Epilepsy, comparative pathogenesis, symptoms, treatment / [Louis Jacob Josef Muskens].

Contributors

Muskens, L. J. J. 1872-1937.

Publication/Creation

London : Baillière, Tindall and Cox, 1928.

Persistent URL

https://wellcomecollection.org/works/jgt2baf3

License and attribution

Conditions of use: it is possible this item is protected by copyright and/or related rights. You are free to use this item in any way that is permitted by the copyright and related rights legislation that applies to your use. For other uses you need to obtain permission from the rights-holder(s).

wellcome collection

Wellcome Collection
183 Euston Road
London NW1 2BE UK
T +44 (0)20 7611 8722
E library@wellcomecollection.org
https://wellcomecollection.org

EPILEPSY

L. J. J. MUSKENS

22102128078

Med
K34992

Digitized by the Internet Archive
in 2017 with funding from
Wellcome Library

https://archive.org/details/b2981358x

EPILEPSY

EPILEPSY

COMPARATIVE PATHOGENESIS, SYMPTOMS, TREATMENT

BY

L. J. J. MUSKENS

M.D., OF AMSTERDAM

FELLOW OF THE ROYAL SOCIETY OF MEDICINE, LONDON;
GENERAL SECRETARY OF THE INTERNATIONAL LEAGUE AGAINST
EPILEPSY; CORRESPONDING MEMBER OF THE SOCIÉTÉ DE NEUROLOGIE
DE PARIS, THE ESTHONIAN NEUROLOGICAL SOCIETY, ETC.

FOREWORD BY

SIR CHARLES S. SHERRINGTON

O.M., G.B.E., M.D., D.Sc.Camb., F.R.C.P., F.R.S.

WAYNEFLETE PROFESSOR OF PHYSIOLOGY, OXFORD

"Epilepsia mirabilis ille morbus."—Boerhaave.

LONDON

BAILLIÈRE, TINDALL AND COX

7 and 8, HENRIETTA STREET, COVENT GARDEN, W.C. 2

1928

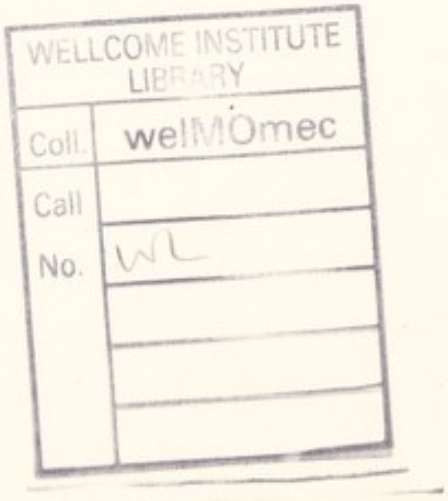
[*All rights reserved*]

(4744797

15070

306112

PRINTED IN GREAT BRITAIN



FOREWORD

THE author has asked me to furnish a few lines of preface to this English translation of his well-known volume on Epilepsy. I have hesitated to comply because I am very conscious of how slight is my competence in all that regards clinical experience. But to that hesitation the author has replied that this work of his is founded upon laboratory experiments as well as upon clinical observation. That is so, and through all the years of my acquaintance with Dr. Muskens, a feature of his activity has been its persevering endeavour to promote neurological knowledge by combining experimental investigation with clinical observation and study. He has, moreover, not been content to know the facts of experiment merely by consulting the literature of laboratory research. He has himself at first hand assiduously prosecuted experiments. His work upon Epilepsy is the fruit of the union of the two methods. The basis of the present volume is therefore twofold, although its results are presented as a united whole. It contains valuable and original views. Some of these are suggestions which will doubtless inspire further work of enquiry. His readers will be grateful to him for a monograph of individual standpoint on a subject of high interest and importance in neurological medicine.

C. S. SHERRINGTON.

OXFORD,
January 17, 1928.

AUTHOR'S PREFACE TO THE ENGLISH EDITION

DURING the period of my training under Winkler (Utrecht) and Dana (New York) my attention was directed towards convulsive diseases, a subject that stood then, as always, in the centre of neurological interest. Physiological research work, under Engelmann and Bowditch, and the influence of scientists, such as Sir Charles Sherrington and Prof. Richet (Paris), tended to orientate me physiologically, when finally, as a clinical clerk to Hughlings Jackson, Gowers, and Horsley, the trend of my own clinical work became fixed. Thus it is that anatomo-physiological work 1900–1916, and clinical work 1900–1924, are incorporated in this volume.

The first part of this book deals mostly with the physiological problems involved in epilepsy, the second part with anatomo-physiological research, while the third or clinical part is based on long experience, many cases having been followed up for twenty years and more.

Thus physiological and clinical work have gone hand in hand, so that my work may be looked upon as a continuation of the life-work of Schroeder van der Kolk, whose "pontine-medullary reflex-centre" I have studied with modern methods, based on the more accurate anatomical knowledge of the central nervous system gained since his time.

I owe thanks to the late Professor de Bruin, Dr. Meuleman, and Professor Laqueur for going over the chapters on children's convulsions, the influence of feminine sexual organs, insulin-cramps and pathological anatomy. I would also thank Dr. Gans for his kindness in examining the chapter on pathological anatomy.

As I am a disciple of the British and American schools of neurology, I am particularly pleased to have my book published

in English as well as in French and German. This English edition has been prepared under my close supervision, so that it is not actually a translation of the Dutch and German editions, but has been revised and brought up to date. Here I had the good fortune to acquire the constant and never-failing co-operation of Mrs. W. Shaw Dunn, herself a physiologist and neurologist, and I am deeply indebted to her for her great interest and painstaking care which have made this publication possible. I have referred to the statements and opinions of others, whenever justice or the importance of facts seemed to render such reference desirable, but exact references are only given to those publications which seem to me to pay most attention to the actual subject dealt with in this book. In such articles many further important references will be found.

L. J. J. MUSKENS.

AMSTERDAM,
January, 1928.

CONTENTS

PART I

EXPERIMENTAL RESEARCH OF THE MYOCLONIC REFLEX AND THE MYOCLONIC EPILEPTIC FITS

CHAPTER PAGE

I. The History of Experimental Research on Epilepsy . 1

§ 1. introduction 1

§ 2. historical section 3

§ 3. localisation of the centre for experimental epilepsy in the cortex . . . 6

§ 4. the production of fits by drugs . . 8

II. The Investigation of Myoclonic Reflexes as a Basis for Myoclonic Epileptic Fits 15

§ 1. special researches 15

§ 2. methods employed in making observations of the fit phenomena 19

§ 3. a comparison of the myoclonic reflexes with other reflexes 30

§ 4. the refractory phase 33

§ 5. the occurrence and mechanism of the so-called spontaneous shocks, series of shocks and fits. groups of muscles involved . . 36

§ 6. a comparison of the motor fit due to bromide of camphor and the epileptic motor fit of the myoclonic variety in man . . 42

III. Mechanism of the Discharges 47

§ 1. on the conception of discharge, "after-discharge" (sherrington's school), and on compensation 47

§ 2. the myoclonic epileptic fit conceived of as the central after-discharge (sherrington) of a myoclonic reflex 52

IV. Further Investigation of Myoclonic Reflexes and of Reflexes related to this Class of Reflex . . 54

§ 1. latency of the myoclonic reflexes and the rapidity of nerve conduction . . 54

§ 2. pflüger's law. stability of the latent period under different circumstances . . 58

§ 3. tactile and acoustic reflex-irritability . 61

§ 4. further research into the bromide of camphor fits 66

CHAPTER PAGE

V. Conditions for the Incidence of Myoclonic Epileptic fits 69

§ 1. Is a certain state of reflex-irritability a condition necessary for the occurrence of epileptiform phenomena—spontaneous shocks, myoclonic after-discharges, and myoclonic fits? 69

§ 2. Is a certain definite length of latent period of the myoclonic reflex associated with the occurrence of epileptic fits? . . . 73

§ 3. Is a change in the refractory phase a condition necessary for the occurrence of epileptic fits? 78

§ 4. The peculiar rhythm of the convulsions and the maximal shortening of the refractory period 81

VI. The Influence of a Narcotic Drug, Strychnine, and Absinthe on the Myoclonic Reflexes and Fits . . 86

§ 1. The influence of ether narcosis on the myoclonic phenomena 86

§ 2. The action of strychnine on the myoclonic reflexes. Fits resulting from the combined action of strychnine and monobromide of camphor 90

§ 3. The action of absinthe 95

VII. Summary of the Reflex and Epileptiform Phenomena described and their Physiological Significance . 98

PART II

THE INFLUENCE OF LESIONS IN THE CENTRAL NERVOUS SYSTEM ON THE MYOCLONIC REFLEXES AND MYOCLONIC EPILEPTIC FITS

I. Introduction 106

II. Extirpation of Various Parts of the Brain and Theca . 109

§ 1. The effect of ablation of a part of the skull and dura mater over the motor area on the myoclonic reflexes, and myoclonic epilepsy. 109

§ 2. Extirpation of parts of the prosencephalon and the results 112

§ 3. The effect of lesions of the cerebellum on the action of monobromide of camphor . 121

§ 4. The influence of lesions in the cerebellum on the incidence of fits 126

CHAPTER PAGE

III. Severance of Various Nerve Tracts . . . 139

§ 1. lesions of the pyramidal tract (the bundle of Monakow being left intact) and the subsequent unilateral exaggeration of myoclonic reflexes and fits . . . 139

§ 2. simultaneous lesions of the pyramidal tract and Monakow's bundle . . . 145

§ 3. lesions restricted to Monakow's bundle . 148

IV. Influence of Different Lesions . . . 151

§ 1. the result of a lesion of the formatio reticularis on the bi-lateral character of myoclonic reflexes 151

§ 2. the results of lesion in the centripetal connections—*i.e.* the posterior roots and the fillet—on the occurrence of reflexes and fits 158

§ 3. myoclonic reflexes where the lumbar cord has been isolated 163

§ 4. concerning direct faradic stimulation of the spinal cord 169

V. Faradic Stimulation of the Motor Cortex and the Medulla Oblongata 171

VI. Résumé of the Results 184

§ 1. incomplete fit-like phenomena in the mutilated central nervous system . . 184

§ 2. intracerebral connections probably involved in the myoclonic reflexes . . . 189

VII. General Conclusions 190

PART III

EPILEPTIC DISORDERS OBSERVED IN MAN AND THEIR TREATMENT

I. Classification of Epilepsy 194

II. Myoclonic Epilepsy 199

III. A More Detailed Description of Regional and Myoclonic Shocks in Man 204

IV. Common or Genuine Epilepsy with Myoclonic Epilepsy as the Starting-Point. Origin and Course . . 210

V. Tonic Spasms and Convulsions in Childhood and their Significance for the Development of Epilepsy . 219

§ 1. various tonic spasmodic convulsions of childhood 219

CHAPTER PAGE

V. Tonic Spasms, etc. (*continued*)

§ 2. The relationship between infantile convulsions and epilepsy. Occasional convulsions, eclampsia in children, and infectious encephalitis statistics 230

§ 3. Conclusion with reference to the attitude of the medical attendant 233

VI. The Influence of Menstruation and Pregnancy on the Occurrence of Epilepsy 235

VII. The Further Description of the Symptoms of Epilepsy and their Significance 242

§ 1. The evolution of the disease 242

§ 2. The great fit 243

§ 3. Prodromal disturbances of sensation: prodromes of short duration or auræ . . . 244

§ 4. The significance of the prodromes and the fit . 250

§ 5. Post-paroxysmal phenomena 254

VIII. The Relative Frequency and Nosological Value of the Symptoms 264

IX. The Statistics of Epilepsy 268

§ 1. Frequency of the disorder 268

§ 2. Heredity and other predisposing factors in epilepsy 271

§ 3. Exciting causes 273

§ 4. Hypoglycæmic convulsions caused by insulin . 281

§ 5. The etiology of the first fit 284

X. Differential Diagnosis of Epilepsy 289

XI. Fainting Fits and Psychisms 295

§ 1. Atypical incomplete discharges or phenomena which may be regarded as such. The substitution of sudden loss of conscious volition or psychical phenomena for the typical epileptic fit 295

§ 2. Dreamy states, confusion, stupor, and mania. Crimes committed in a dreamy mental condition 298

§ 3. Nosological significance of the "absences" and "equivalents" 302

§ 4. The relation of a psychism to a motor discharge 303

§ 5. A psychism depending upon a purely organic lesion 305

§ 6. Psychical symptoms associated with various toxins which produce epilepsy, and the relationship of these symptoms to the fits . 307

§ 7. Relation to other psychoses 310

§ 8. The differential diagnosis of psychical epilepsy from other psychoses 312

§ 9. The permanent psychical condition of the epileptic 315

CHAPTER PAGE

XII. TREATMENT 322

§ 1. COMPILATION OF THE CLINICAL HISTORY . . 322

§ 2. GENERAL PROPHYLAXIS 326

§ 3. SOCIAL HYGIENIC PROPHYLAXIS . . . 327

§ 4. CLASSIFICATION OF PATIENTS INTO GROUPS . 331

§ 5. THE THERAPEUTIC MEASURES TO BE ADOPTED AFTER UNMISTAKABLE EPILEPTIC SYMPTOMS HAVE MANIFESTED THEMSELVES 336

§ 6. THE TREATMENT FOR PATIENTS WHO HAVE HAD A CERTAIN NUMBER OF FITS, BUT WHO HAVE NOT REACHED THE STAGE WHICH COULD BE CLASSED AS INVETERATE 340

§ 7. TREATMENT OF THE INVETERATE CASES . . 349

§ 8. THE PRODROMAL TREATMENT AND PROPHYLACTIC MEASURES IN EPILEPSY 353

§ 9. TREATMENT OF STATUS EPILEPTICUS . . 356

§ 10. PROGNOSIS 359

XIII. PATHOLOGICAL ANATOMY 364

XIV. TRAUMATIC EPILEPSY AND SURGICAL TREATMENT . . 370

§ 1. THE FREQUENCY OF TRUE TRAUMATIC EPILEPSY IN CIVILIAN PRACTICE 370

§ 2. TRAUMATIC EPILEPSY WITH A CRANIAL DEPRESSION DUE TO TRAUMA IN THE MOTOR ZONE . . 371

§ 3. TRAUMATIC EPILEPSY WITH COMPRESSION OF THE SKULL NOT INVOLVING THE MOTOR AREAS . . 373

§ 4. TRAUMATIC EPILEPSY WITHOUT FRACTURE OF THE SKULL, THE INJURY NOT BEING SUFFICIENTLY SEVERE TO CAUSE FRACTURE 379

§ 5. TRAUMATIC EPILEPSY WHERE THERE IS NO FRACTURE OF THE SKULL OR EXTERNAL WOUND. THE FITS ARE UNILATERAL AND ARE ASSOCIATED WITH PSYCHICAL SYMPTOMS 381

§ 6. DOUBTFUL TRAUMATIC EPILEPSY. CASES IN WHICH THE PRESENCE OF A SCAR IS DOUBTFUL, AND THE ASSOCIATION OF THE FITS WITH AN INJURY NOT DEFINITELY ESTABLISHED 383

§ 7. EPITOME 386

§ 8. GENUINE EPILEPSY AFTER ENCEPHALITIS WITH SYMPTOMS OF DEFECT, PARESIS, AND ATHETOSIS . 390

§ 9. GENUINE EPILEPSY NOT PRECEDED BY ENCEPHALITIS. THERE ARE NO SYMPTOMS OF DEFECT, WHILE THE FITS ARE DOUBTFULLY FOCAL 390

§ 10. OPERATIVE TREATMENT IN CASES OF EPILEPSY . 392

§ 11. INDICATIONS FOR OPERATION IN TRAUMATIC AND FOCAL EPILEPSY 395

§ 12. PROGNOSIS 397

§ 13. EPILEPSY IN CASES OF TUMOUR CEREBRI . . 398

§ 14. TRAUMATIC EPILEPSY DUE TO INJURIES GOT IN WAR . 402

§ 15. HISTORICAL NOTE 404

CHAPTER PAGE

XV. A System for the Prevention of Epilepsy, and for the Care of Epileptics 406

Appendix A 414

Appendix B 421

Index of Authors 423

Index of Subjects 431

EPILEPSY

PART I

EXPERIMENTAL RESEARCH OF THE MYOCLONIC REFLEX AND THE MYOCLONIC EPILEPTIC FITS

CHAPTER I

THE HISTORY OF EXPERIMENTAL RESEARCH ON EPILEPSY

§ 1. Introduction.

A CAREFUL consideration of the long history of experimental research devoted to the occurrence of epileptiform phenomena in animals shows that little real progress has been made in the subject. Physiologists and neurologists of the first rank have worked at the subject, but their results are so diverse that it is difficult to form any decision as to the value of the data. This is the case even where the different workers have employed the same methods of investigation applied to the same species of animal.

Much attention has been directed to the localisation of an area or of areas in the brain which, on stimulation, are associated with the production of an epileptic fit. The work done in this effort to produce "Experimental Epilepsy" has resulted in many important contributions to our knowledge of the various centres in the brain. At the same time, this particular type of research does not contribute to the investigation of ordinary epileptiform phenomena.

From a general consideration of the data supplied by earlier workers on epilepsy, two groups of facts may be arranged—those which interest the clinician, and those which concern the physiologist. The clinician is interested in a possible explanation of "Genuine Epilepsy" as he sees it in man, and as it occurs in certain of the higher animals, notably carnivora, and probably in birds. The physiologist, on the other hand, is concerned with the problem of producing an epileptic fit, and of tracing the evolution of such a phenomenon from some closely related but familiar physiological phenomenon.

In my own researches on the subject, I have concentrated my attention on the problem of evoking in animals symptoms closely related to, or identical with, those exhibited by man when suffer-

ing from epilepsy. My investigations have been carried out on physiological and anatomo-physiological lines.

Although I have adopted this particular line of investigation, I would express my high appreciation of the valuable information on the physiology of the central nervous system afforded by the researches on the production of "Experimental Epilepsy." This is particularly the case as regards the establishment of the relationship existing between certain muscular movements and definite cortical areas.

Special reference must be made to the masterly critical review of the important research work done in connection with "Experimental Epilepsy" by Prevost and Samaja.* The study of this review shows that the results of the different workers are very varied, but that three definite theories have been propounded. The first is that the centre for epileptic phenomena is located in the cord, the second that this centre is in the medulla, while according to the third it is located in the cerebral cortex. As I have already indicated, I have not directed my attention to the localisation of a centre for epilepsy; the question I have tried to find an answer to is this:—Is it possible by some experimental method to elicit in animals phenomena comparable in detail with those exhibited in man in genuine epilepsy?

During the fifteen years I have devoted to this branch of research, I have been able to carry on clinical work along with experimental investigations; the combination of the two has proved most helpful. In my investigations, the character of fits produced by stimulation, electrical or otherwise, of the various parts of the central nervous system has been thoroughly examined both graphically and chronometrically. The effect of these methods of stimulation, of drugs, and of operative procedure on the character and length of the latent period, has also been studied.

In all experimental work involving operative measures, a careful autopsy has been made, while the central nervous system has been examined histologically by the Marchi method.

The animals used in this research are mainly cats, dogs, apes, pigeons, snakes, while fish have occasionally been used.

Such, then, is the basis of this investigation, which I can by no means regard as complete.

For convenience in describing my investigations, I have divided them into four sections as follows:

1. Is it possible that stimulation of the spinal cord might produce epileptic phenomena? Such a question involves investigation with electrical stimulation and the use of drugs in any attempt to arrive at a definite answer.

* Samaja, *Rev. méd. de la Suisse romande*, 1904, No. 2.

2. In animals under the influence of certain drugs definite bilateral motor discharges may be observed. Is it possible to alter the character and course of the discharge by an experimental lesion of the central nervous system? If so, which are the tracts or centres in the central nervous system upon whose integrity the phenomena depend?

3. Is it possible to establish any connection between the degree of development of the central nervous system in different types of animals and the occurrence of these phenomena?

4. Can epilepsy be regarded as a phenomenon comparable with such well-known phenomena as fever, inflammation, or cold shivering? If so, is there justification for regarding such phenomena as part of a primordial protective mechanism?

§ 2. **Historical Section.**

A short review of the more important work on experimental epilepsy is necessary before discussing my own investigations.

Marshall Hall,* Kussmaul and Tenner† were the first to examine fits which occur when warm-blooded animals are bled. The work of Kussmaul and Tenner is of particular value, as they describe these fits in great detail. It seems evident from this description that the fits lack a number of the characteristics of an epileptic fit. It is interesting to find that Unverricht also offers this criticism.

In connection with this particular study of fits following on severe and sudden hæmorrhage, it seems suitable to recall the characteristics of a genuine fit in epilepsy; these are briefly:

1. Very rapid muscular convulsions, which are disordered in character and do not occur coincidently in the different parts of the body.

2. Later, the intervals between the convulsions are longer, while the whole body is involved simultaneously in the "terminal beats" of Graham Brown. In no case of genuine epilepsy are the convulsions limited to any set of muscles.

3. In man, consciousness is lost. In animals, a function comparable to consciousness is either partially or entirely lost.

4. In man, motor and sensory as well as psychical pre- and post-epileptic phenomena are well known. In animals, such phenomena are not so readily recognised.

The fits associated with severe hæmorrhage have attracted a great deal of attention, and a good deal of research work has been done upon them. It is now generally recognised that they

* Marshall Hall, "Synopsis of Cerebral and Spinal Seizures," 1822.

† Kussmaul and Tenner, "Moleschott's Untersuchungen," 1857, vol. iii.

belong more or less to the same class as those fits which occur where an animal has been deprived of oxygen, or in the terminal stage of certain nerve poisons. Uspenski* records that in rabbits dosed with strychnine, fits supervene if artificial respiration be suspended. Weisz† describes the appearance of fits in the interval in Cheyne-Stokes respiration. In this interval there is presumably a fall in the cerebral blood supply. Vidal,‡ working with nicotinised dogs, notes that fits develop if the animals be placed on a revolving table. The effect of the motion in conjunction with the drug is to produce cerebral anæmia, and fits follow upon this. Kussmaul and Tenner find that fits do occasionally follow temporary compression of the carotids in man. Hill§ describes the fits which follow when a rabbit is suspended vertically. In this case the fit may be, as Hill suggests, a protective reaction or an involuntary effort to force blood up into the brain. Högyes‖ and Von Schroff ¶ both did a considerable amount of experimental work in connection with fits associated with profound hæmorrhage. They found that if the frontal portion of the cerebrum or the optic thalamus were removed these fits did not occur. They agreed with Uspenski that fits occur when artificial breathing is interfered with, where such aid is necessary to keep the animal alive. Further, they found that if the spinal cord be divided in the neck or at the level of the calamus scriptorius phenomena appear only in the hinder parts of the animal. This is interesting in view of the work of Owsjanninow,** who proved that reflexes pass from one extremity to the other three when the calamus scriptorius is intact. If this region be injured, the reflex will only involve the corresponding limb.

Although the asphyxial convulsions have attracted much attention, I cannot consider that they are suitable for my purpose. The variation which they exhibit from the characteristics of a true epileptic convulsion is manifested in the lack of prodromal symptoms, in the sudden appearance of the convulsion, both during the advance of anoxæmia (Kumao Yamakami)†† and the return of consciousness. Further, the character of these convulsions is not in all instances the same. Hill‡‡ pointed out that

* Uspenski, *Arch. f. Anat. u. Physiol.*, 1869.
† Weisz, *Wien. med. Jahrb.*, 1882.
‡ Vidal, *Comptes. rend. de Séances de la Soc. de Biol.*, 1897, p. 255.
§ Hill, *Philosophical Transactions*, 1900, vol. cxciii., p. 106.
‖ Högyes, *Arch. f. exp. Pathol. u. Pharmakol.*, 1875.
¶ Von Schroff, *Wien. med. Jahrb.*, 1875.
** Owsjanninow, *Leipziger Berichte*, 1874.
†† Kumao Yamakami, *The Tohoku Jnl. of Exp. Medicine*, vol. iii. 11, 1922, p. 295. The blood of a rabbit which is having asphyxic convulsions shows hæmoglobinemia.
‡‡ Hill, in Allbutt's "System of Medicine," vol. viii., p. 24.

where cats or monkeys were under the influence of absinthe, the compression of four cerebral arteries was not followed by clonic convulsions. Steward and Pike corroborated this observation. With dogs, the same result does not follow. Where an animal is either debilitated or over-anæsthetised, death may occur without spasm.

In man, cases have occurred where compression of one carotid artery has been associated with formication and clonic convulsions in the crossed hand.

I do not propose to discuss all the theories which have from time to time appeared regarding the cause of epileptic fits, but attention must be directed to the theory put forward by Schroeder van der Kolk,* for it has found many supporters.

Schroeder van der Kolk describes the medulla oblongata as the centre from whence bilateral reflexes originate. The original arguments for this theory were all based on purely clinical data. Later disciples of van der Kolk, notably Binswanger and Nothnagel,† directed their efforts to the localisation of this postulated centre. Binswanger, in his later work, however, pointed out that it is impossible to produce a genuine epileptic fit by electrical or mechanical stimuli, and therefore it is not permissible to speak of a definite centre for such fits. It is true that under certain conditions stimulation of certain areas of the brain does result in the development of a fit, but not a real epileptic fit.

Brown-Séquard‡ describes convulsions in guinea-pigs after hemisection of the cord, removal of the sciatic nerve, and other lesions of the central nervous system. These convulsions were admitted by Brown-Séquard to be at most epileptiform in appearance and type, although in some cases he found evidence of the condition being hereditary. This last point is disputed, for later work does not afford any confirmatory evidence (Darwin, Romanes, v. Bemmelen, Morgan).§

Hughlings Jackson and Victor Horsley‖ both agreed in regarding the phenomena described by Brown-Séquard as dominated by centres in the cord, since they persist after serious lesions to the cortex.

In connection with this phenomenon described by Brown-Séquard, the work of Graham Brown¶ is of great importance.

* Schroeder van der Kolk, " Bau und Funktionen der Medulla spinalis und oblongata," 1859, p. 893.

† Nothnagel, " Spezielle Pathologie und Therapie ": Art. " Epilepsie," by O. Binswanger, 1904, p. 3.

‡ Brown-Séquard, *Boston Med. and Surg. Journ.*, 1856, p. 337.

§ T. H. Morgan, " Evolution and Adaptation," 1903, p. 255.

‖ V. Horsley, *Brit. Med. Journ.*, 1886, p. 77.

¶ Graham Brown, *Quart. Journ. of Exp. Physiol.*, 1909, vol. ii., pp. 243-275, and 1910, vol. iii., pp. 21-53; vol. iv., etc.

Graham Brown repeated all the experiments of Brown-Séquard and prepared graphic records of each. From this masterly description of these convulsions, it would seem that they display certain symptoms which are regarded as peculiar to experimental epilepsy. Thus the convulsions are provoked by squeezing the skin of the neck or back, or by etherisation of the animal, manipulations causing a certain hypersensibility for the *scratch-reflex*. These convulsions occur at first at the rate of 6 to 10 per second, but they gradually increase in rapidity. Further, it is seen that after a time less stimulation is needed to provoke a fit, and what is still more significant, that a reflex convulsion is more easily induced at the beginning than at the end of ether anæsthesia. This is interesting in view of the well-known fact that in man epileptic fits tend to occur when the patient is at the point of transition from sleep to wakefulness or from wakefulness to sleep. The same holds good in cases of experimental epilepsy.

It is interesting to see that Graham Brown admits that after section of the sciatic nerve a certain area in the skin of the animal develops a degree of hypersensitiveness, a very slight degree of stimulation being sufficient to induce the so-called scratch-reflex. It must be remembered that, although this phenomenon is of great interest, such convulsions cannot be compared with epileptic fits. The animals in question—guinea-pigs—are too far down the zoological scale to allow of comparison with the carnivora or the erect animals. It is only in the latter and higher type of animal that the nervous system has attained that degree of development where an epileptic fit can be produced. At the same time, this so-called Brown-Séquard epilepsy affords an important opportunity for the study of the type of convulsion found in the less highly developed mammal.

§ 3. Localisation of the Centre for Experimental Epilepsy in the Cortex.

As a result of the work of Hitzig, Fritsch, and Ferrier, it became general to regard the probable centre for experimental epilepsy as situated in the cerebral cortex. Albertoni* and v. Bechterew,† who succeeded these workers, contributed very largely to the general knowledge of the physiology of the cerebral cortex. This work, although of the utmost importance physiologically, yet lies somewhat outside the sphere of my research, and is, therefore, not discussed in detail.

* Albertoni, "Moleschott's Untersuchungen," 1881, vol. xii., p. 476.
† W. v. Bechterew, *Neurol. Zentralbl.*, 1897, No. 4.

Bubnoff and Heidenhain* made some interesting observations on the effect of morphia. They found that after large doses of morphia the reflexes, more particularly those associated with auditory stimuli, were exaggerated. Further, they found that the *repetition* of stimuli, not individually strong enough to provoke a reflex, did eventually provoke the reflex. This is a most important observation. These observers also noticed that the shorter the intervals between stimuli the greater was the resulting reflex actions. Both these observations are of peculiar interest in connection with points noted by me in the study of genuine epilepsy, and which will be referred to later. Luciani, a physiologist, concluded from his observations on animals that genuine epilepsy was a phenomenon associated with the cerebral cortex. This conclusion was come to because Luciani observed that, after removal of the cortical motor area for a limb, electrical stimulation of the cortex had no effect upon that limb, although the rest of the animal displayed a condition comparable to epilepsy. The work of Luciani has been criticised a good deal; among the critics are Albertoni, Franck and Pitres,† and Hitzig. These later workers considered that they had sufficient evidence to show that convulsions or fits occurred after destruction of the cortical centres. In replying to his critics, Luciani suggested that the cortical centres had not been thoroughly destroyed. It is interesting to find that Luciani's view was supported by two later workers, Tillman and F. Krause. Although subsequent work has shown that the theory of Luciani is not correct, yet there is much evidence in favour of the view that the cortex does participate to a certain extent in the production of an epileptic fit.

Reference must be made to the work of Vanlair,‡ Legros, and Onimus on choreic dogs. Vanlair was the first to observe that these animals displayed fits most frequently when on the point of falling asleep, while during sleep the fits stopped. This observation, on the time when the fits were most troublesome, has a direct bearing upon this present research.

Unverricht devoted a great deal of study to the cause of epilepsy, and came to the conclusion that both the cerebral cortex and the spinal cord participated in the production of the fit. He also made the suggestion that the subcortical ganglia might play an important part in genuine epileptic fits.

* Bubnoff and Heidenhain, *Pflüger's Archiv f. d. ges. Physiol*, 1881, vol. xxvi.

† Frank and Pitres, "Trav. des. Laborat. de Marey," 1878-79, vol. iv., p. 428.

‡ C. Vanlair, *Rev. de méd.*, 1889, p. 1.

The important work of Wertheimer and Lepage, Probst,* Rothmann, and Prus, lies outside the province touched on in my investigations. I wish, however, to acknowledge our indebtedness to such workers for our knowledge of the physiology of the central nervous system.

§ 4. The Production of Fits by Drugs.

The history of this particular branch of research is very interesting because of the increasing belief in the theory that epilepsy is due to some toxin.

A general survey of the work done on the relationship between drugs and the occurrence of fits shows that the number of drugs which will produce fits is legion.

Magnan† gives a masterly description of the epileptic type of fit associated with absinthe. These fits he observed as a clinician in his patients, while as a physiologist he produced them experimentally in dogs. Experimentally he administered the the drug intravenously and by the mouth, and afterwards made graphic records of the fits. He pointed out that the tonic and clonic stages of a fit are often preceded by separate convulsive seizures.

In one experiment he divided the spinal cord at the level of the twelfth segment, the animal being kept alive by artificial respiration, and immediately after injected absinthe. The result was a series of independent convulsions of the head and hind limbs. From this experiment he concluded that the centre for these fits cannot lie wholly in either the pons or cord. This work of Magnan, done some fifty years ago, is remarkable for the introduction of the graphic method of recording fits, and also for the accuracy and curiously modern attitude to the question of the cause of epilepsy. This writer also made a series of very interesting observations on the condition of the veins in the fundus oculi, and on the character of the heart beat during an epileptic fit.

Horsley, as a disciple of Magnan, followed up this line of research, and as his pupil I had the opportunity of seeing much of his work. From his experiments with absinthe, Horsley concluded that the production of epileptic fits was intimately associated with the functioning of the complete central nervous system. This observation on the narrowness of the dividing line between epilepsy and health is striking and important in relation to my own research.

* Probst, *Jahrb d. Psychiatrie u. Neurol.*, 1901, p. 31.
† Magnan, " Recherches sur les centres nerveux," 1876.

Robert Boyce* carried out a series of experiments on animals under the influence of absinthe. Where he divided the crus cerebri, he found that the recovery of voluntary movement after the initial hemiplegia and the susceptibility to fits went hand in hand.

R. Russell† came to the conclusion that the cerebellum had a definite inhibiting influence on the fits which followed on the administration of absinthe. This conclusion he arrived at from the observation that after removal of one cerebellar hemisphere the convulsions on that side were extraordinarily vehement in character. There is no doubt but that the study of these absinthe fits has contributed materially to our knowledge of genuine epilepsy, but at the same time these fits are not the same as the fits of genuine epilepsy. The onset is too sudden, while the character and after symptoms of the fit do not correspond with the characteristics of genuine epilepsy.

Roeber‡ and Heubel§ investigated the effect of picrotoxin on cold-blooded animals. They described a variety of fits which followed the administration of this drug, and stated that it did not persist after section of the spinal cord. In this point the fit differed from that following strychnine, for with strychnine the fit persists after section of the cord below the medulla.

Turck described fits which followed administration of antipyrine, and Turtschaninow fits which followed strychnine and carbolic acid. Turtschaninow carried on investigations with other drugs, among them camphor compounds and santonine, and described the phenomena following on their use. He found that shivering and trembling resulted most frequently after carbolic acid, while the administration of santonine evoked violent starts. These violent starts were not affected by the removal of the gyrus sygmoideus or after division of the crus cerebri. He suggested that the centre for the movements lay in the medulla, and referred to the work of Schroeder van der Kolk and Nothnagel, who also located in that region a centre dominating convulsive phenomena. One criticism which must be offered on this branch of Turtschaninow's investigations is that he did not call attention to the fact that, after an operation in which the bony skull is opened, five or six times the ordinary dose of santonine is required to produce a reaction. It would seem from these experiments, as well as from those

* R. Boyce, *Brit. Med. Journ.*, 1893, November 18, p. 1097.

† R. Russell, *Transact. of the Roy. Soc. of Trop. Med. and Hyg.*, 1894, vol. clxxxv., part 1, pp. 819-857.

‡ Roeber, *Arch. f. Anat. u. Physiol.*, 1869, p. 38.

§ Heubel, *Pflüger's Arch. f. d. ges. Physiol.*, vol. ix., p. 263.

made by other workers, that the tolerance to a drug is increased after opening of the skull.

As regards the tremors occurring after carbolic acid, Turtschaninow* found they persisted after extirpation of the cortex. Division of the spinal cord stopped the general tremor, but that part of the animal distal to the line of section showed abnormal muscular movement. A general criticism which must be made of Turtschaninow's work is that he did not seem to pay due regard to operative procedure, and was apt to lay all the results to the charge of the drug administered. Apart from this criticism, the work is of great interest, for as a result of his investigations Turtschaninow advanced the view that there was a parallelism between a true epileptic fit and such phenomena as shivering, fever, and the sudden starts frequently seen in early childhood when at the point of sleep, or in adults exposed to sudden noise.

The work on these start phenomena is of great interest, and is in the same line as my own, for I would attempt to show that such phenomena are independent of the cerebral cortex. Further, that in all probability the latent period between the stimulus and the reaction is not influenced by the removal of the frontal or temporal lobes.

The work of Prevost, Batelli, and Samaja is only mentioned, for although their results have formed a valuable contribution to the question of the effect of electrical stimulation of different parts of the central nervous system, they do not assist materially in this study of epilepsy.

Hitzig described the development of epileptic-like fits when localised inflammatory changes had been induced in the cortex. In these experiments it is obviously impossible to exclude complications from pathological infections, and it is absurd—as has been done—to find these experiments referred to as evidence that aseptic exploration of the brain will cause epilepsy or aggravate epilepsy already developed.

Of all the drugs which produce fits in warm-blooded animals, camphor seems to be the best for experimental purposes. The fit produced by this drug is capable of comparison with a genuine epileptic fit. Camphor is a drug which was appreciated by the Chinese in the Middle Ages. Experiments with the drug were begun in the eighteenth century, and valuable data were collected from experiments on animals and personal experiments. The information derived from well-marked cases of camphor poisoning has also been of great

* Turtschaninow, *Arch. f. exp. Pathol. u. Pharmakol.*, 1894, vol. lxxxiv., p. 208.

value. Alexander* and C. Wiedemann† gave a very complete account of the properties of camphor, and it is interesting to find that even the very early workers suggested the term "Epileptiform" as descriptive of the convulsions due to its use. This term may have been adopted because the convulsive seizures are separated from one another by periods of rest. Further, when the experiments were tried on man, it was found that the muscular symptoms were accompanied by psychical symptoms, such as hallucinations, flights of ideas, and definite mental confusion. Purkinje, who carried out experiments on himself, gave an extraordinarily graphic, indeed a classic, account of the symptoms. Purkinje took 2·4 grammes of the drug in the morning before eating, and described the result as follows:

"Movements seemed much facilitated; in walking my thighs rose far above the usual height, but the muscular force required for lifting weights remained unchanged. The sensibility of the skin and muscle nerves seemed somewhat dulled. A storm of thought reached a degree to make loss of consciousness seem imminent, but consciousness was not actually lost, probably because vomiting was induced artificially by deflection of the tongue. The condition continued for four hours, when a feeling of oppressive warmth spread over the whole body, and consciousness was lost." For half an hour, while unconsciousness lasted, the respiratory movements were very slow, a special observer having been provided to watch the condition. On awakening, Purkinje resumed the description: "When I awoke it took a long time to rediscover my own personality in relation to the time and place, for the whole morning and night formed a breach in the sequence of my life, and lay in dark uncertainty in my soul, which laboured to reconstruct my personality. Otherwise I felt well, and by no means fatigued, as in the case of other forms of inebriation."

Such, then, are the effects of this dose on man. In animals, it was found that toxic doses produced paralysis in cold-blooded animals; this is in marked contrast to the convulsions found in warm-blooded animals. Wiedemann, who experimented with warm-blooded animals, pointed out that the rhythmic fluctuations of blood pressure seen after the administration of camphor occurred whether convulsions supervened or not. If the vagi were cut, the fluctuations of blood pressure disappeared, but not otherwise. Further, this worker recognised and de-

* Alexander, *Neue Breslauer Sammlung aus dem Gebiete der Heilk.*, 1829.

† C. Wiedemann, *Arch. f. experiment. Pathologie und Pharmacologie*, vol. vi., 1877.

scribed the wide range of sensitiveness to camphor displayed by all experimental animals.

A consideration of the results described by Lawson* after the use of the monobromide of camphor, and also the symptoms found in a case of poisoning† with this particular compound, attracted my attention to it. It is a compound of camphor where one atom of hydrogen is replaced by one of bromide. The results got with it are extremely encouraging, for the fits produced experimentally by its use are very similar to those of genuine epilepsy of the so-called myoclonic type. I therefore recommend it for the experimental study of epilepsy. The following are some facts relating to the history and properties of the monobromide of camphor.

Schwartz and Deneffe of Ghent,‡ and Hammond§ were the first to write about the drug, but confined their observations to its sedative action.

Pathault‖ published a monograph on the monobromide of camphor, in which he described its first application as a medicine. From this monograph a strong impression is received that it was administered with little apprehension of its toxic properties. This is borne out by the fact that from 1890 to 1900 several cases of serious poisoning occurred through its therapeutic use.

Gubler¶ was the first to call attention to the dangers attending its use, but his article made little impression, for the drug continued to be popular, and was used generously for many maladies. Bourneville and, later, Lawson were the first to carry out extensive experiments on the action of the monobromide of camphor. They administered the drug to guinea-pigs, rabbits, and cats, and found that both the pulse and respirations became slower, while the temperature frequently fell in a striking manner.

A point of peculiar interest is the fall in temperature caused by the drug; the effect of the drug on the central nervous system is seen when the temperature falls. Rabbits, guinea-pigs, and sometimes dogs were found by Bourneville and Lawson to develop a trance-like condition after comparatively small doses; cats, on the other hand, showed convulsive symptoms. In man, the symptoms of monobromide of camphor poisoning are also convulsive. It is the case that the convulsive symptoms found in cats are not well described. Trasbot mentioned them, but

* Lawson, *Brit. Med. Journ.*, 1897, vol. ii., p. 660.
† Wertheim-Solomonson, *Ned. Tijdschr. v. Geneesk.*, 1900, i., ii., p. 506.
‡ Schwartz and Deneffe, *Presse méd. belge.*, 1871, p. 405.
§ Hammond, *New York State Journ. of Med.*, May, 1872.
‖ Pathault, "Monobromure de camphre," Paris, 1876.
¶ Gubler, *Journ. de thérapeutique*, 1874, p. 870.

beyond saying that they resembled strychnine fits, gave no further details.

Pathault investigated the effect of monobromide of camphor on frogs. He described the fits which occurred as being quite unlike those due to strychnine, for he showed in his tracings that a monobromide of camphor fit had a single clonic contraction, while a strychnine fit was tetanic in character.

With regard to the dose of monobromide of camphor, Lawson gave the most useful information—at least, for warm-blooded animals. He found that in cats convulsions followed moderate doses, but not very small or very large doses. The effect of a large dose, he found, was to weaken and benumb the animal: it could be placed in most bizarre attitudes without any resistance.

In connection with the effect of lowering the temperature seen with monobromide of camphor, it is interesting to find from the work of Hess and Harnack* that numerous toxic drugs which cause convulsive symptoms also possess this property. It seems possible there may be some connection between the two phenomena.

Luchsinger† found that with certain drugs a fall in temperature of the animal lessened the toxic action. He attempted to explain this by suggesting that vital phenomena progress at a slower rate with a lower temperature, and therefore less poison is circulated throughout the organism. He also suggested that the resistance of the central nervous system was higher with a low temperature. Harnack, with his pupils Schweigmann, Meyer, Hochheim, and Zuntz, devoted considerable attention to this question of the effect of a fall in the temperature. They concluded that the fall in temperature was primary to the convulsive effect, and considered the two phenomena as being independent. This latter conclusion they arrived at from evidence afforded by the use of ether in association with the special drug. They found that ether caused a fall in temperature, but convulsions did not ensue. It is highly probable that some drugs cause a fall in temperature, through their action on the thermogenic centre (Kreid and Karplus). It must be remembered, however, that the influence of a drug varies in different animals—for example, strychnine produces a fall in temperature with cats but a rise in dogs, and also in man. Harnack suggested that the fall in temperature might be a protective measure. For example, a rabbit dosed with santonine and narcotised with ether had a fall of 13° C., but survived.

* Harnack, *Arch. f. exp. Pathol. u. Pharmakol.*, 1897, vol. xl.
† Luchsinger and Hess, *Pflüger's Arch. f. d. ges. Physiol*, vol. xxxv.

Where the animal was subjected to the same treatment but placed in a warm cage, it died. It is evident that Harnack does not consider the possibility of the fit itself being a protective process whereby toxic elements are dissipated.

There are other facts which must not be forgotten in this attempt to explain the relationship between the fall in temperature and the development of convulsions. Zuntz and Löwy* showed that in persons where more CO_2 was excreted when the temperature fell this increased metabolic activity was accompanied by uncontrollable muscular contractions or shiverings. In this condition of shivering, the consumption of oxygen may be doubled. As has been indicated, these phenomena have been studied experimentally, and centres for such movements described by Turtschaninow, Stephan, and Richet† in the mid-brain. On the other hand, Freusberg‡ and Talma located centres for shivering or trembling in the cord.

Husemann§ recorded the important fact that other drugs besides camphor or its compounds might produce convulsive and narcotic effects at the same time. Among these he found carbolic acid and picrotoxin.

One important property of many drugs associated with the production of fits is that of heightening the reflex irritability. Meihuizen‖ and Sano¶ both recorded that the reflex irritability to tactile stimuli increased after the administration of toxic doses of strychnine. The sensibility to pain in such cases underwent no change.

* Zuntz and Löwy, *Arch. f. Anat. u. Physiol.*, 1889, p. 558.
† Richet, *Arch. de. Physiol.*, 1893, p. 312.
‡ Freusberg, *Arch. f. Psychiatrie u. Nervenkrankh*, 1876, vol. vi.
§ Husemann, *Arch. f. exp. Pathol. u. Pharmakol.*, vol. viii., p. 102.
‖ Meihuizen, *Pflüger's Arch. f. d. ges. Physiol.*, vol. vii., p. 201.
¶ Sano, *Pflüger's Arch. f. d. ges. Physiol.*, 1908, vol. cxxiv.

CHAPTER II

THE INVESTIGATION OF MYOCLONIC REFLEXES AS A BASIS FOR MYOCLONIC EPILEPTIC FITS

§ 1. Special Researches.

FROM a general consideration of the literature describing the results of investigations on the subject of experimental epilepsy, it is evident that little progress has been made in the subject. At the same time, it is true that many important physiological facts relating to the functions of different parts of the brain have been elicited by these researches.

Chemical researches have demonstrated the fact that there are many drugs which do produce fits which display certain symptoms characteristic of epilepsy, such as abnormal muscular movements, mental confusion, or even delirium and hallucinations.

At the same time, these researches have failed to discover one drug which will produce a condition exactly comparable with genuine epilepsy.

In the last few years neurologists have devoted more attention to a certain group of symptoms displayed in genuine epilepsy—namely, the myoclonic and regional reflex shocks and reflex fits. These phenomena are, in my opinion, well worthy of special investigation, for I believe that in their study we may find the key for profitable research. Clinical observations supply sufficient data on myoclonic reflex shocks and fits to allow of the recognition and appreciation of the syndrome when it occurs in experimental animals.

In my early work with monobromide of camphor administered experimentally to animals, I noticed that one of the very earliest symptoms of poisoning was an increased irritability of the forelimbs and back to tactile stimuli. This symptom sometimes appeared before dilatation of the pupils. At a later stage acoustic stimuli produced vehement reflex convulsions, particularly of the head. The more sudden was the noise the greater was the reaction. These reflex movements resembled closely in form, extent, and rapidity the regional convulsive movements familiar clinically in epilepsy. They are also very like the movements described by Turtschaninow as occurring after the administration of santonine. This author describes the movements as "lightning-like contractions" of all the voluntary

muscles. Richet and Broca,* some of whose work I had the privilege of seeing, also describe the same variety of reflex movements in dogs narcotised by chloralose. These movements, they found, were provoked by either tactile or acoustic stimuli. Personally, I have no doubt but that these various forms of reflex movement are in close physiological relationship.

It is quite certain that in epileptics generally, but more particularly in *eclamptic* children, a sudden tactile or acoustic stimulus may cause a general convulsive movement, especially in the period preceding a fit.

From long experience with clinical cases, one is able to recognise periods in the daily cycle when there is a special tendency for the development of *myoclonic epileptiform* phenomena. These periods are particularly the times immediately before falling asleep and immediately on wakening from sleep.

Since I first described these observations, physiological research has thrown some light on the development of the myoclonic fit in man. From a consideration of the work of Waller and Gotch† on reflexes generally, and the action of strychnine in particular, together with the work of Langendorff,‡ it may safely be accepted that myoclonic shocks, series of shocks or fits, are intrinsically of the nature of a reflex phenomenon. At the same time, it must be admitted that this cannot be proved in every case. In my own observations on cats (see page 45, cats 78 and 79) I find that they frequently display myoclonic shocks during sleep. The effect of such a shock is to waken the animal, who is consequently in the condition of hyperexcitability associated with the act of wakening, and the result is often a severe epileptic fit. Even although such a phenomenon cannot be directly observed in man, a certain analogy can be appreciated between clinical symptoms and those symptoms seen in experimental animals.

In my opinion, these myoclonic reflexes are a group which have too long escaped the attention of the physiologists. It is interesting to note that Zwaardemaker, Magnus, and Sherrington, with whom I have discussed this point, agree in this opinion. The reason may be that these reflexes are not prominent in the domesticated animals, neither are they common or well marked in undomesticated animals born in captivity, as seen in zoological gardens. At the same time, a partial or even a complete demonstration of the myoclonic reflex is found in one out of each six or eight domestic cats, while in the bradypus the myoclonic reflex is found to occur very regularly. For humanitarian reasons one cannot study this reflex in man as in animals. It is necessary

* Richet and Broca, *Arch. de Internat. physiol.*, 1897, vol. ix., p. 871.
† Waller and Gotch, *Journ. of Gen. Physiol.*, 1890, vol. v., p. 11.
‡ Langendorff, Nagel's *Handb. d. Physiol.*, 1909, vol. iv., p. 251.

that the stimuli, tactile or acoustic, should be sudden and quite unexpected. It is manifestly impossible to subject patients, or even healthy persons, to such treatment without running the risk of injuring the individual. Since the myoclonic reflexes in the ordinary domesticated animals are never, or very rarely, well marked, it is necessary to intensify them by the use of drugs. It has been found that this can be done by the use of monobromide of camphor, absinthe, or chloralose. The myoclonic reflex phenomenon occurring in such a prepared animal is found to resemble closely the myoclonic convulsions seen in man. The contractions in both cases are localised to a certain definite group of muscles, while the rapidity of the contractions is very striking. A further resemblance is indicated by the occurrence of *spontaneous* myoclonic convulsions or series of convulsions after the simple myoclonic reflex. Sometimes a complete myoclonic fit may follow accompanied by dilatation of the pupils, and occasionally by enuresis.

Where a cat has been prepared by the administration of the monobromide of camphor, the regional reflexes may, in a later stage of the experiment, spread over all the voluntary muscles, not only after tactile stimuli applied to any part of the body, but also after acoustic stimuli. Further, such a cat may show complete shock-like movements, which must be styled spontaneous, as no reflex stimulus can be observed. This spontaneous shock is exactly comparable with the spontaneous shocks seen in epileptic patients. After this stage of spontaneous shocks, the cat may have a complete epileptic fit. In such a case the cycle of events is the same as that seen in epileptic patients. It is evident, therefore, how useful and important is the production of such a condition experimentally in animals for the exact study of the disorder in man. It is interesting and important to find that these experimental animals show other symptoms which are identical with symptoms recognised clinically in epileptic patients. Such symptoms are, first, the animals, like man, have a predilection for developing fits at the periods of falling asleep or of awakening. Second, after a fit, the spontaneous shocks and convulsive reflexes provoked by tactile or acoustic stimuli cannot be elicited. This is the same as in man, where, after a fit, the patient is free, for a time, from all distressing symptoms. Third, if the intoxication with the drug be sufficiently severe, the animal will have a second fit accompanied by all the symptoms of the first, but with moderate intoxication one fit only occurs. A parallel condition is readily recognised clinically.

Indeed, so well is the fact appreciated that an epileptic fit is the terminal manifestation or culmination of a series of shock

phenomena, that the term "discharge" is applied to the fit itself. After a fit the patient is in quite another and better condition, both physically and mentally, than immediately before the fit. The same improvement is seen in cats after a fit, for the pupils regain their normal size, the fur becomes smooth and glossy, while mentally the cats give evidence of increased alertness. There is, therefore, definite evidence that after a fit patients and experimental animals revert to a normal condition both physically and mentally. As has been indicated, there is a definite relation between the character of the motor discharges and the amount of the toxic drug given to an animal. Where a cat gets a moderate dose of monobromide of camphor—that is, half a gramme—it will display intensified reflex irritability to both tactile and acoustic stimuli for a prolonged period, and spontaneous shocks appear later, but a fit may not supervene. If, however, a larger dose be given, or if the animal have the half-gramme dose repeated, it will develop a complete epileptic fit. In the first case the symptoms of intoxication may continue for a comparatively long period, while in the second case they are discharged by one fit. Where the amount of the drug given is still greater, one fit is not sufficient to inactivate its toxic influence, and other fits follow the first. In this case the sequence of events follows that seen in the first fit. There is increased irritability first to tactile, second to acoustic stimuli, the appearance of spontaneous convulsions, and finally the fit itself. If a very big dose be given, the animal may pass into a comatose condition, show little reflex excitability, but pass into a condition of status epilepticus, which will, in all probability, end fatally. This condition of status epilepticus will be discussed later. Where the drug is given intramuscularly the sequence of events is the same, but the whole phenomenon is more rapid. For example, if monobromide of camphor be given by the mouth, generally one and a half to two hours must elapse before symptoms develop, at least with a moderate dose. If large doses are used, spontaneous convulsions may occur in half an hour. If, on the other hand, the drug be given intramuscularly, convulsions generally begin in from fifteen to twenty minutes. If absinthe be injected instead of monobromide of camphor the symptoms appear even earlier.

Certain other factors also influence the action of drugs, such as pregnancy and the condition of nutrition and also the fact of the drug being exhibited in a fasting or replete animal. Where the animal has just been fed, it is more resistant to the drug than when fasting. This variability in the reaction of the replete and fasting animal is very important, and is especially well marked with the monobromide of camphor. This point will be dealt with later.

It must be emphasised that an animal may be discharged in two ways, either by a regular fit or by a long series of reflex shocks produced by definite stimuli, and spontaneous shocks, the stimuli for which are not yet recognised or appreciated.

§ 2. Methods employed in making Observations of the Fit Phenomena.

During this research, which I have carried out for a good many years, I have recorded my experiments by simple observation, and by tracings made in the ordinary way on a revolving drum. Where the graphic method is used, a time

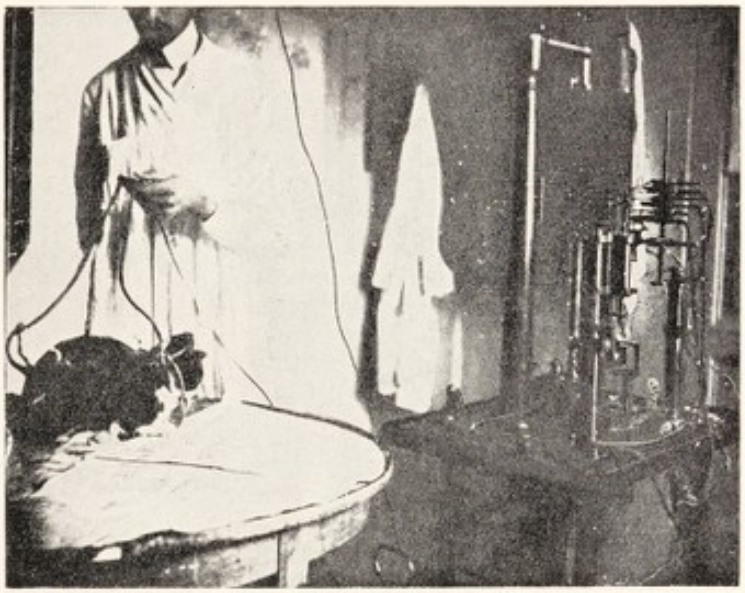


FIG. 1.—METHOD OF REGISTERING MOVEMENTS.

A tambour is placed on the head and one on the coccyx. A rubber tube connects these tambours with a second set of tambours, provided with writing points, which operate on a smoked revolving drum.

tracing is made, representing in the case of a slow drum ten vibrations per second of the tuning fork, and fifty per second for a rapid drum.

In the earlier part of my work, I tried to record the movements of the animals under examination by placing them on an oil-cloth mat, which, in turn, rested on a coil of rubber tubes arranged in a series of twists and turns. Any change of pressure on this coil was recorded by a tambour fixed to the end of the tube and provided with a writing point in contact with a revolving smoked drum (compare Fig. 7, p. 35, and Fig. 15, p. 72). This method had to be given up for several reasons. The tracings did not show a single upstroke, but a complicated series of small up and down strokes. When tactile stimuli were applied to the

animal the record was confused and it was often impossible to distinguish where the tracing actually began to record the reflex movement. Further, it was impossible to tell from the tracing which part of the tube was depressed first; finally, the method was too slow.

Far more exact results were got with the use of Brondgeest's tambours, which I adopted on the advice of Professors Zwaarde-

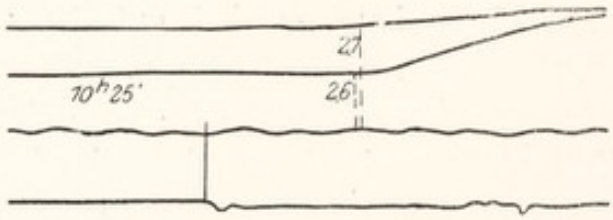


FIG. 2*a*.—TACTILE MYOCLONIC REFLEX IN A NORMAL CAT.

The top tracing is from the tambour fixed on the back, the middle tracing from the tambour attached to the head, the lowest tracing is the time tracing from the tuning fork (50 per second) and Pfeil's signal.

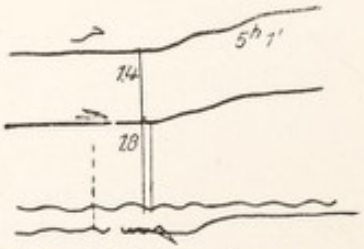


FIG. 2*b*.—THE ACOUSTIC MYOCLONIC REFLEX IN THE SAME CAT.

Tracings are arranged as in Fig. 2*a*.

maker and Magnus. These were attached to the head and haunch of the experimental animal, as shown in Fig. 1. At first this method was used only with the cat and monkey, but later it was found possible to adapt it for pigeons, snakes, and the octopus. Figs. 3*a* and 3*b* show tracings taken from an octopus by means of this method.

Where it was desired to examine the character of fits follow-

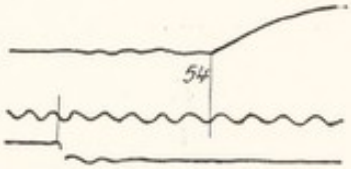


FIG. 3*a*.—TACTILE MYOCLONIC REFLEX OF AN OCTOPUS (*Eledone Moschata*).

Tracings in same order as in Figs. 2*a* and *b*.

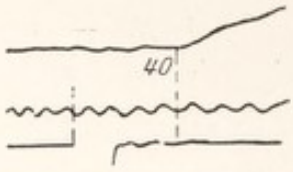


FIG. 3*b*.—TACTILE MYOCLONIC REFLEX IN THE SAME ANIMAL WHERE THE NORMAL IRRITABILITY HAS BEEN INCREASED BY A DRUG.

Tracings as in Fig. 3*a*.

ing on operative procedure, such as section of the posterior nerve roots, after cerebral operations, or with direct stimulation of the cortex, a special procedure was adopted. Reference to Fig. 4 shows that the hind legs of the animal are connected by means of a cord looped round the heel to a specially contrived spring apparatus. This apparatus is constructed on the principle of the Mosso ergograph, and is suitable for recording delicate and rapid movements.

As a rule, in my investigations, experimental animals were examined every three weeks, at least, over a long period, so as to ascertain their susceptibility to the drug used and the character of reaction shown. Small doses of the drug were given at first, and increased gradually. As the examination of any animal extended over many months, frequently over a year or longer, very complete data were got concerning the myoclonic reflexes at different times and in different conditions. It was found that animals rarely, if ever, become accustomed to, or tolerant towards, such a drug as monobromide of camphor. This is, of course, a

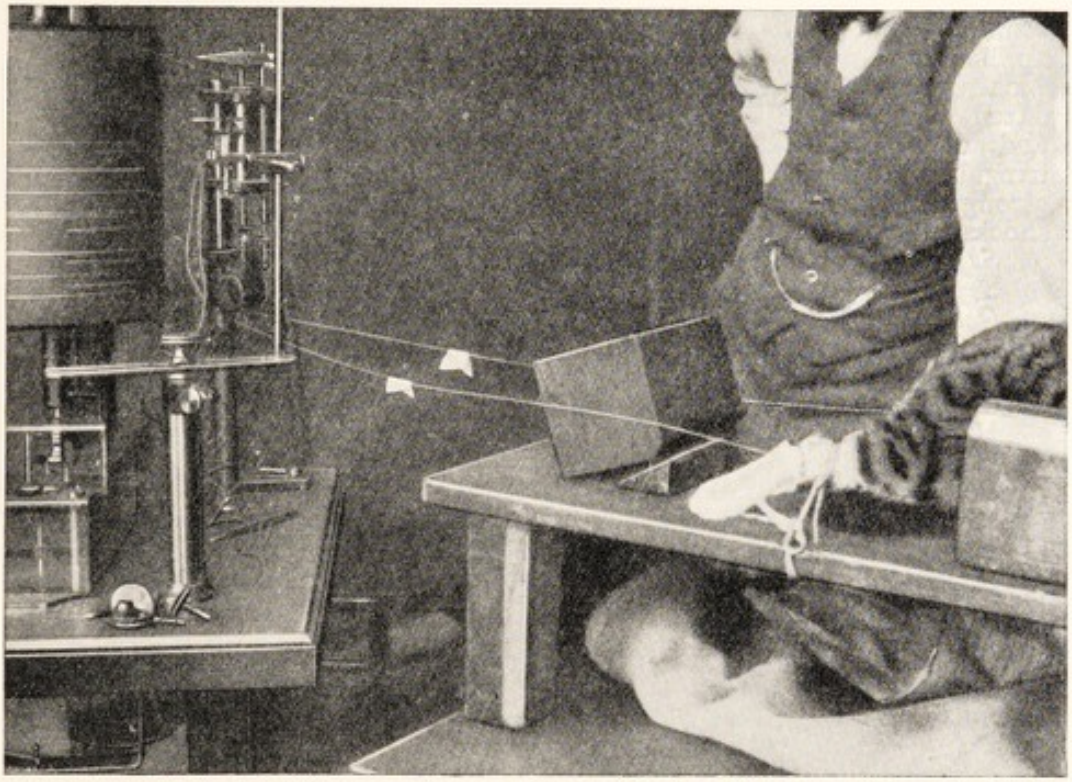


FIG. 4.

most important point. An example is given of a case where successive doses of monobromide of camphor were given to a cat.

Protocol 1, Cat 160. Healthy, strong animal.

October 17, 1907. 9 a.m., injection into quadriceps muscle of 0·25 gramme monobromide of camphor dissolved in warm oil. No result.

October 21. 9 a.m., 0·3 gramme of the drug again injected. No result.

November 8. 0·4 gramme given as before. No result.

November 14. 0·7 gramme given. No result.

December 21. 0·5 gramme given. No result.

January 14, 1908. 0·4 gramme given, this time in ether solution. No result.

January 30. 0·8 gramme given again in ether solution. No result.

February 20. 0·5 gramme given by mouth in capsule. No result.

March 20. 1 gramme again given by the mouth. No result. 0·02 gramme of curare solution injected. No result.

April 8. 1·5 grammes monobromide of camphor given by the mouth *after the morning meal.* No result.

April 27. At 10.10 a.m., 1·5 grammes given by the mouth *before the morning meal—i.e.*, when the animal was fasting. At four in the afternoon, reflex tactile shocks appeared, but neither acoustic shocks nor spontaneous shocks. At 5 p.m. there was a fit. Reflex and spontaneous shocks were present after this fit, and at 5.24 it had a second fit. Immediately after this fit the reflex and spontaneous shock disappeared, and the animal made a quick recovery.

June 16. At 10.30 a.m., 0·4 gramme of a curare solution was injected. No result.

August 12. At 10 a.m., 1·5 grammes monobromide of camphor given by the mouth. At 6 p.m., the pupils were enlarged, and slight spontaneous shocks appeared.

August 26. At 10 a.m., 1·5 grammes given as before. At 1 p.m., the first fit occurred. After this reflex shocks followed on strong acoustic stimuli. At 3.10 p.m., a second fit occurred. At 4.22 p.m., acoustic stimuli, applied at the rate of two per second, were generally followed by reflex shocks. At 4.27 p.m. there was another fit, after which the animal seemed dazed, but when examined ten minutes later responded to both tactile and acoustic stimuli. The response to the acoustic stimuli was somewhat irregular; sometimes a better reaction followed on a weaker than on a stronger stimulus. At 5.30, the animal was playful, and no trace of reflex shocks could be found.

September 9. 1·5 grammes given by the mouth. No result.

September 10. Animal not well.

October 4. At 10.45 a.m., 2 grammes given as before. At 3 p.m. slight tactile reflex shocks present.

October 25. At 5 p.m., 2 grammes again given.

October 26. Animal found dead.

N.B.—During the time this animal was under investigation, intramuscular injections of monobromide of camphor in oil or ether had no effect. During this period as much as 4 grammes of the drug were given at a time. On the other hand, 1½ grammes of monobromide of camphor given by the mouth resulted in "epileptic fits." These fits discharged the animal as a rule, except in September, when it had no fits but did not eat and was unwell for several days.

In addition to those animals (one in every eight or ten cats) which are normally subject to myoclonic reflexes, I found animals which showed another peculiarity. After such an animal had a fit, or a series of fits, as the result of the administration of drugs, it continued to have reflex myoclonic shocks for a shorter or longer period. In some cases this condition might last throughout the life of the animal.

As a general rule, animals subjected to a prolonged course of experimental treatment became more manageable and less shy and timid.

After definite information has been collected on the reaction of a particular animal to monobromide of camphor, some definite operation was performed involving the cerebro-spinal structure. Three weeks after the operation monobromide of camphor was administered in sufficient quantity to produce fits. These fits were recorded graphically. The comparison of the tracing of the monobromide of camphor fits before the operation with the tracings of those later fits demonstrates any change or

changes which may be due to operative procedure. Later, after the autopsy, the central nervous system was examined by the Marchi method, and the lesions due to operation recognised and defined.

The following is an example of a cat which only had *acoustic reflexes.*

Protocol 2, No. 212. Grey cat with white paws and chest. This was a difficult animal to manipulate. During the experiment it was kept on a meat diet.

8.11.11. At 2.30 p.m., ⅜ gramme monobromide of camphor given by the mouth. No result.

18.1.12. At 6 p.m., ½ gramme given as before, only about half swallowed. No result.

19.1.12. ¾ gramme of absinthe injected. No result.

11.2.12. At 10.45 a.m., ½ gramme of absinthe injected, and at 11.15 a.m. a further ½ gramme was injected. At 12.15, a fit resulted. Half an hour before this fit the animal had saliva dribbling from the mouth, and acoustic reflex shocks were present, not tactile. Five minutes after the fit the animal was completely discharged. It seemed in no way disturbed by these injections, which were all administered on the right thigh, but purred steadily through the experiment.

3.3.12. At 9.10 a.m., 2½ grammes of absinthe were injected into the right thigh while the animal was fasting. At 9.35 a.m., two fits occurred in rapid succession. Shocks were elicited by acoustic stimuli, the movements were limited almost entirely to the head. Again at 10.16 a.m. and at 10.35 a.m., fits occurred.

23.3.12. An operation was performed in which both temporal lobes were exposed. The right lobe was faradised, and convulsions occurred on the left side of the face. The temporal lobes on both sides were removed.

11.4.12. At 10 a.m., 1½ grammes of absinthe injected. No result.

12.5.12. The animal was, as it had been for several weeks, in a condition of strong sexual excitement.

12.6.12. At 6 p.m., ½ gramme of monobromide of camphor given.

14.6.12. Two days later the animal developed the condition of status epilepticus and died.

Epitome.—Before the operation this animal did not react to ⅜ gramme of monobromide of camphor; after the operation it succumbed in status epilepticus after a dose of ½ gramme.

Tracings of the reflex shocks due to acoustic stimuli were taken on 3.3.12. These show the latency to be rather prolonged.

Latency at 10 a.m., 64. (It is very rare to find so prolonged a latency with shocks due to acoustic stimuli.)
Latency 10.5 a.m., 60.
Latency 10.6 a.m., 60.
Latency 10.12 a.m., 92.
Latency 10.13 a.m., 44.

After this there were spontaneous shocks in the head and neck.

Latency 10.15 a.m., 90.
Latency 10.16 a.m., 54.

After this last reflex there was a fit which showed a rhythm of 9 to 10 at the beginning.

In order that the reader may appreciate the not unimportant variations shown by different animals, the following protocols are given.

Protocol No. 3, No. 219. A grey tabby cat.

17.8.11. At 6 p.m., ½ gramme of monobromide of camphor given. No result.

8.9.11. At 6.30 p.m., ⅝ gramme given as before. Next day moderate tactile reflexes were elicited by tapping the back of the neck.

2.10.11. At 5.30 p.m., ¾ gramme again given, a slight result followed. The following is the description of experimental reflexes produced in this animal on 3.10.11:

Time.	*Originating Factor for the Reflex.*	*Latency Variation.*	
		Head.	*Neck.*
9.20 a.m.	Clap	64	—
9.23 a.m.	Clap	48	62
9.26 a.m.	Clap	46	—
9.30 a.m.	Touch middle of back	42	50
10.4 a.m.	Touch right hind leg	48	50
10.6 a.m.	Touch right hind leg	64	50
10.10 a.m.	Touch right fore leg	—	54
10.12 a.m.	Touch on rump	60	54

20.10.11. A dose of ⅔ gramme of monobromide of camphor given. Next day tactile shocks were elicited by touching the rump and back. At 11.30 on the same day, a severe fit occurred. The pupils were dilated, and the animal had no appetite. A very slight acoustic reflex shock was elicited from the first of a series of claps.

8.11.11. At 6 p.m., ⅞ gramme of monobromide of camphor given. Next day a fit occurred a little before 9 a.m., while very slight tactile reflex shocks were seen on the same day.

24.11.11. At 7.30 p.m., ⅞ gramme of the drug again given. A little later on $\frac{1}{16}$ gramme was given. Next day there was a fit before 9 a.m.

8.12.11. At 6 p.m., ⅞ gramme given. Next day there was a fit.

3.2.12. At 8 p.m., ⅞ gramme given. No result.

25.2.12. At 6 p.m., 1 gramme given. Next day the animal had a fit, after which it was normal.

15.3.12. At 6 p.m., 1⅛ grammes given. Next day the animal had a fit, after which it was normal.

2.4.12. At 6 p.m., 1¼ grammes given. Next day animal was unwell, and vomited during the night. No shocks could be elicited.

3.4.12. At 9 a.m., 1 gramme given. No result. At 3 p.m., ½ gramme absinthe injected, after this slight tactile shocks could be elicited.

26.4.12. At 6.30 p.m., ⅞ gramme given. No reflex shocks could be elicited. Next day the animal seemed unwell, and had little appetite, but next day it was apparently normal.

13.5.12. At 6 p.m., 1 gramme given followed by one fit.

31.5.12. At 6.8 p.m., 1⅛ grammes given, the animal was subsequently sick.

20.6.12. At 10.30 a.m., ⅕ c.c. of a 1 in 10,000 solution of strychnine injected. No result.

15.7.12. At 6 p.m., ⅛ gramme monobromide of camphor given, this was followed by a fit.

2.8.12. At 6.30 p.m., 1⅛ grammes given followed by a fit.

27.9.12. At 6 p.m., 1⅛ grammes given, followed by a fit. Next day animal was rather unwell, and ate little.

16.10.12. At 6 p.m., 1⅛ grammes given. Animal vomited during the night. No further result.

8.11.12. At 6 p.m., 1¼ grammes given, but the whole was not swallowed. At the same time 1 gramme aspirin was given.

9.11.12. The animal looked ill, and had no appetite. It had one fit during the night. No tactile or reflex shocks could be demonstrated.

31.11.12. At 9.30 a.m., 1¼ grammes given. No result.

3.1.13. At 2.20 p.m., two injections of 1 in 10,000 solution of strychnine injected.

11.3.13. At 6 p.m., 1¼ grammes monobromide of camphor given. No result.

24.4.13. At noon, 1¼ grammes again given. No result, but next day animal refused food.

21.9.13. At 10 a.m., 1¼ grammes given. Next day animal was very sick, and had no appetite, but the reflexes were not apparently increased.

3.10.13. Animal operated on.

Epitome.—During this observation, which lasted over two years, I was struck with the regularity with which the animal reacted to the monobromide of camphor in the early stages of the experiment. A dose of ⅞ gramme of the drug resulted in a fit which completely discharged the animal. Later on in the experiment the animal developed a degree of tolerance, and as much as 1¼ grammes of the drug were required to produce a fit. Further the animal seemed to lose the tendency to develop fits, and reacted to the drug by general indisposition and vomiting.

From the investigation on the character of the latent period, strychnine seemed to shorten it. Further it was found that as a general rule the latent period was less for movements of the hinder portion of the animal than for the head.

Protocol 4, Cat No. 227.

25.9.13. At 6 p.m., ¼ gramme monobromide of camphor given. Slight myoclonic shocks produced by tactile stimuli.

4.10.13. At 6 p.m., ½ gramme given as before. A little later, both forepaws showed slight myoclonic shocks on tactile stimulation. Appetite good.

25.10.13. At 6 p.m., ¾ gramme given. Next day tactile reflex shocks were present.

8.11.13. At 6 p.m., ⅞ gramme given. After this dose tactile stimulation of a forepaw produced a reflex shock limited to the paw.

20.11.13. At 5.30 p.m., 1 gramme given. Next day the animal died, after an uninterrupted series of fits.

Epitome.—This animal had obviously little tendency to develop myoclonic epilepsy, but after a certain increase in the dose of monobromide of camphor it died in a condition of status epilepticus.

Protocol 5, Cat 168.

1.12.08. At 6 p.m., ½ gramme monobromide of camphor given. No result.

5.1.09. At 10.30 a.m., 1/10 gramme curare injected. No result.

24.1.09. At 10.20 a.m., ¾ gramme monobromide of camphor given. No result.

17.2.09. At 6 p.m., ⅞ gramme given. No result.

3.3.09. At 10.30 a.m., 1 gramme given after a meal. No fits resulted, but in the afternoon of the same day, tactile stimuli produced slight reflex shocks. Next day the animal was not well, and had no appetite.

5.3.09. Cat sat huddled up, and evidently had a bad cold (?).

20.3.09. Cat again normal.

Epitome.—Example of a cat which had tactile reflex shocks after moderate doses of monobromide of camphor, but did not have a fit after a larger dose. It displayed, however, after the larger doses, protracted indisposition.

The next protocol, No. 6, like No. 1, illustrates the necessity of increasing the dose of the monobromide of camphor after the animal has been subjected to a series of experimental doses. In protocol No. 6, a case is recorded where the increase in the dose during the year was from ¾ gramme to 1¾ grammes of the drug.

Protocol No. 6, Cat No. 217. Very nervous animal.

10.7.11. At 6 p.m., ⅜ gramme monobromide of camphor given. Next day animal was normal. No result followed.

20.7.11. At 9.30 a.m., ⅜ gramme absinthe was injected. After this injection, a few reflex shocks were produced by tactile stimulation on the rump. At 10.10 a.m. on the same day, the injection of absinthe was repeated. About an hour later, at 11.30 a.m., the animal was found to be breathing rapidly, the pupils were dilated, tactile stimulation produced reflex shocks of moderate intensity. After the lapse of fifteen minutes these tactile reflex shocks became much stronger, and well-marked acoustic reflex shocks were also present. At 11.50 a.m., a severe fit occurred, after which the animal was completely discharged—*i.e.*, became normal in every way.

The following is a table showing the changes in the latent period measured in fiftieths of a second:

July 20, 1911.	Originating Factor for the Reflex.	Variations in Latency.	
Time.		*Head.*	*Back.*
10.40 a.m.	Tactile on rump	—	2·5
	Tactile on rump	2·5	2·6
10.57 a.m.	Tactile on rump	—	2·6
	Tactile on rump	—	2·3
	Tactile on rump	—	2·7
	Tactile on rump	4·4	2·8
11.25 a.m.	Tactile left forepaw	2·4	—
Animal pants, pupils dilated			
11.38 a.m.	Tactile left forepaw	—	2·7
11.40 a.m.	Tactile rump	2·8	2·4
Spontaneous convulsions			
11.40 a.m.	Acoustic clap	4·0*	
11.41 a.m.	Acoustic clap	2·6	
11.42 a.m.	Fit	Convulsions: 7·8; 8; 7·1; 13·1; 14; 7·5; 8·8; 9; 12; 6·9; 9; 13	—
	Tactile rump	—	3·0
	Tactile middle of back	—	3·2
11.58 a.m.	Tactile rump	2·3	2·7
	Acoustic clap	—	—
	Tactile rump	3·6	3·2

* If a convulsion produced reflexly follows too soon upon a spontaneous shock—*i.e.*, before the expiration period—the latency is abnormally long.

15.9.11. At 6 p.m., $\frac{3}{4}$ gramme monobromide of camphor given. No result. Next day slight reflex shocks followed tactile stimulation. At 10.15 a.m. on this day $\frac{1}{2}$ gramme absinthe was injected; this was followed by spontaneous shocks, and at 11.2 a.m., by a fit.

10.10.11. At 6.30 p.m., $\frac{7}{8}$ gramme given. Next day no result.

23.10.11. At 6.30 p.m., 1 gramme given. Next day no result.

13.11.11. At 6.30 p.m., $1\frac{1}{8}$ grammes given. The animal had a fit during the night, and was completely discharged next day.

8.12.11. $\frac{13}{16}$ gramme given. Next day the animal had fits, but was completely discharged during the morning.

19.12.11. At 6 p.m., $1\frac{1}{8}$ grammes given. Next day no result.

20.1.12. Cat seemed normal.

9.2.12. At 6 p.m., $1\frac{1}{8}$ grammes monobromide of camphor given. Next day no result.

1.3.12. At 6 p.m., $\frac{13}{16}$ gramme given. The animal had a fit during the night, after which it was normal.

2.3.12. At 9.30 a.m., $\frac{1}{8}$ gramme given. No result.

20.3.12. At 6.30 p.m., $1\frac{1}{4}$ grammes given. No result, except that the animal had no appetite next day.

3.4.12. At 9.45 a.m., $1\frac{1}{4}$ grammes given. No result, except loss of appetite for the day. Next day it was back to normal.

19.4.12. At 10.5 a.m., one injection of nitrate of strychnine (1 per cent.). At first the animal seemed quite normal, there was no salivation, and the fur was normal in appearance. Suddenly it became convulsed, both fore and hind legs being strongly extended, and the animal fell down. This condition did not last long, and was not accompanied by loss of consciousness. The pupils were not widely dilated. Afterwards the animal got up and walked about, but showed a high degree of sensitiveness to both tactile and acoustic stimuli. Slight movements were accompanied by spontaneous extension fits, during which there was a little salivation of a clear, not foamy character. After three tonic convulsive attacks the animal died.

Epitome.—On the date 19.7.11, 1 gramme of absinthe had no effect on the animal, yet on 26.9.11, $\frac{1}{2}$ gramme of absinthe was sufficient to produce a fit. The reason was that on the second occasion the animal was slightly under the influence of the monobromide of camphor given the day before.

Protocol 7.—This is a case which resembles that described in protocol No. 1, for this animal also showed a greater susceptibility to the monobromide of camphor if given by the mouth than if given intramuscularly. Further, it also showed greater sensitiveness to the drug if it were administered while the animal was fasting. This point is also brought out in the next protocol for cat No. 177.

Protocol 8.—This case shows the effect of an intramuscular injection of monobromide of camphor on a fasting animal.

Cat No. 177. This was a large cat.

29.3.09. At 4.30 p.m., $\frac{5}{8}$ gramme monobromide of camphor given intramuscularly after a meal.

30.3.09. The animal showed a slight tendency to develop myoclonic reflex shocks on tactile and acoustic stimulation. It was in a highly nervous condition, and ate nothing throughout the day.

1.4.09. Animal was still unwell, and continued so on to April 3, that is, for five days after the dose.

10.4.09. At 10 a.m., $\frac{5}{8}$ gramme given as before, *but the animal was fasting*. Next day the animal was in the condition of status epilepticus. It did not eat, neither did it groom its coat.

30.4.09. The spinal arches were removed over the lower six dorsal segments of the spinal cord.

4.5.09. A subdural injection ($\frac{1}{4}$ c.c.) of tropococaine ($\frac{1}{4}$ c.c.) was administered at the site of the operation. Either as a result of this injection, or as a result of some spinal lesion, paresis of both hindlegs developed, and lasted for two days.

8.6.09. At 11 a.m., an injection of tropococaine ($\frac{1}{2}$ c.c.) was administered exactly as before. The paretic condition again was present, and was not completely gone after two days.

30.6.09. The left hindpaw was stiff and covered with ulcers, general analgesia over the paw. Moved about on the forelegs.

30.6.09. At 5.45 p.m., $\frac{5}{8}$ gramme monobromide of camphor given intramuscularly *after a meal*. The animal showed only a tendency to develop acoustic reflex shocks. This is very important, as it shows the effect of a meal is to minimise the action of the drug.

1.7.09. The animal apparently had a fit during the night. During the day it had acoustic reflex shocks, *which were diminished after the animal was fed*. The left hindpaw was stiff, covered with ulcers, and analgesic; it moved about on its forelegs.

16.7.09. On this date 0·75 gramme monobromide of camphor were given by the mouth.

17.7.09. In the morning it was found unconscious and lying on its side. It had a series of fits during the day, and eventually passed into the condition of status epilepticus. From the hours of 9 a.m. to 11 a.m. the cat had no fits; it was too weak. During this period it was unconscious, breathing was shallow, while it made a few automatic movements (petit mal ?). The animal was kept warm with hot bottles, and given the following mixture by the stomach tube: Mixture—Tc. cannabis indica 5 parts, pot. bromide 20 parts, gummi arabis q.s., water 1,000 parts. This treatment resulted in the recovery of the animal,* and it had, as already stated, severe fits when passed into the condition of status epilepticus, in which it died. The reflex shocks and fits were recorded with the panto-kymographion. It appeared that the latency of the tactile reflex shocks increased with the degree of intoxication until it reached 140 mille seconds. Fits only occurred when the latency measured 3·6 fiftieths of a second or less, never if it were longer. See tracings taken from this animal in Fig. 18.

Protocols Nos. 9 and 10.—These are both examples of cats which reacted, like No. 5, to the monobromide of camphor with general indisposition, not with fits.

Protocol 9, Cat 163 E.

30.9.08. At 10 a.m., 1 gramme monobromide of camphor given by the mouth. No fits resulted. The animal was kept under observation up to 4.10.09. It was indisposed, and refused food.

Protocol 10, Cat 168.

6.1.09. At 6 p.m., $\frac{1}{2}$ gramme monobromide of camphor given. No result.

25.1.09. At 10.30 a.m., $\frac{1}{10}$ gramme curare injected.

29.1.09. At 10.20 a.m., $\frac{3}{4}$ gramme monobromide of camphor given after a meal. No result.

27.2.09. At 6.15 p.m., $\frac{7}{8}$ gramme again given. No result.

3.3.09. One gramme given after a meal. Records were got of tactile reflex shocks.

4.3.09. Animal not yet normal. Had no appetite.

5.3.09. Animal more indisposed than on previous day. Sat huddled up, was dazed, the fur was damp.

16.3.09. Cat had a cold.

20.3.09. Animal quite better. Ate and drank well.

---

* Koppang (*Norsk. mag. f. Lægvid.*, No. 12, 1913) found that a rapid recovery from camphor poisoning followed on washing out the stomach.

25.3.09. Anæsthetic administered and a large portion of the bony spinal arch removed. The operation was successfully carried out, and it seemed highly probable that the animal would do well, but it died two days later.

Epitome.—In this last case, after moderate doses of monobromide of camphor, the animal displayed tactile reflex shocks. A larger dose produced indisposition but not a fit.

Protocol 11.—This is a case which shows an increased susceptibility to monobromide of camphor before parturition.

Protocol 11, Cat.

16.3.05. At 10.30 a.m., ¾ gramme monobromide of camphor given, dissolved in oil, and injected intramuscularly. At 12.30 p.m., exaggerated reflexes were present. At 3.30 p.m., the first big fit occurred. At 4.50 p.m., after a second fit, the animal mewed incessantly. On testing it was found not to withdraw its paws from the vicinity of a lighted candle. At 5.20 p.m. recovery had proceeded so far that it did withdraw its paws from the proximity of the candle flame after two minutes. There were no spontaneous shocks.

20.3.05. Partus. Animal gave birth to six kittens, four dead, two alive.

28.3.05. One and one-fifth grammes again injected intramuscularly as before. At 3.30 p.m., a candle flame was drawn slowly along the plantar pads, and the paws were withdrawn, but only after repeated exposure.

4.4.05. At 9 a.m., 1⅓ grammes again given as before. No symptoms followed, except a few spontaneous shocks.

27.4.05. At 9 a.m., 1⅓ grammes again given as before. At 4 p.m., reflex shocks of an exaggerated character, followed on tactile and acoustic stimuli. At 4.50 p.m., there were few violent reflex shocks, then a severe fit, and finally post-epileptic shocks.

In the protocols of the experiments, one finds cases such as Nos. 3 and 6, where approximately equal doses of the monobromide of camphor were given to an animal over a fairly long period, with about equal results. This was done with the object of finding out as precisely as possible the exact effective dose.

It has been seen that several factors influence the amount of the effective dose. A meat diet increases the resistance, so also does the condition of good nutrition, while a larger dose is also necessary where the animal has had a good meal. On the other hand, pregnancy diminishes the tolerance.

It has been found from experiment that where the monobromide of camphor is given in capsules by the mouth, 0·5 gramme to 1·5 grammes is an effective dose for a cat. This dose will produce exaggerated myoclonic reflexes to tactile or acoustic stimuli or fits in practically all animals used experimentally. It would appear as if the mechanism for these phenomena lies latent in the nervous system of animals, and is ready to act on due stimulation. The cases of poisoning with this drug strongly suggest that the same condition holds good for man also. The symptoms of poisoning in man are exaggerated reflex myoclonic shocks, spontaneous shocks, and fits (compare p. 42). In

certain experimental cats, it was seen that the first two phenomena exaggerated reflex myoclonic shocks, and spontaneous shocks were almost wanting. Such cases seem to be parallel to those cases of myoclonic epilepsy in man, where there is no history or evidence for any symptoms before the appearance of the fit. It is, of course, open to question whether one is justified in comparing such cases in man with these peculiar cases in experimental cats. Yet the same sudden onset of the fit is seen in both, although it is true that it is rare among experimental cats (compare Chapter III., paragraph 4).

A point of great interest and importance is that after a fit the cat loses almost at once all pathological symptoms; in other words, the fit has discharged it. This fact is very difficult to explain, unless the fit be looked on as a detoxicating process. This detoxicating effect might be achieved by the action of the fit rendering the toxin inert, or by heightening the resistance of the central nervous system.

I have tried to work at this problem by investigating the amount of monobromide of camphor which may be administered to the animal (short of killing it) after the power of exhibiting a severe motor reaction has been excluded. This exclusion can be affected by section of the motor roots or by injection of cocaine-adrenaline into the subdural space.

These experiments, with the results, are not yet ready for publication, but so far they tend to support the view that the effect of the fit is to render the toxin inactive.

§ 3. **A Comparison of the Myoclonic Reflexes with Other Reflexes.**

Thanks to the researches of Sherrington,* Maxwell, Magnan, Graham Brown, Jordan, and later of Lucas, Adrian, Forbes, Pratt, Kato, and others, considerable progress has been made during the last few years in the knowledge of reflexes in both warm and cold blooded animals. Indeed, so much progress has been made in this line, that it seems probable that a completely new classification of reflexes will soon be necessary. In the meantime, however, a comparison may be made between the myoclonic reflexes, their incidence and time relationship, with the skin and deep reflexes in man and the higher vertebrates.

In the first place, the myoclonic reflexes differ from all other reflexes in that they show the quality of exaggeration when the stimulus is quite unexpected. As is well known, certain reflexes, notably the skin reflexes, exhibit quite another character, for

* Sherrington, "The Integrative Nervous System," 1912.

exaggeration of such a reflex occurs when attention is drawn to the part involved. The deep reflexes are not much affected by the character of the stimulus, whether it be expected or unexpected. In this detail, therefore, there seems to be a certain relationship between the deep reflexes and the myoclonic.

In the second place, with the exception of the vagal cardiac

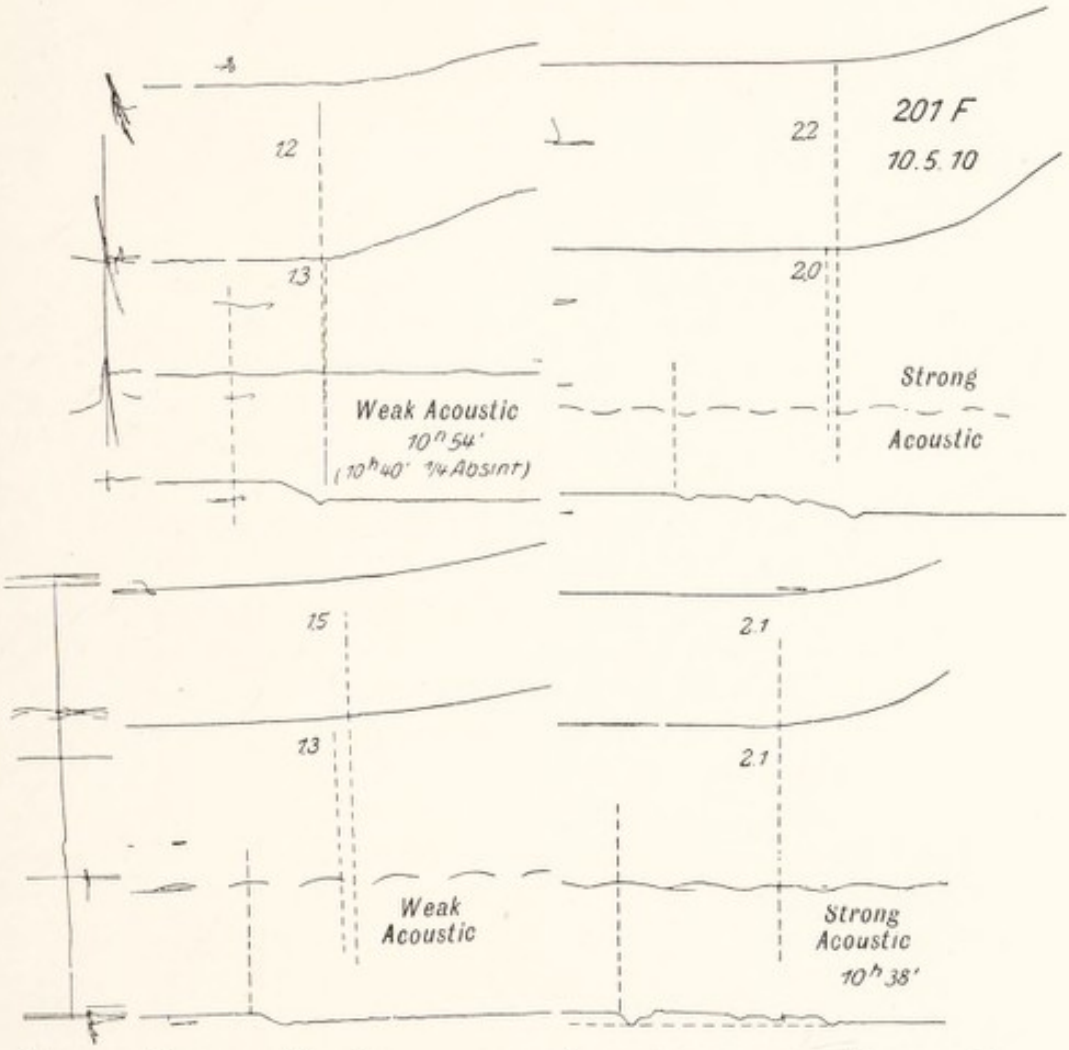


FIG. 5.—CAT 201 F. PARADOXICAL CONDITION OF THE REFLEX TIME WITH WEAK AND STRONG STIMULI.

The topmost curve is formed from the head tambour, the second from the rump tambour. The fourth, or lowest tracing, shows electromagnetically the moment when tactile stimuli or acoustic stimuli were applied. Tuning fork vibrations 50 per second.

reflexes, intestinal peristaltic reflexes and the ejaculatory reflex, there are no reflexes where the mechanism involved displays so long a refractory period as the myoclonic. In this point there is a certain resemblance between the superficial reflexes and the myoclonic. It will be shown in the next paragraph that this refractory period varies according to circumstances from a fraction of a second to several seconds. One of the first points to

investigate is the character of the factors influencing this variation.

In the third place, the latent periods, at least for acoustic myoclonic reflexes, is considerably shorter than that of all physiological phenomena indisputably recognised as true reflexes (see Figs. 5 and 9, clap reflexes). The phrase " indisputably recognised as true reflexes " is used because of the opinion held by some physiologists and neurologists that the so-called deep or tendon reflexes are not true reflexes. I have devoted some attention to this point, and in 1899* published the result of experimental work which rather supported the view that these phenomena are not true reflexes.

The reflex time for myoclonic reflexes has been established by evidence afforded by many experiments conducted over a period of years. The characteristic latent period of the myoclonic reflexes not only distinguishes this class of reflexes from all others, but it may help to explain the nature and character of the so-called deep reflexes. The possible identity of the myoclonic reflexes with those so-called deep reflexes and with the myotatic reflexes of Liddell and Sherrington is a point which must be discussed. It is significant that even in appearance the tracing of a myoclonic reflex shows a striking resemblance to such a " tendon phenomenon " as the knee reflex. It is, on the other hand, quite different from the tracing obtained from a limb when the appropriate area of motor cortex is faradised.

In the fourth place, these myoclonic reflexes possess a very peculiar property. If these reflexes are properly re-enforced by certain drugs, they display an increasing and distinct after-discharge. This after-discharge gradually evolves into what is at present regarded as a pathological phenomenon—an epileptic discharge or fit. The only reflexes which show any similarity to this characteristic are the pathologically exaggerated tendon reflexes, where, as a result of certain lesion of the central nervous system, these reflexes may give rise to clonus (spinal epilepsy of Brown-Séquard), and the shivering fits which may be induced by exposure to cold. In these last cases we are, however, not dealing with true after-discharges. Probably there prevails a condition of tonus which induces alternately stretch and relaxation reflexes, as is shown† in normal conditions in man in the gastrocnemius and tibialis anticus muscles.

* Muskens, *Neurol. Zentralbl.*, 1899, p. 1074.
† *Ibid.*, 1899, p. 1083.

§ 4. The Refractory Phase.

The so-called refractory phase observed in myoclonic reflexes and in most epileptic phenomena is essentially the same as the refractory period or phase which follows any neuro-muscular movement, or the passing of any stimulation along a nerve-fibre (Forbes).* It may be defined as a phase in which the mechanism in question cannot be brought into identical action by means of a repeated identical stimulus. This is a point which has attracted much attention, and about which a considerable amount of physiological information is available. Engelmann† ascribes the refractory phase to the temporary decrease of that function which may be termed the liability to react to a stimulus (Anspruchsfähigkeit). He also considers that this is the basis of the characteristic phenomena displayed in the rhythm of cardiac pulsations. On this last point I do not altogether hold the same views. As a result of my own investigation on the matter,‡ it seems to me that the function of conduction is exhausted after the consummation of each contraction wave of the cardiac muscle. This exhaustion of the function of conduction seems to me to be the explanation of the refractory phase.

It is interesting to find that Engelmann, disregarding the all-or-none principle, confirmed the observation made by Marey§ that the refractory phase is primarily dependent on the strength of the stimulus. In the intoxicated, non-mutilated cat I found the duration of the refractory phase dependent on the nature and character of the after-discharge. For several minutes after a complete after-discharge (a myoclonic epileptic fit) no myoclonic reflex whatever could be elicited. This is found to be true for the reflex excitability of the central nervous system of the cat to both acoustic and tactile stimuli. After an effective slight tactile stimulus applied to an animal which has received a moderate dose of monobromide of camphor, the refractory period for any tactile or acoustic stimulus lasts for several seconds, up to half a minute. Reference must be made to the work of Gotch and Burch, who describe a very much shorter refractory period.‖ Sherrington,¶ whose work was well known before Lucas's revolutionising researches on the subject, regards

* A. Forbes, *Physiol. Review*, 1922, vol. ii., p. 360.

† Engelmann *Investigation from the Physiological Laboratory in Utrecht*, series 4, part 3, p. 53; also *Pflüger's Archiv f. d. ges. Physiol.*, vol. lxii., 1896.

‡ L. J. J. Muskens' *American Journal of Physiology*, 1898, p. 503.

§ Marey, *Excitations artificielles du Cœur travaux du Laboratoire de M. Marey*, 1875, p. 63.

‖ Gotch and Burch, *Journal of Physiology*, xxiv., 1899.

¶ Sherrington, *Brain*, 1910, p. 104.

the refractory period as an inhibitory process. Verworn and Froelich interpret the refractory period as a symptom of fatigue. This explanation cannot, however, be accepted as an explanation of the refractory period in cardiac muscle. This resulted from my own experiments, which were confirmed later by Hering and de Boer. In these experiments it was shown that in pulsus alternans induced by digitalis the entire ventricular musculature does not contract, but only a portion of it. Both phenomena could be reduced to changes in conductibility. Baglioni* looks upon the refractory phase as being exclusively dependent on sensory elements. He illustrates his work on the subject by tracings showing the effect of the use of phenol. Richet and Broca,† in their investigations on the length of the various refractory periods, established the minimum at one-tenth of a second. They also found that the refractory period was influenced by temperature being lengthened in cold. Further, they found that the refractory phase for movements produced by rhythmic stimulation of the cortex in animals dosed with chloralose and for myoclonic shocks produced reflexly is of the same order.

As a result of my own investigations it seems possible to draw another parallel. This is a parallel between the change in latent periods found in the transmission of muscular contractions from the sinus to the auricle, and from the auricle to the ventricle, and the latent periods between reflex stimulation and myoclonic reflex contraction. In both cases the changes seem due to an alteration in the power of conduction. In the heart during diastole, and shortly after it, the time of conduction may be one-fifth second, but it is much shorter immediately before the following systole. Thus stimuli arriving from the sinus or auricle at a rate too rapid to allow of the recovery of the power of conduction will cause an alternate pulse in the auricle and ventricle, while the whole musculature will only be affected by the alternate stimuli. In the same way, when myoclonic reflexes are induced by a rapid succession of tactile or acoustic stimuli alternately stronger and weaker, myoclonic reflexes are produced. Reference to Fig. 6 shows that the latent period increases from 2·7 to 5·6 fiftieths of a second (tuning fork vibrations 50 per second) (54μ to 112μ), while the strength of the resulting muscular movement shows a corresponding decrease.

It must be noted that these differences are of a totally different order from those got in the heart beat observed with direct stimulation. This difference suggests the possibility that in one case

* Muskens' *Journal of Physiology*, vol. xxxvi., 1907, p. 104.

† A. Broca and Richet, *Archives de Physiologie*, vol. xxix., 1897, p. 876.

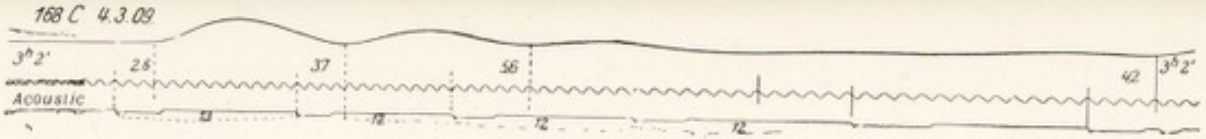


FIG. 6.—CAT 168 C. MARCH, 1909.

The reflexes were slightly exaggerated by the use of bromide of camphor. The tracing shows the effect of acoustic stimuli repeated four times in the second—*i.e.*, the stimuli are applied before the end of the refractory phase. Note the steadily increasing latency and the decrease of the reflex response.

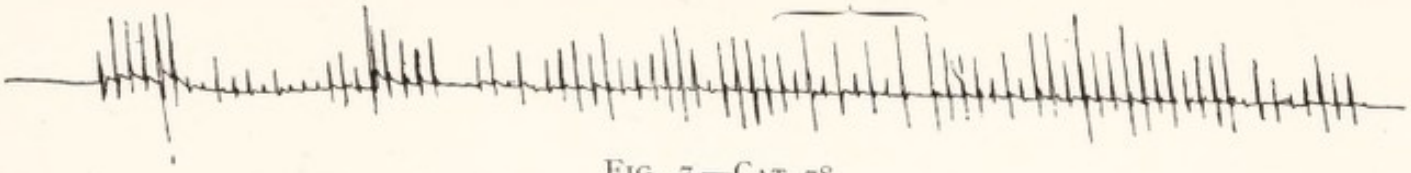


FIG. 7.—CAT 78.

The cat was laid on a mat under which was a twisted rubber tube. By means of this tube changes in pressure were conveyed to a tambour in connection with a recording apparatus. At the beginning of the tracing, acoustic stimuli were applied at intervals of less than 1 inch, and it is seen that the elevations become less and less. After that the stimuli were applied at slightly longer intervals of about 1 inch, and it is seen that the elevations are good either in direct sequence or there is one good and then one poor rise.

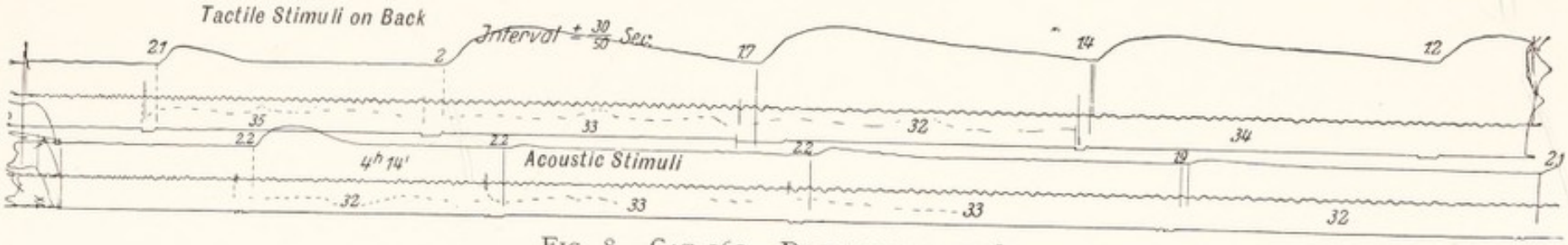


FIG. 8.—CAT 161. DECEMBER 2, 1908.

Tracings are supplied from the back tambour only. Theinterval in time between the tactile reflex tracing (upper tracing) and the acoustic reflex tracing (second tracing) was about $\frac{30}{50}$ second. The tactile reflexes, as is shown, become stronger, the acoustic reflexes slighter (the latter have a longer refractory period). There are only slight changes in the latent period.

the changes are associated with muscular conduction, in the other with nerve conduction.

Where the stimuli succeed one another very rapidly, a tracing reminiscent of one from a pulsus alternans may be got (Fig. 7). If, however, the stimuli follow one another more slowly, the tracing shows properly developed tactile reflexes (top line), although for some time the susceptibility to acoustic reflexes diminishes (lowest line) (refer Fig. 8). When, however, a reflex due to an acoustic stimulus is induced, the latent period is similar to that found with the first reflex. Fig. 9 shows how, under normal conditions, the acoustic reflex time is considerably shorter than that of tactile myoclonic reflexes.

§ 5. The Occurrence and Mechanism of the So-called Spontaneous Shocks, Series of Shocks and Fits. Groups of Muscles involved.

In accordance with the details set forth in the preceding paragraphs, the following conditions in the cat may be distinguished, but it must be remembered that they all merge one into the other.

1. *Complete Absence of Reflex Irritability.*—This is the general rule in the majority of domesticated animals.

2. *Slight Reflex Irritability with a Maximum Refractory Period.*—This is found normally in a few domesticated cats, but is always present in animals after slight intoxication with monobromide of camphor or absinthe. Where a larger dose of the drug is given, this condition exists temporarily until the further action of the drug effaces it.

3. *Greatly Intensified Reflex Irritability as found in Cats after Moderately Large Doses of Monobromide of Camphor or Absinthe.*—It is also found in those rare animals which display myoclonic epilepsy without the administration of drugs. The refractory period for these greatly intensified reflexes is very short.

Further, as a culminating point in respect of reflex irritability and the shortening of the refractory period, two conditions are to be recognized; these are:

4. *The Occurrence of Quasi-Spontaneous Shocks and Series of Shocks with greatly Shortened Refractory Periods.*—Myoclonic tactile reflexes are as a rule easily elicited from all parts of the body, while convulsive jerks, at first limited to the adductors and extensors, gradually involve the entire voluntary musculature.

5. *The Occurrence of Spontaneous Fits of Myoclonic Epilepsy.*—These fits begin with tonic cramps, and are followed by clonic

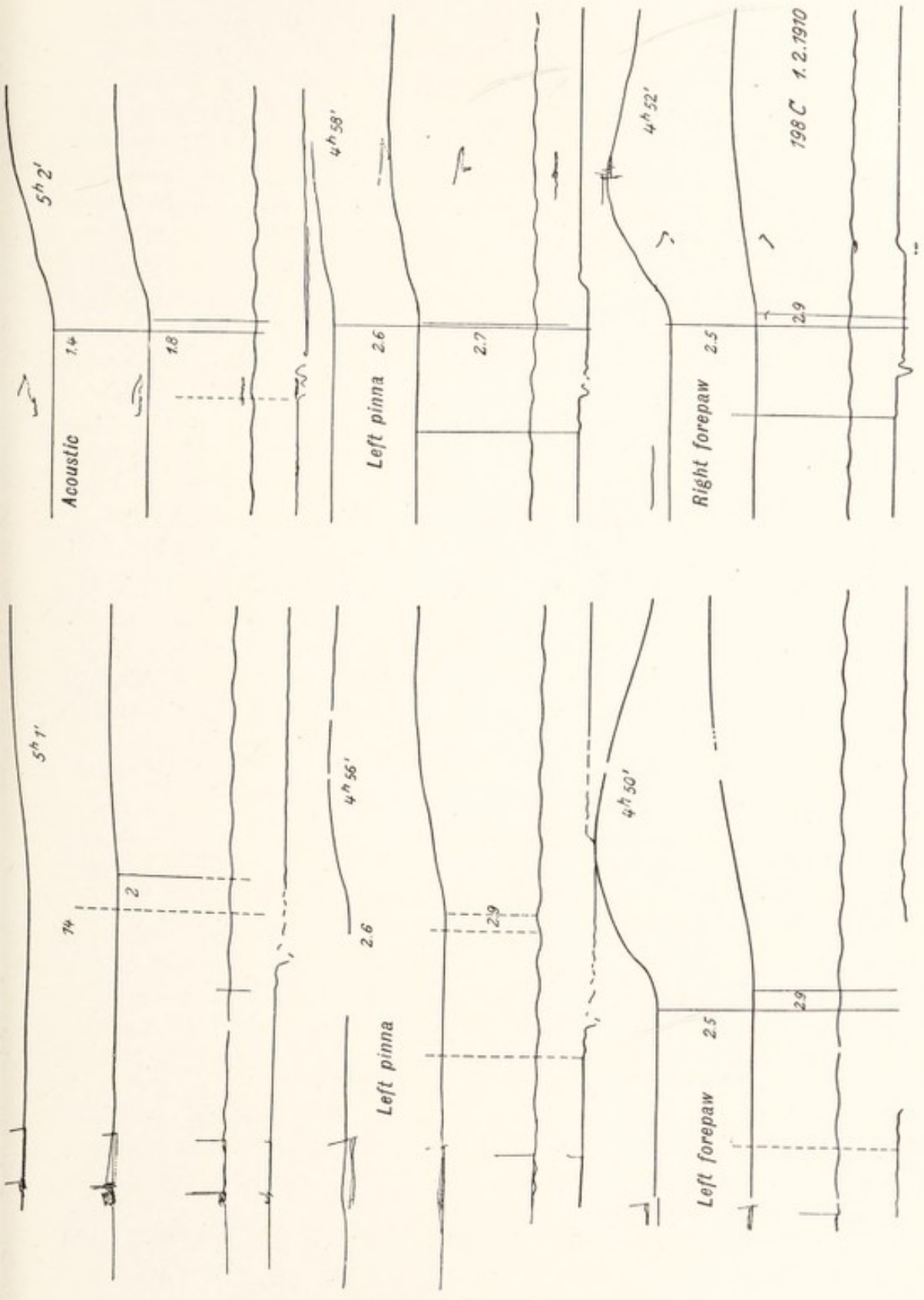


FIG. 9.—CAT 198.

After a moderate dose of bromide of camphor the acoustic and tactile myoclonic reflexes are both increased. The upper tracing was taken from the drum connected to the head, the lower from the drum connected with the back. These tracings illustrate that with the most favourable experimental conditions there is little difference between the latent period of the two sides.

convulsions. The intervals between the convulsions increase while the movements become greater. A stage of numbness and exhaustion follows on this, after which a relatively normal condition supervenes, when the refractory period is at its maximum. This may be called the *stage of discharge*. The last two stages, on account of their kinship to the pathological condition recognised in man as myoclonic epilepsy, are naturally of the greatest interest.

Now as the steady shortening of the refractory period of the reflexes is a characteristic of the first three stages, the question arises whether the last two stages do not show the maximum shortening of this period? This inevitably suggests the question whether the so-called spontaneous shocks are not spontaneous at all, but due to some unknown and unrecognised stimuli. Because we are ignorant of the stimuli, if any, involved in these "spontaneous" shocks, the refractory period cannot possibly be estimated. This being the case, the most that can be done is to collect data from other observations on experimental animals. From observations made on the experimental cat in which these "spontaneous" shocks appear, it seems highly probable that the reflex excitability of the animal has been so increased that certain internal stimuli, normally inadequate, are now adequate, and cause reflex convulsive phenomena. There is no doubt that such stimuli do exist in relation with other phenomena, as, for example, the eyelid reflex. There is sufficient encouragement from the close observation of experimental animals to justify a consideration of such possible subliminal stimuli. The stimuli which deserve consideration are (1) tactile, (2) acoustic, (3) optic (proprioceptive and other sensory stimuli), (4) interoceptive stimuli.

Attention to the work of Stannius, C. Bernard, and H. E. Hering on the spontaneous convulsions in strychnine poisoning helps to the better understanding of the phenomenon. It is interesting to find that these workers all accepted the theory of the reflex origin of these so-called spontaneous convulsions (compare with the work of Sherrington in the "Integrative Nervous System," 1910, p. 107). For the tactile stimuli it is seen that with larger doses of the reinforcing drug the reflex irritability steadily increases while the refractory period shortens. There is, therefore, nothing against the conception that at a given moment the irritability reaches a point when stimuli, unrecognisable as yet but normally reaching the nervous system by tactile channels, becomes active. Should the refractory period at the same time attain a certain minimal value (by whatever mechanism this is obtained), then there is a possibility that not only quasi-spontaneous shocks, but also series of quasi-spontaneous series of convulsions may appear (the after-discharge of Sherrington).

Reference to Fig. 10 shows the tracing from the back tambour registering after-discharges with the frequency calculated in $\frac{1}{50}$ second as 6·5, 6·4, 8·1, 8·2, 8·3, 8·4. With regard to the possibility that subliminal acoustic stimuli could also act in this way, the curious paradoxical characteristics of such stimuli must be recalled. It is found that a decrease in the strength of acoustic stimuli (up to a point) is associated with an increase in the force of the associated reflex. At the same time the refractory period diminishes in length (refer Fig. 5, p. 31). With a certain degree of reinforcement, or of intoxication with suitable drugs, it would, therefore, be peculiarly easy for stimuli of this type to become quasi-spontaneously active and to produce shocks and fits, although no stimuli could be appreciated extraneously. In this connection the possible stimulation by the heart beat suggests

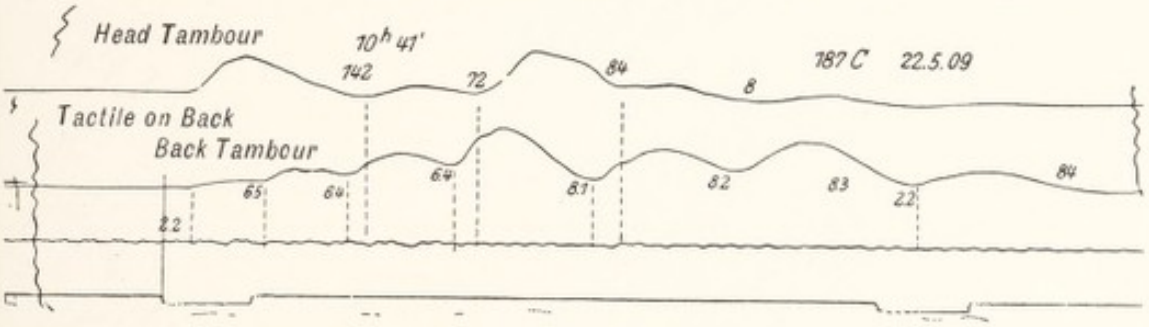


FIG. 10.—CAT 187. MAY 22, 1909.

The reflexes have been reinforced by monobromide of camphor. The top tracing was taken from the head tambour, the lowest from the back tambour. Tactile stimulus to the back was followed, after a normal latency, by a strong reflex movement of the head, and a reflex after discharge consisting of six convulsions within $40\frac{1}{50}$ second. These convulsions are well shown in the back tambour tracing with the freqeuncy of 6·5, 6·4, 8·1, 8·2, 8·3, 8·4. During this series of convulsions, or small myoclonic fits, the pupils were dilated. This is one of the smallest myoclonic epileptic fits I was able to record graphically.

itself. The fact that the frequency of the spontaneous convulsions conceived of as an after-discharge is much greater (up to 8 to 10 per second) by no means excludes this possibility.

Particular attention was not paid in my investigations to optic stimuli and their influence on reflex action, but it was noticeable that the sudden admittance of strong light to an animal dosed with the special drugs seemed to produce a general reflex. Too much attention must not, however, be paid to this, for blindfolded animals showed the same tendency to display these reflexes. The possibility cannot be excluded that certain chemical stimuli (for example, monobromide of camphor) conveyed by the blood to the retina and other parts of the optic apparatus may affect the organ. Nothing is known of the action of stimuli conducted along the sympathetic nervous system, although certain observa-

tions by Langley are very suggestive. It would be necessary to collect data from persons suffering from intestinal disease to supply material for such a theory. As, however, conclusions drawn from observations on pathological conditions are inadmissible in the present investigation, the question of possible intestinal stimuli will not be dealt with.

Setchenow,* in his experiments, proved that slight stimulation of a nerve had, directly and reflexly, a marked influence on the activity of the medulla oblongata (especially if the medulla be isolated from the more proximal parts of the brain). Forty years ago he also established the existence of quasi-spontaneous electric discharges in the isolated nervous system of the frog. This classical description recurs to the mind when observations are being made on myoclonic reflexes.

Gottlieb† distinguished drugs which cause reflex convulsions from those which cause spontaneous convulsions due to the summation of internal stimuli. The former he described as initiated by centres in the spinal cord, while the latter are dominated by centres in the brain. Mattaei‡ suggested that the cause for spontaneous discharges is increased irritability, which persists after the application of a stimulus.

From a consideration of these data the conclusion is arrived at that it is impossible to exclude the possibility that stimuli, inappreciable to the ordinary methods of observation, may be the cause of so-called spontaneous convulsions.

The question as to whether these possibilities can be more closely examined by experimental methods will be dealt with in a later chapter devoted to the influence of lesion of the central nervous system upon the occurrence of reflexes and convulsions.

So far observation has been directed to the question of the cause of spontaneous shocks or series of shocks. The type or form of reflex movement, shown by the muscles involved in a convulsion, forms a separate subject. Where there is but a slight degree of reflex irritability, a touch on a limb of an experimental animal is followed by the stiffening, of a clonic character, of the limb. If the irritability be increased or the stimulus be strengthened, a more or less stereotyped form of convulsion follows, and affects body and limbs of the animal. In such a case the head is turned in, the back bent, the limbs extended or adducted, while fur loses its gloss. This convulsion follows, no matter where the stimulus is applied or what is the character of the stimulus. If the reflex irritability be increased by giving a still larger dose of the

* Setchenow, *Pflüger's Archiv f. d. ges. Physiol.*, vol. xviii., 1882.
† Gottlieb and Meyer, *Lehrbuch der Pharmacognosie*, 1890.
‡ R. Mattaei, *Deutsche med. Wochenschr.*, 1922, No. 35.

drug, the extensors, flexors, and abductors are involved, while the phenomenon known as after-discharge is prominent. In such a case the neck is bent backwards, the tail raised, while flexors and extensors are both convulsed. With stronger intoxication, therefore, there is induced a condition similar to that so picturesquely described by Sherrington for the convulsions in strychnine poisoning. In this description he points out that the movements of the extensors and flexors, instead of inhibiting each other, stimulate each other. He gave the name "conversion" to this change in character of convulsive phenomena.

To explain the establishing of a stereotyped reflex movement in the cat treated with monobromide of camphor, on the supposition that a similar type of "conversion" has occurred, is difficult. It is, perhaps, best to regard the myoclonic reflex as the same as the "start reflex" of Cushny.* It is then assumed that both flexors and extensors are contracted normally in the typical myoclonic reflex as in the "start reflex," and that the drug strychnine or monobromide of camphor only intensifies this reflex.

The question of the character of the refractory phase during a fit or series of shocks will be dealt with later, when the rhythm of the fit is considered.

At this point it must be emphasised that in no case has an extra reflex been seen to occur during a fit.† The question might arise whether the rhythmic character of the reflex contractions during a fit is not dependent, like the heart beat, on the refractory phase. The tonic stage of a fit, at least as observed in cats, is at the beginning of the fit nothing but an extremely rapid succession of clonic contractions (8 to 12 per second). A possible explanation seems to be that, during the initial stages of the fit, the reflex irritability is so great that with the many and varied stimuli reaching the central nervous system each second, a point is reached where the number of myoclonic reflexes is so high (12 per second) that an apparently tonic cramp results.

In any case, I hope to persuade the reader, by means of evidence to be presently discussed, that it is justifiable to infer a *certain physiological equality in the discharging effect of spontaneous convulsions, of reflexly induced convulsions, and of the ordinary complete series of phenomena known as an epileptic fit.*

Attention will be directed later to the inequality in the discharging effect of these various phenomena.

* Cushny, *Quarterly Journal of Experimental Physiology*, vol. xii., 1912, p. 153.

† Engelmann examined the duration of the refractory period by inducing extra contractions between the spontaneous heart beats.

§ 6. A Comparison of the Motor Fit due to Bromide of Camphor and the Epileptic Motor Fit of the Myoclonic Variety in Man.

Such a comparison depends, in the first place, upon the clinical observation of the motor fit due to bromide of camphor as it occurs in man,* and which displays all the phases of the ordinary motor epileptic fit. In the second place, a close study can be made of the different phases and symptoms of the fits as they appear in cats and apes after the administration of bromide of camphor.

Fig. 11 shows automatically a graphically recorded bromide of camphor fit in a cat. In it six periods are to be distinguished.

(*a*) A prodromal period in which reflex as well as spontaneous single convulsions occur with extreme rapidity and ease. (The manner in which this prodromal period may be subdivided has already been described.)

(*b*) The second period is usually short, sometimes only 1 or 2 seconds; during this period the liability to convulsions is temporarily diminished. This stage may be looked upon as a stage of aura. It cannot be regarded as an extended refractory period, although the irritability is as usual lowered. Tactile or acoustic stimuli, applied at this stage, when the animal is usually more or less dazed, produce reflex contractions only after very long intervals. These contractions may merge into a complete fit. This is a definite stage of labile reflex excitability, for in some cases, instead of a lengthened latent period there is a shortened one (compare Fig. 17, p. 75). In this short period important changes probably take place in the function of conduction.† These changes, in all probability, have a distinct influence on the production of the ultimate fit.

It seems possible that an analogous lability in conducting power may occur in the central nervous system of both man and animals at the moment of wakening or of falling asleep. These are phases of the day cycle which are strongly predisposed towards the occurrence of epileptic discharges (Part III., Chapter III.).

(*c*) The third stage is the actual so-called tonic fit, which begins with a series of very rapid and severe convulsions.

These convulsions are followed in a few seconds by convulsions very similar in type, but separated by intervals, which gradually increase in length.

* J. K. A. Wertheim-Salomonson, *Ned. Tijdschrift v. Geneesk.*, 1900, No. 11, p. 506.

† Macdonald and Cobb show that shortly before the absinthe fit commences the cortex blanches and the pressure of the cerebro-spinal fluid diminishes.

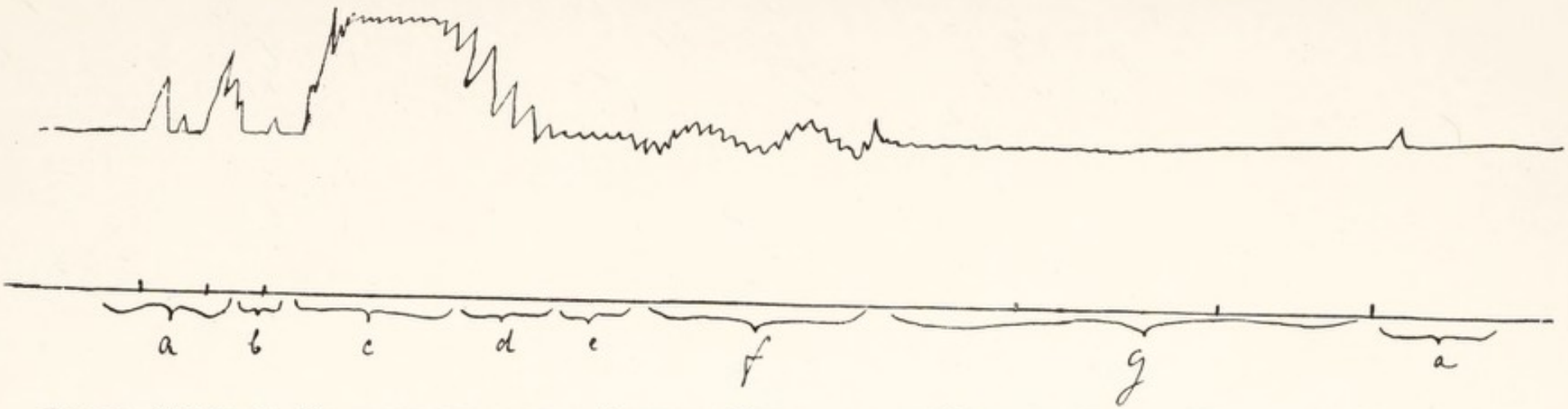


FIG. 11.—SCHEMATIC REPRESENTATION OF THE DIFFERENT PERIODS OF THE MYOCLONIC EPILEPTIC FIT IN THE CAT PREPARED THROUGH THE MEDIUM OF A SLOWLY REVOLVING CYLINDER.

The topmost line is recorded by a tambour attached to the back. Tactile or acoustic stimuli.

(*a*) Stadium incrementi of the reflex irritability.*

(*b*) Phase of lability of the irritability.

(*c*) Spontaneous so-called tonic fit, which consists of rapidly succeeding (10 to 12 per second) complete convulsions (extension is predominant).

(*d*) Very severe convulsions, in which all parts of the body participate simultaneously. These convulsions occur at gradually lengthening periods.

(*e*) Rest, only deep breathing visible.

(*f*) Automatic jumping, running, seeking, plucking movements.

(*g*) Complete rest in a condition of stupor in which tactile and acoustic stimuli (designated in the bottom line) remain uneffectual.

(*a*) Stadium incrementi of the reflex-irritability, first induced myoclonic reflex.

* First comes, after a tactile or acoustic stimulus, a reflex convulsion ; then follows a small spontaneous shock ; next comes a reflexly elicited convulsion, followed by a short lasting after-discharge.

(*d*) From simple observation it would seem as if a tonic condition were followed by clonic convulsions. This impression is, at least in the present instance, only apparent, for the fact is that at the beginning of a fit the severe motor convulsions follow one another so rapidly that they seem to fuse, and so form a tonic phase. It is only later on that the separate convulsions can be appreciated by simple observation. These convulsions involve the whole body simultaneously, and occur at increasing intervals, as has already been described.

(*e*) The fourth stage is a stage of rest, in which the tracing clearly shows rapid breathing.

(*f*) The fifth stage is usually one of automatic movements, and has a characteristic form in different animals. In cats crude jumping movements predominate and are often accompanied by signs of fear. Sometimes the animal is aggressive, even maniacal. The animal evidently suffers from hallucinations.

(*g*) Finally comes the sixth stage, which is a long period of immunity to reflex (and *a fortiori* to spontaneous) shocks.

Where the degree of intoxication has been moderate, it is not infrequently found that a normal condition of the pupils and of the appetite is quickly re-established. Generally, however, there is a phase of increased reflex excitability before the normal level is regained.

If the intoxication be more severe, the reflex irritability gradually increases (*b*) until spontaneous shocks appear, and another fit with all the attendant phenomena supervenes.*

Before proceeding to a closer study of those periods and the factors which influence them, we must point out two facts which place the bromide of camphor fits on a very high level of comparability, if they do not actually prove their identity, with severe epileptic motor fits (myoclonic variety) in man.

One of these is the change in the consciousness of the experimental animals, in which the temporary derangements must be distinguished from the permanent. Immediately after a fit is a period of rest associated with deep breathing; this is always associated with a temporary eclipse of consciousness. This temporary eclipse or loss of consciousness may be conceived of as an acute exacerbation of the dazed condition found to a greater or lesser extent in all animals drugged with bromide of camphor. Lawson describes this very characteristically when he says that after the fits one can "double up," lay, and move the cats as one wishes,

* Franck and Pitres, *Arch. de Phys.*, 1882, p. 111. Their description includes in the general fit, provoked by cortex stimulation, the tonic stage with the tetanus produced by the stimulation. Otherwise the process is identical. They note that during inspiration the series of shocks are greater, just as cold shivers are more pronounced during inspiration.

without evoking any retaliatory movement on the part of the animal.

Further, we observed that those animals who had a large number of fits over a long period, generally become more or less silly, or, as the attendants in the animal house express it, troublesome and quarrelsome animals become tame and good tempered.

This is a permanent change, probably comparable with the varying degrees of dementia associated with frequent and severe fits in man. A further result of frequent or repeated intoxication of an animal is that the sensitiveness to the drug is frequently increased: doses at first ineffective may become active.

FIG. 12.—JACKSONIAN CONVULSION OF THE LEFT FACIAL MUSCLES. CAT 79.

This fact is in accordance with the well-known clinical fact that each fit makes the individual more likely to have another fit.

It must, however, be remembered that it is not infrequent to find animals who do not show any increased sensitiveness, but require the dose of the drug to be increased* (compare Cat 160, August-October, 1908, p. 21).

These two processes—the raising of the threshold as a result of repeated dosing with epileptogenous drugs, or the lowering of the threshold due to the animal becoming habituated to the drugs

* As a rule an interval of two or three weeks took place between the different experiments on the same animal.

—are recorded by other experimenters. Sauerbruch, for example, found that after repeated doses of pilocarpine, smaller doses were needed to induce fits. Macleod* recorded the fact that rabbits dosed with insulin react less and less with convulsions.

We find, therefore, in the details of the myoclonic reflex phenomena produced experimentally in cats—carefully observed and graphically recorded—arguments for establishing a parallel between these phenomena and myoclonic epileptic fits in man.

Very important evidence, sufficient to complete the chain of argument, is supplied by two cats, Nos. 78 and 79. These animals suffered spontaneously from epileptic symptoms—in fact, from complete epileptic fits. In one cat the fits were seen during the transition from the waking to the sleeping state. After a minimal dose of bromide of camphor ($\frac{1}{3}$ of a gramme) the animal died in a state of status epilepticus. This sequence of events was never seen in any other animal. In the other animal, besides a general exaggerated reflex irritability, Jacksonian convulsions of the left side of the body, particularly of the facial muscles, were observed for a whole year (Fig. 12). During the year the left side of the body was far more liable to myoclonic reflexes than the right. Under hygienic conditions this hemi-epilepsy disappeared, but the animal continued in an irritable condition and required only a very small dose of bromide of camphor to display all the earlier epileptic symptoms. The microscopic examination (von Giesen method) of a complete series of sections of the brain showed inflammatory changes in both hemispheres. Cyst formation had also occurred, while the veins were distended. The changes were more marked on the right side, and affected the motor zone.

* J. J. Macleod, *Physiol. Review*, vol. iv., 1924, p. 3.

CHAPTER III

MECHANISM OF THE DISCHARGES

§ 1. On the Conception of Discharge, "After-Discharge" (Sherrington's School), and on Compensation.

In this treatise the term "Discharge" is often used. This is a term which has not yet made its appearance in physiological literature, while in clinical literature it was used for the first time by Schroeder van der Kolk. Later it has been used a great deal by J. Hughlings Jackson. The latter observed that in local affections of the motor cortex partial epileptic fits occurred at certain times. After the fit he regarded the individual as "discharged," because experience showed that immediately after a fit of this kind certain patients are practically sure not to have another fit.

It seems to me that the sense in which we use this term is deeper and more in accordance with Boerhaave's idea. Boerhaave, in his aphorisms, says that the "materia peccans" is rendered innocuous by the epileptic fit. In this way he explains why, after a fit, the epileptic patient feels relieved for several days of both physical and psychical ailments.

In man such an improvement is not usually seen until several hours have elapsed after the fit: the period immediately after the fit is one of exhaustion.

In cats, on the other hand, the recovery is usually rapid and involves more obvious details associated with recovery, such as the dilatation of the pupil and the gloss and smoothness of the fur. This rapid recovery is particularly well shown in cats, where one severe epileptic fit definitely discharges the animal. Sometimes, within a few minutes after being manifestly very unwell, the cat will purr and eat.

In animals who react to one dose of bromide of camphor by several fits, separated by a free interval of half an hour or longer, the same improvement of the general condition may be seen between each fit.

In those rare cats who react to the monobromide of camphor by having fits separated by intervals in which the animal is "discharged" (Protocol 12), the process of events is very similar to that seen in the human patient. In most cases, however, improvement is arrived at only after a short period of maximum

intoxication. So far as one can judge from the temporary maximum dilatation of the pupils psychical symptoms and hallucinations occur in the automatic phase. After the fit there is a period of exhaustion.

Protocol 12. Cat 180 G. Small grey animal.

31.4.09. 0·5 gramme bromide of camphor given after breakfast. No effect.

13.4.09. 10.30 a.m., 0·5 gramme bromide of camphor before breakfast.

14.4.09. Judging from the condition of the sawdust in the kennel, the animal had fits in the night. Next day, however, it was well, and ate and drank normally. It seemed somewhat timid.

18.4.09. Five-eighths gramme camphor bromide given after breakfast. No effect.

26.4.09. Three-quarter gramme bromide of camphor given before breakfast. Shortly after this dose it displayed tactile reflexes, which became greater after the animal had vomited. There were no acoustic shocks, but it was noticed that a loud noise intensified the tendency to spontaneous shocks. Later, series of spontaneous shocks followed each other. After this series came a period in which tactile stimuli did not provoke reflexes.

7.5.09. One gramme bromide of camphor given, with no effect.

13.5.09. The dura was exposed over the left hemisphere and a piece of sterile artery wall, taken from a calf, was inserted under the dura. The wound was carefully closed. During the end of the operation, while the animal was still under the anæsthetic, the right pupil was large and directed downwards, the left was small and directed upwards. On regaining consciousness, the condition and direction of the pupils were reversed.

17.5.09. Animal was quite well.

16.6.09. 5.30, 1⅛ grammes bromide of camphor given after food. No effect.

29.9.09. One gramme bromide of camphor given at 6 p.m.

30.9.09. Had a fit during the night, and again on the morning of the next day. Immediately before the second fit, which occurred at 10.30 a.m., an acoustic shock was seen and recorded. Up to the afternoon of the same day, tactile shocks were quite absent, while tactile reflexes were very slight. In the afternoon the pupils were again dilated, and acoustic shocks were evoked by both tick and clap stimuli. Later in the day, fits supervened, but these acoustic shocks persisted after the fits. In these fits it was noticed that contraction of the left forepaw occurred before the right forepaw.

The animal died during the next night, possibly in status epilepticus.

At the autopsy no trace could be found of the piece of artery wall which had been introduced under the dura. It was with the greatest difficulty that the exact site of the incision could be identified.

Epitome.—As the supposition that a capsule of bromide of camphor took sixteen hours to dissolve can be at once dismissed, the only explanation of this experiment is that the animal was peculiarly resistant to the drug. Each time the fits produced a condition of discharge which lasted several hours. Finally a third wave of intoxication gained the supremacy, and the animal's resistance was completely broken down.

Such cases resemble the condition seen in human myoclonic epilepsy, where days, even weeks, of complete well-being pass before the new minor symptoms (spontaneous shocks) present themselves.

Toxicologists have observed in intoxications (strychnine

arsenic, morphine) that very marked remissions occur, the last attack ending fatally.

We must here lay stress upon the fact that is by no means exclusively through epileptic motor fits that the so-called epileptic charge becomes "discharged." On the contrary, in the lighter forms of intoxication with bromide of camphor, the symptoms of intoxication, such as dilated pupils and dazedness, may sometimes be seen to disappear under the influence of separate spontaneous shocks or series of shocks. Indeed, I saw some animals become discharged as a result of inducing a great number of myoclonic reflex shocks. In such cases a real fit is not developed at all.

In the case of one animal (see Epitome, p. 93) a convulsive seizure due to strychnine, acted as the discharging agent. Cases such as these are referred to in the experimental protocols as follows:

"After a series of reflexes had been induced, the animal is completely refractory to shock, or seems apparently quite well again, eats and purrs." Here, I take it, we have to deal with a fundamental characteristic of the nervous centres, whose function it is to dominate the occurrence of normal and chemically reinforced myoclonic reflexes.

These same nerve centres are called into action in the case of myoclonic epileptic fits. This characteristic is related to, if it is not identical with, the refractory phase which follows upon every reflex action. If, in the latter case, the absence of reaction is due to temporary exhaustion of the mechanism, there is reason to believe in the other case—that of definite discharge—that the mechanism is totally exhausted.

We know little or nothing about the chemical mechanism that lies at the bottom of these discharges.

L. Hill* noted that after anæmic fits the circulation in the brain was restored.

Wiedemann† maintains that camphor fits lead either to death or the animal recuperates. In the latter case the drug is broken up into N-free campho-glycurol acid and uramido-campho-glycuronic acid, both of which are innocuous.

Clinically, analogous symptoms are seen. It is of very frequent occurrence, indeed, it is almost a characteristic of myoclonic epilepsy, that the patients should experience myoclonic shocks, either singly or in a series, when rising in the morning. This period of the day is the period in which shocks are most likely to trouble the patient.

After this shock, or series of shocks, a condition of discharge supervenes, and the patient may have no more trouble until next morning. Next morning the shock, or series of shocks, may be more violent, until one morning the patient has a severe fit. After this severe fit, the patient may be discharged for days, or even weeks, and have no myoclonic manifestation whatsoever.

* L. Hill, *Phil. Trans.*, 1900, vol. cxciii., p. 106.

† Wiedemann, *Handbuch der Artzneimittellehre*, 1884, p. 512.

With the use of the term " discharge," the term " compensation " is closely connected. From the clinical studies on epilepsy the related term of equivalents is well known. By it the classical authors wish to indicate that, in certain persons who are subject at regular intervals to epileptic fits, psychical discharges, such as paroxysms of rage accompanied by vehement muscular movements, really substitute a fit. In other words, they compensate for a fit. According to the views expressed in this work, such substitution or compensation would be easily understood.

From my experiments there is reason to believe that, toxicologically speaking, greater expansion may be given to the term " compensation " both in experiments and in clinical observations.

In our experiments on the cat we repeatedly observed that after a certain dose of bromide of camphor an epileptic fit occurred. If, however, before a fit occurred a great number of reflexes were arbitrarily elicited, these reflexes might act as the " discharge," and a true fit did not develop.

The completeness of the discharge was shown by the disappearance of the secondary symptoms of intoxication, such as dilated pupils, hallucinations, and the ungroomed appearance of the fur. Here the reflex shocks act as the paroxysm of rage, and compensate for a fit.

In the clinic one observes that a large number of spontaneous myoclonic shocks may act as a discharge in a patient, and the epileptic fit, which was due, does not occur. In the chronic auto-intoxication process which many neurologists consider myoclonic epilepsy in man (and often rightly), another form of compensation is seen. An ever-recurring history given by patients while being examined is as follows:

Regular headaches, localised above the eyes, lasting for hours. These headaches do not yield to drugs, but are relieved by a short sleep. They frequently occur in adolescent patients. At a given moment, sometimes after years, myoclonic convulsions appear, first in the morning, later during the night, and eventually during the day. As this stage develops, the headaches recede into the background. In the third, or final stage, epileptic fits appear, the headaches disappear, and the daily shocks are limited to those heralding in a fit.

Here, in the development of this disorder, is a two-fold manifestation of the phenomenon of compensation. Shocks replace the headaches and prevent them, then the big fit compensates for the shocks as well as the headaches.

At this borderland of physiology and physio-pathology, it behoves us to remember the original and very attractive description given by Sherrington of the reflex after-discharge, which led to the conception of the myoclonic epileptic symptoms as a complicated *after-discharge*. This word was first introduced by Sherrington to characterise the protracted reflex movements which occur in the spinal animal after a very strong reflex stimulus. There can be no objection to this purely descriptive term as used here.

Further, Graham Brown considered that the so-called epileptic convulsions in guinea-pigs (the epileptic nature of which has been questioned in an earlier part of this book) as being nothing but a special reflex after-discharge of the "scratch reflex." Independently of this, the myoclonic fits of carnivorous animals, which occur under the influence of bromide of camphor and absinthe (considered as a true epileptic manifestation), were recognised or conceived of by me as complicated epileptic after-discharges.

Graham Brown* now goes so far as to speak of after-discharges, wherever epileptic fits present themselves after a local irritation of the motor cortex, either of the grey or white matter. This is quite a new application of the term, and seems not to be sufficiently justified. Up to the present time, "after-discharge" is a term applied to a reflex after-discharge, and in this sense is a useful physiological term. If, however, this term should be applied to every cortical discharge, one departs from the correct standpoint that at least a real reflex action must precede it. Certainly no one at present regards cortical movements as reflex in character. Further, there arises the danger of confusion. We have, like our predecessors, to distinguish carefully between cortical and subcortical discharges.

Later in this work the role of this subcortical centre will be discussed.

In this matter great circumspection is needed, for the mechanism of a simple reflex with its centre and tracts is almost unknown to us.

In the second part of this work (dealing with the influence of lesions of the central nervous system on myoclonic reflexes and myoclonic fits) we hope to present to the reader some more exact information about the centres and tracts involved in the reflexes to which our attention is especially directed.

We have repeatedly expressed the opinion, in the course of this work, that myoclonic reflexes slowly merge into myoclonic epileptic manifestations. Not only have we repeatedly laid stress upon the comparability of the myoclonic reflexes with the fits (p. 44) and the refractory phase after the reflex with the state of discharge after the epileptic fit, but we also pointed out that the myoclonic fit could hardly be anything but a specially organised reflex after-discharge. This presupposes the adoption of at least a partial identity of the centres whose co-operation is necessary for the occurrence of myoclonic reflexes, and of myoclonic fits. In this way data about the centres and tracts dealing with the fit, will throw some light upon the tracts and centres

* Graham Brown, *Quarterly Journal of Physiology*, vol. ix., 1915, p. 44 *et seq.*

whose function is involved in the simple, normal, myoclonic reflexes.

As the study of reflexes proved to be the way to learn the real biological significance of epileptic fits, so the study of the influence of cerebral lesions upon the fits may throw light upon the centres and tracts which influence the normal reflex.

§ 2. The Myoclonic Epileptic Fit conceived of as the Central After-Discharge (Sherrington) of a Myoclonic Reflex.

We owe to Sherrington the proof that many reflex movements associated with a certain intensity of stimulus are followed by a protracted effect consisting of a number of similar rhythmic movements. In some of them, as for instance the "scratch-reflex," attention was attracted to the "slight lengthening of the duration and sequence of the terminal beats." This phenomenon is very striking in the spinal animal—*i.e.*, where cerebral inhibition of the spinal reflexes has been removed.

From a consideration of the foregoing chapters, it is not difficult to recognise in the myoclonic fit a central reflex after-discharge. In the first place it has been shown that with larger doses of the drug, where the reflex irritability is intensified, a single acoustic or tactile stimulus is followed by a series of shocks. Later on these shocks are followed by a myoclonic fit. In this fit it is seen that the succession of rhythmic convulsions are at first very rapid but gradually slow down so that the terminal beats stand out separately. Hence it would seem that the tonic cramp is caused by a rapid succession of beats—so rapid that they seem to merge. Later on the separate beats, or convulsions, become apparent as the "terminal beats."

Further, the rhythm of the reflex movements observed by Sherrington in the decerebrated dog, and the rhythm just described in the cat, are of the same order. Sherrington finds a rhythm of 7·5 to 12 per second for a flexor reflex. The rhythm of the myoclonic fit was found by me to be approximately the same (Fig. 10, p. 39). Further, Sherrington finds that the reflexes show relatively greater resistance to a single stimulus. This resistance is, however, easily overcome if stimuli be applied rapidly at intervals of less than 1·5 seconds (*loc. cit.*, p. 30). The same phenomenon is seen in cats with exaggerated myoclonic reflexes, but a fit may follow a series of tactile stimuli applied at a rapid rate. It must, however, be remembered that in the cat the rate of stimuli has no influence on the rhythm of the discharges. However rapidly the stimuli are applied, the result, should a fit supervene, is always of the same type.

Schaefer (Textbook 2, 1902, p. 710) found very rapid faradic stimulation transmuted into a stimulus applied at the rate of from 8 to 10 per second. This transmutation, according to Sherrington, takes place in the grey matter. Sherrington has estimated the refractory period for an afferent sensory nerve as 0·01 second. (Baglioni estimates this as a longer period.)

Another point is that the intensity of the stimulus did not, in my experiments, appear to influence the character of the fit or central after-discharge. In the same way Sherrington found that the intensity of the stimulus did not affect the after-discharge

Here one is reminded forcibly of the " all or nothing " law for nerve and muscle fibre (Lucas, Pratt and Eisenberger*). The question naturally arises whether a similar law holds good for the particular form of after-discharge described here as the myoclonic epileptic fit.

* Pratt and Eisenberger, *American Journal of Physiology*, 1919, vol. xlix., p. 1; and G. Kato, *Further Studies on Decrementless Conduction*, Tokyo, 1926.

CHAPTER IV

FURTHER INVESTIGATION OF MYOCLONIC REFLEXES AND OF REFLEXES RELATED TO THIS CLASS OF REFLEX

1. Latency of the Myoclonic Reflexes and the Rapidity of Nerve Conduction.

It is first necessary to recall certain facts found in the literature concerning the latent period of the muscle itself after electrical or mechanical stimulus, and under the influence of cortical and reflex stimulation. It is first of all important to know the latent period of normal muscle, because in measuring reflex action this must be taken into account. Helmholtz described the latency of muscle as the time which elapses between the impact of the stimulus on the muscle and the contraction. The duration of this period has been the subject of much investigation—more especially in cold-blooded animals. Place,* Marey, Volkmann, are three names amongst the many who have studied the subject. Most workers agree that the latency of normal muscle in man is about 10 milli-seconds.

Later the subject was worked on by Paukul† and Fischer,‡ and they agreed in finding the interval between electrical stimulation of the sciatic nerve and the muscular contraction 10 milli-seconds. Piéron published the result of investigations on the same subject in 1917, but he found the interval between stimulation and contraction 8 milli-seconds. In later years, the influence of such drugs as strychnine and absinthe on the latent period of muscle have been investigated. It also seems probable that an inflammatory condition of the cortex exercises a distinct influence on the duration of the latency of muscle. In all such cases the irritability of the muscle was found exaggerated, while the latency was shortened (refer work of Fr. Franck and A. Pitres§). *Ceteris paribus*, the latency is increased in length if the electric stimuli are weakened, if fatigue supervenes under the influence of cold (Richet), and after the administration of certain drugs.

Mendelsohn‖ found the effect of fatigue demonstrated when

* Place, *Nederlandsch Archiv voor Natuur. en Geneeskunde*, 1867.
† Paukul, *Archiv. f. Anat. u. Physiol.*, 1904, p. 100.
‡ H. Fischer, *Pflüger's Archiv.*, vol. cxxvi., 1908, p. 351.
§ Fr. Franck and A. Pitres, *Travaux du Laboratoire de Marey*, 1878, p. 413.
‖ Mendelsohn, *Travaux du Laboratoire de Marey*, 1880, p. 150.

stimuli were applied at the rate of 40 per minute. The latency in this case was increased from 8 to 21 milli-seconds in eighteen minutes.

The latent period is also found to be lengthened after certain pathological changes, as in long-standing hemiplegia, disseminated sclerosis, Parkinson's disease, and after degenerative changes in the muscles.

Various theories are offered as an explanation of the latent period.* It is said to be due to the inertia of the neuro-muscular system, also it is explained as a phenomenon dependent on the elasticity of muscle. Tigerstedt explained the latent period as the time required for the diffusion of the stimulus, while von Regeczy considered it to be the time needed for the diffusion of the contraction wave. Bernstein and Yeo explained it as the time required for certain molecular changes necessary for contraction. The theories propounded by Engelmann and Ranvier on the essential characteristic of muscular contraction tend to make this latter explanation acceptable. According to Engelmann and Ranvier, muscular contraction is associated with a change in the water content of the isotropic and anisotropic layers.

The other three factors, which, together with the latency of the muscle itself, comprise the entire latent period, have been less the matter for study. These factors are the rate of conduction, or the time occupied by conduction of the stimulus along the centripetal and centrifugal parts of the arc, and the time required for the transition of the stimulus across the synapse. Franck and Pîtres, and A. Waller,† investigated this part of the problem. Franck and Pîtres examined the difference in the latency when the cortex was stimulated so that the paws on opposite sides of the body were convulsed, and measured the difference in time of reaction of the front and hind paws. The retardation was found to vary, and is not easy to explain. Franck and Pîtres also analysed the latency found when the grey matter of the cortex was stimulated as follows: for the latency of the muscle, 10 milli-seconds; for the conduction through the motor nerve to the forepaw, 10 milli-seconds; latency of the grey matter, 45 milli-seconds. Further, they found that the latency, when the white matter underlying the motor cortex was not less than 20 milli-seconds, shorter than that following stimulation of the motor cortex. A. Waller and Miss Buchanan investigated the effect of strychnine poisoning on the latent period. They concluded that the lengthening of the latent period was due to the delay in

* G. Guerini, *Arch. italiennes de Brodogie.* 45, vol. ii., p. 72, 1888.
† A. Waller, *Quart. Jour. Exper. Physiol.*, vol. i., 1908.

the transition of an impulse from the centripetal to the centrifugal arc (synapse). For the centrifugal factor, Franck and Pîtres ascertained that after a short stimulation the hindpaw jerks were 45 milli-seconds after those of the forepaw. They estimated the length of the spinal cord as 20 centimetres, and calculated the rate of conduction in the cord as 4·5 metres per second. It is interesting to find that Novi and Grandis* found quite contrary results, for, according to them, the latency of the forepaw is greater. As I have not worked at the question I can do no more than give those two results without any attempt at explaining or discussing the findings. It must, however, be pointed out that the constant results got in measuring the latent periods of the myoclonic reflexes of the fore and hindpaws in the cat tend to support the figures given by Franck and Pîtres.

Helmholtz, Place, Donders, and others, have supplied data regarding the latent period which exists after stimulation of the peripheral nerves at different points. With the data available, it is possible to ascertain the rate of conduction in a nerve. Piper,† one of the latest workers at the subject, has been able to adapt the electrograph for purposes of accurate measurement. The conclusion he arrived at was that the latent period of the nerve terminals or end-organs, and of the muscle itself (that is, the electric changes which precede muscular contraction), amounts to 3·5 milli-seconds in the flexors of the under-arm in man. He calculated the rate of conduction of the motor nerve at 117 metres per second, Forbes and Gregg at 120 metres.‡ Helmholtz, on the other hand, estimated the rate of conduction in a motor nerve at 60 metres per second, while for a reflex—*i.e.*, the transition from the centripetal to the centrifugal elements—the rate was 9 metres per second. Helmholtz also endeavoured to measure the rate of conduction in a sensory nerve by stimulation of such areas as the foot or the neck. Here, however, the psychical factors offered such difficulties that reliable data could not be got. The question now suggests itself whether the myoclonic reflexes, which are apparently outside the psychic influence, might not offer a better field for such an investigation ? Such data as exist on the question of the rate of conduction in the sensory nerves are supplied by Munnich and Schaffer.§ Munnich calculated the rate of conduction as 66 metres per second, while Schaffer gave it as 59 metres. For the motor nerves, Schaffer gave the rate of conduction at 54 metres per second, just slightly

* Novi and Grandis, *Arch. Ital. de Biologie*, 1888.

† Piper, *Pflüger's Archiv*, vol cxxiv., p. 592.

‡ Forbes and Gregg, *American Journal of Physiology*, 1915, vol. xxxvii., p. 120.

§ Schaffer, *Berliner klin. Wochenschrift*, 1921, vol. i., p. 380.

slower. In some of my experimental animals graphic records have been made which would serve as material for a calculation of the centripetal and centrifugal rates of conduction, but the rate of conduction in the spinal cord and in the peripheral nerves could only be estimated approximately. Another objection would be that these experimental animals were under the influence of some drug which lowers the temperature. Forbes and Gregg estimated the rate of conduction in cooled parts at 30 metres per second. Therefore such calculations, even if carried out, would not be helpful for the normal animal. It must, however, be remembered that animals are occasionally found who demonstrate myoclonic reflexes without the administration of drugs, or after the administration of very small doses of the drug. Such animals would be suitable subjects for basing calculations upon.

It is certain that the reflex time in the animal I selected for making the calculation on did not differ materially from that found in other animals normally subject to myoclonic reflexes.

Cat 201, 3.2.1910, had a small dose of monobromide of camphor. Acoustic and tactile stimuli were used, and the average reflex time established. The stimuli, acoustic to the tympanum, and tactile to the back and tail, impinged on the animal at approximately equal distances apart (3 d.m.).

	Reflex Time in Fiftieths of a Second.	
	Head Movement after Stimulus.	*Back Movement after Stimulus.*
Acoustic-Clap	1·7	2·2
Tactile to back	2·5	2·6
Tactile to tail	3·1	3·3

From this one may estimate that the time necessary for the stimulus applied to the tail to reach the medulla amounts to 1·4 if the head movement, and 1·1 if the back movement, is taken into account.

Further, it would appear that the transmission of conduction through the spinal cord was slower in the oral than in the caudal regions. From a simple calculation it is seen that centripetal conduction in this animal is at the rate of 24 metres per second. In the spinal cord the rate of conduction is slower than this, while in the peripheral nerves it is greater, perhaps double.

For the rate of conduction in the centrifugal direction, only a rough calculation can be made, based on the difference in time between the movements of the head and back. It amounts to approximately 25 metres per second.

In the case of another animal, E. 175, which had received $\frac{7}{8}$ gramme monobromide of camphor and whose reflexes were also

examined, the centripetal conduction was found to be at the rate of 25 metres per second, for the centrifugal 60 metres. However, until there is further information about difference in rate of conduction in the spinal cord and peripheral nerves, it is obvious that little real value attaches to these calculations.

§ 2. Pflüger's Law. Stability of the Latent Period under Different Circumstances.

It has been shown that in most animals (cats) at the period of intoxication with a drug, when the reinforced myoclonic reflexes are elicited by tactile stimuli applied to any of the four extremities, acoustic myoclonic reflexes also appear, but second to tactile in order of appearance. In some animals, however, the acoustic and tactile reflexes appear at the same time. At this stage of intoxication, the slightest touch on the fur, particularly if the fur be stroked the wrong way, is sufficient to produce a myoclonic reflex. In order to avoid confusing a graphic record of such a reflex, the tactile stimulus provoking it must be of the slightest. Should, however, an error arise, it is comparatively easy to correct the record, for the signal of the stimulus is recorded 4 to 8 milliseconds after the stimulus (rate of conduction in rubber tube). As a rule, tracings prepared from animals in the early stages of intoxication show that the part of the animal which was touched makes the first convulsive reflex movement. This is in accordance with Pflüger's law. It must, however, be appreciated that the difference in movement of the different parts of the body is very small, and, further, the rule is not invariable. Where a tactile stimulus is applied to the head, the movement of the head and neck precedes that of the back as a general rule; but if the stimulus be applied to the back, the movements of the back may or may not precede that of the head. For acoustic reflexes the head movement was always found to precede that of the back, except in one case. In one normal cat (E. 175), the movement of the back following on an acoustic stimulus preceded that of the head by 18 milliseconds on the tracing. In normal cats and in animals which have had but a small dose of the drug, the movement is often limited to the head and neck. The tracing given by the head movement after acoustic stimuli is often anacrotic in character. A slight and slow elevation precedes the true head movement. At first this initial movement seems difficult to understand, but it seems possible that it may be due to the extensors of the neck preceding the head flexors. In view of Pieron's work on the knee reflex, it seems probable that this initial rise

indicates the beginning of the myoclonic reflex as distinguished from the slightly later myotonic contraction.

If the latent period for reinforced myoclonic movements (after the administration of monobromide of camphor) be compared with the latent period shown by animals who demonstrate normally tactile and acoustic reflexes capable of being recorded graphically, no important discrepancy is found. In this observation there is evidence of complete agreement with the stability shown by the knee reflex under varying conditions. It is true as a result of the researches of Broca and Richet, no doubt can be entertained upon the effect of a fall of temperature of 10° on the latent period of a reflex convulsion. With so marked a fall in temperature, the latent period would, in all probability, be doubled. Nevertheless, at the present time there is no justification for regarding the fall in temperature as the primary effect of monobromide of camphor and the development of fits as the secondary. In comparing the acoustic with the tactile reflexes, it is evident that the acoustic reflexes show far more modifications or variations than the tactile, and are much more sensitive.

Under ether anæsthesia, the latent period for the acoustic reflexes may be greatly lengthened, while other changes are often seen. In the course of anæsthesia, the acoustic reflexes disappear much earlier than the tactile, and also return far later than the tactile on the cessation of anæsthesia. Another important difference is that the latent period of the acoustic reflex, unlike that of the tactile reflex, is apparently influenced by the strength of the stimulus. Both in the animals who show the reflexes normally, and in those who require the administration of monobromide of camphor, the latent period of the acoustic reflexes is distinctly longer after a strong than after a weak stimulus. In the case of Cat 201, this difference of latency after a strong or weak stimulus amounted to $\frac{1}{1000}$ second. In Cat 205, on the day following the injection of $\frac{3}{4}$ gramme monobromide of camphor, the latent periods shown by the acoustic reflex were as follows: After a slight noise 1·6, after a moderate noise 2·5, after a loud clap 2·1, calculated in fiftieths of a second. In Cat 178, the latency shown after different degrees of acoustic stimuli were as follows (also given in fiftieths of a second): Soft clap, 1·9 and 1·8; after a loud clap, 2·6 and 2·6; after a very loud clap, 2·1. Although this paradoxical result has been got in a number of animals, yet it would seem advisable to reserve a final conclusion on the matter. This suggestion is made in view of the fact that in a number of other reflexes it is definitely proved that the latency decreases with the increase of the stimulus. It seems desirable that the myoclonic reflexes should be re-examined by other methods than those I

have used, so as to exclude certain possible sources of error unavoidable with my apparatus. Certain facts may come into play with acoustic stimuli. For example, with a cat a comparatively slight acoustic stimulus may have a short latent period, because it is the type of acoustic stimulus to which the cat is physiologically extremely sensitive. On the other hand, a loud sound may be followed by a long latent period, because some warning of the stimulus has been conveyed to the animal who is therefore on guard. Further, the acoustic stimuli applied in the experiments under consideration are so arranged that a record is made by the lever at the moment of production. It is conceivable that the sharp blow of metal on metal, which produces the stimulus, may cause an instantaneous rebound which vitiates the exact recording of the stimulus by the lever. Both the drum and the rod used in the acoustic experiments were covered with staniol-paper to avoid this vitiating circumstance. Physiologically this paradoxical condition finds a parallel in the Wedensky effect, which has played an important role in the recent studies on the propagation of stimuli in the nerve-fibre. Lucas, Adrian and Forbes have shown that a stimulation of higher frequency under certain conditions must necessarily be inhibited.

The stability of the latent period of the myoclonic reflexes is a prominent feature of the phenomena; it is, therefore, peculiarly surprising to find this latency prolonged where an acoustic reflex is provoked immediately after or within a few seconds after a spontaneous shock. This was seen in the case of Cat *217a*. In this animal the acoustic reflexes were very strong; tracings taken from the head and back showed a latent period of 50 to 54. Immediately after a spontaneous shock this latent period became 80. Further, the movement seen on the tracing was slow and slight in extent. Here is undoubtedly a refractory period not completely expired, at least so far as the motor result is concerned (refer " final common path " of Sherrington).

The form of the myoclonic reflex curve, as recorded graphically, show the same characteristics as the beautiful reflex tracings prepared by Sherrington. In both cases a perfect sharp curve is recorded on the tracing.

It was also found that cross section of the posterior nerve roots had a distinct influence on the tracing supplied by the limbs after stimulation of the cortex.

Fig. 13 shows the effect of section of the posterior lumbar nerve roots for the left hindleg of a cat. Stimulation of the motor cortex for the movement of the hind limbs showed that the tracing from the left hindleg was much sharper than that of the right, where the posterior lumbar nerve roots were intact.

§ 3. Tactile and Acoustic Reflex-Irritability.

As was described in Chapter I., the first symptom of bromide of camphor poisoning of the central nervous system seems to be exaggerated irritability of the animal to myoclonic reflexes, especially if the stimulus, whether tactile or acoustic, be applied suddenly. In the incipient stage only powerful tactile stimuli are effectual, whereas later on weaker stimuli suffice. The strength and extent of the convulsive movement following upon the stimulus serve as a gauge for this irritability. In the incipient or early stage this convulsion remains local, but later on it involves the entire musculature. At first this hyper-irritability is noticeable only on certain parts of the body, especially the rump and the skull, and only with strong stimuli. As the intoxication increases, the local regional convulsions spread over the whole

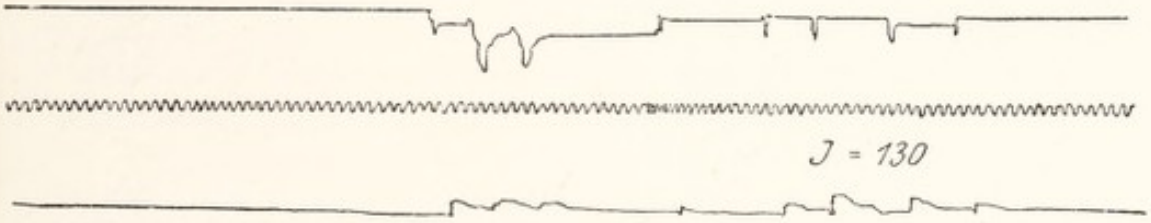


FIG. 13.—CAT 88. FARADIC STIMULATION OF THE MOTOR CORTEX AFTER INCISION OF THE LEFT CRUS CEREBRI.

While stimulation of the left cortex had no effect, a result followed stimulation of the right cortex $i = 130$. The left hindfoot supplied the upper tracing, the right the lower. The difference in the character of the tracing is ascribed to the section of the posterior lumbar nerve roots on the left side.

back, forepaws, hindpaws, belly, tail, and finally includes the whole body.

So far as my observations go, the spread of these convulsions is not quite in accordance with Pflüger's law, which maintains that the point of contact of the stimulus with the animal is the source from which the convulsions spread* (compare p. 57).

In more than one case a whole series of tracings have been obtained which show the increasing extent of a myoclonic convulsion.

Where the animal is but slightly under the influence of bromide of camphor, myoclonic reflex-movements are often provoked by sudden noises, more especially if the animal has been undisturbed for some little time previously. These movements are at first limited to the head, but as the effect of the drug increases, reflex-

* Nagel's *Handbuch der Physiologie*, 1905, vol. iv., chap. 8, p. 56, Langendorff's article, "Reflex." No preference of propagation from oral to caudal was observed as in the case of strychnine (McGrugan, Keeton and Sloan, *Journal of Pharmacology*, 1916, vol. viii., p. 150).

movements involve the back muscles. In the third stage of the intoxication spontaneous shocks appear. At first single shocks occur, to be followed later by a series of shocks. Fig. 10 (p. 39) and middle tracing of Fig. 22 (p. 81) illustrate this point.

Spontaneous myoclonic movements, recorded graphically, do not differ from those provoked reflexly. On the other hand, the series of shocks do differ, because in them the individual convulsions follow each other with a rapidity never seen in reflex-movements which have been provoked.

Whatever may be the direct cause of these spontaneous movements, whether due to an endogenous cause or not, it may be taken for granted that the refractory period of the nervous elements involved is at its minimum at the time of these phenomena. If this stage of spontaneous convulsions is well developed, one may see the first *fit* occur, generally after a short period of rest, but sometimes directly after a shock provoked reflexly (in which case it is suggestive of the rhythmic after-discharge, described by Sherrington in the decerebrate animal) or after a spontaneous single shock.

After the fit, which is composed of apparently tonic, but in reality clonic, contractions, follows a period of rest, in which rapid breathing is very noticeable, and is recorded on the moving drum. After this is the stage of automatic movement, such as jumping, etc., after which the animal reverts to its first condition, before the phenomenon began to develop (compare Fig. 11, p. 43).

In this phase, immediately after a fit and for some time to follow, reflexes cannot be induced, neither are there any spontaneous shocks. The animal seems somewhat dazed.

Gradually, and in the same sequence as just described, the various phenomena reappear, first the tactile, then the acoustic reflexes, then the spontaneous contractions, which, in turn, culminate in an epileptic fit.

The question arises, Is this the phenomenon observed in the majority of the experimental animals? Certain exceptions are found.

In some animals the phase of prodromal shocks is but slightly marked and may be of very short duration. There are also animals in which the usual absence of reflex-irritability after a fit is preceded by several spontaneous isolated shocks.

It seems appropriate to designate this period of quiescence which follows upon a fit, the period or condition of complete discharge. It must, however, be remembered that this condition of complete discharge is not always arrived at after one fit, but may only be induced after several fits.

In all the cats observed, the form or the phenomenon of charge

is the same. The pupils show maximum dilatation, the fur is dull and tangled, there is some change in the consciousness of the animal, while there is a general insensibility to pain. The mesial lines of the extremities and certain parts of the tips of the extremities remain sensitive.

Attention must be directed to those cats who display indifference to small or moderate doses of bromide of camphor. Such animals, when given a large dose such as 1 gramme of the drug, may display but a slight increase of reflex-irritability, but they may pass into status epilepticus and die. The reason for this is not known (compare Protocol 4, p. 25).

It is curious that in these animals the pre-mortal fits follow the usual rule and deviate in character from ordinary fits. The convulsions are very slight and the animals collapse without any stiffness of the extremities. Just before death the temperature goes down considerably.

Animals that have been weakened by disease or lack of nourishment also show the same lack of reflex-irritability and absence of spontaneous shocks.

The impression is received that these atypical fits sometimes closely resemble the forms of petit mal seen in human subjects.

In such cases almost all the symptoms of the big fit are absent, except for dilatation of the pupil, loss of consciousness, and flabbiness of the muscles. If, however, such cases be very carefully analysed, it is often possible to recognise the different phases, although in a very abbreviated form. The phase of exaggerated irritability, for example, may only last a few seconds, and is most likely overlooked altogether unless very careful observations be made.

As has already been indicated, if instead of bromide of camphor essence of absinthe is used to intensify the myoclonic reflexes, the symptoms or characteristics of the condition of charge remain the same. In the case of absinthe where it is injected subcutaneously, and especially if injected in a vein, the whole process runs its course rapidly, in a few minutes a fit occurs, whereas it lasts hours in the case of ingestion of bromide of camphor. It is of the greatest importance for our theoretical conception concerning experimental epilepsy to note that, under normal conditions—*i.e.*, without the administration of any drug—one animal in ten reacts to certain tactile stimuli, and frequently to acoustic stimuli with myoclonic reflexes. This fact, together with the well-known observation that some animals, such as puppies, are subject during sleep to myoclonic manifestations (without any known cause), prove, in my opinion, that the excitability brought about by bromide of camphor is but an

exacerbation of a condition found in healthy individuals under normal circumstances. A cat under observation who had an epileptic fit every two or three weeks died after a small dose of monobromide of camphor. This animal was subject to sudden complete myoclonic manifestations before falling asleep. These manifestations were so severe as to wake the animal completely and prevent its falling asleep for some time. Such a condition is frequently seen in patients suffering from myoclonic or regional epilepsy.* It is a phenomenon which is not at all uncommon among relatives of epileptics, although it might be termed a physiological phenomenon.

Amongst a large number of cats some animals are found which react, before any camphor has been given to them, with mild myoclonic shocks to sudden tactile and acoustic stimuli.

It is, however, more common to find animals who require a small dose of bromide of camphor administered once or twice before they react to tactile and acoustic stimuli with myoclonic reflexes, and develop for the time being a tendency to reflex convulsions.

This irritability may last for several months (no more of the drug being given) and generally disappears very gradually.

The latent period of these "normal" myoclonic convulsions tallies with that observed in animals drugged with bromide of camphor. In these normal animals, as in the drugged animal, the tactile shocks are elicited more easily than the acoustic. Where an animal is subject to acoustic reflex shocks, it also reacts regularly to tactile stimuli. The question arises, What is the relation between those rare animals who normally display a tendency to myoclonic reflexes and the majority of animals in which myoclonic irritability can only be brought about by the influence of drugs which produce convulsions?

In view of the fact that with a certain degree of intoxication all animals show myoclonic irritability, is it not conceivable that these reflexes, like those discovered later by Sherrington, Philipson, Graham Brown, and others, are inhibited under normal conditions by central and peripheral influences?

It is probable that this inhibition already present in wild animals is far more developed in tame or domesticated animals?

At this point it is interesting to recall the experiments of Setchenow,† who demonstrated that certain reflexes only became

* This form of epileptic discharge must be distinguished from the so-called Jacksonian focal or local convulsions, which depend upon stimulation of the motor cortex.

† Setchenow, *Pflüger's Archiv*, vol. xxvii., 1882, p. 534. After having exposed the cerebral spinal axis of a frog, Setchenow observed that after removal of those parts which are anterior to the cerebellum, electromotor

apparent after removal of the inhibiting influence of the frontal and mid-brain. It is well known that slight mechanical influences, such as vibration of the air, may influence the activity of the medulla oblongata. This would explain how stimuli, which are not observable to us under certain conditions of the central nervous system, may become active or appreciable at such a peculiar time as the transition from the waking to the sleeping state.

The other effects of bromide of camphor have not been the subject of special study, but it is seen that the pupils dilate at a very early stage along with development of the narcotic effect.

After the fit the pupils resume their normal size. If one fit discharges the animal, the pupils remain normal, but should fresh symptoms appear, indicative of an approaching fit, the pupils gradually dilate again. The close association between the size of the pupils and the epileptiform phenomena is shown in those not infrequent cases where the pupils dilate abruptly with each spontaneous shock and reassume their normal size immediately after the shock.

Further, I believe that I have been able to observe the gradual development of disturbances in the sensibility to pain in certain definite areas just before a fit. (Needless to say, such observations are extremely difficult, and have to be carried out with the greatest discrimination). In some few cases, I believe, I was able to recognise the return of this sensibility after the fit.

From observations made on many cases, there does not seem to be a close association between the psychical disturbances, the myoclonic discharges, or the disturbances in sensation. At the same time these three phenomena—physical dazedness, myoclonic discharges, and disturbances of sensation—may be regarded as prodromal symptoms of an epileptic fit or of the intoxication of the central nervous system.

From a general consideration of these facts, it is evident that in bromide of camphor we have a drug which, apart from other symptoms of intoxication, intensifies the myoclonic (tactile and acoustic) reflexes found normally in certain animals, without drugs.

Further, bromide of camphor in certain doses produces the phenomena of discharge as evidenced by shocks. These shocks are at first reflex, but later become spontaneous, and finally culminate in a regular epileptic fit.

Hand in hand with these phenomena goes the shortening of the refractory phase as described by Broca and Richet.

---

phenomena occur spontaneously and with a certain regularity. The galvanometer showed important diminution of these phenomena if peripheral nerves were stimulated.

After the fit is over, the refractory phase gradually assumes its normal condition, but if more fits follow the first the refractory phase undergoes repeated shortenings and recoveries. These facts seem to point to the fluency of the transition from physiological to physiological-pathological phenomena. They also illustrate how accurate are the laws relating to reflexes generally, both where these occur normally, and where they have been increased by drugs and have assumed a definite pathological character.

§ 4. **Further Research into the Bromide of Camphor Fits.**

There is now at our disposal a series of observations on a certain group of physiological reflexes which lead in an unbroken sequence up to pathological and especially to epileptiform symptoms. These observations also afford an opportunity for a better understanding of the myoclonic type of human epilepsy. In the unbroken chain of phenomena referred to, there are examples showing the gradual transition from the physiological reflex to regular and complete epileptic fits of the myoclonic type with prodromal symptoms, pre-epileptic and post-epileptic phenomena. This is, in fact, in accordance with the postulate given in the introduction. It must also be pointed out that clinical observations made on myoclonic and regional convulsions in man demonstrate the fluent transition of such reflex phenomena as are frequently seen in the normal human subject at the moment of wakening or falling asleep, to complete epileptic discharges. It may be here noted that the peculiar preference shown by epileptic phenomena for appearing at the moment of transition from sleep to wakefulness or *vice versa* is also seen in animals (see p. 101).

This particular fluent transition to epileptic phenomena has been recorded graphically with a slow revolving drum, and the definite series of events during a myoclonic fit analysed.

The first stage of the fit comprises rapidly successive and powerful contractions, in the second stage these contractions become larger but are separated by gradually increasing intervals, in the third stage is a pause after which come automatic movements. If reference be made to Fig. 7, p. 35 and Fig. 15, p. 72, the movements of the whole animal will be seen recorded. Fig. 13, p. 61, shows a record taken by means of the Mosso ergograph from two symmetrical muscles (gastrocnemius). In most cases, however, the movements were recorded from the head and rump simultaneously with Brondgeest's tambours. The tracing shown in Fig. 11, p. 43, illustrates the type of fit which occurred in the great majority of cases, but there are exceptions to this type which must be referred to.

There are fits which show very slight convulsions, and indeed recall the appearance of petit mal. This type of fit only occurs where large doses of the drug have been given (compare p. 73 and Fig. 16, p. 74). Although such fits are characterised by very slight convulsions (and are therefore very difficult to record graphically), they are accompanied by the phenomena associated with the ordinary type of fit—dilatation of the pupil, loss of consciousness, and salivation. Such fits usually follow one another with great rapidity while consciousness often does not return in the intervals.

The curious complete flabbiness of the muscles, particularly noticeable between the fits, is suggestive of the discharges of the inhibiting centres upon the importance of which Sherrington and Liddell lay much stress. It seems possible that this type of discharge may be a phenomenon which is related to the pathogenesis of petit mal (inhibition of the motor phenomena).

There is another form of fit which really consists of two fits. After the ordinary prodromal and preparatory stage, the animal has a series of powerful convulsions which lasts only for one, or at most a very few, seconds. Then comes a short pause, and immediately after a definite big fit sets in.

In my own observations I found only one animal who showed this type of fit from beginning to end. In this one case it was noticed that after the big fit the animal retained a strong tendency to myoclonic convulsions. This type of convulsion is also seen after median incision of the medulla oblongata.

Finally, there are other varieties of experimental fits which appear after operations affecting the central nervous system, but these will be discussed later in Part II.

Attention must be called to fits of short duration but in all other respects very similar to those produced by bromide of camphor. These fits are induced by the subcutaneous or intravenous injection of absinthe in animals who have already received a dose of bromide of camphor, the amount of bromide of camphor given not being enough to induce a fit.

Instead of a regular myoclonic fit sometimes the animal has a crisis of violent quasi-spontaneous movements. In some cases these crises appeared to bring about a complete discharge as do the regular fits (compare Part III., Chapter XI).

Before leaving this section reference must be made to the very important question of the dose of bromide of camphor which is necessary to produce fits or to elicit symptoms other than fits.

From a long series of observations it seems correct to say that for most animals $\frac{1}{2}$ gramme given by the mouth produces a tendency to shocks and dilated pupils, while 1 gramme produces

severe fits. In some cases status epilepticus will result after 1 gramme, while in others it is a fatal dose. (Where an animal is very collapsed after bromide of camphor, it may be revived by hot milk and bromide of potassium given by the stomach tube.)

Other animals show little susceptibility to the drug, and after a dose of 1 gramme merely develop shocks. This is the type of animal which inevitably succumbs to the drug after a little larger dose, and dies in the condition of status epilepticus.

There are also animals who react to the drug by general indisposition. They remain for days in a dazed condition, untidy as to their coats, and manifestly unwell, but as a rule they never develop fits or even definite myoclonic phenomena (compare Protocol 5, p. 25).

If one wished to determine the conditions necessary for the occurrence of fits in relation to the acoustic and tactile reflexes, it might be said that the conditions for regular fits are present only when the tactile reflexes are peculiarly well developed and when acoustic reflexes are also evident (sometimes also spontaneous shocks). The tendency to develop a fit may be intensified if a myoclonic reflex be elicited, say every second, by a sudden clap; also in animals deeply under the influence of the drug, a sudden noise may precipitate a fit. The impression in such a case is that the animal is primed for the fit, and requires but the necessary stimulation afforded by the noise to demonstrate the complete phenomenon. Physiologically speaking, this represents an extreme case of what Liddell and Sherrington*† call "recruitment." It is interesting to note, on one hand, that these authors find the after-discharge recruitment, and terminal beat-formation of the extensors stronger and of longer duration than that of the flexors; and, on the other, that in man particularly the myoclonic reflexes and shocks usually manifest themselves first in the extensors of the extremities.

* Liddell and Sherrington, *Proc. Roy. Soc.*, 1924, vol. xcv., p. 154.
† Cleghorn and Stewart, *American Journal of Physiology*, 1901, p. 281.

CHAPTER V

CONDITIONS FOR THE INCIDENCE OF MYOCLONIC EPILEPTIC FITS

§ 1. Is a Certain State of Reflex Irritability a Condition Necessary for the Occurrence of Epileptiform Phenomena—Spontaneous Shocks, Myoclonic After-discharges, and Myoclonic Fits?

THE answers to these three questions are beset with difficulties, because the conditions of the animals vary a great deal and are subject to wide fluctuation. This applies to the ordinary reflexes in the normal animal where these reflexes have not been exaggerated with drugs. The cause of this variability of the normal reflex is as yet unknown, although it has been recognised by Fano and other workers.

Certainly, from a prolonged series of experiments, it seems justifiable to say that as a rule there is a condition of increased reflex irritability before the fits. Reflex shocks may be induced by slighter stimuli than are needed with the normal animal.

There are, however, many variations of this general rule.

First of all this period of increased irritability before a fit varies considerably in duration, but is usually about the same in any one animal subjected to one particular dose of the drug. Quite frequently the period may last several hours, but it may be much shorter. It must be remembered that there are cases where the condition of increased reflex irritability is so short as to pass unnoticed. The phase probably always exists, but unless carefully looked for may quite easily be missed.

This last point is of importance in connection with myoclonic epilepsy in man. It is easy to diagnose myoclonic epilepsy in a patient giving a history of increased reflex irritability as evinced by starts on slight noises, which lead in turn to spontaneous shocks. It is more difficult where the history merely includes spontaneous convulsions severe enough to awake the patient from sleep.

The data obtained from experimental work on cats certainly help to clear up some of these doubtful and difficult cases.

It can be proved experimentally that just before a fit there is a marked fluctuation of the reflex irritability in almost every case.

Example of a fluctuating reflex irritability shortly before a myoclonic fit:

Protocol 13, Cat 106. Black animal.

1.9.06. The right occipital lobe was exposed and lifted over to the left side with a spatula. The attempt was made to remove the right anterior or posterior corpus quadrigeminum. When the animal regained consciousness after the anæsthetic it was found that moving the hand in front of the left eye did not cause the eyelid to wink, whereas on the right side it did.

3.9.06. Nothing very unusual could be observed. The animal was rather uncertain and irritable in temper.

4.9.06. No disturbance noted in gait or freedom of action.

18.9.06. At 9 a.m. an intramuscular injection of 6 grammes of a lukewarm solution of bromide of camphor in oil was given. The convulsions which followed this dose were recorded graphically from 2 to 4 o'clock, and included two severe fits. The reflex shocks were elicited mostly by means of acoustic stimuli, tactile stimuli were not very potent. These shocks consisted of the sudden raising and adducting of the right fore-paw (the result of the operation ?). In the severe fits a general convulsive movement took place; both fore and hind paws moved simultaneously.

After the first fit (at 3.49) acoustic reflex shocks and spontaneous shocks reappeared fairly soon, while after the second fit the hyper-irritability disappeared.

In the preparatory stage, before these severe fits, it was noticed that after a series of spontaneous shocks, or even after a single acoustic reflex shock, another reflex shock could not be evoked for 30 to 60 seconds. This is seen on the tracing. When five acoustic reflex shocks were administered at intervals of a second, it was often seen that a reflex was elicited by the second clap; after this the reflex movement increased in power up to the fifth clap. At other times only the first or the last clap of such a series elicited a response, while in some cases no response was evoked at all.

Fig. 14 shows clearly how at 3.20 none of the five hand claps (visible in the time tracing) are followed by a shock.

At 3.23 only the second; at 3.25 all five in a moderate degree, as also at 3.26; but at 3.26½ the second and third claps are followed by spontaneous shocks; at 3.27 a series of spontaneous shocks follows upon the first clap, less so half a minute later, but in that case the last clap is followed by a vigorous convulsion.

At 3.23 the second stimulus of the series gave a reflex movement. At 3.26½ two reflex after-discharges appeared. At 3.27 a mild fit supervened, after which there was diminished reflex irritability (incomplete discharge). At 3.28 the irritability began to increase and remained in a fluctuating condition until 3.49, when a severe myoclonic fit occurred.

At 3.28 the reflex movements decreased in force until the last, which was stronger.

At 3.49, immediately before a short fit, the second clap in a series of five was followed by a reflex movement, which led to a reflex discharge in the form of spontaneous small shocks. Spontaneous shocks occurred between the fourth and fifth claps of the series, while the fifth clap was followed by a violent reflex shock, after which came several additional shocks.

At 3.49½ spontaneous and violent shocks occurred at intervals of a

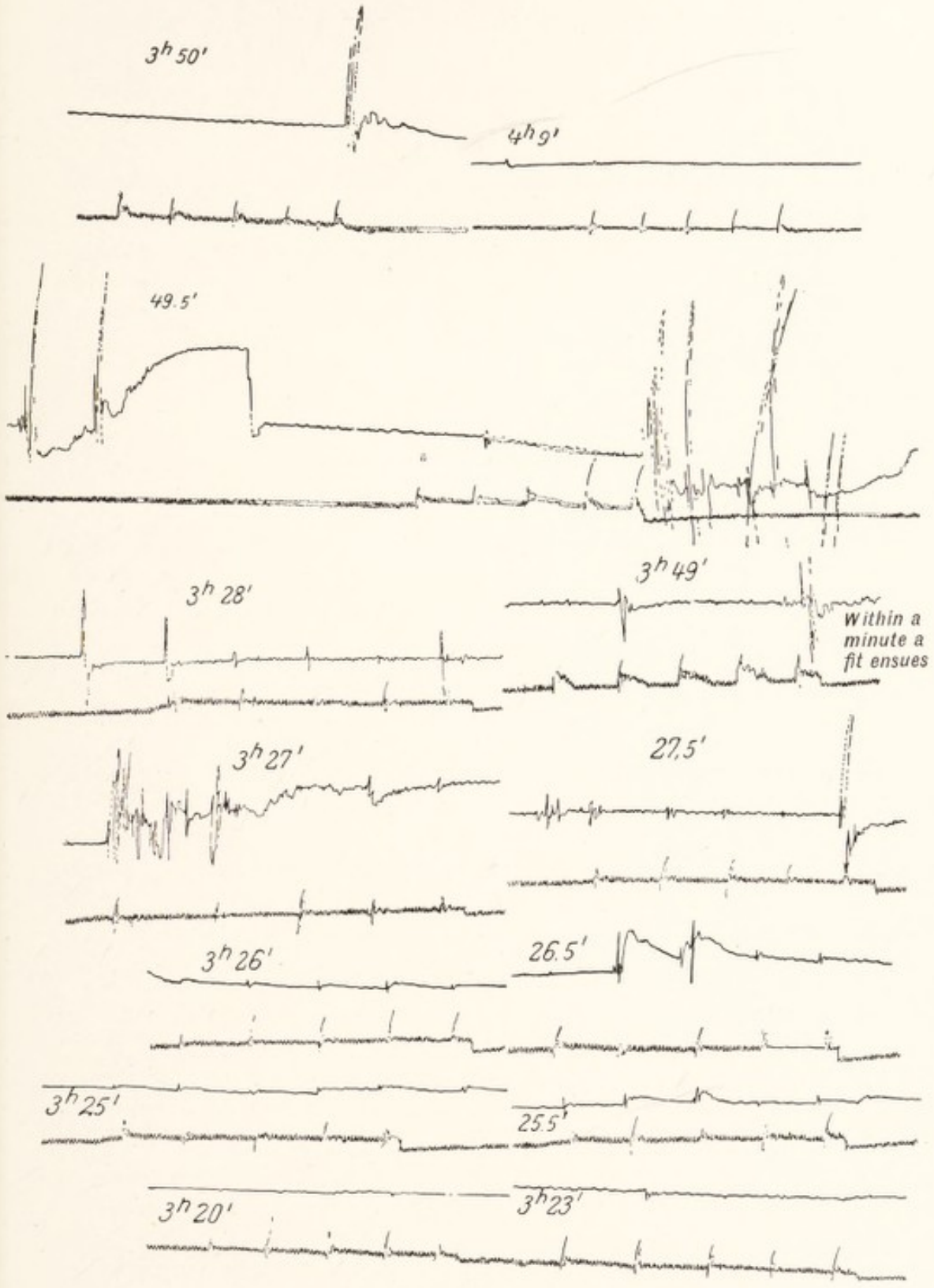


FIG. 14.—CAT 106. SEPTEMBER 18, 1906.

The animal was placed on a mat of oil-cloth, below which were rubber tubes connected with tambours to record any change in pressure in the different parts of the mat. Such change indicated movements on the part of the cat. Each minute a series of five acoustic stimuli (claps) were administered at intervals of one second. Stimuli visible in tracing.

few seconds, after which came a short tonic fit, followed by a period of complete rest, which lasted about ten minutes.

After the second fit the pupils became smaller, but the animal was impervious to pain. An hour later the coat became glossy. Shocks could not be provoked by either tactile or acoustic stimuli, but followed psychical stimuli. These stimuli were afforded by anything passing close to the animal.

23.9.06. The animal did not recover its normal condition after the injection. It ate, but could not walk well, tending to fall to the right, while it co-ordinated badly. It was weak on its paws and stiff. It was subject to shocks which involved the whole body.

24.9.06. At 8 a.m. an injection of 10 grammes of a warm solution of

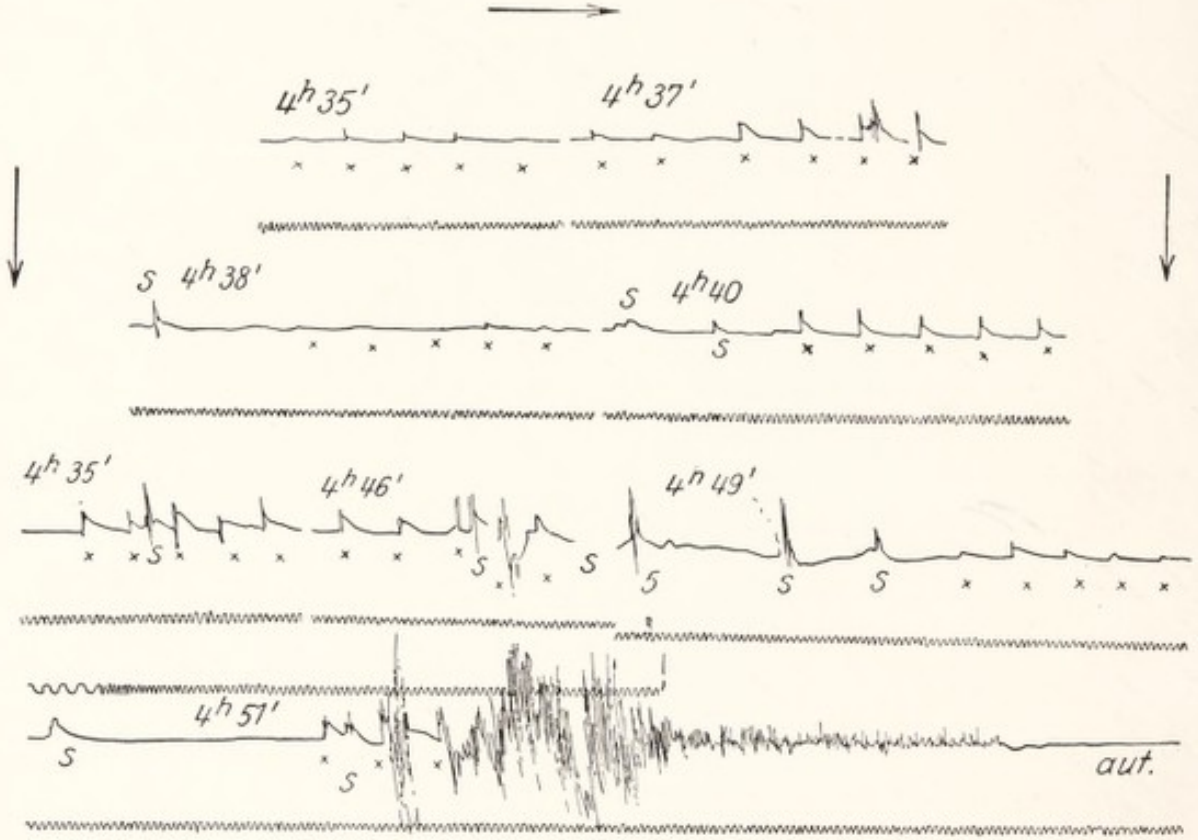


FIG. 15.—CAT 93. JULY 4, 1906.

Record taken by recording changes of pressure transmitted from a plate upon which the cat rested. Tracing reads from top to bottom. From 4.35 to 4.45 p.m. the reflex movements elicited by acoustic stimuli applied at intervals of one second increased in power (marked with ×). After this, as seen up to 4.50, spontaneous shocks appeared. At 4.51 the first clap reflex was followed by a spontaneous shock, while the second clap reflex of the same series was followed by a small fit. The third clap reflex was merged in a severe myoclonic fit. Tuning-fork vibrations 10 per second.

bromide of camphor in oil was given. After this the animal had several fits, and died at 10 a.m.

Autopsy.—A series of Marchi preparations were made of the brain. It was found that there was only a small lesion of the right anterior corpus quadrigeminum. There was some degeneration in the right tecto-pontine tract.

From this experiment, which has been repeated in other animals, it seems safe to conclude that the intensifying of the

reflex irritability with small doses of bromide of camphor induces a condition favourable for the development of a fit. It would seem that the more abrupt are the changes in reflex irritability the sooner will the fit supervene.

In Cat 92 (Figs. 19*a* and 19*b* in the Dutch edition of this book) examination at 2.13 continued up to 2.42½ showed an increase of reflex irritability which was lessened by a series of spontaneous convulsions. At 2.46½ a fit followed a moderate tactile reflex. At 2.48 a severe spontaneous shock occurred, after which the reflex irritability was distinctly decreased (compare fit shown in Fig. 15).

A somewhat parallel condition to this type of reflex irritability is described by Bowditch and Warren, and by Sherrington in connection with the knee reflex.

Sherrington shows that the act of kneading the muscles antagonistic to this reflex has the effect of inhibiting the reflex, but immediately after the kneading is stopped the reflex is intensified.

§ 2. Is a Certain Definite Length of Latent Period of the Myoclonic Reflex associated with the Occurrence of Epileptic Fits?

In order to ascertain whether there is any connection between the length of the latent period and the occurrence of fits, it is necessary to know the length of this period in the prodromal stage, immediately before and immediately after a fit.

The cats which were found most suitable for this branch of investigation were those who exhibited fits or even status epilepticus for a certain period, after which came a period when they were immune from either fits or any associated phenomena.

Protocol 14, Cat 177. Large grey-and-white cat.
16.7.09. 6 p.m., ¾ gramme bromide of camphor given.
17.7.09. Found lying on its side unconscious. Had several fits during the day at shorter and shorter intervals. Later it was unconscious for two hours, apparently too ill to have motor fits. During this period the pupils were small. Periodically the animal passed into a condition which resembled a fainting fit. In such a state the latency of the slight myoclonic reflexes which could occasionally be provoked were abnormally long—6 to 8 fiftieths of a second (Fig. 16, second tracing).

Warm milk, containing potassium bromide, was given by the stomach-tube. The animal recovered somewhat, and the reflex shocks showed a latency of 4 to 6 fiftieths of a second. Later the condition improved still further, and the latency displayed was about 3 fiftieths of a second. (Fig. 16, tracings 1 and 3).

When this degree of latency was reached the animal began to have fits. Towards evening it died, after a series of very slight fits.

From the foregoing protocol it is seen that the latent period in this animal under the influence of bromide of camphor increased

from 2 to 3 and more fiftieths of a second. When the latent period reaches 4 fiftieths of a second, the conditions necessary for the occurrence of a motor epileptic fit were wanting, while further lengthening of the latent period was associated with failure to elicit even slight reflex shocks.

As regards the relationship between the latency of tactile and acoustic reflex shocks and the occurrence of spontaneous shocks, it appears that a slight lengthening of the latent period (from 50 to 56 or 58 milli-seconds for tactile reflex shocks) is associated with the occurrence of spontaneous shocks. If the

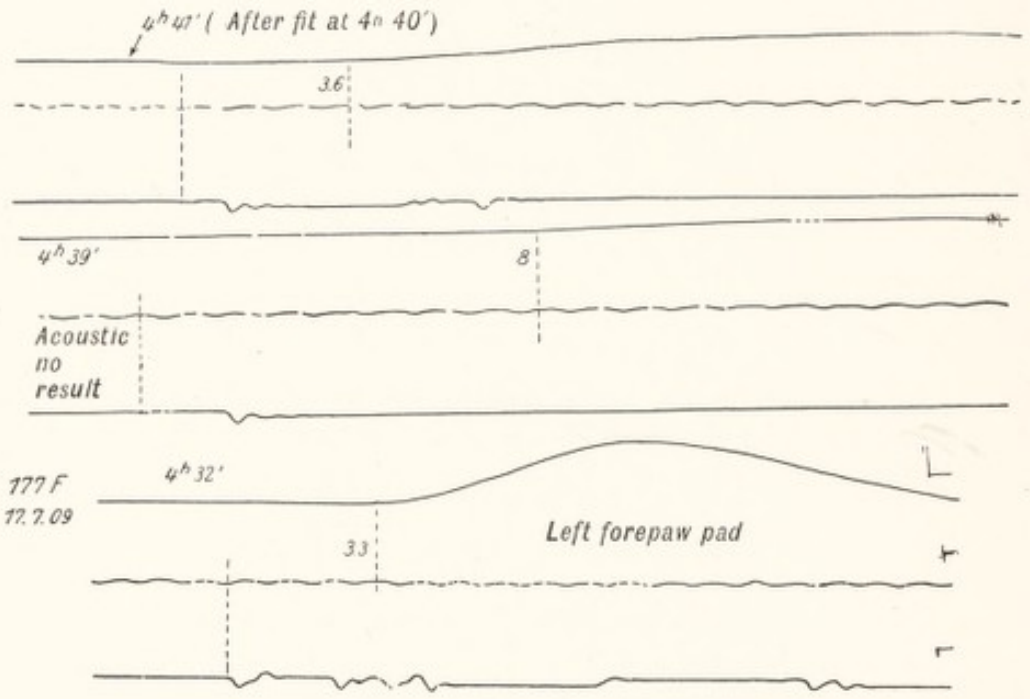


FIG. 16.—CAT 177 F. JULY 17, 1909.

At 4.32 p.m., shortly after the administration of warm milk by the stomach tube tactile reflexes were seen in the sole of the left forepaw. At 4.39 p.m. there was an abortive fit or momentary collapse after a stimulus. At 4.41 p.m. myoclonic reflexes were first recorded after the abortive fit at 4.40 p.m. The tracings read from below up.

latency of the tactile and acoustic reflex shocks reaches 65 to 80 milli-seconds, definite fits are likely to occur. From these investigations, therefore, it would appear that a certain (optimum) length of latency for tactile and acoustic reflex shocks is associated with the development of either spontaneous shocks or epileptic fits.

Similar observations have been made for the acoustic reflexes. Fig. 17 shows the increase of reflex time from 1·0 to 1·3 fiftieth seconds to 1·9 within a very few minutes. The last reflex of this series merges into a big motor convulsion.

We have here a group of consecutive observations which seem

to prove that a certain lengthening of the latent period is either a co-effect of the manifestation of myoclonic phenomena, or is associated with the origin of these phenomena.

There is, however, one group of observations made on tactile

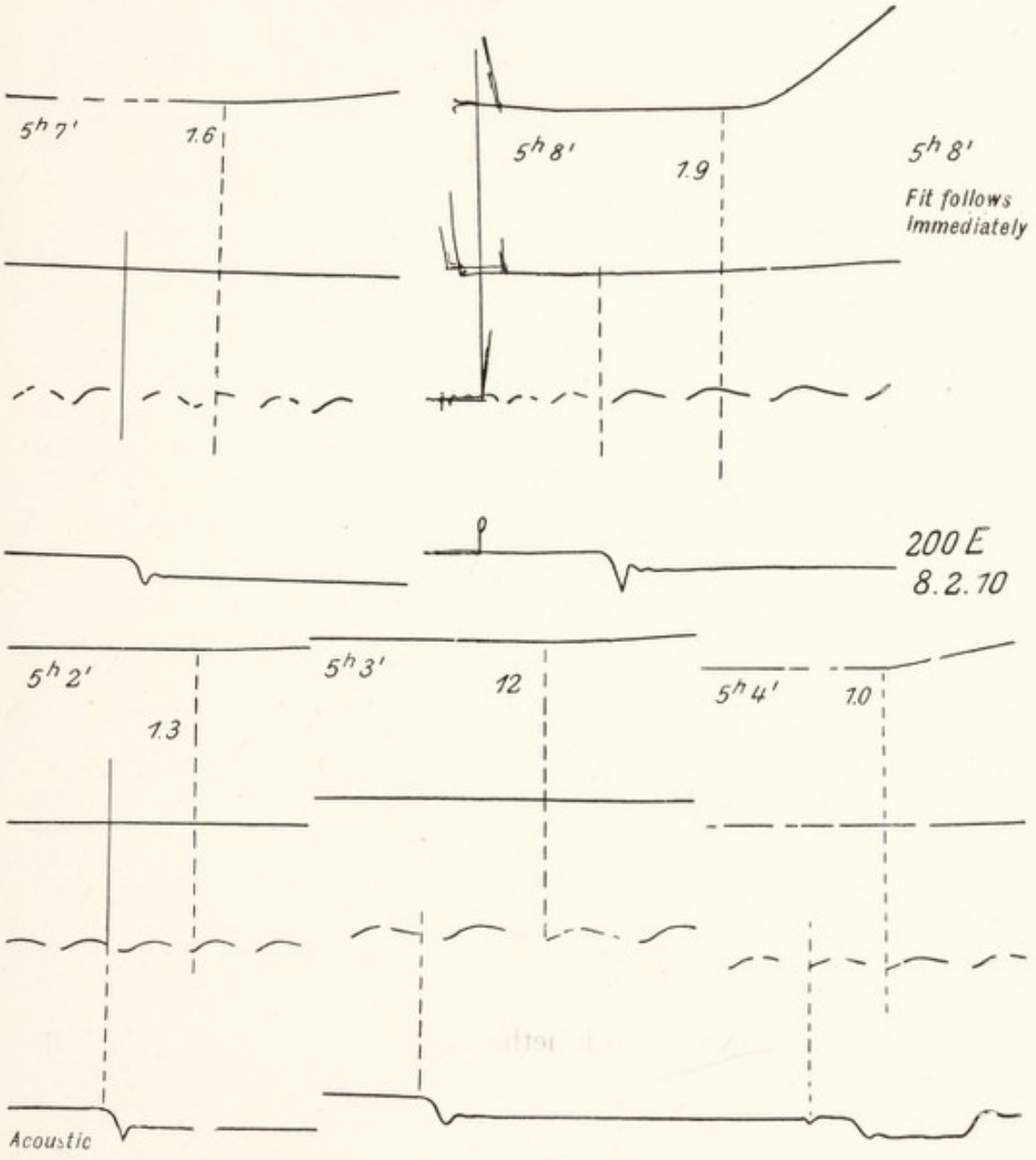


FIG. 17.—CAT 200. JANUARY 8, 1910.

Acoustic myoclonic reflexes with varying length of the latent period. Record made from 5.2 p.m. to 5.4 p.m. The latent period lengthened until 5.8 p.m., when there was a myoclonic fit.

reflexes which would seem to prove the contrary—*i.e.*, that a shortening of the latent period precedes a fit.

This is shown in Fig. 18, where tracings are seen taken from a tambour applied to the back of the animal. Tactile stimuli were

applied regularly to the back (except at 5.20, when the head was touched). At 5.16 the latent period was 2·2; at 5.19, 3·4 fiftieths of a second, while the sharp rise in the tracing shows that the myoclonic element is becoming prominent. At 5.20 (tracing 2 from below up) the latent period is shortened to 1·8, while a comparatively violent convulsion is evoked by the stimulus. After this last response to a tactile stimulus, reflex after-discharges

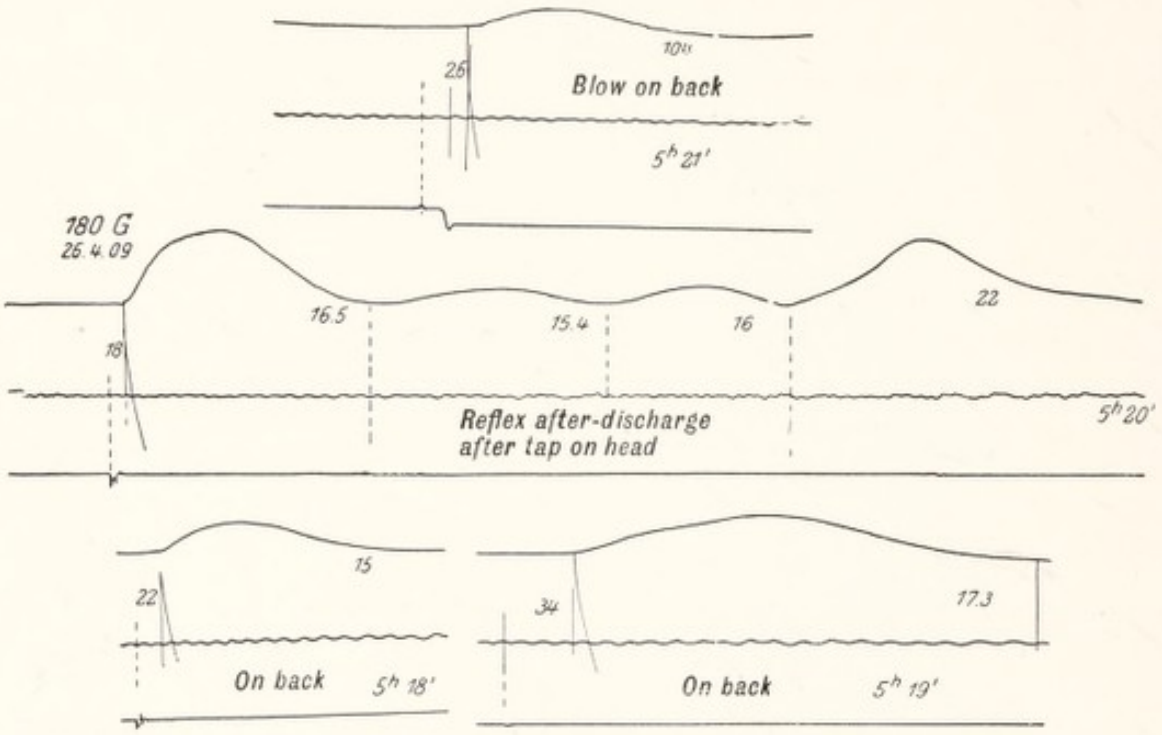


FIG. 18.—CAT 180 (REDUCED ONE-HALF).

Tambour on back. Tactile reflexes from the back. The latent periods at 5.16 p.m. and 5.18 p.m. were 2·2 fiftieths of a second, at 5.19 and 5.20 they were 3.4, and 1·8 fiftieths of a second respectively. A slight myoclonic shock followed the last reflex, with dilatation of the pupil. At 5.21 the latent period was 2·6 and at 5.23 1·1 fiftieths of a second. A fit occurred, and the latent period reverted to 2·6 fiftieths of a second.

follow at intervals of 16 fiftieths seconds—*sit venio verba*, a small epileptic fit occurs.

During this fit the pupils are momentarily dilated. After this fit the latency again lengthens to 2·6, subsequently to 2 (not shown in the figure), but shows a sudden shortening to 1·5 immediately before a slight fit. After this fit the latent period again lengthens to 2·6, when a slight reflex with some after-discharge phenomena occurs. This is at 5.30 p.m. This last observation shows that an after-discharge or fit is not invariably associated with a violent reflex discharge. From the foregoing observation, which has been repeated several times, it seems permissible to formulate this conclusion

"A definite lengthening of the latent period occurs some time before a fit, and under certain circumstances a marked shortening of the latent period may occur immediately before a fit."

It seems justifiable to assume that the organism as a whole

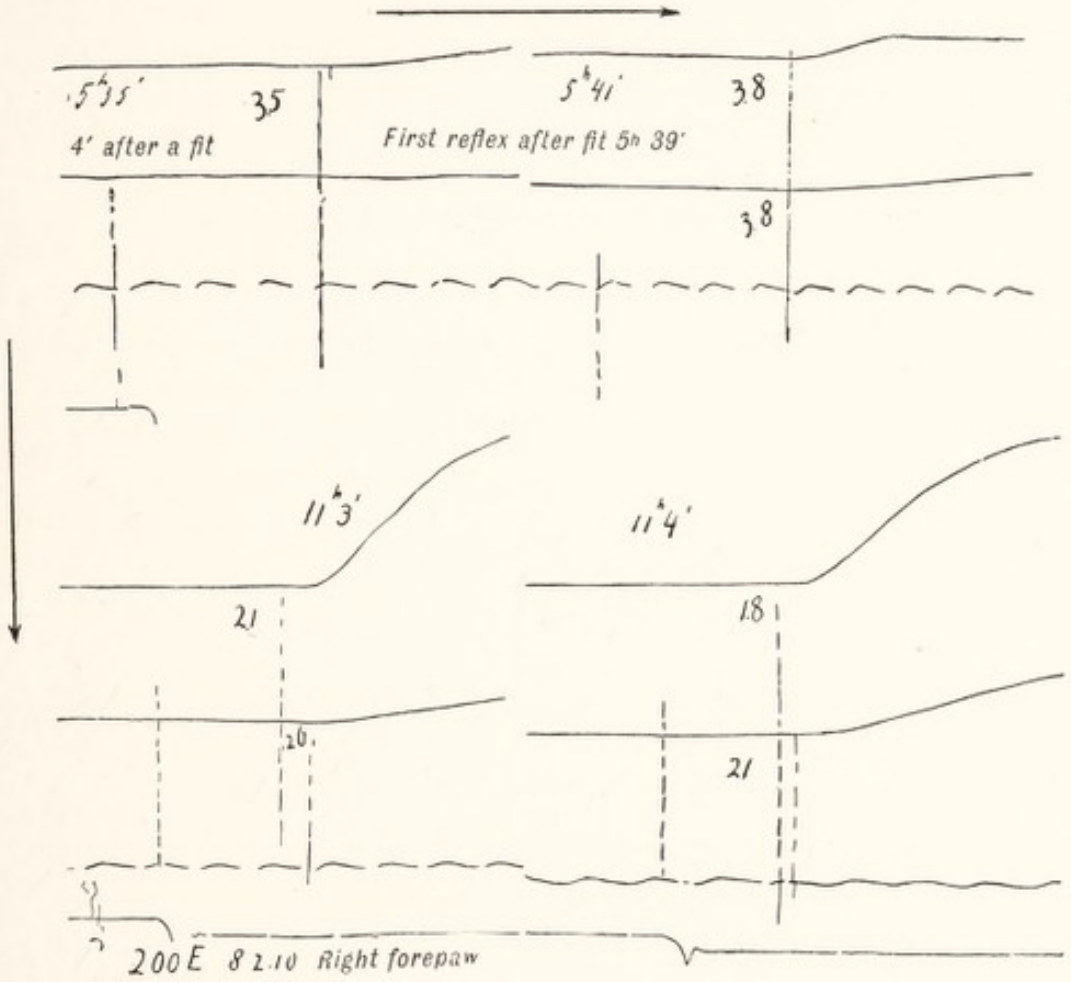


FIG. 19.—CAT 200. FEBRUARY 8, 1910. (REDUCED ONE-HALF).

Top tracing taken from head tambour, lowest from rump. Tactile myoclonic reflexes. Before the myoclonic fits (lowest tracing) the latent period amounted to 2·1, 2·6, 1·8, and 2·1 fiftieths of a second. The first reflexes recorded a few minutes after the fits show latent periods of 3·5 and 3·8 fiftieths of a second.

may display a certain lability just before the occurrence of a fit.

It would appear as if the changes in the condition of the latency (or the lability of the power of conduction that is the cause of this change), like certain changes in the reflex irritability of myoclonic patients, favour the occurrence of epileptiform phenomena. It has already been pointed out that in human epilepsy (not only in the myoclonic form) the moments of tran-

sition—*i.e.*, waking from sleep or falling asleep—are the times when fits most commonly occur. This applies both to spontaneous and isolated shocks and epileptic fits. As has been said, the latency is generally longer than normal after a fit. Fig. 19 offers an example of this lengthening, where the first reflexes recorded after the fits at 5.31 and 5.39 p.m. show a latency of 3·5 and 3·8.

Finally I should like to point out, as a matter of interest, that in an extremely short fit recorded in second tracing Fig. 18 (perhaps

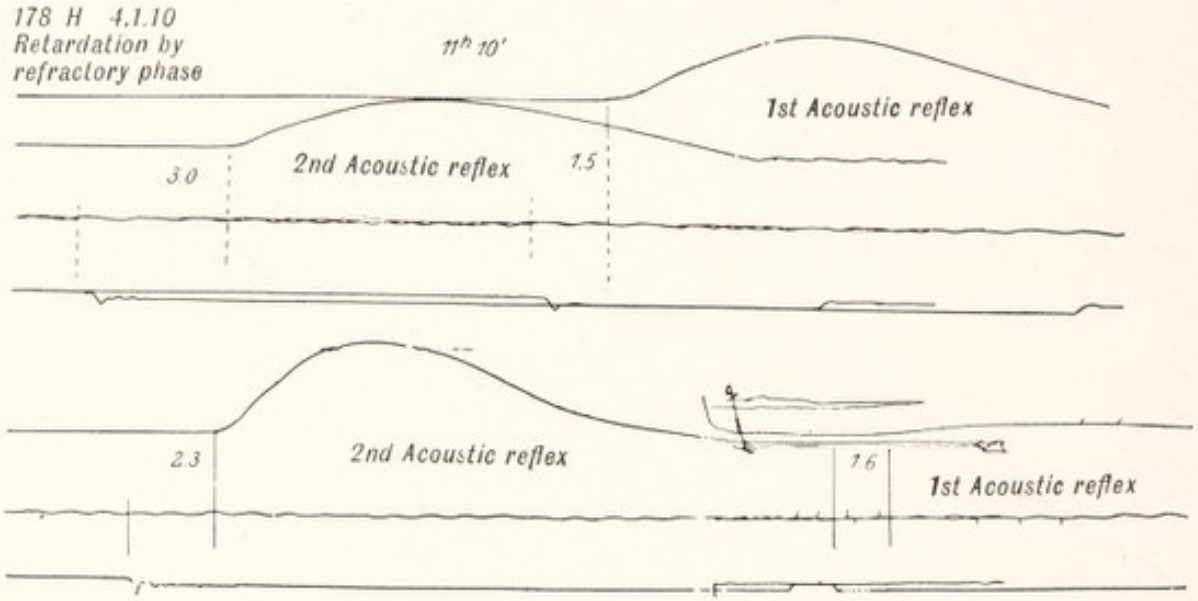


FIG. 20.—CAT 178. JANUARY 4, 1910.

This shows the effect on the latency and form of the tracing of repeating a moderate stimulus twice in one second. In the first tracing the latent period before the first acoustic reflex is 1·5, before the next 3 fiftieths of a second. In the second tracing the latent period is 1·6 and 2·3 fiftieths of a second. Further, in the first tracing, the two reactions are about equal, while in the second tracing the second reaction is much greater.

the shortest fit ever recorded) dilatation of the pupils was present. The importance of this symptom in human epilepsy is well known.

§ 3. Is a Change in the Refractory Phase a Condition Necessary for the Occurrence of Epileptic Fits?

It has been seen from the foregoing pages that by applying a stimulus at regular intervals one may produce regular myoclonic reflex shocks. Thus, in Tracing 1, Fig. 8, p. 35, where there is an interval of 30 fiftieths of a second between the stimuli (tactile stimuli applied to the spinal column) a definite and regular reflex is produced. In this tracing may be seen, probably as a result of the so-called "Bahnung," the increase in size of the reflex movement and the shortening of the reflex time. The reflex time shortens after each stimulus, changing from 2·1 to 1·2 fiftieths

of a second. The lowest tracing shows that this rule does not hold in the case of acoustic stimuli which were applied at the same rate as the tactile stimuli.

With a quickly moving drum the latency for acoustic stimuli remains about the same, but the size of the reflex movements becomes smaller. In the case of regularly repeated tactile stimuli the reflex irritability increases, but this does not happen with acoustic stimuli.*

The refractory period is therefore longer for acoustic stimuli. In Fig. 20 two acoustic stimuli are applied within a second. In the first the latency is 1·5 (fiftieth of a second), in the second case it is doubled. In both cases the extent of the movements is about equal.

In the same experiment the lowest tracing shows how the first reflex stimulus was followed by a slight movement with a latency of over 1·6, while the second reflex was a strong one, but the latency was 2·3. In this tracing we see therefore the pro-

FIG. 21.—CAT 168. MARCH 4, 1909.

Slight exaggeration of the reflexes with monobromide of camphor. The effect of repeating an acoustic stimulus four times in one second results in the arrival of the second stimulus before the termination of the refractory phase of the first. The final result is a lengthening of the latent period and the reflex reaction is less.

tracting after effect of the refractory phase on the latency, while the ascent is enforced by the effect of the facilitation (Bahnung). Thus, where a stimulus is repeated within a second, we see various effects on the latency and on the character of the ascent of the reflex tracing, while the phenomenon of "Bahnung" seems to manifest itself quite independently. If the acoustic stimuli be repeated still more quickly, about four times per second, one may see the latency increase from 2 to 5·8 fiftieths of a second (see Fig. 21, p. 79). After some time a stimulus-effect, very limited in extent, again occurs, but only after a lengthened period (4·2 fiftieths of a second).

From this we may conclude that the phase of the refractory period in which the stimulus is applied is certainly one of the factors which exercise an influence upon the latency. Here it

* On July 20, 1911, an acoustic reflex was elicited from a cat (217) at least half a second after a spontaneous shock. This is evidence of greatly increased irritability. Whereas the latency for an acoustic reflex is rarely or never more than 2 fiftieths of a second, here the latency was not less than 4 fiftieths. This is also evidence that the refractory phase for acoustic stimuli lasts much longer than for tactile stimuli.

must be remembered that Mendelsohn* found that in the muscles of the frog the latency (in this case the time between the moment when the stimulus arrived in the muscle and the beginning of the contraction) changes from 8 to 21 milli-seconds in 18 minutes when the stimuli are applied at 40 per second.

The refractory periods of the reflexes at present under consideration are much too long to be compared with those which may occur in voluntary muscle. See experiments made by Dubois-Raymond† and Richet.‡ These workers proved that there is intensified irritability in tetanised muscle, and that a stimulus applied during a contraction has a shorter latency.

Where a series of very rapid and strong myoclonic contractions occur as a reflex after-discharge, they present an appearance which cannot be produced by artificially provoked reflex movements The conclusion seems admissible that the refractory phase is abnormally shortened. This supposition seems to receive strong confirmation from the observation seen in Fig. 10 (p. 39) where, as a result of a reflex produced from the spine, a series of spontaneous convulsions occurred as a reflex after-discharge. These convulsions have the unprecedentedly short intervals of 6 to 8 fiftieths of a second. Immediately after this series of spontaneous convulsions a fresh reflex was elicited artificially which showed a normal latent period. Now under normal conditions, after the occurrence of one reflex shock, there is a long refractory period, or if the reflex is elicited artificially, the latent period is a long one; it is evident, therefore, that in this case there must exist abnormal conditions of irritability and conduction. In discussing the origin of the reflex after-discharge, Sherrington propounds the following question, Why is it that in the spinal and decerebrate animal reinforcement and rhythmic repetition of the original stimulus occurs? Further, Sherrington calls attention to the comparable phenomenon of cardiac pulsation. Lewis, referring to the exposition on the parts played by anti-peristaltic and retrograde waves in auricle and ventricle of the turtle and frog by the writer,§ extends the argument to explain the mechanism of auricular fibrillation. The suggestion is made that where the power of conduction is reduced, the contraction wave travels round and round, until finally a simultaneous contraction of the whole chamber results. The suggestion is made by Sherrington‖ that a comparable mechanism exists in nervous structures after a stimulus has been received.

* Mendelsohn, *Travaux du Laboratoire Marey*, 1878-79, p. 99.
† Dubois-Raymond, *Gesammte Abhandlungen*, vol. ii., p. 94.
‡ Richet, *Comptes Rendus de l'Académie des Sciences*, July 28, 1879.
§ L. J. J. Musken's, *Journal of Physiology*, 1907, p. 108, and *American Journal of Physiology*, 1898, i., p. 486.
‖ Sherrington, *Libro en honor de D. S. Ramon y Cajal*, 1922, p. 97.

§ 4. The Peculiar Rhythm of the Convulsions and the Maximal Shortening of the Refractory Period.

Even a superficial examination of the tracings recorded by separate convulsions during a fit and series of shocks is sufficient to show that there is a certain definite rhythm in these phenomena. This is the case both for the incipient stage, erroneously termed the tonic stage, and the later stage. These tracings show that at the beginning of a fit induced by monobromide of camphor

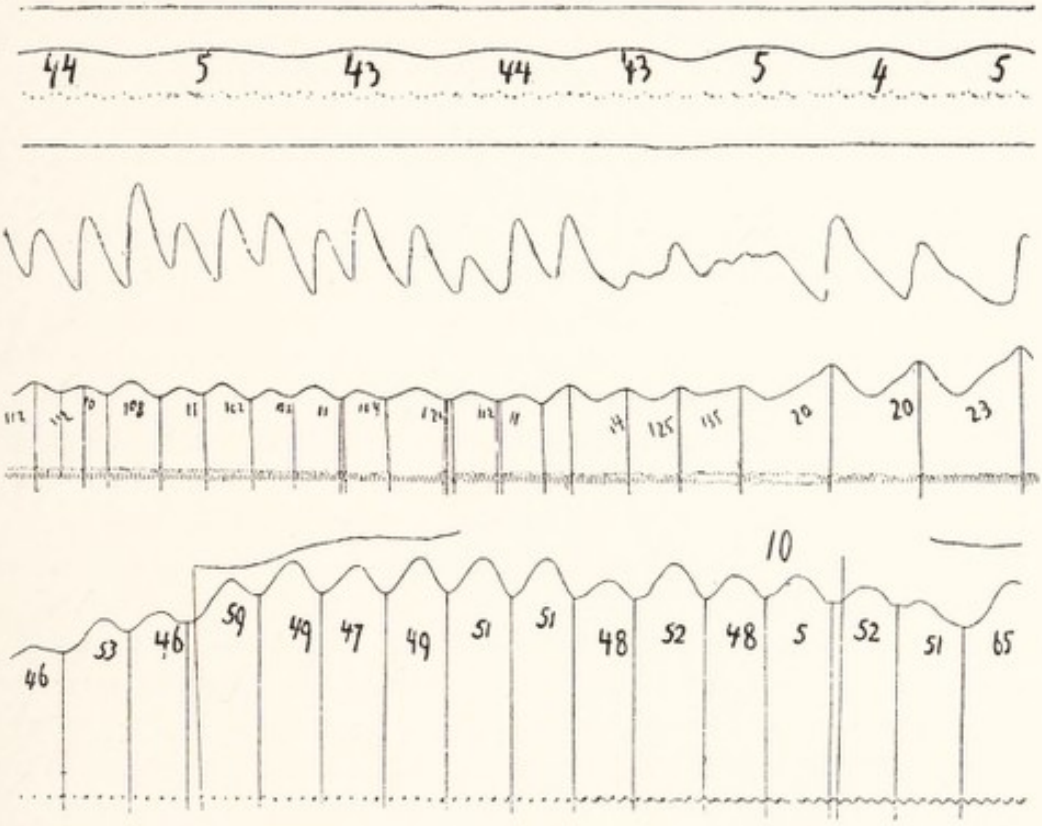


FIG. 22.

Various graphic records of convulsions during the so-called tonic stage in the cat. The lower three tracings show a transition to a considerably lower frequency, in which the period is approximately a multiple of the previous period.

the rhythm fluctuates round about 10 per second (Fig. 22, second tracing).

The results got with a slowly revolving drum must be taken with a certain reserve, as also tracing got by means of elastic tambours. In both these instances vibrations of the lever due to elasticity are a source of possible error. The tracing got with the spring ergograph certainly suggests that during the whole fit the same rhythm is maintained, but that at the end of the fit one or two convulsions drop out. This seems the only explanation why the measured period of the greater wave at the end of a fit is frequently double or treble, or a simple multiple of the previous period.

It certainly would be of theoretical importance if a fixed rhythm were maintained throughout the whole fit, as it would tend to show that the whole phenomenon—spontaneous shocks and reflex shocks and the fit—were due to one mechanism.

What is got in a tracing is that at the beginning of a fit the lever records a series of equal elevations; next comes a short transient stage, when the elevations are alternating in type, one large one small; next comes a stage when there is one big elevation, then two small, followed quickly by a tracing similar to the first part.

The same type of tracing is shown in a series of reflexes produced by a series of stimuli (Fig. 7, p. 35).

The question arises whether each individual has a peculiar rhythm, the rate of which does not change during the fit. This point I could not investigate. So far as I know this point has not been investigated for other reflex after-discharges either, but it seems to me to be one of great importance. It would be desirable to repeat this particular section of my work, using Enthoven's wire galvanometric method.

It will also be remembered that J. Hughlings Jackson repeatedly gave it as his opinion that the tonic convulsions were nothing but extremely rapid and consecutive clonic convulsions. This opinion I entirely endorse from the evidence obtained in this investigation.

In the second part of this book the effect of lesions of the central nervous system on the phenomena just described will be considered, but first the possibility of there being an innate tendency to rhythmic discharge in the central nervous system must be discussed.

In 1879 Sewall* described the electrical stimulation of a voluntary muscle at short intervals, the tracing showed reactions at intervals of 0·026 per second (frequency 38·4 per second). With a greater frequency, say 38·8 per second, everything merged into a tetanus-like record. Stimuli at the rate of 20·8 per second gave, he found, the best effect for summation of stimuli, for at this rate the succeeding stimuli arrived at the top of the preceding contraction. L. Hill† found that he could get optimal contractions from a voluntary muscle at 40 per second. E. Liddell and Sherrington noted that in decerebrate cats stimulation of the afferent nerves fusion of the resulting contractions occurred when the number reached 35 per second.

The work of Pipier‡ is well known. He showed that the salvo-like discharges of the voluntary muscle impulses prove, with

* L. Sewall, *Journal of Physiology*, 1879, vol. ii., p. 172.
† L. Hill, *Journal of Physiology*, 1921.
‡ Pipier, *Pflüger's Archiv*, 1907, vol. cxix., p. 301.

the wire galvanometer, to have a frequency of 47 to 50 per second. As regards the frequency of stimuli from the cortex, Broca and Richet* found that 10 stimuli per second is the normal rhythm, and they further established that physiological tremors, such as cold shivers, also have their rhythm of frequency. Horsley and Schäfer† found that both stimulation of the cortex and of the corona radiata and reflex contraction (muscle-tone) have their own peculiar rhythm of 10 per second or somewhat less. Von Kries‡ recorded tetanic muscular contractions with the myographion, and found that the rhythm varied from 8 to 40 per second. The rate was considerably slower with strong contractions. It has been found that the quickest voluntary movements—say, in piano-playing or typing—are about 10 per second.

More recent investigations have been made on the effect of different rates of stimuli on nerve-muscle preparations in decerebrate cats. The frequency of motor nerve impulses involved in sustained central activity, such as occurs in voluntary movements, should lie between 300 and 600 (Forbes, Ray, and Griffith).§ On the other hand, Cooper and Adrian‖ found that in the spinal cat the muscle reacts 320 times to 320 stimuli per second applied directly to the motor nerve. If the stimuli arrive via a synapse, the muscle reacts irregularly should the stimuli exceed 200 per second.

Schäfer¶ has shown that the rhythmic contraction of muscle controlled by the will shows a variation from 8 to 13 per second.

Broca and Richet** proved that if electric stimuli were applied to the cortex in dogs under the influence of chloral at too frequent a rate, then here also one discharge alone followed on 2, 3, or 4 stimuli. They further proved that both the reflex time and the refractory phase of these reflexes was shortest at a temperature of 35° to 40° C.—*i.e.*, 50 μ and 100 μ†† respectively.

This observation, taken in conjunction with my own observations on cats treated with monobromide of camphor, suggests that a maximum shortening of the refractory phase and latent period is the basis of the explanation of the fusion of numerous single convulsions into one tonic condition. Of course, such a hypo-

* Broca and Richet, *Archives générales de Physiologie normale et pathologique*, 1897, p. 864.

† Horsley and Schäfer, *Journal of Physiology*, vol. vii.

‡ Von Kries, *Arch. (Anat. u.) Physiol.*, 1886.

§ Forbes, Ray and Griffith, *American Journal of Physiology*, 1923, vol. lxvi., p. 606.

‖ Cooper and Adrian, *Journal of Physiology*, 1924, vol. lix., p. 61.

¶ Schäfer, *Journal of Physiology*, vol. vii.

** Broca and Richet, *Comptes Rendus de la Société de Biol.*, 1897, p. 333.

†† It is interesting to find that investigations made for other purposes have shown that the maximum frequency of various voluntary movements is also 10 per second.

thesis presupposes the arrival of a maximum number of stimuli at the discharging centre.

It would appear as if the rhythm of the convulsions in a fit is determined by the maximum shortening of the refractory phase. As has been said, it would appear that there is a specific rhythm for different animals.

Loven,* in his experiments, showed that in strychnine convulsions the rhythm varied from 7 to 9 per second. Although it is not yet possible to give one explanation for all these results, which, indeed, show a fair amount of variation, yet there is evidence in support of the teaching of Broca and Richet that the rhythm of the central nervous system is approximately 10 per second.

In agreement with this the kymographic records of a convulsion due to monobromide of camphor shows in the so-called tonic stage a frequency of 8 to 10 per second. Since, in the periphery, a far more frequent stimulus seems to concord with its own rhythm, it seems possible and probable that in the spinal cord or in the higher centres in the brain this quicker rhythm is converted to the slower rhythm typical of the central nervous system.

From a general consideration of the data obtained, I have come to the conclusion that the monobromide of camphor and absinthe are toxic drugs which produce fits in animals comparable in detail with myoclonic and regional fits in man.

In the second part of the book the effect of lesions of different parts of the central nervous system on these phenomena will be described. The records of the various shocks, convulsions, and fits that we have to deal with point towards the existence of a rhythm which persists in its different phases all through the motor fits, and which does not vary much from the rhythm of 10 per second. It is only in the early stages of the fit that the contractions show the maximum frequency. In the later part of the fit the muscles respond only to a certain number of all the stimuli which reach them from the central nervous system.

The question next arising is what is the difference in the condition of the animal during the series of convulsions and fits as contrasted with the condition in the intervals? It is found that in the intervals the refractory phase is much longer, it may amount to almost 1 second, while during the fit this phase is short, but a fraction of a second, perhaps one-tenth. Whether this radical change in the refractory period is primary or secondary to other fundamental changes, or whether there is a direct connection between the shortened refractory period and the changes in the latent period, are questions which I cannot as yet answer.

* Loven, *Central. f. d. Med. Wissenschr.*, 1881.

One of the most striking phenomena connected with the fit was the protracted period immediately after a fit when no myoclonic reflex could be produced by any form of stimulus. Further, there were no spontaneous shocks in this period. In those cases where but one fit occurred, this period was peculiarly striking, for here the extraordinary influence the fit had on the condition of the animal was clearly seen. The discharging effect was demonstrated by the reversion of the animal to the normal condition. The fur became glossy, the pupils regained their normal size, the animal ate and conducted himself as a normal, healthy animal. Further tests showed that any abnormality of sensibility to pain or heat had passed off. The effect of the fit had been wholly beneficent, changing an unhealthily abnormal animal into a healthy normal one.

One question which must have occurred to the reader has to be dealt with. Why is a tonic stage, such as is seen in human epilepsy, wanting in those fits produced experimentally in animals? It may have been noticed that some care has been taken to avoid the word " tonic " as far as possible, the reason being that during my investigations my conceptions of the meaning of the two words " tonic " and " clonic " underwent a change.

Ordinary observation of the initial stages of a fit shows the body stiffening in a tonic or cramp condition, but a graphic record of the phase did not show a corresponding tracing. On the contrary, all the tracings recorded by each of the four different methods showed the same evidence, that if the condition were recorded with sufficient precautions, separate convulsions are individually discernible. Only at the end of the fit, when the single convulsions are more isolated, the clonic character becomes more pronounced, because the locomotor effect of the muscular contractions was allowed more space. This is why I have come to the conclusion that the whole doctrine of tonic and clonic convulsions which postulates a certain fundamental difference between the tonic and clonic convulsions requires revision. This is more particularly the case, because some physiologists and clinicians tend to regard tonic and clonic convulsions as functions of different structures in the central nervous systems. Those who are inclined to question the proposition that essentially there is no difference between clonic and tonic convulsions are referred to the electro-myographical studies of Cobb.* In this investigation Cobb shows that the concomitant electrical changes are absolutely the same, the difference merely being that the 70 to 90 action currents per second occur in clonic convulsions in groups or showers, while in tonic convulsions they are continuous.

* S. Cobb, *Brain*, 1924, p. 78.

CHAPTER VI

THE INFLUENCE OF A NARCOTIC DRUG, STRYCHNINE, AND ABSINTHE ON THE MYOCLONIC REFLEXES AND FITS

§ 1. The Influence of Ether Narcosis on the Myoclonic Phenomena.

As an example of the effect of ether narcosis on the myoclonic phenomena, Protocol 15, on Cat 201, is given, because in this case the animal demonstrated myoclonic tactile and acoustic reflexes normally without the administration of any drugs. Such an animal, therefore, afforded a good opportunity for studying the effect of ether narcosis. Other observations made on this animal were also important, as, for example, the duration of the latent period after strong and weak stimuli.

Protocol 15, Cat 201.

21.1.10. At 6 p.m., $\frac{3}{8}$ gramme of monobromide of camphor given by the mouth.

22.1.10. Tactile shocks alone seen.

2.2.10. At 10 a.m., $\frac{3}{4}$ gramme of monobromide of camphor given. Both tactile and acoustic shocks recorded in the afternoon.

3.2.10. A number of tracings made. The latent period from a tactile reflex elicited by a touch at the root of the tail was on the average 3·4; from the middle of the back, 2·6; of an acoustic reflex 1·9.

9.3.10. At 6 p.m., $\frac{3}{4}$ gramme of monobromide of camphor given.

10.3.10. Tracings were again made, and the latent period estimated; it was found to be the same as in the first case.

24.3.10. Animal had a severe fit at 9 a.m. The only reason that could be found for this fit was that the animal may have eaten the vomitus of another cat which shared the hutch. This other animal had been sick during the night after having had a dose of 1 gramme of monobromide of camphor.

8.4.10. At 5.45 p.m., $\frac{7}{8}$ gramme of monobromide of camphor given. No effect.

22.4.10. At 5 p.m., 1 gramme of monobromide of camphor given. No effect.

9.5.10. A number of tracings were made of active tactile and acoustic reflexes. Before a fit the pupils were small, dilated during a fit, and again became small after the fit. . Even simultaneously with every spontaneous shock the pupils dilated momentarily.

9.5.10. At 6 p.m., 1 gramme of monobromide of camphor given.

10.10.10. Examination of reflexes, without reinforcement, by means of bromide of camphor or absinthe, before, during, and after ether narcosis. Latency in fiftieth seconds. (See Table on p. 87.)

It appears, therefore, that in this animal, after the narcosis, the conduction in the centripetal direction was the first to recover (compare 10.32).

Furthermore, the knee reflex returned first, shortly after came the myoclonic reflexes of the toes and hindlegs, then those of the forepaws, and finally the acoustic myoclonic reflexes. The first knee and myoclonic reflexes after the narcosis displayed the sudden rise of the myoclonic part of the contraction in the tracing more distinctly than before.

	Time (*a.m.*).	Latency of Reflex.	
		Head Tambour.	*Back Tambour.*
Clap of hands	9.40	—	1·9
Left foreleg	9.42	—	3·0
Left hindleg	—	—	3·9
Right kneejerk	9·45	2·7	2·7
		2·7	2·7
		2·8	1·5
Right idem	10·5	—	2·5
Right foreleg		2·7	3·0
Right hindleg		3·7	3·2
Sacrum		3·6	2·7
Head		1·7	—
Clap		2·2	2·2
Right kneejerk		3·2	2·6
Ether narcosis. Pupils large. No reflex could be elicited. The animal is quite flabby. Uncertain kneejerks		1·7	—
		1·2	—
First brisk kneejerk		—	2·4
Idem			2·4
Idem			2·2
No acoustic nor tactile reflex elicitable			
Lightest tactile reflex		1·3	?
Right foreleg			2·1
Kneejerk			2·3
Idem	10.26		2·3
First tactile reflex of right hindleg. Convulsion of hindleg much more powerful than that of the foreleg	10.27		3·1
Knee reflex			2·3
Idem			2·3
Idem			2·2
Animal somewhat drowsy after narcosis			
Knee reflex		2·6	
First acoustic reflex after narcosis ..	10.31		3·1
Right knee reflex	10.32		2·1
Pupils react	10·32½		
Right kneejerk			2·5
Clap			2·3

The absence of the reflexes (and of the myoclonic fits), observed in a number of animals under the influence of ether narcosis, can only be regarded as being in accordance with the experience of other research workers with regard to the effect of narcosis on the reflexes. Bayliss* proved that the effect of a rise in blood pressure caused by the irritation of a nerve is converted into a fall in blood pressure and therefore a lowering effect.

Sherrington saw a stimulating, increasing effect, on the reflex transformed into an inhibiting effect under the influence of narcosis. Magnus† proved for vertebrates that various reflexes may change in character, according to the position of the animal in space.

* Bayliss, *Journal of Physiology*, 1893, xiv.

† R. Magnus, *Archiv für der ges. Physiologie*, 1910, vol. cxxxiv., p. 567.

Graham Brown* saw an effect on the flexors converted, under certain conditions, into one on the extensors.

In Cat 201 (Fig. 23) and others it was proved that the myoclonic reflexes, exaggerated by camphor monobromide, do not drop out simultaneously during the narcosis, nor do they return simultaneously. After the narcosis, I saw that, without exception, the knee reflex returned, followed first of all, after little or no delay (Fig. 23, 10.18), by the tactile reflexes in the hindlegs (toes); then by those of the forepaws, the nose, and finally by the acoustic myoclonic reflex. It is of importance to remember this sequence when considering what could be the cause of this dissociation. These results appear to be in accordance with the general dictum that, in ether narcosis, first the prosencephalon, then the mesencephalon, then the medulla, and finally the medulla oblongata, come under the influence of the narcotic. This mode of the return of the reflexes is by no means a general phenomenon, for after the epileptic fit—whether this was caused by monobromide of camphor or absinthe—tactile reflexes appeared, as a rule, first in the nose, next in the forepaws and rump, then in the hindlegs, finally followed by the acoustic reflex. In this last point, therefore, there is resemblance between the return of the myoclonic reflex after narcosis and after the fits. After the fit these reflexes reappear in the same sequence, as was described in Chapter II., § 6, p. 42, as a result of drugging a cat which, in normal conditions, was *not* subject to myoclonic reflexes with monobromide of camphor.

Whereas it appears that, as a general rule, the reflexes are very constant as far as the latency is concerned, both before and after the narcosis, yet some important exceptions must be noted. It was seen that, at the beginning of the narcosis, first the reflexes elicited from the head show retardation and finally drop out, and return last of all—long after the reappearance of the knee reflexes and those of the toes of the hind and forepaws. Also, in one case (198), I saw a lengthening of the latency of the first reflexes that were registered after the narcosis, and also of the tactile reflexes provoked from the tail. Later on the acoustic reflex was registered with, however, a normal latency. It would therefore seem very probable that a certain amount of retardation of the reflex may be a rule both at the beginning of the narcosis when the reflexes tend to disappear and when they return at the end of the narcosis. Further, this retardation occurs only during a very short period, so that it is only rarely demonstrable. I could by no means prove this in all cases.

I also frequently saw the latent period prolonged on the return

* Graham Brown, *Quarterly Journal of Physiology*, 1911, vol. iv., p. 287.

of the reflexes, after a fit brought on by the monobromide of camphor or absinthe, but here again I could not establish it as a rule. From the general survey of the evidence I obtained I am inclined to believe that the lengthening of the latent period, after

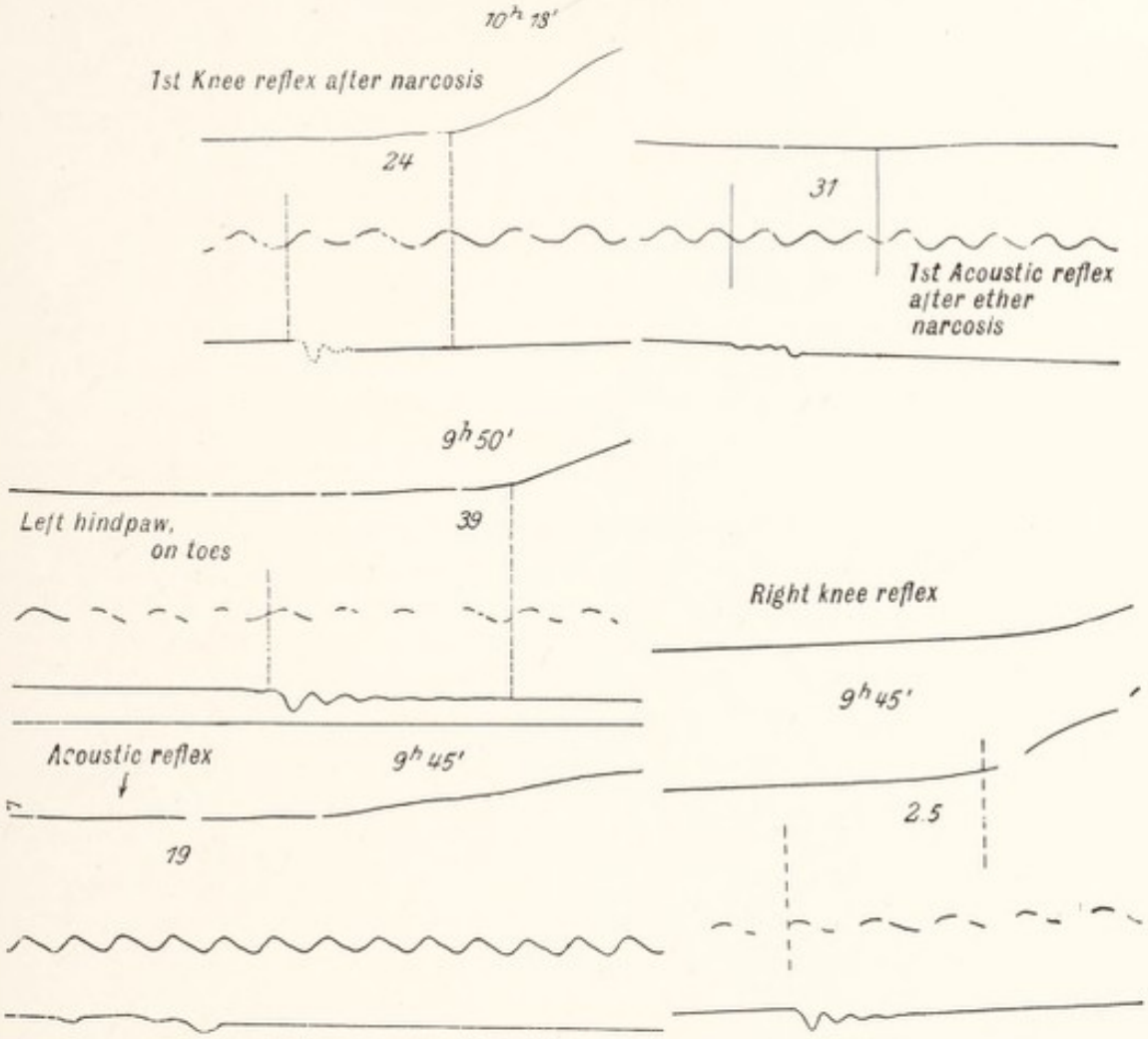


FIG. 23.—CAT 201.

In this cat monobromide of camphor was not required to strengthen the reflexes. Curves read from below upwards, and from left to right. Before narcosis the following data were secured. Tactile reflex from the toes of left hindpaw has a latent period of 3·9; with an acoustic reflex the latent period is 1·9; the knee reflex latent period 2·5. After ether narcosis (at 10.18), the first knee reflex had a latent period of 2·4, while the first acoustic reflex which was elicited much later had the abnormally long latent period of 3·1 fifteenths second.

an epileptic fit, really depends on the same condition as the lengthening of the latent period at the end of narcosis.

Cat 220 affords material for the belief that the centripetal conduction in the spinal cord recovers after narcosis earlier than the centrifugal. In the transitional period after the narcosis the first reflex elicited from the left forepaw showed a latent period of 4·5 fiftieths of a second. This is an abnormally long

latent period. In this case, further, the reflex was limited to a convulsive movement of the head, the limbs and trunk being at rest.

On the other hand, it was frequently seen that after the knee reflex returned, a reaction was got in the hindpaws and the forepaws; but reaction of the hindpaw and rump did not follow on tactile stimulation of the forepaw.

In many experiments with ether narcosis a change was noticeable in the form of the tracing of the recorded movement. Whereas a contraction which before had followed the ordinary course now showed a sharp initial rise.

It may be described as a very sharp myoclonic initiation of the tonic reflex contraction. This is very similar to the sharp rise seen after the administration of strychnine, but is not so clearly shown.

§ 2. The Action of Strychnine on the Myoclonic Reflexes. Fits Resulting from the Combined Action of Strychnine and Monobromide of Camphor.

It has long been known that strychnine intensifies the irritability to tactile stimuli, just as the monobromide of camphor has been shown to do. It is proposed to consider the points of similarity and dissimilarity between the actions of those two drugs.

This is a subject which has already been worked at by Pathault, Trasbot, and Bourneville. As it is not necessary to discuss all aspects of the action of strychnine, the work of Verworn and Baglioni is only alluded to; they maintained that only the sensory elements of the spinal cord were affected by the drug. In the same way the work of Hammet* can only be mentioned. He considered that the action of strychnine was limited to the transition from motor nerve to muscle. This conclusion he arrived at after curare-strychnine experiments. McGrugan, Keeton, and Sloan† admit, with Sherrington and Barenne, the action of strychnine on the motor nerve elements, and note that the spread of the effect, if applied locally to the spinal cord, is more effective caudally than orally.

A big question which shall be left untouched is whether, as Baglioni thought, the tonic action of strychnine spasms are brought about by the reflex movement itself producing a fresh reflex stimulus and so maintaining the mechanism of tetanus,

* Hammet, *Journal of Pharmacology and Experimental Therapy*, 1917, vol. vii., p. 175.

† McGrugan, Keeton, and Sloan, *Journal of Pharmacology*, 1916, vol. viii., p. 150.

or whether, as B. Sanderson and Buchanan state, this view is incorrect.

Husemann* had already classified strychnine as a convulsant drug which at the same time did not produce narcosis, and monobromide of camphor as one which had a narcotic effect combined with the convulsant effect. In this research, so far as could be ascertained, consciousness was not much disturbed during strychnine convulsions. Another important distinction is that in strychnine convulsions the extensor groups of muscles are alone affected, whereas with monobromide of camphor this distinction is not so pronounced—at least, with larger doses. In experimenting with the two drugs it seemed to me that with strychnine the tambour from the back registered stronger and earlier reactions than that from the head tambour. Further, with strychnine, the acoustic reflexes were not so prominent. Further, the pupils with monobromide of camphor are dilated practically always during the action of the drug, even through a very brief spontaneous convulsion, when they dilate very suddenly (compare Cat 217, 19.4.12, p. 27, and Cat 201, 10.5.10, p. 87). With strychnine the pupils are practically never dilated.

Generally speaking there is very little unanimity of opinion shown by those who have investigated the action of strychnine.

A. Waller† found that the latent period with strychnine was lengthened, Mendelsohn‡ that it was shortened. In this respect my own experiments showed that the conditions were not easy to determine. This is shown in the notes made on Cat 219, p. 24.

In my opinion these experiments I have made do not justify a categoric statement as to whether strychnine shortens or lengthens the latent period. As far as the acoustic reflexes are concerned, these are not intensified so early or so potently as the tactile. In some animals, as in Cat 224, I even found the latent period for the acoustic reflex lengthened, with the result that the tactile reflex, especially of the tail, seemed to be shortened.

Further, I found no additional evidence in support of the theory put forward by Bayliss and Starling regarding the conversion of inhibiting into stimulating effects.

Bremer§ came to this conclusion also as the result of a quite different series of experiments.

In contradistinction to the experiments made with monobromide of camphor, I found that with strychnine not only did the

* Husemann, *Archiv f. exp. Path., and Pharmac.*, vol. viii., p. 102.
† A. Waller, *Quarterly Journal of Experimental Physiology*, 1908, vol. i.
‡ Mendelsohn, " Travaux du Laboratoire de Marey," 1878-79, p. 99.
§ F. Bremer, *Comptes Rend. de la Soc., de Biol.*, November 4, 1922, p. 1055.

head react first, as shown by the head and forepaw experiments, but the back movement is seen first after stimuli applied to the tail and hindlegs. In strychnine, therefore, that part which is directly affected reacts quickest;* this is especially the case with the pelvis. This may be assumed to be a proof that the spinal arc reflex is more in evidence in this case than with the monobromide of camphor. This is in agreement with the observation that in slight strychnine poisoning the reflexes tend to be limited to the part of the animal affected by the tactile stimulus (at least, this is more definitely the case than with monobromide of camphor). This is peculiarly well seen in tactile stimuli to the hindlegs. As soon as the strychnine action comes into evidence the beginning of the myoclonic part of the contraction comes into sharper relief than usual against the myotonic part of the tracing. Head and back react at the same time. With larger doses of strychnine, some complete extension convulsions appear, preceded by spontaneous convulsions and some shuffling extension movements of the forepaws. The animal succumbs after the second or third general tonic extension. In contradistinction to the status epilepticus, caused by the monobromide of camphor, the general condition of the animal is little affected by the preceding fits, while consciousness is little if at all interfered with (compare the observation made on 19.4.12 on Cat 217, p. 27). As an example of the curious combined effects of strychnine and absinthe the following excerpt of Protocol 16, Cat 228, is given. Strychnine and absinthe in their action seem to interfere with one another, although, like strychnine and monobromide of camphor, they also support one another.

Protocol 16, Cat 228 E. Black back, white breast.

25.9.12. At 6 p.m., 0·25 gramme of monobromide of camphor. No effect.

14.10.12. At 6 p.m., 0·25 gramme of monobromide of camphor. No effect.

9.11.12. Yesterday 0·75 gramme monobromide of camphor. Last night a fit. At 9 a.m., spontaneous and acoustic convulsions. Appetite good. Is lively.

29.11.12. 6 p.m., 0·75 gramme monobromide of camphor. In the night following this a fit.

30.12.12. 5.30 p.m., 0·75 gramme monobromide.

31.12.12. In the night two fits. Is lively. Had the whole morning spontaneous fits. 2.30 p.m., 2 c.c. strychnine injection of $\frac{1}{10000}$ per cent. At 2.45 p.m., still 1·5 c.c. At 3 p.m., 2 grammes absinthe, equally subcutaneously.

A slight reflex followed by three spontaneous shocks.

After this came a fit as the result of the combination of strychnine and absinthe. During the fit clonic contractions, due to absinthe, were followed by tonic convulsions, when the hindlegs were extended backwards, the forepaws forward.

* Exceptions to this rule occur. This is especially the case after a tactile stimulus to the forepaws, where the back tambour is the first to react.

Consciousness was retained throughout the fit. The corneal reflex was present, while the tongue was discoloured, and became blue, almost black. The recovery after the fit was instantaneous.

The hindlegs were paralysed for some time. A few myoclonic shocks succeeded the fit, after which the animal was completely discharged. At the same time the movement of the back stopped. The hindlegs were paralytic for some time.

11.3.13. ¾ gramme of bromide camphor given at 6 p.m. A fit at night.
12.3.13. Ulcer on left hindleg.
1.3.13. Slight tactile reflexes in the morning.
29.3.13. Animal quite recovered from the ulcer.
8.4.13. At 12 a.m., ¾ gramme of bromide of camphor given. Fits during the night.
28.5.13. At 1 p.m., ¾ gramme of bromide of camphor given.
29.5.13. Fits during the night, slight tactile reflexes next morning.
31.9.13. ¾ gramme of bromide of camphor given at 10 a.m. No effect.
3.10.13. Animal operated on.

Epitome.—In this case tactile reflexes occurred first and were followed by acoustic. The condition of the pupils and the fur, together with the exaggerated nervous irritability present two hours after the administration of the strychnine-absinthe dose, heralded an absinthe fit. The astonishing thing was that, in spite of these prodromal symptoms, a typical strychnine seizure followed. This was shown by the discoloured tongue, the unaltered pupils, and the conservation of consciousness.

As this is the only animal who recovered from so severe a strychnine fit, and on recovery seemed completely discharged, I am inclined to believe that the strychnine stiffening which occurred before the absinthe fit could develop had a discharging effect similar to that of an absinthe fit. This interpretation of the case necessitates the conclusion that strychnine and absinthe given in such proportions had a cumulative effect, and that the reflex charge of both toxins may be discharged by an absinthe fit or a single convulsive extension fit typical of strychnine poisoning.* From the evidence of this experiment there arises the question of the possibility of a moderate strychnine charge induced by a very small dose being discharged by a single strychnine fit.

Protocol 17, Cat 226. Black, with a black and white breast.
18.9.12. At 6 p.m., 9·5 grammes bromide of camphor given. No effect.
5.10.12. At 9 a.m., 0·5 gramme bromide of camphor given before a meal. No effect.
25.10.12. 6 p.m., 9·75 grammes bromide of camphor given. No effect.
16.11.12. 6 p.m., 9·75 grammes bromide of camphor given. No effect.
2.12.12. 6 p.m., 9·75 grammes bromide of camphor given. No effect.
17.1.13. 6 p.m., ⅞ gramme bromide of camphor given. No effect.
20.1.13. At 2.14 p.m., injection of 2 syringes of absinthe, ether narcosis, animal retched.

* Loss of consciousness appears therefore not to be essential to the discharging effect of the fit, a conclusion to which also other observations lead: discharge by a series of myoclonic shocks (p. 48), or incomplete fits (pt. iii., ch. vii., § 4), violent muscular movements (pt. iii., ch. ix., § 3) or a fit of fury (pt. iii., ch. vii., § 1, and ch. xi., § 7).

	Time (p.m.).	Latency of Reflex.	
		Head Tambour.	Back Tambour.
Right foreleg		2·3	2·0
Middle back		2·1	2·3
Left foreleg		1·7	3·0
Middle back	2·30	1·7	
Clap	2.36	2·4	2·8
Clap		2·2	3·0
Ether narcosis (slight)	2.43		
Right hindleg	2.40	3·3	4·0
Left hindleg		2·7	2·8
Right foreleg		2·8	3·0
Wakes up from slight narcosis			
Left foreleg		2·5	3·0
Clap		2·4	3·0
Right foreleg		2·7	3·1
Left hindleg		2·7	2·9
Two spontaneous convulsions and then a fit when recovering ..	2.53		
Two injections of strychnine ..	2.56		
Right foreleg	2.58	5·0	2·6
Left foreleg		2·2	3·2
Absinthe fit. Right foreleg ..	2.59	2·2	2·7
Right foreleg	3.0	1·8	3·0
Right foreleg	3.8	2·3	2·8
Right hindleg		2·3	3·0

Now strong myoclonic reflexes. Tonic extension of forelegs as first strychnine symptom

Three more injections of strychnine	3.10		
Soft clap		3·6	
Soft tick on right hindleg		2·7	3·2
Absinthe fit	3.15		
Right hindleg	3.16	2·4	
Absinthe fit	3.17		
Clap	3.20	2·2	2·2
Idem		2·1	2·1
Idem	3.26	2·2	2·5
Absinthe fit	3.28		
Right foreleg		2·5	2·3

3.29 p.m. Beginning like absinthe fit, but immediately followed by strychnine cramp, in which no separate convulsions are to be seen in the tracing. 100 grammes warm milk administered per os.

Right foreleg	3.38	2·0	—
Lelf hindleg		2·8	
Right hindleg	3.39	2·5	3·0
Left foreleg		2·5	3·0
Clap		2·5	3·0

3.41 p.m. Beginning of a fit like an absinthe fit. Immediately followed by stiffening, with blue tongue, as in strychnine.

Left hindleg	3.41	3·1	—
Left foreleg	3.50	2·7	(slight)
Clap	3.51	2·5	—
Tick on nose	3.51½	2·5	—

3.52 p.m. Weak stiffening cramp, with hindlegs stretched backwards as with strychnine, in which animal died.

Epitome.—As a result of four hypodermic injections of strychnine this animal, who had reacted badly to bromide of camphor, had exaggerated reflexes. On the tracing taken from this animal the characteristic strychnine nose appears.

The movements of the back were pronounced, but that of the head were very slight.

After the animal had two hypodermic injections of absinthe on 20.1.13 it displayed exaggerated myoclonic reflexes. When the animal woke up from the slight narcosis it had a fit. Two injections of strychnine were given, exaggeration of the myoclonic reflexes followed, and after a short interval of some three minutes, an absinthe fit occurred. Three more injections of strychnine were given, after which the animal had an absinthe fit (within twenty minutes of the injection) followed by two strychnine "stiffenings," after the last of which the animal died.

As the same dose of strychnine was given to the cat on 31.12.12, and it was shown that the animal had little tendency towards fit, the effect of the second administration of strychnine illustrates the cumulative action of the drug. Gurber found an adjuvant action to strychnine with picrotoxin.

§ 3. The Action of Absinthe.

Among epileptogenous drugs, the essence of absinthe has long attracted the attention of both French and English workers. We owe much of the available knowledge of the action of this drug on different types of animals to the early workers, more especially to Magnan.* He found that intravenous injections were the quickest method of producing "secouses" of the muscles of the head, neck, and forepaws in dogs. This phenomenon was followed by the development of fits and symptoms of delirium. In the delirious stage warm-blooded animals displayed tonic extension, except in birds where opisthotonos and falling to one side were seen. It was found that the vessels of the fundus dilated when convulsions begin.† If an opening has been made in the skull the brain is seen to be congested, and tends to protrude during the convulsion. Further, it was noted that the temperature rose with every fit. Magnan concluded from the observations that the loss of consciousness which accompanies the fit cannot be due to cerebral anæmia. Another point brought out by this worker was that after section of the medulla, about the level of the twelfth

* Magnan, *Achives générales de Physiologie*, 1873, p. 125, "Recherches sur les Centres Nerveux," Paris, 1876.

† I noted the same thing in a cat during a bromide of camphor fit. The fundus was kept constantly under ophthalmoscopic examination and the vessels were seen to contract suddenly when the animal died.

cranial nerve, alternate convulsions were seen in the head and hinder part of the animal. This observation was in direct opposition to the view expressed by Kussmaul and Tenner, that the only centres for epileptic convulsions lay in the pons and medulla oblongata.

Cadéac and Meunier,* Horsley, Boyce, Russell, and Graham Brown, investigated the influence of certain lesions of the central nervous system upon the incidence of fits; this subject will, however, be dealt with later.

Fr. Franck and Pîtres both concluded that absinthe, like strychnine, intensified the irritability of the motor cortex.

My own observations have convinced me that the essence of absinthe is a valuable epileptogenous drug. Intravenous injections of this drug will produce in a very few minutes the same series of phenomena which have been described as occurring after the administration of bromide of camphor by the mouth.

The only difference being one of time—with absinthe the result occurs in a few minutes, while with bromide of camphor several hours must elapse. With absinthe, as with bromide of camphor, the tactile reflexes are first enhanced, then the acoustic reflexes, after which come a series of shocks eventually followed by complete fits. The fact that the temperature rises under the influence of absinthe, while it falls after bromide of camphor, contradicts the supposition that the lowering of the temperature might play an important part in the bromide of camphor fits.

Absinthe has a very definite effect on consciousness, the injection of even a very small quantity will produce a certain degree of dazedness. There was no special characteristic in the automatic movements after a fit to distinguish either the absinthe or the bromide of camphor fit.

It was particularly noticeable that the pupils dilate under the influence of absinthe just as they do with bromide of camphor, the dilatation in both cases increasing until a fit has supervened, after which they resume their normal appearance. The pupils seem less sensitive to light immediately before and after a fit.

In Chapter II., § 6, some protocols are given of cases of cats poisoned with absinthe. Among these Cat No. 217, p. 26, and Cat No. 219, p. 24, are especially worthy of consideration. In the case of the first cat enhanced reflexes were present normally—*i.e.*, without the administration of any drug. Both these cases, as well as many others, show that there is definite and constant alteration of the latent periods as the effect of absinthe. In the case of Cat 217, however, it was striking to find on one occasion (20.7.11) a lengthening of the latent period from 2·6 to 4·0 fiftieths

* Cadéac and Meunier, *Lyon Medical*, 1889, vol. i., p. 443.

second if a spontaneous shock occurred immediately before (a fraction of a second) the provocation of a reflex. This phenomenon was also observed in cases of bromide of camphor poisoning and is physiologically strongly suggestive. Under analogous circumstances in the heart an extra contraction of the auricle before the expiration of the refractory period may result in the interval between the auricular and ventricular systoles being lengthened.

Occasionally the lengthening of the latent period is more pronounced when a record is made of the first reflex after a fit.

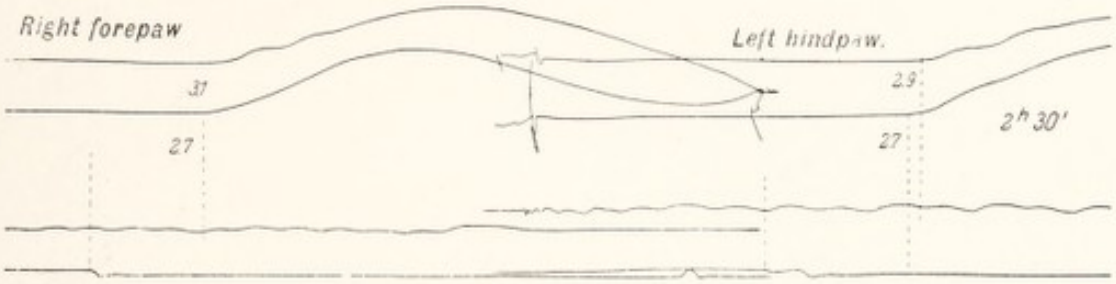


FIG. 24.—DISSOCIATION OF THE TRACING. NOSE FORMATION UNDER THE INFLUENCE OF ABSINTHE, SHORTLY BEFORE A FIT.

Protocol 18, Cat 240. This animal was given ¾ gramme of bromide of camphor in its food at 6 p.m. on 31.10.1911. Next day it only showed moderately enhanced reflexes. At 10.10 a.m., ⅔ gramme of absinthe was given, and at 11.20 exaggerated reflexes were registered. At 11.22 a fit occurred. In this case the reinforcement of the bromide of camphor by absinthe was very evident. At 11.24 the first reflex, also of the right forepaw, was registered, the latency being 4·5 (fiftieths of a second). A minute later the same reflex was again elicited, the latent period was normal (see Fig. 17, p. 75).

With absinthe as with bromide of camphor, the moment of wakening from sleep or of emerging from an anæsthetic, are the times at which a myoclonic fit is most likely to occur (see Cat 226, p. 93).

In one case, Cat 240, where ¾ gramme of monobromide of camphor had been given, the reflexes were exaggerated, but the tracings were of the smooth character one is accustomed to get in such a case. When, however, 2 grammes of absinthe were injected subcutaneously, a change in the character of the tracing was seen within five minutes (see Fig. 24), where two, three, and four "noses" are seen. This certainly proves that it is absinthe which particularly predisposes to this variety of dissociation in the tracing. In another similar case prolongation of the latent period was seen as a result of the administration of absinthe.

CHAPTER VII

SUMMARY OF THE REFLEX AND EPILEPTIFORM PHENOMENA DESCRIBED AND THEIR PHYSIOLOGICAL SIGNIFICANCE

THERE is a group of reflexes which has been little studied and yet is common among undomesticated, warm-blooded animals. These reflexes involve both extensors and flexors of the trunk and extremities. They are elicited by some unexpected touch or an unexpected noise. Richet and Broca described those reflexes in dogs after they produced exaggeration of the reflexes by giving chloralose. The unco ordinated "start-reflex" of L. Cushny,* which involves extensors and flexors, and which is usually intensified with strychnine, may be regarded as identical with the phenomena now described as "myoclonic reflexes." To a certain extent the "Klopfreflex" of German observers is a myoclonic reflex, but not completely, because it is evoked by stimulation of the periosteum, whereas the true myoclonic reflex is evoked by a touch on the skin or fur, or by a sudden noise. The periosteal and tendon myotatic reflexes, clinically so important, may be looked upon as related to the myoclonic group of reflexes. This fact is demonstrated by the latent period of the tendon and periosteal reflexes, by the characteristics they display in ether narcosis, after cerebral lesions, and also during an epileptic fit. It is interesting to find that a normal epileptic reaction, as described by Rosett, corresponds with the phenomenon here described as a myoclonic reflex.

Such reflexes, when recorded graphically, show at first a rapid myoclonic movement, followed by a slower myotonic element. Such a tracing is very clear if strychnine be administered, and also in the prodromal period of an epileptic fit, in an experimental animal. In the cases of two patients suffering from myoclonic epilepsy, a similar change in the tracing of the knee reflexes was seen during the periods preceding the fit, when spontaneous shocks occurred.

Where no method of chemical reinforcement is used, it is very rare to get tactile myoclonic reflexes in the ordinary domesticated cat; on the other hand, the acoustic reflex is rarely absent. Whether the stimulus be slight or strong, these reflexes remain

* Cushny, *Quarterly Journal of Experimental Physiology*, 1919, vol. xii., p. 153.

regional in extent, and may even be limited to the flexor or extensor muscles of an extremity.

Under the influence of bromide of camphor or absinthe, the irritability increases, and the convulsion may spread over the entire musculature, while reflex after-discharges (Sherrington), with their own rhythm, may also occur.

Spontaneous convulsions also occur, which seem to be quite independent of any stimuli. A series of such convulsions is accompanied by dilatation of the pupil, and may be followed by a myoclonic epileptic fit and loss of consciousness. Such a fit is accompanied by dilatation of the pupils, salivation, probably enuresis. In short, such a fit is exactly comparable with the myoclonic epileptic fit in the human being.* A fit of this kind, when examined graphically, is found to have at first a phase when the individual convulsions follow very rapidly one after the other at a rate of 10 to 15 per second. Later the single separate convulsions begin and are gradually separated by ever increasing intervals. At one point, when the toxic influence is at its maximum (apparent by the dilatation of the pupils and certain psychical phenomena), the respirations become more frequent, while, in cats, automatic movements occur, and monkeys give evidence of hallucinations. After one big fit, the animal is often discharged (*i.e.*, appears to be detoxicated), consciousness returns, the coat becomes glossy, the pupils become normal, shocks do not occur and the appetite is quite normal. Where the intoxication is more profound, a second or third fit may occur. It is noticeable that the reflex irritability increases before each fit, but decreases immediately after. The general observation has been made in the case of the functions of the central nervous system that every reflex paves the way for the next, or recurring, reflex. This observation applies more directly to the regional reflexes, and is also applicable to the myoclonic after-discharges and fits.

In the phenomena described above—*i.e.*, enhanced myoclonic reflexes, reflex after-discharges, spontaneous shocks, series of shocks, finally the fit—the gradual curtailing of the refractory phase is the characteristic feature. This phase of non-reaction after a reflex lasts for several seconds in normal cats and in cats which have had a very small dose of some reinforcing drug. During this period it is impossible to evoke a myoclonic reflex. It is this phase which is so drastically curtailed in the progressive stages of the phenomenon, culminating in a fit.

An interesting point in the latent period for myoclonic reflexes is the constancy of the period under different circumstances. For acoustic stimuli the latent period is always short, shorter than

* "Epilepsia," 1911, vol. ii., p. 161.

for any other reflex examined by mechanical methods. In the case of the tactile reflexes Rosenthal's law holds good—that the greater the intensity of the stimulus, the shorter the latency—but for the acoustic reflexes, the reverse seems to be true. The stronger the stimulus, the longer the latency. This suggestion is however made tentatively, as all sources of error could not be excluded. Evidence accumulated in this research would suggest that shortly before an epileptic discharge a certain lability of latency is present. Probably this fact, together with a refractory period shortened to a minimum, is typical of the sensory-motor apparatus before a fit. After a fit the latency is lengthened; this is also seen after narcosis. Apart from these special conditions, the latency of the myoclonic reflexes is very constant. Piéron found the same to be true of the knee reflex.

It seems difficult therefore to explain a myoclonic epileptic fit except as a method of discharging an organism from the influence of a toxic substance. It is a phenomenon capable of being examined by physiological methods. The myoclonic epileptic fit is to be conceived of as a special complex reflex after-discharge, depending upon certain associated conditions and important as a detoxicating agent. The useful effect of such a fit is quite different in extent and character from the regional myoclonic reflex which is its starting-point. There are transitional conditions between the physiological reflexes and pathological phenomena which must be examined. The connection existing between these transitional conditions and lesions of the central nervous system requires to be established. It would appear that under the influence of certain nerve poisons phenomena appear which are transitional in character between the myoclonic reflex and the myoclonic epileptic fit.

A parallel condition is described by Graham Brown as the relationship between the scratch reflex and the special form of cramp described by Brown-Séquard.

The myoclonic reflexes cannot originate in the cortex, because the latent period is too short. Novi and Grandis* and Franck and Pitres demonstrated that reflexes originating in the cortex have a much longer latent period. Franck and Pitres showed in their experiments that the cortex only plays a certain part in the production of fit-like phenomena. The convulsions which they describe as first tonic then clonic, they consider originate in the subcortical centres. They agree with Albertoni that the convulsion spreads, *e.g.*, from the right forepaw onwards to the right hindleg, left hindleg, left forepaw. Fuchs also agrees with this observation, and the evidence collected in this research further supports this conception.

* Novi and Grandis, *Rivista sperimentale*, 1887, vol. xiii.

Physiology teaches little about the structures in the central nervous system which serve as centres for these convulsions. Harnack described phenol convulsions in the leg as occurring after section of the sciatic nerve; other writers described the tremors occurring after carbolic acid poisoning as being stopped by section of the crossed crus-cerebri. Cold shivers have also been described as ceasing after the same operation.

In the pharmacological literature the only observations which may be referred to here are those of Turtschaninow on santonine. With santonine the convulsions are somewhat similar to those got with monobromide of camphor. At first the animal has extension convulsions, then general stiffening, finally epileptic fits, at first tonic then clonic. In no other epileptogenous drug was the discharging effect so clearly seen as with the monobromide of camphor and absinthe.

In many ways the phenomena exhibited by animals under the influence of monobromide of camphor or absinthe are comparable to the myoclonic epilepsy in man. In patients under certain conditions and at a certain age, reflex shocks and spontaneous shocks occur at the moment of wakening or of falling asleep. After a series of such shocks, probably extended over several days, the patient has a fit, after which he is in a condition of discharge—*i.e.*, no reflex can be elicited.

In many cases these reflex shocks will occur when the patient is in bed or just getting up and increase in violence up to the fit, which is the climax; after this the patient may have freedom from all reflex shocks for days, or even weeks. After a time the shocks reappear and the cycle is again gone through (perhaps it is better to call such shocks spontaneous shocks, for no stimulating factor can, in many cases, be recognised). Once fits occur regularly and fairly frequently, the shocks become less prominent, while the tendency to have fits steadily increases. The difference in the sequence of the phenomena in man and the experimental animal is that in man the spontaneous shocks appear first, while in the animal, very distinct reflex shocks precede the spontaneous shocks. It is well not to attempt to draw too close a parallel between the condition in man and in the experimental animals. In the experiments made on animals it was not uncommon to find that early in the case, when the reflexes were exaggerated, only a local convulsion was produced by a tactile stimulus. Thus a touch on the forepaw would induce reaction only in the forepaw. In man such a phenomenon seems very rare indeed.

It must be realised that clinical observation, without some physiological knowledge of the condition, is not sufficient.

This is evident from the fact that Lundberg, who gives the most explicit description of myoclonia in man, described the senso-clonic reaction (*i.e.*, reflex shocks after a sudden noise) as a regular symptom, but it is evident that what he really had to deal with were the exaggerated tactile and acoustic reflexes. In the same way it is not surprising to find that the changes in the condition of the knee reflex, which must accompany the condition of myoclonia, have been overlooked by clinicians.

Among patients the same diversity of symptoms is met with as with experimental animals. In the normal individual, the myoclonic reflexes are little, if at all, developed. This is the same in the domesticated animals. In both, however, there may be a normal, transient, slight increase of irritability on falling asleep or when awakening. This is a point I have frequently to give prominence to, for these periods of the daily cycle are the chosen moments for early manifestations of epileptic phenomena. It is interesting to note that Landois and Zwaardemaker, working on quite another subject, noticed this increased irritability at the moment of falling asleep.

Although the action of monobromide of camphor and absinthe are much alike, yet they are not exactly the same. Other drugs of the epileptogenous class exercise very diverse influences on the tactile and acoustic reflexes, the groups of muscles involved, the order and sequence of phenomena, the occurrence or absence of such symptoms as loss of consciousness, psychical disturbances, and so on. Turtschaninow's work, which has already been referred to, would illustrate this. The action of strychnine described in Chapter VI., § 2, shows that consciousness, in this case, is not lost, while the fit phenomena show little resemblance to myoclonic phenomena, apart from the dissociation of reflex movement immediately before a fit. This is also seen with absinthe. The effect of ether narcosis is peculiar, in that it causes the reflexes to disappear in a certain order and reappear in the same order.

I take it that there is a special affinity between certain drugs and certain reflex phenomena—*i.e.*, one drug affects one group, another drug another group. It is conceivable, for example, that monobromide of camphor and strychnine act upon different elements in the reflex arc (perhaps, as Baglioni suggests, on the motor or sensory elements), and in so doing they reinforce each other producing the curiously mixed type of fit.

It was also noted that the character of the myoclonic fit was changed, the tonic-clonic convulsions dropping out entirely, as soon as the condition of nutrition of the animal—*e.g.*, as a consequence of a severe intoxication—had suffered. Loss of consciousness, enlargement of pupils, enuresis, etc., persisted, so that the fits adopted the characteristics of petit mal of man. Under certain conditions one may see in man so-called petit mal take the place of myoclonic fits.

These circumstances suggest the question whether a reflex-complex develops secondarily to the ordinary reflexes so common in birds, fish, and molluscs—that is, reflexes which are common to animals with widely different degrees of development. Is it possible that such animals exposed to certain drugs may develop this new reflex-complex whose function is to protect the organism from the toxin ?

In the introduction to this book it was pointed out how many nerve poisons induced convulsions of one type or another in warm-blooded animals. It is conceivable that the entire nervous system, not only the spinal cord, may play a part in this (hypothetical) phenomenon. In the study of nerve poisons myoclonic reflexes are peculiarly important, for they form the bridge between what is a physiological phenomenon and the quasi-pathological phenomenon—the fit.

Another point of interest and importance is the variation

displayed by the experimental animals in their reaction to the drug. Animals with a natural tendency to myoclonic epileptic fits stand a larger dose than those not so disposed. Further, in many animals, it was possible to fix a dose which would produce one complete fit, preceded by certain phenomena such as exaggerated reflexes and spontaneous shocks, and followed by a shorter period of exaggerated reflexes and general symptoms of disturbance, dilatation of the pupils and psychical symptoms. After this the animal was completely discharged.

Whether the phenomena concomitant to an epileptic fit, such as loss of consciousness, dilatation of the pupils, vaso-motor and psychical abnormalities and occasionally enuresis, are of significance in discharging the central nervous system, I am not prepared to say. Certainly it seems significant that even in a rapidly passing reflex after-discharge and spontaneous shock dilatation of the pupils and slight torpor are observed. It is of course possible that the dilatation of the pupil, which is so constant a phenomenon, is caused by the convulsion itself. It is certainly obvious from these observations that there is great need for careful investigation into the constitutional phenomena, which attend reflex after-discharges. It may also be recalled that in petit mal, which appears to be a condition peculiar to man, these concomitant phenomena are also present—*i.e.*, vaso-motor disturbances, unconsciousness, and dilatation of the pupils. It is important to note that in recovery from a fit, and in the condition of emerging from ether narcosis, there is the same lengthening of the latent period. Further and protracted use of a drug, particularly of bromide of potassium, will produce dilatation of the pupil and chronic torpor, similar to that found in individuals long subject to repeated fits, without the use of bromide.

These physiological observations give the impression that in incipient myoclonic epilepsy we deal with a physiological condition which leads to a pathological one. This certainly is the case where frequent after-discharges and fits have produced alterations, such as permanent dilatation of the pupils, torpor, gastro-intestinal disturbances and segmental disturbance of sensibility.

Viewed from this standpoint the epileptic phenomena come into line with other reflex phenomena with a physiological basis, such as inflammation, pyrexia,* cold shivering, or rigors. These latter reflexes are fundamentally protective, although ultimately they merge into well-recognised dangerous pathological conditions. I submit that an epileptic fit is essentially a protective measure

* Lauder Brunton, *St. Bartholomew's Hospital Reports*, 1871, p. 416, and Stokvis, *Geneesk.*, 1900, p. 284.

on the part of the central nervous system. The epileptic fit, called into operation by some special chemical combination, against which the central nervous system must protect itself at all costs, is from the first a potentially pathological condition of great danger to the organism. In a healthy organism such a protective measure is seldom, if ever, resorted to, but if once permitted to occur it is very liable to recur. Each fit makes it easier for the next, and in a short time the definite pathological condition of epilepsy may be established.

Probably the hiccough reflex exhibits on a small scale a more definite relation to the myoclonic reflex than any other reflex. This reflex occurs only under special circumstances, such as in gastritis. With a certain degree of irritability, the hiccough reflex assumes a clonic character with a very short refractory period, and also shows two, three, or four post-convulsional after-discharges.

All clinicians know how troublesome the hiccough reflex can be, although it undoubtedly must have some useful function. Where a patient has had one attack of hiccough often the slighest error in diet, either as to quality or quantity, may bring on a relapse. Each relapse makes the patient more prone to have another.

The comparison goes even further. To prevent the recurrence of the hiccough reflex the patient is put under conditions which reduce the chances of the needful irritant arousing the reflex. Briefly, effort is directed at giving the patient the opportunity of having a hiccough-free period in which to build up his resistance to the reflex. Exactly the same holds good for the treatment of the epileptic patient. Treatment is directed wholly to securing for the patient a fit-free period in which to build up a quasi-normal resistance to the fits.

The question is raised in the literature on epilepsy as to the possible connection between the fall in temperature produced by such a drug as bromide of camphor and the occurrence of fits.

Magnan, on the one hand, shows that where fits are produced by absinthe, the temperature is higher after each fit. Harnack considers that the influence of bromide of camphor on the temperature is completely dissociated from its epileptogenous action.

In my own researches I have not been able to collect data on the matter which I regard as one of purely academic interest.

Finally the question arises, What is the position of the myoclonic reflex in the animal economy ?

The answer to this question can, in my opinion, be found in the explanation of the significance of tendon-reflexes given by Hoffmann. Hoffmann points out the enormous importance of both the shortening and lengthening tendon-reflexes for the conservation of a certain definite position of the extremities under the strain of a change in weight. For example, if a person is holding a wooden block in his hand in a certain position, if this block be struck with a hammer, the supporting hand would fall down or give way under the sudden added strain, were it not for the so-called tendon reflex. A voluntary counter-movement to

support the added strain is too slow. The reaction time for such a movement in man is 0·15 of a second, whereas the tendon reflex comes into play after 0·015 of a second, and is therefore efficient in maintaining the posture and in correcting for the change in weight and pressure.

The problem of localisation and the question of the influence of reaction and stimulation of various parts of the central nervous system will be dealt with in another section.

PART II

THE INFLUENCE OF LESIONS IN THE CENTRAL NERVOUS SYSTEM ON THE MYOCLONIC REFLEXES AND MYOCLONIC EPILEPTIC FITS

CHAPTER I

INTRODUCTION

It has already been shown in the history of experimental epilepsy that the literature on this subject contains accounts of numerous experiments where the animals received doses of certain drugs, and in addition had been submitted to various experimental lesions of the central nervous system. This method seems to me to be too uncertain and liable to inaccuracies. Physiological and pathological phenomena are involved, while as yet we are ignorant of the simple physiological phenomena in the intact nervous system. It is only after these normal or physiological phenomena are properly appreciated that we may approach the question of pathological conditions. Further, it is only by acquiring exact physiological data that a correct appreciation of what epilepsy really is can be arrived at. All sorts of abnormal muscular manifestations have been labelled epilepsy.

It is only after extensive preparatory work of this kind that it is of value to examine the results of lesions or of stimulation of the central nervous system.

The need for great care and patient and prolonged examination of each experimental case cannot be too strongly urged. There are so many pitfalls for the unwary. An example of such a pitfall is here given. In the pharmacological literature it is frequently stated that after certain lesions, such as after-removal of half the cerebellum, fits of a particular character no longer occur, or can only be induced by large doses of specific drugs. The futility of such a statement is evident, when it is known that an opening made in the skull and through the dura mater will give the same result. In this case the brain is quite uninjured, yet the symptoms are at first the same as when ablation of half the cerebellum has been performed. The results of all isolated experiments must be received with much caution, and are very rarely of great value.

We know from a perusal of the literature that practically all

parts of the cerebro-spinal axis have been described as the focus, or centre, for epilepsy. Clinicians are most persevering in their efforts to localise a centre.

It seems very likely that there is no such thing as a centre associated with fits. It is more probable that a fit is due to the interplay of various complex nerve nuclei, and that it is essentially a physiological process, not an anatomical entity.

It is interesting to note how, during the last few years, the sharp line drawn by Hughlings Jackson and Gowers between genuine epilepsy, which is certainly not localised to a definite focus, and cortical epilepsy associated with a definite lesion has become much less well defined. At the present time many clinicians accept the doctrine of Albertoni and Luciani and assume that all forms of epilepsy are ultimately associated with the motor cortex. Any facts in the case which do not support this theory are either neglected or coerced into agreement. If necessary it is assumed that the epilepsy is associated with lesions due to encephalitis in youth. Here it is interesting to note that no explanation is given as to why these remote encephalitic lesions never leave cicatrices.

A careful consideration of the work dealing with the effort of fixing a centre for epileptic phenomena shows the results to be very discouraging.

The early workers hunted for the centre in the medulla. Later the medulla was abandoned, and the cerebral cortex was examined also with unsatisfactory results. Is it not time to break away from these old and preconceived ideas of a definite anatomical centre ?

In my opinion the centre of the myoclonic reflex is also the centre for the reflex after-discharge—*i.e.*, the epileptic fit—with the additional factor that from the cerebral cortex come facilitating influences which exert a control on the resulting phenomena.

One point with which I am in agreement with the clinicians is in the acceptance of the old definition of Hughlings Jackson of Jacksonian epilepsy as contrasted with genuine epilepsy.

In the former the fit is one-sided, or at least starts from one limb or part of a limb, whereas in genuine epilepsy the fit is bilateral, and is accompanied by unconsciousness and biting of the tongue. In experiments involving lesions to the brain it is important to note whether the resulting fit, if any, is similar to a fit produced bilaterally in the same animal before operation with such a drug as bromide of camphor. *If the fit following the lesion remains one-sided the conclusion suggested is that the operation has thrown some structure or intracentral connection out of action.*

In all the experimental operations on the brain undertaken in this research, the entire central nervous system has been examined by Marchi's method, so as to localise as exactly as possible the lesion and the structures involved.

Graphic tracings have also been taken of all fit phenomena or muscular movements of a peculiar type before and after operation.

CHAPTER II

EXTIRPATION OF VARIOUS PARTS OF THE BRAIN AND THECA

§ 1. The Effect of Ablation of a Part of the Skull and Dura Mater over the Motor Area on the Myoclonic Reflexes, and Myoclonic Epilepsy.

EARLY in this research on the influence of cerebral lesions on the myoclonic reflexes and myoclonic epilepsy in cats and dogs I investigated the effect of simple ablations of the skull, of openings made in the dura mater, and of the removal of the dura mater over a large area. The ablation of the skull was performed aseptically in three cases, one dog and two cats. It did not appear to exercise any important or regular influence on the dose of monobromide of camphor necessary to produce fits. In one case, as shown in Protocol 2, p. 109, it appeared as if big doses of the drug were less active than before.

Protocol 1, Cat J. Small black animal.

25.4.01. A dose of 0·25 gramme of monobromide of camphor was given by the mouth. Within 1 hour the animal had fits so frequently that the stomach was washed out to remove any of the drug still in the stomach.

22.5.01. The bony skull was removed over the greater part of the right hemisphere.

26.5.01. At 3 p.m., 0·25 gramme monobromide of camphor given. There were no fits nor exaggerated reflexes. At 6 p.m. the animal took food.

5.6.01. A dose of 0·75 gramme monobromide of camphor given. After twenty minutes the animal had a severe fit which chiefly affected the left side. The head showed the tendency to turn to the left. In subsequent fits, the symptoms were bilateral.

14.6.01. The wound was opened and numerous openings made in the dura

21.0.01. After a dose of 0·75 gramme monobromide of camphor a fit occurred within twenty minutes, but only affected the left side. This was also the case with four subsequent fits.

Protocol 2, Cat A.

11.5.01. At 11 a.m., 0·375 gramme monobromide of camphor given. At 1.15 p.m., the animal had a severe fit. It panted, was evidently dazed, while the salivation was copious.

14.5.01. The convexity of the bony skull was removed over the right hemisphere. The animal was listless for days.

5.6.01. At 4.20 p.m., 1 gramme monobromide of camphor given. At 7.40, animal had a fit; at 11.20 there was a second fit, also bilateral.

14.6.01. The wound was opened and seven openings made in the dura mater over the right hemisphere. During the narcosis, the eyes were inclined to the left, while contractions occurred on the left side of the body.

20.6.01. At 1.20 p.m., 1 gramme monobromide of camphor given. At 6 p.m., there was a fit, and after the lapse of half an hour, contractions

of the general musculature were seen, but they were much more pronounced on the left. In the evening the animal sat still, but did not eat. A few exaggerated myoclonic reflexes were elicited. Tapping on the back produced a fit, in which the convulsions seemed more marked on the right. The beginning of this fit was not observed. Some hypalgesia was found on the right half of the body.

27.6.01. 1 gramme monobromide of camphor given. No effect.

2.7.01. 0·75 gramme monobromide of camphor given. No effect.

18.7.01. At 10 a.m. 1·25 grammes monobromide of camphor given. At 10.35 a.m., a severe fit occurred involving both sides.

The effect of making openings in the dura mater, as shown by these experiments, seems to be the production of a temporary change of condition, during which the convulsions were more pronounced on the side of the body opposite to the hemisphere over which the openings have been made. It seems probable that the changes in tension in that hemisphere may facilitate the occurrence of convulsions on the opposite side. When the skull is open and the cerebral hemisphere exposed during a fit induced by bromide of camphor, the brain is seen to be much congested and to protrude during a fit. As has been indicated, this effect produced by opening the dura mater is only temporary, lasting probably a few weeks. Further, these experiments show that the removal of the bony skull and the opening of the dura mater evidently do not have an important or lasting effect on the size of the dose of monobromide of camphor necessary to produce fit phenomena.

The following protocols describe cases where the dura mater was removed over the greater part of the cerebral hemisphere, particularly over the motor zone.

Protocol 3, I. Male cat.

20.7.01. The bony skull was removed over the right hemisphere. The motor cortex was stimulated electrically through the dura. The dura mater was removed over the convexity of the right hemisphere.

10.9.01. At 1.30 p.m., 0·75 gramme monobromide of camphor given. At 4 p.m., slightly exaggerated reflexes were got on the right side. These reflexes continued to become more exaggerated, and at 5.30 p.m. there was a severe fit. At the beginning of the fit, the animal walked round in a circle five times.

17.9.01. At 1 p.m., 0·6 gramme monobromide of camphor given. No effect.

1.10.01. At 2.5 p.m., 0·75 gramme monobromide of camphor given. No effect.

8.10.01. At 2.20 p.m., 1 gramme monobromide of camphor given. No effect.

15.10.01. At 2 p.m., 1·25 grammes monobromide of camphor given. At 4.40 p.m., two fits immediately after each other. Fit began in right forepaw.

15.10.01. The dura was removed from the left hemisphere also.

30.10.01. A dose of 0·75 gramme monobromide of camphor given. Slight exaggerated myoclonic reflexes on right side. Animal somewhat dazed.

8.10.01. 1 gramme monobromide of camphor given. No effect.

22.11.01. A dose of 1·5 gramme monobromide of camphor given. After one and a half hours animal was found to be but slightly sensitive to a pin prick. The myoclonic reflexes were exaggerated.

2.12.01. At 2 p.m., 1·75 grammes monobromide of camphor given. No effect. This animal was used for other experiments; it was noticed that in all operations requiring ether, a very small amount was necessary to anæsthetise the animal.

Epitome.—After a double ablation of the dural covering of the hemispheres, over 1·75 grammes of monobromide of camphor—*i.e.*, over twice the ordinary dose—was not sufficient to produce myoclonic fits. Before the operation, 0·75 gramme of the drug had been sufficient. When the dura was removed over the right hemisphere only, the myoclonic reflexes were exaggerated almost exclusively on the right side, and a myoclonic fit began in the right forepaw.

The following experiment, however, seems to show that this necessity for increasing the dose of monobromide of camphor, after removal of the dura, is only temporary:*

Protocol 4, Cat No. 5. Grey animal.

21.7.01. At 2.10 p.m., 9·75 grammes monobromide of camphor given. At 4.30 exaggerated myoclonic reflexes were present.

11.8.01. At 1 p.m., 0·5 gramme of fresh monobromide of camphor given. At 3 p.m., after a few preliminary symmetrical shocks, there was a severe extension fit, the tonic stage being peculiarly prolonged.

20.8.01. The dura was removed over the right motor zone, a good margin being allowed.

26.8.01. At 2 p.m., 0·5 gramme monobromide of camphor given. No effect.

30.8.01. At 2 p.m., 0·75 gramme monobromide of camphor given. No effect. At 5 p.m., no exaggeration of the reflexes had appeared.

3.9.01. At 2 p.m., 1 gramme monobromide of camphor given. Shortly after exaggerated reflexes appeared on the right side. At 2 p.m., there was a fit, which started on the right side and was transferred to the left.

9.9.01. At 8.45 a.m., 1·25 grammes monobromide of camphor given. At 10.30 a.m., exaggerated reflexes seen on the right side, then a fit occurred, followed by several others. At first these fits occurred exclusively on the right side, so that the animal fell to the left. It also made circus movements to the left. Exaggerated reflexes continued on the right side. Several fits occurred during the night.

13.9.01. At 2 p.m., extirpation of a large portion of the dura over the left hemisphere. Faradic stimulation of the cortex showed that extensor movements of the fore and hindlegs were most easily elicited. The frontal sinuses were opened freely. It was noticed that this animal required a comparatively large dose of ether for anæsthesia to be produced. Wound closed.

18.9.01. A dose of 0·75 gramme monobromide of camphor given. No effect.

1.10.01. The same dose was repeated, the drug being finely powdered. No effect.

5.10.01. At 1.30 p.m., 1·25 grammes monobromide of camphor (an old sample) given. No effect.

16.10.01. At 1.30 p.m., 1·25 grammes monobromide of camphor again given, but this time it was fresh.

17.10.01. The cat shared a hutch with another animal who had had several fits during the night. It is therefore not possible to exclude the influence of a certain psychical infection (I have observed this influence on several occasions). At 10.10 a.m., the animal had a severe bilateral fit. It was striking to find that fifteen minutes before this fit the reflexes were scarcely exaggerated. During this fit, some serous fluid exuded

* These observations may help to explain the temporary effect of trephining in the case of certain epileptic patients.

from the wound. After the fit the animal was in the condition of " discharge "; there were no exaggerated reflexes.

30.10.01. At 2 p.m., 1 gramme monobromide of camphor given. The animal remained perfectly well, and ate as usual.

9.11.01. At 2 p.m., 1·25 grammes monobromide of camphor given. No effect.

16.11.01. At 10 a.m., 1·5 grammes of the drug again given. Fits occurred in the evening at 10 p.m. and 11.30 p.m., but were not severe. The animal had been found to be analgesic earlier in the course of the experiment.

23.11.01. At 2 p.m., 1·75 grammes monobromide of camphor given. Salivation seen at 6 p.m. It was insensitive to pin pricks. The reflexes were slightly exaggerated. There were no fits.

2.12.01. At 2 p.m., 2 grammes monobromide of camphor given. At 4 p.m., two hours later, exaggerated reflexes were present. At 5 p.m., a fit occurred, involving both sides of the body equally. There was involuntary defæcation during the fit.

26.2.02. An injection of absinthe given. No effect.

4.3.02. 1·25 grammes fresh monobromide of camphor given. Animal died in status epilepticus.

From these protocols, the conclusion may be drawn that, at least during the weeks following removal of the dura, the dose of monobromide of camphor given by the mouth must be increased to obtain the exaggeration of myoclonic reflexes. It is also noticeable that the exaggerated reflexes are later in appearing than before operation. As a general rule, removal of the dura on both sides produces the most marked results. Cases are met with, however, where the free removal of the dura mater over one motor area diminishes the effect of monobromide of camphor on both sides of the body. It is obvious that in the subsequent experiments now to be described, where removal of parts of the brain takes place, this result, got from removal of the dura alone, must be allowed for. In certain experiments it is also noted that fits occurring at short intervals, even status epilepticus, are cut short when the dura is opened. This is also seen with patients in the operating theatre.

§ 2. **Extirpation of Parts of the Prosencephalon and the Results.**

In many cats the myoclonic reflexes were examined before and after extirpation of the forebrain, including the motor zone.

In all the cases it appeared that on the side of the body opposite to the cerebral lesion the myoclonic reflexes, hitherto present, either disappeared or, in some cases, became very slight and were characterised by a prolonged refractory period. After a dose of monobromide of camphor or absinthe (as a rule the doses of these drugs have to be increased after operation) exaggerated reflexes could only be elicited on the same side of the body as the lesion. If a fit occurred, the same rule was followed—*i.e.*, a right-sided lesion would, under these circumstances, show right-sided exaggeration of the reflexes and fits. If, however, the fit is very severe, the other side of the body is also involved. This is in accordance

with the observation of Fr. Franck and Pitres, who showed that groups of muscle deprived of their cortical motor centre were drawn into the general convulsions occurring in a fit.

Unverricht* admitted this also. I do not think that the convulsions and myoclonic fits at present under consideration should be put in the same category as those elicited by Franck and Pitres with electrical stimulation of the motor zone. I do think, however, that there is a point of similarity here which goes to prove that the motor cortex plays a certain part in the production of myoclonic convulsions and fits. As a rule there was no change in the latent period of the tactile or acoustic reflexes before and after operation. Only in one case did some changes occur, which could not be satisfactorily explained. This case is given in detail.

Protocol 5, Cat No. 205. Black animal.
1.8.10. At 9 a.m., ⅜ gramme monobromide of camphor given.
2.8.10. At 8 a.m., a fit occurred. At 9 a.m., reflexes still exaggerated, but afterwards became normal.
30.8.10. At 6 p.m., ⅜ gramme of the drug given.
31.8.10. Displayed tactile myoclonic shocks.
17.9.10. For the last few weeks the animal showed tactile myoclonic shocks without the use of monobromide of camphor.
8.10.10. Reflexes were recorded, no monobromide of camphor having been given.

Reflex.	*Latency Head-tracing (In fiftieth seconds).*	*Latency Back-tracing.*
Tactile middle back	2·0	2·2
Tail root	2·35	2·35
Right forepaw (toes)	1·8	2·0
Right hindleg	2·5	2·7
Left hindleg	2·1	1·8
11.9 a.m. Clap	1·6	2·5

Ether narcosis began. On emerging from the narcosis three knee reflexes were provoked, first of all with intervals. The back tambour alone reacted.

First knee reflex : 4·0; second : 3·1; third ; 2·8 ;

11·20 a.m. Right forepaw ..	—	3·5 (forepaws and hindlegs reacted)
Right hindleg	—	2·3
Right forepaw	2·7	2·2
Left forepaw, reacted less than right forepaw	—	2·5
First clap which elicited a reaction	2·0	—
Clap	1·5	1·0
Right hindleg	3·4	2·7
Right knee reflex	2·8	2·2

As is usually seen with ether narcosis, the myoclonic reflexes appeared in the hindleg sooner than in the forepaws. First the

* Unverricht, " Epilepsie: Sammlung klinischer Vorträge," 1897.

knee reflexes, then the tactile reflexes of the toes, then the fore-paws, and finally the acoustic reflexes return.

1.11.10. Operation performed on the left cerebral hemisphere (severe hæmorrhage occurred). The grey matter was removed as thoroughly as possible from the left hemisphere. In the afternoon of the same day, the bandage slipped. Later, when eating, it was noticed that the animal turned its head sharply to the left.

3.11.10. Animal was quite well. There was a continuous flow of serous fluid from the wound, which was partly open. It was noticed that after the first few days following the operation the animal always walked to the left. Tactile shocks sometimes present on the left side.

10.11.10. Myoclonic reflexes were present on the left side of the body.

2.2.11. Over the right hemisphere dura mater removed as far as possible. After this the right pupil is wider than the left one.

20.2.11. Circus movement to the left, as before the second operation. 6 p.m., 1 gramme monobromide of camphor given.

21.2.11. Before 9 a.m., a fit. Reflex irritability was greater before than after feeding. In the convulsions after a touch the left half of the body is more involved than the right half.

10.3.11. 6 p.m., ¾ gramme monobromide of camphor given.

11.3.11. 10 a.m., an injection of absinthe given. 10.20, spontaneous convulsions. 10.30, a fit; the right half of the body appears to remain quiet.

Time (a.m.).	*Reflexes.*	*Latency Head-tracing (in fiftieths of a second).*	*Latency Back-tracing.*
11.26.	Left hindpaw	3·0	0
	Left forepaw	2·2	2·5
	Clap	2·2	2·4
	Clap	2·1	—
	Slight clap	2·1	2·6
	Hard clap	2·4	3·1
	Hard clap	2·3	2·7
	Animal becomes more lively.		
	Slight clap	2·2	—
	Slight clap	2·2	—
	Hard clap	2·2	—
	Very slight clap	2·1	—
	Hard clap	2·2	—
	Slight clap	2·3	—
	Left forepaw	2·1	—
	Left forepaw	0	0
	Reacts less and less.		

19.7.11. Since the operation there was hemianopsia of the right side. It was obvious that the animal only saw its food and tried to get it, when it came within the range of the left field of vision. Myoclonic reflex shocks only occurred on the left side of the body. No monobromide of camphor had been given.

6.10.11. Circus movements towards the left were still a pronounced phenomenon (radius 2 to 5 dm.). Occasionally the animal took a few steps to the right or straight ahead. The fits were still exclusively on the left side. In walking, the left forepaw was lifted high.

27.10.11. 1 gramme monobromide of camphor given. Next night it had a fit. After this it ate well.

Time (p.m.).	*Reflexes.*	*Latency Head-tracing (in fiftieths of a second).*	*Latency Back-tracing.*
3.47	Left forepaw	3·4	3·3
	Left thigh	3·0	3·5
	Left forepaw	2·4	2·8
	Left hindpaw	3·4	2·6
	Left knee jerk	3·0	—
	Right knee jerk	2·0	—
4.1	Left forepaw	3·0	—
	Left hindpaw	4·3	3·0
	Left ear	2·0	—
	Left hindpaw	3·3	—
	Left knee jerk	2·7	—
	Right knee jerk	3·5	—
4.30	Another injection of absinthe.		
4.35	No reflex elicitable.		
5.0	Left forepaw	3·7	4·4
5.4	Left forepaw	3·6	4·4
	Left hindpaw	3·6	3·4
	Left hindpaw	3·5	3·5
	Left forepaw	2·8	3·2
	Left hindpaw	3·3	—
5.20	Clap	1·0	1·4
	Left forepaw	2·4	3·0

The animal is dazed. On the right half of the body no reflexes could be elicited.

29.10.11. Animal still had some spontaneous shocks. At 11 a.m., it had a fit.

8.12.11. At 5.30 p.m., 1 gramme monobromide of camphor given. Animal died in status epilepticus. At the autopsy it was seen that what remained of the left hemisphere had undergone softening. This was seen best in the cortex and corpus striatum. After hardening, secondary atrophic changes were found far advanced in the thalamic nuclei (the medial nuclei were least affected). The cornu ammonis which escaped was much enlarged. Nothing was left of the internal capsule. The ganglion habenulæ, Meinert's bundle, the optic nucleus, the corpus Luysii, and the mammillary region were but little changed (Fig. 25). The front part of the globus pallidus had undergone softening. (See article now ready for publication in *Brain*, by the writer).

Epitome of Cat 205.—The myoclonic reflexes, in this case, were recorded graphically at intervals of approximately three weeks over a long period. After the removal of the grey matter over the left hemisphere to a depth of 4 millimetres the effect on the occurrence of fits and reflexes was observed. It was found that this operation did not affect the quantity of monobromide of camphor necessary to produce enhanced reflexes. Further, it was seen that the myoclonic reflexes were elicited easily on the left side—*i.e.*, the side of the operation as compared with those on the other side. The knee reflexes were normal only on the right side. It is interesting to find that, in this case, the knee reflex followed the course seen in ether narcosis. In ether narcosis the knee reflexes disappear after the myoclonic reflexes, but return before them. From a general consideration of the observations

made on this case it was seen that the various lesions had no appreciable effect on the latent period of the reflexes. There were certain exceptional observations, notably those on 3.11.10 and 11.1.11, when monobromide of camphor and absinthe had been given, but on 11.3.11 the latent period was longer than on the earlier date. Again, on 8.10.10, when no drugs were given, the latent period was again prolonged. No explanation is offered to account for these deviations.

FIG. 25.—CAT. 205. ATROPHY OF THE LEFT THALAMUS AFTER EXTIRPATION OF THE PALLIUM (?) AND FOREMOST PART OF THE NUCLEUS LENTIFORMIS AND GLOBUS PALLIDUS OF THE LEFT HEMISPHERE.

Protocol 6, 186 A. Black and excitable animal.

9.7.09. At 10 a.m., ¼ gramme monobromide of camphor given. At 4 p.m., slight tactile shocks in back.

26.7.09. At 5.45 p.m., ½ gramme monobromide of camphor given. At 10 p.m., a severe fit, after which the animal was discharged.

24.9.09. At 1.30 p.m., monobromide of camphor ½ gramme given fat are meal.

25.9.09. Slight tactile shocks observed. At 9 a.m., ⅛ gramme monobromide of camphor given. Numerous reflexes observed and recorded.

4.10.09. The dura was opened freely across the left hemisphere. The frontal pole on the left was removed. Early in the afternoon of same day the cat was walking about and evidently feeling quite well.

5.10.09. Displayed no tendency to fall.

9.10.09. There was a tendency to walk to the left and the dorsal surface of the left forepaw was put to the ground, but the animal did not stumble. Abundant lacrimation from the left eye. The left half of the body, particularly the left half of the head, displayed well-marked tactile reflexes. The animal ate well. There was a certain insensibility to pain; for example, the paw was not immediately withdrawn if exposed to a candle flame or pricked with a pin. It was evidently in a dazed condition, and no longer appeared intractable.

2.11.09. The left hemisphere was partially extirpated, piecemeal. After four hours, there were circus movements to the left. As regards the actual gait the animal walked quite well when left to itself.

15.11.09. The animal died as a result of a chill. At the autopsy, it was found that the frontal and temporal lobes had been completely removed. The most lateral part of the lentiform nucleus and part of the globus pallidus were injured. The entire pyramidal tract was degenerated. A strand of fine fibres which had degenerated were traced from the affected part of the corpus striatum to the red nucleus (compare article in *Brain*, 1914, p. 410, also p. 60 of the separate publication).

Epitome.—In this animal also the removal of the grey matter of the prosencephalon affects the occurrence of myoclonic reflexes on the opposite side, for they are elicited with difficulty, if at all.

FIG. 26.—CAT 186. DEGENERATION OF THE PYRAMIDAL TRACT.

Protocol 7, 191 B. Tabby cat.

28.7.09. At 5.45 p.m., ⅜ gramme monobromide of camphor given after a meal.

29.7.09. Tactile and acoustic shocks well marked.

24.9.09. At 5.30 p.m., ½ gramme monobromide of camphor given.

25.9.09. Another ¼ gramme monobromide of camphor given before a meal. After the lapse of half an hour animal ate and drank well. At 11.30 a.m. both tactile and acoustic shocks were recorded.

	Fiftieths	*Second.*
Average latent period for 6 tactile shocks of right forepaw	2·1	2·6
Average latent period for 6 tactile shocks of left forepaw	2·2	2·9

15.10.09. At 5.40 p.m., ⅜ gramme monobromide of camphor given. No effect.

16.10.09. At 8 p.m., ⅜ gramme monobromide of camphor given in oil, injected intravenously. At 10 a.m., tactile shocks were observed.

1.12.09. At 5.30 p.m., ¾ gramme monobromide of camphor given.

2.12.09. Tactile and acoustic shocks observed.

7.12.09. Under ether the left cerebrum was exposed and stimulated with the faradic current. Flexion of the hindleg was particularly well shown. The frontal lobe was removed. For the next few days, the animal walked to the left. The right forepaw was peculiarly flaccid, and could be put in all sorts of positions without eliciting any response. Marey's

falling test positive—*i.e.*, the animal fell on its paws. Animal was dazed, yet playful. Right hemianopsia was present. Animal groomed itself badly.

12.1.10. After a meal, ¾ gramme monobromide of camphor given.

13.1.10. No effect.

13.1.10. At 9.15 a.m., ¼ gramme monobromide of camphor given. Animal did not eat, but otherwise seemed quite unaffected by the dose. At 11 a.m., some tactile shocks appeared in the left paws. Circus movements to the left present.

28.1.10. At 6 p.m., ½ gramme monobromide of camphor given.

29.1.10. Animal had a severe fit at 6 o'clock.

10.3.10. At 10.54 a dose of absinthe was injected The animal was found to be less sensitive to a pin prick on the left side of the body. Reflex shocks seen in the left forepaw shortly after the injection. There were no spontaneous shocks. At 11 a.m., reflex shocks were recorded. The animal was dazed, but evidently not quite at ease. On the left side a distinct reflex was elicited in the pinna, but not on the right side.

	Fiftieths	*Second.*
Average latent period 7 times right forepaw ..	2·5	0
Average latent period 10 times left forepaw ..	2·2	2·9

1.4.10. At 5.30 p.m., ⅝ gramme monobromide of camphor given. No effect.

15.4.10. At 5.30 p.m., ⅝ gramme monobromide of camphor given. No effect.

29.4.10. At 5.30 p.m., ⅞ gramme monobromide of camphor given. A fit followed which discharged the animal. This fit began on the left half of the face, passed to the left forepaw, then to the left hindleg, and then to the right side of the body. Towards the end of the fit, the animal jumped round and round to the right.

14.5.10. ⅞ gramme monobromide of camphor given.

15.5.10. Reflex shocks were recorded. At 11 a.m., animal had a fit.

9.6.10. Climbed about well in its hutch, jumped well. Marey's falling test normal. No longer excited.

14.9.10. Late in the experiment it was noticed that the animal made some abnormal movements with the right limbs. They were stretched out as if trying to feel for the floor. These movements occurred so rapidly that they resembled a convulsive movement. Marey's falling test was imperfect at half a metre. When the animal tried to walk quickly it stumbled. It often put the right forepaw in the water-saucer when drinking. Knee reflexes were equal on both sides. On testing the sensibility of the hindlegs it was found that sensibility was better on the right side, but on both sides it was subnormal. The left pupil was noticed to be larger than the right.

Epitome.—In this case, after extirpation of the left frontal brain, the reflexes did not disappear completely on the right side of the body. When they were present, they were somewhat retarded and characterised by a long refractory period. Such reflexes which remain were generally limited to the head. The fits which began on the left side of the body also involved the right side. In this case the autopsy was not obtained, but it is probable that there was injury of the corpus striatum; this is suggested by the protracted circus movements.

Protocol 8, 198 C. Large animal.

14.1.10. At 6 p.m., ½ gramme monobromide of camphor given.

15.1.10. At 9 a.m., ¼ gramme monobromide of camphor given. Tactile shocks appeared first, then acoustic. Then came a fit, after which the animal was discharged.

1.2.10. At 9 a.m., ¾ gramme monobromide of camphor given. Tactile and acoustic shocks were recorded. At 3.17 p.m., 1 gramme absinthe injected. No important change in the latent period of the reflexes.

21.2.10. At 9.25 a.m., ¾ gramme monobromide of camphor given. No effect.

12.2.10. At 10 a.m., Chloral was injected. After this the animal was seen to have a waddling gait.

23.2.10. At 3.15 p.m., 1 gramme monobromide of camphor given. No effect.

17.4.10. At 5.35 p.m., 1¼ grammes monobromide of camphor given. No effect.

2.5.10. At 5.30 p.m., 1½ grammes monobromide of camphor given. No effect.

16.7.10. At 10 a.m., the animal was lightly anæsthetised with ether, and absinthe was injected in the auricular vein. This was done at 10 a.m. At 11 a.m., tactile shocks could be elicited only at the root of the tail. The latent period, as a rule, decreased with the weakening of the reflexes.

3.8.10. At 10 a.m., 1½ grammes monobromide of camphor given. At 3.40 there were exaggerated reflex shocks.

17.9.10. At 10.30 a.m., 1 gramme of absinthe was injected. At 4.41 p.m., the dose was repeated, but intravenously into the auricular vein. Up till midnight animal showed reflex shocks to soft claps; if the claps were loud, the response was not so good. Numerous records were made from this case.

11.10.10. The left frontal portion of the prosencephalon was removed, also that part of the cortex, which on faradic stimulation produced convulsive movements of the face, fore- and hindpaws. The operation was attended by severe hæmorrhage.

12.10.10. Right forepaw was held in an extended position. The left pupil was smaller than the right.

15.10.10. Walked mostly to the left, displayed circus movements. Tactile shocks seen over left side of the body.

24.10.10. Jumped reluctantly out of the hutch. Animal had a fistula at site of operation and the cerebro-spinal fluid oozed out. At 10.40 a.m., a hypodermic injection of absinthe was given in the left thigh. A fit followed five minutes later, while six more fits occurred within the next fifteen minutes. After these fits, the animal breathed deeply, and displayed tactile shocks. Spontaneous shocks were seen occurring constantly in the left forepaw. The reflexes were, as a whole, exaggerated on the left side of the body. Between the fits, the pupils contracted, but during the fits they were dilated.

At 11.20 there was a left-sided fit and again at 11.40 a.m., after which the animal was discharged.

23.11.10. At 10 p.m., ⅝ gramme monobromide of camphor given. No effect; probably because animal vomited. Fistula had closed.

10.12.10. At 3.30 p.m., ¾ gramme monobromide of camphor given. Animal vomited it.

29.12.10. Animal developed nasal and bronchial catarrh and died.

Epitome.—In this animal only left-sided fits were seen after removal of the left frontal portion of the brain, the corpus striatum being intact. There was no difference in the latent period before and after the operation.

In relation to these experiments attention is directed to the different character of the tracings taken from the paws of the cat, during stimulation of the cortex, and stimulation of the subjacent white matter after removal of the cortex; also to the changes in the tracings taken from myoclonic reflexes under those two conditions. Bubnoff and Heidenhain* and Fr. Franck and Pîtres† have described how, after removal of the cortex, stimulation of the subjacent white matter produced convulsions with a shorter latent period and a shorter contraction.

* Bubnoff and Heidenhain, *Pflüger's Archiv.*, 1881, vol. xxvi.

† Fr. Franck and Pitres, *Archives de Physiologie*, 1882.

It has been seen that immediately after the cortex (the grey matter) on one side is removed, it is difficult, if not impossible, to elicit myoclonic reflexes on the opposite side of the body. This indicates that the cortex plays a certain part in the development of the myoclonic reflex phenomena. On the other hand, it is obvious that these reflexes are by no means completely dominated by the cortex, for removal of the cortex does not affect the latent period of such reflexes as may occur later (Protocol 7, on 10.3.10, p. 117). It is at least certain that the mechanism of the myoclonic reflex is quite different from that concerned with convulsions due to direct stimulation of the cortex. It seems fairly certain that although the cortex does exercise a certain influence over the myoclonic reflex, yet the centre for myoclonic reflexes must be looked for lower down in the cerebral axis.

Attention is directed to certain points on which I am not in agreement with the results of other workers. Libertini and Fano* described the myoclonic reflex in the hindleg as exhibiting a longer latent period than the foreleg; with this I do not agree, for if there be any difference it appears to me that the latent period in the foreleg is the shorter. Boyce,† in his writings, described the disappearance of absinthe convulsions on the side of the body opposite, after section of the pedunculus cerebri. This is in agreement with the result got in the majority of my experiments. L. Hill's work is well known, in which he showed that, after removal of the cerebrum, asphyxial convulsions became less vehement. Victor Horsley‡ also found that convulsions in guinea-pigs, due to absinthe poisoning, did not occur, if the cortex of the cerebrum were removed before the administration of the absinthe. S. Cobb and Uyematzu§ found that injection of oil of wormwood caused enlargement of the pupils and fits both before and after decerebration; but after decerebration the dose had to be increased. Pike and Elsberg‖ disagreed as to the necessity of the presence of cortical matter for the production of clonic convulsions, as was claimed by Ziehen.

In my experiments no direct proof is obtained as to the direct influence of the corpus striatum upon myoclonic reflexes and fits. Yet I have observed in the pigeon that for some time after lesion of the mesostriate body on the heterolateral side of the body myoclonic reflexes are absent, to reappear later again. This suggests that also in this function the striate

* Libertini and Fano, *Archives Italiennes de Biologie*, 1895, vol. xxiv., F. 3, p. 438.

† Boyce, *Philosophical Transactions*, 1893.

‡ V. Horsley, Reports Brown's Institution, 1886.

§ S. Cobb and Uyematzu, *Archiv. of Neur. and Psych.*, 1922, vol. vii., p. 660.

‖ F. Pike and Elsberg, *Am. Journ. of Physiol.*, 1925, vol. lxxii., p. 338.

body, which is developed enormously in birds, may replace the prosencephalon of the mammals. I will resist the temptation of discussing the theory that the greater the development of the non-striatal motility (especially of the pyramidal tract), the greater is the development of the myoclonic reflex after-discharge —*i.e.*, epileptic fit. This theory is tempting, especially in the light of the observations made by Féré,* Dexler, P. Clark,† and myself on epileptiform convulsions in birds. Such convulsions show a predominance of the tonic fit and post-epileptic paresis. Such phenomena are possibly connected with the great development of the corpus striatum in birds at the expense of the cortex cerebri.

As regards quadrupeds other than those already referred to, Lafosse‡ found four epileptics in 130,000 solidungulates, while among 25,000 dogs 255 were epileptics. Rabbits also seem to be prone to fits; reference need only be made to the use of rabbits for the hypoglycæmic fit, which serves as a test for insulin. Macleod also pointed out the frequency with which myoclonia is met with in dogs. From a general consideration of these experiments, the conclusion is come to that ablation of the cortex cerebri has no permanent destructive influence upon the occurrence of myoclonic reflexes on the opposite side of the body, neither does the latent period of these reflexes undergo any noticeable change.

§ 3. **The Effect of Lesions of the Cerebellum on the Action of Monobromide of Camphor.**

During a long series of experiments I was repeatedly struck with the fact that, after a lesion of the cerebellum or close to the cerebellum, an experimental cat required a very large dose of camphor monobromide to produce the well-known exaggeration of the reflexes and fits. This was all the more striking since, as Luciani and others have pointed out, lesions involving the cerebellum lead to a rapid diminution in weight. With diminution in body-weight, it would have been natural to expect a fall in the dose necessary to produce myoclonic symptoms instead of a rise. In order to ascertain what particular lesion might be followed by this necessity for increasing the dose of the drug, I have prepared a table showing the nature of the lesion and the dose subsequently required to produce enhanced reflexes.

Space is also given for some animals which were not examined before operation, and to three cases, 212, 211, and 108, which had had an operation, involving the cutting off of the frontal brain. These are for purposes of comparison.

* Féré, *Comptes Rendus de la Soc. de Biologie*, 1894, vol. i., p. 937.

† P. Clark, *American Journal for Nervous and Mental Diseases*, 1904. No. 8.

‡ Lafosse, *Traité de Pathologie vétérinaire*, Toulouse, 1867,

TABLE I.

THE DOSE OF MONOBROMIDE OF CAMPHOR AND ITS EFFECT BEFORE AND AFTER OPERATIONS ON THE CEREBELLUM AND OTHER PARTS OF THE CENTRAL NERVOUS SYSTEM.

Number.	*Dose before Operation.*	*Operation.*	*After Effect.*
78*a*.	0·6 gramme monobromide of camphor in oil. After twenty minutes' salivation, within an hour a fit. Within two hours five fits.	Right cerebellum, part of cortex softened, injury to right bundle of Monakow.	$2\frac{1}{5}$ grammes monobromide of camphor in oil. After some hours status epilepticus.
Cat C.	1 gramme monobromide of camphor in capsules.	Right cerebellum, part of cortex and nucleus dentatus removed.	2 grammes monobromide of camphor in capsule salivation, but no fits. Motor cortex on right and left exposed; some reaction only with very strong current.
69.	1·3 grammes monobromide of camphor in oil. After six hours shock and analgesia; no fit.	Entire cerebellum exposed. Right and left cortex removed.	3·0 grammes monobromide of camphor in oil; after this status epilepticus and death.
221.	$\frac{5}{8}$ gramme monobromide of camphor. No effect.	Needle stabs right and left middle line, through nucleus tecti, into the medulla.	$\frac{3}{4}$ gramme monobromide of camphor, also an injection of absinthe. After this shocks and fits. The animal died after repeated experimental stimuli and opening of the anterior cavity.
70.	1 gramme monobromide of camphor in oil. After five minutes a fit.	Longitudinal incision on right of pons.	$2\frac{3}{4}$ grammes monobromide of camphor per os. After ninety minutes death in status epilepticus.
212.	$\frac{3}{8}$ gramme monobromide of camphor. No effect.	Motor cortex exposed on both sides.	$\frac{1}{2}$ gramme monobromide of camphor. Died in twenty-four hours.
203.	After $\frac{5}{8}$ gramme monobromide of camphor in capsule, myoclonic reflexes exaggerated. After $1\frac{1}{8}$ grammes shocks for a whole day.	Cortex of cerebellum completely removed on right.	$\frac{5}{8}$ gramme in capsule, plus large dose of absinthe ($4\frac{1}{2}$ c.c.) led to fits. Death in stimulation experiment.
118.		Stab through Deiters' region, and through the formatio reticularis on the right at the point of transition of the middle and lateral fillet.	$2\frac{1}{5}$ grammes monobromide of camphor in oil given. Dose was followed by two severe fits and death. During the fourteen days before death, absinthe had been given hypodermically in alternate doses of 1, $\frac{1}{5}$, $\frac{1}{3}$, $\frac{2}{3}$, and $1\frac{1}{5}$ grammes with no effect.

TABLE I.—*Continued.*

Number.	*Dose before Operation.*	*Operation.*	*After Effect.*
86.		Stab in Deiters' region and through the formatio reticularis laterally.	1½ grammes monobromide of camphor in oil given. No fits.
133.		Formatio vermicularis destroyed.	⅔ gramme bromide of camphor in oil given. Animal exposed to cold. Died next day, but had no fits.
139.		Posterior cranial sinus opened. Stab through cerebellum in posterior, longitudinal bundle.	1½ grammes bromide of camphor given in oil. Animal again kept in a cold room. Dead next day.
241.		Cranium opened over right hemisphere. Stab made through posterior commissure.	Died after 1¾ c.c. absinthe, given hypodermically.
241.		Stab through right nucleus tecti and posterior longitudinal bundle.	½ gramme bromide of camphor given in capsule also a hypodermic injection of absinthe. Dead during stimulation experiments.
108.		Stab through middle brain after the right hemisphere had been exposed. Hæmorrhage in both formationes reticulares mesencephali.	1⅔ grammes bromide of camphor given in oil. Animal died in fits.
88.		Stab in corpus trapezoides on right.	2 grammes bromide of camphor given in oil. Died after extensive exposure of cord.
92.		Stab through the medulla, causing lesion of both formationes reticulares.	2 grammes bromide of camphor given. After eight minutes animal had a fit; motor zones were exposed. There were no important changes upon faradic stimulation, except in the forepaw centre. In this centre, on the right side, the left paw was drawn up, but the same current gave no result on the left side.
222.	1 gramme bromide of camphor. Fits and exaggerated reflexes seen next day.	Stab through the right cerebellum and through the formatio reticularis pontis laterally.	2 hypodermic injections of absinthe given. In thirty-five minutes reflexes were exaggerated. This was better seen on the right side. (Experiment repeated three times.)

TABLE I.—*Continued.*

Number.	*Dose before Operation.*	*Operation.*	*After Effect.*
229.	¾ gramme bromide of camphor. No effect.	Lesion involved restiform body and adjacent tissue. After eight days the descending ramus of the eighth nerve and the nucleus of the tenth were pierced.	¾ gramme bromide of camphor. Animal was dead next day.
VII.	0·75 gramme bromide of camphor. After 100 minutes severe fit the left side of the body was most involved.	Lesion in the right cerebellum (nucleus dentatus and Deiters nucleus).	2 grammes bromide of camphor given. Motor zone exposed. Faradic stimulation. No important change shown, but in the centre further forefoot stimulation on the right was followed by movement of the left foot, but no movement followed stimulation of the left centre.

From these experiments it seems indubitable that, after operations involving the cerebellum, the dose of bromide of camphor must, as a rule, be increased to obtain the same effect. By this effect is meant the exaggeration of the myoclonic reflexes and the occurrence of myoclonic epileptic fits. In such cases the most striking changes were seen in cats. In some of these the operation involved the cerebellum only, in others the cerebral cortex (69, 203), while in others the cerebellar nuclei were injured (78, Cat C). In some cats the skull was partially removed, the dura freely opened, but the lesion restricted to the pons and medulla (221, 70, 118, 88, 92).

Careful consideration of these results leads to a conclusion that the exposure of the cerebellum may itself be the deciding factor. The observations of laying bare the effect of the cerebrum have certainly led to this same conclusion. Further, this would be in agreement with the observations made by Bouché.* His observations were made with the use of absinthe, and it is but fair to state that the increase in dose was not so remarkable as it is with monobromide of camphor.

From this the question arises whether the condition of cerebral pressure is really a factor in the occurrence of myoclonic reflexes and fits. Further, do the more striking results following operation involving the posterior cranial cavity depend on the

* Bouché, *Epilepsia*, 1914, vol. v., p. 34.

greater influence of the bony skull and the dural coverings in this part of the brain on the cerebral pressure generally? Another possibility is here suggested. Is it the case that the medullary centres situated within this small cranial cavity are normally, under certain conditions of pressure, the principal factors in the occurrence of reflexes and fits? These questions are formulated, but as yet answers are not forthcoming.

The latter supposition is perhaps best supported by the only case in my experiments of cerebellar lesion in which an inflammatory condition in or near these centres was found to exist. In this case an abnormally small dose of monobromide of camphor caused status epilepticus.

Protocol 9, Cat 35.

8.4.04. The bony skull over the right cerebellum was removed. At time of operation a swelling was seen under the right ear which seemed to grow worse during four weeks following the operation, but there were no symptoms pointing to middle-ear disease. Four weeks after the first operation, the animal was anæsthetised with chloroform-ether, and the dura was freely opened, the cerebellum being pushed to the left with a wooden spatula and *de visu*, the N. vestibularis (or what was taken to be it) was severed.

20.4.04. The animal had still a strong tendency to roll to the right. The eyes were held in a peculiar position; this seems an integral part of the forced position assumed by the animal.

12.5.04. Still walked as though creeping carefully along the ground. Scarcely titubates any more; position of the eyes normal.

At 12.36 p.m., three capsules of 0·125 gramme bromide of camphor given—*i.e.*, 0·375 gramme in all. At 3 p.m. the animal had had four fits, which started on the right side but were not restricted to that side. After the fits the animal fell to the right side. This may have been because the dazed condition of the animal prevented the compensating movements necessary to correct the rolling movements from being performed. The animal died in status epilepticus.

Autopsy.—The Marchi stained preparations were, for the most part, unsuccessful. Further, the traces of the operation were indistinct. There were evidences of lesion in the corpus restiforme where it forms the boundary of the medulla. Fatty degeneration was seen in the N. descendens of the trigeminal nerve and in the region of the bundles of Monakow and Gowers. Higher up, the corpus restiforme was seen to be shrunken, probably due to degeneration. Only a few sections through the spinal cord and pons were well stained. In the spinal cord the bundle of Monakow and the anterior antero-lateral fibres on one side were degenerated. In the pons the mesial fillet was degenerated on one side.

Epitome.—This observation is too incomplete to lay claim to exactitude. I think, however, that I cannot exclude the possibility that in this case a purulent process, starting from the internal ear, had caused the local irritation in the medulla. This may explain the extraordinary susceptibility to myoclonic reflex enhancement by means of the administration of the monobromide of camphor.

§ 4. The Influence of Lesions in the Cerebellum on the Incidence of Fits.

Among the experimental operations involving the posterior cerebellar cavity in cats, a distinction must be drawn between those in which some definite lesion of the medulla oblongata was inflicted during the operation, the cerebellum also being injured; and those operations where the cerebellum alone was injured. In many respects great significance must be ascribed to lesions of the medulla, for lesion of the so-called convulsive centres may occur, and also of the great centrifugal tracts. For this reason attention will be devoted first to those operations belonging to the second group, where the lesion, as revealed by the Marchi stained sections, is limited to the corpus restiforme of the middle and anterior crus cerebelli. It may be said that in no other cerebral operations are there greater discrepancies between the lesion which is intended to be inflicted and the lesion which is actually inflicted. In this area the conditions of brain pressure are very delicate and are very liable to be influenced by hæmorrhage or œdema. There are other possible complications, such as thrombosis in certain vessels, or severe and unexpected hæmorrhage. All these factors tend to complicate the result of what is technically and essentially a " clean " operation.

The first case of this class is No. 203, in which the cortex of the cerebellum was affected almost exclusively. Only a few fibres of the superior crus were degenerated. Next come cases where lesions involved the nuclei, and lastly, lesions involving the medulla and truncus cerebri. In the table a short note has been made, descriptive of the lesion, as revealed by the Marchi stain.

First of all, Case 203 may afford the proof that an affection of the cortex cerebelli exercises a certain influence on the irritability of the contra-lateral motor cortex (both for the mechanical and faradic irritability) It is found to diminish it. On the other hand, no alteration of the bi-lateral character of the fits is seen.

In Cats 79 and 80, the nucleus dentatus in the cerebellum was injured in such a manner that a large number of degenerated fibres were found in the superior cerebellar crus. In this case the myoclonic reflexes on the operated side were more easily elicited than on the other. Further, the myoclonic fits started on this side, and might be limited to this side. It was also seen that other reflexes, such as the plantar reflex, were unequal in the case of Cat 79*a*. In this animal they were better marked on the operated side This point has been also proved by other research workers. Risien Russell found that, after extirpation of a cerebellar hemisphere,

the epileptiform convulsions on the side of the body on which the operation was made are more intense and show less co-ordination than on the other side. In agreement with this observation, the myoclonic reflexes are found more pronounced on the operated side, while the myoclonic fits also start on that side of the body.

In Cat 78*a*, the lesion was more extensive, the truncus cerebri was pierced in its whole length up to the red nucleus, while the whole of the crus superior cerebelli was degenerated. In such a case there were necessarily many complicating factors. In this case the results are apparently not in agreement with those of the preceding case. If, however, it is remembered that through the lesion of the red nucleus on the right side the cerebellar influence from the left side was even more completely cut off than the influence of the right or injured side, the results of the operation *would* seem to be in accordance with the former case. In the same way, in Case 221 (operation involved a stab through the right cerebellum and only left-sided reflexes persisted after), the fact that the formatio reticularis was pierced on the right side (Chapter V., p. 175) should be taken into account. In Cases 239 and 68 the internal capsule or the pyramidal tract was injured on the right side and exaggerated reflexes were seen only on the right side, where the pyramidal innervation was intact. Fits were also restricted to the right side.

In Case 239, where the cerebellar influence was cut off on the right side, while the left side of the body was deprived of pyramidal innervation, the effect was that exaggerated reflexes occurred only on the right side.

Case 68 is also very instructive, because here the uncrossed pyramidal tract and the bundle of Monakow are both injured. As a result the rubro-spinal innervation is wanting on the right side, while the pyramidal innervation on the left side is, to a large extent, lacking. In this case the reflexes and fits appeared on the right side only (Fig. 35, p. 149). From this experiment, therefore, it may be concluded that the pyramidal influence predominates over the rubro-spinal. It is indeed a matter for question whether the influence of the rubro-spinal tract really exists. As a result of these observations, I hold that the conclusion is justified that the cerebellar nuclei or cerebellum is one of the structures, a lesion of which gives a unilateral character to what was previously a bilateral phenomenon. In agreement with Russell, I hold that the ablation or lesion of these nuclei causes reinforcement of the reflexes on the side of the lesion, while the reflex after-discharges or myoclonic fits occur earlier and more completely on this side of the body. The same results followed lesions of the inferior and superior crura cerebelli.

TABLE II.

INFLUENCE OF THE CEREBELLAR LESIONS ON THE REFLEXES AND FITS.

No.	*Lesion in Question.*	*Degeneration found according to Marchi Examination.*	*Condition of the Myoclonic Reflexes and Fits.*	*Remarks concerning Faradic Stimulations, etc.*
203.	(See Protocol 10). Ablation of a considerable part of the cortex from the right cerebellum.	The nuclei remained practically intact.	Reflexes and fits were bilateral. During the fit, the forepaws were stretched right out; after which only left forepaw drawn up, head bent markedly backwards.	Faradic cortex. On the right hemisphere feeble current, on the left cortex strong current was necessary. After absinthe injection, total convulsions (right and left part of the body, dura reflexes ?) could be elicited, even with slight mechanical stimulation of the dura over the motor cortex to the right. The right cortex reacted to the current, longer than the left.
79*a*.	Stab with Probst's needle in the cerebellum (to the striæ acust. ?)	Lesion only of the right cerebellum, including cerebellar nuclei (nuc. dent. and crus cer. sup. partially degenerated).	After administration of bromide of camphor the reflexes in the right paws were more pronounced than the left.	
80.	As above.	As above. More pronounced degeneration in the crus sup. cerebelli.	Right part of the body only reacted, particularly spontaneous shocks on the right. If both paws reacted upon acoustic stimulus, then the right paw preceded by 50 milliseconds.	After exposure of both motor cortices, strong, powerful movements could be elicited both from the right and the left centre, but less from the right side. Fits could not be elicited with powerful faradisation, either from the cortex or from the exposed dorsal part of the spinal cord. Faradic stimulation of upper dorsal part of spinal cord (longitudinally placed electrodes) gave only contractions of the left paw.
78*a*.	Attempt to sever ascending vestibularis connections with Probst's needle.	Longitudinal incision in right cerebellum, and right crus sup. (penetrating to the red nucleus with Forel's fascicles). Degeneration of right corp. restif., ram. desc. N./V., crus. sup. cerebelli and Monakow's bundle (slight).	During the acoustic myoclonic reflexes, the convulsion of the left forepaw was noticeable first, and this contracted most forcibly.	After semi-lateral severing of the topmost dorsal part of the spinal cord (r.) faradic stimulation of the neck part of the spinal cord only gave movements of the left hindpaw.

TABLE II.—*Continued.*

No.	*Lesions in Question.*	*Degeneration found according to Marchi Examination.*	*Condition of the Myoclonic Reflexes and Fits.*	*Remarks concerning Faradic Stimulations, etc.*
68.	Attempt to hemisection the truncus cerebri.	Right cerebellum affected by the hæmorrhage. The cerebral trunk was damaged only in the pons. Degeneration of the r. pyr. bundle and of Monakow's (r.) bundle.	Myoclonic reflexes on the right side of the body only, as also the fits. (Tracing Fig. 29, p. 137).	Abscess formation.
70.	Superficial incision in r. crus cerebelli ad pontem.	R. corpus restiform, r. crus cerebelli sup. and r. Monakow's bundle degenerated.	Reflexes on left side of the body only. Fits began on the left, but later on on the right too.	Rolled to right for several days. Died during preparation for faradic stimulation.
221.	(See Protocol 21, p. 175). Needle stab right through cerebellum.	R. nuc. dentat. and crus cereb. ant. touched and degenerated. In the r. pyr. bundle (*i.e.*, opposite the left in the spinal cord) there were but few degenerated fibres. Through the stab the medial part of the form. retic. was also pierced on the right.	Myoclonic reflexes could only be elicited on the left side of the body. (No fits, on account of speedy exposure.)	Faradic cortex stimulation. R.: every alternate stimulus produced a convulsion on the left. L.: every fifth faradic stimulus produced convulsion on the right. The medulla oblongata reacted on the r.=l.
239.	1st Lesion: Stab in right thalamus opticus. No results observed. 2nd Lesion: Not consummated, because on opening the foramen magnum the medulla was inadvertently damaged.	2nd Lesion: Only the right corpus restiform injured and degenerated ascendingly where it was loosened from the medulla. Left pyr. lateral tract moderately degenerated as a result of the first lesion.	Right side of the body more sensitive to touch than the left paws.	The animal could be induced to rotate and fall more easily to the left than to the right (effect of secondary lesion of the ram. desc. N./VIII.)
VIII.	Right hemisphere of the cerebellum wounded.	Lesion right cerebellum (including nuc. dentatus and Deiters' nucleus).	Very exaggerated reflexes (no record concerning one-sidedness).	Faradic cortex stimulation: from right motor zone much better reaction with weaker current than from left cortex.

Literature contains certain facts relating to the physiological reciprocity between the motor cortex and the crossed cerebellum. Thus Rossi* found that the faradic irritability of the motor cortex diminishes after extirpation of the crossed cerebellum. This is in accordance with my own data supplied by Case 203 (Protocol 10, p. 130), where the lesion was almost exclusively localised in the cortex, and by Case 221 (Protocol 21, p. 175), where the dentate nucleus was injured. On the other hand, R. Russell found exaggerated irritability in the crossed motor zone some minutes after extirpation of a cerebellar hemisphere. My own observations which were that faradic irritability of the motor cortex decreased after ablation of the cortex cerebelli, and also after extirpation of the subjacent cerebellar nuclei, do not tend to simplify the problem of the origin of myoclonic fits.

Further, I found reinforced myoclonic reflexes on that side of the body where the cerebellar nuclei were injured, while at the same time the irritability of the crossed motor cortex was decreased. It can therefore not be assumed that there is a simple relation between increased irritability of the motor cortex and exaggerated myoclonic reflex irritability on the crossed side of the body. This was, however, the view taken by Boyce.† This is shown in the case of Cat 203, where I found a very distinct difference in faradic irritability of the motor cortices (43 and 49 millimetres coil distance) in association with bilateral myoclonic reflexes which were equal on the two sides. In the physiological study of the interdependence of the cerebellum and the crossed cerebrum difficulties in the interpretation of the facts found have been met with more than once. Beck and Bikeles‡ found by measuring the action current on the cerebellum, when thermal stimulation was applied to the cerebrum, that while in most cases the positive effect was crossed, there were cases in which the cerebro-cerebellar influence was prominently homolateral. As far as the anatomy of the cerebro-cerebellar connections are concerned, von Gudden had already noted that in many cases hemicerebral lesion was followed by atrophy of the crossed cerebellum, but in some cases by atrophy of the homolateral cerebellum.

Protocol 10, Cat 203.
25.2.10. 6 p.m., ¼ gramme bromide of camphor.
26.3.10. No effect.
2.4.10. 9 a.m., ½ gramme bromide of camphor. No effect.
22.4.10. ½ gramme bromide of camphor. No effect.
27.6.10. ½ gramme bromide of camphor. 28.6.10. Reinforced tactile reflexes, two fits, after which discharged.
27.7.10. ½ gramme bromide of camphor. No effect.

* Rossi, *Archivio di Fisiologia*, 1912, vol. x., section 3.
† Boyce, *Philosophical Transactions*, 1894, also *Neurologisches Centralblatt*, 1894, p. 466.
‡ Beck and Bikeles, *Pflüger's Archiv*, 1911, vol. cxliii., p. 283.

23.8.10. $\frac{3}{8}$ gramme bromide of camphor. No effect.
9.9.10. $\frac{1}{2}$ gramme bromide of camphor. 10.9.10. Slightly exaggerated tactile reflexes.
29.9.10. $\frac{5}{8}$ gramme bromide of camphor. Moderately reinforced tactile reflexes.
14.10.10. 6 p.m., $\frac{7}{8}$ gramme bromide of camphor. 15.10.10. But little reflex exaggeration.

Time (a.m.).	*Reflexes.*	*Latency Head Tambour.*	*Latency Back Tambour.*
9.41	Narcosis begins. The animal is very playful.	1·7	
9.47	Left knee reflex		2·6
	Nose from above	0	0
	Right knee reflex		2·6
	Right forepaw		2·0
10.0	Paws and nose no longer react. Animal tries to get up.		
10.2	*Entirely under narcotic,* weak.		
	Knee reflex		2·7
	Right knee reflex		2·8 (Very weak).
10.6	Right nose		2·9
10.7	Nose does not react		
	Knee reflex	1·5 (?)	2·5
	Shortly after the knee reflex a proper nose reflex is visible.		
	Right forepaw		1 9
	Right knee reflex		2·4
	The animal comes out of anaesthetic.		
10.18	Right knee reflex	2·3	

28.10.10. 6 p.m., 1 gramme bromide of camphor. 29.10.10. No effect.
16.11.10. 6 p.m., $1\frac{1}{8}$ grammes bromide of camphor.
17.11.10.

	Right forepaw	2·6	3·8
10.1	Right forepaw	1·8	2·9 (Immediately following two successive spontaneous shocks.)
	Left forepaw	2·5	0
	Left forepaw	2·6	3·0
10.12	Acoustic	1·6	2·8
	Clap	2·0	2·6
10.14	Right forepaw	2·6	3·1 (Seems to be discharged.)
11.50	Right forepaw	2·9	1·3
	Left forepaw	0	3·0
	Clap	2·1	3·3
	Some reflex irritability present only after many tactile stimuli on back.		
11.58	Right forepaw	2·8	3·5

6.12.10. Posterior cranial cavity opened. The cerebellum was removed with a spoon on the right side, but a small portion of the left

cerebellum was removed also. In this operation the dura mater was opened freely. The animal revived, but slowly, after the operation.

8.12.10. Could not walk, tended to deviate to the right. Lay on its stomach, forepaws stretched out in front. It pawed the air at times in an uncertain fashion with the left forepaw. Was evidently bewildered mentally, the pupils were dilated. Milk and minced meat were given by the stomach tube.

10.12.10. Ate on its own initiative, but did not walk well. Titubated constantly, when it attempted to walk; it deviated to the right or left.

13.12.10. Was quite well. No forced movements present, but the animal reeled on walking. Was mentally placid.

30.12.10. Still preferred to lie on its stomach. Marey's test was positive. No forced movements present. Left forepaw seemed less sensitive to the candle flame than the right. Both the hindpaws were keenly sensitive to the candle flame and were withdrawn at once, while both forepaws were only withdrawn after four to seven seconds.

4.1.11. Jumped somewhat clumsily from the table. Walked fairly steadily to both sides. If a limb were hooked over the finger, the animal stretched out all its paws easily and co-ordinately with the exception of the right forepaw. If this limb were hooked over the finger, the animal left it in this position for some seconds and only withdrew slowly.

6.1.11. At 6 p.m., $\frac{1}{2}$ gramme monobromide of camphor given. Within two hours the animal had a fit. Immediately after the fit the animal was in the condition of discharge. It purred and seemed quite normal. At 6 p.m., $\frac{5}{8}$ gramme bromide of camphor given.

7.1.11. Animal completely discharged. At 9 a.m., a hypodermic injection of absinthe given in the thigh.

Between 9 and 11 o'clock four hypodermic injections of absinthe were given. The animal panted as if suffering from asthma.

Time (a.m.).	*Reflexes.*	*Latency Movement of Head-tracing.*	*Latency Back-tracing.*	*Latency Head-tracing.*	*Latency Back-tracing.*
9.40	Two acoustic stimuli	0	0 (Ditto	0 within $\frac{28}{50}''$	2·2 interval)
9.42		2·0	2·2	0	0
	Left forepaw	3·1	3·2		
	Right forepaw twice (within $\frac{34}{50}''$)	2·4	2·8	2·9	3·2
	Right forepaw twice Spontaneous shocks	0	3·1		
10.10	Left forepaw twice (within $\frac{34}{50}''$)	1·7	2·5	2·6	3·6
	Clap twice	2·6	2·8	3·3	2·3
10.11	Fit, of which the rhythm was 4·12—7·11—11·3—11—10·10.				
	The animal is in coma.				
	2 claps	1·8	2·5	0	0
	First come acoustic shocks, then tactile shocks, followed by a fit.				
	2 claps (within $\frac{30}{50}''$)	2·6	2·8	1·5	2·7
	Tick right forepaw twice (within $\frac{39}{50}''$)	2·3	4·2	1·2	4·7
	Left forepaw twice ($\frac{26}{50}''$)	2·3	0	2·8	4·0

In the fit at 11 o'clock both forepaws were stretched right out, after that the left forepaw was drawn up, while the right forepaw remained stretched out, head bent well back. The convulsions in the face were bi-lateral.

11.5 a.m. Stretched out and cerebrum exposed, dura mater opened. Contraction of hindleg observed from crossed motor zone: left cortex i=43; from right cortex i=49. From left cortex stronger stimuli required everywhere. Just before an epileptic fit, *general convulsions* could be produced, starting from the motor zone with comparatively weak current. Another hypodermic of absinthe at 11.30. After that, continual spontaneous shocks, on the *mechanical touch* of the motor cortex. Also a short current in the spinal cord (electrodes applied lengthways) produced general shocks in the hind body. During the first five minutes after a fit, such convulsions could only be produced from the spinal cord; and only later on from the cortex. When status epilepticus started, the cortex was no longer irritable (even for i=15); the spinal cord less irritable. Jacksonian cramps could not be elicited at all. During a longer interval between two fits, the irritability of the spinal cord returned first, then that

FIG. 27.—CAT 203. SLIGHT DEGENERATION OF A PORTION OF THE SUPERIOR CEREBELLAR CRUS ON THE RIGHT SIDE.

of the brain. Just before the fit, the spinal cord reacted upon i=48, the cortex upon i=30.

11.25 a.m. Fits grew weaker. The right cortex reacted better than the left.

11.35 a.m. Convulsions could only be elicited from the right cortex. A fit at 11 a.m. showed a rhythm of 3·8—4·2—4·4—4·6—10·8—11.

Autopsy.—A fairly complete series of sections of the brain were made and stained by the Marchi method. The caudal portion of the cerebellum was found to be but slightly injured on the right side only. The nucleus dentatus was free from injury except on the upper side. There was no sign of damage in the sections involving that point where the restiform body disappears under the cerebellum. More anteriorly the superior crus showed degenerative changes in about three-fifths of its fibres (about 120 fibres). The hook-like bundle of Russell, on the left side, was not quite free from degenerative changes. A few fibres of the descending ramus, from the superior crus to the formatio reticularis, showed degenerative changes. The spinal cord was free from degenerative change.

Protocol 11, Cat 239. Small cat.

10.4.14. Right cerebellum exposed. The brain was penetrated with a fine knife in the region of the corpus striatum. After the operation the animal kept the head down and turned to the right. Conjugate deviation of the head and eyes to the right was seen when the head was raised. The animal was able to look to the left, but only for a moment; there was a marked inclination to conjugate deviation to the right. The left forepaw was drawn backwards under the body; this caused a tendency to fall to the left. The left hindpaw lagged behind. Two hours later the animal still inclined to look to the right; occasionally there was a tendency to look upwards and almost backwards. The animal did not rear up.

11.4.14. The animal showed a slight tendency to fall to the left.

12.4.14. Animal walked in a perfectly normal fashion.

13.4.14. The application of the falling experiment of Marey showed considerable deviation from the normal. The animal, however, stepped quite well. It jumped voluntarily from a table, and performed the act very well. Fairly frequently the left paw was put down on the dorsal side. No sign of any forced movements was present.

14.4.14. No rolling to the left was present. The animal seemed normal. The falling experiment, repeated at 1 dm. from the floor, gave a normal result. The left feet still hung over the edge of a table when the animal was put in an appropriate position.

17.4.14. Nothing beyond a slight ataxia of the left feet was seen.

21.4.14. The right side of the cerebellum was exposed, and the foramen magnum opened. Owing to a slip of the instrument the animal's breathing stopped, but with suitable manipulation it recovered. The descending ramus from the eighth nerve was stabbed with a needle. During narcosis it was noted that the right eye was directed downwards. When put on the ground immediately after the operation it rolled to the left side and while regaining consciousness showed a tendency to fall to the left side. The head was slightly rotated, and directed downwards. Scratching movements were made by the forepaws, while the hind feet were tremulous. The head was also tremulous and swayed to the right. When the animal regained consciousness and was able to stand, it was noticed that it had great difficulty in standing at all. It swayed to and fro, and finally fell to the left side. Half an hour later—*i.e.*, at 5.40 p.m.—circus movements were present to the left, with rolling movements to the right. Ten minutes later much the same phenomena were present, except that the animal reared up. Five minutes later the animal showed a distinct inclination to fall to the left. It lay, as a rule, on the left side. An appearance of circus movements to the left was simulated by the fact that in order to prevent itself from falling to the left, it put out its right foot.

22.4.14. Left foot ataxic. Animal walked better, but got very shaky if it attempted to climb. It would not jump, and fell if it were forced to try. It crept along the ground on its belly. It could be rotated to the right or left with equal ease, as it made no resistance. The falling experiment was normal at ½ metre distance, but not with a shorter drop. Later, in the same day, the animal jumped voluntarily from a table, but the hind limbs showed a limp flapping movement. From both right feet definite reflex shocks were elicited; this was not seen on the left side. Rotation of the whole animal was easier to the left than to the right.

24.4.14. At 4 p.m., an injection of absinthe was given. The reflex shocks from the right feet became more active. Reflex shocks could also be elicited from the left feet, and in both the latent period was the same—*i.e.*, 2·3 fiftieths of a second.

A table is given on p. 135 showing the strength of current (distance of coils) with which faradic stimulation of the left motor cortex induced extension of the right hindpaw and of the left hindpaw, with stimulation of the left side of the medulla.

From this table and other experiments it appears that the faradic irritability of both those areas was diminished *after* a *fit*. This diminished irritability was more apparent in the motor cortex at one time, and in the medulla at another.

Time (p.m.).	*Motor Cortex, Distance of Coils.*	*Time (p.m.).*	*Medulla Distance of Coils.*
4.59	22		
(After that epileptic fit.)			
5.0	17		
5.1	22	5.1·5	23
5.3	21	5.2·5	24
5.4	21	5.4	24
		5.5	30
5.6	21	5.6	30
5.7	20		
5.7·5	Fit	5.8	20
5.8	20		
5.9	20	5.10	28
5.11	20	5.11·5	28
5.12	20	5.12·5	27
		5.13	21
		5.13·5	27
		5.14	
		(1 gramme of absinthe injected. Right forebrain exposed.)	
5.15	Fit		
5.16	Fit		
5.17	20	5.18	28
5.18·5	Fit		
5.19	15	5.19	26
5.19·5	18·5	5.20	25
5.20·5	17	5.22	24
5.22·5	17	5.23	24
5.23·5	16		
		5.24	Fit.
5.25·5	20	5.25	22
5.27	17		
		5.28	24
5.28·5	17	5.29	26
5.30	22	(Continuous spontaneous convulsions.)	
5.30·5	18	5.31	24
(Immediately after the convulsions.)			
5.32	18	5.32·5	21
5.33	16		
Exitus.			

Autopsy.—A series of sections stained with Marchi's method were prepared of the brain. The first lesion was found to pass through the right lateral thalamic nucleus and pes pedunculi; it touched the optic nerve. There was some degeneration in the middle part of the peduncle, slight degeneration towards the globus pallidus on one side and on the other side toward Forel's lenticular bundle. In the second operation the left restiform body was injured, but there was no spread of the degenerative changes as the animal only survived the operation two or three days.

Epitome.—The greater reflex irritability of the right side of the body was probably due to the pyramidal bundle on that side being intact. Reasons are given in Chapter IV., § 2, showing that injury of the sensory thalamic nuclei are not the cause of unequal irritability on the two sides.

Protocol 12. Cat 68. Small male animal.

25.5.05. It was intended to perform hemisection of the crus cerebri on the right side just in front of the cerebellum. After the operation there was no trace of rotation. The animal kept the right eye shut, while the right feet seemed paretic. The head was deviated to the left.

28.5.05. Deviation of the head to the left. The right eye had suppurated. Slight percussion of the right side of the body induced convulsive movements. This was not seen on the left side.

5.6.05. There was some serous exudate at the line of incision. The animal could not walk nor stand. It had grown thin. The head was rotated to the left.

6.6.05. The animal lay on its left side, it would not lie at all on the right side. The head was held so that it rested on the right cheek, this

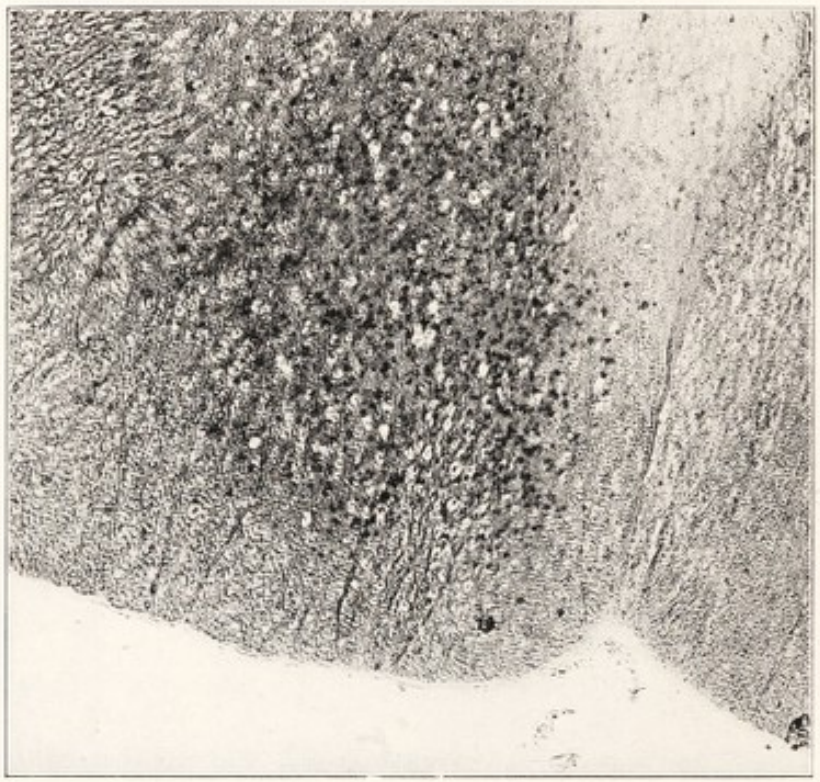


FIG. 28.—CAT 239. DEGENERATION OF THE LEFT PYRAMIDAL TRACT IN THE MEDULLA SPINALIS DORSALIS.

necessitated rotation of the head. No spontaneous movements occurred for long periods.

8.6.05. At 9 a.m. about 10 grammes monobromide of camphor dissolved in oil were injected. As a result fits developed on the *right* side, and also shocks (see Fig. 29). When later the whole cerebrum and cerebellum were exposed, the animal still showed the same deviation of the head to the right. Animal died.

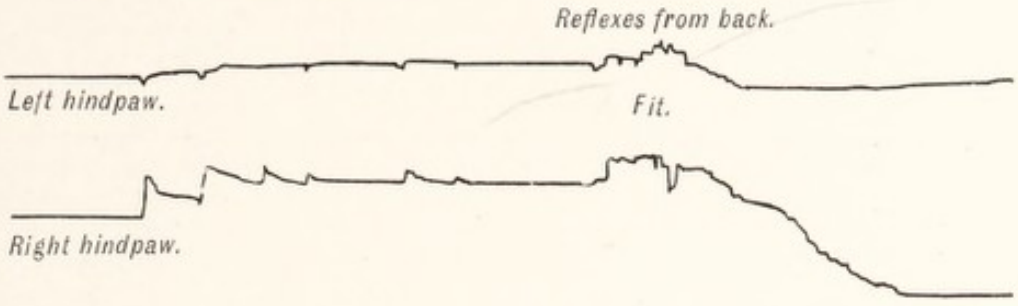
Autopsy.—A series of sections were made of the brain and stained by the Marchi method. It was found that there was degeneration of the right cerebellum and nucleus dentatus. The right half of the pons was partially softened (Fig. 30), including the medial crus, a part of the pyramidal bundle, Monakow's bundle, the descending trigeminal fibres and the lateral fillet.

Protocol 13, Cat 221. Small grey animal.

25.3.12. 6 p.m., $\frac{3}{8}$ gramme bromide of camphor. No effect.

10.4.12. 7 p.m., $\frac{1}{2}$ gramme bromide of camphor. Vomited during the night.

3.5.12. 6.30 p.m., ½ gramme bromide of camphor given. No effect.
24.5.12. 6 p.m., ⅝ gramme bromide of camphor given. No effect.
2.7.12. Animal narcotsied. Cerebellum exposed. The dura was



Cat 68.

FIG. 29.—CAT 68. 8.6.06. ACOUSTIC REFLEXES EXCLUSIVELY FROM THE RIGHT HINDPAW. (MOSSO APPARATUS.)

The upper curve is from the left hindpaw, the lower from the right. Tuning fork vibrations 2 per second. Lesion w. s on the left half of pons. The degeneration was found in the right pyramidal tract and the right bundle of Monakow and in the right lateral fillet.

FIG. 30.—CAT 68. HEMISECTION OF THE PONS, DEGENERATION ON THE RIGHT SIDE.

Degeneration and softening are shown by discoloration of the area. There is also hæmorrhage into the posterior longitudinal bundle. The formatio reticularis is only laterally involved. The pyramidal tract and Monakow's bundle show ascending and descending degeneration.

incised, and the posterior longitudinal bundle pierced in two places. This was done to both the right and left posterior longitudinal bundles, but on the left side the punctures were more lateral. After the operation the

animal staggered and showed a certain degree of restlessness. It reared up as it tried to walk, and seemed to sway more to the right, but this observation was doubtful.

The day after the operation it walked about in a crouching position, and occasionally showed deviation of the head to the left or right. It resisted being laid on the right side, but lay contentedly on the left side. One day later—*i.e.*, on the third—it manifested an extreme objection to lie on the right side, but lay readily on the left. The left forepaw was extended. The gait was still low and crouching, such as is characteristic of an animal whose medulla has been punctured in the middle line.

5.7.12. Animal showed marked disinclination to walk about. If the eyes were covered, it remained quiescent, and did not walk backwards in the excited fashion seen in the ordinary cat. It now lay contentedly on either side.

6.7.12. The creeping gait was still present, the forepaws were rather stiff. The animal could not spring upwards to obtain a piece of food offered, but made a definite attempt to do so. If dropped from a height of a metre, it fell on its feet, but fell on either the right or left side if dropped a greater distance.

19.7.12. 6 p.m., ¾ gramme bromide of camphor given.

20.7.12. Myoclonic shocks occurred on the left side of the body. At 10.15 a.m., an injection of absinthe was given. The cerebrum on both sides was exposed and subjected to faradic stimulation. Powerful shocks were produced on the opposite sides of the body from the area stimulated.

11.16 a.m. A second injection of absinthe was given.

11.18. The left side of the body reacted strongly to mechanical stimuli, while the right side reacted but feebly.

11.19. With faradic stimulation violent shocks resulted, whether the stimulation was applied to the right or left side of the cerebrum. Current 80.

11.20. When the right motor cortex was stimulated, each alternate stimulus gave a well-marked convulsive movement of the forepaw. On the left side, this effect only occurred with each fifth stimulus. Current 90.

11.22. A mechanical stimulus applied to the right forepaw brought about a shock at each *third stimulus*. Mechanical stimuli applied to the left forepaw were, *in each case*, followed by a violent shock. (There is, therefore, a shorter refractory phase in the left forepaw, as there is a shorter refractory phase with the right motor cortex.)

11.36. A cross incision was made at the distal end of the optic thalamus. After this, stimulation of the motor areas was in no case followed by contractions.

11.45. The medulla oblongata and the cerebellum were laid bare. Faradic stimulation was applied to the medulla at the point where the restiform body disappears under the folia cerebelli. Convulsive movements were elicited in each forepaw on stimulation of the corresponding sides. On the right side, the movement was about 120 cm., while on the left side the rate of movement was about the same.

11.50. The experiment was repeated with the same result.

11.52. The experiment was repeated, but the coil of convulsive movement was 150 cm. Faradic stimulation of the cerebellum gave no result.

11.54. Mechanical stimulation of the left hindpaw gave good myoclonic shocks. The same stimuli applied to the right hindpaw gave no result, or at best, very uncertain results. Spontaneous shocks or fits were never observed in this animal.

Autopsy.—See p. 176, Fig. 40, p. 175.

CHAPTER III

SEVERANCE OF VARIOUS NERVE TRACTS

§ 1. Lesions of the Pyramidal Tract (the Bundle of Monakow Being Left Intact) and the Subsequent Unilateral Exaggeration of Myoclonic Reflexes and Fits.

UNDER this heading come four experiments 158, 186, 239, 240, all of which are given in Table III., p. 140.

Additional experiments in which there was a pyramidal lesion are 191, 68, 202, 233, 240 (see § 2, p. 158).

These examples, of which numerous tracings were taken, illustrate sufficiently clearly the effect of division of these tracts on the acoustic and tactile reflexes. As the tracings show, these reflexes are absent in the first two weeks after operation and are diminished for a still longer period.

No notes were prepared regarding the occurrence of fits in these animals, neither whether these fits (where present) were located to that side of the body corresponding to the pyramidal fibres which had been cut, or whether the fits were localised to one half of the body. From the work of Boyce it seems probable that this is the case. This is a point, however, which would need further investigation. Further, in Cat 91, the right half of the body, at least the right forepaw, was deprived of innervation from the pyramidal fibres, while the left side of the body was deprived of innervation from the bundle of Monakow (Fig. 32, p. 146). The fact that convulsive movements appeared first in the left forepaw would prove that the pyramidal fibres were the dominant fibres for the forepaws. The same point is seen in Case 68, p. 136.

In Cat 158, the pyramidal fibres were very completely destroyed. For not only were the left motor centres destroyed, but the left pyramidal tract in the medulla was punctured by a needle (Figs. 36, 37, pp. 164, 165). During the short time the animal was kept alive after operation, reflex shocks and spontaneous myoclonic convulsions occurred exclusively on the left side of the body.

Finally, from the evidence afforded by Cats 205 (p. 113) and 186 (p. 116) and 191 (p. 117), it is shown that removal of the motor zone had no permanent effect on the latent period of the myoclonic reflexes. In Cat 239, where the pyramidal fibres on the left side were divided and the right corpus restiforme was injured, the result was a difference in the reflexes on the two sides of the body.

TABLE III.

LESIONS OF THE PYRAMIDAL TRACT AND BUNDLE OF MONAKOW.

No.	*Site and Extent of Lesion.*	*Reflexes and Fits.*	*Notes.*
114.	A stab was made in the mesencephalon about the region of the corpus quadrigeminum posterior. As a result there was complete degeneration of the right bundle of Monakow, and in the medial part of the right pes pedunculi and right fillet. Ascending degeneration was present in the right crus cerebelli superior, which was completely degenerated. The left crus cerebelli superior, like the right fillet, was almost completely degenerated.	Left-sided fits followed on the administration of $\frac{1}{3}$ gramme of monobromide of camphor. Immediately after these fits tactile myoclonic reflexes could be elicited on the right side of the body.	There were no motor disturbances, except staggering movements during the first four days after operation. The right bundle of Monakow was degenerated to the level of the sacral region. There was slight pyramidal degeneration, but not below the medulla.
108.	A stab was made in the region of the red nucleus. This was followed by degeneration in the left bundle of Monakow and left pyramidal tract. In neither case did the degeneration reach the sacral level.	After the administration of $1\frac{2}{3}$ grammes monobromide of camphor (in oil) the animal had status epilepticus and died. There are no notes on the course of the fits.	For ten days after operation the cat tended to fall to the left. There was ataxia of the left hind-paw. These were the only changes.
113.	A stab was made entering the right corpus restiforme by Deiters' region, and passing through the lateral part of the formatio reticularis and tegmentum to the right pes pedunculi (Fig. 31, p. 145). There was complete degeneration in the spinal cord of the right bundle of Monakow and lateral pyramidal tract.	After 1 gramme of monobromide of camphor (in oil) animal had myoclonic shocks and status epilepticus and died. No further particulars.	Circus movements to the right, rotation of the head to the right, staggering and titubation persisted for some time. No motor disturbances of the limbs.
118.	A Probst needle was passed below the cerebellum in Deiters' region through the lateral part of the formatio reticularis pontis up to the right pes pedunculi. Degeneration was found in the spinal cord of the right bundle of Monakow and the left lateral pyramidal tract. This was less completely degenerated than the bundle of Monakow.	The administration of $\frac{1}{5}$, $\frac{1}{3}$, $\frac{2}{3}$ and $1\frac{1}{3}$ grammes monobromide of camphor in oil had no effect, but $2\frac{1}{3}$ grammes in oil resulted in two fits, after which the animal died.	There were no motor disturbances, except a tendency to walk to the right and to fall to the right.

TABLE III.—*Continued.*

No.	*Site and Extent of Lesion.*	*Reflexes and Fits.*	*Notes.*
158.	The frontal pole of the left cerebral hemisphere was removed. At the same time the vermis was pierced a little to the left of the middle line, the Probst needle being passed to the base of the skull, after which it was brought forward and rotated, and then drawn back, so that the cerebellum was pierced, but the line of section was very small.	After 2·5 grammes monobromide of camphor exaggerated acoustic reflexes were got on the left side only. Spontaneous shocks were seen on the left side. After a myoclonic fit shocks were limited to the left side.	Walked to the left. Circus movements to right. This may be due to lesion of middle part of the left posterior longitudinal bundle, and also to the lesion of the left corpus striatum. The left pes pedunculi was completely degenerated, while in the medulla the left pyramidal bundle was again involved. Complete degeneration of right pyramidal tract (compare Figs. 36 and 37, pp. 164, 165).
186.	The left frontal pole was removed. After four weeks the left hemisphere was completely removed. The next night the cat died.	Without the administration of monobromide of camphor the tactile reflexes, especially of the head were more prominent on the left side. There was no definite difference in the latent period on the two sides of the body.	Animal became more dazed. Circus movements to left were present for one week. The pes pedunculi was degenerated in its whole extent. The crossed pyramidal tract was much more degenerated than in Cat 158.
91.	A Probst needle was passed through the formatio vermicularis to the bottom brought forward and rotated. The cerebellum showed little sign of injury. The left longitudinal bundle was cut. Further, the left formatio reticularis and fillet were pierced, and the distal part of the pes pedunculi destroyed, more particularly the lateral part.	Tactile stimuli elicited myoclonic reflexes. the hindpaws convulsed together, but the left forepaw first and more strongly. After 2 grammes monobromide of camphor, fits affecting both sides occurred. Cortical irritability, when tested i = 180 to both right and left sides of the cortex, produced convulsions of the crossed extremities.	Clock hand movements to the right for ten days. Lateral part of pes pedunculi degenerated (slight degeneration of the pyramidal tract seen in the spinal cord). Further degenerative changes were seen in the left bundle of Monakow, the posterior longitudinal bundle (ascending and descending), the predorsal bundle, and the medial fillet (Fig. 32, p. 146).
239.	At the *first operation* a Probst needle was passed through the unopened dura into the lateral part of the right thalamus, so that the lateral thalamic nucleus and internal capsule were pierced. The lat-	Myoclonic reflexes were best marked on the right side. Sometimes they only occurred on this side. The administration of monobromide of camphor was not necessary to produce them. There	During the first day and a half there was unnecessary rotation of the head to the right, while the animal was more easily rolled to the left than to the right. The left paws were

TABLE III.—*Continued.*

No.	*Site and Extent of Lesion.*	*Reflexes and Fits.*	*Notes.*
239.	eral part of the pes pedunculi showed degeneration to the sacral region. At the *second operation* the right restiform body was severed near the foramen of Monro. The animal survived the operation too short a time for degenerative changes to be followed up.	were no notes on the effect of large doses of this drug or of absinthe and the occurrence of fits. When the motor cortex on both sides and the medulla were exposed and tested with the faradic current, it was found that irritability was decreased after a fit. The diminution of irritability varied, sometimes being greater in the cortex, at other times in the medulla. There was no difference in the irritability of the two motor cortices (p. 135).	ataxic up to the time of the animal's death (right nucleus ventralis thalami was cut). After the second operation the animal tended to stagger and to creep flat along the floor.
240.	*First Operation.*—In the right hemisphere in the frontal lobe a small knife was inserted and the right nucleus caudatus and the frontal part of the right nucleus lentiformis were injured. Subsequent examination showed degenerated fibres passing to the corpus striatum, while other degenerated fibres, although not so numerous, passed through the lamina medial ventralis to the hypothalamus. The internal capsule was intact. *Second Operation.*—A Probst needle was passed through the cerebellum to the medulla a little to the right of the middle line: as a result the longitudinal bundle, the olive, the fillet and the pyramidal bundle were destroyed. Degeneration of the right pyramidal tract could be traced to the sacral region.	After the first operation tactile and acoustic shocks were elicited mostly from the right side. The day of operation was, however, an exception, for on this day these reflexes were best on the left side. For two days there was astereognosis of the forepaw left. Conjugate deviation of the eyes and head to the right. Animal lay with head directed forwards. It allowed itself to be rolled to the left. There was lateral limitation of the visual field. The reflexes on the left side were regular, but weak. After the second operation there were no forced movements. The myoclonic reflexes were almost wholly on the right side. Numerous experiments showed no peculiar changes in the latent time. With faradic stimulation it was found that much stronger currents were needed for right motor cortex than for left to produce convulsions in the limbs of the opposite side (p. 179).	After the first operation the degenerative change was limited to the frontal part of the corpus striatum, and the frontal cortex including the septal nucleus. After the second operation, the right pyramidal tract was degenerated to the lower sacral region. The right posterior longitudinal bundle (antero-lateral bundles) and vestibulospinal bundles all showed changes down the cord. Degeneration was also seen in the distal portion of the corpus trapezoides and trapezoides olivocerebellaris (Winkler and Potter). Ascending degeneration was seen in right lateral fillet, the left was also degenerated, but not so much as the right.

The slight cortical irritability of the right hemisphere between the fits was certainly associated with the presence of a lesion in the pyramidal tract.

In Cat 240, where the lesion of the frontal brain did not affect the internal capsule, only a slight, although perfectly definite, change was produced on the myoclonic reflexes. In contradistinction to this a very marked change in the reflex irritability was seen on both sides of the body when, in the second operation, both the pyramidal tract and the fillet were divided. On the left half of the body which was deprived of both the pyramidal and fillet fibres no myoclonic reflexes could be elicited.

From these experiments it is evident that injury of the pyramidal tract at some point between the motor cortex and the anterior horns results, at least in the first instance, in a marked diminution of the myoclonic reflexes and fits. Can we infer from this that the fits and reflexes originate in the motor cortex and are conducted by the pyramidal fibres?

This is not so, as will be shown by further evidence.

Very soon after this operation an epileptic fit which originated in the normal side of the body spread to the other side from which the pyramidal fibres had been cut off.* Further, as was shown in Cat 191, the administration of bromide of camphor in large doses resulted in the demonstration of reflexes and reflex after-discharges in the abnormal side of the body from which immediately before no reflexes could be elicited at all.

As was shown in the first section of this book, these reflex after-discharges slowly merge into complete myoclonic fits, the refractory phase gradually shortening. Further, from the experimental evidence there is no reason for believing that there is any fundamental difference between the localisation of the myoclonic reflexes and the myoclonic fits.

It would be pointed out that the experiments by Turtschaninow, carried out immediately after lesion of the motor cortex or of the pyramidal tract, do not seem to be very reliable. This applies especially to the observations made after section through both pyramidal bundles. The anatomical evidence for this experiment does not seem very satisfactory, and it would seem that far more injury was done to the surrounding tissue than is supposed.

The results of pyramidal lesions on the different myoclonic reflexes are very varied. The knee reflex, for example, will persist after lesion of the pyramidal tract, while the tactile ear

* M. Rothmann (*Zeitschr. f. klin. Medizin*, 1902, vol. xliv., p. 184). He also found that after section of the pyramidal tract for one side of the body recovery did occur, for in a few weeks both sides reacted simultaneously to faradic stimulation of the cortex.

reflex will disappear and remain absent after other myoclonic reflexes have reappeared in the limbs. Finally, in Chapter IV., § 3, proof will be given that after complete elimination of the cortex, even after section of the spinal cord, myoclonic reflexes, although of a different character, persist.

From the evidence supplied the conclusion is arrived at that the pyramidal fibres exercise a facilitating influence on the more caudally situated centres—that is, the injury of these fibres by interrupting this facilitation makes the development of ordinary myoclonic reflexes more difficult, at least for the first two weeks after operation.

Oebeke,* a clinician, observed that in an epileptic who had a unilateral cerebral hæmorrhage the fit was subsequently limited to the same side as the hæmorrhage. This observation is in line with my own experiments, for in those cases where the cortex on one side was removed myoclonic shocks and fits occurred only on the same side of the body—*i.e.*, on that side which was still under full nervous control. This condition lasted for fully two weeks after operation. Luciani, the physiologist, who first suggested that epileptic fits originated in the motor cortex, asserted that in the experiments made by Hitzig, Franck and Pitres, and Albertoni, some grey matter of the cortex had, in each case, been left after operation.

Their experiments. he maintained, were clear proofs of his theory. According to Luciani,† the corpus callosum was the conductor of the impulses coming from both sides of the cortex. On this point he was shown to be wrong by the work of Prus, Probst‡ and Karplus.§ The relative value of the motor cortex as a starting-point for fit phenomena is shown in von Monakow's‖ case, where a fit started in the left arm, although all the right side of the motor cortex had been destroyed. In such a case it is possible that the lesion involving the internal capsule may have given the impulse to the crossed medullary centre.¶

It must, however, be remembered that, according to Collier, genuine epilepsy is the condition which most frequently causes unilateral convulsions—that is, the presence of unilateral convulsions does not of necessity prove the existence of cortical epilepsy.

* Oebeke, *Berliner klin. Wochenschrift*, 1880, No. 37.
† Luciani, *Rivista sperimentale*, 1878, p. 617.
‡ Probst, *Jahrbücher f. Psych.*, 1901, p. 31.
§ Karplus, *Wiener klin. Wochenschrift*, 1914, p. 645.
‖ v. Monakow, *Archiv f. Psychiatrie*, p. 407.
¶ Bubnoff and Heidenhain, like Franck and Pitres, deny the possibility of eliciting complete fits by the stimulation of the white matter of the cerebrum.

§ 2. Simultaneous Lesions of the Pyramidal Tract and Monakow's Bundle.

The case shown in Cat 91 is important for two reasons.

First, because after section of the lateral half of the left pes pedunculi (that is, the part of the pyramidal tract for the supply of the right forepaw), both hindpaws showed active reflex movements, while the reaction in the right forepaw was not so active.

Second, in this case the left bundle of Monakow was found to be completely degenerated. It would appear, therefore, that the

FIG. 31.—CAT 113. INJURY OR LESION OF DEITERS' ZONE.

bundle of Monakow has but little influence on the convulsions in the opposite side of the body.

On the other hand, the evidence afforded by Cat 114 is interesting.

(A photograph of part of the lesion in this case is shown in Fig. 38, p. 166). In this case the left bundle of Monakow was cut, and part of the right pyramidal bundle—that is, the right side of the body was deprived of the innervation through the bundle of Monakow, while the left side was deprived of part of the pyramidal innervation. In this case fits occurred on the left side—that is, where the bundle of Monakow was intact, its influence can replace that lost through a high and partial section through the pyramidal tract.

From the available evidence, then, it seems that the bundle of Monakow has a certain influence on convulsive phenomena. This evidence would only be annulled if it transpired that lesion of the right tegmentum in the region of the posterior corpora quadrigemina exercised a destructive and homolateral influence on the possible influence of the tegmentum on the occurrence of epilepsy.

From the evidence afforded by case of Cat 108, it is seen that epileptic fits may occur after section of the pyramidal tract and the bundle of Monakow on the same side at the level of the red

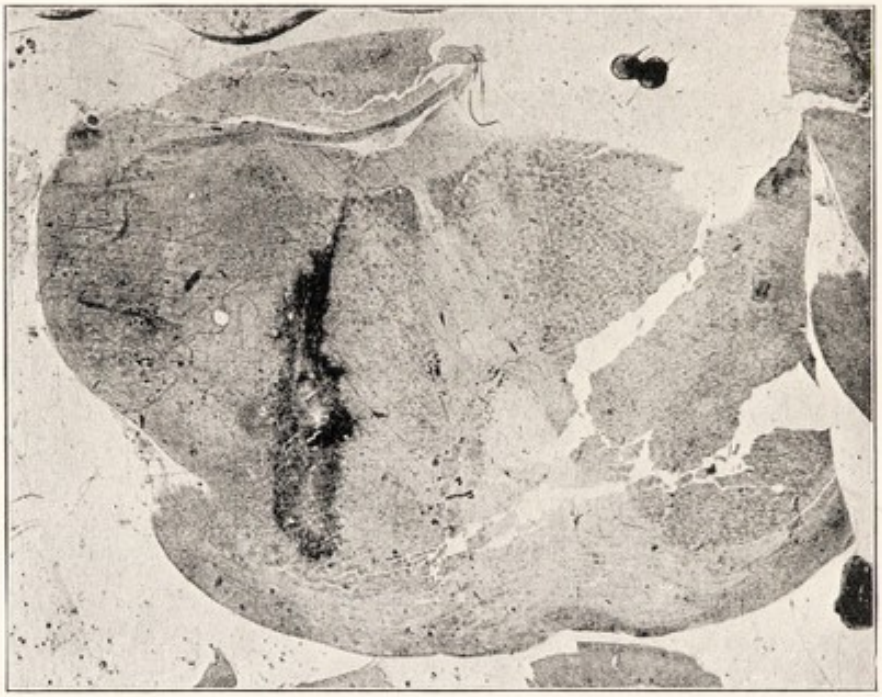


FIG. 32.—CAT 91. LESION OF THE LATERAL HALF OF THE LEFT PES PEDUNCULI.

nucleus (descending degeneration) (compare Fig. 33, and also refer *Brain*, 1914, Figs. 7*a* and 7*b*, p. 370). The same occurs after lesion of the tegmentum at the level of the corpora quadrigemina anterior, but only if large doses of bromide of camphor are administered. No details can, however, be given about those fits.

The evidence afforded by Cats 113 and 118 (Cat 113, Fig. 31, p. 145, photograph *Brain*, 1914, p. 360, Figs. 3*a* and 3*b* (Cat 118, p. 140), shows that enhanced reflexes and fits may occur after extensive lesion of the lateral part of the formatio reticularis, associated with complete degeneration in the spinal cord of the right bundle of Monakow and the left pyramidal tract. In both these animals, however, a very large dose of bromide of camphor was necessary to produce these phenomena.

It is shown in Part II., Chapter IV., p. 153, Cat 91, that in the same lesion (loss of the pyramidal innervation on the right and of innervation through Monakow's bundle on the left) the reflexes were enhanced particularly in the left forepaw and fits occurred.

From this evidence it may be concluded that in case of Cat 91 the enhanced irritability of the left forepaw was due to the lesion of the left pes pedunculi being localised exclusively to the lateral

FIG. 33.—CAT 108. LESION OF THE MID-BRAIN WITH DESCENDING DEGENERATION IN THE RIGHT TRACTUS INTERSTITIO-SPINALIS (FIBRES HERE ARE THICK), AND THE LEFT TRACTUS COMMISSURO-MEDULLARIS (WITH THIN FIBRES).

There were also degenerative changes in the left bundle of Monakow and the left pyramidal tract, but these do not appear in the figure.

region. In this case, as is known, the pyramidal innervation of the right forepaw was lacking.

From a general consideration of the effects of simultaneous lesions of the pyramidal bundles and the bundle of Monakow it seems to be the case that the bundle of Monakow has a certain influence on the production of enhanced reflexes and the occurrence of fits.

This is shown in the case of Cat 114.

The only alternative to this would be if the tegmentum of the mid-brain were proved to have a homolateral influence on the occurrence of myoclonic phenomena.

§ 3. Lesions Restricted to Monakow's Bundle.

Case 92 is important because of the sharp limitation of the lesions (here the left formatio reticularis pontis, left bundle of Monakow, the cerebellum and pyramidal tract are all intact), and the definite unilateral character of the symptoms (compare Figs. 34 and 35, pp. 148 and 149). Further, it would appear that Monakow's bundle must be intact for the occurrence of reflexes or fits, unless evidence is forthcoming that these phenomena depend upon the integrity of the formatio reticularis pontis. Case 78 may be

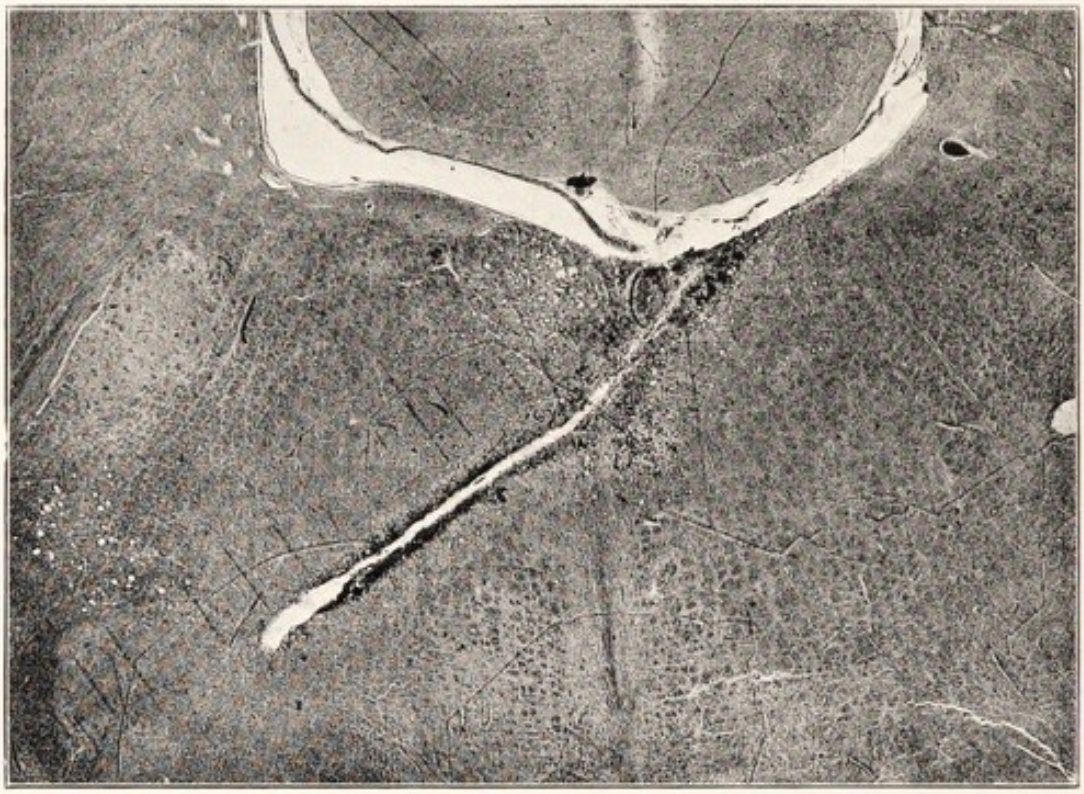


FIG. 34.—CAT 92. LESION (ORAL PART) OF THE DORSO-MEDIAL AREA OF THE MEDULLA OBLONGATA.

The fillet and pyramidal fibres are intact. The bundle of Monakow on the left side is degenerated.

put in the same category as Case 92. Here the explanation may be offered that the normal bilateral phenomena shown at the beginning of a fit are dependent on the integrity of the bundle of Monakow. Here, again, a complication arises in that the formatio reticularis pontis is involved, although in a more oral position in the brain stem than in the Case 92.

Cases which show lesions involving the bundle of Monakow with very slight complicating injuries are Nos. 8 and 36. Cases are also available which show that degeneration of the fillet and cross-section of the posterior roots have no influence on the bilateral character of convulsive myoclonic symptoms. These facts might support the view that changes occurring in the bilateral character are due to lesions in Monakow's bundle.

In Case 8 the irritability of the right motor area to faradic stimulation was shown to be diminished. It has been shown that this lowering of faradic irritability may be seen after lesion of the crossed cerebellar nuclei. In some cases such lesions have been found associated with enhanced myoclonic reflexes on the same side of the body. In this case, however, the nuclei were intact, but the right corpus restiforme was degenerated. The suggestion, therefore, is that cross-section of the posterior crus cerebelli has the effect of lowering the faradic irritability of the cortex. It is very probable that in this case the rubro-spinal tract was injured, and this may be an incidental complicating factor.

In the case of Cat 36, more evidence might have been got for the influence of the rubro-spinal bundle on myoclonic phenomena were it not that the notes were limited to asymmetry shown by the abdominal muscles.

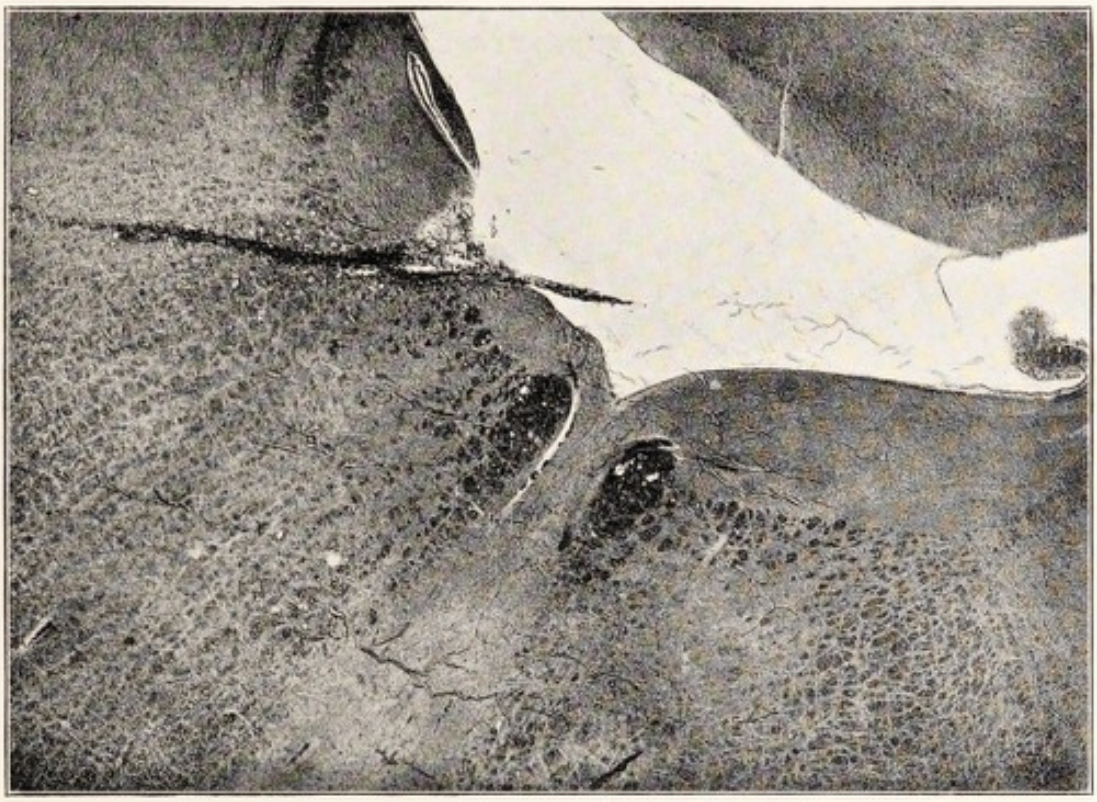


FIG. 35.—CAT 92. CAUDAL PART OF THE LESION.

It is evident, therefore, from the results of the different experiments that Monakow's bundle cannot be excluded as a conductor of the impulses in myoclonic convulsions in cases where the pyramidal tracts are not available. If Monakow's bundle does act in this way its conducting power for convulsive phenomena is far inferior to that of the pyramidal bundle. The question whether the bundle of Monakow does conduct such impulses is not quite certain, neither can it be settled from the available experimental evidence. Further research is necessary to decide whether a lesion of the formatio reticularis of the pons and medulla (eventually also a lesion involving the tegmentum of the mid-brain) might not have the effect of preventing or inhibiting convulsive phenomena and myoclonic reflexes on the corresponding side of the body.

Consideration must now be given to the evidence procured by other workers on the phenomena of reflexes, the conduction of

cortical impulses, and the convulsions associated with cortical stimulation. It will be found that there is a lack of systematised research even on such well-known phenomena as the knee reflex. This reflex is probably one which has had most attention paid to it. An exception to this rule is seen in the recent work of Magnus and de Kleyn on the influence of posture on reflexes.

Clinically, discussion still goes on as to whether or not complete cross-section of the spinal cord is or is not followed by the disappearance of tendon reflexes.

The close relationship between the tendon and the myoclonic reflexes would suggest the question whether the conflicting data may arise from the fact that the disappearance of the reflexes is associated with destruction of cerebro-fugal bundles. This condition is recovered from, for it was shown that after section of the pyramidal bundle the reflex reappeared in two weeks, although it was changed in character. This also occurred even where the bundle of Monakow was excluded, but later. In this connection the experiments of Turtschaninow are important, for he showed that after section of the pes pedunculi the "Blitzartige Zusammenfahren," or "lightning convulsion," which follows poisoning with santonine still persists. From the description given by Turtschaninow there seems some doubt whether these are really reflexes due to tactile and acoustic stimuli.

If these convulsions are identical with or related to the myoclonic reflexes described by me, this result is of great importance, for it would show that the reflexes persisted immediately after removal of the influence of the cerebral hemisphere, while the red nucleus was not injured. The positive result got by Turtschaninow, more especially if supported by further evidence, would demonstrate more vividly than my own experiments the independence of these phenomena from the cortex.

The question whether picrotoxin in sufficient doses will give the same result as bromide of camphor or absinthe, and enhance the myoclonic reflexes and induce complete myoclonic fits, has not yet been proved. In the meantime it is important to note that G. Holmes, L. J. Pollock, and Treadway* found that picrotoxin fits persisted after decerebration. In the same way the myoclonic reflexes, enhanced by monobromide of camphor in the case of Cat 242 (p. 181), persisted after decerebration. This case is described in *Journal of Physiology*, 1928. Considering my results as a whole, the conclusion is come to, that it is only possible to deny the influence of the rubro-spinal bundle on myoclonic phenomena, if later research make it apparent that a lesion of the formatio reticularis pontis, and probably, also, of the tegmentum in the mid-brain, has a positive influence on these reflexes.

* Holmes, Pollock and Treadway, *Archives of Neurology and Psych.*, 1923, vol. ix., p. 609.

CHAPTER IV

INFLUENCE OF DIFFERENT LESIONS

§ 1. The Result of a Lesion of the Formatio Reticularis on the Bi-Lateral Character of Myoclonic Reflexes.

It is obvious that the lesions of the formatio reticularis which are most important are those which do not involve much destruction of other important parts, such as the ascending or descending tracts. A distinction must be drawn between the results got from a strictly localised lesion and those which follow accidental injury of other structures, which we already know exert a definite influence on myoclonic reflexes, spontaneous shocks, or fits.

Such structures are the pyramidal tracts, the cerebellum, and probably the rubro-spinal tract. Lesions which involve structures such as the posterior spinal nerve roots, the fillet, and the vestibulo-spinal bundle do not, so far as is known, effect these phenomena.

As a negative case, No. 86 (p. 152) is important. In this case the lateral portion of the formatio reticularis was injured at the level of the facial nerve root. Still, after the administration of large doses of bromide of camphor bilateral myoclonic reflexes could be elicited, but no fits.

Should it become evident in later researches that either the pontine or medullary portions of the formatio reticularis participate in the production of myoclonic reflexes, the lateral part of the medullary portion of the formatio reticularis may be excluded.

Also, in Case 108, the lesion involved a large part of the formatio reticularis in the mesencephalon on the right side, yet the animal showed bilateral fits after a very large dose of bromide of camphor. In this case $2\frac{1}{2}$ grammes of monobromide of camphor in oil were administered (photos showing the descending degeneration from the site of injury in Fig. 33, p. 147). It would appear, therefore, that that portion of the formatio reticularis situated in the mesencephalon has no important function in the production of myoclonic reflexes.

The other cases in the tables are those where the lesions were situated in the pons or medulla, areas where it is impossible to conceive of a sharply localised injury. Great circumspection is therefore necessary in interpreting the results.

In Cat 88, a distinct difference was found in the myoclonic reflexes on the two sides, those on the left side being much weaker. In this animal a right-sided lesion involved the lateral part of the formatio reticularis. It was shown in an earlier chapter that there was not much evidence for the bilateral symmetry of myoclonic reflexes being affected by a slight lesion of the bundle of Monakow; it seems possible, therefore, that the differences in the reflexes on the two sides may be due to injury of the medio-dorsal portion of the formatio reticularis. It is possible that the medial portion of the formatio reticularis is of significance for myoclonic reflexes.

Case No. 221 is still more important in this connection. Here the lesion consisted of a stab through the right cerebellum and medulla. The result was, reflexes could only be elicited on the left side (Fig. 40, p. 175). In this case the difference of the reflexes on two sides of the body must be ascribed, either to the injury to the cerebellum, which was accidental, or to a lesion of the formatio reticularis.

TABLE IV.

LESION OF THE FORMATIO RETICULARIS.

No.	*Lesion.*	*Reflexes and Fits.*	*Notes.*
92.	Stab in medio-dorsal part of the form. ret.; moderate degeneration of left pyramidal and left Monakow. (Figs. 34 and 35, p. 148).	Faradic stimulation of left cortex: convulsion of both paws at the same time. Faradic stimulation of right cortex: left paw convulses more.	Only right forepaw is involved in the reflex convulsion, rarely the right hind-paw. Fits especially on right side.
86.	Lateral stab of the needle with intact cerebellum, in the lateral part of the form. retic. at the level of the exit of the 7th nerve and not exceeding that level. The 7th nerve is involved in the middle, the oliva superior from above. Degeneration of the reticulo-spinal fibres in the anterior columns to the sacral region (see Table III., p. 140).	After 1 ½ grammes bromide of camphor, myoclonic reflexes, on both sides at the same time are observed; no fits occur.	Persistent pronounced ataxy; swallowed badly.
88.	Lesion of right tuberc. acustic. by a stab, with intact cerebellum, starting from the 4th ventricle; 5th and 7th root are injured, also Monakow's bundle; degeneration of right Gowers' bundle and corpus trapezoides at the right very limited and involving this bundle laterally.	After 2 grammes bromide of camphor (in oil) tactile; no acoustic reflexes. The left half of the body reacts much better.	Head rotated strongly to the right.

TABLE IV.—*Continued.*

No.	*Lesion.*	*Reflexes and Fits.*	*Notes.*
221.	Two vertical stabs through the right form. retic., sharply limited and causing no further malacia (Fig. 40, p. 175); degenerations compared.	Left half of body reacts strongly on tactile stimulation. Motor cortex more irritable on the right side than on left.	Tendency to lie upon the right side and to stagger.
235.	In the first operation a stab is made, penetrating near the middle line, via right posterior longitudinal bundle, in the form. retic. till the area Monakow, where the lateral fillet (lateral part) and the pyramidal bundle are pierced and degenerated. This lesion causes only diminished reflexes on the left (as a consequence of the lesion of the fillet and of the pyramidal tract). After 14 days a stab is made right through the 1st lesion, which has grown purulent, and so an abscess was formed over the whole right form. retic., and the myoclonic reflexes of the right half of the body diminished or disappeared.	For the observation of myoclonic reflexes the supply of bromide of camphor proved superfluous.	After the first stab, as a consequence of the lesion of the nervus vestibularis (perhaps also of lateral part of the posterior longitudinal bundle), tendency to roll to right. As a consequence of the lesion of the ramus desc. 8th nerve after the second stab more rolling tendency to the left.
91.	Probst's needle penetrated from above the cerebellum in the upper part of the pons, on the left side, causing a lesion of the lateral part of the pyramidal and lateral fillet. Left Monakow's bundle degenerated moderately; right crus sup. cerebelli slightly degenerated. At the left side the medial part of the form. retic. pontis is hurt (Fig. 32, p. 146).	Only tactile, no acoustic myoclonic reflexes, in which both hindpaws convulsed, but of the forepaws the left convulsed more than the right. After 2 grammes bromide of camphor bilateral fits. Faradic cortex irritation; no difference between right and left.	Circus movements to the right; lies flat on the ground, left forepaw stretched forward.
114, 241 and 242 (see pp. 162, 163).			

The dilemma may be settled from my own observations as well as from those of Russell, which show that if the lesion had been cerebellar the effect would have been the opposite of that found. That is to say, the reflexes would have been exaggerated. This interpretation seems to make the case of Cat 235 clearer.

Protocol 14, Cat 235. Yellow animal.

22.9.13. The bony covering was removed from over the cerebellum. Profuse hæmorrhage followed, which was stopped with use of prepared wax. With a Probst needle the cerebellum was pressed forwards, and

pierced anteriorly. It was noticed that during anæsthesia the breathing was more pronounced on the left than on the right side of the abdomen (right fasc. solitarius ?). The corneal reflex returned first on the right side, the reflex in the left eye was late and slight (secondary ascending trigeminal connection ?). When the animal was coming round after the anæsthetic, the pupils dilated, while it moved the right forepaw much more than the left (right lateral fillet). Tactile reflexes seemed stronger on the right side; if the right hindpaw were placed in an abnormal position, it was at once withdrawn. This was not the case with the left paw (fillet ?) When the animal regained consciousness it showed a tendency to lie on the right side (right nerv. vestibularis). There was a tendency to circus movements (right posterior longitudinal bundle) to the left. One and a half hours after operation the animal held its right forepaw crossed over its breast against its left cheek. Strong myoclonic tactile reflexes were present, and could be elicited in any region. The animal rolled spontaneously to the right side. It held its head far forward (the neck stretched out) and tended to show titubation forwards (nucleus raphe ?). In walking it tended to roll to the right (this may be a symptom of irritation of the vestibular nerve or irritation action of the descending ramus of the auditory nerve).

After four hours. The animal lay on the left side (this may be due to result of a lesion of the right nervus vestibularis ?), but not absolutely on its flank. When put into another position it rolled to the left again. The head was rotated to the left. The animal coughed continually, and there was a tendency to titubate forwards.

After six hours. It sat on four feet, but not in a normal position. Head and eyes were rotated to the left (right posterior longitudinal bundle). The hind limbs were flat on the ground (nuc. raphe). Cat avoided walking (lesion of both posterior longitudinal bundles). When his mate in the same kennel had a violent fit he seemed frightened and staggered forward, with the belly on the ground. In this way he closely resembled an animal who had had both posterior longitudinal bundles cut. Sometimes he showed a tendency to retrogression (nuc. raphe); sometimes too he fell to the right, sometimes to the left. The left forepaw could be put in abnormal positions (right lateral fillet ?) The bandage had fallen off.

23.9.13. The animal lay on the right side (right nerv. vestibularis). At intervals about every ten minutes, he tried to sit on the ground, in a normal position. There was always a tendency to deviate both head and eyes to the left. He fell to the right and showed slight titubation (nuc. Deiters). In the evening of the same day the animal lay on the right side, the head deviated to the left. It could not be induced to move (posterior longitudinal bundle).

24.9.13. At 10 a.m., animal fell on the right side. There was moderate conjugate deviation to the left. Left forepaw sometimes put down on the dorsal aspect (right lateral fillet). The eyes were rotated to the right, the right eye was at a lower level than the left (right nerv. vestibularis).

25.9.13. Walked unsteadily. It was inclined to bend over to the right (right nerv. vestibularis). There were no circus movements. When it walked, the belly was on the ground (nuc. raphe). In the evening of the same day, animal showed high stepping gait (symptom of nuc. tecti, nuc. raphe, and vertical deep fibres). It refused to lie on either side, but it allowed itself to be placed on either side. Once it was seen to fall to the right side, once to the left.

26.9.13. Was very ataxic. There was a slight inclination to droop to the right side rather than the left. There was a tendency to go towards the right rather than the left. The forepaws showed high stepping gait, while the feet were held well apart. The trunk was lowered towards the ground (nuc. raphe).

27.9.13. When dropped from a height of 8 dm. back downwards, it fell with a thud on its belly and knees (nerv. vestibularis). It was somewhat rotated to the right as it fell and made rolling movements towards the right (right nerv. vestibularis).

28.9.13. Walked about in a normal manner and was evidently quite cheerful, with the exception that the forepaws were rather stiff and showed

the high stepping gait. When tested by making it walk over a piece of lattice work it walked quite well.

There were no tendencies towards forced movements or rotation of the head. It would not allow itself to be pushed down either to the right or left.

From the right half of the body, including the right half of the back, myoclonic reflexes were more easily elicited than before the operation, while on the left side of the body they were less easily elicited than before the operation.

It is possible that this change in the character of the myoclonic reflexes may be due to some local and slight irritation at the site of the lesion (lesion was produced by an aseptic needle) in the right formatio reticularis and to the local lesion in the right lateral fillet. This was shown from the microscopic preparations.

29.9.13. Animal anæsthetised with ether. Examination showed the presence of fluid in a cavity in the wound. Precautions were taken to avoid the extension of infection in the cranial cavity.

30.9.13. Animal was well. Still showed the high stepping gait. When subjected to the falling experiment from a height of 1 metre, it fell to the right side as before.

31.9.13. Jumped spontaneously out of his kennel. When the left forepaw was pulled, he did not seek to draw it back. When the left hindpaw was pulled, he pulled it back, but not readily (lateral part of fillet more involved than the medial). Both the right paws were smartly and promptly withdrawn on being pulled. Cat could climb upwards well, and ate well. Animal was again anæsthetised, and a fine needle passed through the first wound which was found dilated with exudate. The object of this second operation was to touch another portion of the posterior longitudinal bundle. When the cat was coming out of the anæsthetic, it fell twice to the right. After an interval of ten minutes, it allowed itself to be pushed over towards the left, but not to the right (this was a result of the lesion, produced at the second operation, to the nuc. ram. desc. n. VIII.) The head was sometimes rotated to the right. It stood with its left flank pressed against or resting against a wall (ram. desc. vestibularis). Later, the head was slightly rotated to the left (right ram. desc. vestibularis?). An hour after the operation it lay on the right side, and would only permit itself to be pushed over to the left. The falling experiment was again negative. The animal fell to the left. When it jumped down, the hind portion of the body came down with a little thud (nuc. raphe). Head was now somewhat rotated to the left.

1.10.13. Animal allowed himself to be rolled to the left, but resisted being rolled to the right. Very slight ataxia. At 3 p.m., *i.e.*, on the afternoon after the above observation, the head was rotated to the left. When excited fell to the left. Was manifestly interested in his surroundings. Stretched himself more than after the first operation. It permitted itself to be put on the left side, but not on the right. The falling experiment was negative. *Myoclonic tactile shocks more pronounced on the left side.* Evidently did not feel well, but walked well and moved freely.

2.10.13. Was rather dazed. Allowed himself to be pushed down to either side. If he shook himself he fell to the left. Walked unsteadily, the belly was lowered and the animal tremulous.

3.10.13. Cat allowed himself to be pushed over more easily to the left than to the right side. When the feet on either side were placed in an abnormal position it speedily corrected this. The left half of the body was more susceptible, tactile reflexes being more easily evoked than on the right. The animal walked somewhat stiffly, but was not awkward. Occasionally the animal fell to the left. When the falling experiment was tried it went well from the height of 1 metre, but badly from half that distance. There was slight rotation of the head to the left. The animal was rather apathetic and allowed such manipulation as holding up the chin with indifference. At 8 p.m., $\frac{1}{2}$ gramme bromide of camphor was given.

4.10.13. Animal was found dead. The brain and spinal cord were removed and examined in serial section by the Marchi method. The lesion was found to have penetrated the fourth ventricle and to have pierced the left posterior bundle; it touched the nucleus dorsalis raphe,

and pierced the formatio reticularis. It touched the medial nucleus, partly pierced the lateral nucleus and the facial root. The distal vestibular fibres were involved and the lateral fillet, but the descending ramus of the fifth nerve had escaped, also the bundle of Monakow and the restiform body. Around the original site of the injury softening had taken place, but as the reaction with osmic acid was only faint, it was probable that this softening followed after the second operation. In the degenerative change the formatio reticularis was involved to a considerable extent. Ascending degeneration as a result of the first operation was seen in part of the posterior longitudinal bundle on the right and in the fillet. Descending degeneration was seen in both posterior longitudinal bundles, in the predorsal bundles, in the vestibulo-spinal bundle, and in Monakow's bundle. The traces of the second lesion were found to be caudal to the first, and right descending ramus of the eighth nerve was pierced, also the ramus descendens of the fifth, and the internal arcuate fibres and the olivary body; the lesion terminating in the right pyramidal tract.

In this case the reflexes which were at first increased on the right side were probably due to the lesion in the right cerebellum. The increased reflexes on the left side of the body, found after the second lesion, cannot be due to a lesion of the right pyramidal tract. This we know, because we have seen that the result of such a lesion would have been increased reflexes on the right side. I am inclined to explain these increased reflexes on the left side as being due to an infection of the first canal after the second operation and the formation of septic foci involving the formatio reticularis.

Had the malacia been associated with the first operation, there would have been much more extensive degenerations both upwards and downwards. The microscopic evidence is in favour of the degenerative changes being of comparatively short duration.

In Cat 68 (Protocol 12, p. 136, and Table II., p. 128) there was found a comparable softening, but in this case only the lateral part of the formatio reticularis pontis and medulla were involved. It will be recalled that the fits were almost entirely localised to the right side, and were ascribed to the suppression of the functioning of the cerebellar function, due to this softening. Now, in Case 235 the cerebellum was not involved. If we conclude from the evidence of these cases that the formatio reticularis, more especially in the medial part, has a direct influence on the occurrence of myoclonic reflexes and fits, the interpretation of other cases, which will now be described, is possible. The evidence of these later cases would also afford some evidence of the localisation of that part of the formatio reticularis which is of importance for these phenomena.

Cat 91.—This cat had an extensive lesion of the medial portion of the formatio reticularis on the left side. It had increased tactile reflexes and bilateral fits (Tables III. and IV.). It was seen that both hindpaws were equally affected by the fit, but the left forepaw was more affected than the right. In this animal the

lesion had involved the lateral part of the pyramidal bundle (Fig. 32, p. 146). This would seem to indicate that the difference in the reflexes might be ascribed to this lesion of the pyramidal bundle on one side. As it has been found that both bilateral fits and reflexes may be present where there is a lesion involving the medial portion of the formatio reticularis pontis, it seems permissible to conclude that only the medullary part of the formatio reticularis is associated with the occurrence of such phenomena. Further, this case affords evidence that for the normal occurrence of myoclonic reflexes the fillet must be normal. This latter point will be referred to in the next section.

In Cat 92 (see Table IV., p. 152), on the other hand, the fillet and pyramidal bundle are intact, but caudally the medial portion of the left formatio reticularis medulla is destroyed. The lesion is shown in the photograph, Figs. 34 and 35 (pp. 148, 149). The fact that the fits started in the right forepaw, while the left rubro-spinal tract was degenerated right down to the sacral region of the spinal cord, in my opinion affords evidence concerning the function of this tract. In this case we were faced with a difficulty—either the fact that fits started on the right side was to be ascribed to the degeneration of the left bundle of Monakow, or to the lesion in the left formatio reticularis. We now have evidence which makes it fairly safe to conclude that the medial portion of the formatio reticularis medulla has a positive influence on the occurrence of reflexes and fits. Hence it is a matter for grave doubt whether the rubro-spinal tract has any connection whatsoever with these phenomena. This is made obvious by the fact that in Cat 92 it was found degenerated right down to the sacral region. The case is better understood and comes into line with other cases if we conclude that in this case a group of nuclei for the right side were involved and that the nucleus for the forepaw was more involved than that for the hindpaw.

Case 114 is more difficult to explain, for the fits in the condition of status epilepticus followed an uncommon course. The course of the phenomena was first two left-sided fits, then separate spontaneous shocks, more especially on the right side. Further, immediately after a severe fit, right-sided reflex (?) shocks were seen. This is unusual, for the severe fit, as has been pointed out, almost invariably precludes any reflex phenomena for some time (the refractory phase). The lesion in the case of Cat 114 is shown in the photograph in Fig. 38, p. 166 (Fig. 2 of the paper in *Brain*, 1914, p. 358). The question arises whether the comparative independence shown between the two sides of the body may be due to a lesion in the medial line which would sever cross connections. Further, the severe lesion of the fillet, which was

degenerated completely on the left side, might account for the exclusion of the right side of the body from the fits. Nothnagel* considered that it was impossible to localise his convulsive centre accurately by means of electrical stimulation on account of the escape of current. He tried to map out the centres by injecting an irritant material. With this method he found that the lowest point at which he could produce general convulsions with the development of the pupil symptom was the point of the ala cinerea, while the highest point he found to be near the locus cæruleus. Binswanger,† in his cross-section localisation, came to practically the same result. In connection with the work of Binswanger it is interesting to find that he records how, after mechanical interference with this region, a sudden jerk of the table elicits fresh and violent shocks. This is of special interest, since the centre Binswanger describes coincides approximately with the centre described here for myoclonic reflexes.

It is shown from my experiments that the occurrence of complete epileptic fits is not dependent alone on the ponto-medullary convulsive centre described by Schreuder van der Kolk and Binswanger. Further, it is apparent, not only from my own experiments, but also from the work of Bechterew, that a fit induced by a stab in this ponto-medullary centre, which involves the seventh nerve at its mid-portion, is stopped at once by cross-section of the crura cerebri.

§ 2. **The Results of Lesion in the Centripetal Connections**—*i.e.*, **the Posterior Roots and the Fillet**—**on the Occurrence of Reflexes and Fits.**

From the position of the fillet in the brain it is hardly possible to injure it without injuring other structures. If the lesion be attempted in the antero-posterior direction it is almost certain to involve the pyramidal tract, while it is very difficult to avoid injuring the formatio reticularis and other important structures. Although it must be granted that we have as yet no clear experiments demonstrating the single action of the fillet, a table has been prepared (Table V., p. 161), showing the results in cases where centripetal conduction has been interfered with by lesion of the posterior roots, posterior bundles, the fillet, the ventral thalamic nuclei, and certain portions of the cortex. Clear and definite results were only obtained in cases of section of the posterior nerve roots. This is shown in Cat 175. After such an operation the tactile

* Nothnagel, *Virchow's Archiv*, 1869, vol. xliv.

† Binswanger, *Archiv f. Psychiatrie*, 1888. It is interesting to find that L. Pollock arrives in a different way at the same localisation of his "epileptogenous zone" (*Archives of Neur. a. Psych.*, 1923, p. 611).

myoclonic reflexes were absent in the limb affected. In such an experiment care is necessary in order that the bones and tendons of the part are not stimulated mechanically; if this occurs the stimulus may be conveyed to sensitive areas not affected by the lesion and the result vitiated. In such an animal where a sufficient dose of bromide of camphor is given, spontaneous shocks occurred which affected the extremity in association with the lesion, and other adjacent muscles. When a complete myoclonic fit occurred it was seen that this limb also participated.

The result got in this case may help to throw some light on the question whether so-called spontaneous shocks and also those induced by strychnine and occurring in tetanus convulsions are reflex in origin. (This question was discussed in Part I., p. 40.) It is very plausible to explain these spontaneous shocks as being due to stimulation from proprioceptive end-organs such as may occur in the gut. At the same time from the evidence afforded by Cat 175, one cannot exclude the possibility that chemical stimulation may be the cause of the phenomena.

As regards the observations made after section of the posterior nerve columns, reference will here be made to only one case, that of Cat 222 (p. 177). After cross-section of the posterior columns in the upper dorsal regions, no change was observed in the reflexes. When a deeper incision in the cord was made, no reflexes were elicited from the region caudal to the line of section at least immediately after the operation. The cortex irritability was unchanged.

A number of experiments were made to ascertain the result of simultaneous lesions involving the secondary centripetal tract for tactile sensation and the pyramidal tract both in the truncus cerebri and the cortex. It was found that the result was the same as where the pyramidal tract alone was cut—that is, the myoclonic reflexes were destroyed, at least, temporarily on the side of the body involved (Chapter III., § 1).

In Cat 114, the fillet was almost completely penetrated, while the pyramidal tract was but slightly injured. This case is important, because the lesion was directed mostly in an antero-posterior direction, so that all the fibres which cross orally to Wernekink's decussation were severed. This is the only case in my series of experiments where complete independence of the two halves of the body, as regards myoclonic reflexes, could be observed. The fits in this case were best marked on the left side (see p. 140, lesion, Fig. 38, p. 166). A deviation from the ordinary rule was seen in this case. As a rule after a myoclonic fit, whether it is better marked on one side or not, myoclonic reflexes cannot be elicited from any part immediately after the fit; this applies to both tactile and acoustic reflexes. This is the refractory phase described in Part I. In this case, however, tactile reflexes could be

elicited from the right side of the body immediately after the fit. Now, in this animal, the left half of the body had been deprived of innervation through the fillet and of a small part of the pyramidal tract. The right half of the body had been deprived of innervation through Monakow's bundle. In Chapter III. it was shown that unilateral lesion of this bundle did not exert a marked influence on the bilateral character of myoclonic phenomena.

We must therefore admit that some more important element has been interfered with. It is known in the case under discussion that the lesion was extensive and lay near the middle line on the right side. It must be remembered that near the middle line a complex group of cells lies (substantia reticularis). This structure appears to have a homolateral positive influence on reflex phenomena. It may be the case that on the left side where this region is intact, as well as the homolateral descending nerve tracts, fits occur, while on the right side, with injury of this region, the tactile myoclonic reflexes alone persist.

It is interesting to find that G. Holmes* came to the same conclusion as regards the homolateral influence of the formatio reticularis as applied to certain tremors, as also did Bouche† in relation to absinthe fits.

The importance of the evidence afforded by Cat 114, as to the influence exerted by groups of cells in the truncus cerebri, is enhanced by experiment No. 241, where the incision was made oral to the incision in Cat 114. In Case 241 nothing special was seen.

In Cat 242, hemisection of the mid-brain cuts off the left prosencephalon (Fig. 41, p. 181), with the exception of the pyramidal tract, while a middle line incision had been made oral to that made in Cat 114. After this operation the myoclonic reflexes were found equal and normal on both sides. The results of this experiment were recorded in tracings, while a complete series of sections showed the extent of the lesion. We are therefore able to draw definite conclusions from the experiment.

(*a*) The fillet may be excluded as an important or stable factor in the occurrence of myoclonic reflexes. In this experiment it was cut through on the left side. (*b*) In contradistinction to the condition found for the substantia reticularis pontis, a lesion in the mid-brain exerts no influence on the occurrence of reflexes—at least, not on the simultaneous appearance of the convulsions on both sides of the body. (*c*) Hemisection of the mid-brain—the pes pedunculi remaining uninjured—shows that with the exception of the pyramidal tract already referred to, all parts of the brain oral to the pontine region appear to have no effect or influence on the myoclonic reflexes and convulsions.

* G. Holmes, *Brain*, 1904 (Autumn).
† Bouché, *Epilepsia*, 1914, vol. v., p. 36.

TABLE V.

No.	*Lesions and Degenerations.*	*Myoclonic Reflexes and Fits.*
175.	Cross-section of the right posterior roots from 5th cervical to 3rd dorsal. Ascending degeneration in right posterior tracts, Gowers' and Flechsig's bundles, descending degeneration in antero-lateral tract.	Right forepaw did not react to tactile stimuli applied to the skin, but it did react when the stimulus was transferred through the bones. To an acoustic stimulus both right and left forepaws reacted simultaneously. Spontaneous shocks were seen in the left forepaw, while it was also involved in a general convulsion.
68.	A large abscess was found in the right cerebellum. The truncus cerebri was involved in the pontine region only. The lateral part of the lateral fillet showed ascending degeneration, while descending degeneration was present in the right pyramidal tract and bundle of Monakow.	Reflexes and fits occurred exclusively on the right side. (The left side was deprived of innervation from the fillet and pyramidal tract.) (Figs. 29 and 30, p. 137.)
91.	Ascending degeneration was present in the lateral fillet, descending in the left bundle of Monakow, and the lateral part of the left pes pedunculi (Fig. 32, p. 146).	Myoclonic reflexes were got best from the left forepaw. (The right forepaw had lost innervation from the fillet and pyramidal tract).
158.	Extirpation of the frontal pole of the left cerebral hemisphere. The cerebellar nuclei were intact.	Myoclonic reflexes were enhanced on the left side only, while fits also occurred on this side. (The right side lacked innervation through the fillet and pyramidal tract (see Table II., p. 128, and Figs. 36 and 37, pp. 164, 165).
191.	The frontal pole of the left cerebral hemisphere including the marginal convolution was removed. Ataxia of the right paws followed, better marked in the forepaws (see p. 118).	Tactile reflexes were absent from the right fore- and hindpaws. After the lapse of months these reflexes returned, but were weak, with a long refractory period and lengthened latent period. Further, a large dose of either the monobromide of camphor or absinthe was necessary before they could be elicited. Tactile ear reflexes were absent. Myoclonic epileptic fits in this animal started on the left side of the face, passed to the forepaw, the hindpaw of the same side, then crossed to the right side. Towards the end of the fit the animal jumped to the right side. After the fit it walked to the left, while it was dazed, but uneasy as soon as absinthe was given. The right side of the body was insensitive to pain for an hour after, while tactile stimulation induced convulsive movements in left paws only, and mainly in forepaw. Knee reflexes were present on both sides.

TABLE V.—*Continued.*

No.	*Lesions and Degenerations.*	*Myoclonic Reflexes and Fits.*
198.	The lesion was the same as for Cat 191. Degenerative changes occurred in the pyramidal tract and in some cortical association fibres with the oral portion of the thalamic nuclei. The corpus striatum was intact.	Right hindpaw was ataxic. It was held straight and stiffly forwards. Left pupil smaller than right one. The animal showed circus movements to the left for the first few days after operation. Tactile reflexes normal on the left side; usually absent on the right. Sometimes a weak tactile reflex was seen in the right forepaw, but there was no change of the latent period. After the injection of absinthe, spontaneous shocks and fits were seen on the left side. The animal was killed after five weeks.
202.	The grey matter of the left cerebral hemisphere was removed as far as possible.	This animal had, prior to operation, very active myoclonic reflexes —*i.e.*, without the use of monobromide of camphor. After operation the animal showed occasional circus movements, but later this movement became constant and with conjugate deviation of the eyes persisted up till the death of the animal thirteen months later. There was right hemianopsia. Reflex and spontaneous shocks were seen on left side, and at times, after the administration of large doses of monobromide of camphor, on the right side. There was no change in the latent period. In shocks and fits, the left side of the body was frequently involved alone. Knee reflexes were present on both sides, and the latent period was the same on both sides.
235.	(See Table IV., p. 153, Protocol 14, p. 153). Lesion of the fillet and pyramidal tract on the right side of the medulla.	The myoclonic reflexes were diminished, but not absent on the left side of the body.
24.	Lesion of the fillet and pyramidal tract.	On that side of the body which had been deprived of pyramidal and fillet innervation the myoclonic reflexes could hardly be elicited.
114.	A median incision was made so that all fibres crossing orally to Wernekink's decussation were cut. Degeneration was also present in the right fillet (compare Protocol 16, p. 166, and Fig. 38, p. 166).	There was a striking difference on the two sides. After a small dose of monobromide of camphor, fits occurred on the left side, while myoclonic reflexes could be elicited on the right side, more especially after a left-sided fit. If both sides of the body were convulsed in a fit, the rhythm of the convulsions on the two sides was quite different.
241.	At the first operation a median incision in the mid-brain severed the commissura posterior and the intra-rubral connections.	After the first operation no difference in reflexes was seen. After the second, the myoclonic reflexes were much more pronounced

TABLE V.—*Continued.*

No.	*Lesions and Degenerations.*	*Myoclonic Reflexes and Fits.*
	Degeneration was found in the ascending oral connections of the nucleus ruber (left less than right), the lamina medullaris ventr., the thalami (right less than left) and in various hypothalamo-striatal connections. Descending degeneration was found in both posterior longitudinal bundles. At the second operation the foramen magnum was exposed and an attempt made to cut the vestibular nerve with a needle. This failed, however, and the right nucleus gracilis and cuneatus were injured.	on the left side. This may be due to lesion of the nucleus of the funiculus posterior. It must, however, be remembered that, in this case, the homolateral tractus reticulo-spinalis was involved. The animal only lived six days after the second operation, so verification by the examination of degenerative changes was not possible.
242.	Incision in thalamus on the right side. This was done seven days before the animal died. Four days before it died an injection of formol was made between the nuc. tecti cerebelli and median incision at the level of the red nucleus, so that only the pes pedunculi and the lateral part of the tegmentum escaped (Fig. 41, p. 181).	The animal was decerebrated in the second operation; still, after the administration of ½ gramme monobromide of camphor (in oil) and a dose of absinthe, myoclonic reflexes could be elicited from both sides simultaneously. Tracings demonstrating this phenomenon were prepared. Further, the latent period of these reflexes did not seem altered.

§ 3. **Myoclonic Reflexes where the Lumbar Cord has been isolated.**

In some of my later experiments I frequently recorded myoclonic phenomena occurring in animals where the spinal cord was partially or wholly divided, either unilaterally or bilaterally. In none of these experiments was the result so successful as in the case of a dog where several segments of the dorsal spinal cord had been removed some time before.

Protocol 15, Poodle.

26.2.01. The dura mater was exposed under ether-anæsthesia over some five to six dorsal spinal segments and opened freely. The wound was closed in layers. Knee and plantar reflexes were both found in the paraplegic animal on the day following the operation.

2.3.01. The wound was opened, and five segments of the dorsal cord removed. The wound was again closed in the layer method. After this operation, knee and plantar reflexes had quite gone. The animal became much emaciated, had incontinence of urine and fæces, and developed ulcers on the hinder part of the body.

12.3.01. At 9 a.m., 1½ grammes monobromide of camphor were given. The animal whined. Tapping on the bones of the hinder part of the body elicited a retarded myoclonic reflex. The reflexes in the forepaws were normal. There was no plantar reflex.

At 10 a.m., quasi-choreic convulsions were observed as occurring

constantly over the voluntary musculature of the anterior part of the animal. Slight acoustic stimuli, produced by tapping the hands together, produced a well-marked acoustic reflex. The left hindpaw hung completely flaccid, but the right hindpaw showed rhythmic extension movements every five or six seconds. During this examination it was found that the knee reflex was present, but it was the biceps and not the quadriceps which contracted.

At 10.10 a.m., the animal had a fit localised to the frontal part, it salivated, and had convulsive movements of the jaws. During this fit the right hindpaw showed the extension movements already referred to, but they were slower. Before and after the fit, there was no reaction to a pain stimulus from any part of the animal.

At 11 a.m., animal had vehement fits with salivation and tonic and clonic convulsions followed each other. It did not make any cry. The fit

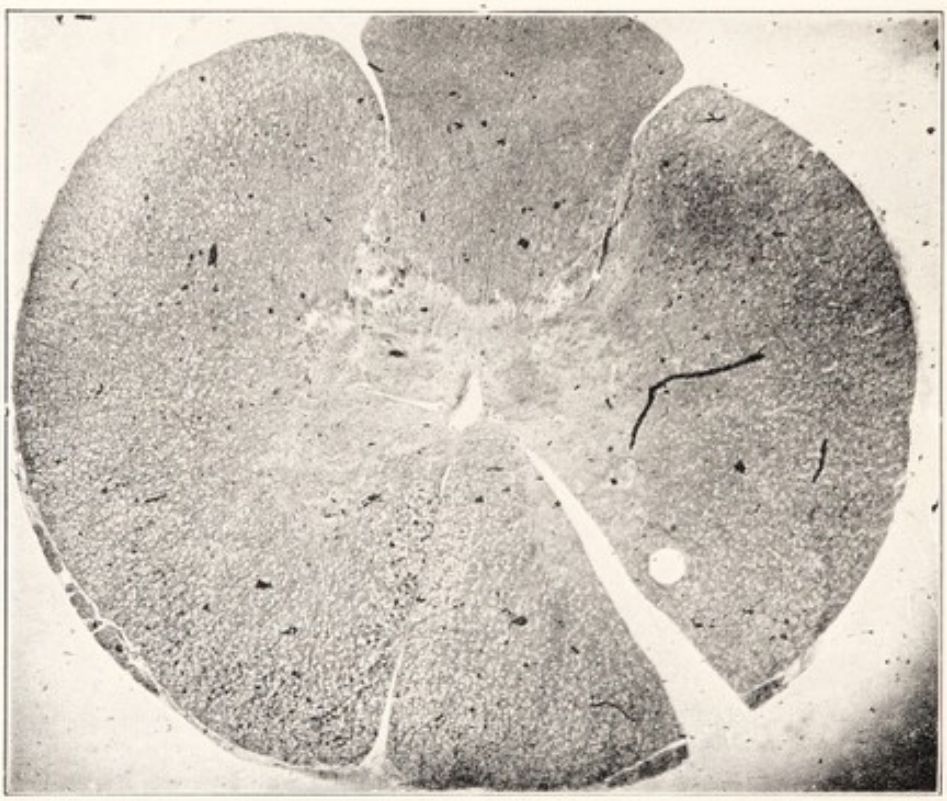


FIG. 36.—CAT 158. DEGENERATION OF THE RIGHT PYRAMIDAL TRACT AS A RESULT OF A LESION IN THE LEFT PYRAMID; ALSO DEGENERATION OF THE LEFT ANTERIOR LATERAL TRACT AS A RESULT OF A LESION IN THE MEDULLA.

was again localised to the front region. The plantar reflex of the right hindpaw could be elicited during the fit; it was slow, but quite active, and had a definite refractory period. A short time after this "frontal fit," the movements of the hindpaw ceased. *This phenomenon of stoppage of the rhythmic extension movements of the right hindpaw after a fit was seen after each subsequent fit.*

13.4.01. Animal died. The rigor mortis was more pronounced in the left hindpaw than in the right. Incisions of the musculature failed to produce any sign of blood. There was deformity of the thorax, due to the lower six ribs having lost their normal position, and they were found lying along the spinal column. The whole aperture in the spinal cord was filled with gelatinous granulation tissue. This mass was 6 cm. in length and 1½ cm. in depth. There was no trace of pus. When the spinal cord was more closely examined, it was found that there was a zone of venous con-

gestion for 3 cm. above and below the lesion. There was no malacia. There were no further changes beyond the degenerative changes inevitable to the lesion; these were demonstrated by the Marchi method.

The occurrence of the apparently retarded reflex movement in the hind limb in this animal, produced by tapping or touching the bone, may give rise to some difficulty, for it is true that it is not easy to exclude the possibility of the propagation of shock to the frontal animal. The reappearance of the plantar reflex, under the influence of monobromide of camphor, is also difficult to explain. There is, however, no doubt but that the spontaneous rhythmic movements in the hindpaw of the animal are due to, or are called forth by, the effect of the drug on the isolated lumbar

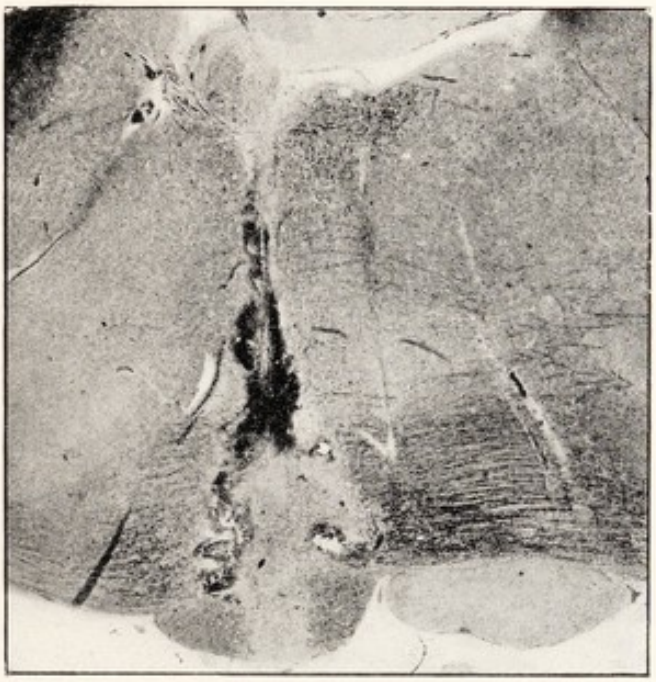


FIG. 37.—CAT 158. SHOWS A STAB IN THE MEDULLA ON THE LEFT OF THE MIDDLE LINE.

cord. That these rhythmic movements cease after the fits in the frontal part of the animal seems to me to be of great interest, when considered in relation to certain facts dealt with in Chapter III., § 1, p. 47. It would appear in this case that the fit in the frontal part of the animal exerted an influence on the hinderpart. In all probability the effect of the fit was to render the toxin—monobromide of camphor—inert. The cessation of motor phenomena in the frontal animal after a fit might be ascribed to the influence of the central nervous system, by assuming that there was a long refractory period. This explanation would, of course, not apply to the hinderpart of the animal, for it was cut off from all nervous connection with the frontal animal.

The observations made on another experimental animal,

Cat 114, already referred to (see Table 3, p. 140), are of the same type. In Cat 114, where the spinal cord was divided, monobromide of camphor had a distinct influence on the hinderpart of the animal. This was the only one of my experimental animals where the two halves of the body displayed independent action in relation to myoclonic fits (middle line lesion at junction of pons and mesencephalon).

Protocol 16, Cat 114.

28.10.06. Lesion, refer p. 140. Monobromide of camphor dissolved in oil was administered. It had shocks but no fits.

30.10.06. The same dose repeated.

31.10.06. At 11 a.m., a kymographic record was taken of both fits and reflexes. At 1.15 p.m., both cortices were laid bare. Faradic stimulation

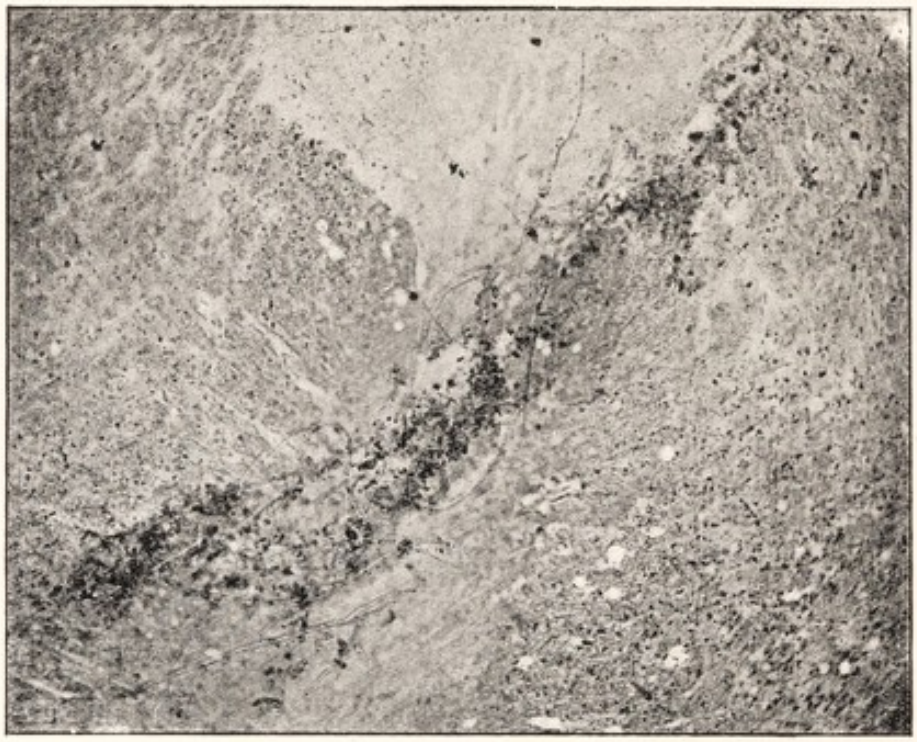


FIG. 38.—CAT 114. MIDDLE LINE INCISION IN THE MESENCEPHALON. (SEE P. 140).

of the left cortex gave convulsive movements of the right hindpaw, stimulation of the right cortex gave convulsive movements of both hindpaws. About the level of the sixth dorsal segment hemisection of the right side of the cord was performed. After this, convulsive movements of the right hindpaw was only got by tapping on the back of the animal.

After the spinal cord was cut through completely, percussion on the animal's back produced a weak convulsive movement of both hindpaws. These movements were purely extensor; before this the flexor movement had been predominant. If the cortex were stimulated the frontal portion of the animal alone reacted. The autopsy showed that the spinal cord had been completely cut through.

Although in this case, also, there is no means of determining finally that the act of tapping or percussing the back was not

transferred to the hypersensitive and strongly reacting frontal portion of the animal, yet the change in the character of the movements from flexion to extension seems to indicate the great probability that, in the isolated hinderpart of the body, a tactile reflex, although much weakened and altered, can still be elicited. Further attention must be drawn to the conversion of the myoclonic reflex. Normally, this reflex involves chiefly the flexors, but after isolation the extensors take their place. This was also seen in the dog just described, where a portion of the dorsal cord had been removed some weeks previously (23.3.01).

It therefore seems to me justifiable to conclude that immediately after cross-section of the lumbar cord, and several weeks after cross-section of the dorsal cord, this change, or conversion of a flexor into an extensor reflex, occurs. Wiedemann and Gottlieb* stated that they never saw true convulsive fits in the hind limbs of animals, but in birds, under the influence of picro-toxin, convulsive movements had been observed in the legs. The observations made on Cat 175 are in agreement with these descriptions.

Protocol 17, Cat 175.

6.6.10. The posterior nerve roots from the fifth cervical to the third dorsal were cut through.

6.7.10. 1½ grammes monobromide of camphor given by the mouth.

7.7.10. At 8 a.m., ¾ gramme monobromide of camphor was given, and the same drug dissolved in oil was injected at 10 a.m., followed by a dose of absinthe. Notes were taken from 9 a.m. From 10 a.m. the animal had epileptic fits which recurred at shorter and shorter intervals, gradually displaying the condition of status epilepticus. Between the fits it was impossible to make any notes on the condition of the reflexes.

The animal was arranged so that it was fixed in front while the hind legs pulled against a spring. After a fit a movement of the left hindpaw could always be elicited by tapping on the table. During the fit it was noticed that both forepaws convulsed at the same time, in the same position and direction, but in the course of the fit the right and non-sensitive paw was altered. It was held straight down, pressed towards the trunk. If the right shoulder were touched the right forepaw alone was convulsed. A spontaneous shock was seen only in this paw. Complete cross-section of the cord was made at the level of the middle of the scapula. After this operation, the knee reflexes were found on both sides. Further, when a bony prominence of the hind animal was touched a (reflex) shock was produced in the hind animal. This part of the animal did not, however, participate in a fit of the frontal portion. Fibrillar and fascicular contractions were constantly present in the muscles of the hind animal. Tapping on the table was sufficient to augment the irritability of the frontal animal up to the point of producing myoclonic fits. Sometimes it looked as if the whole animal shared in such a fit. *Immediately after a fit, the frontal animal was in the condition of "discharge." Knocking on the table produced distinct extensor movements* of the left hindpaw; the right hindpaw was not affected. The same phenomena are seen after resection of the left frontal cerebral pole. At 12.15 p.m., the right frontal pole of the cerebrum was also resected. After this, knocking on the table caused the left forepaw to react, but had no effect on the right.

The next step in the operation was the joining of the cross-section

* Gottlieb, *Archiv. f. exp. Path. u. Pharmacodynamie*, 1892, vol. xxx., p. 30.

through the right and left frontal poles by an incision through the thalamus. Walking movements were subsequently seen in both forepaws, but mostly in the right. The left forepaw still reacted to knocking on the table. The right fore and hindpaws did so also, but to a much less extent.

The animal died. The brain and spinal cord were examined. The skin was also kept for examination for changes in the fur.

This experiment also seems to show that with the isolated lumbar cord myoclonic tactile reflexes may be elicited, but they are changed in type. Instead of adduction and flexion the movement is extension. Further, after resection of both frontal poles, involving the front portion of the thalamus, a tactile myoclonic reflex can still be demonstrated.

Although all writers on the subject from M. Hall (experiment made with a dog, the spinal cord cut across, both carotids cut, anoxæmia convulsions only seen in frontal animal) up to Olmstedt and Logan (who recorded the absence of insulin convulsions in a

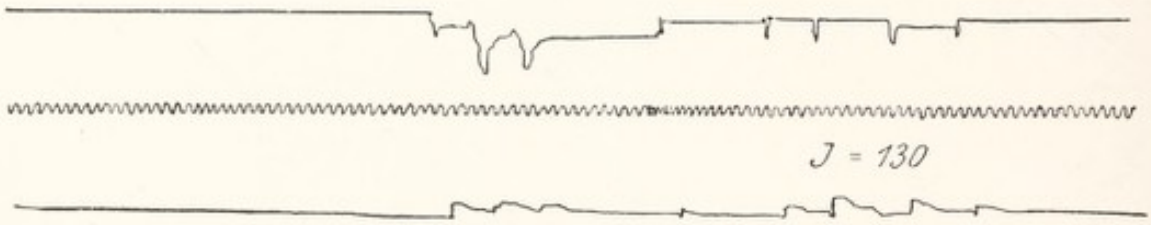


FIG. 39.—CAT 88. FARADIC STIMULATION OF THE MOTOR CORTICES AFTER SECTION OF THE LEFT CRUS CEREBRI.

Stimulation of the cortex on the left side has no effect, the effect of stimulating the right cortex is here shown; i=130. The left hindpaw supplies the upper curve, the right hindpaw the lower. The difference in the curve must be ascribed to the section of the lumbar posterior nerve roots on the left side, which preceded the taking of this tracing.

dog with the spinal cord cut) agree that complete fits cannot be the function of the spinal cord. There is, however, a difference of opinion as regards myoclonic and choreic convulsions. Chauveau, Legros and Onimus,* and Harnack† observed that, in a dog, chronic convulsions disappeared after section of the cord. Quincke,‡ on the other hand, did see periodic convulsions in the hindpart of a dog in which the cord had been cut. In the same way, Magnan (Part I., p. 8) saw convulsions following the administration of absinthe to such an animal, and Bertet and Joliet§ after the administration of carbolic. Perhaps in this last case the convulsions were fibrillar and fascicular and might be regarded as a symptom of poisoning. Experiments on the fœtus to determine

* Legros and Onimus, *Journal de l'Anatomie et de la Physiologie*, 1870, No. 4.

† Harnack, *Arch. f. exp. Pathol. u. Ther.*, vol. vii., p. 188.

‡ Quincke, *Arch. f. exp. Pathol. u. Ther.*, 1885, p. 370.

§ Bertet et Joliet, *Gaz. méd. de Paris*, 1872, p. 187.

the early appearance of some reflex power in the spinal cord seem to point in the same direction also.*

Finally, attention must be called to the case of an experimental animal, Cat 175. In this animal I found cross-section of the posterior spinal nerve root for a limb, did not prevent this limb from participating in spontaneous shocks, series of shocks and fits, some weeks later.

Reference is here made to cases similar to that of the experimental animal, Cat 88. In this animal the cross-section of the posterior nerve roots was not done several weeks before the observations were made, but observations were made immediately at the time of operation. It was definitely proved that the laying bare of the cord and cross-section of the posterior nerve roots had a decided influence on the effect of stimulation of the cortex and on myoclonic phenomena. In Cat 88 the spinal cord was exposed at 4.45 p.m., and from that moment no myoclonic phenomena could be got from the extremities distal to the site of operation. At 5.30 p.m., the posterior nerve roots for the left hindleg were cut. The motor cortices were stimulated with the faradic current. From the left cortex convulsions of the right hindpaw could be produced, but no result followed stimulation of the right cortex. With a strong current applied to both cortices convulsions of the crossed extremity did appear (Fig. 39, p. 168), but the tracing from the non-sensitive paw was much sharper than that from the right.

§ 4. Concerning Direct Faradic Stimulation of the Spinal Cord.

Cat 203 (compare Table II., p. 128) had on 6.1.12 ½ gramme monobromide of camphor and on 7.1.12 a dose of absinthe. The animal breathed asthmatically. A severe fit occurred in which both forepaws were stretched forwards, while the head was bent strongly backwards. After the preliminary stretching forwards of the forepaws the left one convulsed, but not the right which retained its position. The face was convulsed homolaterally.

At 10.5 a.m., the animal had a dose of absinthe. It was thereafter suitably secured and the cortical motor areas exposed. When the right cortex was touched with the electrode, i=48, the left hindpaw convulsed. When the left cortex was touched, i=43, the right hindpaw convulsed. At 10.30 a.m., a very much larger dose of absinthe was injected into the thigh (right). After this, touching of the cortex produced a continual series of shocks, even if no current were passing. The mere touching of the left cortex caused a general shock, but the result was much more potent if the current were employed.

The dorsal cord was exposed and stimulated; shocks of the hind portion of the body followed.

In the first five minutes after a fit, induced by stimulation of the motor cortex, no reaction could be provoked by repeated stimulation of the cortex; but if the electrode were applied to the dorsal cord, shocks followed in the hind portion of the body. These were too slight to record. After repeated stimulation of the cortices had induced status epilepticus, the cortices remained insensitive to stimulation, but the spinal cord still reacted with i=30.

* Minkowski, *Schweiz. med. Wochenschrift*, 1922, Nos. 29 and 30.

Some considerable time after a fit the irritability of the cortex was again enhanced, so that immediately before the next fit a moderate current stimulating the cortex might produce shocks. Jacksonian convulsions could not be elicited between the fits. Some moments before a fit, the cortex reacted to i=38, the spinal cord to i=48.

11.25 a.m. The fits became weaker. The irritability increased as before, slowly before a fit. The right cortex reacted better than the left.

11.30 a.m. Only from a certain point in the right cortex with a current of i=40 could a reaction be got. This was not the case with the left cortex.

Complete cross-section of the spinal cord was performed. Stimulation of the proximal portion produced shocks in the head. It could not, however, be decided whether this head shock was not caused indirectly as a reflex to a mechanically conducted shock due to the local convulsion which followed on application of the electrode.

From this experiment the conclusion is drawn that direct irritability of the spinal cord, like the reflex irritability of the isolated lumbar cord (p. 168) increases before a fit, and is at its lowest for some time after the fit. The changes in the irritability of the dorsal cord are not so striking as in the motor cortex. Further, it was demonstrated that in this animal, where the cerebellum was severed on the right side, the left motor cortex was permanently less irritable.

I got a similar result in an animal with the same lesion (Cat 2.7.01) and also in other animals in the condition of charge, where I stimulated the dorsal cord with the faradic current, with no result save single convulsion in the hind animal.

CHAPTER V

FARADIC STIMULATION OF THE MOTOR CORTEX AND THE MEDULLA OBLONGATA

DURING part of this research it was the rule to use the animals for further observations after preliminary observations on the effect of monobromide of camphor and absinthe had been recorded. In such cases the animal was suitably arranged and, after being anæsthetised, the brain was exposed. Warm salt solution was used to keep the cerebral tissues moist and warm; faradic stimulation of the brain or ablation of certain areas was performed and the effect noted. As a result of numerous experiments it was seen that stimulation of the motor cortex and also of the lateral portions of the medulla, which are all but covered by the cerebellum, is followed by tonic convulsions on both homolateral extremities. This is more particularly the case where a dose of monobromide of camphor or absinthe precedes the stimulation. In the case of faradic stimulation of the motor cortex, the effect, of course, varied with the centre stimulated (this was first seen on the crossed half of the body); in the case of the medulla, stimulation was followed regularly and immediately by a convulsive movement of both hind- and forepaws, or, where the current used was very weak, by a movement of the homolateral hindpaws only. These movements of a convulsive character are similar to those which usher in a myoclonic fit. It must, however, be remembered that in stimulating this lateral area of the medulla, there is great danger of the current escaping through the spinal accessory nerve. Indeed, only the convulsive movement of the hindpaw, usually adduction, is generally taken to be due to the actual stimulation of the medulla.

In these stimulation experiments it was shown that the degree of irritability (measured by the distance of the coils—Dubois-Raymond coil used) of the cortex or the medulla, first for the crossed effect, and secondly for the homolateral effect on the hindpaw, varied greatly with the condition of charge or discharge in which the animal was—that is, the condition of maximum irritability was found shortly before a spontaneous fit, the minimum effect shortly after a fit. This difference, however, is seen in many cases to be less evident for the medulla than for the motor cortex, and also lasts for a shorter period.

In a normal cat—*i.e.*, a cat not operated on (No. 166)—the

motor cortices were exposed during status epilepticus, and faradic stimulation was applied through the dura to the motor area.

Protocol 18, Cat 166. Not operated on.

30.11.08. 0·5 gramme bromide of camphor. No effect.

10.12.08. 9.45 a.m., 0·75 gramme bromide of camphor. No effect. 3.10 p.m., a fit heralded by spontaneous shocks. Tactile reflexes much clearer than the acoustic reflexes.

1.3.09. 1 gramme bromide of camphor after the meal. No effect.

25.1.09. 10 a.m., 1 gramme bromide of camphor before the meals. 6 p.m., fits, always preceded by spontaneous shocks.

7.4.09. 12.45 p.m., 1·5 gramme bromide of camphor. 3 p.m., the fits appeared, which became more vehement up to exitus (4.55). 4.10 p.m., the animal was fixed in position. 4.15, 155 mm. (position of coil), stimulation to left cortex. Slight reaction of the right hindpaw. As an after effect a fit followed at 4.16. 4.17, irritation of right cortex, current the same as above: slight convulsions of right and left paws. 4.19, right cortex i=180: slight convulsions left paw. 4.31, a spontaneous fit. Shortly after this: left cortex i=180. No effect. 4.31·5, right cortex i=150: convulsions of left paw. 4.32, left cortex i=150: convulsions of both paws. 4.33, spontaneous fit. Shortly after; right cortex i=150: convulsions of the left paw. 4.34, left cortex: convulsions of the right paw. 4.31, right cortex i=150; convulsions of both paws. 4.35·5, a slight fit. 4.37, right cortex: slight convulsions of the left paw. 4.37·5, left cortex; convulsions of the right paw. 4.38, right cortex: both paws. 4.39, left cortex: both paws (always at same current i=150). 4.40, right cortex: both paws slightly. 4.41, left cortex: both paws (right more than left). 4.42, right cortex: both paws slightly. 4.43, left cortex: both paws (right more than left). 4.44, a slight fit. 4.45, right cortex: left paw more than right. 4.49, right cortex: left more than right. 4.50, cortex: right more than left. 4.50·5, a fit. 4.51, right cortex: left paw ver weakly. 4.53, right cortex: both paws almost invisible. 4.54, left cortex: no effect. 4.55, left and right: no effect. Exitus.

In the case of this animal, where no operation had previously been performed, the irritability of the cortex seemed to increase before a fit and to diminish after the fit, with the exception of those occasions where a second fit followed quickly on the first; when this happened, the increased irritability persisted. The diminution of irritability after a fit was further demonstrated by the fact that stimulation of the cortex immediately after a fit resulted in convulsive movements of the crossed hindpaw only. Later on, both hindpaws reacted, at first slightly, then more actively, until finally a fit supervened.

The next case (No. 224) shows the effect of stimulation of the right motor cortex and the left side of the medulla. It further demonstrates that the irritability of these two regions is not always the same in relation to the occurrence of fits.

Protocol 19, Cat No. 224:

3.8.19. 9.50 a.m., ether narcosis. Over the right frontal brain the dura was laid bare. Cortex stimulated through the dura. With a current i=90 slight convulsion of left forepaw. 10.20, the medulla oblongata was also laid bare; there was a cyst in this region below the thickened dura. On the left side the dura was removed, and the medulla was irritated at the point where the corpus restiforme disappears below the cerebellum. With a very weak current i=250, only a convulsion followed in the muscles, which are innervated by the nervus accessorius. With a current i=120 and i=100 slight movements of the toes of the left

hindpaw, or also extension of the hindpaw with movements of the toes could be seen.

10.44. Cortex stimulated as before i=90; slight convulsion of left forepaw. 10.50, ¾ syringe of absinthe. After four minutes, slight tactile reflexes of back and hindpaws.

10.55. Left frontal brain i=90 as before. 11 a.m., right corpus restiforme. When i=140, shock-like convulsions of the left forepaw and right hindpaw (altered pyramidal effect ?). 11.5, another syringe of absinthe. 11.6, left frontal brain i=80; convulsion of right forepaw. 11.8, a fit followed by stimulation of the medulla; i=160, convulsion over the right half of the body. Five minutes later this was no longer the case with i=120. 11.10, left cortex i=70; left medulla i=100, left half of the body. 11.15, another syringe of absinthe. 11.16, immediately after a slight fit cortex i=10 (?).

11.18. Left medulla i=180 (convulsion left half of the body).

11.20. Another syringe of absinthe. 11.21, cortex i=70, medulla i=200, no fit. 11.25, cortex i=70, medulla i=245 (weak current).

11.26. Fit elicited by manipulations. Shortly after irritability of the cortex i=70, and medulla i=160. 11.40, another 1½ syringe of absinthe of the medulla, convulsions on right and left i=245, till a fit followed. After this for a long time nothing could be elicited from the medulla with i=200, but this was the case with i=170.

11.45. Threshold is found in the cortex i=170, in the medulla i=245. Immediately after this a severe fit, with vehement general convulsions and cries. Then from the medulla nothing was observed with i=190, and this was also the case with i=150. 11.48, the animal was still discharged; cortex i=40, medulla i=150. 11·50, still discharged. So much so that with stimulation of the medulla exclusively a crossed (pyramidal) effect was obtained. Slowly the irritability increased and homolateral shocks were observed again in response to stimulation of the medulla. In this stadium incrementi of the irritability, immediately after a homolateral shock, elicited by faradic current, no reaction could be obtained with the same current (refractory phase). This was never observed at the cortex, at least not in that degree. 12 o'clock, crossed incision in the mid-brain causing decerebration. The tactile shocks persisted, whereas with i=130 homolateral shocks could be elicited from the medulla. Also with a much stronger current ,such as i=120, homolateral shocks were elicited. Fits were no longer seen. Exitus.

This observation seems of importance to me, because here it is plainly proved that absinthe increases the irritability of the centres in the medulla oblongata. The increase in medullary irritability is not in this case so marked as the increase of the irritability of the motor cortex. This increased irritability persists shortly after a fit, and then diminishes rapidly in the next few minutes to increase again for a brief period. In the stadium incrementi, after a homolateral convulsion, elicited by unilateral faradisation of the medulla, or after a spontaneous double-sided shock, no fresh shock can be elicited; this is therefore a refractory period. In the stadium incrementi the duration of the refractory phase connected with stimulation of the medulla is of the same order as that of the tactile reflex shocks with a moderate degree of monobromide of camphor intoxication. There is, therefore, good reason to believe that the mechanism of the refractory phase with the myoclonic reflexes does not find its seat in the spinal cord as Sherrington suggests, but higher up in the centres and connections which play a part in these experiments where the medulla

is stimulated. After decerebration there is no change in the homolateral shocks which may be elicited by stimulation of the medulla, but no regular complete fit is seen to follow medullary stimulation. This experiment, just as the experiments recorded in Chapter II., § 2, p. 113, and Chapter III., p. 139, shows that the tendency to exhibit fits appears to depend on the pyramidal tracts being entire. Like this experiment, the present experiment shows that, although the normal reflex shocks have their centre in the medulla, yet the influence of the cerebral cortex is important, both for the occurrence of reflexes and more especially for complete myoclonic fits. The observations with Cat 233 also show clearly the strong influence of the fits in diminishing the irritability of the lateral area of the medulla without the intervention of the cerebral cortex. This animal, three weeks previously, had an experimental lesion performed which induced conjugate deviation to the right and a tendency to fall to the left. The conjugate deviation persisted up to the death of the animal.

As in the case of Cat 233, the motor cortex was intact (there were no degenerative changes in the pyramidal tracts), while there were definite differences in the reflexes on the right and left sides, it therefore proves that the influence of the frontal brain on the myoclonic reflexes is not exclusively dependent on the motor area, or even on the cortex as a whole. This conclusion is also arrived at from the data supplied by another experimental Cat 240, pp. 142 and 180.

Protocol 20, Cat 233.

3.8.13. Animal had ½ gramme monobromide of camphor. The myoclonic reflexes produced after the dose were much weaker on the left side. Absinthe was injected. A general fit followed, after which there was marked deviation of the head to the right; maximal rotation of the head to the left. This marked deviation of the head to the right was seen after all the subsequent fits. At 11.45 p.m., continuous shocks and fits supervened. Both cortices were exposed, when a strong odour of absinthe was noticed. With a strong current, no convulsions could be produced by stimulation of the cortex. The medulla was then exposed and the lateral area of the medulla stimulated. Homolateral convulsions followed, particularly well marked in the hindpaw; these convulsive movements were induced with a weak current (i=180). It was noticed that after a fit a much stronger current was required to elicit these movements (i=150). After breathing had stopped, slight convulsive movements could still be seen. From an examination of the sections of the brain it was seen that at the operation, performed on the cat three weeks before death, the lateral part of the right lateral fillet and the nucleus ventralis thalami had been severed, while the nucleus lentiformis was pierced at the right side. The internal capsule had escaped.

That the "tonisating," or, perhaps, better termed the "facilitating" (Graham Brown), influence of a certain condition of the cerebral cortex on the medullary centres is reciprocal is proved by the observations on Cat 221. These observations afford data which make it possible to establish more accurately the centres

and tracts which are associated with the refractory phase of the myoclonic reflexes.

Protocol 21, Cat 221. Operation on 2.7.12, p. 153.

Two vertical stabs were made through the right cerebellum and through the formatio reticularis; the pyramidal tracts remained intact (Fig. 40, p. 175).

20.7.12. At 10.15 a.m., absinthe was injected. Afterwards some

FIG. 40.—CAT 221. LESION IN THE RIGHT FORMATIO RETICULARIS. TWO STABS MADE IN IT WITH A NEEDLE.

tactile shocks were elicited, but only on the left side. Both frontal poles were exposed.

11.15 a.m. The motor areas were stimulated with a current i=80, with the result that powerful convulsive movements were produced on crossed sides of the body, both right and left.

11.16. A second dose of absinthe was injected. At 11.18 the left side showed well-marked tactile reflexes; on the right side these reflexes were weak or absent.

11.19. The cortex was again stimulated with the same strength of current as before (i=80); powerful shocks were produced as before on both sides.

11.20. With a current of i=90 it was found that *stimulation of the*

right cortex resulted in a single convulsive movement of the forepaw at every second application (interval of stimuli ± 1 inch), while on the left side the convulsion followed every fifth application of the stimulus.

11.22. Tactile stimuli applied to the forepaw on the right was followed by a tactile reflex shock at *every third application—i.e.*, there was a long refractory period. On the left side each stimulus was followed by a well-marked shock.

11.36. The thalamus was divided on both sides. After this, stimulation of the cortex was quite ineffectual.

11.45. Cerebellum and medulla exposed. Faradic stimulation of the lateral aspect of the medulla on both sides, the current i = 120, gave convulsive movements of the homolateral forepaw. With the current of i = 150 the same movements followed. It was found, however, that these movements were due to escape of current through the spinal accessory nerve (see Cat 222). Tactile stimulation to the left hindpaw was followed by a reflex; this did not happen on the right side.

Autopsy.—The white matter of the cerebellum on the right side showed areas of degeneration. There was marked degeneration of the superior crus cerebelli following severance of the nucleus dentatus. The posterior longitudinal bundle had been divided, and, as a result, well-marked ascending and descending degeneration had followed along the bundle. As the right substantia reticularis was divided, the predorsal bundle showed descending degeneration, mostly on the right side. (See Fig. 40.)

Epitome.—As a result of the observations noted in Chapter II., § 4, p. 126, the suggestion that the unequal reactions shown on the two sides of the body is due to an affection of the cerebellum may be excluded at once. If such were the explanation, then the irritability would in this case be better marked on the right side. As, however, the pyramidal bundles and the bundle of Monakow are both intact, it seems to me that the better marked reaction seen on the left side of the body may be ascribed to the lesion of the right formatio reticularis.

I therefore think that the long refractory period met with when the left cortex is stimulated, or when tactile stimuli are applied to the right hindpaw, must be ascribed to this lesion. From this experiment the conclusion can be drawn that a lesion of the right medullary centre does not alter the irritability of the crossed cortex, but only lengthens the refractory phase for faradic stimulation of the left motor cortex, as well as that of the tactile myoclonic reflex of the right hindpaw.

In this way the medullary centre seems to exert a certain tonic (facilitating) influence as well on the homolateral myoclonic reflexes as on the crossed cortex, and especially so by influencing the refractory phase.

It will be recalled that in Part I., Chapter IV., p. 55, and Chapter V., p. 69, it is shown that in the physiological analysis of the myoclonic phenomena, the shortening of the refractory phase progresses steadily after myoclonic reflexes, series of shocks, or complete myoclonic fits. It is clear, therefore, that the pontine-

medullary centre plays a very important part in the production of myoclonic reflexes and fit phenomena.

The observations made on Cat 222 show quite definitely that the dorso-lateral tracts are not, at least exclusively, the conductors of the ascending stimuli which call forth myoclonic reflexes.

Protocol 22, Cat 222 H.

27.7.12. At 10 a.m., animal was lightly anæsthetised and a large injection of absinthe administered. The motor area and the medulla were exposed.

11.5. First spontaneous shocks seen.

11.15. Current i=200 stimulation of margin of medulla on the right, followed by convulsive movement of the hindpaw (right).

11.30. Dura opened over both cortices. Stimulation with the current i=85 on both sides was followed by convulsive movements of the crossed forepaw.

11.35. Current i=180 stimulation at the margin of the medulla (corpus restiforme) resulted in a convulsive movement of the homolateral hindpaw.

11.45. Section of the dorso-lateral tracts on the right side at the level of the first cervical vertebra.

11.46. Result as described at 11.35.

11.48. Tactile myoclonic reflexes elicited from fore- and hindpaws.

11.50. The posterior half of the spinal cord incised about the level of the first cervical vertebra. After this operation the irritability of the cortex was unchanged. Stimulation resulted in movements of the crossed forepaws, as seen at 11.30. The convulsive movements of the hindpaws, produced by stimulation of the margins of the medulla, were less regular in occurrence, and were better marked on the right than the left. After cross-section of the right optic thalamus, stimulation of the medulla margin still produced convulsive movements of the hindpaws; the right side was less marked than the left. After section of the thalamus on the left, the same result followed. Stimulation of the margin of the medulla still elicited convulsive movements of the forepaw. After breathing had stopped, and cross-section of the spinal accessory nerve, convulsive movements occurred in the shoulders, due to escape of current through this nerve.

From this experiment the conclusion is drawn that the conducting tracts for the ascending stimuli associated with peripheral reflexes, and the descending stimuli associated with hindpaw convulsive movements produced by stimulation of the margin of the medulla, are not situated in the posterior columns, but lie more ventrally in the spinal cord. The experiment made at 11.50 a.m. seems to indicate that the centrifugal conduction of such stimuli from the medulla lies near the level of the central canal.

The next experiment serves to show that the supposition regarding the escape of current through the accessory nerve already referred to is perfectly right. This being so, no value attaches to the convulsive movements, seen during stimulation of the medulla, in the forepaw. In Cats 239 and 240 stimulation was applied regularly to the cortex and the margin of the medulla during status epilepticus.

Protocol 23, Cat 239. Lesions and their results compare Chapter III., paragraph 1, p. 134.

Without a stronger dose of bromide of camphor the myoclonic reflexes of this animal were more pronounced over the right half of the body.

24.4.10. At 4 o'clock an injection.

Time.	*Reflex after.*	*Time.*	*Reflex after.*
4.6	Right forepaw, 2·4	4.11·5	Right forepaw, 2·2
4.8	Left forepaw, 2·2	4.12	Left forepaw, 2.2
4.9	Right forepaw, 3·0		Spontaneous shocks.
4.10	Left forepaw, 2·2	4.13	Right forepaw, 2·3
Another two-thirds syringe of absinthe.			
4.11	Blow, 1·7	4.14	Fit.
		4.16	Right forepaw, 3.3
		4.18	Fit.

(Rhythm of the tracing of the fit: 5—6—12, 5—6—5—9—6—12—23—6, 5—8.)

The left frontal brain and left medulla oblongata were exposed. Faradic stimulation.

The following experiments refer to the left motor cortex and left medulla. Stimulation with faradic current.

Left Motor Cortex.		Left Medulla Oblongata.	
Time.	*Minimal Strength of Current.*	*Time.*	*Minimal Strength of Current.*
5.0	170	4.59	220
5.0·5	Fit		
5.1	220		
		5.1·5	230
		5.1·5	250
5.2	210		
		5.2·5	240
		5.3·5	240
		5.5·5	300
5.6	210		
		5.6·5	300
5.7	200 (weaker)		
5.7·5	Fit		
		5.8	230
5.8·5	200		
5.9	200		
		5.10	280
5.11	220		
		5.11·5	280
5.12	220		
		5.12·5	270
		5.13	210
		5.13·5	270
5.14	210		
5.15	Two fits. After this one syringe of absinthe.		

Right Motor Cortex.	
Time.	*Minimal Strength of Current.*
5.17	200
5.18·5	Fit.
5.19	150
5.20·5	170
5.22·5	170
5.23·5	160
5.27	170
5.28·5	170
5.30	220
Immediately followed by 180.	
5.32	180
5.33	160
	Exitus.

Right Medulla Oblongata.	
Time.	*Minimal Strength of Current.*
5.18	280
5.19·5	269
5.20	250
5.22	240
5.23	240
5.24	Fit.
5.25	230
5.26	230
5.28	240
5.29	260
Spontaneous shocks.	
5.31	240
5.32·5	210

Protocol 24, Cat 240. Lesion, etc., see p. 142, 11.5.14.

Time.	*Reflex after.*
a.m.	
10	¾ gr. br. ca.
	Right forepaw, 1·6
p.m.	
2.37	Right forepaw, 2.2
	Left forepaw, 1·9
	Left forepaw, 2·2
	Right forepaw, 2·2
2.40	Back, 2·6
	Crossed, 2·2
	Right forepaw, 2·2
	Right forepaw, 1·6
2.44	Right forepaw, 2·2
	Right forepaw, 2·2
Ate some meat.	
2.50	Right forepaw, 2·6
2.52	Right forepaw, 2·6
	Right forepaw, 2·9—1·4
3.2	Two syringes of absinthe
3.4	Right forepaw, 2·5
	Right forepaw, 2·6
	Right forepaw, 2·4
	Blow, 3·0
	Blow, 3·0
Up till now smooth tracings. Now spontaneous shocks appeared. Afterwards dissociation of the tracing occurred regularly.	
	Right forepaw, 2·6
	Right forepaw, 2·8—1·8—1·7
Strongly pronounced dissociation. The animal almost had a fit.	
3.7	Right forepaw, 2·5—1·1—1·1

Time.	*Reflex after.*
p.m.	
3.8	Right hindpaw, 1·7—1·0—1·2—1·6
3.18	Right forepaw, 3·5—1·1—1·2,
Shortly after followed by a fit.	
3·24	Right forepaw, 3·1—1·3
	Right forepaw, 2·6
	Right forepaw, 3·0—1·6
3.25	Right forepaw, 2·7—1·5—1·1
3.26	Right forepaw 2·4
	Right forepaw, 3·0—1·6—1·1
Another third syringe of absinthe.	
3.27	Right forepaw, 3·0
	Right forepaw, 2·8
	Right forepaw, 3·0—2·6—1·5
3·32	Right forepaw, 2·2—1·5
3·34	Right forepaw, 2·7—1·0
Spontaneous shocks.	
	Right forepaw, 4·0
	Left forepaw, 3·0—1·0—1·1
	Right forepaw, 3·3—1·9—1·1
	Right forepaw, 2·9—2·0
	Right forepaw, 2·7—0·9

In these latent periods the first cypher indicates the real latency; the following cyphers indicate the distance of subsequent elevations of the tracing. Both frontal lobes and the medulla were exposed and stimulated with the faradic current.

STIMULATION EXPERIMENTS.

Time.	*Frontal Brain.*	*Time.*	*Medulla Oblongata.*	*Time.*	*Frontal Brain.*	*Time.*	*Medulla Oblongata.*
5·37	55 Followed by a fit.			5·59	Left, 60	6.0	Right, 100
						6.1	Left, 130
5·38	45			6.1·5	Right, 40		
		5·39	150	6.2	Left, 70		
		5·41	120	6.2·5	Fit.		
5·41·5	60					6.3·5	Right, 110
5·42	80					6.4	Left, 100
5·42·5	Fit.			6.4·5	Right, 40		
5·43	80			6.5·5	Left, 70		
5·44	Small fit.			6.7·5	Right, 65		
5·44·5	70			6.8	Left, 70		
5·5·51	50					6.9	Right, 169
5·51·5	70					6.9·5	Fit.
		5·52	135	6.10	Right		
		5·53	140		maximal		
		5·53·5	130		current.		
		5·54	120	6.10·5	Left		
		5·54·5	90		maximal		
5·56	Right, 40				current.		
5·57	Right, 70					6.11	Right, 90
		5·58	Right, 150			6.11·5	Left, 90
						6.12	Left, 100
		5·58·5	Fit.	6.12·5	Right, 20		
5·59	Right, 30						

From these stimulation experiments, made between 5.37 p.m. to 6.12 p.m. on Cat 240, I consider that it is justifiable to conclude that the irritability of the motor cortex and also of the margin of the medulla are decreased after a fit. Immediately after the brain had been exposed, this decrease in irritability is less striking, but after the experiment had been in progress some time the decrease is quite evident. Further, it was found that in Cat 240, the strength of current necessary for stimulation of the cortex was about twice that necessary for the medulla, while the faradic irritability disappeared first in the cortex when the animal was dying. It is seen from a study of the tracings taken of the reflex phenomena displayed by this animal, that on the left side, which had lost the pyramidal innervation reflex, convulsions only occurred rarely and after a moderate dose of camphor monobromide. When such a reflex did occur, the reflex time did not differ much from that shown on the right side (latency at the beginning of the experiment was $\pm 2/50''$ seconds). Striking variations in the irritability of the cortex and medulla are *not* seen under normal conditions neither in cats dosed with absinthe or camphor bromide, but who have not displayed the ordinary sequence of fits.

Protocol 25, Cat 242.

Animal received ½ gramme monobromide of camphor and a dose of absinthe. The motor cortex and medulla were exposed. These two regions were stimulated faradically. The weakest current which would produce from the cortex a contra-lateral convulsion and a homolateral convulsion of the hindpaw from the medulla was ascertained. (See p. 163 and Fig. 41, for further details.)

Motor Cortex.			Medulla.		
Time.	*Left.*	*Right.*	*Time.*	*Left.*	*Right.*
4·40	50	50		90	
4·46		90			
			4·47		90
4·46·5	50	50			
			4·47		90
			4·48	120	
			4·51	120	120
4·52		65			
4·53	50				
4·59	65	65			
5.0	1 syringe of absinthe.				
			5.1		70
			5.2	100	
			5·5	100	100

Fig. 41.—Cat 242. Hæmorrhage at the Level of the Lesion of the Mid-Brain.

Although these stimulation experiments cannot be regarded as all-sufficing in supplying the requisite evidence, yet the conclusion is to be drawn from those already done—that in the brain there are two areas which develop increased faradic irritability under the influence of epileptogenous drugs. These areas are the motor areas in the two cortices and the lateral margins of the medulla. Further, this irritability to faradic stimulation shows fluctuation. Shortly before a discharge the irritability reaches, usually, its maximum and decreases after the fit. Certain exceptions do occur to this rule; some can be explained on the theory that a second fit supervened very speedily on the first; other exceptional cases may remind us that a short period of enhanced reflexes is found immediately after a fit (p. 216). In some cases, it seems as if the difference in irritability before and after a fit is better seen in the marginal medullary area; in other cases, sometimes in the cortex; while at other times the medulla shows the greater degree of alteration.

For the cortex, the changes in irritability were observed both with the dura closed or open. As would be expected, the first and strongest reaction is in the crossed extremities. In one case where the irritability was much increased, a general shock followed the mechanical stimulus of touching the cortex with the electrode, no current being passed. This happened during the stadium incrementi preceding a fit. The irritability of the cortex was found to be diminished in two cases, where some weeks previously the nucleus dentatus in the crossed cerebellar lobe had been severed (see Cat 203, pp. 130 and 133). When the medulla was stimulated the homolateral side of the body reacted, especially the hindpaw, while a stronger current produced a myoclonic convulsion in all the extremities. It is very probable that the irritability of the medullary area is affected by a lesion of the motor cortex; this is certainly the case for the peripheral reflex irritability of the crossed half of the body. There is further reason for believing that a lesion in the pontine and medullary centres, or in their descending tracts, has a distinct influence on the irritability of the motor cortex (Cat 221, p. 175). In connection with the question of the centres and conducting tracts involved in these stimulation experiments, reference is here made to two cases, 221 and 222.

The observations made in Case 221 tend to support the view that the lesion in the formatio reticularis inferior is responsible for the difference in the reflex irritability on the two sides of the body, and also for the difference in reaction shown by the two motor cortices. On the left motor cortex, every fifth stimulus evoked a reaction, while on the right side every second stimulus was followed by a reaction. For tactile stimuli the right side

of the body reacted after each third stimulus, while the left side responded to each stimulus.

This proves that between the cortex and medullary centres for the myoclonic reflexes there does exist a certain relationship. The cortex exerts an influence over the medulla, and the medulla over the cortex.* If this were not so, it would be quite incomprehensible why the cortices in Case 221 should show any change in the refractory phase when neither they nor the pyramidal tracts had been injured. The fact that stimulation of the medullary areas in this case showed no difference in the irritability of the two sides of the medulla does not contradict this view. It must be admitted that faradic stimuli, applied to these lateral areas in the medulla, usually do not reach the reflex centres directly, but only the descending centrifugal connections of these centres. From the observations made on Case 222, the conclusion may be arrived at, that, in any case, the centripetal stimuli are not conducted by the dorso-lateral tracts alone, for the cross-section of these tracts has no influence on the occurrence of the reflexes. Further, the last experiment shows strong evidence for the supposition that the conducting tract from the medullary (pontine) centres downwards may be the tractus reticulo-spinalis. This supposition or suggestion is based on the fact that no myoclonic reaction followed stimulation of the lateral medullary area after the cross-section of the posterior bundles in the cord had reached the level of the central canal.

* Beritoff, *Journal Russe de Physiologie*, 1917, vol. i., and *Ergebnisse der Physiologie*, 1919, vol. xx., p. 418.

CHAPTER VI

RÉSUMÉ OF THE RESULTS

§ 1.

In the first part of this book it has been shown how the conclusion was arrived at that myoclonic fits were a special form of reflex after-discharge (Sherrington). This reflex phenomenon, it was shown, developed from tactile and acoustic reflexes, when the irritability was increased as the result of experimental methods. These reflexes and reflex after-discharges were examined by the ordinary physiological methods.

Although it was found possible to produce myoclonic reflexes in all animals used in the experiments, yet it was found that such phenomena were best developed and eliminated toxic material from the system most completely when the pyramidal tracts were fully developed. It was suggested that these tracts, so important in conveying voluntary impulses, also played a part in reflexes and reflex after-discharges.

Experimental work gave definite support to this theory, and some more exact information was obtained about the centres and tracts closely associated with these phenomena.

It was found that any lesion in the central nervous system which involved the pyramidal tract hindered or impeded the occurrence of myoclonic reflexes or reflex after-discharges.

It was shown in several cases where myoclonic reflexes (tactile) could be demonstrated without the use of either monobromide of camphor or absinthe, that if a lesion were caused in the motor cortex, so as to involve the pyramidal tracts, these reflexes could not be elicited, at least not immediately after the operation. Later, it was found that they occasionally reappeared. If such an animal had a myoclonic fit after the operation, the side of the body opposite to that involved in the operation participated in the fit only when it started in the healthy side and was carried over to the injured.

It was also seen that after removal of the temporal convolutions the acoustic reflexes were more difficult to produce, but with the administration of large doses of monobromide of camphor (which has been shown to reinforce the reflexes) this reflex returned. If the non-motor cortex were removed, the tactile reflexes were diminished but not lost.

It is important that in none of these cases where the portions

of the cortex were removed, or where the pyramidal tract was cut, was there any change in the latent period.

A closer study brought to light certain facts connected with the persistence of a rudimentary form of myoclonic reflexes after operations involving destruction of portions of the motor cortex and section of the pyramidal tracts. Such persistence on the part of these reflexes is not due to any incomplete destruction of the motor cortex or to incomplete section of the pyramidal tracts. It was found that after extirpation of the complete hemisphere the reflexes persisted. This phenomenon is not so astonishing when it is remembered that Wertheimer* and Lepage demonstrated the presence of connecting fibres between both sides of the motor cortex and both halves of the spinal cord. Further, Rothmann† and Probst found that after both pyramidal tracts were cut stimulation of the cortex, by a strong current, was followed by epileptiform convulsions on both sides of the body. It was also shown by Goltz and Rothmann that epileptic fits may occur after removal of both cerebral hemispheres.

On this latter point the present research throws some light, for it shows that there are centres for the myoclonic reflexes in the pons and medulla. It also appears that the centres in the cortex exercise a facilitating effect upon the pontine and medullary centres. The observation of Sherrington and Leyton, of Magnus and de Kleyn, and of Saito and Nikishawa, are in agreement with the view that reflex centres in the medulla are relatively autonomic.

Further, Olmsted and Logan have shown that insulin convulsions occur in cats after decerebration. It has also been shown that in cases where the spinal cord is completely isolated from the brain a modified myoclonic reflex may be elicited in the lower part of the body.

It would appear from the present research that many parts of the central nervous system other than the motor cortex and the pyramidal tracts exert an influence on the occurrence of reflexes and fits. It was found that, after lesions of the pons and medulla, myoclonic reflexes, series of shocks, and fits were in some cases restricted to one side of the body, although they had been shown to be bilateral before operation. After the operation, tactile reflexes could be elicited from one side only, while the myoclonic fit was definitely restricted to the same side. If the motor cortex, in such cases where there was a lesion of the lower centres or tracts, were tested by the faradic current, its irritability was found equal on both sides, but the refractory phase for the crossed motor zone was lengthened. In some of these cases

* Wertheimer and Lepage, *Archives de Physiologie*, 1897, vol. xxix., p. 876.

† Rothmann, *Zeitsch. f. klin. Med.*, 1902, vol. xliv., p. 184.

the difference in reaction of the two sides of the body could be ascribed to cross-sections of Monakow's bundle. Normally, this bundle seems to have some influence on the normal occurrence of bilateral myoclonic shocks and fits.

In certain cases the lesion involved the formatio reticularis of pons and medulla oblongata, while neither the bundle of Monakow nor the pyramidal tracts were injured. The results of such an operation showed that a double centre for myoclonic phenomena must be situated at this level. A unilateral lesion of this centre apparently inhibits myoclonic reflexes on the corresponding side of the body. Experiments made with lesions at a higher level had no effect on the bilateral occurrence of myoclonic reflex phenomena, unless the pyramidal tracts or the bundle of Monakow were involved.*

Another series of experiments which would lead to the same conclusion were those of faradic stimulation of the medulla and the comparison of the result with that got from stimulating the motor cortical zone—*i.e.*, the two regions from which convulsions may be elicited. The faradic irritability of the motor cerebral cortex is apparently enhanced by the administration of such drugs as monobromide of camphor or absinthe, while the character of the resulting phenomena is altered. A very slight current will give focal convulsions of the crossed limbs, but these convulsions are more abrupt than those occurring before administration of the drug. Further, the local convulsions spread more rapidly along one side of the body and involve the other half. This holds good whether the dura be intact or not during stimulation of the cortex. In one of my experimental cases the irritability of the cortex was so increased with the monobromide of camphor that the mere touch of the electrode, without the passage of current, induced convulsions in the crossed limbs. This phenomenon I never found in an animal not treated with some epileptogenous drug. Data were not collected as to latent period of cortical response to faradic stimuli before and after drugging. Experiments, however, were made by stimulating the medulla with the faradic current during the condition of status epilepticus which had been induced by drugs. The electrode was applied to the medulla oblongata through the dura mater, more particularly at that point where it passes under the cerebellum. The result was a hemilateral convulsion which became bilateral as the irritability was enhanced.

Unlike the convulsion induced by the stimulation of the motor cortex, this convulsion was chiefly homolateral.

* In the case of Cat No. 233 (p. 174) a lesion of the lenticular nucleus seemed to diminish the crossed reflexes. It is possible, however, that such as an influence really is exerted by the ventral thalamic-nucleus as a tertiary centre for the fillet, the pathway for tactile sensations.

(It was evident that short circuiting of the current occurred very easily at this point of stimulation through the spinal accessory nerve, therefore the convulsions of the hindleg alone could be considered as " Massgebend.")

From a comparison of the strength of current necessary to evoke convulsions, either from the motor cortex or from the medulla, it is evident that the irritability of the medulla was enhanced about twice as much as that of the motor cortex in these experiments. Further, it appeared that the irritability of both the motor cortex and the medulla underwent alteration during the condition of status epilepticus, rising and falling with the corresponding conditions of " charge " and " discharge." As a general rule the irritability increases before a fit while it falls after a fit, except for a very short period of hyper-excitability immediately after a fit. If, however, the fits follow one another closely, the irritability does not decrease (compare p. 178, 24.4.10). These observations apply to both the medulla and the cerebral motor cortex, except in some few cases where there seemed evidence that the irritability of the motor cortex was alone decreased, the condition in the medulla being unchanged. In other cases, the evidence indicated persistence of irritability in the cortex, the medulla showing a change.

An important point in connection with the significance of this ponto-medullary centre for myoclonic reflex phenomena is that in the stadium incrementi of irritability after an epileptic discharge, the refractory period after stimulation of the medulla was of the same order as that of myoclonic reflexes examined at the same time (Cat 224, p. 173).

A similar agreement between the refractory period of rhythmic irritation of the cortex and of reflex shocks was observed by Broca and Richet (working with dogs poisoned with chloralose).

In Cat 221 (p. 175, 11.20) it was seen that after lesion of the medulla on the right side the refractory phase for irritation of the opposite motor cortex and for the myoclonic reflexes on the same side of the body were lengthened. It would appear that it is not the threshold of stimulation of cortex and periphery which is influenced, but rather the refractory period, one of the elements of reflex irritability.

The question is, are we entitled from such evidence to assume that the centre for the myoclonic reflexes lies in the medullary-pontine area? It is impossible to make this assumption, for experiments made where the spinal cord was completely isolated from the brain demonstrate that rudimentary myoclonic reflexes persist. In such an experiment, however, the reflex has been seen to take the form of extension instead of flexion and adduction.

The myoclonic reflex phenomena seem curiously ubiquitous in relation to the various parts of the central nervous system.

It has been seen that from the spinal cord alone rudimentary myoclonic reflexes may be produced; these reflexes are profoundly influenced by the pyramidal tract and the motor cortex. At the same time they only attain complete development when the double centres in the medullary-pontine region and in the cerebellum on the same side are intact. Although Hughlings Jackson did not make any experiments, and his reasoning depended mostly, if not exclusively, on clinical observations, one cannot help to think here of the possibility of epileptic discharges of the three levels in the central nervous system of this author.

Experiments on the cerebellum were attended by some peculiar difficulties. It was found that after removal of the portion of skull necessary, more especially if the dura mater were opened, a larger dose of an epileptogenous drug was necessary than before operation to get a similar result. This was also found where the operation involved the motor cortex, but the dose of the drug had not to be increased so much. It is known that an operation involving the posterior cranial bones is found to be beneficial in conditions associated with high intracranial pressure. It seems possible that the ponto-medullary centres may be influenced to a certain extent by the intracranial pressure.

In cases where the cortex of the cerebellum on one side was removed the irritability of the motor cortex on the opposite side was diminished, but the bilateral character of the myoclonic reflexes and fits was unaltered. As soon as the operation involved the cerebellar nuclei, it was seen that the myoclonic reflexes on the same side of the body were more easily elicited.

These data do not permit the conception that there is a certain identity of function in the cerebellar nuclei on one side with that of the red nucleus of the other, although it seems certain that both would exert their influence through the bundle of Monakow. It has been shown that lesion of the right dentate nucleus reinforces the myoclonic reflexes of the same side, but it does not follow that lesion of the left red nucleus will give the same result. Indeed, it has been shown that if any effect on the myoclonic reflexes should follow section of the bundle of Monakow they are diminished.

Where the posterior nerve roots were cut across, no myoclonic reflexes could be elicited from the limb involved, but it participated in spontaneous convulsions or fits affecting the whole body. The experiments did not show that cross-section of the fillet was able to inhibit completely either the myoclonic reflexes or fits.

§ 2. Intracerebral Connections probably involved in the Myoclonic Reflexes.

In the endeavour to ascertain which are the nerve tracts along which the myoclonic impulses pass, a list is given of the results of this research.

1. Rudimentary myoclonic reflexes can be elicited from the spinal cord entirely isolated from the brain.

2. The most important centripetal tracts for myoclonic reflexes are the tactile sensory and the acoustic.

3. The duration of the refractory period (the element upon which the occurrence of the reflex after-discharge and fits depend) depends on the medullary *convulsive centres*. These lie at the junction of the pons and medulla, and influence reflexes on the *homolateral* half of the body.

4. That part of the cortex which, as a result of direct stimulation, shows a refractory phase of the same order as is seen in the crossed medullary centre, or in the reflex produced by direct stimulation of the periphery, exerts a distinct facilitating influence upon the reflexes. This influence is conveyed through the pyramidal tract, and also in a lesser degree through the bundle of Monakow and possibly through other nerve tracts.

From these conclusions, drawn from a consideration of the preceding experiments, the following deductions are drawn. An elementary or simple reflex has its origin in the individual spinal segments, while the excitability of these centres is directly under the influence of the medullary centres whose excitability is in turn controlled through the pyramidal tract. A characteristic true tactile myoclonic reflex, with its characteristic rapidity and regulation of the refractory phase, only occurs if the medullary centres co-operate. The ponto-medullary centres influence the homolateral side of the body. Is it possible with the present knowledge of anatomy to decide more exactly what are the connections between the spinal nerve roots and the medullary centres ? It is known that the tactile stimuli reach the medial fillet after crossing the median line, while the acoustic stimuli travel upwards in the lateral fillet. Further, it is known that the posterior corpora quadrigemina act as a nodal point for this important junction, and that from this level descends the tractus tecto-reticularis.

The fact that here is a double crossing in this chain while the acoustic and tactile tracts reach the same point in the mid-brain indicates very conclusively that further research is required for the exact appreciation of the full significance of this region. This is more obvious because,as has already been pointed out, the localisation of the reflex paths in the central nervous system is only beginning.

CHAPTER VII

GENERAL CONCLUSIONS

At the end of the first part of this book the conclusion was come to that myoclonic epileptic fits in the higher vertebrates are reflex after-discharges which serve mainly as a method of rendering certain toxins inactive. The object of the second part of this book has been to establish as accurately as possible the significance of these fits in the physiological economy and to ascertain how far localisation of these phenomena in the central nervous system is possible.

Although the elements necessary for the occurrence of the simple tactile myoclonic reflexes are present in the isolated spinal cord, yet in the pons and medulla there are two sets of centres which dominate the homolateral side of the body.* These centres are necessary for the development of the reflex after-discharge (a series of simultaneous convulsions of the complete voluntary musculature).

These centres are endowed with this function because they dominate the refractory phase. It was shown in Part I., Chapter V., § 3, that the alteration of this refractory period was apparently the fundamental factor in the transition of simple reflexes to fits. It is possible that the formatio reticularis pontis and medulla are wholly or partly identical with the localisation of these centres. It was certainly found that lesions of this area more than of any other had the effect of changing the bilateral myoclonic fit into a unilateral fit. Other physiological and clinical data show that this region has a special significance in the conservation of consciousness.† This is both interesting and important in reference to the question why loss of consciousness is so early and regular a symptom in myoclonic fits. (In Jacksonian epilepsy, on the other hand, consciousness is not lost early.)

A similar explanation may be forthcoming for the other phenomena which accompany the complete discharge in man and animal, such as salivation and dilatation of the pupils.

* Another important group of reflexes the Magnus de Kleyns reflexes in rotation of the head and in the tonic reflexes of voluntary musculature are, according to these authors, dependent on centres about the same region. Further, the homolateral influence seemed to predominate. This point needs, we think, more research.

† It is well known that tumours in this region are earlier and more frequently associated with coma. The experience of the war would also show that the slightest lesion in the medulla oblongata was accompanied by loss of consciousness (Breslauer, *Deutsch. med. Wochenschrift*, 1919, No. 13).

Although evidence was got of the importance of these medullary centres in reflex and convulsive phenomena, there was evidence also showing the importance of the influence of the cerebral cortex through the pyramidal tracts on these centres.

Further, a regular fluctuation of the cortical excitability was seen immediately before and after a fit. This evidence went to prove the existence of a *certain interrelation between the motor cortex and those medullary convulsive centres.*

The suggestions, or prognostications, of Schroeder van der Kolk, Fr. Franck, Pitres, Binswanger, Ziehen, Redlich, Sarbo, and A. Fuchs* are thus experimentally confirmed.

We must therefore decide that myoclonic epilepsy is a mechanism present in all higher animals which will respond so soon as a certain degree of intoxication in the circulation is exceeded. This being the case, the symptom complex, known as myoclonic epilepsy in man, now gets its true nosological place. It is no more looked on as a rare type of epilepsy, but as a prototype of genuine epilepsy.

It was shown that in cats the enhanced tactile reflexes may be overshadowed by the spontaneous or regional shocks, so that the true beginning of the myoclonic condition is in some cases obscured.

Clinical experience also shows that myoclonic epilepsy is the most common amongst the different types of epilepsy. Russell Reynolds in his old records noted that 81 per cent. of his epileptic patients had interparoxysmal convulsive symptoms. As a matter of fact, the only other forms of symptoms are petit mal or psychical equivalent conditions (conditions of mental dreaminess porio mania, etc.).

In the third part of this book it will be seen that these may be regarded as atypical fits or incomplete discharges, where the patient, mentally or otherwise, is still under the influence of the toxin—that is, he is still in a condition of charge. The severe complete fits are the typical form of discharge.

Up to the present I have not attempted to bring the results of my experiments into line with the clinical researches of other workers on the phenomenon of so-called myoclonia. My own clinical observations were made at the same time as the experimental researches. In the first place, stress is laid on the fact that the results of experiments have not been very helpful in explaining clinical facts, the phenomena, obtained as the results of experiment, being very different to those found clinically.

Reference is here made to the important report by Pierce Clark† which has recently appeared and which deals with the occurrence of myoclonia and myoclonic epilepsy in the last fifteen years. It is interesting to find out how far physiological and clinical data lead to the same conclusions, more particularly with regard to localisation. Pierce Clark states that the characteristics of myoclonic convulsions are that they are "short, sudden, and lightning-like." Further, he points out that the

* A. Fuchs, *Wien. klin. Wochenschrift*, April 28, 1910.

† Clark, *Journal for Nervous and Mental Diseases*, 1919, vol. ii., p. 17.

intensity of the clonus shows great variation in each individual case, while the rhythm also varies considerably. The range may vary from 10 to 240 per minute. Further, it is found in the cat, that the rhythm did go up to 15 per second in the fit. The difference in rhythm for both phenomena seems fundamental. (Compare Part III., Chapter II., p. 199). Clark also emphasised the variability in degree, interval, and synchronism in these phenomena (p. 33).

Clark and Shanahan agree in regarding the matutinal single convulsion as " motor manifestations of petit mal," not as myoclonic phenomena. In the preceding chapters, special stress has been laid on the fact that the transition from the waking to the sleeping state, both in animals and in human beings, is one when there is a special predisposition for myoclonic manifestations.

Dealing further with the question of localisation, Clark considers that myoclonia can be observed in cases of cortical lesion, such as dementia paralytica and also in spinal lesions. This observation I would associate with the observation of modified reflex myoclonic phenomena noted in animals where the spinal cord has been isolated from the brain.

In the geniune myoclonic epilepsy of Unverricht (progressive type) and Lundborg (stationary type), good days and bad days are prominent until late in the course of the disease. After a large number of discharges, days of comparatively normal life follow. This normal period or period of discharge might be compared with the refractory period. That is, the patient has had a definite reflex phenomenon, and after it has been accomplished, he enters a refractory period. This was seen after a myoclonic fit in the experimental cat. In the later stages of the malady the good days disappear until finally the myoclonic phenomena become continuous, interfere with the nutrition of the patient, and lead directly or indirectly to a fatal termination.

Now, in true myoclonia, autopsy has never revealed any focus or centre of disease; this being the case, clinical deductions are as yet purely theoretical. On the grounds of clinical evidence, Clark compares these convulsive phenomena with the extra-pyramidal motor syndrome and paralyses which have attracted so much attention. In the literature on postencephalitic disorders there are many cases of spasticity, contracture, tremor, choreic movements, athetosis or symptoms resembling paralysis agitans, general rhythmic automatic movements and continuous myoclonic activity, where the pyramidal tracts are intact, but where some alterations are recognised in the hypothalamus, corpus striatum, and mid-brain.* Clark would attempt to prove that these myoclonic phenomena are dependent on alterations in the mid-brain, and attempts to explain the gradual merging of athetosis or choreic movements into myoclonic movements. The cases recorded by Flatau and Sterling are both interesting and important, but unfortunately no definite evidence, as afforded by an autopsy, is forthcoming.

It must be admitted that, according to Clark, Flatau, and Sterling, clinical facts tend to show that the truncus cerebri has some connection with these myoclonic phenomena. These authors do not, however, agree with Schroeder van der Kolk, Nothnagel, Franck, who maintained that there was a convulsive centre in the medulla oblongata, which dominated the whole of the epileptic phenomena. Clark is of opinion that, from clinical evidence, myoclonic phenomena in man must be due to ultra-microscopic changes in the mid-brain, yet this does not prevent Clark from agreeing with many other clinical observers that epileptic fits always originate in the motor cortex.

In comparing the result of a consideration of *pathological* data with the study of *lesions* of the truncus cerebri, performed on *animals* and the influence of these lesions on epileptiform phenomena, one is impressed with the common difficulty of ascribing a certain part of the phenomenon to the motor cortex, and a certain

* Compare Muskens, *Revue Neurologique*, 1927, vol. ii., p. 155, and Wilson's *Review of Neurology*, next volume.

part to the pontine and medullary centres. At the same time, both clinical and experimental evidence indicate the cerebral trunk as the main origin for myoclonic phenomena. From a pathological standpoint, we have to deal with an influx of stimuli from the striate body and mid-brain which crosses to the other half of the body. From the experimental standpoint, we have to deal with an influx of stimuli which induce homolateral reflexes, which come from the region of the substantia reticularis. It is not impossible that both results may be brought into agreement, if further research were to demonstrate a crossed connection between those parts—*i.e.*, the mid-brain and the medulla. There might be a supranuclear hypothalamic or mesencephalic centre, which would dominate the crossed medullary convulsive centre. Or it might be that a nucleus was not stimulated in my experiments, but a terminal tract which has its crossing at a higher level. (Chapter III., § 3, p. 148, shows this could hardly be the rubro-spinal tract.) If the latter is the case the difficulty of admitting such an anomaly as a direct connection between the reflex centre in the medulla and the periphery of the same side is avoided. This is obviously a difficult admission, for it is known that all motor and sensory supranuclear connections cross the median line (pyramidal tract, supranuclear vestibular connections).* From the present research, more evidence is got for the suggestion of Monakow that, for the occurrence of cloni, the cortex, thalamus, pons, medulla oblongata, and the spinal cord must all functionate. Long ago, Unverricht stated that for true myoclonic phenomena the cortex cerebri and the spinal cord must both participate.

Regarding the myoclonic movements in various infectious diseases, such as chorea electrica Dubini (where epileptic fits also occurred) and in malaria,† and also after the epidemic of grippe in 1919, Schupfer and Brush‡ concluded that the whole cerebro-spinal axis participated in the phenomenon.

My opinion is that, from a physio-pathological point of view, this most important group of epileptic fits, the myoclonic group, can be explained as developing from a group of reflexes, tactile and acoustic, which have been extensively investigated and described in this book.

* Muskens, *Brain*, 1914, p. 404.
† Bastianelli and Bignani, *Atti de l'Accademia di Roma*, 1893-94, p. 221.
‡ Brush, *Amer. Jour. Med. Science*, December, 1899.

PART III

EPILEPTIC DISORDERS OBSERVED IN MAN AND THEIR TREATMENT

CHAPTER I

CLASSIFICATION OF EPILEPSY

Difficulties of Classification in the Present Chaotic Conditions. Incipient Cases the Most Important Scientifically and Socially. Various Endogenous and Exogenous Poisons and their Effect at Different Periods of Life, and Traumatic Epilepsy.

THE chaotic state of the present knowledge of epilepsy is nowhere more evident than in monographs and manuals dealing with the classification of this disorder. Some authors face the difficulty and draw up some sort of scheme, while others attempt no classification at all. This difficulty is due partly to the lack of any systematised method of examination or description of epilepsy, and also to the practical difficulty met with by every clinician in keeping in close touch with cases.

A further difficulty is that most of the cases of epilepsy that come to the clinics or consulting room are well-established cases where a varied complex of symptoms have developed. In a case which has lasted over a period of several years, three, four, or five different groups of symptoms may have developed. Early in the case such symptoms as automatic movements or mental changes are but vague and transient, but become fixed by the passage of time.

Gowers, Féré, and Binswanger gave up the attempt at classification, and adopted the plan of describing exactly and in detail the symptoms of the disorder. The more modern writers on epilepsy, Turner, Vogt,* and Cestan,† confine themselves to a classification based on the supposed cause. The chronic cases of epilepsy met with in epileptic institutions or in hospitals for the insane are, in my opinion, the end-product of various pathological processes. They are not suitable cases for basing any classification upon. Those cases which afford the best material for classification, by comparison with the data arrived from the experimental animals, are the early cases where there is no mental impairment.

* H. Vogt, *Allg. Zeitsch. f. Psych. u. Neuro.*, 1907, vol. lxiv., p. 418.
† Cestan, "Les Épilepsies," Paris, 1922.

The importance of the early cases will be dealt with very fully in chapters on prophylaxis and treatment. These early cases are the important cases socially, for it is at this stage that one can hope to arrest the progress of the disorder and procure for the patient at least a comparatively normal life. Clinically and pathologically, these early cases have for long proved a stumbling-block, and it is the hope of clearing up some of the difficulties that I have devoted so much attention to this class of case.

The following is a classification which, I think, demonstrates clearly the position of myoclonic epilepsy as it occurs in man and other animals in relation to other well-known clinical groups.

(*a*) Myoclonic epileptic fits elicited by well-known toxins. Whether this intoxication is made available through the gastro-intestinal tract or through the circulatory system, the cessation of the condition of intoxication as a rule stops the fits.* Such extraneous toxins as bromide of camphor, absinthe, lead, carbolic acid, and certain gases, all produce, under certain circumstances, fits. Further, myoclonic epileptic fits appear in persons revived by artificial respiration from conditions of suffocation as induced by submersion in water or snow—*i.e.*, during the transition from unconsciousness to consciousness, more particularly where the unconsciousness has been associated with anoxæmia.

Under this heading fall the experimental myoclonic epileptic fits produced in cats and monkeys by bromide of camphor or absinthe. Also, those clinical cases occasionally seen where fits follow on the accidental poisoning with bromide of camphor (compare pp. 12, 42) or after a single dose of absinthe.

Here also belong cases where *chronic* epilepsy follows on the single fit occurring at the time of resuscitation, although this fit, with the motor and probable psychical symptoms, is the very first manifestation of the disorder the patient has had.

In this class different forms of convulsions or fits, as the result of various intoxications, have been studied and classified by Turtschaninow. From this classification the myoclonic variety would seem to be the most frequent.

(*b*) To this class belong those epileptic fits caused by certain toxins produced endogenously.

Probably the greater number of the cases of genuine epilepsy belong to this group. They form the majority of cases seen by the neurologist displaying the well-known diversity of symptoms, and probably includes some cases of petit mal with psychical changes.

* It has been found that in man acute alcoholic intoxication may be followed by chronic epilepsy, in the same way chronic epilepsy may follow on absinthe poisoning. I never found this in the hundreds of cats I have observed, but I did get diminished tolerance to the drug (see p. 196 under *b*).

From the view expressed in this book it is obvious that I cannot regard such patients as being in the same category as those who have developed epilepsy after some lesion or injury to the brain. The patients of the class referred to under (*b*) are originally sound individuals who have developed epilepsy as a result of often repeated epileptic discharges (reflex after-discharge effects). Such persons acquire the epileptic habit as a result of myoclonic phenomena due to some toxin. This toxin, or this condition of intoxication, is frequently alimentary, associated with constipation. Such people are effectively and repeatedly poisoned by this endogenous toxin, and react to it by such symptoms as myoclonic shocks and fits. With the passage of time the natural resistance against such phenomena is weakened, and a less and less amount of the toxin is required for the production of these phenomena. This point was brought out clearly in some of the experimental cats, where it was found that after fits had been induced by the toxic drug the animal required smaller doses for a repetition of the fit. The same point was brought out by Sauerbruch in his pilocarpine experiments. W. Timme* gave the term "lowering of the threshold" to this phenomenon. It must be appreciated, however, that in most experimental cats the animals developed a natural protection, probably anti-bodies, so that, as already indicated, an increase in dose was required to produce the fit. The tendency to epileptic phenomena is certainly often hereditary, but, in man at least, it may appear suddenly in a healthy stock.

(*c*) To this class belong those cases of epilepsy due to some local affection of the brain, not to trauma. The fits result probably as a release-phenomenon in defective lesions, or from the stimulation of the central convolutions and ponto-medullary centres as a result of tumour, or by some general increase in brain pressure due to a factor not directly involving these structures. To this class also belong cases of genuine epilepsy due to encephalitic processes, either prenatal or occurring very early in life.

(*d*) *Traumatic Epilepsy.*—These are cases which, on account of their favourable prognosis, occupy a peculiar place. (It must, however, be understood that this favourable prognosis appears only to apply to those cases of traumatic epilepsy met with in civilian practice. At least this is the only class of practice of which I can speak with first-hand knowledge, and, so far as I can find from the literature, cases of traumatic epilepsy, due to injuries received in warfare, do not offer the same prognosis.) Epilepsy

* W. Timme, *Arch. of Neurology and Psychology*, 1923, vol. ix., p. 549.

of this type is caused by injuries of the head or in some rare cases to injuries of the peripheral nerves.

It is this classification, based on the etiology and the symptoms of the disorder, which will be followed out in this book.

In a classification based only on the etiology the following varieties of epilepsy are distinguished:

Eclampsia in infants; reflex-epilepsy, due to a lesion of the peripheral nervous system, the ear, eye, or stomach; epilepsia gravidarum, or eclampsia, occurring in the pregnant women and in the puerperium; traumatic epilepsy, local at first—at least, as a general rule—but later becoming general; epilepsy associated with alcoholism, plumbism, cardiac affections, such as Stokes-Adams disease; epilepsy associated with arterio-sclerosis and senility; epilepsy following on almost complete suffocation; epilepsy after operation or injury to the limbs, or after orthopædic treatment, due to fat embolism; and the epilepsy found to occur in certain diseases affecting the spinal cord.

Up to the present time it has not been found possible to make any important distinction in the symptoms of these forms of epilepsy etiologically so varied. In any of them grand mal may occur alone, or petit mal or its equivalent, as well as myoclonic symptoms. It is, however, rare to get genuine malign progressive myoclonic epilepsy developing in the cases where some distinct etiology can be indicated.

There is yet another useful classification based on the symptoms and form of development of the epilepsy. It is as follows:

1. *Partial or Jacksonian Epilepsy.*

2. *Primary Grand Mal.*—The other forms of discharge (petit mal and myoclonic manifestations) develop secondarily to this.

3. *Primary Petit Mal.*—The other forms of discharge (grand mal or myoclonic fits) are secondary in development to the slighter fits.

4. *Primary Myoclonic Epilepsy.*—The other forms of discharge (grand mal and petit mal) develop only as a result of the myoclonic fits. This is probably the most frequent form, the incipient myoclonic manifestations frequently passing unnoticed.

There is yet a fourth classification based on the period of life at which the disorder appears. The classification is as follows:

1. *Infantile Convulsions.*—In the very young the tendency to convulsive movements (viz., myoclonic reflexes and fits) is very marked, and is demonstrated with great regularity. The incidence of epileptiform convulsions at the onset of an acute infectious disorder might therefore be looked on as almost physiological. It is necessary to discriminate very carefully here.

Care must be taken to exclude such convulsions as may occur

in early childhood, as in laryngismus stridulus, the carpo-pedal spasms, or fits of temper. The first two are found not only in spasmophilic children, but occur also in meningitis and other local and general diseases of the brain. On the other hand, the so-called "occasional fits," which are preceded by enhanced myoclonic reflexes and have themselves all the characteristics of a myoclonic fit, like the fits due to encephalitis not caused by traumatic injury to the brain, belong definitely to the group of regular epileptic phenomena. The tendency to epileptiform phenomena in infants undoubtedly is a consequence of the fact that myoclonic reflexes are normally very well developed in children; this is shown by the violent general contraction which may be seen in young children exposed to a sudden noise or touch. It seems probable that these "occasional" fits of infancy are, in reality, myoclonic epileptic fits, and are preceded by enhanced myoclonic reflexes and spontaneous reflex shocks as seen in the experimental cats. In one boy this was proved to be the case (E. M., p. 224).

2. *Adolescent Epilepsy.*—This time of life has a most important significance for those children who in early infancy have had some sort of fits. Gowers found that one-seventh of his cases of epilepsy began between the ages of 12 and 15. Among my own case I found 65 per cent. started in the second decade of life.

3. *Menstrual Epilepsy.*—This will be dealt with in a subsequent chapter.

4. *Epilepsy in the Pregnant Woman and Eclampsia.*—This also will be dealt with later.

5. *Climacteric Epilepsy.*—Just as the climacteric period of life is frequently one of psychical instability, it is not uncommon to find that a patient who has previously suffered from epilepsy becomes worse. In some rare cases epilepsy may appear for the first time at the climacteric, while cases occur where the disorder is arrested.

6. *Senile Epilepsy.*—Arterio-sclerosis is considered to be the immediate cause in this type.* There is no marked difference in the symptoms in senile epilepsy from those found in epilepsy earlier in life. The prognosis is no worse with persons over fifty. Probably it is, on the whole, better than in younger patients.

* Lüth and Schupfer, *Monatsschr. f. Psych. u. Neur.*, 1901, vol. viii., p. 282.

CHAPTER II

MYOCLONIC EPILEPSY

The Word or Term "Myoclonia" is used for Two Very Different Types of Phenomena. Great Frequency with which Myoclonic Symptoms appear in Various Forms of Epilepsy.

It has been shown that the myoclonic reflexes (which in a sense protect an animal) are brought into play by an unexpected noise or touch; and myoclonic epilepsy (which protects the animal when exposed to certain toxins and infections) plays, as we have seen, a very important part already in the lower quadrupeds. It seems very probable that where the nervous system is highly developed as in man, these phenomena should also play an important rôle. This applies less to the myoclonic reflexes proper, for it has been shown repeatedly that domestication—*i.e.*, living habitually under conditions of a special form of safety—tend to relegate these reflexes both in man and the lower animals to the background.* In such cases the inhibition afforded by the cerebrum is so strong that, unless the reflexes are enhanced artificially by means of drugs, they are almost, if not quite, quiescent. On the other hand, there is ample opportunity for observing the many epileptic manifestations other than myoclonic epilepsy which appear in man. Such manifestations may be complete myoclonic fits with or without preceding myoclonic reflexes and spontaneous shocks, slighter forms of epileptic discharges without convulsions or psychic phenomena, traumatic epilepsy, and so on. In man may also be seen different forms of epilepsy due to degenerative causes (see 3 (*a*), p. 200). Further, the immense importance of hereditary predisposition is made manifest. Cases are also met with where, in a family, a greater tendency to myoclonic discharges than is quite normal, and epilepsy (a sudden variation of Darwin, or, as it is now called, a "mutation") suddenly appears as a recessive character.

Up to the present time myoclonia and myoclonic epilepsy in man have been studied quite apart from experimental myoclonia. It may therefore be useful to recapitulate, briefly, the history of the subject. Spontaneous shocks, as a prodromal symptom

* Under certain conditions of danger these reflexes may reappear. C. Darwin relates how that in his journey through the Argentine, where he was in danger from Indians, he noticed that his two comrades, a guide and a half-caste, started at the slightest noise coming from the thicket. Here he exclaims: "What a life these men lead!"

before an epileptic fit, are so frequent that they could not escape the notice of such keen observers as Boerhaave, Tissot, and Russell Reynolds.*

These spontaneous shocks were described by them as " petites secousses," " epilepsia minor," and so on (see 3 (*c*) below). The description of the condition and the term " myoclonia " appeared in medical literature in 1881, when Friedreich gave the name " peramyoclonus " to a pathological form of movement which appears rarely and sporadically and always in association with other myoclonic symptoms. These rapid involuntary convulsions produce no locomotion of the limbs, and have nothing to do with epilepsy. Possibly because the description of the muscular movements given by Friedreich resembles more or less superficially the movements seen in epilepsy, this term has been adopted by later workers, among whom are Unverricht, C. van Lair,† and Lundborg, and applied by them to epileptic phenomena.

The best description of myoclonia and myoclonic epilepsy is given by Lundborg.‡ In his book on the subject Lundborg gives a critical review of all the literature connected with the subject and a very clear exposition of the phenomenon as he himself has seen it. He distinguishes the following types of myoclonic disorders:

1. *Myoclonia Symptomatica.*—This occurs in certain nervous diseases, also in infectious diseases such as malaria, diphtheria, typhus and influenza.

2. *Myoclonia Simplex s. Essentialis s. Myoclonus Multiplex.*—This is a chronic affection depending on (*a*) an hereditary tendency towards nervous disorders (hereditary family myoclonia); (*b*) a definite intoxication. Some types of this intoxication are recognised to be uræmia, mercury, and lead poisoning.

The following myoclonic phenomena are always associated with epilepsy:

3. *Myoclonus Epilepsia* (*Myoclonia Epileptica*).—Which includes three different forms—

(*a*) The progressive form, Unverricht's familial disease.
(*b*) Rabot's intermittent (sporadic form).
(*c*) Genuine epilepsy commencing with myoclonic epilepsy.

The last is the largest group and will be more fully discussed.

* Russell Reynolds estimated the number of epileptics who displayed slight motor symptoms in the inter-paroxysmal periods as 74 per cent.

† C. van Lair's definition of (*Revue de Médecine*, 1889) of myoclonic movements is completely applicable to spontaneous myoclonic convulsions in epileptics. He applies the terms: " Contractions forcées, brusques, incoordinées, rhythmiques ou arhythmiques, avortées ou suivies d'un déplacement." Spratling's description applies to many cases. (*Pediatrics*, December, 1905, p. 767). " Lightning-like contraction of trunk and proximal muscles of extremities which are not possible at will."

* H. Lundborg, " Die progressive Myoklonus-Epilepsie," Upsala, 1903.

Lugaro* lays stress on the artificial subdivision of myoclonic symptoms on the grounds of their various localisations in the central nervous system. He calls attention to Brissaud's somewhat arbitrary dictum, "the tics are cerebral, myoclonia is bulbar." Lugaro, on the other hand, is not less didactic in his statement, "there exists a status neuroclonicus, the abnormality of which is the rapidity of the movement and the absence of a stimulus. This status may arise in all levels of the central nervous system, and therefore all manner of possible changes and combinations may be found. As extreme examples are the 'maladies des tics convulsifs,' with its psychical phenomena, and the spinal myoclonias with their peripherally seated abnormal rapidity." I quote these excerpts from the literature on myoclonia to show that if the study of myoclonia is not begun from its natural and physiological starting-point—the myoclonic reflex—there is much danger of being led astray. Lundborg quite justifiably devotes most of his book to myoclonia-epilepsy. He points out (see p. 27) that there are all sorts of stages between intermittent myoclonia and myoclonia-epilepsy. The extraordinary frequency of the myoclonic convulsions (corresponding to the spontaneous shocks already described in the first part of this book, pp. 41, 61, 65, 95, 98), which becomes so evident in the careful examination of incipient epilepsy, has never been so well described as by Russell Reynolds.†

The confusion in the literature dealing with myoclonic phenomena is really due to the fact that two quite different anomalies of muscular movement were first described about the same time. These were: (*a*) A somewhat rare involuntary continuous movement of the voluntary muscles; more rapid than myoclonia, but less rapid than chorea electrica. It shows an irregular rhythm of 100 to 200 per minute (Marinesco and Gorn), and rarely leads to locomotion of the parts involved. (*b*) The second type of movement is the far more frequent myoclonic contractions of voluntary muscles occurring in epilepsy. These movements involve the muscles of a limb or part of a limb, but locomotion does not always follow. These movements are produced reflexly by a tactile or acoustic stimulus, but they may occur spontaneously or at least without a *known* stimulus. The frequency of these movements has already been dealt with in the first part of this book, where it has been described as similar to that of a reflex after-discharge or myoclonic fit—viz., 12 to 15 per minute.

It has not yet been proved that these two forms of movement are even intimately connected so there can be no question of their being identical.‡

* Lugaro, *Rivista di Neurologia*, 1896, p. 389.

† Russell Reynolds, *Epilepsie*, German edition by H. Beigel, Erlangen, 1865, p. 66.

‡ Besides the fact that the rhythm of these two anomalies of muscular movement are fundamentally different, certain clinical facts plead against their being related. Thus one observer records that in certain cases of myoclonic undulation in and after infectious diseases (grippe) the knee reflexes are feeble (Ramsay Hunt, *Amer. Jour. Med. Assoc.*, September 11, 1920, p. 713, and C. Roger, Aymès and Pourtal, *Revue de Médecine*, 1923, p. 385). Such a combination never occurs where the myoclonic reflexes are increased. So tabes and genuine myoclonic epilepsy are never found

The first form of myoclonia is described in such brain diseases as general paralysis (Lambrani, Souques, Moniz) and in lesions of brain (hæmatoma—Murri, Chauffard, Ferrannini, Fragnito, Hoch). It has also been described in association with spinal diseases, such as myelitis (Raymond), in disseminated sclerosis (Strumpell, Heilig, Remak, Farge, Goria), in intoxication with alcohol (Lafargue, Mott, Söldner), with lead poisoning (Marie, Meinertz), in uræmia (Perrero, Levi, Follet), in syphilis (Dana, Muratow, Strassmann, Simonelli, Hermann, Leubuscher), in auto-intoxication from the alimentary canal (Peiper), in hypo-parathyroidism (Lundborg, Wagner, Falconer), in infectious diseases (Marinesco, Lalage), after parturition (Clark, Prout, Feinberg), in hysteria (Möbius, Böttiger, Huchard, Fiessinger, Murri, Carrière), in other cases by Starr, Schupfer, Homen, Bechterew, Koschewnikoff, Lugaro, Eussière, and Maillet, Goldflamm, Bregmann, Lenoble and Aubinau, Meyssier, Papillon and Gy, Valobra, G. Stewart, Hunt, Poggio, Gorn, Abadie and Molin de Teyssiere, Zylberlast, Roger and Robitschek. The word " myoclonia " was coined by Seeligmüller and also used by Ziehen and Bressler to denote epileptic shocks. These shocks had already been observed by R. Reynolds, Rabot, Turtschaninow (in carbolic acid poisoning), Unverricht, van Lair, Lundborg, Seppilli, and d'Alloco, Lambrani, Verga and Gonsalez, Buzzard and myself in relation to co-existent epileptic fits.

From his experience Reynolds found that in a group of fifty-seven cases, 81 per cent. had clonic symptoms in the periods between the fits. From my own observations, based on 2,000 to 3,000 cases, I can endorse this statement completely. This is important, for Lundborg and others were inclined to doubt the observation made by Reynolds, on the ground that he had so few cases. Further, from my own observations I have come to the conclusion that Reynolds' description of the frequent occurrence of shocks between fits, in the cases which have not reached the chronic or inveterate stage, is absolutely correct, and in no way exaggerated. As a doctor rarely sees a myoclonic shock, and the patient himself and his friends are rarely impressed by their occurrence, it requires very careful, patient, and thorough examination before one can satisfy oneself that they are or are not present (see Part III., Chapter III., p. 204). In most cases, the shocks occur many years before the fits; this is in principle the same as in the development of myoclonic epilepsy—as has been demonstrated in experimental animals.

In these animals, it will be remembered, myoclonic shocks as a rule preceded the fits. From actual experience it is found that this symptom is only recognised by the laity after the patient has had a fit or fits. In some rare cases one is told that these shocks only appear after a severe epileptic fit. This latter observation is certainly incorrect in many cases, and only due to faulty observation, because the severe fits occupy the whole attention

co-existing (according to the literature) except in the case of Veit (*Allgem. Zeitsch. f. Psychiatrie*, vol. lxii., p. 430). This case has been questioned and, indeed, contradicted by Bödeker and Kalischer. Only Jelliffe and White (" Diseases of the Nervous System," 1919, pp. 871 and 880) have, so far as I know, clearly differentiated between myoclonic prodromal shocks and what they call " real myoclonia."

of the patient's friends, yet cases do occur when this is quite true. In 1907-1908 I investigated three groups of fifty patients, both male and female, with reference to the relative frequency of the myoclonic shocks at any stage in the disorder. In 1920 I again investigated the matter in the cases of fifty male and fifty female cases.

Relative Frequency of Myoclonic Shocks at any Stage of the Disorder.

	Females.	*Males.*
First fifty cases	35	22
Second fifty cases	36	34
Third fifty cases	32	26
Fourth fifty cases	26	29
Total	129	111

These cases are in nowise selected, but were taken just as they came.

Cases where there was a question of a focal or traumatic character were only occasionally included in the list; while cases where there was mental disturbance, or where hystero-epilepsy was complicated with functional disturbance, were excluded. The value of these statistics was increased by the fact that the patients were drawn from all classes of society, but no essential difference could be recognised in the symptoms.

From the fact that myoclonic shocks are found to occur in 55 per cent. of the male cases, and in 65 per cent. of the female cases, it is evident that they are, as Russell Reynolds pointed out, most important nosologically. From a purely pathognomonic point of view, it is evident why so much interest should be paid to this symptom. In a group of 200 female cases, 51 had myoclonic shocks for long periods ranging from months to years; 46 had myoclonic shocks after the first severe fit; while 32 had no clear history of the occurrence of the shocks. In a group of 200 male cases, 28 had myoclonic shocks over a long period; 52 had myoclonic shocks after the first severe fit; 31 had no clear history. It would seem, therefore, that the frequency of myoclonic shocks which occur in more than half the total cases is more frequent in women than in men.

Further, it appears that in man, as in the experimental cat, shocks appear most frequently before the appearance of fits. In cats the whole phenomenon of shocks preceding fits may occupy but a few hours, while in man it may extend over months or years. The other condition where the fits appear first and are followed by shocks is very rare in the experimental cat, while in man it is relatively rare, but not nearly so unusual as with the cat.

CHAPTER III

A MORE DETAILED DESCRIPTION OF REGIONAL AND MYOCLONIC SHOCKS IN MAN

Peculiarities during Sleep, while Waking Up and at Transition of Waking and Sleeping Condition. Matutinal Shocks. Significance of Night Rest for the Origin of Myoclonic Phenomena. In Man Less Clear Climax in the Myoclonic Phenomena as in Experimental Animals.

If the myoclonic convulsions seen in an epileptic patient be carefully observed we may compare them either to choreic or Jacksonian convulsions, or to the sudden local jerk found in true paramyoclonia, or still more to partial convulsions known as fibrillar or fascicular contractions. With this wide range of comparison it is not difficult to differentiate between *regional* (affecting certain limbs) and *local* (affecting only a muscle or part of a muscle) movements.

The larger movements, or regional convulsions, are associated with locomotion of the body, as, for example, when an arm or arms are thrown forward or sideways and the head jerked forwards or backwards.

The muscular movements not associated with locomotion of any part of the body are termed "myoclonic convulsions," but in a narrower sense. Both these types of convulsions may be seen in one patient, but as a rule one type of convulsion tends to recur in a patient. These movements or convulsions are never painful, and are usually only complained of by the patient because he recognises in them a prodromal symptom of an epileptic fit. Sometimes both the patient and his friends require educating in the recognition of this simple connection.

These movements certainly occur in sleep, and frequently awake the patient. Very frequently such a convulsion occurs just at the moment of dozing off and awakes the patient, while the early hours of the morning are very frequently the time for myoclonic manifestations. From my own experience with cases of myoclonic epilepsy, the moment of getting up, or in some cases the moment of sitting up in bed, is peculiarly associated with the occurrence of myoclonic convulsions.

In many other cases the myoclonic convulsions may occur first during the process of dressing, and may be of so severe a

character as to throw the patient on the floor. It is not infrequent for two or three convulsions to follow one another, just as they may do experimentally. When this occurs, patients frequently say that they are able to appreciate a momentary loss or obscuration of consciousness. Where patients are very observant, they may complain of a swiftly passing blurring of consciousness when there has been but one single shock-like convulsion. So slight is this that these patients are immediately aware of pain from impact with the floor should they fall.

If patients, subject to matutinal shocks, develop a complete fit, it generally takes place before breakfast. In not a few cases the taking of food has a soothing effect (compare p. 27, Protocol 7). In other cases the severe discharging fit develops later, some time after the breaking of fast. Here follows an example:

Case 1. G. H., age 30, unmarried. Works in a factory. He was the only child of a mother who was deserted by her husband, and was brought up in necessitous circumstances.

1. *Shocks.*—Patient complained of shocks which occurred almost exclusively when he was getting up in the morning. These shocks had lasted one and a half years, from the seventeenth to the nineteenth year. They were of a character to inconvenience him while dressing, for he dropped such articles as he was using, and occasionally they were severe enough to cause him to fall. He realised that when this occurred he must have lost consciousness, just prior to the fall, for he never remembered falling, although he was always conscious of the painful impact with the floor. Experience taught him to save himself from falling, either by clinging to articles of furniture or propping himself against them. As a rule these shocks troubled him every morning, but occasionally he might escape once or twice in a week. During his nineteenth year these shocks disappeared, but were replaced by shocks during the night. These occurred whether he was awake or asleep. Further, he found that if he had shocks during the night he had a fit during the day.

2. *Fits.*—Patient also complained of fits which came on suddenly with no immediate prodromal symptoms. At first these fits only troubled him in the morning, but gradually they appeared at any time during the day, although they were most frequent in the morning. In these fits, he fell backwards or forwards and frequently hurt himself. He did not scream at the onset of the fit, but became very pale. No history of enuresis was got. The convulsions involved both sides of the body, but only the left side of the tongue was bitten. Ten minutes after a fit he recovered, but was drowsy and dizzy, but there was no loss of memory. He had to go to stool always immediately after a fit. These fits occurred thrice monthly for a period of eleven years.

Personal History.—Patient was a full-term child; the birth was normal, but the mother stated that the pregnancy had been for her a time of severe emotional strain and worry. Patient was breast-fed. No history of infantile convulsions was got. At the age of 13 he went to work in a factory. When he was 14, enuresis developed with no apparent cause. At the age of 17, myoclonic shocks began, and eighteen months later, severe epileptic fits. After the appearance of the epileptic fits, the shocks were much less prominent. At the present time the patient showed no organic aberrations, but his memory was evidently failing. The teeth were bad and the tongue coated. He was sent to the institution for chronic epileptics at Heemstede.

The following histories illustrate the peculiarities shown by some patients before the advent of shocks:

Extract from history No. 1. A. M., age 28, a county council workman. When at school patient made but very moderate progress, but he may have been handicapped by a severe cranial injury he received at the age of 3. His grandfather on his mother's side was said to have been a drunkard, while one of his mother's brothers was an epileptic and had been drowned in a fit.

Patient had suffered from myoclonic shocks, characterised by extension forwards of both arms, for six years. These shocks came on if he lay down, particularly if he dropped asleep; he therefore avoided the recumbent position as much as possible. He also found that shocks supervened if he had to concentrate, as on a difficult piece of work, or playing a card game of skill, or if he had to do dull tiring work. Soon after the shocks appeared, patient also had fits. These fits occurred sometimes twice a month, but might be so frequent as twice a week. At first the epileptic fits seemed to protect him from myoclonic shocks, but latterly the shocks were also very troublesome. When under observation in the clinic, he seemed to have shocks only when awake, for at night, if he slept well, none were ever observed.

As a rule such symptoms as biting of the tongue, enuresis or discoloration of the face do not appear in conjunction with shocks or series of shocks. At the same time the careful observation of certain phenomena which may accompany shocks makes it difficult to believe that they are entirely dependent on peripheral causes. For example, consciousness is momentarily disturbed in many cases of severe shock. The patient finds himself on the floor, appreciates the painfulness of the impact, but has no memory of the actual fall. Further, in certain cases, particularly those where single shocks follow one another in rapid succession, a momentary enlargement of the pupil is seen (reflex after-discharge, Part I., pp. 40 and 63). This is also seen in experimental animals, and has already been described.

Certain attention must also be paid to the not infrequent statements of patients' friends and relatives that regular and recurrent shocks do affect the memory and mental functions of patients. It is a general rule, however, with some exceptions, that in the more pronounced cases of myoclonic epilepsy a certain amount of mental dulness is present. This is seen in the cases given on pp. 205 and 206. This fact has been noted by other observers.*

The falling backwards or forwards of the patient, which may occur in a myoclonic shock, is clearly associated with the predominance of the flexors or extensors of the spinal column. It seems needless to deal with the explanation put forward by R. Hunt, that the fall in *myoclonic shocks* is a static disturbance. Nor is the interesting theory of this author,† that the myoclonic convulsions should be regarded as merely a momentary compensation for a local and momentary loss of muscular tonicity, borne out by the numerous tracings made in my experiments,—that is if one regards the convulsions produced by monobromide of

* N. Wyllie, Critchley, and Macdonald, *Brain*, 1925, p. 141.
† Reid Hunt, *Revue Neurologique*, 1922, vol. i., p. 201.

camphor in experimental animals as identical with the phenomena in man.

An important question is, Why is the beginning, and particularly the end, of the night's sleep so conspicuously the time chosen above all others for myoclonic manifestations ?

In the first place, it must be pointed out that many normal persons habitually awake shortly after having fallen asleep, in a condition of general shock or fright, which seemingly rounds off a dream. This is particularly the case, with nervous highly strung persons. Where such a symptom is very prominent, careful investigation often shows that such a person is related to some one who either suffers from myoclonic or genuine epilepsy. This curious manifestation of psychic or emotional disturbances, powerful enough to awake a sleeper and to imbue him with a definite sense of fear or shock, is of great interest. The fact that it is so common among all sorts of persons would suggest that it is somehow connected with the physiology of sleep (Wiersma). It must be also understood that in other conditions of transition from unconsciousness to consciousness epileptic phenomena are prone to occur. In the second place, many myoclonic epileptics complain that if they rest during the day, especially if fatigued, myoclonic shocks tend to ensue. This seems to point to a predisposition to myoclonic symptoms in the quiescent person after exertion.

Careful enquiry has shown that in the very earliest stages of epilepsy the shocks occur usually shortly after the patient has fallen asleep, perhaps half an hour after. This shock awakes the patient, and is followed quickly by a fit or a very severe shock. Later on in the disorder, fits may occur at any time, but at the early stages the fits all tend to occur at this period in the twenty-four hours. Reference is made to the work of Fischer and Leyser,* who suggest that in sleep the cerebral cortex is out of action and the hormonal and intestinal functions have full play.

It would be both interesting and important to know whether any explanation of these phenomena might be got from the facts known regarding the physiology of sleep. According to the researches of Michelson,† and Lambrani,‡ there are two types of healthy sleep. The first type is that experienced by most healthy persons. They fall into a deep sleep early in the night, while towards morning sleep becomes lighter and more fluctuating in character. In the second type, the sleep is light and fluctuating at first, but becomes deep as morning approaches. From this type of sleep a person generally wakens unrefreshed.

Mosso§ and Czerny‖ made a series of observations on a patient with a cranial defect. They observed that cranial pulsations deepen in character at the beginning of sleep, and gradually assume the character of the pulsations seen when a patient is awake, but has his mind completely concentrated.

Whether one agrees with Preyer and other workers that the cause of sleep is the accumulation of the products of fatigue, or if the view of L. Hill be accepted that sleep is essentially a temporary anæmia of the brain, it must be admitted that in the first period of sleep physiological changes occur which are apparently associated with a greater tendency to myoclonic shocks or fits. MacWilliam¶ first drew attention to the strange and surprisingly extensive changes in blood-pressure during sleep. These changes are partly due to dreams, but by no means wholly dependent upon dreams.

It is difficult to explain why wakening in the morning should be associ-

* Fischer and Leyser, *Monatsschrift f. Psychiatrie u. Neurol.*, 1924, vol. lvi., p. 216.

† Michelson, "Dissertation," Dorpat, 1891.

‡ Lambrani, *Atti d. Accad. delle Scienz mediche*, Ferrara, 1099.

§ A. Mosso, "Der Kreislauf im Schädel," Leipzig, 1881.

‖ Czerny, *Jahrbuch der Kinderheilkunde*, 1896, vol. xvi.

¶ MacWilliam, "International Physiological Congress of Edinburgh," 1923, *British Medical Journal*, September, 1923.

ated with myoclonic movements, but it is just as difficult to explain why sitting up, and more especially getting up, should be a signal for a myoclonic epileptic fit. From our present knowledge it can only be concluded that the period of sleep is associated with chemical and other changes as little understood, and that these changes are associated with an increased tendency to myoclonic convulsive phenomena. From the observations made on the experimental cat, it is evident that this phenomena is not limited to man. (Part I., p. 49.)

Although the accurate mechanism underlying this phenomenon is at present unknown to us, we certainly can utilise the experience clinical practice has gained us.

It is common experience that myoclonic epileptics often have a fit if wakened suddenly. Therefore one of the directions I am in the habit of giving to relatives and intimate friends of patients concerning the prophylaxis of fits is that the patient must never be wakened suddenly with a sharp knock on his bedroom door. If he has to be called in the morning the tapping must be begun very softly and gradually increased in force. Further, while the patient is getting up and while dressing all sudden noises must be avoided.

It is very rare to meet with myoclonic epileptic patients who complain voluntarily of senso-clonic reactions.

(" A senso-clonic reaction is the myoclonic shock or series of shocks displayed by patients when exposed to some sudden noise or touch "—Lundborg).

At the same time it is not uncommon to learn from the patient's friends that they do have a convulsion when exposed to a sudden noise, such as the banging of a door. This is particularly the case in children (compare p. 219). It is interesting to find that a nurse who was in charge of an incubator ward, for very delicate or premature infants, noticed that the sudden banging of the door resulted in the immediate and simultaneous convulsive reaction of all her small charges.

It is evident that there are a number of points in common between the myoclonic reflexes of animals and the myoclonic manifestations in man, and especially in the myoclonic epileptic.

Yet we cannot identify the conditions in man and in animals, because the tactile and acoustic reflexes are much less regularly found normally in man than in domesticated cats. Nor can a parallel be drawn between the incipience of the myoclonic fit in man and in an experimental animal.

In an experimental animal there are first reinforced myoclonic reflexes affecting certain parts of the body, these gradually involve the whole body, spontaneous shocks occur next, and finally the complete myoclonic fit.

In man, on the other hand, reflex shocks are often wanting, while there may be no trace of a spontaneous shock before the big discharging fit. A slight myoclonic manifestation (just a few spontaneous shocks, as a prodrome, preceding the fit), which is described as usual for man, may occur in animals also, but it is extremely rare.

At the same time it must be admitted that there are points of striking similarity between the two types of convulsion.

At a certain stage of reinforcement of the reflexes (reflex after-discharge) in experimental cats an enlargement of the pupils is observed. This is also seen in epileptic patients during a series of shocks not associated with loss of consciousness.

In both man and animals we recognise the existence of an incompletely developed epileptic fit, which, so far as somatic symptoms are concerned, is almost entirely similar.

CHAPTER IV

COMMON OR GENUINE EPILEPSY WITH MYOCLONIC EPILEPSY AS THE STARTING-POINT. ORIGIN AND COURSE

Typical Development of Myoclonic Epilepsy. Various Forms of Compensation. Cases given as Examples. Contrast between Intoxication and Detoxication, or Charge and Discharge.

If myoclonic epilepsy be taken as the starting-point in the description of common or ordinary epilepsy it is but in agreement with the observations of Russell Reynolds, who pointed out how very frequently myoclonic shocks occurred in epilepsy. Further, such a starting-point is also justified by the tendency to myoclonic epilepsy found in all the higher animals. It is recognised clinically that monosymptomatic epilepsy is a rare phenomenon. In the ordinary course headaches and myoclonic shocks are frequently associated with absences and psychical symptoms. It is proposed to include epilepsy in the human subject characterised from the start by severe motor fits in the class of myoclonic epilepsy. It will be recalled that among the experimental cats cases were met with where the ordinary climax (enhanced myoclonic reflexes, spontaneous myoclonic shocks, myoclonic fits, status epilepticus) was absent. In such cases the administration of a certain dose of monobromide of camphor produced at once severe motor fits, apparently with no prodromal symptoms (compare pp. 30 and 69).

It will be shown in the chapter on infantile convulsions that the enhanced tendency to myoclonic reflexes found in the first years of life are to be regarded as physiological phenomena. When we come to the discussion of myoclonic epilepsy in the exact sense, it will be seen that this enhanced myoclonic reflex is frequently demonstrated in night terrors which persist, in some children, to the age of puberty. In children where the normal enhanced myoclonic reflexes of infancy are not inhibited by the normal development, there is always the danger that a sudden emotional strain or some toxin may precipitate a myoclonic epileptic fit. When this occurs, a doctor is called in; but it must be realised that this phenomenon is very probably but the climax to other manifestations, such as myoclonic reflex convulsions and spontaneous shocks. Even when this is appreciated it is often very difficult

to get a satisfactory history of the case. In many cases parents do not observe or appreciate lesser phenomena and persist in looking on the fit as a single unprecedented event. Pædiatrists class these children as spasmophilics. There are other danger-signals to be looked for amongst children, such as headaches associated with confinement in close or over-heated rooms, or over-exhaustion when playing or straining at stool. Other children of this class exhibit mental slowness, they either fail to make progress at school or progress very slowly.

One is able to recognise the phenomenon of compensation in the symptoms in almost all cases. This applies especially to the two first groups. A child who has had persistent frontal headaches which do not yield to medical treatment, but are relieved by sleep, begins to display myoclonic symptoms and the headaches cease. This form of compensation was also described by Webber.* A further display of compensation is frequently seen where both the headaches and the myoclonic symptoms disappear when the severe epileptic fits become regular. The following cases illustrate this important phenomenon of compensation.

History No. 2, G. P., age 18, cigar-maker. (1) Patient complained of fits; on an average he had one a week. They were preceded by pain in the stomach, and came on at first in the morning before rising, sometimes after he rose, but before breakfast; but on two occasions they had come on at other times. These attacks were sometimes preceded by a day of mental disturbance, either he was moody or dazed. Shocks always preceded the fits. In these fits he gave a loud cry and fell down, the hands and feet were convulsed; he was cyanosed, the eyes were rotated to one side, usually the tongue was bitten, there was no enuresis. The unconsciousness lasted half an hour. After he had regained consciousness he had a headache and felt ill. These fits had lasted for eight years.

(2) When this patient had shocks he occasionally lost consciousness and fell down. If the shocks were very severe, he was made giddy, and felt most unwell; sometimes he vomited. He stated that these shocks had troubled him for six years. This is probably an inaccurate observation on his part, for it is very probable that the shocks preceded the fits.

(3) The patient suffered much from gastric symptoms, and before a fit he used to have sour eructations. He was not troubled with headaches, while the action of the bowels was regular and normal. Mentally he was normal.

Personal History.—There was nothing abnormal about his birth, and he was breast-fed. In his second year he had convulsions. In these convulsions the eyes were rotated to one side, and unconsciousness lasted for hours. While still unconscious patient used to have several slight convulsions. This occurred several times in a couple of months. When he was 9 he fell downstairs and was unconscious as a result. When he was in his sixteenth year he was standing one day on a roof, working with his pigeons under a strong sun, when he suddenly fell down in a severe fit. He was dazed for a long time afterwards. Later on the fits began to occur at intervals, and a little later shocks were also noticed. *When examined he had alternative periods.* For weeks he would have no severe fits, but during the whole day myoclonic shocks might occur, then he had weeks when he had no myoclonic shocks but severe fits. These fits were not accompanied by myoclonic shocks. He said he preferred the fits to the

* Webber, *Boston Medical and Surgical Journal*, 1893, p. 481.

shocks, because the fits generally came on at night, and he felt safe during the next day and could work. With the shocks, he never knew when he would be well enough to work.

Family History.—The patient's father was of a nervous disposition, and worked in an institution for the blind. His mother had suffered from fits, if she were annoyed or distressed, up to the age of 70. The patient had four brothers and two sisters. All were healthy, except one sister who had migraine. When seen on 1.10.06, the patient was well-built and well-nourished. His face was scarred with the bromide rash. There was no analgesia; neither was there any organic abnormality. When seen again in 29.9.23, he came as the result of a special invitation. He had been lost sight of for years. He said that for six years he had had no shocks. On the other hand, he had a fit regularly every three weeks. He had no prodromal symptoms before a fit. The fits were much shorter than in the earlier part of his illness. He bit his tongue in the fit, and as the fits usually happened at night, about an hour after he fell asleep, he only knew he had had a fit, because his tongue was sore when he awoke. If he, perchance, did not bite his tongue, then his parents, with whom he lived, told him he had had a fit, otherwise he was quite unconscious of the event. He still earned his living as a cigar-maker. Neither his memory nor his judgment had suffered appreciably since he was last seen, while his temper had improved and he was less nervous. He still had some gastric trouble and had to be careful with his diet, and avoided certain articles of diet, such as pork. He always took moderate doses of bromide. One point to be noted is that at this examination the patient was found to be entirely anæsthetic, including even the eyelids.

Epitome.—This case is not a common one, in the fact that the mentality remained practically unimpaired, although the myoclonic epilepsy had persisted for so long. Further, it is evident that a state of equilibrium was arrived at when the shocks disappeared and the fits became comparatively slight, occurred at night, and caused the patient little trouble. That is, the single fit compensated for the series of shocks which were formerly so troublesome. In the early stage of the case the myoclonic shocks dominated the clinical aspect of the case, but finally they were entirely superseded by the abbreviated discharges which occurred at regular intervals.

In the next case compensation is again demonstrated.

Extract No. 2, C., age 25. Patient had had shocks for six years, fainting fits for four years, while fits had occurred in the last six months before examination. The first fit came on after a fall on the head at the age of 18. In this patient, menstruation had begun very late, and some days prior to the first period the shocks first began. Two years later petit mal developed. Later the patient had severe fits, when the shocks and petit mal symptoms entirely disappeared. The fits disappeared under treatment, and when seen twelve years later (1923) she had had no recurrence.

Extract No. 3, S., age 9. Patient had shocks from infancy. For two years he had had attacks, when the head and eyes were deviated to the right; he fell down, but did not lose consciousness. Regular epileptic fits had been present for three months. After the establishment of these severe fits there were no more minor symptoms. (In 1923 it was ascertained that the patient had been for four years in an epileptic institution.)

Extract No. 4, L., age 20. For eight years the patient had had fainting fits (twenty in all) and shocks daily. In the fourteenth year headaches began and later on, fits, but the patient did not have any more fainting fits.

Extract No. 5, B., age 20. Patient's father drank and a sister had convulsions. Patient had had headaches since the age of 13, while shocks had been present at the periods of wakening or falling asleep from the age of 4. He had had epileptic fits for four years. When these fits began the shocks stopped, but reappeared later on.

Extract No. 6, in C., age 12. Patient had fits and shocks from the second year. She was treated successfully for these symptoms four years ago, but attacks of nervous apprehension appeared. Father was an epileptic.

Extract No. 7, M., age 18. Patient fell on his head when he was 2. After this he had numerous fits, generally they occurred in a series. These fits were occasionally replaced by a series of fainting fits. After such a series of fainting fits the patient had severe headaches for several days.

Extract No. 8, P., age 15. Patient had convulsions at the age of 2. After this she was much troubled with persistent headaches, accompanied by a dazed mental condition. When she was 8, shocks accompanied the headaches. After this, she was free from any mental symptoms, except for a dazed condition which usually preceded a fit.

Extract No. 9, E., age 15. When the patient was 7 he had a bad attack of diarrhœa, which recurred several times in the next two years. Gradually the diarrhœa passed off, but the patient developed severe headaches. Later, he had an epileptic fit, or severe shocks during one night, alternately each week.

Many patients complain that epileptic phenomena follow even a slight degree of constipation.

Extract No. 10, B., age 22. This was a case of traumatic epilepsy. Patient had an injury to the skull, which resulted in a cranial defect. If this patient were constipated for even one day he inevitably had shocks. If he took proper precautions by taking an enema he escaped the shocks. This fact he discovered for himself.

Extract No. 11, W., age 30. This was a case of myoclonic epilepsy. The patient had shocks if the bowels were constipated for one day, and also if he had too heavy a meal. He found for himself that the eating of a light meal the first thing in the morning made the shocks much less troublesome, as they occurred at longer intervals.

Many patients realise the value of eating a little immediately after they waken in the morning. In many cases a severe fit may be warded off by this means.

Extract No. 12, P. Sw., age in 1906, 24. When seena t first this patient had a severe fit immediately before breakfast. He found that if he had a light meal, such as roll or piece of bread, the fit did not occur. This statement he made in 1916.

Extract No. 13, J., age 28. This patient had suffered from headaches from the age of 12 (when he was 4, he had convulsions which lasted for six hours without intermission). At the age of 17, fits and shocks began. He found that he had more shocks during the day if he did not have a plentiful breakfast. There was no history of hereditary epilepsy in this case.

It is the case with many patients that the act of lying down to rest seems to induce both shocks and fits. This is shown in Cases 12 and 13, but Case 14 was one where the taking of rest, or the assumption of the resting position, seemed to ward off a severe fit. It is not uncommon for patients to say voluntarily that they can prevent a severe fit by taking violent exercises. These apparently contradictory conditions are of frequent occurrence.

Extract No. 14, G., age 20. This was a case of myoclonic epilepsy. This patient very frequently had shocks about eleven in the morning if she had been very busy the day before. She had learned by experience, that if she lay down about eleven she only had a few shocks and the symptoms passed off. If she neglected to do this she had a series of shocks, and finally a severe fit.

Extract No. 15, V., age 25. This was a case of chronic progressive epilepsy, where myoclonic shocks had appeared late in the case. The patient claimed to be able to prevent these shocks by walking. If he lay down or sat down, the shocks were not so troublesome; but if he were to stand still for a short time, he had very severe shocks which sometimes terminated in a fit.

Extract No. 16, C.K., age 17. This patient was one of four brothers who all suffered from myoclonic epilepsy. The father was a drunkard, while epilepsy appeared in the family history of the mother. While this patient was yet asleep in the morning the shocks began. When he got up the shocks persisted, while he was often unconscious for a few minutes on first getting up. In these shocks the trunk was bent backwards, while the hands were thrown upwards; if a fit supervened, the trunk was bent forwards. This case was under observation for fifteen years, and when last seen patient had about five fits in the week.

Extract No. 17, K., age 39. This patient had fits for fifteen years. These fits came on when the patient was resting quietly or when she slept later in the morning. She used to seize hold of heavy objects and try to shake them when she felt a fit coming on. She succeeded in some cases in warding off the fit. Later, the fits became so troublesome during the night that she slept in a chair to prevent her disturbing her husband. Later these fits cleared up and for twenty years the patient had no more fits.

In Cases 15 and 17 severe muscular exertion evidently compensated for the fits (compare p. 93 footnote). Compensation between other symptoms is not entirely lacking, but is comparatively rare.

Extract No. 18, W. B. S., age 4. This child was the son of a physician; there was a history of epilepsy in the family. Before this child had regular fits, he used to become red and cyanosed; after the fits began he did not have these changes in colour.

Extract No. 19, P. M., age 18. This patient had a fall on his head (frontal region) at the age of 2. After this he had convulsions, and later fits. Later on, he had fainting fits, while later still, headaches and shocks became troublesome. The fits alternated with fainting fits, but it was noticed that the patient was dazed for a much longer time after the fainting fit than after the ordinary fit.

Extract No. 20, C., age 12. Patient had fits and myoclonic shocks from the age of 2. These fits were successfully treated with drugs, but the patient had instead attacks of mental terror.

An interesting point I noted in at least two of my patients was that epistaxis, which had previously been very troublesome, ceased when the patient had fits.

The headaches which have frequently been referred to are all alike in certain points (see Differential Diagnosis, p. 288). It is rare to get patients with headaches atypical in distribution and character. The headache in epilepsy has attracted a considerable degree of attention from neurologists, among whom are Schuller,* Spitzer, and Marburg. These latter investigators attempted to

* Schuller, *Jahrbucher f. Psychiatrie*, 1907, p. 287.

establish some changes in the intercranial pressure as an explanation, but failed to find any definite facts. The fact that the headaches in epilepsy are frequently more troublesome when there are few or no fits suggests that they are alternative manifestation of the effects of the intoxication associated with epilepsy. This point will, however, be dealt with later.

If one takes a careful survey of a case of epilepsy, one sees a chain of symptoms running down the history—sometimes one symptom is prominent, sometimes another. Thus shocks, headaches, fits appear prominently at different stages in the history. Thus a patient may have several days when he has a large number of spontaneous shocks (" bad days " of Unverricht). These shocks are particularly troublesome before breakfast and while rising and dressing in the morning. Finally, the climax comes, and the patient has an epileptic fit. After this the patient usually has a free period until the shocks reappear. Again, an epileptic patient, after taking a little alcohol, may have either a fit, headache, or a series of shocks. Such a phenomenon recalls the experimental work on cats, where it was seen that the reaction of an animal to a drug, such as monobromide of camphor, varied within certain limits—either it would have a severe fit and revert to the normal, or it would react by a series of shocks lasting several days. This interchange of symptoms is so common in epilepsy, that I do not consider it necessary to give separate clinical examples. One point, however, I would emphasise, and that is: that as a rule, at least in the first years of the disorder, the patient may be fairly sure to have immunity from shocks, certainly from fits, for the first few days after a fit. Friends find this out themselves, in some cases, and relax vigilant supervision. This is not to be encouraged, for there is always the danger that shocks of a severe character may occur in which a patient might be injured.

It is not uncommon to find the symptoms of shock complicated with symptoms of giddiness and vasomotor disturbances, or even petit mal. After a severe fit it is not at all uncommon to have a complete cessation of all the symptoms for a longer time.

Along with those physical symptoms go psychical symptoms—changes of temper, loss of memory, and so on. Here it is difficult to draw a parallel between this class of symptom as seen in man and in the experimental animals. At the same time there was a certain amount of evidence that these animals were also affected mentally to some extent.

When a cat has had a fit as a result of poisoning with bromide of camphor (as described in the chapters devoted to the experimental work) very interesting phenomena were sometimes seen in the stage of so-called automatic movement. The animal was sometimes seen to make movements as if fighting an enemy. Also in some cases, violent progressive

movements occurred both before and after a fit similar to those seen in epilepsia procursiva in man.

Where monkeys were treated with bromide of camphor one frequently got evidences of hallucinations of sight and taste, such as smacking of the lips, after a fit. It would appear from the experimental and clinical evidence that the maximum psychical effect of the toxins appears, not before, but immediately after a fit. It may be recalled that in the section devoted to the experimental work, attention was drawn to the fact that the motor cortex and the medullary centres both showed an increased excitability immediately after a fit. This temporary increase of excitability, for it passes quickly, is, I consider, due to the fit. The immediate effect of the fit is, I hold, to dispel the toxin, but there is a temporary and passing increase of the toxin in the blood immediately after the fit. A fit raises the excitability, but as the toxin is in process of expulsion the effect is transient. This may also explain the occurrence of the post-epileptic automatic stage. In none of my experiments with cats did I get petit mal alone with no definite fits. In one case of a cat, where a very large dose of the toxin had been given, the animal simply collapsed and had no convulsions (see p. 74, Fig. 16; also p. 67).

The question arises whether the two conditions—the toxic epilepsy of the experimental animal and epilepsy in man—are two separate entities? In the first case, the myoclonic symptoms form the basis of the condition, while in epilepsy in man the myoclonic symptoms are generally temporary. I consider that the two conditions—the experimental epilepsy in animals and the clinical epilepsy—are essentially one and the same phenomenon. It is, of course, well known that psychiatrists, among whom may be mentioned Aschaffenburg, Jelgersma, and P. Clark, regard epilepsy as a psychological condition, at least primarily. This opinion, I think, arises from the fact that psychiatrists see the cases of epilepsy when well-advanced mental changes have supervened. I freely admit such changes do occur, and that an advanced case of epilepsy has frequently many psychological symptoms, but essentially epilepsy is not psychological.

It is interesting to note that cases of reflex epilepsy were described at the end of the last century. Auboin, Raynaud, and Cérenville* described epilepsy, due to reflex irritation of the pleura following irrigation, after resection, with carbol and thymol solutions. These authors all agreed in considering that the epileptic fits, following the irrigations of the pleural cavity, were due to the reflex irritation of the pleura, and not to the drugs used. Indeed, these cases were accepted by Féré as evidence that epilepsy was here due to reflex irritation. This mistake seems the more extraordinary, since it was fairly generally known among pharmacologists and physiologists that carbolic compounds and their allies would produce fits if administered in sufficient doses.

It must be remembered that the production of myoclonic epilepsy in the experimental animal is an instantaneous process

* Cérenville, *Revue médicale de la Suisse Romande*, 1887 and 1888.

as compared with the progress of epilepsy in the human subject. Here the process is so slow and so subtle that it is generally well advanced when it is recognised. The symptoms so prominent in the experimental animal are prominent largely because they are looked for. It is obvious that such a symptom as an increase in reflex irritability might pass quite unnoticed in a supposedly healthy individual. Here arise the numerous misunderstandings about the initial stages of epilepsy. Both the laity and the profession are inclined to regard the first unmistakable symptom, such as a fit or some mental symptom, as the beginning of the disorder. It is, indeed, extremely difficult to ascertain the actual start of the disorder. I have tried to prepare some figures, and with that end in view drew up tables for 500 male and 500 female cases, giving the ages at which they came for treatment. The results I got agreed with practically those given by other workers (see p. 198). It would appear from these figures that the disorder develops most frequently in the second decennium of life, and that the majority of male cases begin in the first half of that decennium, while the female cases tend to occur later in the second half (earlier development of puberty in the female—Bolk*). It must, of course, be remembered that one has always to allow for patients where the disorder has been present as nocturnal fits, which have never been recognised by the patient nor his friends. The course of the disorder varies enormously. It is, we know, in accordance with the physiological law, that the fits should tend to recur more and more frequently (see pp. 45 and 78), but variations do occur to an extraordinary extent. There are malign cases which go rapidly from bad to worse, in spite of any care or treatment. Such cases not infrequently have some complicating factor, such as encephalitis. Again, there are patients who have fits only at certain times of life, and show no psychic changes whatever. It is recognised, as a general rule, that atypical discharges are generally associated with mental deterioration, but here again exceptions to the rule are not infrequent. Again, long intermissions occur in the disorder which cannot be satisfactorily accounted for. In some cases, certainly, as Turner points out, intermission of the disorder is the direct result of treatment. It is not uncommon to see cases where the intermission has been terminated by some complicating factor, such as a confinement, some infection or disease, or by injury or shock. I am not yet prepared to give a final report on the patients, some 600, which were treated by me some fifteen to twenty years ago, but certain facts can even now be appreciated. Those patients who had suffered from epilepsy for some considerable time before

* L. Bolk, *Ned. Tijdschr. v. Geneesk.*, 1923, vol. i., p. 1530.

I saw them have almost all become chronic epileptics, or have developed mental symptoms, in addition to those cases which have died either in the condition of status epilepticus or from some intercurrent malady—generally tubercular. The patients, on the other hand, who were seen when the disease had not been established have as a rule done well. This is in agreement with Herpin's dictum that after a hundred fits the prognosis is bad. In Part III., Chapter VII., evidence afforded by clinical cases will be used to supplement the evidence afforded by the experimental work in demonstrating that the conditions in epilepsy are those of charge before a fit and discharge after a fit. That is, there is a condition of intoxication before a fit, which, by the action of the fit, is dissipated, with the result that the organism is detoxicated after the fit.

It must be assumed that in every individual there is a certain natural or inborn tendency towards the development of fits. It is proposed to discuss these etiological conditions which, as Redlich points out, bring out or make manifest the first actual manifestations of a fit. Apart from extraneous causes, such as disease,* there are periods in the natural course of life when the tendency to develop fits is higher than at others. Such periods occur in infancy, when convulsions are very prone to appear, and again, more especially among women patients at the various stages of life associated with the menstrual function and child-bearing.

* B. J. Stokvis, *Geneeskundige Bladen*, 1901, No. 11, p. 284. Lauder Brunton, "St. Bartholomew's Reports," 1871, p. 206, and Richet, "Dictionnaire de Physiologie," Art. Chaleurs, p. 87.

CHAPTER V

TONIC SPASMS AND CONVULSIONS IN CHILDHOOD AND THEIR SIGNIFICANCE FOR THE DEVELOPMENT OF EPILEPSY

§ 1. Various Tonic Spasmodic Convulsions of Childhood.

INFANCY has always been regarded as a period when the individual is, for a variety of reasons, particularly prone to the development of convulsive phenomena accompanied with loss of consciousness. It is, therefore, strange that so close an observer as Gowers,* although he was aware of the close relationship between this condition and epilepsy considered clinically, yet does little more than distinguish between the eclampsia in rickets and that due to encephalitis. On the other hand, it is surprising to find pædiatrists, such as Thiemich, Comby, and Hochsinger, describing the different forms of infantile convulsions, but omitting that form associated with encephalitis, although this is the form neurologists are most impressed with. Even in the writings of such eminent authorities as Schroeder van der Kolk, Féré, or Binswanger, one fails to find an adequate description of the different forms of infantile convulsions.

It is evident that this omission is appreciated by pædiatrists, for papers appear dealing with the question. Henoch† described convulsive movements which involved the whole body in perfectly healthy children. It is the case that even in the careful analysis of infantile convulsions by Hochsinger‡ there is not an accurate description of *the activity of the myoclonic reflexes in normal children* (Muskens).§

I feel that an acknowledgement of this physiological fact is the basis for a more exact understanding of the origin of a great number of infantile convulsions.

Numerous theories have been put forward by pædiatrists to explain this tendency for myoclonic infantile convulsions. Soltmann suggested that the cerebral cortex in young animals was

* Gowers, "Epilepsy," 1901, p. 23. "Even a single fit in infancy indicates the need for careful supervision." This is valuable advice too often neglected. *Idem*, Baginsky: *Lehrbuch der Kinderkrankheiten*, 1902, p. 585.

† Henoch, *Vorlesungen über Kinderkrankheiten*, 1887, p. 151.

‡ Hochsinger, *Deutsch. Klinik*, 1912, vol. vii., p. 469

§ Muskens, "Myoclonic Reflexes. Kon. Akademie van Wetenschappen. Natuurkundige Afdeeling. Zitting van Dec. 1921," *Zentralblatt f. Physiologie*, 1912, vol. xxvi., p. 533 and *Epilepsia*, 1913, vol. iv., p. 174.

not yet capable of exerting an inhibiting effect on the impulses in the nerve fibres which already were fully developed. He based this theory on the supposition that the cortex at this stage did not react to electrical stimulation. This last point—the non-irritability of the cortex—was contradicted by Paneth, while clinical observations are also opposed to it. For example, it is a well-known clinical fact that focal epileptic convulsions can be produced by a cerebral hæmorrhage occurring at birth. Jenner admitted that rickets was an etiological factor for infantile convulsions, while Gowers agreed with this view, and suggested that the retarded development of the bones of the skull caused disturbances in the development of the cerebrum which, in turn, resulted in the tendency to have fits.

Czerny and Stheemann* ascribed both rickets and the hyper-irritability of the nerve centres to a deficiency of chalk in the diet.

Erb found that in tetany in the adult there was a hyper-irritability of the peripheral nerves; this was also observed in children with convulsions by Hansen and Thiemich.† Trousseau reported a case where a fit of tetany could be produced by pressure on the sulcus bicipitalis. Chvostek reported a case where percussion over the facial nerve resulted in the spontaneous contraction of the adjacent muscles. Hochsinger, at a later date, confirmed this observation of the hyper-irritability of peripheral nerves in cases of infantile convulsions. These many theories and suggestions do not seem to me to explain the condition satisfactorily, and it appears to me that the fundamental factors for the occurrence of infantile convulsions are not properly appreciated or understood.

Cases of infantile eclampsia nearly always occur in association with incorrect or insufficient nourishment, more especially where the children are not breast-fed. Gastro-intestinal disturbances are common in such children, while both glottic spasm and inspiratory spasm are frequent symptoms. Such children, it is found, often suffer from lack of sufficient fresh air.

The fact remains that at the present day the different forms of infantile convulsions have not been properly classified, neither is there a proper appreciation of the connection which may exist between different convulsive symptoms seen by the pædiatrists and the adult with fits or allied phenomena seen later by a neurologist. When a case of epilepsy in an adult comes under the care of a neurologist, it is often impossible to get a satisfactory early history of the case. Even where the patient has had infantile convulsions, and has been attended by a pædiatrist, he has almost certainly been lost sight of by the pædiatrist during the lapse of

* Stheemann, H. A., *Nederl. Tijdschrift v. Geneeskunde*, 1917, vol. i., p. 1436.

† Thiemich, *Revue d'Hygiène et de Médecine infantile*, 1903, p. 309.

years. The parents or near relatives can rarely give a correct history, for years have dimmed the memory of observations, which probably were very incomplete and inaccurate. Further, it must be remembered that even amongst the profession there is not a clear classification of the different forms of infantile convulsions. It is obvious, therefore, that amongst the laity the confusion is worse, and all sorts of conditions are referred to under the title of "infantile convulsions."

An attempt is here made to separate out the different phenomena, which may be described under the heading of Infantile Convulsions.

1. Involuntary muscular contractions. These occur during suckling and during sleep. This phenomenon is seen very well in young puppies. The characteristic movements are twitching of the lips and eyelids, and also twitchings in the extremities. When watching such a case, one will see twitching of the muscles of the lips, the mouth may be drawn into different positions, twitching of the eyelids, close gripping movements of one or both eyelids, fascicular twitchings of the muscles of the face, and twitchings in the limbs. So far as I know, this phenomenon has no deep significance, and it generally disappears after the first few months of life.

It is interesting to recall the work of P. Flechsig,* who showed that the nerve sheaths were developed in the gyrus centralis posterior in the first months of life. It is probable that the development of the nerve sheaths in the motor gyrus may be the fundamental reason for this phenomenon.

2. In very young children, under 1 year, who are very ill, particularly with hereditary syphilis, tonic cramp or tonic convulsive movements, sometimes occur (compare Poynton†). This phenomenon is frequently seen just before death.

The observations made by Soltmann are of interest for this type of convulsion. Soltmann stated that at this stage of life the pyramidal tracts are not yet functioning as in the adult; it is probable, therefore, that these tonic convulsions are due to a change or disturbance in the corpus striatum and not to the pyramidal tracts.

Another interesting observation was made by Soltmann. He found that 16 stimuli per second will induce tetany in the newly born animal, whereas in the adult 50 stimuli per second are required. There is, therefore, a greater tendency to tonic convulsions in early life. Further, the muscular contraction curve is slower in type than with the adult. These two observations

* P. Flechsig, "Anatomie des menschlichen Gehirns," Leipzig, 1920, vols. vii. and viii.

† Poynton, *Lancet*, October 31, 1908, p. 1244.

suggest the possibility of there being some etiological connection between the convulsive movements described under Class 1 and myoclonic convulsions occurring later in life. Certainly the convulsions of Class 1 are much slower than real myoclonic convulsions.

3. When examining the history of chronic epileptic patients, more especially those who show some differences in the symptoms on the two sides of the body, the mother or near relative frequently gives a history of some serious illness in youth. Such an illness may be associated with loss of consciousness lasting for several hours or days, the development of a certain degree of hemiplegia, and loss of speech so far as it had been learned. As the patient recovers, he recovers more or less from the hemiplegic symptoms, learns to speak again, and gradually resumes his normal development.

It would be pointed out that the special class of case referred to is not one where the patients show definite or persistent hemiplegia or athetosis, but those with more illusive unilateral symptoms, such as a more or less one-sided character of the fit, or the presence of exaggerated reflexes on one side between the fits.

Neurologists regard such a train of symptoms occurring in a young patient as an indication of encephalitis of infectious, embolic or thrombotic nature.

It is generally difficult to get a reliable history of the case, or to ascertain whether the encephalitis was primary or secondary.

Sometimes such a case may occur as a sequel to, or coincident with, the course of some infection, such as scarlet fever, diphtheria, whooping cough, typhoid, cerebro-spinal meningitis, erysipelas, septic infection from the ligature of the umbilical cord.

From the fact that such convulsions do frequently appear in the history of epileptic patients, neurologists have agreed that encephalitis, or rather, according to Ford and Schaffer* vascular, disturbances must play an important part in the development of epilepsy later in life. Féré, for example, found that in 100 cases of epilepsy infantile convulsions occurred in 34. In 40 cases of epilepsy, which I took without any selection, I found in 11 a history of convulsions, accompanied with unconsciousness lasting for many hours. In 6 of these 11 cases there was a direct history of heredity—*i.e.*, epilepsy in near relatives. Only in 2 cases did I find that the epileptic fits had followed immediately upon the encephalitis. Both these cases showed symptoms of hemiparesis, and were more or less backward mentally. It is curious and important to find that there was a tendency to constipation, and the tongue was coated in those cases where the epilepsy was directly associated with encephalitis, just as in ordinary cases of genuine epilepsy.

* F. R. Ford and A. J. Schaffer, *Archives of Neurol. and Psych.*, 1927, vol. xviii., p. 323.

It seems reasonable to believe that either the lesion in the brain or the resulting fits produce the same gastro-intestinal disturbance (compare Chapter XV., § 10), or, as is more probable, the cerebral lesions only lead to epileptic manifestation where gastro-intestinal disturbances are prone to occur. On the other hand, one is led to believe that many cases of severe infantile convulsions, which suggest encephalitic lesions, are really brought about by an intoxication due to intestinal infection (compare § 2 of this chapter).

Attention must be called to Gowers' description of the phenomena associated with encephalitis. It is as follows:

(*a*) A fit involving one side at least at the beginning.
(*b*) The occurrence of a severe general fit, which is associated with some infectious disorder or cranial trauma.
(*c*) Temporary paralytic symptoms.

Such a description does not seem to me effective enough to allow of differentiating the cases from those of so-called "occasional convulsions." As regards the question of the influence of cranial trauma at birth, Turner found such a history in 5·8 per cent. of his cases of epilepsy.

4. To this group belong *Occasional Convulsions*. These are distinct from any of the foregoing types, and tend to occur in children with febrile disorders, peculiarly after the first rise in temperature. The age incidence is from 2 to 8. Such fits may occur in otherwise perfectly healthy children coming of a healthy stock. It would appear, however, that genuine chronic epilepsy is only likely to follow such fits where there is a family history of epilepsy. Turner maintains that a history of infantile convulsions is only got with those epileptic patients who have an hereditary family history of epilepsy. Féré also attaches great importance to the hereditary character of infantile convulsions in general.

These occasional convulsions show all the characteristic symptoms of genuine myoclonic epilepsy to a greater degree than other forms of infantile convulsions. An important resemblance is the enhancement of myoclonic reflexes present several days before and after the convulsions. The close resemblance between the phenomena suggests strongly that here we have an analogous condition to the myoclonic fit, seen in the cat after intoxication with such a drug as bromide of camphor. Some children apparently develop these convulsions as a result of some intoxication, either due to micro-organisms or to some metabolic product associated with the rise in temperature. If the latter explanation be correct, it would account for the occurrence of the convulsions in certain children in different circumstances characterised by

rise of temperature, but not by the presence of any particular organism. Such children will have a fit after an attack of bronchitis, or at the initial stage of pneumonia. The effect of some definite toxin is seen in the convulsions occurring in children after small doses of carbolic acid, as described by Comby and Hochsinger, or those following in breast-fed children upon the taking of alcohol by the mother or wet-nurse; and sometimes where the child is breast-fed by an eclamptic mother. Such occasional convulsions may also follow on overloading of the stomach, or after psychical shock (Thiemich and de Bruin).

There are children, who, from the age of 2 to 10, react with a fit at the commencement of any febrile disorder, such as recurrent bronchitis. They have no fits apart from this condition. There are other children, who will only have such a fit once. This fit may be very severe, and may be accompanied by unconsciousness, slight hemiplegia, and aphasia. In all cases, where a fit occurs in young children, with no history of other fits or allied phenomena, the temperature should be taken at once, and a careful examination made of the chest. The following is an example of this particular type of case.

Case No. 3, E. M., age 2½ years. Up to this time patient was perfectly healthy. In July of 1915 he was taken to stay in a country boarding-house. It afterwards transpired that in the preceding winter a tubercular case, in the last stages, had been nursed in this house. From July 15 to August 1 the little lad played in the garden and was perfectly well. On the August 1 another family arrived and stayed in the same boarding-house. In this family there were two children, and on August 5 a four-year old boy fell ill. He had a long and severe fit with both tonic and clonic convulsions, which involved the whole body; the pupils were dilated, and unconsciousness lasted five hours. After he regained consciousness, the temperature rose to 39·5° C., and half a day later the child had symptoms of aphasia. This boy had had a similar convulsion on three occasions a year previously, and had had bronchitis immediately after. The younger brother, aged 2, had a convulsion just like his brother, and, like him, had bronchitis after. E. M. was evidently infected from those children, for two days later he awoke crying in the night, his hands shook nervously, the pupils were dilated, the eyes staring during general convulsions, but there was no enuresis. The next day he had bronchitis.* Later, on November 24, 1915, the patient again had a noisy and excited day, and again looked very ill. At one o'clock a.m. his mother wakened to find him in a fit. The fit lasted almost a minute, and was followed by a period of unconsciousness, lasting about half an hour. After this fit, the reflex irritability was a very prominent symptom, while the temperature was 38·7° C. During the same night, when the patient had fallen asleep, several convulsive movements occurred; these were very similar to those seen in young puppies when asleep. In the four years after this fit the child had four to six fits of this type. They were all accompanied by a rise in temperature and a recrudescence of the bronchitic symptoms. The later convulsions generally took the form of

* The question arises whether in such cases the "occasional fit" does not replace the so-called "cold shiverings," which in so many adults is associated with an initial rise of temperature heralding in some infectious disorder. One is led to think that such a child as the one under discussion, who has reacted repeatedly with a complete fit, would react to slight rises in temperature with a fit instead of "cold shiverings."

shivering movements over the whole body, the legs alone showed convulsive movements of the ordinary type. In all cases the reflex irritability for the myoclonic reflexes in the period preceding this fit was increased.—During the whole period the child made quite satisfactory progress at school, while physically he kept well, with the exception of some catarrhal trouble of the right ear. The bronchitis troubled him less and less, but when he was 9 he had measles and again had a fit, which was associated with a bronchitic attack.

As regards the two other children who were ill in August of 1915, I learned in 1922 that they had had no more convulsions and had made good progress at school.

Epitome.—In the case under consideration, it is evident that E., the patient, was not infected in the first place by any infection lingering in the house. (One cannot dogmatise on such a point, but it is highly probable that the house, at least in certain parts, would retain infected matter from the former tenant.) When, however, the other children arrived, they speedily developed respiratory trouble, which was passed on to E. This infection produced a sufficient degree of intoxication to break down the natural resistance against fits in this child. It is highly probable that E. ran a grave risk of becoming a myoclonic epileptic. Fits were brought about, for a number of years, by a degree of toxæmia, characterised by a rise in temperature and bronchitic troubles. But this case, as well as the cases of the two other children, yielded to care and proper treatment. Probably, also, the fact that E. had no hereditary history of epilepsy helped.

These fits or convulsions were, I consider, defensive in action, and were a method of discharging a toxin injurious to the organism. It is true that, in the cases of two of the children, a certain degree of aphasia and hemiparesis was seen after the severe fit, but these symptoms were, in all probability, due to some intoxication of the cerebrum, and not to a definite lesion (Ashbey).* In the case of E. there were no cerebral symptoms. These three were children, who reacted to certain toxins by increased myoclonic reflexes in the first place, and finally, by fits. Although it is true that in one case aphasia was present for several hours after the fit, and a certain degree of right-sided hemiplegia was noted, it still seems somewhat slight data to diagnose a tangible lesion from. It is rather a condition of temporary intoxication, which may be regarded as a transition stage to an encephalitic lesion. The observations of Osler and Sachs† are very interesting. They record a case of severe cerebral hæmorrhage and resulting hemiplegia associated with a severe *occasional* fit. This occurred possibly in the same way as, after an ordinary epileptic fit, subconjunctival hæmorrhages occasionally occur. It is probable that intracranial hæmorrhage is more common than is generally realised.

* Ashbey, *Lancet*, January 21, 1905.

† Sachs, " Nervous Diseases of Children," 1905. Compare also Spriggs and Higgs and Shore, *Practitioner*, 1885, vol. xxxiv., p. 434.

Notes are here given of a second case, which could not be followed so completely as that of the first. In this case there was more chance that the disorder would develop into genuine epilepsy, for the father was an epileptic, while the patient suffered from two grave symptoms—enuresis and headaches.

Case 4, W. An. Patient was seen first at the age of 3, and was kept under observation for thirteen years, from 1908 to 1921. When seen first, the history was that the child had been feverish and irritable for two days. Suddenly she became pale and had a definite convulsive attack in which she salivated, bit her tongue, lost consciousness and displayed twitchings of the hands and feet. After consciousness returned the patient had a headache. Within a year, a fit of this type occurred seven or eight times; on each occasion she was feverish, or had distinct malaise at the time of the fit and immediately after it. She occasionally displayed enuresis, sometimes twice a week, and suffered from headaches. The bowels were inclined to constipation. In the family history certain points of significance were found. The father had had fits up to the age of 13, accompanied by epistaxis. Her grandfather on the paternal side had also had fits, while a brother of her father had fits up to the age of 20. In the patient herself no abnormality could be detected. In January of 1908 she had a very severe bout of fits, having as many as seven in one night, after which she entered the epileptic hospital for one month. During this period she had milk diet, a minimal dose of a bromide salt, and meticulous care bestowed on the hygienic routine of her life. In 1911 she had a nocturnal fit, when she was suffering from a cold, and during the next year, on one occasion, twitching of the mouth was noticed during sleep. In 1913 she had a slight and evanescent attack of facial paralysis, preceded by sickness and nausea the day before. In 1915 menstruation began; this gave her no trouble, but in the same year she had diphtheria. When seen in 1921 she was a strong, stout girl of sixteen. She was perfectly well and never had fits. Mentally, she was slightly below the average.

Epitome.—This was a patient, with an hereditary history of epilepsy. She had occasional fits over a long period, which were associated with a rise in temperature. It was a case which gave rise to considerable anxiety, yet careful treatment was successful in *arresting the decided tendency* to epilepsy.

Occasional convulsions which occur up to the tenth year of life should always be looked on with suspicion. Pædiatrists explain them—partly, at least—as spasmophilic in nature, and describe a hyper-excitability of the peripheral nerves. This hyper-excitability, I consider to be increased myoclonic reflex irritability. Certainly, in the first case of E., I was able to detect a peculiar sensitiveness to touch and to sudden noises several hours before a fit. A sudden noise would be sufficient to produce a distinct myoclonic shock, involving the general musculature. It is important to note that the glottis is never involved in these occasional convulsions.

5. *Eclampsia in Children.*—This is a subject which has been studied almost exclusively by pædiatrists. In fits of this type the glottic and respiratory muscles are involved, while there is marked hyper-excitability of the peripheral nerves and loss

of consciousness. It is important to note that glottic spasms seem to be a form of reaction peculiar to the very young, for they occur apart from general convulsions, and in cases of meningitis and encephalitis. Henoch* also describes hemilateral, cramp-like spasms associated with gastric disturbances and constipation. The observations of Henoch also make it clear that there are transition stages between myoclonic reflexes and fits, and occasional convulsions and eclampsia in children. From the description of these spasmophilic convulsions given by pædiatrists, it is seen that they tend to occur in winter, more particularly in rachitic children. This may be associated with the lack of fresh air from which the children tend to suffer in severe weather. It is also thought that a calcium deficiency may be the cause. There is no doubt but that gastric disturbances and lack of fresh air are important etiological factors. Escherich thinks that the lack of breast-feeding is an important cause, at least with very young children; and this may be true. It seems to me that pædiatrists tend to pay too much attention to the standard of excitability of the peripheral nerves. This point has been investigated by Mann and Pirquet,† who, however, got divergent results. Too much attention is also, I think, given to the symptoms of Chvostek and of Trousseau. As far as the symptom of Chvostek is concerned, one has only to go into an obstetric clinic and look at a number of healthy new-born infants, to find how often the contraction of the mimical muscles may be elicited by a tap on the cheek—that is, if the children are not asleep or crying. In very young children, it is surprising how often one gets either acoustic or tactile (myoclonic) reflexes. A sister who had charge of a number of premature infants in incubators used to describe how all her young charges reacted simultaneously to a sudden noise, displaying a spasmodic contraction of the whole body. It would also appear that too little attention is paid to the myoclonic reflexes found in many normal children, at least this is to be concluded from the work of Henoch and Bossert.‡ For example, if a young child is asleep, particularly if in a light sleep, a sudden noise may produce a shock or a glottic spasm. This is more particularly the case with spasmophilic children. In short, the question arises whether the Chvostek and Trousseau signs are not merely manifestations of myoclonic hyper-excitability. It is becoming evident, from the literature, that pædiatrists are dissatisfied with the old classification of spasmophilic disorders. This is shown particularly clearly in the writings of Reyher.§

* Henoch, *Vorlesungen über Kinderkrankheiten*, 1882, p. 159.
† Pirquet, *Wiener medizinische Wochenschrift*, 1907.
‡ Bossert, *Zeitschrift f. d. ges. Neurolog. u. Psychiatrie*, 1921, vol. lxvii.
§ Reyher, *Klinischer Wochenschrift*, 1923, vol. ii.

There is no doubt but that there is a connection between the cramp-like phenomena, eclampsia in children, and encephalitis. All these disorders frequently tend to run in families, and may be replaced or represented in one family by epilepsy. That is, one generation, or several members of one generation of the family, may have one or other of these disorders, while others have epilepsy.

In many cases of these associated eclamptic disorders, phosphates and cod-liver oil give excellent results, and arrest the fits. As regards prognosis, this form of eclamptic fit which usually occurs in the first three years of life is rarely dangerous in itself, unless glottic and respiratory spasm develop. Thiemich and Birk have pointed out that about 50 per cent. of children from this form of disorder are backward mentally.

An example is here given of a case which is considered to belong to this spasmophilic type. This child, it may be noted, was breast-fed.

Case 5, M. v. V., 15.5.19. Patient, aged 3, was the fourth of five children. Three had died of convulsions, aged respectively eighteen months, 1 year, and 4 years. Patient and his surviving brother both had rickets. The convulsions which the patient suffered from were similar to those from which the three children had died. The child had a fit of temper, made a deep inspiration but did not expire, became more and more deeply cyanosed and displayed tonic and clonic convulsions. Patient sometimes had as many as six of these fits in a day, but when examined rarely had more than four in the course of a week. The first untoward symptom had appeared when he was not quite a year old. During the previous day he had played and been apparently normal, had been fed as usual (child was breast-fed), but suddenly became rigid, while the eyes were deflected to the right. There were no febrile symptoms. The next morning the child was quite well. The next fit occurred three weeks later, when he was in a heated room. The mother noticed after this that a fit frequently followed if the child hurt himself or if he were startled or annoyed. She said that all her children had shown the same difficulty in stopping crying. They all tended to take a deep inspiration and then seemed to hold their breath—*i.e.*, they could not expire (expiratory spasm). Patient was never altogether free from fits, and when examined had had about forty. He had more fits in warm than in cold weather. After a fit he was tired and slept when put to bed. Apart from the fits patient was a troublesome child, being passionate and easily annoyed. He was very easily frightened, and often showed a powerful reaction after a very slight stimulus (the senso-myoclonic reaction of Lundborg). The mother said that she had had a very difficult pregnancy with the child and had been much worried during the whole time on account of sadistic symptoms displayed by her husband's patron. The family history showed that the mother's mother and two sisters had died in a lunatic asylum. There was no history of epilepsy in the family. Three of the children had died of convulsions, as has been stated.

When seen in April, 1921, patient still had fits. These fits were often associated with diarrhœa, or they sometimes occurred when the child was very preoccupied with his games. He was put on phosphates and cod-liver oil, and seemed to improve. Later it was found possible to place him in better hygienic surroundings, and he had no fits for quite a long time.

Extract Case 20, L. K. This patient was the daughter of one of my female epileptic patients. During the pregnancy the mother had many fits. The confinement was normal, but about seventeen days later the infant was seen to become cyanosed. This occurred several times in a week. When the child was seven months old, just as breast-feeding was

to be stopped, she had a definite fit. Since then, up till the present age of 17, the patient has had a regular series of epileptic fits. It was impossible for this patient to lead a normal social life because of her passionate temper.

6. *Tetany in Children* is to be considered as the same disease in adults.

7. *Emotional or Anger Convulsions.*—Such phenomena may be seen in very young children of neuropathic tendencies. When the child is annoyed, it reacts by holding its breath after a deep inspiration, the head drops back, the face becomes cyanosed, and sometimes the child appears unconscious.* The whole phenomenon is very like the respiratory convulsions of the so-called spasmophilic child, but the two conditions are not the same, and must not be confused. These anger or rage convulsions have a good prognosis. Like the two syndromes, glottic and carpo-pedal spasms, I consider this reaction as peculiar to the infantile age, and not in any way analogous to the occasional convulsion. It will be remembered that the occasional convulsion, which I consider to be in reality a myoclonic epileptic fit, has already been described as performing a definitely protective role inactivating certain toxins.

8. *Habitual Forced Movements in One of the Three Planes*† (*Jactatio capitis nocturna*).—This is a condition which is quite different from infantile convulsions, although pædiatrists are inclined to class them together. In this condition we have to deal with automatic movements which occur partly in sleep, partly when awake, and are related to the development of the semicircular canals. The complete functionation of the semicircular canals is developed late (this is curious, since the secondary vestibular nerve fibres are among the first to acquire a medullary sheath in the fœtus). As is well known, all children love to swing, to ride on merry-go-rounds, or to be rocked. Further, when children are quite young, especially before they can walk, they exhibit a curious immunity to sea-sickness. It is quite common to see a nurse or mother violently ill on board a boat while the child is quite well. This immunity generally passes as the child grows older. The habitual forced movements may persist in children up to the age of twenty. They seem to have no pathological significance.

9. Frequent petit mal in children or pyknolepsie (see Chapter XI., § 9, p. 315).

* E. Feer, *Lehrbuch der Kinderkrankheiten*, 1907, p. 494; Friedmann, *Allg. Zeitschrift f. Psych. u. Neurolog.*, 1912, vol. ix., p. 257; Neumann, *Archiv. f. Kinderkrankheiten*, 1905, p. 99, recommend sharp stimulation of the skin, when a child holds its breath.

† Compare J. Thomson, "Traité des Maladies de l'Enfance," 1905, vol. iv., and Corn. de Lange, *Nederlandische Tÿdschrift v. Geneesk.*, 1915, vol. ii., p. 1142.

§ 2. The Relationship between Infantile Convulsions and Epilepsy. Occasional Convulsions, Eclampsia in Children, and Infectious Encephalitis Statistics.

Pædiatrists meet with great difficulty in keeping trace of their cases as these cases grow up and pass out of their clinic. The neurologists, on the other hand, are beset by the difficulty of getting reliable historical data for their cases. Everyone is agreed that it is of the utmost importance, if the problem of epilepsy is to be solved, that a complete record of all cases of convulsions or fits should be accessible. With this aim with others in view, the establishment of a central clinic in the Netherlands was recommended in 1903.

In the foregoing part of this chapter we have discussed seven different types of convulsions, but of these, types 1, 2, 6, 7, 8, and 9 may be disregarded at once, and full attention paid to types 3, 4, and 5.

Turner* says that "The most common demonstrable cause of epilepsy is infantile convulsions"; it is, therefore, important to ascertain which type or types of infantile convulsions are principally involved. This problem is not directly approached by the various writers. Féré is the most sweeping, for he asserts that infantile convulsions are ætiologically and symptomatically identical with epilepsy; he found that 34 per cent. of his cases of epilepsy had had infantile convulsions. Turner and Gowers† give this figure at 10 per cent., Patrick and Levy‡ found that 19·6 per cent. of their 500 cases of idiopathic epilepsy had had infantile convulsions. They also took the trouble of examining non-epileptic children. They found in unselected cases of children 4·2 per cent. had had infantile convulsions; further, they found infantile convulsions more frequently among country children than among those of the town. They concluded that if all children have a chance of developing epilepsy, those children who have had infantile convulsions have this chance multiplied by five. Further, they concluded that epilepsy was more likely to develop if the infantile convulsions were varied in character, and if tonic convulsions had occurred.

These authors do not specify exactly what type of infantile convulsion is referred to; and this I take to be the most important point.

Binswanger quotes Féré and Voisin, who assert that eclampsia in children is practically a prodromal symptom of epilepsy in the

* W. A. Turner, "Epilepsy," 1907, p. 48 (Macmillan and Co.).

† This percentage is, according to Burr, 15 per cent. (*Archiv. Pediat.*, May 22, vol. xxxix., p. 303). This author considers that the interval between infantile convulsions and epilepsy is a long remission.

‡ Patrick and Levy, *Journal American Med. Assoc.*, 1924, p. 376.

adult. He then proceeds to draw up a table showing the differentiating symptoms between the forms of convulsions in the occasional and adult stages. Here I do not agree with him, for both eclampsia and epilepsy show so many and various forms of discharge, it is impossible to make any hard-and-fast dividing line between them. The suggestion that the eclamptic fits in children are more like the " Brown-Séquard epilepsy " in guinea-pigs than ordinary epilepsy seems to me quite mistaken.

From my own experience, I found that out of 1,000 male patients 99 had a definite history of occasional convulsions in childhood. In these cases the convulsions were sometimes associated with teething, some were indefinite in character and not associated with any concomitant condition, while in a few the convulsions merged into epilepsy. I thought I was able to recognise encephalitis in the history of 143 male cases out of the 1,000, and 11 cases of glottic spasm. In 1,000 female epileptic patients I was able to trace infantile convulsions in 75 cases, encephalitis in 116, while glottic spasm was apparently present in 12 cases. The total numbers were, therefore, 253 cases showing a history of infantile convulsions in 1,000 male cases, and 203 in 1,000 female cases.

In a small group of 200 cases of genuine epilepsy, to which I gave special attention, I found I was able to trace infantile convulsions (this is taken to include occasional convulsions, encephalitis, and eclampsia) in 27·5 per cent. Too much attention cannot be paid to this figure until we are in a better position to get a reliable history of the occurrence of occasional convulsions in healthy persons. Personally I consider 27·5 per cent. to be too high a figure.

Similar objections may be raised to the interesting table of percentage given by Thom.* He found among 300 cases of early epilepsy (before the end of the first year), in the Monson Epileptic Home, 150 cases with a history of infantile convulsions. Further, in 111 children examined eight years after they had had convulsions in children's hospitals, Thom found that in 42 cases, where gastro-intestinal trouble had been the primary cause, the convulsions had continued in 15. Of these, 5 were mentally deficient, and 7 were physically subnormal.

The question now before us is, what light do the researches on myoclonic reflexes and myoclonic epilepsy, described in the earlier part of this book, throw on this problem ?

Firstly, it must be recognised that enhanced myoclonic reflexes are a physiological condition of childhood; secondly, that children who are disposed to have occasional shocks or convulsions

* Thom, D. A., *Archives of Neurolog. and Psych.*, 1924, vol. x., p. 664.

display these enhanced myoclonic reflexes to a very marked degree. In one case, that of Case 4 (p. 225), the mother saw a number of her children become convulsed at the same time, owing to a strong acoustic stimulus. Such children also have nocturnal spontaneous shocks. In the third place, it is the case that in the occasional convulsions of childhood, more especially those associated with febrile disorders, we find fits of exactly the same variations as those occurring in epileptic adults. I therefore cannot agree with Binswanger, who claims to be able to distinguish infantile convulsions from ordinary epilepsy. Neither do I agree with Féré, that infantile convulsions are merely symptomatically similar to epilepsy. The occasional convulsions are, I maintain, identical with myoclonic epilepsy, but etiologically they cover a larger field. In the young child a rise in temperature may be followed by an occasional convulsion, but it is not known that a slight rise in temperature of an adult is ever associated with an epileptic fit.

Put briefly, the conclusion is as follows:

From the experiments made on animals, and described in the earlier part of this book, we learn that myoclonic fits are a means of defence of the organism against certain toxins. In infancy there is normally an enhanced myoclonic irritability as contrasted with the adult. This being the case, the occurrence of occasional convulsions is easily brought about by what in an adult would be a wholly inadequate stimulus. The occasional convulsion of infancy is essentially not a pathological process at all. As the child grows older, the inhibition or checking of these myoclonic reflexes develops, favoured largely by the condition of tranquil security in which the majority of children in civilised countries live. A parallel condition was seen in the cat. An ordinary domesticated cat rarely exhibits myoclonic reflexes (except occasionally at the end of pregnancy), without treatment with bromide of camphor. If, on the other hand, the cat is wild, the myoclonic reflexes are very active, and require no fortification with drugs.* Not only early youth and pregnancy, but also puberty, the menstrual period, and the climacteric are all periods of enhanced tendency towards epilepsy.

To get a clear picture of the association of epilepsy, and occasional convulsions, it is necessary to have a full report of the cases as they appear to the pædiatrist (*i.e.*, the frequency of occasional convulsions in children generally), and a later report, either from the pædiatrist or from a neurologist, of the cases of epilepsy in young children which were subject to these convulsions. The association of these two reports would show the connection between the various forms of infantile convulsions

* H. Frisch, *Allg. Zeitschr. der Psych. u. Neur.*, vol. lxv., p. 231.

and epilepsy (see p. 230). It must, however, be remembered that pædiatrists are quite frequently not interested in convulsions, and therefore do not record them very carefully. One must keep in mind that the observation of occasional convulsions is a delicate matter. Many quite intelligent parents fail to observe them, or to attach any importance to them. For the diagnosis of the occasional convulsion, one has to rely on the brief duration of the phenomenon and the subsequent rise of temperature. For the diagnosis of eclampsia, the accompaniment of respiratory disturbances is important. Encephalitis can only be diagnosed where the loss of consciousness lasts over a long period, and is followed by hemiplegic symptoms of some duration.

From an observation of many cases, the conclusion is arrived at that encephalitis is certainly of significance for the development of epilepsy, as also are occasional convulsions and eclampsia. It is also possible that spasms associated with emotional disturbances may have some significance.

For purposes of classification, occasional convulsions should be placed next to the myoclonic fits seen in experimental animals. As has been suggested, these occasional fits seem to fulfil a protective function, guarding the organism from certain toxins.

In conclusion, it is noted that there is no parallel between the glottic spasm, the carpo-pedal spasm and the emotional spasms of young children, and the epileptic fit of the adult. (These phenomena, glottic spasm and carpo-pedal spasm, are not found in the adult.) These two phenomena are peculiar to infants or young children. They are probably due to toxic substances associated with metabolic disturbances. Further, it must be pointed out that cases of occasional convulsion do occur which are followed by transient aphasic or paralytic symptoms. There is no reason for believing that there is always a focal, vascular, or other organic cause for such symptoms.

§ 3. **Conclusion with Reference to the Attitude of the Medical Attendant.**

When a doctor is called in to see a young child who has fits, he must focus his attention on certain definite points. He must take the temperature in each case as soon as possible after the convulsion. Where the temperature has risen, and where there is further evidence of some infection, he is generally able to give a favourable prognosis. At the same time, he must follow Gowers' direction, and insist on special prophylactic measures being adopted, which must be kept up at least until puberty. Where, however, the child exhibits prolonged unconsciousness with the fit, and this is followed by definite hemiplegia or aphasia,

the case is very probably one of encephalitis. As has been already pointed out, this encephalitis may give rise to epilepsy later on in life. Where the fit is accompanied, or followed, by respiratory spasms the prognosis is not so good, the result may in some rare cases be fatal, but the child may do well, while the pathological significance seems slight. We are not yet in a position to say exactly whether there is any tendency in such patients to develop epilepsy later on.

In my statistics on the etiology of epilepsy, and in my observations of infantile convulsions, I have been impressed by the number of cases where the mother's pregnancy was attended by emotional strain or disturbance. Such an observation suggests that a definite prophylactic measure against epilepsy would be the protection of the pregnant woman rom emotional disturbance.

Sometimes, in practice, the question arises as to whether one is dealing with a case of infantile convulsions or infantile epilepsy. Vogt* points out that eclamptic fits generally occur in a series, while this is not seen in epilepsy. Certainly, this point serves as a distinctive diagnosis from the occasional fit which has already been described as identical with the myoclonic fit. Further, eclamptic fits are usually associated with rickets, and respiratory disturbances are practically always present.

The question naturally arises, is there any symptomatic or fundamental difference between the forms of convulsions associated with uræmia, eclampsia in the pregnant woman, the fit due to camphor bromide, cocaine (Feinberg), absinthe, santonine (Jelliffe), apomorphine (Amsler†), hypoglycæmia (Macleod), chinchonidine (Albertoni), picrotoxin (Pollock, Grunewald), morphine, arsenic, etc.? I consider that these phenomena are essentially identical, although differences occur in the form of the convulsions, the implication of consciousness and other details. (Refer to the work of Pollock‡ on the action of the pupil.) The experience of toxicologists and veterinarians is in agreement with the widespread occurrence of the syndrome of myoclonic epilepsy and its varieties, which we here postulate. Just as in Case 3 (p. 224) enhanced tactile and acoustic reflexes were seen before the occasional convulsions, so Vogt found a case of infantile epilepsy where a fit was produced by the acoustic stimulation provided by the falling of a box. (This was a myoclonic fit, produced by or following an acoustic myoclonic reflex.) Here we have to deal with one reflex mechanism which responds to many different forms of toxins. These may be endogenous toxins, associated with metabolism or pregnancy, or exogenous toxins. The various forms of cerebral injury, such as encephalitis, or an hereditary predisposition towards epilepsy, are, so to speak, the mine, while the toxin is the spark, the "agent provocateur," which precipitates the explosion.

Where there is any doubt in the differential diagnosis between infantile convulsions and infantile epilepsy, it is best to begin the prophylactic treatment against epilepsy as described in Part III., Chapter XI., § 4, at once.

* Vogt, "Epilepsie im Kindesalter," 1910, Berlin.
† Amsler, *Archiv. f. Exp. Path. u. Pharm.*, 1923, vol. xcvii., p. 11.
‡ C. P. Pollock, *Archives of Neurology and Psych.*, 1923, vol. ix., p. 604.

CHAPTER VI

THE INFLUENCE OF MENSTRUATION AND PREGNANCY ON THE OCCURRENCE OF EPILEPSY

The Different Effects of the Beginning of Menstruation on Initial Epilepsy. Examples of Cases and Treatment. The Varying Effect of Pregnancy and the Menopause on Epilepsy. Epilepsy in Pregnancy. Eclampsia.

WRITERS on the subject, from Delasiauve to Gowers and Binswanger, have all appreciated the fact that menstruation has a great influence on epilepsy. Turner has furnished valuable statistics on the point. It is recognised that, in many cases, a patient has more fits about the menstrual period, and that it is not infrequent to find the disorder aggravated for a few days before and after the period. Further, not a few authors point out that epilepsy frequently begins with the first menstrual period. On this latter point I am not in complete agreement, although doubtless it is true of many cases. It is not infrequent to find cases where epileptic fits are already occurring once in every four weeks before the ordinary habit of menstruation has been established. In such cases the fits may be regarded as true molimina menstrualis. The following are some interesting and significant cases which illustrate this condition:

Extract history, Case 21, M. S., 15 years old, 25.3.05. (1) Patient had fits every four weeks for a period of three months. Two days before these attacks, patient was pale and had abdominal pain, constipation, and polyuria. In the fits the left side was most involved, while the tongue was badly bitten. (2) Shocks had occurred during the night for four months. (3) She had suffered from headaches over the eyes for years. Patient had typhoid in her tenth year, but as her mother had died recently no good history could be got of her early life. It was known that her mother had had a very difficult labour at the time of her birth. Patient had never menstruated. *Family History.*—Mother had had convulsions, while a sister's child is an idiot.

Careful clinical examination merely revealed an intermittent segmental analgesia, but no reflex abnormalities. The patient was given pills as follows: ℞ Permanganat. kal., 50 mg., fiat pil.; three pills daily, with instructions to take up to twenty during the days when the abdominal symptoms appeared. She was also directed to take a hot hip-bath. The first time this treatment was tried she menstruated. She was kept under observation for four months, during which she menstruated regularly, and had no fits.

Case 22, J. de L., age 15 years. This patient had never menstruated.

Family History.—An aunt on her father's side had had fits from the age of 4 to 40. Patient had had fits for the last two years, occurring

every four to six weeks, sometimes accompanied by abdominal pain. As a child she had had a tendency to shocks. On the 30.10.07 she was admitted into the institution for epileptics, when she complained of abdominal pain. She was given nine permanganate pills (as above) and at once had a hot hip-bath; immediately after, menstruation began. For six months she menstruated regularly and had no fits. Then she began having fits during the period. The method was thereupon adopted of giving her doses of two tablespoonfuls tinc. cannabis indica-bromide mixture (compare p. 348) on the fifth and fourth days before the menstrual period was expected, and three tablespoonfuls on the third, second, and first days before the period. She left the institution improved, but had to return later, when she was put on the following prescription: A definite quantity of bread per day, which contained the daily dose of 0·3 gr. borax, pot. brom. 1 gr., sod. brom. 1 gr. In addition, five days before the menstrual period was expected, four tablespoonfuls of the mixture described above were given, five tablespoonfuls on the fourth day and up to and during the period, gradually diminishing the dose after the period. For two years she remained quite free from fits.

Another class of case is that where the patient has had epileptic fits at all times during the month. After the establishment of menstruation, these symptoms become grouped to that portion of the month at which the menstrual period occurs.

Case No. 23, A. D., age 19 years. Patient was a delicate girl. She had suffered from headaches of an epileptic type from her sixth year. From the age of 15, when she first menstruated, these headaches occurred regularly on the first day of menstruation. Myoclonic shocks also were present.

Case No. 24, C. H., age 22 years. Patient had had fits or convulsions from the age of eighteen months. Fainting fits began at the age of 10, definite fits at 15, fits of staring at the age of 19, and series of epileptic fits at 20. These series of fits appeared regularly just before menstruation. When the patient reached the age of 22, all the symptoms were grouped round the function of menstruation; if menstruation were delayed, the epileptic symptoms were also in abeyance. Father's sister was insane.

Case No. 25, M. B., age 13 years. Patient had had fits from the age of 7. These fits were preceded by shocks and occurred once in four to eight weeks. Patient did not menstruate until the age of 13, but had the prodromal symptoms of pain in the abdomen and thighs. After menstruation was established, the fits stopped and did not recur for six years, when she had a fit during pregnancy. Patient's father was addicted to alcohol. He had had epileptic fits before his marriage, and had one fit four years after his marriage, when playing boisterously with his children. This fit was not associated with the taking of alcohol.

There is fair evidence for the conclusion that in some cases the monthly menstrual cycle has already begun before there is a definite discharge. There may be some definite cause, such as a passing toxæmia, due to some internal secretion which may account for the curious grouping of epileptic symptoms round the period. Attention is called to the case recorded by Filia,* where a baby who was breast-fed had a fit when his mother menstruated.

It may be pointed out that, according to Brierre de Brismont (1842), menstruation is closely associated with ripening of the ovum. This physiological process, we know, precedes menstruation by a few days. This coincides with the period when patients are very liable to have fits.

* Filia, *Revue d'Hygiène à de Médecine infantile*, 1903, vol. ii., p. 526.

It is not infrequent for older patients to state that the fits appear just at the beginning of menstruation. Such patients often complain of the severe pain associated with the function. It seems obvious that the pain, and possibly the fit, are associated with a tonic closure of the os uteri. Many physicians recommend dilatation. From my own experience, the results are moderately encouraging; personally, I never recommend dilatation for any patient under the age of twenty.

Case No. 26, H. U., age 14 years. Patient had a fit, five weeks before coming to the clinic. The fit was not attended by vehement convulsions, but was preceded by shocks and headaches. This fit coincided with the beginning of the menstrual period, and recurred at the next period. Patient had a very distant relative who had had fits.

Case No. 27, J. B., age 42 years. Patient had epileptic fits and headaches for twenty-one years. These occurred always at the beginning of menstruation. When the climacteric was reached, the fits stopped.

Case No. 28, R. B., age 18 years. This case was kept under observation from 1903 to 1921.

When the patient was a year old, she had a severe fit. When seen in 1906, she had had one to four epileptic fits each month for the past two years, preceded by a night of broken sleep. She was ordered special bread containing a bromide salt, and had no fits for two years. She came back in 1915. This patient started to menstruate at the very late age of twenty-five. For two years after the beginning of this function she had fits at each period. Stronger doses of bromide were given and the fits stopped completely (*post* or *propter*).

Case No. 29, A. P., age 16 years. Patient had had five fits in the seven months preceding her visit to the clinic. The first four of these coincided with the beginning of the menstrual period. The fits were preceded by shocks and headaches; the last fit coincided with the administration of cocaine, when attending a dental clinic. Bromide bread was given in this case, and the region of the lumbar plexus was faradised. The patient had no more fits for six months, after which she was lost sight of.

The treatment for cases of difficult or painful menstruation associated with epileptic fits—namely, potassium permanganate—is found to be very successful. In some cases it is necessary to have further treatment by a gynæcologist. It very often happens that where the pain of the menstrual period is relieved the epileptic condition is improved. Where a patient can be treated so that her menstrual periods are easy and normal in amount, a distinct alleviation of the epileptic symptoms is frequently found. In addition to this, there is no doubt that special care must be taken just before the menstrual period begins. The special treatment must often be temporarily fortified, either by additional and suitable drugs, or by giving larger doses of the medicaments in use.

In some cases the mother demonstrates a particular form of fit during pregnancy, and this is repeated, or almost repeated, by the child, should it be a girl, when she approaches the menstrual period.

Case No. 30, C. S., age 18 years. At the age of 12 the patient had fainting fits every four or six weeks. At the age of 15, shocks occurred along with the fainting fits; at one of these periods, menstruation supervened. The history showed that the mother of the patient had suffered from fainting fits during all her pregnancies: it must be noted that she was not worse while pregnant with the patient than with the other children.

Case No. 31, E. H., age 11 years. Patient had epileptic fits from the age of 5. An aunt on the maternal side was in an institution for chronic epileptics, while another aunt on the same side was insane. The mother was very nervous and had myoclonic shocks in all her pregnancies. These shocks increased in number the further the pregnancy progressed.

It is not uncommon for epilepsy to manifest itself first during a first pregnancy, with a severe fit.

Case No. 32, A. P., age 32 years. Patient suffered from dizziness when menstruating. At the age of 18 she married, and in her sixth month of pregnancy she had her first epileptic fit; this caused a miscarriage. After this she had myoclonic shocks every four weeks, and also had epileptic headaches. Later, pregnancies were often interrupted with epileptic fits. After the climacteric she had both ordinary epileptic fits and fainting fits. Patient's father had severe headaches, and her sister was an epileptic.

Handfield Jones and Aldren Turner are both of the opinion that such physiological phenomena as menstruation or pregnancy are only followed by epilepsy where there is an hereditary history. From my own observations, I do not altogether agree with this opinion, for I found 29 out of 1,000 cases of female epileptics in which the epilepsy appeared with the commencement of the menses, where there was no hereditary history of epilepsy. The case of Elliotson,* where a woman who had infantile convulsions until menstruation was established, thereafter was free from fits until the climacteric, when she again had fits, is also an exception. De la Motte also records a case where a woman had five daughters and three sons; when pregnant with sons, she always had epileptic fits, but never with daughters. One of my own cases was a woman who had suffered from headaches and fits of vomiting from infancy. At the age of fifteen she menstruated and developed epileptic fits. While pregnant on three different occasions with daughters, she had neither myoclonic shocks nor fits; but when pregnant with a boy, she had many fits. After her last confinement she had no more fits. The mother of a patient with myoclonic epilepsy stated that during her pregnancies with three sons she always had fainting fits, but the symptoms never occurred when pregnant with three daughters.

Nerlinger† doubts the occurrence of pregnancy-epilepsy; in this, I consider that he is wrong. If care be taken in the examina-

* Féré, *loc. cit.*, p. 247.

† Nerlinger, "Epilepsie und das Fortpflanzungsgeschäft," Diss., Strasburg, 1889.

tion of patients, it will be seen how very often epileptic phenomena occur in pregnancy. No doubt is left in the mind as to the occurrence of the complication. (The experimental work with bromide of camphor given to pregnant cats showed that a cat in this condition displayed myoclonic epileptic fits with a much smaller dose than the normal non-pregnant cat.) Landois, Blumreich, and Zuntz* also showed that creatin applied directly to the cortex, or injected into pregnant animals, produced convulsive fits—a result rarely obtained in the control of non-pregnant animals. On the other hand, there is no doubt that pregnancy does, in some cases, induce a complete remission of epileptic symptoms. Nerlinger, Eusière, Delmas,† and Redlich called attention to this fact. Bechterew‡ also records a case where a remission of myoclonic epilepsy occurred with a pregnancy. In my own experience I have seen a similar case. There is a popular but ill-founded belief that the climacteric frequently brings about a recovery from epilepsy.

Gowers reported ten cases of epilepsy, which began with a pregnancy, but which grew rapidly worse when the climacteric was reached.

Apart from the classical literature on epilepsy by Tissot and Delasiauve, very little literature exists on the subject of the influence of pregnancy on epilepsy. Curschmann§ and Westphal‖ described cases of ordinary epilepsy and focal epilepsy which they consider to be directly associated with pregnancy. Nolen also described cases of recurring encephalomeningitis serosa in pregnancy. Westphal and Gowers recorded cases of ordinary myoclonic epilepsy associated with pregnancy.

A question of great importance is the relationship between epilepsy and eclampsia in the pregnant woman. Féré is of the opinion that eclamptic patients frequently have an hereditary predisposition. He maintains that in many cases, where sufficient care is taken, a history of epilepsy can be elicited. Further, he points out that the children born of an eclamptic woman are often subject to infantile convulsions. In my own cases I have only met with two cases which are of special interest. In one the patient was eclamptic in a pregnancy, and after the pregnancy was over she continued to suffer from petit mal associated with mental symptoms. In the other the patient had three relatives—a mother, a daughter, and a brother—all epileptics. She had fits during the first pregnancy, and also in the second, when she had twins. After this second pregnancy, fits persisted, and the

* Blumreich and Zuntz, *Zentralbl. f. Gynæcol.*, 1902, p. 562.

† Eusière and Delmas, *Montpellier médical*, March 27, 1910.

‡ Bechterew, *Archiv. f. Psych., und Nervenkrankheiten*, 1880, vol. xix., p. 88.

§ Curschmann, *Deutsch. Zeitschrift u. Nervenheilk.*, 1922, pp. 85, 96.

‖ Westphal, *Deutsch. med. Wochenschrift*, 1919, vol. ii., p. 1320. Compare Muskens, *Epilepsia*, 1910, vol. ii., p. 53.

patient remained epileptic for many years. The fact that I only found two cases of eclampsia in almost 1,200 cases of female epilepsy may be because I did not pay particular attention to the question. Gowers certainly does not attach much importance to eclampsia as a cause for epilepsy; but Turner and Féré consider eclampsia to be an acute form of series epilepsy, and they present a large number of cases in support of their opinion.

Féré points out that, although in many cases of eclampsia there are the usual symptoms of nephritis disorder, prominent among these being the presence of albumin in the urine, yet there are not infrequently cases of genuine eclampsia where there are no evidences of nephritis. Chirée* and Edel† both did a number of experiments on pregnant dogs, and their results seem to support the view taken by Féré. Jardine‡ found three epileptics in 100 cases of eclampsia. Nerlinger points out that epilepsy very rarely interrupts a pregnancy,§ whereas it is very common for eclampsia to produce miscarriage or abortion. He regards eclampsia and epilepsy as two separate diseases, and points out that eclampsia rarely recurs in a woman. Personally, I consider the fact that eclampsia diminished so markedly during the Great War, when there was a shortage of albuminous food, very significant. Even were it granted that eclampsia is a species of endogenous poisoning (Donath's gravidity toxæmia) from the metabolic products of the mother and the fœtus, it does not separate it definitely from epilepsy. In genuine epilepsy, as is known, endogenous and exogenous toxins, or both acting together in one individual, frequently play an important part (compare Part III., Chapter IX., p. 273 and p. 95).

A widespread and popular belief is that marriage has a beneficial effect upon epilepsy. From a medical and professional stand-point, there is no doubt that it would be extremely ill-advised to encourage marriage amongst epileptics; statistics show too plainly the dangers of heredity in this disorder. Apart from this, the mental and physical strain which marriage involves is, in itself, prejudicial to the average epileptic patient. At the same time it is certainly the case that marriage does improve or is associated with the improvement of quite a number of cases. These cases are mostly among the working classes, and here the reason may be the regularity of life and perhaps the greater degree of routine comfort.

Case No. 33, M. K., 35 years of age. Patient's father had screaming fits and convulsions. At the age of 6 patient had fainting fits, attacks

* Chirée, *Annales de Gynæcologie*, 1908, vol. v.
† Edel, *Allg. Zeitschrift f. Psych.*, 1908, p. 1000.
‡ R. Jardine, *Lancet*, 1907, p. 1432.
§ Durlacher, *Wien. klin. Wochenschrift*, 1906.

of tachycardia, and myoclonic shocks. Sometimes she fainted as often as thrice daily. After she married her condition improved until the fifth month of her first pregnancy, when she reverted to the pre-marital condition in which she remained during this pregnancy.

Case No. 34, M. C., age 30 years. Patient had fits first at the age of 15. These fits were associated with overstrain, and occurred once in one to three weeks. These fits were aggravated if the patient rose early. After her marriage she was much better, but always, during her pregnancies, shortly before confinement, she had two fits each week. One of her children, aged 4, had crying fits at night, and convulsive movements during sleep.

Case No. 35, L. A., age 25 years. Since the age of 2 patient has had two to three shocks daily. Patient is now married, has seven children, and has had no fits for fourteen years. A sister of the patient also had fits, as many as two to three a day, but had no more after marriage.

Turner supplies figures which afford the same evidence (pp. 43-46). In this connection mention is made of a case where epilepsy apparently followed removal of the ovary.

Case No. 36, B. age 46. During four years the patient had about fifty dizzy fits. In the last three years, myoclonic shocks accompanied the dizzy attacks. She had an ovary removed, after which menstruation was scanty and irregular. Further, she developed headaches of the epileptic type, above and behind the eyes, while dizzy fits also were troublesome.*

---

* All sorts of curious ideas exist about the connection between epilepsy and the sexual organs. Not many years ago, a young lady was treated for epileptic fits by double ovariectomy! Because the number of fits increased during menstruation, the conclusion was come to that the disorder was dependent on some affection of the ovaries.

CHAPTER VII

THE FURTHER DESCRIPTION OF THE SYMPTOMS OF EPILEPSY AND THEIR SIGNIFICANCE

§ 1. The Evolution of the Disease.

THE three great symptoms in epilepsy are myoclonic shocks, headaches, and fits. In the earlier stages of the disease there is a certain degree of compensation apparent between the symptoms. (pp. 49 and 211). It is fairly common to find that both the myoclonic shocks and the headaches tend to disappear when the severe type of fit appears. Frequently these symptoms reappear, more particularly the headache, after the disease has been established some time, whether the fits have been stopped, or partially stopped, by treatment or not. This phenomenon of compensation is comparable with that seen in animals dosed with bromide of camphor. In these animals it was seen that after a severe fit the myoclonic reflexes and the spontaneous shocks were both absent for some little time.

This phenomenon of compensation is recognised and taken advantage of by many epileptic patients. For example, they may avoid walking in the streets or appearing in public places, except at those periods immediately following a severe fit, when they know that they are practically certain to be free from myoclonic fits.

An important point is the change in the character of the fits after they have persisted for a number of years.

Besides the severe fit, generally recognised by the laity as an epileptic fit, other fits of different character appear in many cases. These fits are abortive in type, are associated with little myoclonic disturbance, but the symptoms are pallor, loss of consciousness for a very short period—only rarely does the patient fall or foam at the mouth.

These fits are preceded by prodromal symptoms, similar to those which precede the severe fits; but the post-epileptic period, or stage of automatism, is much shortened. Except in cases where a number of these fits succeed one another at short intervals, there is no discharging effect, as in the case of severe fits (compare pp. 50 and 303, and atypical fits, pp. 67 and 93).

Between the severe fit and the abortive fit there are many transitional types of seizure. Among these transitional forms are fainting fits. The fainting fit which may occur in epilepsy is

peculiar, in that it is very rare to find it completely dissociated from some form of movement (compare Chapter XI., § 1).

Where the severe fits persist for a considerable period, they may tend to become less severe both in character and duration. The prodromal symptoms, frequently, are less pronounced, while the post-epileptic stage of general malaise and dazedness is distinctly shorter. Briefly, in a favourable case, a condition of greater or lesser equilibrium for the patient is reached (C., No. 3, p. 212).

In unfavourable cases, on the other hand, the period of automatism becomes more pronounced, while the psychical symptoms increase in character and severity. The fits also become more frequent, and occur at all periods of the day or night.

One point must be emphasised, that where the result of treatment has been to procure for the patient a long interval between the fits, then when a fit does occur the prodromal symptoms are usually much *more pronounced* than where the patient was having frequent fits.

§ 2. **The Great Fit.**

Considered apart from the pre-epileptic symptoms, such as headaches and spontaneous shocks, the typical fit of epilepsy may be said to appear suddenly after certain more or less developed prodromes. The patient falls with a loud cry, generally on to his face, while the whole voluntary musculature is involved in tonic convulsions. Consciousness is lost. The face is very pallid, but may become cyanosed from the asphyxia or from the rigidity of the thorax.* The legs are extended, the arms more or less adducted and flexed, while all the muscles partake of the general tonic convulsion. At this stage the tendon reflexes are decreased or lost (p. 255); the plantar reflex is generally extensor in type, the pupils are dilated, and do not react to light, while the corneal reflex is wanting.

These convulsions may last 10 or 20 seconds, or even longer, the patient meantime becoming more cyanosed and looking as if he would be suffocated. The tonic convulsions now pass into clonic form; at first these occur in rapid succession. These clonic convulsions occur at first rapidly, and succeed each other not simultaneously in the different extremities and in the trunk. Like the clonic convulsions induced by bromide of camphor, they have a definite rhythm of 12 to 15 per second. As the fit progresses, these

* Franck established the fact that in experimental animals epileptic fits, induced by irritation of the cortex, could not be stopped, except by the development of asphyxia. Extirpation of the portion of cortex, under experiment, failed to stop the convulsions. It is, therefore, suggested that, in epilepsy in the human subject, the development of asphyxia, through fixation of the thorax, automatically stops the fit.

convulsions occur at wider intervals, and are simultaneous over the entire body, so that the whole body musculature convulses at the same time in the final shocks. At this point the first irregular respiratory movements begin, and the saliva or foam appears at the lips. If there has been biting of the tongue, this will be blood-stained.* The blood-pressure is highest when the clonic convulsions are most rapid. At this stage cranial prolapse may occur, should a cranial operation be in progress.†

Enuresis is not an infrequent symptom, and may occur in the tonic and clonic stages. Defæcation during a fit is rare.

As the patient emerges from the fit the complexion becomes more natural; the corneal reflex begins to reappear, although the pupils are still dilated. The tendon reflexes return.

At this point begins the so-called automatic stage. The patient moves his limbs in an aimless fashion, mutters incoherently, and expresses by vague, aimless speech and acts that he has some misty ideas, probably connected with getting up and getting away. He may offer resistance, and fight imaginary foes. He may begin to undress, or exhibit aimless plucking movements of the fingers. At other times he appears to be eating something, or to imagine he is eating, from the chewing movements and smacking of the lips. In some cases the patient passes through this stage into slumber ; in others he emerges complaining of a headache, and he may feel sick. Speech is gradually restored, and orientation for time and space return gradually. Where a patient falls asleep immediately after the automatic stage, he recognises that he has had a fit, when he awakes, from the pain of his tongue (from bites while in the fit), and from the tiredness of his limbs. Sometimes, in addition to these injuries and pains, a patient may dislocate a joint in a fit. It is not infrequent to find punctiform hæmorrhages in the face and neck, and suggillation of the eyelids after a fit.

§ 3. Prodromal Disturbances of Sensation : Prodromes of Short Duration or Auræ.

It has long been recognised that there are certain profound changes in a patient before, during, and after a fit. This change may manifest itself in many different ways, one of the most striking being the alteration in sensation in certain segmental areas. These alterations or disturbances generally disappear after a discharge or series of discharges. Among those who were among the

* I have seen blood-stained foam fairly frequently where there has been no biting of the tongue.

† Magnan and Robinowitch, Congrès de Neurologie et Psychiatrie, Amsterdam, 1907.

first to devote special attention to this side of epilepsy may be mentioned Claus and van der Stricht, Krainsky, Agostini, Haig, and Voisin.

Considering the phenomena of prodromes as a whole, one has to group them into two classes: the prodromes, which occur at some considerable period before a fit, and those which immediately precede the fit. Those of the second class, or prodromes of a short term, are those which come more under the notice of the

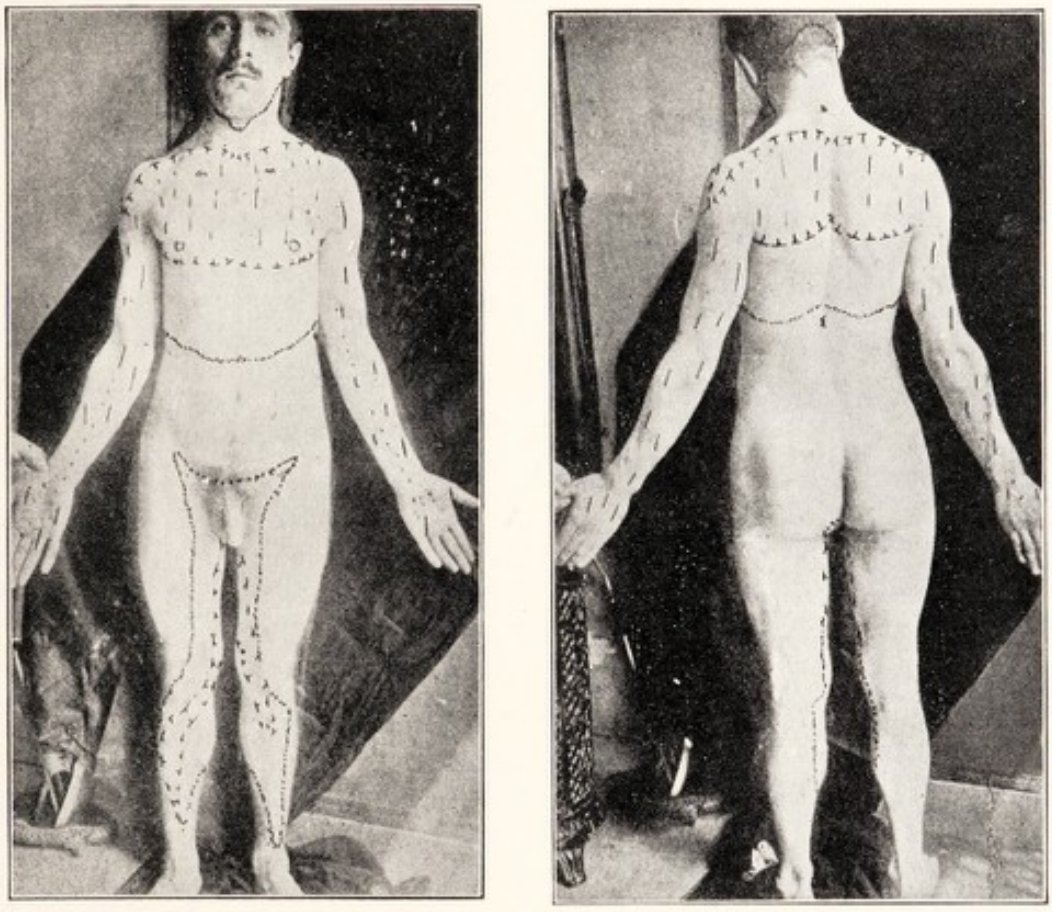


FIG. 42.—THIS FIGURE SHOWS THE MAXIMUM EXTENSION AND THE MINIMAL LIMITATION OF THE AREAS OF DISTURBED SENSATION.

The maximal fields are marked by dotted lines from neck to the umbilical cross-line and caudal to the dotted line on the lower extremities; the minimal fields, generally before a fit, by crosses. (Further details in the paper referred to p. 247).

layman, whether he be the patient or the attendant. Gowers, in describing these prodromes, styled them "aura," and regarded them as part of the fit. The frequency with which prodromes of the long period type occur is very much underestimated by the different writers. Turner, for instance, gives it at 15 per cent. It is certainly the case that one generally gets a denial of such prodromes on first examining a case. If, however, care be taken and the general peculiarities of the case studied, and the

patient or his friends be closely questioned, later on one often gets another reply. For example, if the friends are asked if they did not notice for several days before the fit that the patient had myoclonic shocks in the morning, or attacks of headache, or whether he had restless nights, was irritable and moody, they frequently recognise that such a condition had been present. They explain their first denial by explaining that these symptoms were so disconnected in their minds from the fit that they thought them quite irrelevant. Indeed, these prodromes are *interparoxysmal* in type. This being so, the patient's friends affirm unhesitatingly that there are no prodromes (p. 323). Further, they do not appreciate that a discharge may occur in any other way than by a fit.* It must be stated, in conclusion, that there is only *one* way for establishing a proper knowledge of the prodromes, and that is by observation, either in a hospital or at home by a trained nurse. Under these conditions the attention can be directed on the prodromes so varied in character, which may, in the same patient, precede a fit. Such symptoms as dilatation of the pupils, congestions, hæmotaxis, numbness of the fingers, and other vasomotor disturbances, not generally recognised by the laity, can be properly appreciated.

Among the prodromes one must distinguish two groups—those which continue over a long period, and those which are short. To the first group belong such prodromes as a coated tongue, dilated or unequal pupils, complete analgesia, headache lasting several days, a curious feeling of oppression, a very irritable temper, a state of sleepiness ("dreamy state"). To the latter group belong vasomotor disturbances, transient anorexia, periods of pollakiuria, passing sensations of oppression, fainting fits, attacks of yawning, or sneezing, eructations and gastro-intestinal disturbances. Apart from these important symptoms, one must recognise other symptoms which have more the character of a discharge. Among these are the myoclonic shocks, and series of shocks, and fainting fits which resemble petit mal, and are seen both before and after a severe fit. Indeed, these latter symptoms frequently increase just before a discharge, so that the patient's family learn by experience when a fit is imminent. It is not at all uncommon to find the fainting fits accompanied by psychical symptoms, and sometimes, also, hallucinations.

The prodromes, which exist only for a short period, manifest themselves both when the patient is asleep or awake. It was shown clearly for the myoclonic shocks that the time of predilection was the transition from sleep to wakening, and this holds good also for the prodromes of this class.

* P. Hartenberg, *Presse médicale*, 1919, No. 22.

Prodromal Disturbances of Sensation.—There is no doubt but that the prodromal disturbance of sensibility to pain with segmental limitations* has induced a closer study of the prodromal symptoms lasting over a long period, and has had practical results for treatment. The regular disturbance of the sensation of pain has been confirmed by Maes and Claude,† Kinnier Wilson, Balint, Baugh,‡ de Crinis,§ and others. Maes and Claude estimated the frequency of occurrence at about 70 per cent. It is a question whether these areas of hypalgesia do not get more extensive before a fit, and shrink or disappear after a fit. The close examination of cases has shown that sometimes the condition of charge can be diagnosed from an extension of these areas of disturbed sensation.

In many cases one does get slight alterations in such areas before and after a fit, but there are also many cases where the area of hypalgesia is not altered by the fit. It has been noticed that the zone of hypalgesia may shrink suddenly after a copious evacuation of the bowels as well as after a fit (compare Maes and Claude).

The most frequent zone involved in this hypalgesia is limited above by the mesial line of the upper extremity, and below by D5 and D6. The post-axial segments are, therefore, mostly involved. The zone of the ulnar nerve is a skin zone, by which one can orientate oneself without difficulty. Fig. 42 (see p. 245) indicates the different limitations and extensions found in the same patient. (For closer, more exact details, see the above-mentioned discussions by the author.) It is, therefore, not surprising to find that Biernacki was long ago struck by the insensibility of the ulnar nerve in epileptic patients.

The change in the hypalgesic areas are quite independent of any psychical disturbances. Where there is doubt as to the diagnosis of a condition being an epileptic equivalent, segmental disturbances of sensation are in favour of the case being one of epilepsy.

It is important to remember that in the incipient stage of the disorder disturbances of sensation to pain may be quite wanting.

Considering the phenomena of prodromes as a whole, it may be said that the greater the distance between the fits the more distinct and prominent are the prodromes. This is very important for treatment directed to the prophylaxis of fits. When clear and fair warning is given of the approach of a fit, it is easier to inter-

* L. J. J. Muskens, *Epilepsia*, 1909, vol. i., p. 249; *Archiv. f. Psych.*, 1903, vol. xxxvi., pt. 2, p. 347; and *Ned. Tijdschr. v. Geneesk.*, 1901.

† Maes and H. Claude, *Annales d'Électrobiologie*, 1907, F. 4-5.

‡ Baugh, *Journal of Mental Science*, 1914, vol. lvi., p. 693.

§ M. de Crinis, Art. "Epilepsie" (F. Kraus und Th. Brugsch), "Spezielle Pathologie und Therapie innerer Krankheiten," 1922.

vene successfully with the treatment and to ward off the threatening fit. Another important point is, that the character of the prodrome may change after a long interval between fits. For example, where gastro-intestinal disturbances have served as prodromal symptoms, and the patient has had no fit for a long period, the next prodrome may be of a vasomotor type.

Where the fits are frequent, the prodromes tend to diminish, and become less and less significant before a fit.

Some examples of cases are given, illustrating the points dealt with.

No. 37. This was a case of a girl of 25, who had an hereditary predisposition for epilepsy. For two days before a fit she was subject to a feeling of sadness. One day before the fit she also had an unnatural craving for food and could not be satisfied. She was moody, had a tired feeling in her legs, and curious sensations travelling upwards to the throat from the stomach, while at times she talked incoherently. After the fit all the symptoms disappeared.

No. 38. This was a case of a boy of 17. He had had infantile convulsions. From the age of 5 he had had fits, preceded for three days by borborygmi in the stomach. There were no other prodromes. It was found that, when for the first time he had had no fits for a considerable period, he was moody and had red spots on his face, some days before the fit.

No. 39. This was a man of 24. He had had fits for nine years, fainting fits for one year, while he had headaches for years. There was no hereditary history, neither had he had infantile convulsions. When he was having fits regularly, he had epistaxis shortly before a fit. When a long interval intervened between fits, he was in a bad temper for three days before a fit. When the patient was seen in 1923, he had had no fits for fifteen years.

No. 40. This was a man of 24, with no hereditary history of epilepsy. After having had convulsions, he had diurnal fits for years, preceded by myoclonic shocks. Later, he had only nocturnal fits, and had no prodromes.

Finally, it seems to be the case that where there is an hereditary history of psychoses, the prodromes are more frequently of a psychical character.

Where a patient is being treated at home, special attention must be paid to such prodromes as psychical disturbances, increase of myoclonic shocks, increased frequency of fainting fits, uncertain temper, restless and broken sleep, unreasoning fears, or the repetition of the disagreeable feeling known as false reminiscence (disagreeable feeling, as if one had been the same situation more than once). Such prodromes as disturbance of sensation appeal to the medical profession, but do not attract much attention from the patient's friends.

It is a curious fact that in some cases the prodrome may take the form of a special appetite for a particular article of diet, or an exuberant feeling of well-being. Also, there are cases where a psychical depression lasting many days, precedes a fit, but is replaced immediately before a fit by a feeling of animation. There are yet other cases where a sensation that everything is unreal is the prodrome to a fit.

"*Prodromes of Short Duration—Aura.*"—The work of Hughlings Jackson did much to stimulate the study of these phenomena and subjective aura. It was he who first described, or drew attention to, the peculiarities of the so-called focal convulsions. He pointed out how they began slowly, "deliberately," with convulsive movements, starting first in the fingers, then passing to the hand, arm, and leg of the same side; then involving the other side of the body. From my own experimental work, it appears as if the local irritation in Jacksonian fits is *slowly* conducted to the medullary centres when the fit becomes general.

Arguing from the data found for focal epileptic fits (*i.e.*, fits starting from a cortical focus), it is not surprising to find Gowers devoting much attention to the establishment of some parallel explanation for genuine epilepsy. He was much impressed by the frequency of all varieties of physical symptoms which may introduce the first epileptic fits. So much was he impressed, that he thought the cortex played an analogous part in all convulsions to that found in Jacksonian epilepsy. Here I think he was mistaken. Gowers made very careful investigations as to the occurrence of aura, and found that they occurred in not less than 57 per cent. Other writers have given this figure as 30 per cent. Other writers, on the other hand, among whom is Delasiauve, do not attach any importance to the differentiation of prodromes from an aura, both of which may occur in infinite variety.

The word "aura" in itself is interesting, for it proves how prejudices persist. Galenus had a patient who had a feeling of wind ("aura") passing from the extremities to the head before a fit. Such a sensation before a fit is very rare, but still the term "aura" persists.

It is a fact that, in many cases, a fit is preceded by an aura or a sensation in an extremity or in the epigastrium, when it may apparently pass upwards to the neck or throat. Further, one may get strange hallucinations of smell, taste, sight, and hearing. Where the sight is involved, and a visible aura is appreciated, red is the predominant colour (Magnan, Rochet, and Caers).*

Herpin had, previous to the work of Gowers, recognised certain rules, which he considered dominated the relations between the preludium, or aura, and the fit. These rules are still of value in a well-developed case of epilepsy. They are as follows: Herpin recognised three groups of epileptic phenomena:

1. An aura or preludium occurring alone—that is, the sensation which as a rule precedes a fit, if it occurs alone.

2. The incomplete fit. Here the aura which, according to rule would precede a complete fit, is followed by some part of the

* A. Rochet and F. Caers, *Archives de Neurologie*, 1907, p. 180.

fit, such as dizziness (this is most common), or a temporary dazedness (" dreamy state "), and sometimes, according to Turner, by dropping down of the patient without convulsions.

3. The classical fit. Here the aura precedes a complete fit.

Those three types of epileptic attack, which generally occur in chronic epilepsy, therefore represent three stages of the same phenomenon. Turner agrees with Gowers in considering that the aura indicates that the cerebral cortex is the origin of the fit. At the same time Turner describes bilateral myoclonic shocks as aura, although, so far as I know, there is no locality of the cerebral cortex where electrical stimulation would produce shock-like phenomena of this character.

§ 4. The Significance of the Prodromes and the Fit.

Comparison of phenomena observed in quadrupeds. Tolerance of convulsive phenomena. Significance of the loss of consciousness. Disturbances of the circulation. Changes in the pupils.

Although I appreciate fully the value of the observation made by Herpin on the character of the initial symptoms of the various forms of discharge in special cases of chronic epilepsy, yet, from arguments brought forward in earlier chapters of this book, I showed that chronic epilepsy is a residual condition, the result of very many fits.

Although I do not ascribe the same nosological value to the aura that my predecessors have done, yet I think it very probable that myoclonic shocks, and the different aura seen before a fit, are due to intoxication symptoms of certain subcortical centres. It was seen in the cat intoxicated with bromide of camphor, that a comparable condition of myoclonic shocks, with a condition of dazedness and symptoms of mental terror, appeared some considerable time before a fit.

There are both experimental and clinical arguments against these prodromes being cortical in origin (p. 250, l. 12, and p. 393, l. 15, and also p. 120, l. 20).

Another point of similarity between the conditions found in the experimental cat and man is the recurrence of a special type of phenomena before a fit. It was seen in the cat that the myoclonic shocks which preceded the fit in the cat varied for each animal, but were always the same for the same animal. This is in agreement with the law of Herpin, and it would appear that in chronic epilepsy the stimulation of those centres (probably subcortical, ponto-medullary) which react most easily to the toxin always precede the fits, severe or slight. It appears, therefore, that the significance of the aura is limited, and for practical purposes of treatment second in importance to prodromes of the long period type.

Although this reference is made to Gowers' and Herpin's work, yet I would emphasise how diverse are the forms or auræ, and how limitless their variation. For example, under the heading of psychical aura, one finds very complicated sensations. For example, I had a case where the psychical aura took the form of the patient imagining himself in a well-lighted room, filled with well-dressed people, while he heard very delightful music. Another phenomenon, which not infrequently precedes a fit, is the feeling that everything has suddenly grown much smaller or much larger than normal.

There are also aura where the patient displays automatic movements, such as running, undressing, trying to fight his surroundings, or becoming ecstatic; generally this latter condition is associated with religion. These demonstrations of automatism are different in different patients, and often occur *after* as well as *before* a fit.

It is interesting to find the same pre- and post-epileptic automatism was shown by some of the experimental cats.

From the similarity of the automatic phenomena before and after a fit, it certainly suggests that the same mechanism produces both symptoms. This may be some chemical change.

A general consideration of the fits as they occur in the experimental animal and in man leads to the conclusion that symptomatically they are the same. The post-fit symptoms, such as certain psychical changes, and changes in the pupil are, I hold, to be considered as systemic phenomena, complicating the after-discharges.

This statement may be quite satisfactory for epilepsy due to toxins—*i.e.*, the group to which genuine epilepsy belongs—but it does not explain the phenomenon of epilepsy due to defects or injuries of the central nervous system (encephalitis in youth, or multiple sclerosis, etc.). Here it seems possible that the fits are due to changes in inhibitory tracts or centres. Thus, a fit occurs during the acute illness, and owing to injury of certain tracts or centres the inhibitory influence is lost, and the fits are not checked. Each fit predisposes to the next, and the patient reacts ever more readily to certain toxins. It is conceivable that the end result of epilepsy due to toxins, and that due at first to lesion of the brain in early life, is the same. It is for this class of epilepsy, associated with cerebral lesion in early life, that Cajal's law of the avalanche-like spread of a stimulus holds good. Jelliffe and White described a fit as a pathological dispersion of energy in three directions—physio-chemical, physiological, and psychical.*

* Jelliffe and W. White, "Diseases of the Nervous System," 1919, p. 868.

From my standpoint, both the conditions of charge and discharge are based on chemical processes of intoxication and detoxication. The different experimental and clinical facts show that the fit throws the toxins into the circulation, and that this accounts for the temporary post-epileptic disturbances and automatism.

If this theory is to work, it must also explain the occurrence of automatism after a fit, produced experimentally in an animal by stimulation of the cortical centres (Franck and Pîtres; also compare p. 305), and fits occurring in traumatic epilepsy (see p. 387). It is interesting to find in the other workers indications of the view which I hold very strongly, that epilepsy is a certain condition due to a toxin. Redlich recognised in a fit a manifestation of "epileptisch Reaktionsfähigkeit"—that is, a mechanism present in every individual. Raymond recognised an epileptic fit as "une crise salutaire," Frisch* described a condition which he called "convulsive Toleranz," Wiersma described the constitutional improvement seen after a fit. All these contain suggestions of the theory I here put forward that the epileptic fit is a complicated after-discharge, that such a mechanism is present in all individuals, that it is called into action by certain toxins, and that in effect the fit is primarily beneficial.

I consider that epilepsy, or an epileptic fit, is a parallel phenomenon of the "frissons toxique" described by Richet,† who admitted that the question whether a patient would react to a toxin by a shivering fit or an epileptic convulsion depended solely on the dose of the toxin. (Compare also the work of Dana and Timme).‡

The Significance of the Loss of Consciousness in Fits.—The question arises whether there is any relation between the loss of consciousness in an epileptic fit and that due to syncope. Gowers§ explained fainting, or loss of consciousness in syncope, as being due to insufficient action of the heart, so that the cerebral centres became anæmic. This explanation will not answer for the unconsciousness in epilepsy, for the patient loses consciousness first, then becomes pale. Further, after this loss of consciousness, automatic movements or a dreamy mental condition may follow; this never happens in syncope. These facts are all against there being a close relation between the two conditions. At the same time, it is the case that the parents and friends of epileptics often

* H. Frisch, *Allg. Zeitsch. f. d. Neur. und Psych.*, vol. lxv., p. 231.
† C. Richet, *Archives de Physiologie*, 1923, p. 316.
‡ Dana and Timme, *Archives of Neurology and Psychiatry*, May, 1923, pp. 549 and 553.
§ Gowers, *Lancet*, 1907, p. 565.

relate that the patient had been prone to faint before the occurrence of fits. In some cases the syncope gradually merges into the epileptic condition.* A case which illustrates this point is given.

Extract C., No. 41, T. G., age 34. The father of this patient had often had fainting fits due to fright. Her mother had had fits since birth, while a sister had fainting fits. The patient had never had convulsions. She had had scarlet fever and once an accident, when she fell on her head, but there were no scars. From the age of 24 to 30 patient had fainting fits, especially if over-tired, or if she delayed taking food in the morning, or if she took a little alcohol. When she was in the sixth month of her pregnancy, she had a fit, in which the tongue was bitten; immediately after this she had influenza. She stated that after a fit she was blind for a short time. When seen eighteen years later, the patient stated that she was much better, and only had a fit three or four times in the year.

A second point to be remembered is that posture influences the epileptic phenomena as it does syncope. This is especially the case for myoclonic epilepsy. Frequently a patient has shocks when stooping at work. Further, it has been seen, experimentally, where the cortex is stimulated, and also in traumatic focal epilepsy, that the patient loses consciousness slowly, often without pallor. This loss of consciousness may occur after a focal convulsion has passed. It would appear, therefore, that consciousness is very slowly lost in the transition of the stimuli from the motor cortex to the centres in the pons and medulla. Cases seen in the war also showed that injury to the posterior part of the brain were attended by unconsciousness. It would appear, therefore, that the loss of consciousness in epilepsy is due to some failure of functionation in the centres in this region of the brain (compare p. 292).

Are the Symptoms observed in the Circulatory System and in the Pupils necessarily associated with the Motor Fit, or are these Symptoms relatively Independent of the Fit?—Franck found, from stimulation of the cortex in a curarised animal, that increased action of the heart occurred, just as it does during tonic convulsions; this would indicate a certain independence of these phenomena associated with the sympathetic system. The pupil symptoms must be regarded as very loosely connected with the fit phenomenon. For it is seen that, in a creatinine fit, they get smaller instead of dilating (Fürstner), while this also occurs often with picro-toxin fits (Pollock).

Forced Movements as Aura.—Bourneville and Bricon,† Mairet and Mingazzini,‡ made a special examination of forced movements (circus movements, procursion or rolling movements), which

* E. A. Russell considers that frequent fainting fits in people of unstable cardio-vascular apparatus (T. Solis Cohen) is bound to go over to epileptic phenomena.

† Bourneville and Bricon, *Archives de Neurologie*, 1878, vol. xvii., No. 39, p. 321.

‡ Mingazzini, *Riv. sperimentale di Freniatina*, 1894, vol. xx.

occur either as an aura or as an atypical fit. Such aura are often found in organic lesions of the cerebrum.

I do not think that these movements are due to any hypothetical disturbance of cerebellar circulation. From the evidence afforded by experimental research, it appears that they depend on the palæo-striatal nuclei.* Normally, the conditions of cerebral compensation are such, that forced movements are prevented, but where this inhibition is excluded by loss of consciousness the forced movements appear. In experiments where half the cerebrum was removed in a cat, circus movements appeared after the operation, but after the lapse of some time they disappeared. At the same time, they reappeared in the animals during the period of unconsciousness preceding and following a fit. Nothnagel† injected certain stimulating solutions into the region of the palæo-striatal nuclei, and got procursion, retrogression, and circus movements as a result.

The question of the part played by the striate body in the epileptic attack cannot yet be answered, neither can the problem whether chronic epilepsy ever follows as a sequel to encephalitis. See the literature dealing with the subject by Lhermitte-Cornil, Stern, Sterling, Paulian, Lemos Magelhaes, and Muskens.‡ The case recorded by Wimmer§ is very suggestive. In this case, however, the patient had not suffered from grippe, but his parents had.

§ 5. Post-Paroxysmal Phenomena.

Reflexes. Paresis. Amblyopia. Gastro-intestinal disturbances. Metabolic changes. Physical phenomena. Significance of post-paroxysmal symptoms. Inter-paroxysmal symptoms.

The symptoms which appear after a fit deserve the careful attention of the physician. At the same time, it is impossible to consider them of the same importance as the symptoms which precede a fit; for, by the careful observation of these, the prophylaxis against the fits may be undertaken.

Symptoms which appear after a fit may be subdivided into four groups:

1. Motor Symptoms.
2. Sensory Symptoms.
3. Symptoms associated with the Autonomic System.
4. Psychical Symptoms.

1. Under the *Motor Symptoms* the reflexes are to be considered. After a fit it is often seen that the knee and Achilles

* L. J. J. Muskens, *Brain*, 1917, p. 352, and 1922, p. 414.
† Nothnagel, "Eulenburg's Handbuch des Nervenkrankheiten," 1877, p. 242.
‡ L. J. J. Muskens, *Revue Neurol.*, 1927, vol. ii., p. 822.
§ Wimmer, *Revue Neurol.*, 1925, vol. ii., p. 822, and Wilson's "Review of Neurology," 1928.

tendon reflexes return some time before the pupil or corneal reflexes. In status epilepticus, or after a very severe fit, these reflexes may, on the other hand, be absent for a long time. The plantar reflex is nearly always of the Babinski type. Indeed, the presence of this reflex after a fit is almost diagnostic of the character of the fit, but the absence of the Babinski reflex is not necessarily an argument or proof against the fit being epileptic.

One can be fairly positive about the condition of the reflexes after a fit, but it is quite otherwise as regards the paresis which sometimes follow on fits.

Since the work of Todd and Hughlings Jackson, a great deal of attention has been paid to post-paroxysmal paralysis.

In the first place, there is a great deal of general weakness of the muscles after a fit. Féré demonstrated this by means of dynamometer tests. This symptom is admitted by practically all the observers, and is attributed to the exhaustion following the fit. Discussion has gone on for a long time, on the question of the occurrence of monoplegia and hemiplegia after a fit. This is a subject about which there is much disagreement. The workers of last century unanimously agreed that such a paralysis did occur. Not long ago it was generally held that epileptic fits were cortical discharges, and that there was a great increase in the irritability of the motor area associated therewith. Franck and Pîtres demonstrated that the irritability of the motor cortex was much decreased after a cortical discharge. In the literature one finds great divergence of opinion, some writers maintaining that temporary paralysis may follow an ordinary epileptic fit, while others, among whom are Clark and Prout, deny the possibility of such an occurrence. Turner also doubts that paralysis could follow on an ordinary epileptic fit, if there were no local lesion. Personally, I consider that the occurrence of a genuine paralysis after an ordinary epileptic fit has not been satisfactorily demonstrated. In my 2,000 cases of epilepsy I did have several, where notes were made, describing post-paroxysmal paralysis, but these cases were found later to be complicated with cerebral tumour. If careful notes were kept of cases, it seems probable that any post-paroxysmal symptoms of a paralytic nature could be explained by the presence of some definite cerebral tumour or lesion.

Jackson, who believed in the existence of post-epileptic paralysis, thought it might be due to exhaustion, but Gowers points out that this would not explain why post-epileptic paralysis was more common after a fit which had only involved a part of the musculature (Jacksonian epilepsy) than when the whole body had been involved. Turner was inclined to admit the possibility

of there being an exhaustion of the cortex, because he thought this would explain why the knee reflexes remained exaggerated for several days after severe fits.

The explanation of the latter fact, we think, is supplied by what might be termed the myoclonic theory of epilepsy, as set forth in this book. According to this theory, the presence or absence of the tendon reflexes depends on whether the discharges have been sufficient to bring about a complete condition of discharge. It was noticed that where a myoclonic fit had incompletely discharged the animal, the myoclonic reflexes were very active. Where the knee reflexes, related as they are to the myoclonic reflexes, in view of their conduct during narcosis, etc., are slow in returning, as in status epilepticus, it most probably indicates a condition of complete discharge. The observations of earlier workers on post-paroxysmal paralysis cannot, therefore, be regarded as consistent with present knowledge.*

The question whether motor or sensory aphasia ever occurs after a genuine epileptic fit is one to which I have paid considerable attention, and as a result I most unhesitatingly state that it does not occur. Cases where a fit is followed by such phenomena are always complicated by some organic lesion.

It may be recalled that in an earlier chapter it was pointed out that occasional convulsions occurring in children were classified along with genuine epilepsy. In both cases organic lesion of the cortex was excluded. The possibility must not be lost sight of, that in both types of fit, as after a myoclonic fit, the faradic irritability of the cortex may be lowered. Where the fit has been most marked on the right side of the body, it is conceivable that the speech centre might be depressed, so that there might be some initial slowness in speech, or in the comprehending of speech.

The subject of the possibility of post-epileptic paralysis must not be concluded without pointing out that an extreme degree of muscular exhaustion might simulate paralysis. The muscular exertions in some fits is extraordinary, sometimes being sufficient to dislocate a joint or actually tear the muscular attachments.

2. *The Occurrence of Post-Paroxysmal Sensory Disturbances.*—The investigation of sensory disturbances after a fit is made difficult because of the period of unconsciousness which supervenes after a fit.† One may succeed in marking off segmental zones of disturbed sensation, but one cannot secure data as to finer shades of blunting of sensation. This applies especially to the tactile and stereognostic tests.

* Féré, *loc. cit.*, p. 476.

† Burgé, "Étude des Paralyses post-épileptiques," Thèse, Paris, 1882.

When a patient is examined immediately before and after a fit, it is sometimes found that areas which displayed sensory disturbances immediately before the fit are quite normal when the fit has passed. Sometimes the areas have been increased, or they may have remained stationary. In some cases one could prognose the occurrence of further discharges from the persistence of these areas of sensory disturbances after the first discharge. In other cases the disturbance of sensation may persist for quite a long time, and only passes off slowly.

Amblyopia has often been described as a transient symptom after an epileptic fit. Thomson and Oppenheim both found that there was a diminished field of vision, particularly after fits attended by marked psychical symptoms. Féré also records it in other cases. From my own cases I have not been able to find a good case of amaurosis, although one patient told me she was blind after a fit (Extract C., No. 41, p. 253). In these cases it was, however, impossible to exclude functional or hysterical symptoms which might account for the phenomenon.

From the point of view of the patient, the presence of a headache and the painful tongue are the two post-epileptic symptoms of importance. From these he knows he has had a fit.

The post-epileptic headache is characterised by its deep-seated localisation, and appears to the patient to be in his head; it is quite definitely not frontal. Like the pre-epileptic headache, it is little influenced by drugs, but will pass off if the patient sleeps. In many cases the headache alternates with a period of sleep; that is, if the patient falls asleep, he awakes refreshed and free from headache, while if he does not fall asleep the headache troubles him for some time.

3. *Post-Paroxysmal Symptoms asssociated with the Autonomic System.*—It is not uncommon to find a rise of temperature after a series of fits (Bourneville, Marchand, and Rohde). A. Turner and Hallager found evidence that the body-weight diminished after a fit, but this has been contradicted by Jolly, Lehmann, and Krantz.

Symptoms which indicate intestinal intoxication are common. It is usual to find anorexia and a foul tongue for several days after a fit. Constipation, pollakiuria, and dryness of the skin are also common symptoms.

It was confidently expected that much light would be thrown on epilepsy as a whole by the examination of the secretions and excretions, but the results have been most disappointing. The urine has been examined for albumen, sugar, urea content, carbarmine acid, and ammonia by many workers, among whom are Krainsky and Caro, Bisgaerd and Noervig, but the results are

very contradictory. Bouchard and Albrecht examined the urine before and after the fits, in the attempt to isolate some toxin. The constituents of the blood, both before and after a fit, have been examined by Claus and van der Stricht, but no result of the least practical importance has been found. Roncorini* came to the conclusion, after a general survey of this type of research, that the methods were evidently not along the right lines for the elucidation of the problem of epilepsy.

As yet, the methods of chemical research do not seem to have reached the degree of delicacy necessary for the estimation and appreciation of very fine grades of alteration. One is hopeful that later on it may be found possible to repeat these disappointing investigations under more favourable conditions.

At the same time, it is important that the researches which have already been done should be known; a brief résumé is here given.

H. Kersten† found that the blood sugar increased during the occurrence of severe fits. This result was supported by Lugiato and Wuth. They also found that there was a distinct fall in the blood sugar in fainting fits. Further, Fischer‡ propounded the theory that the whole chromaffine system, including the kidneys, central nervous system, peripheral nerves and the musculature take part in the mechanism of the convulsions. Kersten injected adrenalin, which causes changes in the percentage of blood sugar. According to Benedek,§ seven out of nineteen epileptics reacted to such an injection with a fit. No result followed the injection with non-epileptics. Macleod and Best found that the experimental glycæmic animals frequently had convulsions. For the changes in the blood (1916), Dide found that the specific weight of the blood decreased before a fit. Lui, Lambranzani, Charon, Briche, and Pugh, found the alkalinity of the blood diminished before a fit; this was contradicted by Haldane, Schultz, and Vollmer. Brown, Vidoni, and Gutti found that the viscosity of the blood diminished after a fit. Pighine and Juschtschenko found certain ferments in the different organs. Bolten‖ and H. Claude¶ conclude that endocrine disturbances play an important part, but this is contradicted by Marchand.**

The cerebro-spinal fluid has been examined by many workers. Donath,†† Dide, Saquepée, and Pellegrini found it toxic for

* Roncoroni. *Archiv. di Psychiatria*, 1900, vol. xxi., p. 6.

† Kersten, *Allg. Zeitschr. f. d. ges. Neurol. und Psychiatrie*, 1921, vol. lxiii.; 1923, vol. lxx.

‡ Fischer, *Idem*, 1918, vol. lvi.

§ L. Benedek, *Wien. klin. Wochenschr.*, 1918, No. 52.

‖ G. C. Bolten, *Epilepsia*, 1914, vol. v., p. 300.

¶ H. Claude and Lejonne, *Epilepsia*, 1910, vol. ii., pp. 1-13.

** L. Marchand, *Revue neurologique*, 1922, p. 1434.

†† Donath, *Medical News*, 1905.

animals, but were unable to define the chemical properties of the toxin. Fuchs and Rosenthal found the freezing-point slightly lowered, while Hartmann and di Gaspero found that the albumen slightly increased in status epilepticus. Hamilton * found the calcium content of the blood and cerebro-spinal fluid normal in seventeen epileptics examined.

A certain unanimity has lately become apparent among the various workers on the changes in the number of the corpuscles in the blood, at the time, or about the time, of the fit. The first important work was done by Schlecht, Hartmann, di Gaspero, and they thought they saw in the fit the leucopenia of the anaphylactic shock.

Among those who have devoted attention to this question are de Buck, Lunwall, Bruce-Perbles, Hoesslin, Krumbmiller, Rohde, P. Niewenhuyse, Naegeli, Morselli, Jödicke, Wuth, Sauer, Gorieri, Campioni, Schultz, Zimmermann, and Brühl. Among the recent workers M. de Crinis † is outstanding. He examined a number of epileptic patients, and found that each fit was preceded by leucopenia, and followed about six hours after a fit by hyperleucocytosis. At the same time, a fit did not always follow on a condition of leucopenia. This agrees practically with an observation I made on the alternation of segmental disturbances associated with a fit.‡ De Crinis also examined the percentage of albumen in the blood-serum, and found it to be higher in epileptics. This observation was partially confirmed by Anthéaume and Trepsat,§ but denied by Meyer and Brühl. Further, de Crinis found antitrypsine and cholestrine in the blood increased before a fit, while coagulation of the blood was distinctly slower than normal after a fit. Besta and Perugia found that the coagulability of the blood diminished shortly before a fit. In some cases Cuneo ‖ found albumen in the blood immediately after a fit, this was absent in the interval between the fits.

It is known from the work of Franck, and also from the observation of a temporary prolapse seen in the brain of persons who have a fit, while in process of being trepanned, that the blood-pressure rises during a fit. Clinical observation shows that during the tonic stage of a severe fit the patients show peculiar hæmorrhagic points, particularly noticeable on the face (the eyelids very frequently show them, and neck). The boundary line for the neck

* Hamilton, *Journ. Amer. Med. Assoc.*, 1925, p. 1253.

† M. de Crinis, "Monographien der Neurologie und Psychiatrie," 1920, pt. 22., and Art. Epilepsie (Kraus and Brugsch); "Spezielle Pathologie und Therapie" 1923. Vienna: Urban und Schwarzenberg.

‡ Muskens, *Archiv. f. Psychiatrie*, 1903, vol. xxxvi., pt. 2.

§ A. Anthéaume and L. Trepsat, *Encéphale*, 1922, No. 2, p. 103.

‖ G. Cuneo, *Riv. sperimentale di Freniatria*, 1914, vol. xl., p. 837, and 1922, vol. xlv., p. 408.

is about the third segment, and is often so sharply demarcated that the explanation was given that it was due to pressure from the collar. This is not the case, or not altogether the case, for it is seen in patients who are in bed, and where no collar is worn.

Féré, Vaquez, Nobécourt, Sérieux, and M. de Fleury demonstrated that there was a condition of hypertension before a fit, and hypotension after a fit.

4. *Post-Paroxysmal Phenomena of a Psychical Nature.*—Although it is recognised that there are great differences in the mental reaction of patients after a severe fit, yet one may say that there is always a certain degree of mental dazedness for a shorter or longer period after a severe fit. Immediately after the fit, there is a stage of automatism, where apparently voluntary acts are performed, such as undressing, looking for something, attempting to go away hurriedly. No memory is left of this stage. At this stage one sees the so-called "plucking movements of epileptics." It is interesting to record that I once saw such movements after a bromide of camphor fit in a *Macacus rhesus*.

If those who are near the patient attempt to interfere with these automatic movements, and to prevent him from performing acts he manifestly wishes to perform, he may resist vehemently, and the result may be dangerous. The sensible thing to do is to leave the patient as much as possible alone. It is not uncommon to find a patient passing from this stage into an hysterical fit, while even "arc de cercle" may occur. This stage of automatism is of immense importance forensically, especially as it is associated with loss of memory for the period. In a number of non-criminal cases I have repeatedly examined patients as speedily as possible after a fit, to find out how far back they could remember. It was found that not infrequently the loss of memory after a fit was accompanied by a loss of memory for a shorter or longer period before the fit. In many cases one could find out quite definitely the exact moment when memory was lost.

Sometimes, when such a patient was examined later, the reconstruction of memory could be made right up to the fit. From the general examination of patients who suffered from single fits as well as from a series of fits, the amnesia was found to go further back after the series of fits than after the single fit.

What is the Significance of the Post-Paroxysmal Phenomena?—It was pointed out that according to my theory the prodromal symptoms and the aura in epilepsy are to be regarded as being symptoms of charge or intoxication, analogous to those described in the experimental cat. It would be illogical, therefore, to ascribe the post-paroxysmal symptoms to some other cause.

As was seen, the prodromal symptoms involve particularly the

motor sphere, as shown by enhanced reflexes, and the sensory sphere, while after the fit the disturbances pre-eminently affect the psychical side. The disturbances show themselves in the form of complicated acts, such as undressing, fighting, or reactions due to hallucinations.

The explanation of the condition is based on the evidence got from the study of the cat after bromide of camphor intoxication. In some cases it will be recalled a single severe fit discharged the animal—that is, in a very short time after the fit it behaved normally—purring, eating, and attending to its coat. This marked improvement does not, however, occur immediately. During the first few minutes after the fit the animal displays automatic movements, behaving in an excited fashion, or fighting with some imaginary foe. These movements, I hold, are due to the action of the fit itself, which throws certain toxins into the circulation. These toxins have the effect of inducing these automatic movements. (Compare p. 48, l. 2; p. 99, l. 17; p. 103, l. 6; p. 173, l. 42, and p. 187, l. 13.) On the other hand, there were cases were the cat was not normal after a fit, it still suffered from myoclonic shocks, and was in a dazed, abnormal condition. In the same way patients are seen who have a very brief post-epileptic stage, with only brief automatic phenomena, while others display a longer period of automatism, which may last until more fits occur. The conclusion is therefore come to, that in man as in the cat the effect of the fit has been to throw the toxin into the circulatory system, so that the complete discharging effect is delayed for a varying period. Where the amount of toxin has been large, it is possible that one fit may not discharge the animal. The sequel of events in such cases has already been described. Again, the rapid precipitation of the toxins in the blood by a fit explains the occurrence of certain post-paroxysmal phenomena. The same explanation applies for the stage of automatism with psychical disturbances seen after fits, where no known toxin has been recognised as causing the fit. It may be recalled that evidences of hallucination were found in animals immediately after fits due to experimental irritation of the cortex, and psychical disturbances are seen in certain cases of traumatic epilepsy. This is more particularly the case where the patient has an hereditary predisposition to psychosis.

Inter-Paroxysmal Conditions or Symptoms.—It is certainly the case that there are no regular and unfailing symptoms which can be considered as characteristic for genuine epilepsy. There are many symptoms which may occur, but it is impossible to give a hard-and-fast classification such as is possible for some other maladies.

Segmental disturbances of sensation are always to be examined for, as they do have a certain objective significance, especially from a legal aspect, where the question of a certain individual being an epileptic has to be decided. The disturbance of the sensation for pain should, therefore, always be looked for, but if absent, the fact has no diagnostic significance.

The examination of a patient for such segmental disturbances of pain is not too simple, for the phenomena are transient, and in many case brief. It is necessary to examine a patient at certain periods at least twice a day to get any reliable data. It is only in chronic cases where complete, or almost complete, analgesia is got (Thomson and Oppenheim).* Certain small fields are excluded, such as the mesial lines in the extremities, the balls of the thumbs, and round the eyes. Ritterhaus, Redlich, Stier, and

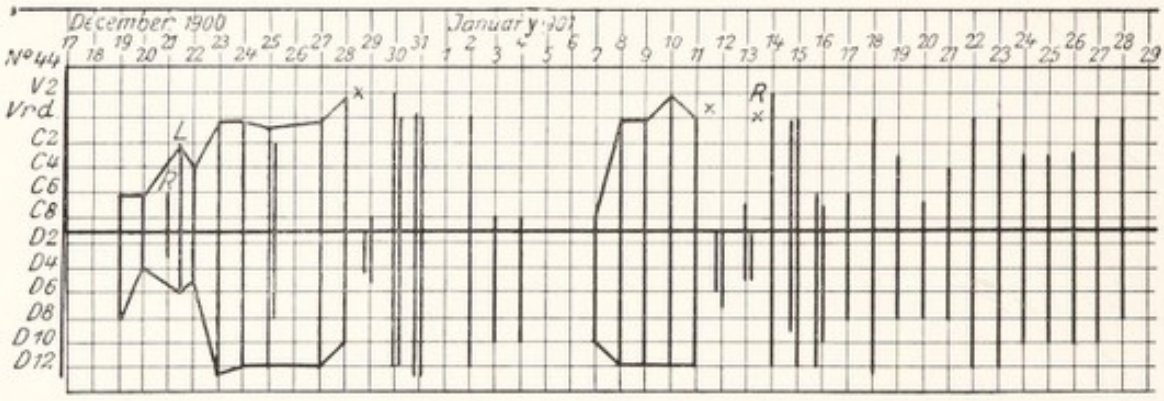


FIG. 43.—THE VERTICAL LINES INDICATE THE EXTENT OF THE SEGMENTAL DISTURBANCES OF THE SENSATION OF PAIN (IN THE THORACIC FIELD).

Generally there is an increase in extent before a discharge; the discharge is indicated by a cross. This is taken from Table XIII. of my paper referred to on p. 247 of this subject.

especially Wiersma, devoted special attention to the examination of the so-called epileptic character. Reference must here be made to the inter-paroxysmal psychical condition. The first workers examined patients by a method of association, while the later worker adopted an ingenious system of definite reaction experiments. It was found that, on the whole, epileptics tended to show a sudden loss of attention. It is interesting to find that Jelgersma, Clark, and Spratling looked upon the psychical symptoms as the nucleus of epilepsy.

Godefroy's examination of the disturbances of co-ordination in epileptics between the fits, if found in early cases, will be of importance in relation to the work of Wiersma.

* R. Thomson and H. Oppenheim, *Arch. f. Psych. u. Nervenkrankheiten*, 1884, vol. xv., p. 559.

One symptom which has certainly not attracted enough attention (T. Schilling) is the coated tongue. A coated tongue is seen as a prodromal symptom to a fit, and also after a fit. It occurs in cases where there is no history of gastro-intestinal disturbance, and is also found in traumatic epilepsy (p. 387). Rollin thought that it might be due to acidity of the blood. Felsen* examined the gastric content in a number of epileptic patients taken at random, and concluded that the gastric content in epileptic patients had a higher degree of acidity than normal.

In cases where there is an hereditary predisposition, the so-called signs or symptoms of degeneration are not infrequent. These may be a high palate, or abnormal growth of the hair, but these symptoms should not be considered too seriously.

Spratling ascribes the so-called epileptic face seen in cases of long-standing to the dementia, the acne pustules, and scars. The horrible breath so frequent in chronic cases, is also thought to be due to gastro-intestinal disturbances and the use of bromides.

To this drug also is due partly, at least, the inequality and dilatation of the pupils. Tremor of the hands is common (often related to myoclony), also cold moist fingers, with sometimes the condition of numbness.

It must be realised that all the fluctuating symptoms described as prodromal may occur inter-paroxysmally. Indeed, they may be true inter-paroxysmal symptoms in that the fit itself may not occur, the discharge having come about in another way. Careful notes show a varying picture of symptoms, such as fluctuating segmental disturbances of the skin, enhancement of reflexes, occurrence of spontaneous shocks, headaches, changes of temper, changes in the condition of the pupils, condition of the tongue, and so on. That is the demonstration of a fluctuating condition of charge preceding the discharge.

This interplay of inter-paroxysmal and prodromal symptoms, if carefully noted, is most illuminating. This refers especially to the fluctuations of the segmental disturbances of sensation (Fig. 43). (Refer also to Table 12, *Arch. f. Psychiatrie*, vol. xxxvi., 1903.)

* Felsen, *Archives of International Medicine*, August, 1924, vol. xxxiv., p. 147.

CHAPTER VIII

THE RELATIVE FREQUENCY AND NOSOLOGICAL VALUE OF THE SYMPTOMS

The Most Frequent Combinations of the Conditions of Charge or Discharge. The Great Frequency of Myoclonic Shocks.

As the clinical material which formed a basis for this work was not of the class of inveterate or chronic cases so familiar in institutions, it offers a far better opportunity for the study and appreciation of the different symptoms.

An exact and complete account of symptoms in carefully examined cases of early epilepsy, at least not chronic epilepsy, is by no means redundant or unnecessary. Any one who goes into the matter carefully cannot but be struck with the varieties and combinations of the minor symptoms apart from the three cardinal ones—the epileptic fit, the myoclonic shocks, and the headache. The old chronic cases of epilepsy are so complicated, any catalogue of symptoms becomes valueless. Such cases are not suitable for contributing data for this research. The question arises, which group or combination of symptoms is most prominent in the early stages of epilepsy when the patient has little or no mental symptoms. I would hope that by a careful study of this question some light might be thrown on the pathogenesis of epilepsy. The available statistics which I present are taken from 1,000 carefully examined male and 1,000 female cases. Even in these cases circumstances prevented me from going into all the cases as fully as I wished, yet in all circumstances a careful history was taken of the condition as seen at the first examination. The complaints of the patient, the different forms of discharge, and the various forms of charge were carefully recorded, and also the duration of the disorder. From these notes experience teaches how to form an estimate as to the development of the case.

In the first place, the percentage of cases which *suffered exclusively from one form of discharge* were investigated. As the cases were non-chronic, a higher percentage was looked for. The figures obtained were 11 per cent. in males, and 8·7 per cent. in females.

It must be conceded that among these 2,000 cases were included cases seen when I began the special study of epilepsy, and where lack of experience might influence the establishing of

the particular type of discharge. It is probable, therefore, that these figures are a little too high. Among the 110 male cases and 87 female cases with one characteristic symptom, myoclonic shocks occurred in 8 male and 15 female cases, fainting fits 9 cases in either sex, headaches as an exclusive symptom in 3 male and 3 female cases. In the great majority of the cases included in the 11 per cent. males and 8·7 per cent. female cases—*i.e.*, in 90 men and 60 women—*severe epileptic motor fits* were the sole mode of discharge.

Although I have not as yet examined more particularly the further course of these monosymptomatic cases, yet from the evidence already obtained it is evident that the prognosis is more favourable where the only manifestation is a solitary severe fit, than where there are complicated symptoms such as fainting fits.

The examination of cases with regard to the *absence of great motor discharges* shows that such cases are relatively rare.

This is a very important fact, because it confirms the statement made elsewhere in this book that the nucleus of the disorder is *the great epileptic fit*. It is interesting to find that the result of the experimental examination of myoclonic epilepsy in warm-blooded animals led to the same conclusion.

In 37·9 per cent. of the male cases, and 36·9 per cent. of the female cases, *myoclonic shocks were present*. These figures are not nearly so high as those given by Russell Reynolds, but they extend parallel between the epileptic fit due to bromide of camphor in warm-blooded animals and myoclonic epilepsy in man. There is further good reason for believing that these figures considerably understate the occurrence of myoclonic shocks in the course of the disorder. These reasons are:

1. During the research, as I became more experienced, the nosological significance of these myoclonic shocks became more and more significant, both as an actual symptom and from their appearance in the histories of cases. It is very likely that the figures given are too low, because the condition was missed at the beginning of the investigation.

2. Experience teaches that with adults as with children (pp. 202 and 220) myoclonic shocks, where they occur alone, are often entirely overlooked; neither the patient nor his friends appreciate them.

It is not to be wondered at that such cases—*i.e.*, those with simple myoclonic shocks—rarely get medical attention. I was able to find only 8 male and 15 female cases of this class. It is interesting to find that several of these patients were seen later on, when they had regular epileptic fits. In accordance with the

principle of compensation, the myoclonic shocks had fallen to the background.

The same holds good, though in a less degree, for those cases where the fits were preceded by (*a*) myoclonic convulsions accompanied with headaches; of these there were 8 male and 7 female cases; (*b*) myoclonic shock and fainting fits, 14 male and 14 female cases; (*c*) myoclonic shocks with headaches and fainting fits, 9 male and 14 female cases; (*d*) myoclonic shocks with fainting fits and psychical symptoms, 6 male and 6 female cases; (*e*) myoclonic shocks accompanied only by psychical symptoms, 1 male and 1 female case. From the evidence of these cases it is shown that those cases where the myoclonic shocks follow the fits are atypical, and occur comparatively rarely. Atypical, also, are those cases where (*a*) fainting fits occur alone, as seen in 21 male and 34 female cases, and (*b*) cases where headaches and fainting fits preceded the fits, 15 male cases and 28 female cases. The small number of cases in which headaches alone preceded the fit (3 male and 3 female) does not give a very accurate impression of the frequency with which headaches are the symptom ushering in the disorder of epilepsy. I have, however, only included those cases where the later course of the disease made the diagnosis of epilepsy legitimate, or where a very strong hereditary history admitted of the diagnosis.

If an examination be made of the combination of symptoms apparently characteristic for myoclonic epilepsy in the experimental animal—*i.e.*, myoclonic shocks and fits—it is seen that this combination also occurs in 32·8 per cent. of the male cases and 36·7 per cent. of the female cases, or in 328 men and 367 women. This seems to me to prove that the choice of myoclonic epilepsy as a starting-point for this description was correct.

The fact that in more than half the cases fits, shocks, and headaches occur, shows that these three symptoms are interdependent, and of intrinsic significance.

The close association between myoclonic shocks and fits has been demonstrated by the experimental work, but of course no information is available from this source for the headaches. This part of the syndrome must have all its data collected from clinical cases. From the clinical evidence it appears that the headache is so far independent of the other two symptoms, for it very frequently occurs between the fits in the inter-paroxysmal period; is, in some cases, permanently present. The evidence shows that the headache occurs just as often along *with* the fits and shocks as *without* them.

From a general consideration of these 1,000 male cases and

1,000 female cases, it is seen that in nearly half the epileptic fits were combined with shocks or headaches.

It must be remembered that in a number of cases the myoclonic shocks give very little trouble, and appear only shortly before a fit, and disappear or become insignificant after a fit, and that the headaches also tend to form a passing phase of the disorder. Such an observation justifies the conclusion that at the beginning of epilepsy the three cardinal symptoms (myoclonic shocks, headaches, and fits) have been present, although, when the case is seen, one or other may have become obscured.

I do not think I exaggerate when I say that, in my opinion, more than half the cases of genuine epilepsy may be regarded as myoclonic epilepsy in a wider sense.

From the nature of my clinical material—early cases of epilepsy—it is natural that little evidence could be got for psychical changes. It must, however, be admitted that in many of these cases such changes have developed later. At the same time, the fact that I did not get such changes in the cases demonstrates the inaccuracy of the opinion held by many psychiatrists that a psychical change is the nucleus of the disorder.

Syndromes.	*Among First* 1,000 *Cases.*		*Among Second* 1,000 *Cases.*		*Together.*	
	500 *Males.*	500 *Females.*	500 *Males.*	500 *Females.*	1,000 *Males.*	1,000 *Females.*
Myoclonic convulsions, fits, headaches	86	100	89	113	175	213
Myoclonic convulsions, and fits, without headaches ..	55	70	98	84	153	154
Cases with psychisms	49	30	33	30	82	60
Inter - paroxysmal headaches present	188	245	207	240	395	485

CHAPTER IX

THE STATISTICS OF EPILEPSY

§ 1. Frequency of the Disorder.

THE question of the relative frequency of epilepsy is one which has always formed part of the programme of the International League against Epilepsy from its inception in 1908.

It is evident that, apart from the statistics available from the examination of conscripts, one can only get reliable data from small communities. Statistics, of course, do exist, which claim to represent the prevalence of epilepsy in the larger countries.

For example, the figures given for France, about the middle of last century, represent the disease as occurring in 1 in 200 or 1 in 1,500 of the population depending on the department under examination. At the end of last century the statistics prepared in Germany from the examination of conscripts gave the figure as 1 in 400.

A Dutch table, prepared from 1914 to 1918, gave the figure as 1 in 1,800. Where a small division of Holland was examined, or one of the smaller islands where the entire population had but one physician,* the average result worked out at about 1 in 300 or 350 of the population. In Switzerland, where the cantonment system is peculiarly suitable for the preparation of statistics, the average was 1 case in 200 of the population;† in England‡ only an approximate figure can be got as yet. From the work of Davenport, it would seem that epilepsy is relatively less common amongst the negroes and Polynesians.

In preparing, or attempting to prepare, the statistics for epilepsy, one is always met by the practical difficulty of ignorance. The disease is present in many cases where it is not recognised by the physician, the friends and relatives, or by the patient. This applies particularly to cases where the fits occur at night, when the patient is asleep, and where the tongue is not bitten. Further, if it be remembered that epilepsy may exist in many different types and degrees from the migraine with some epileptic symptoms, or slight epileptic phenomena appearing only at certain times, such as during pregnancy, up to the severe and chronic

* J. Casparie, Annual Report of the Dutch Branch of the International League against Epilepsy, 1920, p. 11.

† Amman, *Epilepsia*, 1913, vol. iv., p. 483.

‡ Comsie, *Lancet*, 1919, vol. ii., p. 959.

cases seen in epileptic institutes and asylums, it is obvious that the diagnosis is not simple, or in many cases straightforward. In many cases it is difficult to distinguish between epilepsy, hystero-epilepsy, and hysteria. It was hoped that some useful facts might be got from an inquiry amongst school children. Such an inquiry was initiated by a branch of the League, but the only result arrived at was that epilepsy amongst school children was almost unknown. This type of investigation could only be of value if the parents were questioned as to the occurrence of infantile convulsions, the prevalence of headaches, and the presence of slight diurnal or nocturnal shocks, which may all be prodromal symptoms of epilepsy. The mere examination of children for the presence of epilepsy or putting a few isolated questions to them are valueless.

Some critics go so far as to discuss the admissibility of investigating the frequency of epilepsy, for they maintain that epilepsy as a separate entity has not yet been defined. How therefore, say they, are we to ask if patients have or have not epilepsy, when we have not yet decided what epilepsy is?

The whole question is one beset with difficulties. Which of the different forms of infantile convulsions are to be looked upon as distinct precursors of epilepsy? Are all the people who have had a fit or fits but once or twice in their lives, associated with unusual phenomena, such as the inauguration of the menses, starvation, over-indulgence in alcohol, over-exertion, or after certain toxins such as lead, to be classed as epileptics?

It seems to me that what is needed, in the first place, is a better appreciation of the symptoms of epilepsy, before we attempt to make any hard or fast definition of the malady.

The next questions which come up are—In what proportion of the case where there is an hereditary history of epilepsy will epilepsy develop? How many of these cases will become chronic (*a*) with treatment, (*b*) without treatment? Again, how many epileptics, or what proportion of epileptics, become insane?

In answer to the last question I have examined the returns from the Dutch Asylums for the period from 1880 to 1926, and found the percentage to be from 7 to 9.

RELATIVE PERCENTAGE OF EPILEPTICS IN THE MENTAL HOSPITAL IN THE NETHERLANDS

Year.	*Number of Male Cases of Insanity.*	*Percentage of Epileptics.*	*Number of Female Cases of Insanity.*	*Percentage of Epileptics.*
1850	618	9·9	615	9·2
1880	2,117	10·5	2,216	7·6
1900	4,096	9·0	4,043	7·0
1926	6,890	8·06	5,814	6·5

These statistics are so far inexact, as the total number of insane patients in 1926 was about 10,000. I have used for 1926 only the information sent to me from the superintendents. The fall in the percentage in the last term is probably the favourable result of the different efforts made to combat epilepsy; such agencies are particularly active in the Northern provinces of the Netherlands. This appears the more probable, as the percentage in the asylums of the Southern provinces amounts to 8·6 and 7·6.

In countries where there are no special institutes for chronic epileptics, one finds that there is a much higher proportion in asylums. These cases are often exceedingly pitiful, for they have arrived in asylums not so much on account of their psychical condition, but because there was nowhere else to put them. So we find them almost normal mentally, and yet condemned to spend their days amongst the insane.

The question of the relative proportion of epilepsy in the sexes has been investigated by different workers. From my own investigations I found that the proportion in my own patients was 1,000 males to 1,080 females, thus showing a preponderance on the female side. It seems to me that the conditions in the two sexes balance fairly well. In 1,000 maie cases of epilepsy I found that 253 had had infantile convulsions, but only 203 out of 1,000 female cases. The increase in the female cases in the second and third decades of life is most probably associated with the crisis of menstruation. Gowers also found that women were more liable to develop epilepsy as a result of fright or great emotional strain. In the male cases one more often finds a history of cranial injury, and after the third decade syphilis and alcoholism are important etiological factors.

As regards the period of life at which epilepsy most frequently appears for the first time, all the authors agree in describing the fourteenth to the twentieth years as being the period at which most cases begin.

Some attempt has been made to get statistics relative to the time of year at which epileptic fits are most common, but nothing of importance has been found. Amman* thought February and June were the times of the year when epileptic fits were most frequent. He also thought that the hour after falling asleep and dawn were the two periods of the day when fits were most likely to occur. He agreed with Arrhenius, who had a theory that at these periods there was some change in the aerial electrical conditions. This was contradicted by Gallus.† Lomer‡ thought that the occurrence of fits was in some way associated with changes in air pressure.

* Amman, *Epilepsia*, vol. iii., p. 383.
† Gallus, *Epilepsia*, vol. iii., p. 46.
‡ Lomer, *Arch. für Psych. u. Nerv.*, vol. xli., p. 1009.

§ 2. Heredity and Other Predisposing Factors in Epilepsy.

Heredity has always been regarded as an important factor in the occurrence of epilepsy. It is only quite lately that some of the younger workers, among whom may be mentioned Klessens, have begun to cast any doubt on this view.

From the examination of my 2,000 cases of epilepsy certain facts are deduced which illustrate the importance of heredity.

From these 2,000 cases, 89 males and 101 female cases have to be excluded owing to incomplete data in the sense that no reliable hereditary history was got, although in other particulars the cases were complete. It is seen that 233 male cases and 245 female show direct epileptic heredity. Direct heredity indicates that epilepsy occurred in the parents, the grandparents, the brothers or sisters, or the children of the patient.

Series of 2,000 Cases of Epilepsy, 1,000 are Males, 1,000 Females.

		1,000 *Males.*	1,000 *Females.*
Incompletely examined cases		89	101
Direct heredity (epilepsy migraine)		200	218
Cases where the mother had epileptic symptoms during pregnancy		33	26
	Total	233	245
Indirect heredity (epilepsy migraine) up to third generation		78	91
	Total	311	336
Insanity — Direct		91	83
Insanity — Indirect		51	38
	Total	142	121
Alcoholism — Grandparents		7	11
Alcoholism — Parents		41	52
Alcoholism — Patient		43	7
	Total	91	70
Syphilis — Grandparents and parents		24	17
Syphilis — Patient		16	5
	Total	40	22

Indirect heredity includes those cases where epilepsy occurred in the uncles, aunts, nephews, nieces, or cousins of the patient. In my table this indirect heredity was seen in 78 male cases and 91 females. We therefore conclude that in over one-third of the cases a history of epilepsy was found (31·1 per cent. males, 33·6 per cent. females).

From my table the number of epileptics who show an hereditary tendency is probably greater than that given by other workers. The reason for this is because I have included among them those where epilepsy occurred in brothers, sisters, and children of the patient. Turner is the only other worker who gives a higher

figure for the influence of heredity; this figure is 37 per cent. Heredity seems to have most influence with the young. The older a person is at the beginning of the disorder, the less is the importance of heredity. The practical difficulty must not be forgotten, which is that it is more difficult to get an accurate history with older patients. This is because those members of the family who would have known the history of the patient and his family have died or been lost sight of.

It was found in my series of 2,000 cases that there was a direct history of insanity in 91 male cases and in 83 female, while it was found in the family, but not so closely associated with the patient, in 51 male cases and 38 female. (These figures are in all probability not very different from those which would be got from the family histories of any thousand healthy persons.) In this point my data do not differ much from that given by other workers, with the exception of Binswanger, who investigated 150 cases of epilepsy and gave the number who had an hereditary history of insanity as 29·5 per cent. The influence of heredity seems to vary remarkably with the different forms of epilepsy. Turner states that 35·9 per cent. of traumatic epileptics have an hereditary predisposition to epilepsy and 68·7 per cent. of psychogenic epileptics.

It is not uncommon to find several brothers and sisters in the same family spoken of as epileptics. Generally, the investigation of such a case shows that one or two of the number has genuine chronic epilepsy, while the others, either have occasional discharges or suffer from chronic headaches of the epileptiform type, or have epileptic fits only at certain periods, such as during gravidity. In one case where there was an alcoholic father, four out of a family of six boys all suffered from the same definite form of myoclonic epilepsy.

Generally speaking, epilepsy seems to pass more usually from father to son, and from mother to daughter, than from father to daughter, or mother to son.

It is not uncommon to find peculiarities of the disease, such as the reaction to treatment, transferred by heredity.

A male patient (K. O.) suffered from his youth from epileptic fits associated with bouts of passion. From the age of 30 to 50 he had no fits. The man was twice married, and by his first wife had a son who had epilepsy exactly similar to his own. By his second wife he had a son (the first-born), who died of fits at the age of 2, after having had fits since his birth. The second child, also a son, had fits practically from birth. The mother stated that the movements of this child in utero had been excessive. The third child, also a son, was healthy. After this came six girls. The eldest, born at the eighth month, died in a convulsion the second day after birth. The next kept well, but developed fits after her marriage. The third girl died the day after birth, the fourth was an imbecile and had fits from her fourth year; the fifth had fits from birth, became mentally affected, but lived to the age of 60; the sixth girl was healthy.

Among the English and American authorities on epilepsy, due significance is given to the first fit and the probable provoking factor. It is recognised that the first fit indicates the breaking down of the inherent resistance, and that once this has been broken down the tendency is for the fits to recur. The importance of infantile convulsions, the influence of menstruation and gravidity, and the significance of heredity on epilepsy are to be considered predisposing factors.

Where no other cause can be found for epilepsy, it has been asserted that consanguinity has a very important influence (p. 327).

§ 3. **Exciting Causes.**

Alcoholism, syphilis, trauma, shock psychical or physical from falling into water, starvation or prolonged abstinence from food, over-eating, impure air, chemical laden atmosphere, smoking, metabolic toxins.

Among the various forms of intoxication or infection are those which may of themselves break down the inherent resistance of the individual, or they may precipitate a fit where the patient has a predisposition to epilepsy. Alcohol and syphilis are two very important toxins. Alcoholism in parents or grandparents is a definite predisposing factor. Alcohol used to excess, or syphilis, may induce such constitutional changes that epilepsy may result apart from predisposing causes. It is, further, not infrequent to find, where a patient has a definite predisposition to epilepsy, that a single dose of a toxin, such as a bout of drinking, or an infection with syphilis (Fournier), precipitates epilepsy. The epileptic fits manifest themselves at the time of the infection, but tend to recur, and at each successive recurrence need less and less stimulation. This development of the disease is described by Müller Schürch.*

The influence of alcoholism of the parents on the genesis of epilepsy is a point on which workers in different countries are not agreed. For example, in Russia (Kowalewsky), Italy (Batti), and in Germany (Moeli), the percentage of epileptics having a history of alcoholism in the parent is comparatively very high.

It is, of course, well known that delirium tremens is frequently associated with fits, while in some cases fits follow twenty-four to thirty-six hours after a drinking bout, due to metabolic changes (de-alcoholisation of the system). Atwater and Benedict found that 2 per cent. of the alcohol leaves the system by the lungs, skin and alimentary canal. It is not infrequent to find fits occurring in a breast-fed child when the mother has taken alcohol, even in quite small quantities. Where a patient is a chronic epileptic, a small dose of alcohol is one of the most certain means to provoke a fit.

* Müller Schürch, *Epilepsia*, vol. iii., p. 340, and Bechterew, Anfimow, Tamburini, Claude, Redlich, *Epilepsia*, 1912, vol. iv., p. 16.

Extract C., No. 42. One of my own patients exhibited the effect of a small dose of alcohol in a striking fashion. His father related how his son was delayed in hospital for a long period in the effort to establish the existence of epilepsy from which he suffered. (Epileptic fits, when *seen* in the military hospital, exclude the patient from military service.) The father asked the military doctor to observe his son, after having given him two glasses of Moselle wine and to keep him under medical observation for several hours. An epileptic fit resulted in a short time, and the patient was sent from the military hospital as unsuitable for conscription.

Cases have also been known where an epileptic patient with only petit mal has displayed an epileptic psychotic condition or a severe fit after the first dose of alcohol. In some favourable cases of epilepsy, the patients gradually lose their extreme sensitiveness to alcohol.

Extract C., No. 43, J. H., aged 20. Patient fell from a staircase at the age of 14 and injured her foot. The injury was attended to at once and put up in a plaster bandage. Within twenty-four hours of the injury patient had two fits and continued to have fits until treated. These fits were preceded for days by visual hallucinations when she saw the landscape gaily coloured. Amnesia was a very marked symptom, and the patient had also attacks of psychic unconsciousness. She became quite analgesic. A year after the accident when these symptoms were all prominent the patient was brought for treatment and put on bromide bread. The result was excellent, for she had no more fits, while the analgesia cleared up.

In 1907 the patient took a little alcohol, and on one occasion after a half ounce of brandy had two severe fits. For a long period she remained free from fits, even during pregnancies, but on one occasion she had a fit after a glass of beer. Later when I saw her after 17 years she did not have fits even after larger doses of alcohol than those which before caused a fit and seemed to have lost sensitiveness to the drug. It was interesting to find that this patient's mother had had epileptic fits in all her pregnancies up to the fifth month, and that her maternal grandfather had also had fits.

With regard to congenital syphilis, there is no doubt but that it is associated with the occurrences of epilepsy, but, according to Gowers and Turner, not so frequently as was at one time supposed. The application of the Wassermann method in the examination of epileptics confirms the opinion of those workers. Secondary syphilis is sometimes associated with the occurrence of epilepsy, but it is frequently the means of aggravating an epileptic predisposition already present. Tertiary syphilis is often the cause of organic epilepsy, and not infrequently closely resembles in its course genuine epilepsy.

We can appreciate a certain degree of resemblance between the action of the two toxins—syphilis an endogenous toxin, and alcohol an exogenous toxin—and the action of bromide of camphor in the experimental cats, where myoclonic epilepsy resulted. In the case of syphilis or alcoholic intoxication, the resistance of the organism is considered to be weakened by the toxin, and the first fit may be induced by quite a trifling factor. After the first fit the tendency is for another fit to follow, as Gowers has said the nature of the disease is "self-perpetuating." In the

same way it is conceivable that physical or psychical trauma, endocrine or metabolic changes might produce chemical substances which would be similar in their action to alcohol or syphilis.

It must be pointed out that epilepsy may occur as a result of changes due to tertiary syphilis in other organs than the brain. A non-specific dyscrasic epilepsy may result as the end-product of metabolic changes induced by syphilitic changes in organs other than the brain.

As a general rule, it may be stated that epilepsy originating after the age of forty is as a rule due either to syphilis or alcoholism. In such cases the syphilitic changes are not always found in the brain. According to Gaucher, it is not uncommon to get epilepsy following on hereditary syphilis traced to the grandparents. In such patients I have not infrequently found hystero-epilepsy with such tabetic symptoms as the Argyll-Robertson pupil.

Trauma Capitis.—Where epileptic fits supervene suddenly and unexpectedly in a patient, it is very natural to raise the question of there having been some recent and severe injury to the head. Where the patient is a boy, the relatives or friends will almost certainly give a history of some such injury (compare discussion on this matter, pp. 370-371).

There are certainly cases where some definite association exists between a cranial injury and epileptic fits. In such cases the patient generally suffers from severe headaches, followed by other symptoms, which gradually terminate in epileptic fits. It is always an important point where the question of insurance or compensation arises to decide whether the epilepsy is due to an injury. Gowers has stated definitely that only a few months should elapse between an injury and an epileptic fit due to the injury. This is a good and safe rule, but it must be modified if the patient contracted the injury on military service. It has been found in the war that a longer period may elapse between the injury and the fit if the injury be contracted on military service. It is at best a difficult matter to decide whether a specific cranial injury is associated with epileptic fits, more especially where there is no tangible sign of bone injury. Such cases do exist, but each case has to be judged on its own merits, and the diagnosis is always difficult. An X-ray photograph is sometimes a valuable help and of course very careful clinical examination after shaving the scalp.

The following is a table showing the association between epilepsy and different types of trauma or shock. Those cases which show palpable cranial defect form a class by themselves—the real traumatic epilepsy. The prognosis in such cases is very good. This subject is dealt with fully elsewhere (Chapter XV.).

	1,000 *Males.*	1,000 *Females.*
Trauma of head	107	42
Trauma with scars	28	10
Trauma with cranial defect	9	2
Fall or blow on other part of body ..	82	26
Fall with loss of consciousness ..	6	1
Falling into water	17	6
Almost drowned	6	2
Difficult confinement (on infant) ..	20	10

The large proportion of cases associated with falling into water is accounted for by the fact that these data were collected in the Netherlands, where the natural features of the country allow ample opportunities for such accidents. It must be remembered that in all these accidents the emotional strain, as well as the physical, has a direct influence on the result. It is not infrequent to find the recovery, or resuscitation, of a patient attended by an epileptic fit. This may be, and in the cases under consideration was the first fit the patient had had, but it may be followed by others, and chronic epilepsy may supervene.

It may be recalled that in both man and the experimental animal there is a strong tendency for epileptic phenomena to occur at the time of transition from sleeping to waking or *vice versa* (compare p. 191). I* have repeatedly laid stress on this fact. It is really remarkable that epileptic fits are so rarely heard of as occurring either at the beginning or end of surgical anæsthesia.†

Epilepsy associated with Interference with the Circulation in the Brain.—Where the circulation of the blood through the brain is interfered with, chemical changes immediately follow. Pflüger has shown that if the cerebral circulation be interfered with for a few seconds, the natural neutral reaction of the cerebral tissues is altered to acid. T. Lewis has shown that an interruption of cerebral circulation for the space of time occupied by a cardiac systole is sufficient to suspend all mental processes. Leonard Hill proved that recovery of the cerebral tissue is impossible after interruption of the circulation for fifteen minutes.

Where epileptic fits occur in patients who have been resuscitated from drowning, suffocation, hanging, or after very severe hæmorrhage, or in Stokes-Adams disease, such fits are associated with two factors. One is the hypoxyhæmy, the other is the predilection all fit phenomena show for the moment of transference from the unconscious to the conscious state. It has already been pointed out how frequently fits occur just when the patient is on the point of falling asleep or of wakening. In such cases as those just referred to, the fit again selects the moment of transition from the unconscious condition associated with impending death to the recovery of consciousness.

* Muskens, *Epilepsia*, 1904, vol. i., p. 168.

† Discussion in the *British Medical Journal*, Autumn, 1927, on "The Frequency and Causation of Epilepsy," pp. 276 and 288.

Cases are reported in the literature, of patients who had epileptic fits associated with loss of consciousness due to aneurism, insufficient development of the circle of Willis, pressure on the carotids or any other factor whereby the cerebral circulation was temporarily interfered with (compare p. 288). Where the interference was due to temporary pressure on the carotids, the fits came on when the patient sat upright. Cases of this type have been reported by Ogle, Savory,* W. Moore, and Wolffhügel.†

In epileptic fits caused by pressure on the carotids, the vagus is very probably also involved, and contributes towards the result (Ziemssen and L. Hill reference on p. 4). Langendorff and Zander showed that in a chloralised rabbit stimulation of the vagus caused stoppage of the heart, and induced an epileptic fit. Finally, when non-epileptic patients are undergoing narcosis either with chloroform or ether, they not infrequently have an epileptic fit. Such a fit is an isolated experience, and has no further consequence (Patch).‡

A point of great interest and importance is the agreement between these pathological fits and the myoclonic epileptic fits produced experimentally in cats. This agreement is seen in the time of occurrence of these fits. In the pathological fit—*i.e.*, the fit due to trauma or disease, and associated with unconsciousness—the point of time when the patient is emerging from unconsciousness to consciousness is the most likely time for a fit, and in the experimental myoclonic fit it is also the time of wakening from sleep or the time of falling asleep. In both it is a point of time when the patient is undergoing a physiological change. What exactly this change is is not known, but there is much evidence to show that it is definite and far-reaching (compare p. 207).

Another point is that emphasized by Roll,§ that convulsions due to hæmorrhage only occur in well-nourished animals. This observation agrees with the results got experimentally where typical myoclonic convulsions could be produced only in well-fed, healthy animals (compare also p. 284, 2).

Elsberg and Stookey note that the anoxæmic fits which may be produced in the cat by compression of both carotids may be prevented if the cerebrum be perfused with Ringer or saline solution. They suggest that the action of this fluid is to wash away certain metabolic substances, probably derived from the blood, and which would irritate the convulsive centres.

In recent papers on anoxæmia, this condition has been described as one which not only "stops the machinery, but wrecks the machine."‖

* Savory, "Medico-Chir. Transactions," 1856, vol. xxxix.
† Wolffhügel, "Inaug. Diss.," 1888. Strasburg.
‡ Patch, *Lancet*, 1922, vol. ii., p. 813.
§ Roll, "Leerboek der gerechtelijke Geneeskunde," 1908, vol. i., p. 153.
‖ Barcroft, *Lancet*, 1925, p. 590, and Koehler, Behnermann, Bonell, and Loewenhart, *American Journ. of Physiol.*, 1925, vol. xxiv., p. 590.

K. Yamakumi* found that rabbits on the point of death from drowning developed fits, and that hæmoglobinuria was present.

Emotion as a direct cause of epilepsy is a controversial point. Gowers gives fright or anxiety as the sole cause of the disease in one-third of his cases. Spratling† finds only 5 to 6 per cent. of his cases associated with emotional disturbances. Féré, on the other hand, pays little attention to emotion as a cause of epilepsy, but points out that it might be easy to mistake the prodromal condition of anxiety for the cause of the fit. Binswanger, also, does not think emotion a sufficient cause in itself for epilepsy, but considers that severe and prolonged mental overstrain may produce the malady. Probably a combination of overstrain, anxiety, and distress may suffice to precipitate a fit. Certainly, the fact that a first fit sometimes occurs when the patient is undergoing such a combination as playing cards for higher stakes than he can afford, supports this suggestion. Turner finds that in 388 cases of epilepsy emotional strain could be proved to have caused 16. Out of these 16 cases 11 had a family history of epilepsy. In my own cases I have been able to establish emotional disturbances as a cause in 13·1 per cent. among males, and in 4·7 per cent. among females. Among the male cases severe mental strain—such as working for examinations—or bodily exhaustion caused by repeated hæmorrhages were often associated with the breakdown. In females, a condition of chronic depression or shock after some assault of a sexual nature was sometimes the psychical forerunner of the breakdown. In this connection there is some doubt that the repetition of the sexual act is frequently associated with a fit, but it is incorrect to regard the act as the sole cause of the fit. This was pointed out by Féré.

Masturbation as a cause of epilepsy must be disregarded. It is a bad habit too widely practised; it is impossible to associate it with the occurrence of epilepsy.

Gowers and Binswanger both observed that some time frequently elapsed between the emotional or mental strain and the first fit. This is not surprising in view of the experimental work on cats with bromide of camphor. It was shown that after a condition of charge was induced by intoxication with the drug a peripheral stimulation brought on a fit. In the same way an emotional disturbance may bring about some endocrinous change or some metabolic variation, which induces or produces the condition of charge, so that the fit may be precipitated by some passing stimulus. Camson, Crile, Gley, and de Allende Navarro

* Kumao Yamakumi, "Drowning Hæmoglobinuria," *The Tohoku Journ. of Exp. Med.*, 1922, vol. iii., p. 295.

† Spratling, *Epilepsia*, 1909, vol. i., p. 279.

certainly consider that good proof has been obtained that emotion produces an endocrinous disturbance in the form of a hypersecretion of adrenaline. T. Uno* found that in rats who had been induced to fight for hours there was an enlargement of the hypophysis, and the effect of this extract on the excised gut was to reverse the normal action.

L. P. Clark and Ferenczi admit that, as a consequence of the epileptic diathesis, an accumulation of disagreeable impressions, which in a normal person lead to a furious outburst of temper, elicit an epileptic fit. It may be recalled that they consider (according to the teaching of Freud), a fit as a "striving for expression of the libidinous energies in the unconscious," or that the "epileptic psychological mechanism is a too intense and prolonged parental fixation of the libido." . . . Although it is a fact that in most epileptics the sexual instincts are not strong, such a psychological theory has certain advantages over a doctrine, which is based on the physiological observation of animals as described in Parts I. and II. in this work. It is interesting, however, that both theories lead to the same conclusion that, therapeutically, a hygienic regime and well chosen physical exercises are important.

Other Incidental Causes.—Occasionally I have seen cases of well-marked epileptic fits associated with long fasting, but more frequently cases due to too rich or to too full a diet. In two cases of the latter class fats were quite evidently the exciting cause.

Smoking seemed to be the cause of the fits in not less than fifteen of my cases. In three cases the epileptic phenomena ceased when the smoking was stopped. Two of these were boys at the age of puberty; one was older (compare p. 299, l. 20).

It is well known that many epileptics are liable to have a fit if sitting in a crowded room, at a concert, play, or social function. Some few cases one meets where the very first fit has occurred when the patient was in a crowded room. Here, however, there are too many agencies at work; it is impossible to ascribe the disease merely to the circumstance of a crowded room. Such a circumstance, associated as it is with a vitiated atmosphere, may induce metabolic changes, which in turn induce a fit. In one of my cases a fit occurred first when the patient was exposed to fumes from a process in the manufacture of sulphuric acid, while another succumbed to the inhalation of coal gas. Clinical observation shows that there is a considerable degree of variation in this type of reaction. For example, a man had three epileptic fits—two at the end of two strenuous days, the third after inhaling fumes from a stove newly in use. This man's

* T. Uno, *American Journal of Physiology*, 1922, vol. lxi., p. 203.

wife, who was an epileptic, was exposed to the fumes also, but merely had a headache. This personal variation in reaction is emphasized by P. Masoin,* Slosse, and Godart.

It is very difficult to estimate the number of cases which are due to constipation caused by hereditary slowness of the intestinal peristalsis (Harryman and Donaldson),† or the "kink in the colon" described by Arbuthnot Lane. It is certain that the number cannot be small, for so many cases of epilepsy are alleviated, if not cured, by attention to the regular functioning of the colon. Recently operative removal of cæcum and ascending colon has been proposed.‡

In many chronic cases I found the presence of colitis membranacea; whether it has any relation with the disorder, or is perhaps a result of repeated enemata, I cannot tell. Many arguments have from time to time been brought forward to support the view that there is an accumulation of some toxic substance in the organism of epileptics, which has the effect of producing the condition of "charge." (See part of this book devoted to experimental results.) The blood and excreta of chronic epileptics has been examined, and different workers have ascribed the fits to different toxic compounds which they have found in them. Krainsky considers carbamic acid as an important toxic substance, but this is denied by Hoppe.

Bisgaerd and Noervig found an accumulation of ammonia in the blood of chronic epileptics and considered this to be the toxic substance. Donath thinks choline the convulsant factor; this is not confirmed by Handelsmann. Rivano, Alessian, and Heinrich regard a phosphorus compound as the toxic agent; this is denied by Buck. Haig and Tintemann and Loewe agree in finding the cause in uric acid; but this also is denied by Putnam, Pfaff, and Mainzer. Bickel ascribes the condition to bile sulphates. Lately, attention has been directed to the diminished alkalinity of the blood or, better still, the inconstancy of the acido-basic equilibrium (Bigwood§) which is productive of enhanced irritability. Such a condition has been described by Elsberg‖ and Stookey for absinthe and anoxæmic fits.

Cuneo and Osnato¶ suggest that in epileptic patients organic acids are formed from the starches which are not properly alkalinised and detoxicated, but Goldbloom and Lennox** and O'Connor Wright, with a protein-carbohydrate diet, found no confirmation of this supposition. Kennedy supposes carbohydrate fermentation occurs in the intestine.

Ceni, Cololian, Meyer and Masoin found the blood-serum of epileptic patients, taken just before a fit, would produce epileptic symptoms if injected into dogs. Mairet and Ardin Delteil found the same result from the sweat of these patients, if taken just before a fit. This result was questioned by Hebold and Bratz. Agostini, Galdi, Tarugi, and Tramonti found the urine of epileptic patients toxic at certain periods.

These researches on the metabolism in epileptic patients have been directed to establish the presence of some chemical change demonstrable in the blood or excreta before and after a fit. Rohde, Allers, Guidi, Guerri, and Kaufmann found the secretion of uric acid diminished before a fit, but increased after. Rodiet was further able to detect the increase of indoxyl sulphuric acid before a fit. The recent researches of de Crinis on the chemical and corpuscular change in the blood before a fit are important and suggestive (see p. 259).

* Masoin, "Mémoires couronnés de l'Académie Royale de Belgique," 1904.
† W. Harryman and S. Donaldson, *Journ. Amer. Med. Assoc.*, 1923, p. 813
‡ Armstrong, *Practitioner*, 1926, November, p. 288.
§ Bigwood, *Annales de Médecine*, 1923, vol. xv., p. 24.
‖ Elsberg and Stookey, *Arch. of Neurol. and Psych.*, April, 1913, p. 6.
¶ Osnato, *Arch. of Neurol. and Psych.*, April, 1913, p. 491 or p. 1191.
** Lennox, *Journ. Amer. Med. Assoc.*, 1923, p. 1138.

Buscaino made an observation of value when he pointed out that the Abderhalden reaction of the blood-serum of epileptics with the thyroid gland of an epileptic is better marked than in the case of non-epileptics.

§ 4. **Hypoglycæmic Convulsions caused by Insulin.**

In Part I. of this book the effects of bromide of camphor and essence of absinthe on cats were discussed. It was pointed out how the administration of these drugs produced myoclonic reflex phenomena and fits. The effect of the fit was to dissipate the condition or state of intoxication. If the poisoning had been carried too far, and the animal was moribund, it could often be revived by the administration of hot milk and the application of hot bottles. When the recovery reached a certain stage, the animal had a fit. For a complete or discharging fit, which has been shown to be so beneficial to an animal under the influence of the drug, the entire central nervous system must display normal conductibility.

All these phenomena may be seen in rabbits who have developed hypoglycæmia with insulin. In the case of fits caused by bromide of camphor, the slower course of the fits resembles the epileptic fit as seen in man. The striking feature in the case of fits due to insulin is the rapidity with which they disappear when glucose is given.

Insulin causes the removal of glucose from the tissue cells; sugar is, therefore, lacking from the blood, for the liver and muscles cannot immediately transform the glycogen to glucose. The administration of glucose has the immediate effect of stopping the fits. It is only *glucose* which has this effect; neither maltose nor saccharose has the same effect. In animals quite collapsed after the administration of large doses of insulin, the injection of a solution of glucose has the same restorative effect as heat and the introduction of hot milk into the stomach in the case of bromide of camphor (Noble, O'Brien). In both cases the first sign of recovery is a fit. It is the same where a person is resuscitated after being nearly drowned or dug out of deep snow. The recovery from almost complete suffocation may be heralded by a fit (pp. 276 and 307). There is a wide degree of individual variation shown between the amount of blood sugar present and the development of fits. Most rabbits will exhibit fits with a blood-sugar of 0·045 per cent., but sometimes fits occur when the blood-sugar has reached approximately its normal figure. Further, after repeated administration of an experimental drug, the animal may develop what might be termed an aptitude for fits; that is, certain toxic substances, previously inert, may become active in the sense of causing fits. It is not yet known whether an animal may continue to have fits long after all experimental interference has ceased (compare § 5, p. 284).

According to Macleod, rabbits grow less and less prone to convulsions after continued experiment.* Further, complete myoclonic fits develop under the influence of either insulin or bromide of camphor, only if the animal be well fed, where there is a relatively slow fall of the blood-sugar percentage (for insulin), and where the central nervous system is intact and functioning normally.

In exhausted or starving animals, atypical fits occur. Where the blood-sugar percentage goes below 0·045 per cent., a dazed and comatose condition ensues instead of a fit.

The insulin fits in rabbits are of a twofold character. They are either typical myoclonic fits, preceded by strongly enhanced myoclonic tactile and acoustic reflexes, or the prodromal symptoms are wanting, and after a short period of dazedness a fit characterised by a wild jumping movement ensues. Rolling movements towards one side and conjugate deviation of the eyes are frequently found. The deviation is generally always to the same side. This conjugate deviation of the head and eyes to one side is frequently seen at the beginning of epileptic fits in men and animals. Some authors (Marie and Benders) suppose this is due to some actual lesion of a nerve tract; there is no proof of it. It is, I hold, due to an asymmetrical manifestation of normal impulses from the vestibular centres. The same is seen in patients under a narcotic, and it disappears as consciousness returns (Banting, Best, Collip, and Campbell).

Yet the observation of Russell Brain† on the reduction of the response of the labyrinth to caloric tests in hypoglycæmic animals tends to show that the labyrinths are affected by the activity of the medullary convulsive centre. This may be due to the proximity of these structures to the posterior longitudinal bundles. Sordelli and Houssay,‡ in their work, support this observation. Frank§ suggests that hypoglycæmic convulsions occur when the sugar content in the ganglion cells of the mesencephalon falls below a certain figure.

Macleod compares these convulsions to those described by Baranyi, as occurring in rabbits after violent rotation. L. Hill, who also investigated this type of fit, considers that it is due to cerebral anæmia caused by the centrifugal movement, and that the beneficial effect of the fit rests on the re-establishment of intercranial blood circulation. Macleod further points out that in the condition of asphyxia the blood-sugar rises more rapidly than in any other circumstance, and suggests that insulin prevents hyperglycæmia, by means of the fits, which induce the condition of asphyxia. In later writing on the subject, he suggests that the fits may be due to a failure of the

* J. R. Macleod, *Physiological Review*, 1924, vol. iv., p. 31.
† Russell Brain, *Quarterly Journ. of Exp. Physiol.*, 1926, vol. xvi., p. 45.
‡ Sordelli and Houssay, *Comptes Rendus de la Soc. de Biol.*, 1923, vol. lxxxix., p. 744.
§ Frank, *Verhandl. Deutsch Gesellsch. f. Inn. Med.*, 1924 ,p. 126.

oxidative processes in the nerve cells, but remarks that placing the experimental animal in oxygen does not relieve the symptoms.

In man, insulin intoxication also manifests itself in two different ways. In one, the reflexes are exaggerated and convulsions occur. Where the blood-sugar stands at 0·07 per cent., it is more usual to find psychic symptoms appearing accompanied by exaggerated reflexes. These symptoms may be classified as general tiredness, anxious emotionalism, developing into definite vaso-motor disturbances ending in delirium, stupor, and coma (compare Part III., Chapter XI., § 3, p. 303).

The mechanism by which a fit restores the blood-sugar content is as yet not fully understood. Much suggestive work on the subject is being carried out in the Toronto laboratories. From what is already known of this work, it seems extremely likely that much light may be thrown on the whole subject of epilepsy.

Olmsted and Logan,* in experiments on rabbits, were able to demonstrate that the condition of asphyxia would double the blood-sugar content within a few minutes. Therefore the brief asphyxia associated with the fit may serve this useful purpose. Macleod points out that certain animals are not restored with a fit, but remain "depressed." This seems an analogous condition to that found in certain cats after treatment with bromide of camphor. A similar condition also occurs in some patients with status epilepticus, where they develop the so-called status psychicus.

Referring again to the work of Olmsted and Logan, these investigators pointed out that the blood of cats treated with insulin, more especially those with a low blood-sugar content, was dark in colour and coagulated easily. This held good for both the normal and decerebrate cat. If this observation could be verified for other animals, it would suggest that the condition of anoxæmia was a condition immediately associated with the fits. In this case insulin fits would form part of the great group of fits due to anoxæmia (see Part II., Chapter II., § 2, p. 276) (Laqueur, Grevenstuk, and de Jong).†

The next question is, what is the effect of the various operative procedures on the fits? After decerebration it is possible to produce fits complete in all respects except for the salivation and characteristic cry.‡ The fits do not occur so regularly as in normal animals. Probably this may be in part due to the hypophysis being out of action. In my own experiments with bromide of camphor the results were much the same, decerebration was associated with loss of regularity in the fits.

Where the cat was decapitated, no complete fit was observed. This is in agreement with the result I got with cats where the spinal cord was isolated. Whether a modified myoclonic reflex movement may be elicited in such cats, as it was in the case of my own experimental animals, is as yet unknown.

Great attention is being paid to insulin, on account of its

* J. Olmsted and H. Logan, *American Journal of Physiology*, 1923, vol. lxvi., p. 440.

† De Jong, while laying stress on the lack of parallelism between the sugar lowering and the convulsive capacity of insulin, admits a relative independence of these two effects.

‡ A decerebrated cat will show genuine asphyxia fits if the larynx be temporarily blocked with mucus.

practical importance as a therapeutic, and from the general mass of information certain definite facts may be elicited. These facts bring the actions of insulin and bromide of camphor very fairly into line. They are as follows:

1. With insulin, as with bromide of camphor, the tendency for an epileptic discharge is greatest at the moments of wakening or of falling asleep.

2. Animals moribund after the administration of bromide of camphor may be revived by heat and the administration of hot milk with the stomach tube, and display as the first sign of recovery a well-marked fit. The same phenomenon is seen in the case of an animal moribund after insulin, and resuscitated with glucose; the recovery of consciousness is again attended by a fit.

3. Where a patient has been rendered unconscious by some accidental process involving almost complete asphyxiation after resuscitation by artificial respiration the return to consciousness may be marked by a fit. The same phenomenon is sometimes seen in a patient emerging from narcosis.

§ 5. The Etiology of the First Fit.

The examination of the patient with a view to ascertain, if possible, what factor caused the first fit, is of great practical importance, as well as of scientific interest. Experience shows that the same hurtful influences which first broke down the resistance of the patient are frequently of importance in the later history of the case.

Such an examination is helpful to both the patient and physician, for, like Redlich, I cannot agree with the view taken by Turner, Hauptmann, and Binswanger, that the first fit in genuine epilepsy has no immediate incidental cause. The influence of infantile convulsions on the occurrence of epilepsy has already been fully discussed.

For infectious diseases it might safely be said that any one of them might serve as the starting-point of epilepsy. Certainly this is the case in more adult life. The fits usually appear during the convalescence. Probably epilepsy follows more frequently after scarlet fever, pneumonia, typhoid fever, influenza, and malaria, but cases occur in association with septic disorders, such as erysipelas, pellagra, herpes, or even vaccination. As a general rule, a chronic epileptic has an alleviation from the malady if he has an acute illness, fits rarely occurring when the temperature is raised. Indeed, in some cases, the condition of the patient is distinctly better after an acute illness. Turnowsky* went so far as to say that such an improvement of the malady was most frequent after pneumonia or scarlet fever. At the same time,

* Turnowsky, *Wiener klin. Wochenschr.*, 1901, p. 35.

rare cases do occur (I have seen two) where the fits occurred right through a severe and acute illness such as typhoid.

Where an hereditary history has been established, it should not be at once assumed that no provocative cause need be looked for. P. Marie* points out how often in such cases the occurrence of encephalitis in extreme youth can be established. Marie suggests that there may be no real difference between genuine and organic epilepsy. Marie's pupil, Lemoine, goes further, and ascribes all febrile convulsions, occasional convulsions, and even convulsions associated with lead-poisoning, to some hypothetical focus in the cerebrum. The assumption, including as it does fits associated with lead-poisoning, seems too comprehensive, for it is well known that such fits are alleviated, if not cured, by the prevention of further ingestion of lead.

Sachs, Peterson, Redlich,† and Stier are also inclined to ascribe a cerebral focus as the cause of slight manifestations of epilepsy, where there is not nearly sufficient evidence to justify such an assumption. Schott‡ gives the dictum that 24 per cent. of all epileptics have a definite cerebral lesion. This dictum has not yet been proved, but there is a certain amount of evidence in favour of its being correct. Personally, I am more inclined to agree with Voisin, who suggests that certain toxins may accumulate in the body during an acute illness, and that they may affect the medullary centres, probably increasing their irritability, and so paving the way for the appearance of fits.

Sunstroke and Life in Tropical Countries.—It would be considered highly probable that sunstroke associated with residence in tropical countries might be the cause of a fair proportion of cases of epilepsy. In my own experience I have not found this to be the case. Indeed, one case I had was a man who, at the age of 19, had severe epileptic fits; at this age he went to India, where he stayed for twenty-three years. During the whole of this period he had no fits, but when he returned to Holland he again had fits. It is interesting to find that van Swieten also records a similar case. At the same time there is no doubt that residence in a hot country does, in some cases, cause rapid deterioration.

Reflex Epilepsy.—In the last half of last century a great deal of literature appeared dealing with reflex epilepsy. First were the cases of Virchow and Billroth (referred to by Gowers), where injury of a peripheral nerve was associated with epileptic fits. After a suitable operation relieving the condition the fits ceased. Later cases were recorded where the reflex epilepsy was

* Marie, *Progrès méd.*, 1887, p. 47.
† Redlich, *Jahrbüchr. f. Psych.*, 1909, p. 287.
‡ Schott, *Jahrbüchr. f. Kindesspiele*, 1919, vol. xc., p. 3.

associated with injury to the eye, ear, nose, teeth, stomach, or genitalia. An attempt was made to establish this reflex epilepsy as a separate entity clinically. As time has gone on this idea has become less prominent. In my own series of 2,000 cases there is not one which is of necessity relegated to this category. The cases described by other workers, such as those given by Ormerod* and Randall† as due to intestinal parasites, or Binswanger's cases associated with nasal polypus, errors of refraction, or gynæcological abnormalities, are regarded with more and more caution, if not scepticism. At the same time, some peripheral irritation, pain, or lesion may, in the case of a predisposed person, be the incidental cause of the first fit.

Attention may here be drawn to an error not infrequently made in connection with so-called reflex epilepsy. It is sometimes said that reflex epilepsy may follow from irrigating the pleural cavity with a carbolic lotion. This is quite incorrect; such a condition has no association whatsoever with reflex epilepsy (compare p. 216). Further, such a case as that recorded by Landeesen, where the stretching of a peripheral nerve under an anæsthetic was associated with a fit, might belong to the same category as the epileptic fit which sometimes appears in a perfectly healthy person when under an anæsthetic, where no reflex irritation exists.‡ The cases described by Rueff§ and Kompe‖ seem to me to belong to the same class.

In this connection it is also interesting to refer to the work of G. Amantea. He points out that after the application of nitrate of strychnine to the motor centre of an extremity a painful stimulus to that extremity is liable to call out an epileptic fit. He suggests that in certain individuals the threshold is so low that they are predisposed to reflex epilepsy.

Bubnoff and Heidenhain also record cases where a very slight stimulus, such as blowing on an extremity, may enhance the irritability of the motor centres. G. Holmes¶ explained the beneficial result which frequently follows in Jacksonian epilepsy when the limb in which the fit starts is bound as a reflex influence.

It seems highly probable that so-called reflex epilepsy belongs to the same class of phenomena as the Brown-Séquard epilepsy. This is a convulsive phenomenon elicited by stimulation of the skin over a certain area in guinea-pigs after an operation involving

* Ormerod, *Brain*, 1884, p. 20.

† Randall, *Am. Journ. of Med. Sciences*, 1905, vol. v., p. 53.

‡ Cohen, *British Medical Journal*, 1920, vol. i., p. 526.

§ Rueff, *Revue de Médecine*, 1903. A patient with cardiac disease, cured of epilepsy for many years, had a fit immediately before death.

‖ Kompe, *Neurologisches Centralblatt*, 1897, p. 312. Where a healthy person was resuscitated after being almost hung, a severe epileptic fit coincided with recovery of consciousness. Later severe psychical epilepsy developed.

¶ G. Holmes, *Lancet*, 1927, vol. i., p. 958.

a peripheral nerve. These convulsions are the reflex after-discharges of flexion reflexes.

Lesions of Central Nervous System.—As regards lesions of the central nervous system it is common knowledge that extensive lesions in the brain, wherever they may occur, may produce epilepsy by means of increased cerebral pressure (compare p. 398). In older persons increase of the blood-pressure in the brain, associated with hæmorrhage, may also produce epileptic fits.

No cases of epilepsy are known, associated with lesions limited to the pons, the subthalamic region, or the corpora quadrigemina, with the exception of the case of hæmangioma of the pons-tegmentum reported by Clingenstein. The cases reported by Luce, von Winkler, and de Vries* of alternating epilepsy associated with pontine lesions are not epilepsy. On the other hand, it is not uncommon to find in persons who have had an encephalitic lesion in youth near the red nucleus epileptic fits affecting one side of the body, while the opposite side of the body shows arrest in growth (Wallenberg,† Halban and Infeld,‡ Marie and Guillain,§ and Ceni).‖

Epileptic fits do occasionally occur in association with disease of the spinal cord. I have seen it in cases of tumour and myelitis. Cases also appear in literature (Leblois, Oppler, Tuffier, Hallon, and Dumesnil), although Westphal and Leyden are both doubtful on the subject.

Occasionally, epilepsy may be due to fracture of the spine; in this case the epilepsy belongs to the class associated with fractures of bones. Epilepsy seems to follow mostly after fracture of the spine or the femur. Notes of such cases are supplied by Calot and Celsus. Aberle is inclined to ascribe such fits to fat embolism, but Tilanus points out that they may occur after orthopædic operations. He records a case of a child of five who developed epileptic fits after the application of a plaster of Paris bandage; the fits stopped when the dressing was removed.

Trauma at Birth.—Féré, Binswanger, and Volland ascribed this as the cause in 45 cases out of 1,500. Thomson gives a higher percentage. Up to the present time there is not sufficient evidence forthcoming to allow of any definite dictum being given on the subject.

Gowers found that the oldest child in a family most frequently showed trauma due to injury at birth; the cases recorded

* De Vries, *Neurologisches Zentralblatt*, 1913, p. 310.

† Wallenberg, *Archiv. f. Psychiatrie*, 1888, vol. xix., p. 97.

‡ Halban and Infeld, "Arbeiten a. d. neurol. Inst. d. Wiener Univ.," 1902, vol. ix., p. 329.

§ Marie and Guillain, "Nouvelle Iconografie de la Salpétrière," 1903, p. 78. ‖ Ceni, *Riv. sperim. di freniatr.*, 1898, vol. xxiv., p. 126.

by Volland* also demonstrated this fact. It is remarkable that among those cases of trauma due to difficult birth there are about twice as many male cases as female.

Epileptic Fits due to Intermissions of the Pulse (Stokes-Adams syndrome).—Intermission of the pulse beat is nearly always due to defective conduction between the sinus and auricles, or between the auricle and ventricle, whether the failure of conduction causes pulsus regulariter intermittens, or where the conduction is definitely interfered with, and the autonomous rhythm of the ventricle has not yet supervened. It will be recalled that the occurrence of the pulsus regulariter intermittens was demonstrated experimentally by me to be associated with the slow restoration of conduction.†

In one case I had of a young woman, loss of consciousness and convulsions occurred each time the pulse missed three beats. Huchard observed the same syndrome of symptoms in a case of arterio-sclerosis of the medulla. Belski thought that such cases were associated with the presence of extra-systoles, while Rosenthal noted epileptic convulsions in animals treated with drugs producing lengthened diastole. Carducelli produced epileptic fits experimentally by pressure on the vagus nerve, and alleviated the symptom by giving atropine.

It seems quite definite that a sudden interference with cerebral circulation is the immediate cause of these convulsions. Gowers regarded such a sudden intermission as equivalent to a blow on the head. Apart from intermission of the heart beat, an insufficient supply of oxygen may be a potent factor in producing convulsions (compare p. 276).

A. E. Russell described the occurrence of a severe fit after a longer intermission of ventricular systoles and a slight fit after a shorter intermission.‡ He further suggests that cerebral anæmia is always associated with epileptic fits.

The association of cardiac irregularity and convulsive phenomena is fairly familiar. I had a case of a boatman from Egmond aan Zee, where the cardiac irregularity was associated with brief absences and slight convulsions. I found from their medical attendant (Dr. Schipper) that a brother and cousin of the patient had the same symptoms. There was no history of hereditary epilepsy, but there had been much intermarriage, and degenerative stigmata were common.

* Volland, *Zeitschrift f. Psychiatrie u. Nervenkrankh.*, 1906, vol. lxiii., p. 735.

† Muskens, *Geneeskundige Bladen*, 1897, No. 4, p. 77.

‡ A. E. Russell, *Lancet*, 1906, No. 4,325.

CHAPTER X

DIFFERENTIAL DIAGNOSIS OF EPILEPSY

Early Appearance of Functional or Hysterical Symptoms in Addition to the Epileptic Objective Phenomena in the Inter-paroxysmal Periods. Characteristics of Jacksonian, Hysterical and Menière Fits.

WHERE epilepsy has been present for some time, and where the symptoms are more or less definitely established, the diagnosis of the disorder is as a rule easy. It is in the early stages, where the symptoms are slight and elusive, that the diagnosis may be as difficult as it is important.

From the point of view of prognosis it is of the utmost importance that cases should be diagnosed early, and put under treatment. Epilepsy, undiagnosed and therefore untreated, is frequently an amazingly progressive disease. The whole life of a patient may be altered and his usefulness destroyed for lack of accurate observation and knowledge in making an early diagnosis (compare p. 383).

Further, it is of the utmost importance that the habit of having fits should not be established. It is a fact that each fit a patient has predisposes him to have another.

Where the physician is thoroughly acquainted with the various symptoms and phenomena which herald this disorder, he is frequently able to gather very useful and important data from the account of the case furnished by friends of the patient, especially where some practical method of case-taking is adopted (p. 322).

As is well known, the laity are notoriously poor and inaccurate observers, but frequently the history of the case, as related by a friend, is all the physician has to start with.

From this history the physician may be able to recognise certain phenomena, such as myoclonic shocks. Further, it may transpire that these shocks occur most frequently at certain definite periods in the daily cycle, and also that they become more marked before a fit. It may be that other symptoms are described, such as headaches or the occurrence of fainting fits, when the patient may escape a fit. The phenomenon of compensation (pp. 18, 33, 42, 48, 49, 211, 243) was noted by Gowers* for migraine. An error in dietary some weeks after an attack provoked a second attack, whereas the same error committed immediately after an attack had not this effect. Certain facts may come to light which may help in the diagnosis—as, for example, that the patient had infantile convulsions, or that there

* Gowers, *British Medical Journal*, July, 1909, vol. i., p. 1401.

is a history of epilepsy in the family. Where the history is elicited very carefully, there is no doubt that it affords help to one well acquainted with epilepsy, but great caution is always needed. At best, such a history is rarely, if ever, sufficient for a diagnosis, but it is at least suggestive, and should never be completely neglected. The only absolutely safe basis for diagnosis is personal observation of the patient over a prolonged period by a nurse, especially trained in observing and recognising epilepsy.

It must not be forgotten that the early stages of epilepsy frequently escape notice because no one knows about the fits. The fits, which are in all probability slight, may occur when the patient is not under observation, and as he himself is unconscious he naturally does not know he has had some kind of a fit.

It is not at all unusual for patients to consult a physician for some subsidiary symptom, such as tachycardia, exhaustion, a tendency to hysteria, or some neurasthenic symptom. Unless the possibility of the patient being an early case of epilepsy is not lost sight of, it is very easy to miss the real trouble.

In all cases where patients complain of vague functional disorders, great care should be taken to exclude epilepsy. It is true that many such patients are not epileptic, but there is no doubt that the early stages of epilepsy are frequently missed.

The results to a patient of such a mistake are so serious and far-reaching that no apology is offered for emphasising the importance of definitely excluding epilepsy in the case of patients with vague general symptoms.

Occasionally the history of a case may furnish important, and indeed conclusive, details. If, for example, one is told that a patient has bitten his tongue in a fit, or falls and injures himself, or that hæmorrhages appear in the conjunctiva, one may be fairly certain that the case is one of epilepsy. At the same time all these symptoms may be absent, and yet the case be one of epilepsy. Sometimes help may be got from a knowledge of the rate of the convulsions. In epilepsy the convulsions are rapid, 12 to 15 per second; hysteria never shows this rapidity. Further disturbances of sensation to pain with segmental distribution and the changes observed in the affected areas (pp. 211, 244, 262) are very important if present.

If the diagnosis of epilepsy be established, the next important thing is to ascertain as soon as possible after the fit the immediate cause of the fits.

This needs very careful investigation. Sometimes it is found that a patient is liable to have a fit after a certain article of diet or after some emotional excitement. The cause may be so closely interwoven with the patient's daily life that neither he nor his friends would light on it unaided.

If it is possible to find out the history preceding the first fit, much may be learned. If some definite fact can be brought to light, such as an excess, physical or emotional, or some shock, fright, or exhausting process, it may serve as a guide for prophylactic treatment, the argument being that a certain combination of circumstances broke down the patient's resistance, and that it is highly probable that a repetition of these circumstances will more readily induce another breakdown.

The personal history of the patient, apart from the history of the present illness, must be carefully investigated.

The presence of organic disease, the chances of some form of intoxication, such as alcohol, lead, etc., and the influence of certain physiological conditions, such as pregnancy or the approach of menstruation, are all important. The fact whether the patient had or had not infantile convulsions is always important.

Great care must be taken over the family history and the hereditary presence or absence of epilepsy established where possible.

In many cases the patient is brought for examination after epileptic fits have been recognised for some time.

Here the symptoms are not nearly so elusive. The characteristic frontal headache above and behind the eyes generally occurs between the attacks, and also is a prodromal symptom of a fit. This headache (p. 266) is frequently a great trial to patients, and they complain that no remedy does any good, but if they can sleep for even a short period the pain is gone when they awake. Sometimes, although rarely, migraine is a troublesome symptom. Curiously enough, migraine is often present in the parents of epileptics. Kowalewski,* Rockford, Haig, and Lambrani, all admit a certain relationship between the two maladies. Apart from this is the curious symptom of regional analgesia, with its segmental distribution (p. 245). The danger which is always pointed out is that of mistaking hysteria for epilepsy. This is a danger which is exaggerated; it is more common to find epilepsy mistaken for hysteria. It must be remembered that in an epileptic patient one is very likely to find hysterical symptoms. One might even go so far as to say that epilepsy is never quite dissociated from hysteria. Indeed, it is very common to find cases of genuine epilepsy complicated by hysterical symptoms.

This fact in itself is a strong argument why no case of "fits" should be finally diagnosed without most careful and prolonged observation and analysis.

This is not the place to enter into a prolonged discussion on the different forms hysteria may assume. It is a curious fact that hysteria has in a sense a national character. For example, the grotesque cases seen in France are never met with in clinics of

* Kowalewski, *Archives internat. de Neurologie*, 1906, vol. xxi., p. 364.

colder countries, with a more lethargic population, while the Jewish nation, as is well known, possesses the hysterical diathesis to a marked degree. One pitfall does exist for the unwary physician, and that is that hysteria may, and does, occur in children and in men. This fact seems not to be properly appreciated.

At one time, the differential diagnosis between the two maladies was based on the condition of the pupil, but the work of Karplus,* Steffens,† and others has shown that this is not a sure guide. The absence of the corneal reflex is, however, very strong evidence in favour of epilepsy.

At one time the effect of treatment was regarded as being diagnostic, the hysterical patient reacting rapidly to heroic treatment, while the epileptic patient remained quiescent. Gowers has shown this to be fallacious, at least to a certain extent, for the hysterical taint in genuine epilepsy may lead to confusion. (Binswanger points out that in degenerated families cases of mixed epilepsy and hysteria are prone to occur.)

It must be remembered that not only is it necessary to differentiate between the epileptic fit and the hysterical fit, which may occur in the same patient, but the fits themselves must be carefully analysed to ascertain whether they are of a dual character, and if so, which part of the fit is hysterical or functional, and which epileptic, in nature.

When called in for the first time to a patient in a fit, it is practically impossible to make a definite diagnosis. The symptoms are noted, and a probable diagnosis arrived at; this is the most that can be done. Given a patient who falls down suddenly in a fit, the condition may be due to a number of causes. If the case be one of apoplexy or cerebral hæmorrhage, the diagnosis is generally evident in a very short time. It must, however, be remembered that Monakow, Nonne (p. 144), and other authorities have shown that it is not uncommon to find unilateral symptoms in genuine epilepsy. Care is, therefore, necessary before concluding that the cause of the fits is some cerebral lesion or tumour.

If the patient be found lying collapsed and pale and unconscious, the condition closely resembles an ordinary fainting fit. The condition of the pulse is a useful guide, for in syncope or severe fainting fits the pulse cannot be felt, whereas in epilepsy the blood-pressure is not diminished.

Sometimes one finds petit mal associated with ordinary fainting. One case I had displayed the first symptom of petit mal after a fainting fit induced by fatigue (p. 253).

In Jacksonian epilepsy the fits begin with clonic convulsions,

* Karplus, *Jahrbucher f. Psychiatrie*, 1901, vol. xvii., pts. 1 and 2.

† Steffens, *Archiv f. Psychiatrie u. Nervenkrankh.*, 1900, vol. xxxiii., p 892

and consciousness is usually lost much later on than in genuine epilepsy. In some cases, consciousness is retained throughout the fit, and may go after the fit is over. Great care is needed in making the diagnosis, for genuine epilepsy may be, as already pointed out, unilateral, while a long-standing case of Jacksonian epilepsy may present many or all the symptoms of genuine epilepsy. Although the propagation of cortical stimuli to the medullary pontine centres is at first slow, in traumatic cortical epilepsy of long standing it is almost instantaneous (Case No. 1, Ch. XV., § 2).

The succession of convulsions—first tonic cramp, which dissolves into rapid convulsions and finishes with steadily increasing *simultaneous* convulsions of all extremities, while at the same time the intervals between the convulsions increase, then the stage of stertorous breathing, of automatic movements, headache and dizziness some hours after—from these phenomena one may draw the conclusion that the medullary cramp-centres are involved, and a genuine epileptic fit is present. If, after an initial cramp of first one extremity or one-half of the face, then one-half of the body is involved, especially if the loss of consciousness comes on deliberately later in the fit when convulsions become general, the evidence pleads strongly for the focal nature of the discharge.

These signs show the transition from the focal cortical convulsions to the ponto-medullary centres (Part II., Ch. V., and Part III., § 10); also it must be recalled that it takes some time before the fits settle down to a certain definite form of discharge.

Relatively frequent are the cases of tumor cerebri, with general convulsions, in which the nature of the disease is cleared up much later by ocular disturbances and paralysis (compare Ch. XV., § 13).

The diagnosis from Menière's Disease is not so difficult. In the fits associated with this disease, the loss of consciousness is incomplete, or, in most cases, absent. There are no interparoxysmal symptoms, while the psychical symptoms are lacking. In addition, there are also the signs and symptoms of disease of the middle ear. Attention must, however, be called to the observation made by Gowers, who had several patients in whom vertigo and epilepsy alternated. The question arises whether the proximity of the vestibular and convulsive centres in the medulla may explain this phenomenon.

Where the diagnosis is required for life insurance purposes, each case has to be judged on its own merits. The debatable point is what should be the attitude towards children of epileptics offering themselves for insurance?

As a general rule, persons do not offer themselves for insurance until grown up, and where a child of epileptic parents has attained adult life without developing epilepsy his chances of developing

it later are reduced by 50 per cent. from those which overshadowed him in childhood and adolescence.

The Examination of Tram and Automobile Drivers.—It is a fact that in these days of congested street traffic passengers do run a certain risk should the driver have an epileptic seizure. It is of course true that other conditions, such as cerebral hæmorrhage or cerebral tumour, could also cause, in some cases, a sudden and complete collapse, while other maladies, such as renal disease and diabetes, are also associated with the development of sudden unconsciousness. Most conditions other than cerebral hæmorrhage and sometimes cerebral tumour can be practically ruled out as danger factors to the travelling public, as the other symptoms and the general ill-health of the patient conspire to set him aside from the active world. Cerebral tumour and general paresis I have found not to be infrequently missed in medical examinations, and accidents have occurred where the patient has sought medical advice and been treated for a symptom, the causal condition being unsuspected. The patient, therefore, continued to drive until the unhappy catastrophe occurred. Although this is true, no malady causes anything like the same number of accidents as epilepsy. The fact that a man may be suddenly incapacitated by a fit is more or less generally recognised, and on some train services it is the custom to have a second man capable of carrying on should the driver be incapacitated. Something of the same kind is arranged in some of the passenger aeroplanes.

The practical question is what can be done to lessen or remove this risk undoubtedly run by passengers. The ideal way would be to have two drivers on at once, one to relieve the other, but this is not practical for many reasons. A second suggestion that the tram or car should stop at once when the man ceases to press the steering wheel is useless, because in many lesser fits there may be practically no change in the pressure on the wheel—indeed, the automatic stage of the fit is more likely to induce a cramp-like grip on the wheel.

The practical way seems to me to lie in examining candidates for the posts of tram or automobile drivers, not only on general medical grounds and in the psycho-technical laboratory (for reaction time, etc.), but especially for epileptiform symptoms. This needs time and training, and could only be done by a neurologist skilled in the recognition of epilepsy. It would be necessary to examine the candidate carefully for physical symptoms, to take an exact family history, and to investigate the presence or absence of any epileptiform symptoms, and for the occurrence of syncope at any period of life. Reference should be made to Part III., Chapter V., for the symptoms which are characteristic or indicative of the possible presence of hitherto unsuspected epilepsy.

CHAPTER XI

FAINTING FITS AND PSYCHISMS

§ 1. Atypical Incomplete Discharges or Phenomena which may be regarded as such. The Substitution of Sudden Loss of Conscious Volition or Psychical Phenomena for the Typical Epileptic Fit.

It has been made evident from the experimental work on cats that a certain discharging influence is exercised by myoclonic reflex shocks and reflex after-discharges. It is not uncommon to have a condition of discharge brought about in cats after administration of bromide of camphor by a series of reflex shocks associated with little or no loss of consciousness. The same drug used in man often causes a violent motor fit associated with a transient fit of maniacal excitement (see Purkinje's experiment on himself, p. 11), followed by amnesia. Where all these symptoms do not appear, camphor bromide generally causes a severe convulsive fit. In cats dosed with bromide of camphor the whole development from the enhancement of the reflexes to the complete epileptic fit can be observed.

As a rule this is not the case in man (or the period of enhanced reflexes passes too quickly for observation), the process being much quicker, the violent fit supervening practically at once.

Epilepsy as a disorder is subject to many variations. It is not at all unusual to find cases where the convulsive element is quite lacking or very slight. In such cases psychical disturbances of longer or shorter duration may form the entire clinical picture.

In this connection it will be remembered that in the cats treated with bromide of camphor some animals had no fits, but reacted to the drug by being sick for several days, or by developing a dazed condition and behaving in an unusual or abnormal manner (pp. 67, 282).

Phenomena comparable to petit mal as observed in man are unusual in animals, but cases do occur where an exhausted cat displays fits in which convulsive movements are absent but where dilatation of the pupils, dazedness, and enuresis are present. It has already been pointed out (p. 67) that this dropping out of the most characteristic feature of the myoclonic fit finds a parallel in other aspects of neuro-muscular physiology. It is interesting

to find that cats show distinct evidence of hallucinations in the automatic stage of the fit.

It is very difficult to give a satisfactory definition of the condition "absence" (unconscious volition): it may present so many different degrees or phases. The most constant symptom is *loss of consciousness*. Yet it is no uncommon thing to see patients pass through an attack without ceasing from their occupation. For example, a cyclist may continue cycling throughout an attack, while another may continue to play the piano. A barber has even been known to continue to shave a customer throughout such a phase.

Next in frequency are changes in colour and dilatation of the pupils. More rare are such phenomena as salivation, enuresis, or collapse. A fainting fit, or the collapse of the patient, might be regarded as an abortive epileptic fit where only the automatic movement is preserved. Gowers and Martin* suggested that cortical inhibition was the fundamental cause of this dropping out of motor phenomena.

Indeed, in many of these "absences" automatic movements, such as chewing, picking movements, acts of dressing or undressing, may be continued. In petit mal, or in a true fainting fit, on the other hand, it is rare to find any sort of movement entirely missing (compare p. 243).

Another variety of atypical fit is one where tonic convulsions occur.† This is associated only under certain circumstances with clonic convulsions.

Case No. 44, X., age 23 years. Patient was the daughter of a skipper. She had had headaches from her early youth. At the age of 10 she fell into the water. During her second pregnancy she had fits which persisted after her confinement. For the first two years these fits took the form of a muscular stiffness associated with loss of consciousness. If she were over-tired clonic convulsions were associated with the tonic fit. Her two youngest children had occasional convulsions.

In other cases an atypical fit may consist of a long spell of unconsciousness, convulsions occurring only at the end of this period. In many cases, this means that the disorder is in process of complete manifestation, and has not yet subsided into a definite form of discharge. The premature use, and abuse, of bromide probably plays a role in such a case.

Case No. 45, V., age 13 years. Patient was always a backward child. At the age of 10 he was over-exhausted and had fits on three different occasions. These fits consisted of loss of consciousness without convulsions or any stiffness. Later the fits were associated with tonic

* S. P. Martin, *British Medical Journal*, 1926, vol. i., p. 760.

† P. Clark, *American Journal of Insanity*, 1898–99, vol. lv., p. 583; Knapp, *Monatsschr. f. Psych.*, 1919, p. 47; both noted that in all such cases the presence of a lesion must be carefully excluded.

and clonic convulsions. These fits occurred after over-exertion or were due to fright.

Case No. 46, L., age 42 years. At the age of 10 patient began to suffer from migraine and had an attack generally once a week. At the age of 37 myoclonic shocks appeared, and three years later he became subject to changes of moods. Afterwards he began to have attacks characterised by loss of consciousness, followed after a period of about 30 seconds by convulsions. Later he had numerous fainting fits; they finally dominated the clinical picture. Under treatment he got rid of them, but they were always liable to return if he underwent any psychical strain.

Here we have an illustration of *the abortive development of epilepsy*. From the close observation of many cases it would seem probable that these atypical fits are in reality stages in the development of the malady. The phenomena displayed are abortive in type, and represent an effort on the part of the various factors to bring about a regular myoclonic phenomenon. In a sense the patient reacts inadequately and incorrectly to the stimulus, which more usually evokes an epileptic fit or some closely associated reaction.

I have had occasion to notice in a number of cases of epilepsy that fainting fits, or "absences," tend to appear in place of the ordinary epileptic fit when the patient has had prolonged treatment with bromides. Where this occurs, I am inclined to regard these phenomena associated with little or no convulsive movement as artificial products associated with the use of bromide.

The question arises whether in atypical fits, such as the fainting fit, petit mal, or in the "absence," prodromal symptoms occur, as in the case of the typical fit.

Prodromal symptoms do occur before these atypical fits, particularly before the fainting fit. Sometimes the psychical prodrome is more severe than that before complete epileptic fits (Janet, Wiersma).

In some cases these atypical faints not only have very definite prodromal symptoms, but they themselves may be but the aura of a severe fit. This is by no means a rule, but it does occasionally occur.

It must be pointed out that there has been a certain amount of misconception regarding the relation of the fits where there is an association of grand mal and petit mal.

Herpin thought that it was the rule that the small fit acted as an aura to the great fit. Gowers pointed out that this was not the case (compare p. 243). All sorts of gradation of loss of consciousness are met with.

It must be remembered that the atypical fit is very prone to variation. Analysis of established cases shows that at least a score of different forms of atypical discharges may be recognised.

The atypical fainting fit is a form of the malady which is

rarely easy to recognise. The spells of unconsciousness are so short that even when the patient is being closely watched they may be quite missed. All the outward evidence may be that the patient slackens his gait for several paces, or he may speak a little slower for half a sentence, or he may merely appear lost in thought for a moment.

To these automatic movements may be added various psychic elements, such as the mental condition of fear or anxiety, or there may be such physical elements as impeded respirations, tachycardia, or enuresis. In both cases the patient generally has no memory of the phenomena. In some cases a patient or his friends will recognise that he has had a fit because he breathed stertorously.

Petit mal as the only symptom of the disease is rare. I found it only in 21 males and 25 females from among 2,000 epileptic patients. Where it does exist alone the attacks are very numerous, and may continue over a number of years. In some rare cases the mental changes are almost if not quite absent.

§ 2. Dreamy States, Confusion, Stupor, and Mania. Crimes committed in a Dreamy Mental Condition.

It is customary to speak of psychical equivalents where the disturbance of consciousness is of longer duration.

The automatic movements are carried on over a longer period, and are of a complicated nature. The patient may undress himself, or he may display exhibitionism, or he may become extremely combative against certain persons. The post-epileptic irritability finds in the experiments on animals its complete counterpart (pp. 174, 261). The normal character of the patient displays itself in his abnormal acts. Where crime is committed in such a state, the question of the degree of responsibility is very difficult to decide. In this respect Binswanger's case is very interesting.

A young working girl who was in such a dreamy mental state conducted herself so that none of her colleagues noticed anything wrong with her. She went home, and on the way annexed an umbrella from a shop. She had desired this article when in her normal condition, and when abnormal, acquired it. It was, however, very difficult for the judge to understand that the girl was not really responsible for her act.

Where this dreamy mental condition is repeated frequently, or where it lasts over a long period, the peculiar characteristic stereotyped movements seen in epilepsy become apparent. The patient tends to repeat a certain series of acts due to a stereotyped series of associations. This may manifest itself in such acts as fire raising, in kleptomania, and so on.

Something similar to this is seen in those who are under the influence of alcohol. It is well known that some men, when partially drunk, always want to fight the same person, weep over the same melancholy suggestions, or propound the same fantastic schemes.

Anti-social acts are not very often performed in the dreamy state, but probably more frequently than is generally known outside the consulting-room.

As a general rule, the patient subject to this dreamy condition has some prodromal symptoms, such as headache, dilated pupils, or loss of appetite. When the dreamy dazed condition supervenes, the patient has often a disquieting sense of unreality. He loses the comforting normal sense of self-possession. He floats off into an indeterminate mental state, where nothing seems real and his own personality vague and elusive. In this state patients frequently wander away—poriomania or fugues. This wandering is quite apart from the movements described as sometimes occurring at the beginning of an epileptic fit. These latter movements are forced, and are dependent on certain organic lesions, probably in the palæo-striatal centres (p. 254).

Poriomania or fugues are quite often seen in epileptic children. They are often associated with the early use of tobacco by such children. Another variation is that described by Falret* as "petit mal intellectual." In this state the patient feels impelled to do all sorts of unusual acts, more especially does he want to destroy things. In some patients this condition is very persistent, and only relieved by the appearance of ordinary motor fits. Here the abnormal psychical condition is a real equivalent, and compensates vicariously for the great motor fit.

Other patients have symptoms of hallucination, which are always of the same vague character.

One patient had an hallucination of taste as an aura to her fits, and at the autopsy it transpired that there was a tumour in the white matter situated near the posterior part of the corpus callosum. It is interesting to note that, according to Hughlings Jackson, hallucinations of taste and smell are generally associated with tumours in the temporal lobe.

Somnambulism is also a symptom in this peculiar psychic state, just as it is in alcoholism and in hysteria.

The most acute types of psychical equivalents to the ordinary motor fit are the following:

1. *Epileptic Delusional Insanity.*—This may be looked on as an intensifying and lengthening of the period of slight confusion which occurs in all cases of epilepsy between the state of unconsciousness and consciousness. Binswanger, writing on this

* Falret, "État mental des Épileptiques," *Archives générales de Médecine*, 1860, p. 66.

subject, considers that the vagueness and looseness of association characteristic of ordinary nocturnal dreams is also characteristic of this condition. Certainly nocturnal dreams and the events occurring in the dreamy stage of an epileptic attack are both very quickly forgotten.

Probably epileptic dreamy states are always of a fluctuating character—*i.e.*, a slight event may transfer the patient from dreamland to reality. In the case described as No. 7 in Chapter XIV., § 5, for a short time the dreamy state alternated with a clear vision.

This patient came home after wandering for two weeks, because he suddenly found his home address. His wife had, as usual, beefsteak for him when he returned from wandering, because he required substantial food. When eating the beef, he said: "This is not nice; you say it is beef, but it is fish. I could not do better than kill you with this knife." As he took the knife (the first of this sort of attack in twenty years of marriage, during which he had had weekly epileptic symptoms), his wife screamed. His face immediately lost its tension, and he looked quietly at her, and said: "I do not feel very well, please forgive me," and, trembling frightfully, he finished his meal. As usual, after two days of sleep he was perfectly well.

2. *Epileptic Stupor.*—This may last for a long time.

3. *A Maniacal Condition associated with Epilepsy.*—This is a very terrible mania, and many horrible crimes have been committed by patients in this condition.

Unlike ordinary mania, which usually develops slowly, and may last some time, epileptic mania comes on abruptly, runs a short course, and passes off suddenly. It quite frequently develops in a patient who has been in the dreamy condition, but the prodromal symptom may be a headache, or that peculiar condition already referred to as "a glittering glance of the eye." The outbursts are very violent, and in no other form of mania is there such a systematic succession of hallucinations. The horrible crime (almost stereotyped in the newspaper reports) where a murderer is found calmly smoking with the repulsive evidences of his crime still apparent on his person is very probably always due to epilepsy.

Le Grand du Saulle and Féré suggest that such a person, having realised that he has committed a crime, always has some reason for his act. Analysis does, in many instances, show that the victim had annoyed the assailant at some time. It seems possible to explain the outburst clinically by regarding it as a repetition of this condition of annoyance when all inhibitory influences are absent. Clinically, this might pass muster, but forensically it is very difficult to make out a good case for the individual who commits a brutal murder.

Féré also points out that an epileptic fit may precede the outburst, or it may follow it, or the maniacal attack may fall in a

period when the patient is free from fits. This latter condition tends to make a medico-legal case still more difficult.

Another important point noted by Féré, which is also strongly prejudicial in the eyes of the law and the laity, is the extraordinary degree of judgment displayed by a patient in a fit of epileptic mania. The fatal blow is given with judgment. Even where such a patient is bent on suicide, he will storm at nurses and attendants in a manner which shows discrimination and judgment.

Where murder is committed by an epileptic mania, the violence and brutality used are excessive. The fatal blow is not only given, but the corpse is maltreated in the most horrible and revolting manner. As already remarked, crimes outstanding in their inhuman brutality and horror are almost invariably the result of this most dreadful disorder.

Needless to say, such excesses occur comparatively rarely, and epileptic mania is often seen clinically as a condition characterised by fits of temper alternating with a worried, harassed mental state, associated with hallucinations. With such an attack, it is possible to recognise other epileptic symptoms, such as myoclonic shocks, tremors, vasomotor, and metabolic disturbances.* The tongue is generally coated, the breath foul, and the digestive system upset.

In all conditions of psychical disturbances from the simple petit mal to stupor and mania, the characteristic amnesia exists.

This was recognised by the early Roman physicians (Cælius).

The degree of amnesia varies. If it extends backwards to the period preceding the psychosis, or the epileptic fit which may inaugurate the psychosis, it is known as "retrograde amnesia."

There are two types of this amnesia, true and false, depending on the presence or absence of pre-epileptic psychosis. (The different stages in the progress of epilepsy merge imperceptibly one into the other.)

In patients without psychical symptoms, the retrograde amnesia extends up to a few minutes before the fit. In cases where post-epileptic psychosis exists, the period of retrograde amnesia may be much longer, and extend over months. Alzheimer† calls attention to the form of retrograde amnesia found after normal sleep. This is generally best seen in persons travelling or sleeping in unfamiliar surroundings, and is a very common phenomenon. As regards the mechanism by which the trance condition arises in traumatic, and probably also in genuine epilepsy (compare Case No. 7, Chapter XIV., § 5).

* Raecke, "Die transitorischen Bewusztseinsstörungen der Epileptiker," Halle a. S. 1903.

† Alzheimer, *Allg. Zeitschr. f. Psych. u. psych.-gerichtl. Med.*, 1907, vol. liii., p. 483.

§ 3. Nosological Significance of the "Absences" and "Equivalents."

The study of these psychical phenomena associated with epilepsy is beset with difficulties. Under the influence of a certain psychic complex, the patient performs certain acts of which he afterwards remembers nothing. Féré points out very correctly that, at the time of committing the acts, the patient may not be unconscious, but he performs the act under the influence of an epileptic delusion. Hughlings Jackson offers the explanation that the acts performed by an epileptic when under the influence of one or other of these psychical disturbances are due to the higher or controlling centres being temporarily quiescent.

This explanation does not, however, help one to understand the condition. A question which has been much discussed is whether these psychoses always occur in association with an epileptic fit.

This is a difficult point to settle, and there are rare cases where a brief psychosis precedes an epileptic fit by several hours.

Case No. 46, M. S., age 25 years. Patient was a domestic servant. The illness began seven years ago with headaches; a year later myoclonic shocks appeared, while for the last four years the patient had fainting fits. For the last three years patient also complained of a curious uneasy feeling on the left side of the body. During the last six months severe epileptic fits occurred. After a severe fit the patient has freedom from the fainting fits for several weeks. There is no history of infantile convulsions.

At school patient made but poor progress. At the age of 6 she fell and struck her head violently against a tree, and was very confused for days after.

Shortly before her first menstrual period she was very confused mentally, and had many myoclonic shocks.

Quite suddenly some years later she developed hallucinations of apprehensions, and imagined she was being followed by a man. This hallucination came on one evening and preceded a severe epileptic fit. Under treatment she improved and eventually married, needless to say against advice. For fifteen years after marriage she had no fits except once when pregnant with twins. Occasionally she had shocks and headaches, but otherwise was perfectly well.

She came back to the clinic bringing with her a son of 15 who had just had an epileptic fit. This woman had no hereditary history of epilepsy.

As regards the relative frequency of pre- and post-epileptic psychically abnormal conditions, varying from extreme irritability to violence frequently with confusion, reference must be made to the statistics of Pagné, who found that in 52 cases of epilepsy, 13 displayed psychical disturbances before the convulsions, 33 after the convulsions.

It is well known clinically, and also from experimental work, that certain toxins—alcohol, absinthe, camphor—may affect the individual differently at different times. This difference is quite independent of the chemical properties of these toxins, but depends upon the condition of the individual. A poor state of nutrition or pregnancy may alter the effect of the drug from the demonstration of an epileptic fit to a passing psychism.

Very little is yet known about the chemical action of many poisons in relation to psychical changes and epileptic phenomena.* Heiman had a patient, a morphomaniac, who took large doses of morphia (2 grammes) daily. To break him of the habit cocaine was given in full doses (8 grs.). After the first dose of cocaine the patient became excited and irritated, this stage passed quickly and was succeeded by a severe epileptic fit.

Very small variations in the chemical composition of a drug will give very divergent results. *Morphineglycol* acid causes a dazed mental condition, but the methyl- and ethyl-ethers are convulsive poisons.† Camphor gives very different results in different individuals. In some the effect is extremely rapid, and consists of myoclonic shocks followed by fits. In others the results are marked restlessness, hallucinations, mania, and general indisposition lasting over a prolonged period. Antipyrine and carbolic acid poisoning both cause enhanced reflexes and fits often associated with psychical phenomena.

Great differences are also shown as regards the pre- and post-epileptic psychisms, in different individuals after the same dose of any one toxin. The works of Wiersma, Jelgersma, and P. Clark‡ are of importance, and supply interesting data on this point.

§ 4. The Relation of a Psychism to a Motor Discharge.

In epileptic patients, it is rare that one can see the immediate beneficial effect of a fit or a "discharge" as one can with the experimental cats. If this be the case for the spectacular and definite phenomenon of a fit, it is still more true for the elusive and transient psychism.

It certainly seems highly probable that a sudden emotional crisis, such as a fit of temper, a burst of high excitement, may discharge the epileptic as surely as a fit of the ordinary motor type. It is definitely known that not a few patients learn to ward off an epileptic fit by violent muscular exercise after they experience the first prodromal symptom (compare pp. 49, 93, 214). In the writings of the keen observer Morel,§ one finds notes of early or incipient epilepsy where mental symptoms have been prominent, but these symptoms have disappeared after the occurrence of motor epileptic fits. The epileptic fit would seem to be the safety valve against the development of mental symptoms. On the other hand, muscular movements of a maniacal type appear to be competent to affect discharge of the organism. Echeverria had a patient who prevented hundreds of fits by taking gymnastic exercises with frenzied energy on the trapeze as soon as he had the first indications that a fit was imminent (compare pp. 49, 93, footnote 215).

A reversal of this may occasionally be seen. Drugs may have the effect of stopping the epileptic fits or discharges and dreamy

* Heiman, *Deutsche med. Wochenschr.*, 1889, p. 232; and *Tageblatt Naturforschergesellschaft*, 1886.

† Barnes, *Schmiedeberg's Archiv*, 1901, vol. xlvi., p. 69.

‡ P. Clark, *Archives of Neurol. and Psychiatry*, 1922, vol. viii., p. 317; and *Brain*, 1920, p. 40: "The epileptic alteration is seen to proceed from the mental make up of the individual."

§ Morel, *Gaz. hebdomadaire de Médecine et de Chirurgie*, 1860; L. B. Clark, *New York Medical Journal*, 1925, vol. i., p. 442.

states may occur. L. P. Clark explains this on a psychoanalytic basis, as the libido, not finding expression normally in fits, gives rise to these dreamy states.

Cases occur where myoclonic shocks alternate with periods of mental depression, or even with delusions. In such cases, myoclonic shocks seem to clear up the patient's mental condition.

Case No. 47, A. V., age 25 years. When the patient was under one year she had severe convulsions, which lasted for three days. From this age onwards she had epileptic fits. At the age of 15 myoclonic shocks began, and at 17 fits associated with amaurosis.

In this patient periods characterised by mental stupor, numerous fainting fits, alternated with periods when the mentality and general subjective sensations were normal, but the patient displayed both severe fits and myoclonic shocks.

So far as our present-day knowledge of the subject goes, one can only recognise an equivalent phenomenon to the ordinary epileptic fit where it occurs at a definite period. For example, if at the menstrual period a patient sometimes has an epileptic seizure, at other times some definite psychical symptom. Even in such cases differences do exist between the associated phenomena. Beevor and Binswanger pointed out that the condition of the knee reflex was different after an epileptic fit from what it was after some equivalent phenomenon or symptom. There used to be, and still is, a tendency among some psychiatrists to consider epilepsy as essentially a psychosis, and cases have been published to support this view.

Doutrebente* described a case where the patient displayed recurrent mania and later had epileptic fits. This case Doutrebente took to be one of epilepsia larvata, which developed into ordinary epilepsy. This opinion he considered to be supported by the fact that before a maniacal attack and before an epileptic attack, the patient displayed the movement of running forward. This conclusion, however, only illustrates the need for careful distinction in diagnosis (p. 254). Although a forced movement occurs as a symptom heralding a fit it must lead to error, if running forward so common in psychopathics is indiscriminately admitted to be of epileptic origin.

The experimental work done to show the effect of a toxin, such as camphor bromide on cats, shows how manifold may be the effects of drugs on the central nervous system. It seems at least probable that the various psychical changes of our epileptic patients are the result of toxic changes in the central nervous system. It seems, however, illogical to consider epilepsy as essentially a psychosis, in view of the fact that the psychical changes noted in experimental work and also those in our patients are usually secondary to the development of fits.

* Doutrebente, *Annales méd.-phychologiques*, p. 177.

§ 5. **A Psychism depending upon a Purely Organic Lesion.**

The question arises whether in cases of purely anatomical cerebral lesion associated with epilepsy psychical changes and hallucinations may appear similar to those found when the epilepsy is due to endogenous or exogenous toxins.

The case of C. Winkler is of significance. He reported a case of epilepsy due to trauma capitis over the right frontal bone. This case had intellectual aura, having false reminiscences of bygone journeys. In the fit the face was turned to the left, and the fit began with convulsions of the left half of the face, associated with loss of consciousness, followed by amnesia. Later on this patient displayed psychical equivalents, which lasted several days, even as many as four. The case was operated on, and after removal of the bone a milky cicatricial patch was seen about the size of a two-shilling piece. This patch was the centre for a cluster of large vessels. In the part of the cortex removed multiple scars were found. Later, after operation, the patient had more attacks.

Binswanger (*loc. cit.*) is doubtful about this case, and questions the occurrence of intellectual aura.

The case recorded by Tomaschewski and Ssimonowitch* can, however, hardly be disregarded, in the evidence it affords of the occurrence of visual hallucinations as an aura to epileptic fits due to cerebral trauma. This was the case of a woman who had multiple cranial traumata, which, however, left no scar or defect in the bone. She had epileptic fits after the injury, preceded first by acoustic hallucinations, later by tactile hallucinations on the left side, and finally she had hallucinations of sight. The convulsions were best marked on the left side of the body. At the autopsy changes in the bone over the lower third of the central convolutions were seen. There were also changes in the temporal convolution, in the gyrus supramarginalis and angularis, while over this area the dura was much thickened and very vascular. It was closely bound down to the cortex, which was evidently thinner than normal, so that the dura lay directly on the white matter at several points. Over the posterior part of the first temporal convolution, and over the posterior central convolutions (there was hemiplegia with pronounced disturbances of sensation on the left side), the ganglion cells had disappeared almost completely.

Of the two or three cases which I have seen myself, where a trauma of the head was associated with hemilateral epilepsy with definite psychical symptoms, I would select the case given on p. 381 as being in my opinion very conclusive. In this case there

* Tomaschewski and Ssimonowitch, *Neurologisches Centralblatt*, 1889, p. 22.

was a purely local lesion associated with fits, which lasted for forty years. These fits began locally, and were associated with pronounced dreamy states, and attacks of kleptomania. After operation, neither the fits, nor the dreamy stages, nor the kleptomania reappeared. The patient has remained quite well since the operation.

Further, Fr. Franck and Pîtres showed that in animals where fits were induced by electrical stimulation of the cortex, hallucinations, fits of anxiety, and violent motions indicative of hallucinations were frequent. The animals also had, in some cases, periods of protracted dazedness, in which there was no reaction to stimuli. I found the same phenomena in cats treated with bromide of camphor and absinthe. I am therefore led to advance the theory that the fit or convulsion produced by drugs or electrical stimulation causes either exogenous or endogenous toxins to be precipitated into the circulation (pp. 48 and 261) which cause certain of the post-fit phenomena. There is, therefore, evidence to show conclusively that pure traumatic epilepsy may be accompanied by pre- and post-epileptic psychisms. Therefore we must regard those psychisms which occur in genuine epilepsy spontaneously (not as the result of a fit) as a direct manifestation of intoxication. That is the condition induced by the toxin—*i.e.*, the condition of charge. When the psychism passes without a fit, then the psychism may itself have acted as a discharge.

Those physical conditions, on the other hand, which occur after a fit, are probably brought on by the fit itself, whether the case be genuine epilepsy or traumatic.

In the literature one finds that many authors ascribe post-epileptic psychical phenomena to the condition of exhaustion consequent on the fit. It must be admitted that the result of fits induced by electrical stimulation supports this view (*cf.* Franck, Pîtres, and Jackson). This theory will not, however, explain the reason for pre-paroxysmal and inter-paroxysmal phenomena of a psychical character.

It would be pointed out here that psychical post-epileptic phenomena must be regarded as peculiarly dependent on the discharges having involved the medullary centres. In pure Jacksonian epilepsy these psychical post-epileptic phenomena only occur when the convulsions become general.

There are, therefore, two important theories as to the cause of the most important of the post-epileptic psychical phenomena.

1. These psychical phenomena are, like those occurring before and between the fits, primarily toxic in character.

2. These post-epileptic psychical phenomena are due to the toxic influences caused by the fit itself.

There is, frankly, a good deal to be said for both theories. It is probable that further physiological research will help to clear up the point, but more exact knowledge of the chemical changes is needed.

If it transpired from further research that certain cerebral lesions resulted in gastro-intestinal disturbances, or disturbance elsewhere in the autonomic system which induce such symptoms as constipation and a coated tongue, etc. (p. 387), then it would be easy to see how a psychism in pure traumatic epilepsy as well as in genuine epilepsy was toxic in origin.

Reference is made to the work of H. Claude and P. Lejonne,* who got analogous results in the convulsions produced in dogs with absinthe. It was found that animals who had had a part of the motor cortex destroyed with zinc chloride when very young reacted later to smaller doses of absinthe than animals treated in another way.

§ 6. Psychical Symptoms associated with Various Toxins which produce Epilepsy, and the Relationship of these Symptoms to the Fits.

In this connection the cases reported by Gerstmann are both interesting and instructive. Six healthy persons were enveloped in an avalanche, rescued, and brought round with great difficulty. The symptoms which occurred were as follows:

First came severe fits very like epileptic fits, then a period of delusion and psycho-motor activity, then a period where the memory was lost, and finally reversion to the normal. The same symptoms are seen in persons who have attempted to hang themselves but have been cut down and revived, also in children saved from drowning. I have seen several patients who developed a chronic epilepsy after a narrow escape from drowning, the first fit having come on after successful resuscitation. It is not difficult to understand why a fit should occur after such a violent strain on the organism as a whole, such as must follow the near approach of death. It is more difficult to understand why a chronic condition of epilepsy should follow. Yet in some cases this certainly occurs. The collapse of the resistance against fits occurring as it does at the same time as the disappearance of anoxæmia is quite in accordance with the tendency to myoclonic and epileptic phenomena peculiar to regaining consciousness (compare p. 206).

Not only does it occur after such a condition of shock or strain, but chronic epilepsy may follow a single attack brought about by lead or alcohol poisoning. One can only surmise that in such

* H. Claude and P. Lejonne, *Epilepsia*, 1910, vol. ii., pp. 1-12.

cases the threshold is lowered or the resistance of the patient has been completely broken down, and that the ordinary sequence of daily life is sufficient to provide the stimulus for succeeding fits. It is well known that one fit always disposes towards another, and the patient gradually becomes more and more prone to fits.

It has been shown that certain lesions of the white and grey matter of the brain may bring about epileptic psychical symptoms and definite sensory aura. These cases do occur in civil life as in war, but in point of fact are very rare. The question arises, is it possible to prove the *cortical* origin of epileptic psychoses from the evidence they afford? One may appreciate the analogy of the motor aura in cases of lesions of the motor areas, but one cannot admit this as direct proof. From my own experimental work my conclusions do not admit of my agreeing with Bechterew and Unverricht that the origin of myoclonic epilepsy and its accompanying pyschoses is cortical.

It must be recalled how, when the irritability of the cortical and medullary centres was measured before and after a fit (p. 178), it was demonstrated that there was a simultaneous increase and decrease of this irritability before and after a fit. Further, the latency of the myoclonic reflex remained constant after extirpation of the cortex cerebri (p. 113). After removal of a cerebral hemisphere, the crossed half of the body eventually participated in the myoclonic reflexes elicited from the other hemisphere. Where both hemispheres were removed, atypical fits occurred (Goltz and Rothmann's dogs).

The question arises, are the psychical phenomena to be regarded, in some cases at least, as a substitute for the regular epileptic fits? In cases where the patient has bouts of almost maniacal passion, the muscular exertion expended in such bouts would, in all probability, have the same detoxicating effect as a fit. In other cases the psychical phenomena would certainly not have this effect.

Further, is the presence of certain psychical symptoms, such as prolonged dreamy states, to be regarded as significant of long continued epileptic fits? On the other hand, is it the case, as Pick,* Féré† and Turner think, such dreamy states may occur as an early symptom, but that only in cases where there is a certain degree of defective mentality, or an hereditary predisposition thereto, do these dreamy states persist and develop? From my own experience there does not seem to me to be an hereditary tendency to psychical symptoms in all the cases, and I consider that both petit mal and psychical symptoms should both be

* Pick, *Journ. of Mental Science*, 1901, p. 485.
† Féré, *Rev. de Médecine*, 1905, p. 670.

regarded as collateral symptoms of genuine epilepsy. Where for some reason, not as yet understood, the organism does not display regular and efficient discharges, such as the complete motor fit, atypical discharges are bound to appear.

Case No. 48. Worked in a shop as messenger for delivering bread. Patient had worked in his father's shop as a shoemaker. He was troubled with fainting fits and had mental disturbances. He stopped working in the shop and got an open-air job as a messenger. He now had neither fainting fits nor mental disturbances, but instead had severe epileptic fits. This change in environment and occupation was repeated several times always with the same result. When kept from the fresh air he never had the epileptic fits, but instead fainting fits and mental symptoms.

Case No. 49, H. A., age 25 years. Patient was the son of a drunkard. He was rather delicate, but had worked hard. He had myoclonic convulsions for several months, after which he became mentally afflicted and had to be put in an institution for treatment. Three days after he went into the institution he had a severe regular epileptic fit, after which he was much better. When he had subsequently severe fits, they were characterised by a stage of automatism, when he fought fiercely against imaginary enemies. Later he apparently completely recovered and went home.

It is well known that there is more tendency towards mental symptoms in cases of frequent petit mal than in grand mal. Further, it is quite usual to find mental symptoms developing where grand mal has been treated successfully—*i.e.*, where the severe fits have been stopped.

Case No. 6, G. v. M., age 17 years. Patient was a mechanic, and already showed great promise and skill. Eighteen months ago he fell into a canal, and saved himself from drowning by swimming. Six weeks after he had, for the first time since the accident, a fainting fit accompanied by slight convulsion of the left side of the body. The whole attack with unconsciousness lasted ten minutes. These fits occurred once in two to three weeks for a period of fifteen months. Three months ago he had a severe epileptic fit one morning after an evening function, where he had exerted himself a great deal.

From the history supplied by the patient's friends it was found that he had suffered from myoclonic shocks during sleep for a year. For six months he had frontal headaches, which gradually became more troublesome. Sometimes in the evenings he had curious fit-like attacks, when he clutched at his chest and gasped. From his mother it was elicited that patient had had no serious illness while an infant. He had displayed somnambulism for a short period, but this ceased after his tonsils were removed. He had been a bright child at school, and had always been alert and pleasant.

In the family history the only points of interest were that the father's mother was insane, and that an aunt, also on his father's side, was "peculiar." A brother of the patient's had been very slow at school.

History of a Particular Attack.—Patient was going home about 10 o'clock on a December evening after having paid a family call. He had a bad headache and decided to take a walk. The last fact he was able to recall on his recovery was that he was in a particular street when he decided to do this. He also remembered, vaguely, that he felt dizzy; that he perspired a good deal, and that he leaned against a wall. After this he can recollect nothing. The rest of the history has been built up from witnesses.

A lady saw him, and as she was well acquainted with him, greeted him. He took no notice of her. She thought he must be annoyed about something, but noticed particularly that his dress was in order, that he walked with his head bent, and when accosted stared straight in front of him.

At 2 a.m. next morning a friend of his brother saw him. He had no hat on, and his collar was torn to pieces, while he stumbled as he walked. At 2.30 a.m. the police found him lying face downwards on some steps, almost benumbed by cold. Some people tried to revive him, but without success, and he was taken to hospital. The first thing he remembered was the clock striking 3 a.m., which it did just after he was in the hospital. He fainted again and remembered nothing more until 6 a.m., when he saw his father at the side of his bed. Even then he was " misty," and it was not until 8 a.m. that he came round completely. He was much fatigued all day, but after a good sleep through the next night he was quite better.

Epitome.—This is a case of an intelligent boy who showed very few of the ordinary symptoms associated with epilepsy. In twelve months he only had about twelve fits.

Instead of the fits he displayed this curious psychic state of dreaminess, with complete loss of memory associated with fainting fits. This case is reminiscent of Case 49, where a dreamy mental condition and fainting fits replaced ordinary epileptic fits.

The patient was put under hygienic conditions in a home; after a very short time the myoclonic shocks disappeared. Patient ultimately recovered, never having either fits or mental disturbances. He never had any drugs, and the satisfactory condition has lasted three and a half years. Then his father came to complain of disorders in patient's financial affairs.

This case is interesting, because the dreamy mental condition was an early symptom. Such cases have suggested to psychiatrists, among whom is Jelgersma, that the psychical disturbances are independent of the motor fits (compare pp. 252 and 304). This is not the case. What really has been the condition in such a case is that the degree of tolerance towards certain toxins has been equally low, physically and psychically. This patient, as has been shown, improved, and was ultimately free from both sets of symptoms as a result of a definite hygienic mode of life. Another interesting point illustrated by this case is that epilepsy may not, indeed usually does not, begin as a fully developed clinical entity. Certain psychical symptoms show themselves along with certain physical symptoms, and in the course of time the clinical picture completes itself.

It is very interesting to note the effect of epileptic fits on the mentality of patients. A very great degree of variation is seen which is very difficult to explain. Some patients show marked mental deterioration after a few fits, while others suffer from the malady for years, and are practically unaffected mentally. Mental deterioration seems to follow more readily where there is a family history of mental disease, but this does not account for nearly all the cases. There must be some other factor as yet unknown.

§ 7. Relation to Other Psychoses.

The psychical side of epilepsy and its relation to allied psychoses is a subject which is so far-reaching that it would be impossible to deal fully with it here. One condition, however, must be discussed—namely, the condition of intoxication mania or what

is known in German as "pathologische Rausch." This is a condition where there is a pathological reaction to alcohol which is etiologically and symptomatically similar to epilepsy.

The following is a case illustrating the disorder. A similar history was published by F. W. Mott (Croonian Lectures 1900, Lecture 4) where there were also 4 cases in one family.

Case No. 7, H. G., age 24 years. Patient was a workman. He suffered from headaches for years. These headaches were localised mainly to the left temple, and often lasted twenty-four hours. He had myoclonic convulsions, more particularly of the right arm and leg. These convulsions were often very severe when he lay down. During sleep he had twitching of the muscles. When asleep, or when under emotional strain, he ground his teeth. He was subject to fits of fury, when he behaved in a maniacal manner, yelling and fighting and manifestly quite unaware of his immediate environment. His friends thought those fits were worse if he had been drinking, but they were not absent if he did not drink. On one of these fits of meaningless fury he caused such a disturbance in a street that he was arrested. Eight policeman, with the help of four onlookers, were required to conduct him to prison, and when he did arrive there, his clothes had been torn from him, so vehemently had he struggled.

Family History.—Patient's father and grandfather were both passionate men and both were addicted to alcohol. The father had suffered from migraine, had nocturnal convulsions, marked analgesia and pronounced intolerance to alcohol.

Patient was the oldest of thirteen children and had had scarlet fever when five years old, after which, his mother stated, he had always been nervous. He did not get on well at school, and quarrelled so violently with different masters that his school had to be changed four times. When he went to work he did no better. He started all sorts of jobs, but never did well. At the age of 18 he drank ale for the first time. After this he was very queer for several hours. Some eighteen months after marriage he had an argument with his wife, when he suddenly fell down, foamed at the mouth, and became unconscious.

After a very violent fit of fury he quite frequently fainted or fell asleep, and remembered nothing at all about the attack.

Patient had three children, the second one, a boy, was of a passionate disposition, and at the age of 2 had complained of headaches, but had not had convulsions. Analgesia was well marked in this little lad.

1907. Patient was a well-built man. His body was badly bruised from blows received when in fits. The pupils reacted normally, the reflexes were also normal. Analgesia was extremely well marked.

Patient was seen four years later. He had been well for some time. His last breakdown had followed the drinking of ale. He had become wild and had been arrested. He had been so violent that five policemen were required to convey him to prison. He recalled nothing of the whole incident. Myoclonic convulsions were still well marked on the right side of the body. His wife stated that alcohol or a sudden fright or shock precipitated an attack. His son, previously noted as being of a passionate disposition, had unfortunately stabbed his brother in the eye in a fit of temper.

Patient was seen again seventeen years later (1924), when no new point of interest could be reported, fits having practically ceased.

Epitome.—This is a case of intoxication, with maniacal symptoms or the so-called "pathological Rausch" of the Germans. The phenomenon is of the same class and type as a psycho-motor discharge in an epileptic patient.

Cases do occur where patients suffer from violent fits of temper, not so severe as just described, but distinctly abnormal in type. Such fits are often associated with the use of alcohol, but they

may be occasioned also by emotion.* A patient, after indulgence in alcohol, will become violent and abusive over a trifle. It is very generally supposed that if the alcohol be stopped the fits of temper cease. This is unfortunately not always the case. Such patients frequently present difficulties as regards diagnosis. Are they merely cases of intolerance towards alcohol, or are they epileptic? The diagnosis has to rest upon very careful examination and observation of the patient. All the minor symptoms of epilepsy have to be carefully watched for—the presence or absence of myoclonic shocks, and also the effect of a rigidly non-alcoholic and hygienic mode of life.

As regards the condition of catatonia, it may form a part of the general epileptic phenomenon. It may alternate with fits (compare Yawges,† Urstein, and Vorkastner), or it may persist for days with an epileptic patient just as in dementia præcox. The fact that catatonia may be found in two such widely different disorders need not be a cause for wonder, when it is realised that in both gastro-intestinal disturbances are of frequent occurrence. The same endogenous toxin may be *the cause in both cases.*

§ 8. **The Differential Diagnosis of Psychical Epilepsy from Other Psychoses.**

Where the ordinary epileptic symptoms are present there is, as a rule, no difficulty in making such a diagnosis—it is in cases where the patient has had the first fit in association with a bout of alcoholism or where some severe shock or fright coincides with the fit. Difficulties also arise where the patient or his family are known to be hysterical. More important are those cases where the mental or psychical symptoms appear before the physical symptoms, or where they are at least more prominent. If an epileptic patient manifests his disease first by passing into a dreamy mental condition in which he may unknowingly perform anti-social acts, the diagnosis becomes difficult for the doctor and most important for the patient. It must be remembered that complete lapse of memory may be found in hysteria, alcoholism, and in epilepsy.

If the patient when first seen is breathing stertorously, and (when conscious again) displays analgesia of the segmental type with dilated pupils which react slowly, a diagnosis of epilepsy is suggested. If it is ascertained that the patient has had similar attacks, it is still more in favour of this diagnosis. Some importance is attached to the fact that epileptic patients are as a

* Aschaffenburg maintains that the hyper-sensitivity to alcohol occurs exactly in the condition of charge as that of the epileptic.

† Yawges, *American Journal of Nervous and Mental Diseases*, 1915, p. 74.

rule notoriously uncertain in temper, but this is not a safe point on which to base so delicate a differential diagnosis.

Where the patient is in a dreamy almost stuporous condition, it is not very likely to be epilepsy unless the stupor passes off after, at most, a few days. This rule, however, does not always hold good. Lasègue had an epileptic patient who fell into a dreamy condition at Havre and awoke from it in Bombay.

Spratling records a similar case which lasted twenty-six days, while Alzheimer had one which lasted still longer.

In all cases where a differential diagnosis is required in a supposed criminal case there should be a special ward in prisons for trained observation. It is impossible to make so delicate and difficult a diagnosis under ordinary prison conditions.

Where a patient can be kept under close observation, it is practically always possible to clear up the case. Great attention must be paid to inter-paroxsymal conditions—such symptoms as headaches, their distribution and character, the presence or absence of myoclonic shocks, the presence or absence of analgesia, its distribution if present (Stoddart), vaso-motor disturbances, reflex exaggerations, condition of the pupillary reflexes, and the changes in the psychical condition.

Falret, writing on this question of diagnosis, pays much attention to what he terms the "glittering glance of the eyes," the headaches and the regular recurrence of the same association heralding in a psychical fit, called by him "manie avec fureur."

It must be remembered that whether an epileptic has performed a criminal act or not, there is often in epileptics a similarity of experience. In one case an epileptic will murder a person, yielding as it were to some impulse which drives him on to perform the act apart from his conscious volition.

Another epileptic will be impelled to throw an article such as a glass; again the impulse is without conscious volition. In both cases all the patient may feel is relief. All recollection of the act associated with the sensation of relief may be lost.

At the same time it would not be ethically sound to plead complete irresponsibility in the case of every possible epileptic appearing in the criminal court. No judge would permit it. All the medical expert in such a case can do is to establish the diagnosis of epilepsy—if possible. Where the individual has not had a motor fit, such a diagnosis must rest on the presence of other symptoms.

In some cases the performance of the act wakes him and he becomes immediately conscious of the act and its significance. In some cases the patient merely has a dream-like memory of the event. In all cases it must be realised that little or no help can be got from the lay associates of the patient. The symptoms are

too delicate for the laity, whose evidence in such cases is generally valueless. The close resemblance between post-paroxysmal and inter-paroxysmal hysterical and epileptic symptoms makes exact diagnosis difficult. Indeed, in many cases, the two conditions overlap. This can be easily understood, more particularly in the case of the young patient who has had a good deal of attention centred on him from anxious parents and friends. Further, the peculiar sensations to which an incipient epileptic is subject to makes it difficult for him to separate the imaginary from the real. In a sense he is not facing life, or his own development in relation to life, quite clearly, his sensations are muffled and distorted, facts are hazy and his imagination has too free a scope. At the same time, it is my experience that epilepsy and hystero-epilepsy are more often mistaken for hysteria than the reverse.

The question as to whether a patient is completely conscious, partially conscious, or quite unconscious, is always difficult. Certain methods have been adopted to try and ascertain the degree of consciousness. The nurse may be instructed to give a special provocative word or number so that the patient automatically reacts with the answer or the next number should he be conscious to the necessary degree. Where this method has been repeated several times with a patient, it becomes a fairly sure way of finding the condition of consciousness.

The corneal and conjunctival reflexes are very important. In epileptic fits both are absent, while they are as a rule present in hysteria. Spasmic closure of the eyelids is common in hysteria, while it is comparatively rare in epilepsy (Karplus and Jauregg).

The extent and character of the injuries are important. In epileptic fits the patients often do injure themselves very severely, while the tongue is often badly bitten. The hysterical patient rarely suffers real injury, neither is the tongue bitten. Enuresis, common in epilepsy, is very rare in hysteria.

The nature and character of the movements is also important. To one well skilled in epilepsy the movements of the hysterical patient in a fit are distinctly more abrupt, but it must be remembered that these patients sometimes do simulate epilepsy remarkably closely. As a general rule the movements are grotesque—animals may be imitated (theriomimy of Gowers). Great care must be observed in forming a decision from the character of movements in a fit. In genuine epilepsy, and in long-standing Jacksonian epilepsy, all sorts of modifications occur. This applies especially to Jacksonian epilepsy, where the passage of years will transform a purely localised convulsion into one involving the whole body.

Not infrequently a good deal can be learned from the reaction to immediate treatment. A sharp clear order, application of wet

cloths to the face, or pressure over the abdomen, often clears up a doubtful hysterical case. Even a bad case of hysteria will react automatically to a sharp distinct order, whereas an epileptic never does. No rule can be laid down, but all neurologists have methods which they find useful for application in suitable cases.

The fact that the patient was emotional before the fit is no argument against it being epilepsy. Many epileptics precipitate a fit by an emotional crisis.

Masturbation is associated with both hysteria and epilepsy.

According to Gowers, spasm of the adductors, laryngismus stridulus, is a functional or hysterical phenomenon. Many neurologists do not agree with this.* Raynaud reports a case of a morphine addict who was suffocated in a fit of laryngismus.

Pierce Clark† and others have advocated the recognition of hystero-epilepsy as a separate clinical entity. Whether this will meet with general approval is questionable, since the enormous influence of emotional life on epilepsy is commonly admitted, and hysterical symptoms, even in individual fits, are variously intermingled.

Whether narcolepsy (Gélineau, Redlich) and pyknolepsy (frequent small fits of children) have to be recognised as separate clinical entities is not yet decided.

Redlich‡ has recently given an exact statement of what we know of narcolepsy. If we exclude the many cases, which are really petit mal or some other definite malady (encephalitis), there remains some cases, mostly adult males, in which the patient falls asleep several times a day, and in which no other symptoms appear in the course of years. In one case I saw, the X rays demonstrated an abnormal condition. In this case certainly some change in hypophysis secretion seemed probable

Uncertainty also exists about pyknolepsy, to which from time to time attention is drawn.§ In many cases it comes later than ordinary epilepsy. Petit mal, without psychical complications, occurs more frequently at the age of 6 to 10 years than later in life.

§ 9. **The Permanent Psychical Condition of the Epileptic.**

The permanent psychical condition of any epileptic is of the very greatest importance. On this factor depends the estimation of the importance of the malady from the social standpoint, as well as from the forensic. It is also a vital factor in deciding on the efficacy or wisdom of adopting the American method of colonisation for epileptics.

* H. Thomson, *British Medical Journal*, July, 1923, vol. ii., p. 715.
† Pierce Clark, *Archives of Neurology and Psychiatry*, 1922, vol. viii., p. 317.
‡ Redlich, *Zeitschr. f. d. ges. Neurol. u. Psych.*, 1925, vol. xcv., p. 270.
§ W. Adie, *Proceedings of the Royal Society of Medicine*, 1925, vol. xvii., p. 19.

The whole question is one of prime importance, and must be considered afresh for each case. Each new case of epilepsy coming under the care of a physician should be considered from the standpoint of the patient's inherent mentality. Is he a case where the mental endowment is such that he can collaborate with the physician in his own treatment, or is he too poorly endowed mentally? Where the patient belongs to the first group where the mental endowment is good, the prognosis is certainly hopeful. So strongly do I feel on this matter, that I am convinced that if 75 per cent. of the financial support forthcoming from the Government for epilepsy were given for the treatment of early cases I should consider it a distinctly progressive movement.

The question may be asked, does psychical deterioration form an inseparable part of the malady? Or, in other words, does it, with the myoclonic convulsions, fits, headaches, fainting-fits, and dreamy mental conditions, form the entity-epilepsy?

The answer to such a question is that mental deterioration may form a part of epilepsy in the same way that infectious processes and furunculosis may be symptoms in a case of diabetes.

There is no necessity for psychical deterioration to be a symptom in epilepsy except under special circumstances. Where the patient starts life poorly endowed mentally, probably there may be a history of hereditary mental disease; or where severe encephalitis has occurred early in life, mental or psychical deterioration is almost certain to be a prominent symptom in the disease. Where, on the other hand, the patient starts with good mental endowment, then, in my opinion, any psychical deterioration is due to the fits.

This point is of great importance, and I would emphasise my opinion that there is no need for any intelligent patient suffering from epilepsy to develop psychical deterioration if he in the beginning is properly treated and the malady be arrested. Where, however, the treatment is neglected or inadequate, the psychical changes inevitably follow. The same result is seen in those cases where a cerebral tumour produces epileptic phenomena; here also the memory fails, while the general mental attitude changes. In some cases one is led to believe that even the first fit itself brings about some alteration in the mental personality. A man, who had always been normal mentally, although nervous, got a first fit after gas-intoxication, followed from time to time by others. Marked and very troublesome agoraphobia appeared after the first fit and for many years hampered his social conduct.

This is a point upon which there is very great divergence of opinion. In no other section of the statistics of epilepsy are there such differences as in this section devoted to the occurrence of dementia with epilepsy. In view, however, of the work of Wilder-

muth, it is fairly generally recognised that such data depend upon the nature and class of case examined by the different writers. For example, the psychiatrist in a mental hospital has ample opportunity of examining the mental condition of the chronic epileptic, such cases forming about 10 per cent. of insane patients. The neurologist, on the other hand, generally sees early cases which, if properly treated, give an entirely different impression as to the frequency of mental disturbances. In the same way physicians in epileptic colonies see another aspect of the malady and draw correspondingly different conclusions.

Although the view is held that the earliest psychical changes in epileptics of normal mental endowment are due to the fits themselves,* it must be remembered that we know little if anything about how those defects originate.† We do not know the cause of the dementia so often associated with epilepsy. It may be due to the fits, to the convulsive phenomena, to the increased blood-pressure, or it may be an illustration of the well-known and generally accepted view that every psychosis, however brief, leaves a lasting change. The dementia would, according to this latter theory, be but the changes due to a long series of transitory psychoses.

If this view were to be accepted provisionally, it would be interesting to see what phase of the epileptic condition constitutes the element which has so pernicious an influence on the mentality of a patient—whether the short phase of automatism or period of moodiness were more hurtful than the loss of consciousness in the fit or *vice versa*. Such an investigation would, of course, require suitable clinical material and much time. Wiersma's work was somewhat on this line, and a statement by his pupil Kramer may be given. He states that the greater the psychical degeneration of an epileptic, the more frequent is the transient loss of consciousness. The longer does it last and the slower is the reaction time. The significance of such data is, however, limited by the fact that the patients in question had all suffered from epilepsy for a great many years. The epileptic psychosis has been studied by P. Clark (*vide supra*) from the psycho-analytic standpoint. His view is that the intense stirrings of the unconscious forces so repeatedly assert themselves that normal consciousness is persistently shattered; finally, the infantile in the unconscious state usurps the domain of conscious memories of everyday life.

In all conclusions drawn from the examination of epileptics,

* Bressot and Bourichet, *Lancet*, 1922, vol. i., p. 645.

† The work of F. W. Ninde is one of the few endeavours to analyse the effect of the disorder on the mental functions. He examined the auditory memory in 2,000 epileptics by using cyphers from 2 to 10. To get dependable and really valuable data on such a point, the same patients would have to be examined at different stages and at different times in relation to the fits.

the fact must not be overlooked that the patients have certainly had drugs such as bromide administered over some considerable period.

Whether the drugs themselves may have a direct influence on the mental condition of a patient is an open question. Although I have examined very many patients, I am not prepared to affirm or deny such a possibility. The point is a difficult one, for a well-marked case of epilepsy which has not been treated with bromide is practically never seen. It seems that the dementia, due to the taking of bromide as a drug—*i.e.*, apart from any therapeutic reason—is closely allied to the dementia caused by the epilepsy. There is the same irritability, loss of memory for recent events, tendency to dreaminess coupled with puerile suspiciousness. The whole matter requires, however, more careful investigation. An important point noted by me in the course of numerous examinations of cases of epilepsy in the young was that the parents frequently stated that the children had not got on well at school, also, though rarely, where no encephalitis was suspected. This fact they had recognised long before any of the ordinary epileptic symptoms such as headache or myoclonic shocks appeared. In the cases I refer to, there was no history of encephalitis or infantile convulsions. This history was given by parents far more frequently than I would have expected, and is a fact to be borne in mind.

It must be mentioned that in many cases epileptic children do well at school. In some rare cases even children who have suffered from encephalitis also do well at school. This fact seems to me to invalidate the claim made by some physicians that they can distinguish epilepsy from hysteria by the fact that epilepsy is associated with slow mental progress.

Turner suggests a very practical scheme for classifying patients according to the degree of mentality shown by them between the epileptic fits. The scheme is as follows: (1) Patients showing normal intelligence; (2) patients showing loss of memory for recent events and a greater or lesser degree of irritability (these patients are still capable of working, and may lead a fairly normal life with certain restrictions inseparable from their malady); (3) patients who are not demented, but who are no longer capable of working or of leading even a comparatively normal life; (4) patients who are completely demented.

This author very sapiently points out that in many cases where the actual fits have been arrested the patients frequently manifest mental changes of the second, third, or fourth types. In other words, the cure of the actual fit phenomena is associated, in some cases, with the development of mental changes.

Turner further raises the question as to the correctness of

applying the name epilepsy to such cases where the epileptic fits only appear at certain periods of life—say, during gravidity or in senility. These fits Turner considers to have no influence whatsoever on the mentality of a patient. The same question in another form is suggested by certain German authors, among them Hoffmann, who hold that the diagnosis of epilepsy should not be made where the fit occurs in consequence of some definite cause, such as indigestion or intoxication. This view does not seem to me to be right, as it is based on the conception that a degree of psychical inferiority is essential for the establishment of epilepsy as a clinical entity. There is no doubt that such cases of epilepsy do occur—indeed, they are not infrequent in families with a strong hereditary tendency or history. These cases, in my opinion, serve as illustrations for my doctrine that, if fits associated with loss of consciousness do not occur except at long intervals, mental changes do not supervene.*

Such cases are those of a boy of 13 and his sister of 16, who were both under my care for epilepsy.

Extract C., No. 50, F. G. The father suffered from shocks, sometimes bit the tongue, more especially if he slept during the day after being on night duty. The mother had one fit at the fifth month in one of her pregnancies.

Personal History.—The boy suffered for four years from headaches, while for three years he had severe shocks especially during sleep, while for the same period he had violent bouts of temper.

The sister had headaches, shocks and definite epileptic fits for three years. The first epileptic fit came on after a period of prolonged fasting prior to being received into the Church. So severe were the fits that she had to be brought out of the church several times on the day on which she was received. Mentally she was dazed and very forgetful. It must also be noted that the boy made good progress at school and held the first position in the class.

Gowers, Binswanger, and Turner teach that cases of petit mal, more especially if it begins before puberty, are very apt to become demented. On the other hand, pyknoleptic cases show nothing of this sort. Further, that those cases of epilepsy where the fits occur in a series, whether consciousness is regained between the fits or not as in status epilepticus, are also very liable to develop dementia. I agree with these statements, but maintain that they do not affect my position, my view being that in the repetition of the fit, or in the repeated loss of consciousness, lies the reason for the mental enfeeblement.

Féré points out very correctly that there are two forms of dementia—the organic, and what he terms the functional.

* Persons who suffer from syncope for some reason, or who have atypical convulsions as in Stokes-Adams disease, do not show any mental change, as seen with epilepsy. I have known a case of Stokes-Adams disease where fits occurred daily for years, and yet no mental changes appeared (compare p. 288).

The first, or organic dementia, is a definite condition which shows no alteration. The second, or functional dementia, may, however, show improvement if the condition of the patient is changed. An interesting case of this type was a man of 54, who for a period of forty-six years suffered almost nightly, at least in his later years, from epileptic fits. The fits were completely stopped, and the man's strangled intelligence began to reassert itself in a most interesting way.

C., No. 8, P. v. d. M., age 54. No employment. From the age of 8 he had had epileptic fits. For the first nine years the fits often occurred in the day-time, but later they came on only at night. In a fit he fell down; both hands and feet became convulsed. Sometimes these symptoms were accompanied by biting of the tongue and enuresis. After the fit he was dazed and fell asleep. The next day he was still dazed and had a headache. At one time he used to have a series of fits, probably as many as thirty in a few days, but at the age of 54 the fits occurred at night. In the day-time tremor of the legs and an ankle clonus appeared, and the diagnosis of spinal disease was given by the family physician.

When examined mentally the patient's memory was found to be very good, considering that he had had fits practically all his life.

Speech was difficult; he stuttered, and he was unable to express his condition or symptoms. He did not read the papers, and had no pleasure or interest in ordinary social life. Occasionally he played Patience. Mentally he was always more or less dazed, and had to be led about as a child. Generally he was more or less irritable, and at times had outbursts of temper, but on the whole he was not difficult to deal with. He complained of compression over the thoracic region, of a lump in the throat, and a girdle-like compression round the waist. The hands were always moist. Headaches were sometimes troublesome, but were not a marked symptom. On examination the deep reflexes were found to be exaggerated, while analgesia was general and complete. He had taken large quantities of bromide, but shortly before coming to the clinic the dose had been reduced.

When admitted to the clinic the patient displayed many minor symptoms. He had hyperhidrosis and very frequent nocturnal shocks. It was noticed that the patient did not wake with the nightly fit, but slept on. He was kept ten days in bed, and given bread, containing a bromide salt and boracic acid, but no ordinary salt (2½ grammes bromide, ⅓ gramme borax).

Under this treatment the nocturnal fits stopped, while the bowels became regular. Mentally the patient grew less morose, read a good deal, was able to go to and enjoy the theatre, and to converse with others. After six weeks he went home, when he had a fit during the first night, but it was noted that he awoke with the fit. Further, from that time, 1907, he never had a relapse into his former condition.

In 1913 he was not so well, being troubled with dizziness, vomiting, irregularity of the bowels, while mentally he was dazed. He was re-admitted into the clinic, and had a course of treatment directed to improving his general condition. This restored him, and up to 1923 he remained well and had no fits. During this period he was occasionally seen by a medical man. Mentally he was well and showed an extraordinary degree of mental development.

In textbooks dealing with epilepsy there is a tendency to lay too much stress on the epileptic character. This is not in keeping with facts observed in patients. There is no doubt that epileptic patients as a class tend to be more irritable than normal people, also they are inclined to be dreamy, but it is not the case that

they are extremely egotistical. It must be remembered that among epileptics, as among normal persons, there are great variations in temperament and natural characteristics. The peculiarly deficient type of mentality so often seen in clinics for epileptics (frequently cases of long-standing) makes one forget that among epileptics are many of the notable men in the world's history, among them Napoleon and Muhammad. Claus and Van der Stricht also include Julius Cæsar, Petrarca, Charles V., Peter the Great, and Gustav Flaubert.

This being the case I do not consider it at all probable that a diagnosis of either epilepsy or of the so-called epileptic psychosis could be made from the contemplation of the patient's character alone. At the same time there is no doubt that if epilepsy is allowed to continue untreated, the patient's character does undergo a change. Such a patient is ever in a changing condition of "charge," hence the changes manifested such as irritability and slight unfitness for work (compare p. 313). The same symptoms appear where the epilepsy is associated with some organic morbid process; here, however, are superadded symptoms due to interference with vital processes. Also it must not be forgotten that life is very difficult for these patients.

Marchand and Nouet describe the epileptic character or temperament thus: "Irritabilité et impulsivité, mobilité des sentiments, variabilité de l'activité." It seems to me that several of these so-called characteristics are really prodromal symptoms of a fit. These authors agree with Féré that many—indeed, a majority of epileptic patients—do not develop a real "epileptic character."

From a survey of the evidence supplied by the examination of many cases over a prolonged period of years, it seems to me that the lasting mental changes are nearly always associated with a persistence of the epileptic fits. Doubtless there may be and are passing mental symptoms associated probably with the motor symptoms inseparable from the phenomenon of a fit, but these are quite different from the symptoms referred to as the "epileptic character."

From the evidence afforded in this chapter it is shown that before one can come to any judgment as to the mentality of a patient one must get them into a comparatively normal condition—that is, the fits must be arrested for at least a couple of weeks.

Further, in patients who have been treated more or less successfully twenty years ago, it is seen that under special conditions of strain they react not by epileptic fits, but by abnormal mental phenomena.

CHAPTER XII

TREATMENT

§ 1. Compilation of the Clinical History.

WHEN the notes of a case of epilepsy are being taken, the following points should be borne in mind: (1) Get a clear picture of the present condition of the patient. (2) Get as quickly and clearly as possible a history of the case up to the time of examination. Such a history is always of value statistically, nosologically and therapeutically. (3) Keep up the history with careful notes, so that the effects of treatment are clearly represented.

In his book Russell Reynolds has dealt with the necessity of careful note-making, and puts forward a plea for a rigorous code of examination. If such a code could be evolved and adhered to, how valuable the results might be.

When examining a case with a view to getting the present and the past history, it is always advisable to allow the patient or his friends to use their own terminology in describing symptoms. Merely give a lead, and then allow the description to be supplied. By so doing one often gets a very vivid and exact description of the case. Never attempt to describe what you conceive ought to be the symptoms; if one does so, patients and their friends will frequently agree irrespective of the correctness of the description supplied, and so error creeps in.

Take careful notes of all the complaints made by a patient, but remember that epileptic patients sometimes stray far from the truth in describing certain symptoms, and further they may fail to recognise symptoms which are present. This latter point is especially true about the presence of an aura before a fit. Frequently patients aver, and aver honestly, that they have no warning at all before a fit (compare p. 245). The truth in such a case is sometimes got by asking them to describe their sensations after a fit. They frequently, indeed almost always, say they feel much better, and may even unconsciously "give away" the truth by saying they did not feel well before a fit. Of course, no matter how carefully one examines a case, or how anxiously a patient or his friends endeavour to help one, a perfectly exact record of any case can only be got by observation in a clinic over a definite period. Still, by careful questionings and patience, one can get a fairly clear picture of the fits, their number, and time of occurrence.

After one has exhausted the subject of the fits, the next point is to enquire into the general health of the patient. A point of

special importance is the condition of the bowels: do they act regularly every day, and are the motions normal or constipated? The mental condition of the patient is of great importance. Find out the condition of his memory and judgment, and also ascertain his attitude towards the outside world. Is he interested and intelligent, or is he self-absorbed and morbid? The mentality of a patient frequently reveals more than one can be told by word of mouth. Where the memory is good, the judgment not deficient, and the whole attitude of mind intelligent, the case is likely an early one, and the prognosis is good. Such a case may be an early one, but cases do occur of long-standing epilepsy where the mentality is good.

One must never forget that it is not at all uncommon to have patients coming alone to complain of all sorts of vague disorders which frequently suggest neurasthenia, when in reality they suffer from epilepsy. It is not that such patients wilfully deceive themselves or the medical attendant, but they do not know that they have fits at all. They are conscious of symptoms before and after a fit, but if the fit occurs when they are asleep or unobserved, and no injury occurs, they simply do not appreciate it at all. It is not uncommon to find such patients very cheerful and optimistic. They do not know they have fits, and the physician should take care not to depress an unconscious epileptic unduly. This is too frequently done where the medical attendant conceives it to be his duty to give a frank diagnosis and prognosis. At the same time, where vague symptoms are complained of, and no other cause can be found, it is the duty of the doctor to keep in mind the possibility of epilepsy and to collect the data necessary for an accurate diagnosis.

Great tact and care are needed when discussing symptoms with adult patients, as they are frequently sensitive and easily upset. Special difficulties are presented to a physician where the case is one where epilepsy and hysteria co-exist. At this point I would enter a protest against the diagnosis of hystero-epilepsy. Hysterical symptoms are never completely absent in true epilepsy, and it is not justifiable to class as a separate entity a form of epilepsy in which the hysterical symptoms are simply more pronounced (compare p. 292).

If the case be taken carefully, one should be in the position of knowing what the patient is like in a fit, when they occur, and how frequently. Further, the general condition between the fits should be known, while a fairly extensive survey has been made of his mental standard. Of course a physician of any experience knows that this is not always attained, but still one must aim for it, and with care and patience it is wonderful how complete an account one can get. Where possible, such data should be ratified by direct

observation in a clinic. Even in a clinic Binswanger's observation must be borne in mind. Binswanger pointed out that it is not sufficient to see a single fit to make a diagnosis; one must observe the condition and symptoms between the fits.

The next point in the clinical history is the history of the patient. Here again patience and care are demanded. Special enquiries should be made as to the presence or otherwise of infantile convulsions. Whether headaches were troublesome; if so, when and what was their character? Whether they were associated with some trauma? Whether shocks appeared before the fits; if so, when and under what conditions? Were they diurnal, nocturnal, or both? Was there any special cause or period of life which could be associated, at least in time, with the first appearance of shocks? Such a condition as the establishment and cycle of menstruation or severe mental or physical overwork are not infrequently associated with early symptoms of epilepsy. It is always of the greatest importance to get all the available data of the circumstances associated with the earliest discharges. If we can ascertain what were the peculiar circumstances which broke down the natural resistance of the individual, we may get a valuable clue to treatment. In this connection it must be pointed out that the view held by Gillès de la Tourette,* that there is generally no special incident associated with the first fit, is not correct. It is quite frequently the case that the first fit occurs after a long period of overstrain, or after alcoholic or other excess, and yet no special cause can be assigned for the fit. It is in such cases that careful examination generally shows a gradual breaking down of resistance as shown by headaches or myoclonic shocks, the actual fit only being the climax to an unrecognised series of symptoms. Gowers, Claus, and van der Stricht all agree in attaching great significance to the first fit which, as the two latter observers phrase it, "produces a *locus minoris resistentiæ* for later provocations." So if we can establish that some form of event or chain of events were associated with the first fit it is always wise to try the effect of excluding such factors from the patient's life as far as possible.

Sometimes one may get valuable indications for treatment from the patient or his friends when they tell how, under certain conditions, the patient had no fits. Always be on the look-out for any hint or suggestion which may lead to the reconstruction of the conditions which seem to be either associated with the occurrence or absence of fits. One must also get the hereditary history of the patient as fully and correctly as possible. Special attention is, of course, paid to the presence of any epilepsy in the family. Where it is present, I have not infrequently found that

* Gillès de la Tourette, "Traitement pratique de l'Épilepsie," 1901, p. 7. Paris: Baillière.

the type or form of the malady tends to be similar in, say, mother and daughter, or father and son.

I give now a copy of the case-sheet which I use in examining patients:

Name. Date. Address. Age. Married or Unmarried. Number of children. (If a female, number of miscarriages.) Diagnosis which they may have got from friends or from a physician. Name of the physician if previously under medical care. History of the patient's complaints.

1. Description of the fits. Type of prodromal symptoms All particulars related to the fits. Causes assigned to the occurrence of the fits. Any phenomena which persist in the fits or in the periods between the fits. Frequency of the fits and length of time during which the patient has suffered from them.

2. History of any slighter or abortive discharges or fits. Whether patient has attacks of dizziness or periods of mental forgetfulness—" absences." Whether enuresis occurs. If any of these phenomena occur, what is their frequency, and how long have they lasted ?

3. Are there diurnal or nocturnal shocks ? If so, what form do they take, and what is their relation to the fits ? Also how often do they occur, and how long have they been present ?

4. Are headaches troublesome ? If so, where are they localised ? What is their significance, if any ? How often do they occur; how long have they been present ?

5. Has the patient changes of mood ? If so, are the changes sudden or not, and what is their degree ? Are these changes related to the occurrence of fits ? Do they occur frequently or not, and how long have they been noticed ?

6. History of the psychical condition. Is the patient subject to attacks or periods of dreaminess ? Does he have fits of temper, or is he irritable ?

Questions which should always be asked are the following:

1. Was the mother of the patient subject to fits, or had she a fit or fits during her pregnancy ? 2. Was the mother exposed to some sudden shock, such as an assault of a peculiarly trying nature during the pregnancy ? 3. Was the confinement normal or otherwise ? 4. Had the patient any form of infantile convulsions ? 5. When did he cut his teeth, learn to walk and talk ? 6. What infectious diseases has he had ? 7. How did he get on at school ? 8. Did he ever have a trauma of the head ? 9. Has he ever suffered from enuresis or exhibited somnambulism ? 10. What was the condition at puberty ? 11. If a girl, have any symptoms been associated with menstruation ? 12. If the patient has ever been pregnant, has this condition any apparent influence on the malady ? 13. What was the cause, or probable cause, of the

first fit? 14. What was the patient like when the first fit occurred? 15. Can any circumstances, psychical or physical, be associated with this first fit or with subsequent fits? 16. Whether the fits occur by day or night, or whether at both periods? 17. Whether they occur at the time of wakening or of falling asleep? 18. Whether they are affected by posture, such as lying down? 19. Whether the fits are affected by emotional disturbances, or by dietetic factors, such as alcohol or by smoking? 20. What is the condition of a patient after a fit? 21. Is he better, or does he feel worn out and mentally jaded? 22. What are the compensatory discharges, if any, for the fits—for example, shocks or headaches? 23. Are there diurnal or nocturnal shocks? 24. What is the sensibility to pain, if the tongue be bitten during a fit; how long after the fit does it begin to hurt? 25. Have such phenomena as menstruation, gravidity, or a high temperature any influence on the fits? 26. Have the seasons any influence—*i.e.*, is the patient better in cool or warm weather? 27. What are the conditions of the memory and the general consciousness after a fit? 28. What treatment has the patient had, and how did he react? 29. Has he had bromide; if so, how long, and in what quantity? Get a short concise history of the whole fit phenomenon arranged in order of appearance of the symptoms.

Examine the patient very carefully on the following points:

1. The motor system. 2. Sensory system, eyesight, hearing, smell, taste, pain, and tactile sensations. 3. Circulatory system, respiratory system, renal and gastro-intestinal systems. 4. Examine as thoroughly as possible the mentality of the patient.

§ 2. General Prophylaxis.

Epilepsy, as described by the present writer, is to be considered as the repetition of a species of physiological reflex after-discharge induced by some form of intoxication. Genuine epilepsy is, in many cases, a permanent and exaggerated form of that group of reflexes which have been so poorly studied—namely, myoclonic reflexes. These myoclonic reflexes are partly dependent upon the integrity of the pyramidal tracts, and are possible reflexes for all vertebrates—at least for those provided with these tracts. Epilepsy so explained is less a specific disease, but rather a manifestation of a physiological reflex that has become pathological under special stimuli. The repetition of the stimuli leads to a repetition of the reflex. To put it briefly and clearly: in every person lies the apparatus necessary for the production of an epileptic fit. Certain stimuli—*i.e.*, some well-known poisons, but many the nature of which is little known*—will induce a fit or bring the mechanism

* R. S. Mackenzie, Wallis, and Nicoll, *Lancet*, 1923, vol. i., p. 741.

into play. In every individual there is a certain resistance to this reflex, but this resistance varies; in some it is easily broken down, in others not. The early signs of breaking down are not a fit but some other manifestation, such as a myoclonic reflex.

It is a curious fact that in man the prototype of the myoclonic after-discharge and the complete motor fit, the myoclonic reflex, is so little noticed. As a symptom it is frequently unobserved by the patient himself. In the lower animals, more especially in the undomesticated animals, this reflex is extremely well marked, and has a definite protective function. This absence or partial development of the myoclonic reflex in man may account for the presence of certain atypical phenomena and special forms of discharge which have already been discussed (pp. 204, 265 and pp. 67, 93), and will be dealt with again later.

The case may never go further, but, given suitable conditions, it may develop into ordinary epilepsy. There are special times in the life-cycle when this proneness to myoclonic phenomena is greater than at others. Where the patient is young it is generally found that the resistance is less than with those who have reached later life. Experiments have shown that the original function of the fit is protective. It is a method which nature adopts to get rid of the toxin. This first protective function soon passes off, and the reflex tends to become a definite pathological process. A comparable condition is seen in inflammatory changes and in cases of fever (compare p. 219). Here again the first aim of the processes is curative, but in a short time they pass beyond this and are definite dangerous pathological phenomena. The first aim of prophylaxis is therefore to ascertain, as far as possible, what are the dangerous stimuli which produce the fits and to avoid them. (It must, of course, be understood that epilepsy due to organic disease, tumour or traumata of the head or brain, does not come under the category of epilepsy as discussed in the foregoing section.) The second aim is to avoid as far as possible such dangerous stimuli. The prophylactic measures against epilepsy fall into two categories—social-hygienic and individual. For the first a general knowledge of the disorder indicates the lines to be followed, while for the second a study of the individual case is necessary.

§ 3. **Social Hygienic Prophylaxis.**

Prophylaxis from the eugenic standpoint. The influence of alcoholism and syphilis. Marriage of epileptics. Education of predisposed children.

From an etiological standpoint almost all, if not all, the writers on epilepsy agree that certain hereditary degenerative tendencies occurring in a family tend to predispose the members of that family to epilepsy. Anyone interested in the causation and prevention of epilepsy cannot fail to realise that prophylaxis must be approached in the first instance from the social side. Such precautions as a medical examination prior to marriage, the discouragement of

marriage between certain degrees of consanguinity, or of persons with a definite history of hereditary nervous disease, are all important. Apart from the direct question of marriage, the health of such individuals must be safeguarded by well-regulated and abstemious habits. Where there is either a family history of epilepsy or some nervous disorder, or where the person in question has already displayed significant symptoms, the prophylactic measures are the same. Such individuals dare not indulge in alcoholism or run any risk of contracting syphilis. Such an additional strain is more than they can endure, and the result in many cases is to change them from potential to actual patients.

The dangers of marriage between persons in the relationship of cousin or niece seem to be very considerable. In my own experience I have had five cases of epilepsy where there was absolutely no trace of any etiological cause such as nervous disease in the family history. These were all cases of offspring from the marriage of cousins. So long as the law allows legal marriage between persons of this degree of consanguinity, such marriages will take place, but it is very desirable that the medical world should urge on the public the great dangers attendant thereto. Where one is consulted as to the advisability of such a marriage, the task is easy, but the advice is not always followed, even when given forcibly and plainly.

Where persons have had epileptic fits it is according to many inadvisable to marry; this is certainly so if the proposed marriage is with a person who is also an epileptic. Such marriages seem absurd to the physician, but they do take place; epileptics marry normal persons or other epileptics in spite of all that can be said or done.

Whatever may be said about the heredity of epilepsy, such a marriage of epileptics with each other involves a double inheritance in one pathological direction. The explanation given by Roger Williams* of the reparatory tendency of nature does serve here as in other circumstances. The French school goes furthest of all, and declares that marriage between persons who are epileptics, including those who have had at any time one or two epileptic fits, should be forbidden, and that this prohibition should be enforced by law.† This seems to me to be a somewhat extreme view and a measure which it would be difficult to enforce.

* Roger Williams, "The Natural History of Cancer." "It has been overlooked that the predisposition of the organism is to normality, and that disease tends to disappear under suitable environment. Under physiological conditions the inheritance of any characteristic whatsoever is the rule and non-inheritance the exception. Under pathological conditions the reverse is true. Hence with favourable conditions morbid conditions (cancer) tend to die out in the course of transmission. Here one has the indication that 'there is assurance of the feasibility of prevention.'"

† Th. Holmes, *British Medical Journal*, 1910, p. 39.

In my own practice I follow the plan of advising against marriage for epileptics on general grounds. I realise only too clearly that such advice is but routine advice and is not followed blindly by patients who really wish to marry. Curiously and fortunately epileptics as a class seem to be lethargic sexually. Where, however, a patient comes for direct advice I go into the case and judge it on its own merits. The character and type of the other contracting party must be taken into account, also the family history. Where this person has never had any manifestation of fits at any period of his life, and there is no history of nervous disease in the family, the prognosis is in a sense good. On the part of the patient himself the epileptic fits should not have been of such severity as to interfere gravely with his social life. Further, they should be of a type which show themselves capable of control by a careful régime, and the judicious use of drugs. Such a case should enjoy freedom from fits for a period of at least two years prior to marriage. Where these conditions are present, the marriage is still to be discouraged, but one cannot, in my opinion, conscientiously forbid it altogether. Experience shows that marriage frequently has a good effect upon patients, and that there is a good chance, if proper care be taken, for the offspring to escape. So far not one of the offspring of marriages of my former patients has become an epileptic. The question of the fate of the children in such a marriage is, of course, the important thing. It is very rarely that all the children of even the most injudicious marriage fall victims to epilepsy, but quite frequently one of the family does. There is always the risk of a nervous diathesis in the family, and the children need very special care.

While it is true that marriage does improve the condition of some epileptics, there is no reason for the popular idea that the sexual act of marriage is in any way curative. This is merely a deeply rooted but entirely fallacious idea. In many cases the worry and cares inseparable from setting up and maintaining a household are very hurtful to the epileptic, and may make him worse. On the other hand, many cases of epilepsy are practically unaffected by marriage.

The effect of alcohol on the occurrence of epilepsy is very important. In tables which I have prepared dealing with this point, my figures are as follows: Male parents were alcoholic in 4·1 per cent. of the cases; female parents, 5·2 per cent. (these are really below the actual numbers); grandparents, 0·8 per cent. to 0·7 per cent. Among the patients themselves I found that out of a thousand male cases 4·3 per cent. had a history of alcoholism as the provoking cause, and out of a thousand female patients 0·7 per cent. These last cases show very dramatically the important

part alcohol plays in this malady. I am persuaded that if alcohol could be ruled out of the lives of the people the numbers of the epileptics would drop. For ordinary people with a stable nervous system alcohol is not without its dangers, but people with a stable nervous system do not generally drink alcohol, at least to excess. It is the nervy individual who turns to it most readily, and he is just the type to whom alcohol is a most dangerous drug.

In examining patients I have occasionally come across the following history: In the case of a child suffering from myoclonic epilepsy, the father was under the influence of alcohol at the time when the child was conceived. In one case in which four children in a family had myoclonic epilepsy the father in each case was intoxicated at the time of conception. These cases are, of course, rare—at least such histories are—but it might serve as a hint for warning. F. Weeks,* who has directed attention to the heredity of epilepsy, calls special attention to alcoholism in parents as a predisposing cause for epilepsy.

Syphilis is a factor of some importance in the causation of epilepsy. The figures I give are in reality an underestimate, but they serve to indicate at least that hereditary syphilis (2·95 per cent.) is much more serious than acquired syphilis (1·05 per cent.) as an etiological factor.

The significance of infantile convulsions and their relationship to epilepsy is not properly understood either by the average medical practitioner or the general public. There is no doubt that a very close connection exists between the two conditions.

It is strongly urged that all cases of fits, occurring more especially in the young, should be treated with utmost care. It is so easy for a fit occurring, from whatever cause, in a young person to recur, and to become a definite pathological condition. Where there is a history of fits, it is not too much to prescribe a stay in a suitable clinic, where careful and trained observation may explain the cause or indicate the treatment. This rule would apply to fits which tend to recur and are not isolated or definitely connected with some strongly provocative cause. Even these cases should be carefully watched and the patient guarded from all avoidable strain or exertion.

Observation indicates that infantile convulsions are often associated, at least immediately, with dietetic disturbances. This being the case, the care of the diet for young children is a direct prophylactic measure against epilepsy.

The general care of nervous or rickety children is very important. Such children should not be exposed to much excitement, late hours, or any strenuous form of sport. Further, they should have a light nutritious diet (no meat under the age of three), and under no circumstances should they get alcohol. Great care should be taken to ensure the regular action of the bowels.

* F. Weeks, *Proc. Amer. Philosoph. Soc.*, 1912, vol. xxi., and *Epilepsia*, 1913, vol. iv., p. 63.

Where a child has a distinctly bad family history, prophylactic measures should start at once and be carried out with exact care. Where it can be afforded it is best to get a specially trained nurse or governess who will devote her whole time to supervising the child. A careful time-table should be drawn up and plenty of rest should be insisted on between the periods of work. Such children must have plenty of sleep, and all excitement or over-exertion must be avoided. The children often have very large appetites and would eat more than is suitable. The diet must be regulated in amount as well as in character. On the other hand, they must have nourishment frequently, every two or three hours, and on awakening they must get one or two biscuits or a little stale bread. In winter they should get cod-liver oil or Scott's emulsion.

When early childhood is passed, the same care must be maintained as regards the régime of life. Alcohol, sexual excesses, excitement, excessive eating or smoking, fasting, or any form of very exhausting sport, must be avoided. As in the case of the child, great care must be taken to avoid constipation.

In all cases where a child or young person receives a severe injury or blow on the head, great attention must be paid to any symptoms which may appear. If headaches occur frequently, the case is one to keep under close observation and, if possible, on the régime indicated for the nervous child.

§ 4. Classification of Patients into Groups.

Prophylaxis of the individual. Prophylaxis of fits. Prodromes as a landmark. Treatment of prodromes. Directions for household of patient. Hygienic measures, especially for nervous system. Physiological principles in pathology. Choice of career.

When the development of the child and a study of the hereditary history make it evident that there are reasons to fear that epilepsy may develop, more especially if some definite phenomena appear which indicate the approach or probable approach of fits, the general hygienic prophylactic course, described in section 2, must be applied, with special modifications for the particular case. Further, distinction must be made between the prophylaxis in a case where fits have already appeared, and those cases where this has not happened.

It is helpful in understanding our cases, as well as in treating them, if we subdivide them into three groups. In the first class are those patients who have shown symptoms which indicate that epilepsy may supervene. The second class are those patients who have had a definite epileptic fit. They have not had many fits, and no regular habit of fits has been established. The third class are those where fits have occurred fairly frequently, and there is imminent danger of a habit being established. The fourth class are

patients who have had regular fits over a long period. The fifth class are patients where the epilepsy is chronic and accompanied by mental deterioration.

The prognosis in these classes varies greatly. For the first, second, and third classes it is, generally speaking, distinctly good, while for the fourth class the results got may be very satisfactory. In the case of the fifth class nothing curative can be hoped for; one can only do a considerable amount of palliative work.

It is a great pity that so many epileptic patients are not brought for advice and treatment early in the disease. It is so often the case that the fifth stage has been reached before the specialist sees the patient. This fact in itself shows how much need there is for educating the public mind on the subject of epilepsy. Just because hopeless cases are so often brought to clinics, the public get the impression that the disease is hopeless. Epilepsy is no more hopeless a disease than tuberculosis, much less so if it be treated properly at the early stages.

Prophylactic measures must not be limited to cases which show prodromal signs of epilepsy, but must be applied on a much wider scale. Children who have a bad hereditary history, either of epilepsy or of some nervous disorder, such as somnambulism or nocturnal enuresis, or who have had severe illnesses, are as much the subject for special prophylactic measures as those who have had myoclonic shocks, infantile convulsions, or who suffer from headaches of an epileptic type.

Any child who has had an injury to the head (p. 331) or encephalitis of any degree is also a subject for special care along with the rickety child or the nervy child of alcoholic parents.

So important is it that prophylaxis should be begun early, that, if it could be arranged, it should form part of ante-natal work. Where the family history is bad, or where the mother has fits either during pregnancy or at other times, she should have special care during the pregnancy. Such care can only take the form of a well-regulated system of life, with carefully regulated rest and nourishment. How difficult it is to get these two last factors in the life of the average woman of the poorer classes any doctor knows. All the same, if we are to deal efficiently with epilepsy as a social problem, we must be prepared to do much. When the child is born, it must receive great care. If possible it must be breast-fed, and as it grows its diet and habits must be carefully supervised. Even when one gets such a child successfully through infancy, the danger is not over; one must not relax any attention, for the prodromal symptoms of epilepsy often make their first appearance at the age of 5 or 8, or at puberty, or even four or five years later.

The prophylactic measures to be followed out for children are on the following lines :

The children must have plenty of sunshine and fresh air. Their day must be arranged so that short periods of work alternate with short periods of rest. It is of the utmost importance that the habit be formed to lie down and sleep each afternoon in an airy but shaded room. Food must be light and given frequently in small quantities. Fasting for periods of over three hours must not be allowed.

I wish to make it clear that in my opinion no special dietetic scheme has stood the test of prolonged observation. This opinion I find shared by Weeks, Renner, Allen, and Wishart,* and by Goldbloom and Lennox, who investigated the effects of protein and carbohydrate diets. Their observations do not support the view taken by Cuneo that more fits occur on a carbohydrate diet.

On wakening in the morning the child should be taught to wash out his mouth and then be given a biscuit or a piece of bread, not too recently baked, in order to break the fast as early as possible. The play of the children must not be of a very boisterous or tiring nature; they must not indulge in sports necessitating severe physical strain. Above all, the arrangement of the child's life must be done unostentatiously. He must not be taught to regard himself as an invalid, but must lead a natural, healthy, busy life, with supervision. They may attend school in the morning, and a moderate amount† of brain work is to be encouraged. When puberty approaches, great care is needed. In many cases the parents are not sufficiently wise or well-trained to carry a child of this type successfully over the difficulties attending the period. Even in the healthy child it is a period of strain, and one which they often have to come through with practically little help—often the lack of help injures them. In the case of the special child under discussion, the strain is proportionately greater, and every help must be given.

I have found parents so astonishingly ignorant of facts relating to the treatment of children during puberty that I have for some time given a short course of lectures, several times a year, for the parents of epileptic children, for near relatives, and for persons in charge of epileptics whether children or adults. Such lectures, I find, are really a help. They must, of course, be of the simplest nature, and absolutely to the point. In the lectures I explain how the very act of sitting in a room involves an expenditure of energy. Many people do not realise that the receiving of a continual stream of impressions and the subconscious reaction to each is a really exhausting process. If you do not explain this properly the parents cannot understand why it is necessary for the patient to lie down and sleep for some time, each day in the afternoon, in an airy shaded quiet room instead of just sitting in the living-room. This habit is difficult to establish, and may take weeks in the case of grown-up patients. Patients often have a fit coinciding with lack of sleep in the afternoon. Employers must be asked to give an opportunity for this rest in the afternoon. The importance of personal

* Weeks, Renner, Allen, and Wishart, *Archiv. of Neurol. and Psychol.*, 1923, p. 683.

† Hammond, of New York, notes that an average amount of mental exercise is highly beneficial for cerebral development.

cleanliness must also be explained in the same fundamental way. Special attention is given to the diet sheet—what it must and must not contain, and why. The patient must masticate his food properly. Long fasts must not be allowed. When the patient wakens in the morning crisp biscuits or some dry bread should be eaten immediately after washing out the mouth, and, most important, the necessity of having a daily evacuation of the bowels is insisted on. Patients should accustom themselves to defæcate soon after breakfast. Where the bowels act irregularly an aperient should be given, but not one containing a high percentage of ordinary salt (Carlsbad salts, etc.). If after administration of an aperient the bowels do not act, an enema must be given.

Instruction must also be given to those whose children are older about the dangers arising from attending plays, concerts, or lectures in crowded rooms, or of playing games productive of strong excitement. Church-going should be allowed, but only to short services where there is no over-crowding. It is also important that they realise how essential it is to keep up the treatment. If the matter be explained clearly and simply, the parents or friends are much more likely to co-operate intelligently with the treatment. Where the patient has also a clear grasp of the why and wherefore of the régime, and has the good hope of recovery put before him, the case is naturally on the best possible footing.

Where a breakdown occurs and disquieting symptoms appear, the directions must be clear and definite. Neither the patient nor his friends must become panic-struck or despondent. Put the patient to bed for several days, give the drugs as directed by the medical man, take special care of the diet, which must be light, and see that the bowels act freely.

Careful notes must be made of the patient's occupations, amusements, and general mode of life, so as to ascertain, if possible, the causes of derangement, and the associated circumstances of the conditions of "charge" and "discharge" Lists, such as are shown in the appendix of Chapter XV., must be given to the patient or his friends or attendants. Those in attendance on the patient, or those in close association with him, such as near relatives, must be instructed thoroughly and minutely, both as regards the symptoms to watch for—*i.e.*, those indicating the condition of "charge"—and as regards the treatment. Should such symptoms appear the patient, who is in the condition of one very liable to have a fit, must be treated as a technically sick person, put to bed. kept quiet and at rest, extra medicines given (as prescribed), and an enema administered.

Under all circumstances, such patients must never take alcohol, even aerated lemonade must not be drunk. Coffee also is forbidden, except where special instructions are given. They must live in rooms with windows widely open summer and winter, day and night, while the bed-stead must be clear of all walls and obstructing draperies.

To prevent any risk from suffocation by heavy feather pillows, the patient should have a horsehair pillow covered with wide meshed material, which will allow of the free passage of air. This is absolutely necessary if no one sleeps in the same room or next door to the patient. I have known of three cases of suffocation occurring where this precaution was not taken.

Where a child has already had myoclonic shocks or headaches of an epileptic type, when brought for treatment, the foregoing prophylactic measures are all the more necessary.

Where such a child is brought, always try to find out whether the first fit, or manifestation of minor symptoms, such as headaches or myoclonic shocks, preceded or coincided with some time of special excitement—a party, a festival, or an examination.

Where the myoclonic shocks and other symptoms do not appear merely at times of very special strain and recur frequently, it is wise to regard the patient as being definitely over the borderline-and therefore a true case of epilepsy.

We have here to deal with the physiological principle that every process performed for the first time has to overcome a certain resistance. When the action is repeated, often enough the resistance is gradually worn away. In the case of a child with an occasional myoclonic shock in response to a tactile or acoustic stimulus, the natural resistance is not yet overcome. If, however, " spontaneous " myoclonic convulsions occur without special cause, it may be taken for granted that the natural resistance is in process of being overcome. Where this resistance has been overcome for a long period, the nerve tracts involved may be described as " frayed."

The same series of physiological events may be seen where a child is taught piano-playing. At first the movements are difficult, the co-ordination awkward, but later it is done practically mechanically. In the same way, if the myoclonic shocks are prevented, the resistance is built up, as, conversely, the mechanical dexterity in playing is lost if not kept up by practice.

The great point to be realised about epilepsy is that it is the *repetition* of the fit which constitutes the great danger. Gowers states the case trenchantly when he says " the disease is self-perpetuating." Where fits have occurred, we know that the natural resistance has been broken down and weakened, but where treatment succeeds in stopping those fits the resistance is gradually built up again. At the same time it must be remembered that it is not certain that a repaired resistance is as strong as one never broken down. Further, in many cases of epilepsy the initial normal resistance is weak. It is this fact which makes all the prophylactic work so necessary. Where there is reason to believe or to know that the resistance is weak, one can take no risks. Such a person must always exercise care, but with certain reasonable precautions the case may practically be a recovery—that is, he escapes the fate of becoming a chronic epileptic. The same applies to other diseases; a person cured of pulmonary tuberculosis is taught to avoid certain risks, although he is, technically speaking, cured.

It is interesting to find that Tissot,* writing in 1813, admits that many cases of epilepsy are curable, and points out that physicians give up hope too soon—so delivering the patient to the quack doctor or charlatan.

Regarding the choice of an occupation, it follows from the foregoing pages that the work of a gardener, porter, or messenger is more to be recommended than that of a builder, electrician, chauffeur, etc. Office and work in a shop need not be specially discouraged, since much depends on the hygienic conditions of the office or shop.

* Tissot, " Œuvres complètes," 1813, p. 26.

§ 5. The Therapeutic Measures to be adopted after Unmistakable Epileptic Symptoms have manifested themselves.

Herpin-Delasiauve argument. Great importance of hygienic rules. Individual treatment of paramount importance. The fate of a possible epileptic patient is as a rule decided by the treatment after the first definite fit. Notes on animal epilepsy.

The fate of the patient is frequently decided by the therapeutic measures adopted immediately after the malady has manifested itself.

About the treatment and prophylactic measures suitable for epilepsy has raged a fierce conflict. Even at the present day the matter is one subjected to much discussion. Reference may here be made to the two leaders of thought on the subject—Herpin, the Swiss neurologist, and Delasiauve, the French neurologist.

Herpin* in his book on epilepsy, which is rightly considered to be a classic, complains of the scanty attention paid to the therapeutics of epilepsy and the small advance made in this branch compared with the progress made in symptomatology, differential diagnosis, prognosis, and pathological anatomy. As he says, physicians of different countries and schools of medicine will agree as regards the symptoms and character of a disease, but differ hopelessly when treatment is discussed.

In scrutinising the cases decribed by Herpin with great scientific accuracy, it is seen that three cases in the first group of seventeen have had but one fit. This fact was criticised adversely by his opponents, but here they were wrong. The diagnosis of epilepsy can most undoubtedly be made after one fit, more especially where a knowledge of the case affords further corroborative data. Herpin also suggests the question as to the possible number of patients who have only had one epileptic fit during their whole life. This question still remains unanswered.† If, however, such patients are more numerous than we are accustomed to think, it would somewhat diminish the correctness of Herpin's dictum, that more than half of the epileptics might be cured, given proper treatment. The word "cured" is one which gives occasion for criticism. Herpin, it is true, merely follows the example of great workers such as Morgagni, Boerhaave, and others in his use of it; still it is an expression which conveys an impression which experience does not support. As Delasiauve says: "The predisposition remains." Still, if a patient remains free from fits for a very long time it is usual to find that the resistance increases again (compare Extract, Case 43, p. 274).

As regards the actual treatment of the cases the impression one gathers from a study of Herpin's cases is that he did not himself appreciate thoroughly the influence of comparatively slight changes in the condition of life he prescribed to his patients. He stipulates that simple medicines must be used, simple modifications in the manner of life, and careful watchfulness of the cases practised.

The second observation of Herpin deals with a case of a girl aged 18, who had a predisposition to epilepsy, and who had convulsive movements of the fingers on the ulnar side, and also had complete epileptic fits. He prescribed zinc oxide, and records that after the taking of 312 grammes the patient had no more fits, with the exception of one relapse, which was treated by changing her bedroom. After this the girl kept well for many years after Herpin's death.

* Th. Herpin, "Du Prognostic et du Traitement curatif de l'Épilepsie," Paris, 1852.

† From my own experience these cases are fairly frequent.

In another case where the patient was a lad of 11 years, it seems more probable that the cure was associated with the control of masturbation than with the administration of ½-gramme doses of zinc oxide. In a third case (No. 13) it is fairly obvious that the control of the " manger d'une manière immodérée " was the curative agent, and in a fourth (No. 16) the control of a drinking habit.

Herpin is plainly of the opinion that to be capable of cure the epileptic fits which have occurred must have been few in number. Up to 100 the prognosis is good, over 500 bad.

Over seventy years have passed since Herpin wrote his book, and during that period the use of bromide and its various compounds for epilepsy has become very general. Are we at the present day so very much further on therapeutically than Herpin? Certainly we have made some progress, but is not this progress more in the lines of general treatment, the recognition and application of the rules of strict personal hygiene extending over all the aspects of the patient's life? Herpin certainly introduced and practised many of these rules, but he did not seem to appreciate how much good he was doing to his patients thereby, and how little their cure depended upon a drug such as zinc oxide. In our opinion he ascribes too much importance to this drug. At the present day the rational and comparatively successful treatment of epilepsy is based on close attention to personal hygiene. All aspects of the patient's life come under the rule, and his whole life must be subordinate to the ceaseless effort to prevent the occurrence of fits. The fact emphasised by Herpin that epilepsy has a good prognosis only when few fits have occurred is an axiom in present-day medicine. Each fit a patient has predisposes him to have another, or in other words each fit makes the next easier. It is therefore obvious that to be successful treatment must start early. This stage so fraught with danger to the patient, and so weighted with splendid possibilities, is practically always in the hands of the family doctor. This may be a matter for regret, but it is so, and the remedy lies in educating all medical practitioners in the knowledge necessary for the correct treatment of early cases. Certainly every practitioner should know that an early case of epilepsy is not one to be treated by narcotising drugs.

Each doctor who has a case of early epilepsy brought to him must realise that upon his diagnosis and proper understanding of the case rests, humanly speaking, the future of the patient. Epilepsy is not a disease with ready-made symptoms or fundamental characteristics, at least in its early stages. Certainly it is not a disease to be studied in a textbook, or to be treated by stereotyped methods. Each case has to be examined on its own merits, and the utmost patience and thoroughness are necessary to obtain an absolute knowledge of all the symptoms, their time, and manner of appearing. Of course, where some cause can be ascribed rightly

or wrongly for the appearance of fits, the physician has something to start on. In the case of trauma, investigations must be directed to the establishment of some connection between the injury and the fits. If the patient has led a markedly intemperate life, here again is a point to work from.

Cases associated with degenerative cerebral conditions are not so important, because so little can be done at the best.

The typical case, which is important to treat correctly, is one where the patient has suffered from myoclonic shocks and headaches, probably for some time, and finally has had an epileptic fit. The fit has alarmed the patient's friends, and he is hurried to the family doctor. As has been shown in Chapter VII., the actual fit is not so distressing a symptom, since it represents a method by which the toxins have been dissipated. The preceding symptoms—headaches, vaso-motor and sensory disturbances, myoclonic shocks and fainting fits—are the important facts; the fit merely is a climax. Gowers and Turner both maintain that the prognosis is better in patients who only have severe fits as contrasted with petit mal. In the second case the discharge or fit does not seem sufficient to dissipate the toxins, and the patient is never in so healthy a condition as after a severe fit. This point was brought out in the experimental work on cats, dealt with earlier in this book. The curious sense of well-being described by patients after a severe fit has been noted by writers on epilepsy for many years (pp. 252 and 282). The therapeutic measures must not, however, be directed to curing the patient's headache, fainting fit, or other symptom; these are merely danger-signals. The treatment must be directed to the underlying condition which gives rise to the danger-signals. What are the conditions of life which place the patient in a condition of danger? No detail is too trivial, no modification too small, to exercise an important influence on such a patient. It may not be irrelevant to recall a case of an ape in the zoological gardens who had severe fits. As treatment I suggested putting him in a sunnier cage; this was done, and the animal had no more fits. True this was an ape, but over and over again I have found some trifling modification of life, some small detail of routine, enough to raise the patient's resistance sufficiently to stop the fits. In this opinion I am not alone. Juarros,* Shanahan,† Allan MacDougall,‡ and others hold the same view, although their interpretation of the significance of the fits is not the same as mine.

In connection with the foregoing experience with the ape in the Zoological Gardens I have been struck with the fact that some simple readjustment in the routine of the life of an animal in these gardens has

* Juarros, *Epilepsia*, 1914, vol. v., p. 172.
† Shanahan, *Therapeutic Gazette*, March, 1912.
‡ Allan MacDougall, *Epilepsia*, 1913, vol. iv., p. 358.

resulted in the complete disappearance of fits. Such "cures" have to my own knowledge lasted ten, twenty, and over twenty years.

With patients I have also found that a more or less simple modification such as a glass of hot water morning and evening, an hour's sleep in the afternoon, abdominal massage to facilitate peristalsis, abstention from long fasts, taking food every two hours in suitably small quantities, abstention from severe and prolonged study, or the regulation of study so as to leave the evenings free, the introduction of some light amusement before going to bed, such as an amusing game of skill where there is no money at stake, stopping all alcohol even light beer, stopping smoking, changing the habitat even so slightly as from a lower to a higher flat, where it may be drier, or to a lower flat where the patient gets out more easily (this applies more especially to children), may have a most beneficial effect. Sometimes the removal of the appendix will act in the same way, or the habitual use of a soap and water enema, where daily evacuation of the bowel does not occur spontaneously. In the case of children, sometimes the fact that they are allowed to go to school only in the morning, or are enabled to play with others out of doors, may have beneficial results. It is true that the criticism may be made that in addition to any of the foregoing modifications the patient is receiving special attention and medicaments, and that they, rather than the modification, are answerable for the improvement. This may be true for a certain number of cases, but there are some where a slight factor seems to have been directly or indirectly the cause of the presence of this unknown postulated toxin, which induced the fits. This factor has been, it is suggested, ruled out by one or other modification of life.

Viewed from the physiological standpoint, the epileptic fit is a last defensive reflex against certain toxins (pp. 99 and 191). Smaller doses of the toxins have evoked the danger-signals, already referred to; but an increase of the dose eventually produces this reflex discharge, the immediate effect of which is a feeling of well-being. With this view as our starting-point, it is obvious how important it is to know the exact circumstances attendant upon the first fit and the first appearance of the danger-signals. We must try to reconstruct the condition of life at that time. It is also very important to know whether the climax or fit was associated with any abnormal or unusual circumstances, such as emotional strain, fasting as for religious purposes, constipation, or alcoholism, or some allied condition. Sometimes this is found to be the case, but by no means in all cases. It must be remembered that where danger-signals have been in evidence for some time, a very small factor would be sufficient to precipitate a patient into a fit. Very often it is found that a combination of factors, probably insignificant singly, but hurtful if grouped, can be recognised as having caused the first fit. Indeed, careful survey of cases goes to show that in a number of them there is no startling factor before a fit.

As a result of years of experience in such work—*i.e.*, the diagnosing and treating incipient epilepsy—I would recommend the erection of a hospital for incipient epilepsy, for such cases do not get the attention and treatment they require in general hospitals. Here the patients would have care, supervision, and reorganisation of the routine of their lives. Personal cleanliness down to the smallest detail of the care of the teeth or artificial dentures, careful super-

vision of their diet, attention to the proper functioning of the alimentary canal, rest, open air, and sunshine, regulated exercises, and definite psychical encouragement, would all be given to them. I would have each patient in the incipient stage know exactly what the chances are of escaping the awful fate of becoming an epileptic. I should explain to him why this great care is being taken, and I should imbue him with enthusiasm to fight for his own recovery. Above all, he must not get depressed, neither must—important detail—resort be made to sedative drugs. Personally I believe the mere fact that such a hospital existed, and that in it people were taught how to protect themselves, would be of immense national value. Epilepsy is such a terrible disease to fight: it is a national duty to do our utmost. Until we get this, all we can do is to ensure, as far as possible, that all doctors realise the awful responsibility devolving upon them when called on to see an early case of epilepsy. To say, "send each case to a specialist," is even now the counsel of perfection. Epilepsy is, unfortunately, too universal a disease, and until we have some national institution early cases are nearly always seen by family doctors. It is they who must exercise the beneficial influence and apply the modern therapeutic measures of personal hygiene. If one could ensure that no case of early epilepsy was merely given bromide or luminal, without any thorough examination, great progress would be made.

§ 6. The Treatment for Patients who have had a Certain Number of Fits, but who have not reached the Stage which could be classed as Inveterate.

Points to be aimed at. To secure a long period free from fits or associated phenomena. To give suitable medicaments to lessen the irritability of the nervous system. Zinc oxide. Zinc lactate. Salts of bromide to obtain results. The action of the bromides. Significance and value of salt abstention. Disadvantages of bromide therapeutic preparations. Acne. Bad effects. Borax. Luminal. Nitro-glycerine. Indian hemp.

Such patients are those whose resistance to fits has been reduced by the recurrence of fits. The object to be aimed at in such cases is the establishment of a long period in which the patient does not have any fits. To produce this, resource must be made to drugs, such as the compounds of zinc, bromide, and borax. This stage is the one which most neurologists see. It must be emphasised that in many textbooks on epilepsy or on nervous diseases this stage of epilepsy is referred to as the typical condition when treatment is necessary and beneficial. In this work one special object is to point out how erroneous this view is. As has been shown in the earlier chapters, this is the fourth stage of the malady, and one where treatment is so belated that palliative results are in some cases all the most hopeful physician may look for.

In his book on epilepsy Gowers begins the chapter on treatment by pointing out that epilepsy is a self-perpetuating disease. Each fit predisposes the patient to have another. This is due to a physiological law which operates in disease as in health (compare p. 335).

If we look at epilepsy from this standpoint, it is really amazing that an arrest, or a partial arrest, of the disease in this stage occurs at all. It is not nearly so wonderful that quite a number of cases are resistant to all palliative measures. What is achieved by drug treatment at its best is that the period between the fits is lengthened, and if care be taken to avoid any combination of circumstances which seems to be associated with the occurrence of fits the patient may regain so much of his original resistance—that is, the resistance which he possessed normally, before it was overcome by some toxic substance, in conjunction with some unfavourable condition of life (Tissot, *loc. cit.*, p. 158). Along with drug treatment the whole condition of the patient must be carefully studied and any possible cause of trouble removed. Among these are intestinal parasites, habitual over-eating of rich foods, alcoholism, or some peripheral source of irritation.

Although the correct and successful treatment of these subsidiary abnormal conditions helps immensely, one cannot forego the direct treatment of the increased irritability of the nervous system. The old dictum, "causa ablata, tollitur effectus," does not work here in many cases (compare also experiences with traumatic and focal epilepsy, p. 395).

In the literature of the middle of last century, the manuals of Delasiauve, Radcliffe, and Herpin contain references to many drugs proudly termed specifics against epilepsy. Valerian was introduced from Italy to the countries of Northern Europe. Boerhaave advised asafœtida, more particularly in cases of hysteria, but certainly got good results in epilepsy. Opiates of different types were exploited, such as opium and belladonna, while digitalis had some reputation.

Zinc oxide, originally used by Paracelsus, was officially introduced by Gaubius, who "discovered it as the secret of a quack." The pills of Méglin, a compound of zinc oxide in 60-milligramme doses, with valerian and jusquian, had quite a reputation. Herpin praises these pills in his writings, and records that he pushed the dose so that some patients took 2·50 grammes of the zinc salt per diem. He found that sickness and diarrhœa usually prevented the increase of the dose to this amount. Sir William Gowers also used this formula along with bromides. An attempt has been made to give this compound in bread, the so-called zinc bread, but patients found it too offensive. Gowers found it best to give the zinc oxide in powders, and found that 100-milligramme doses could be given daily without bad results. Schroeder van der Kolk and Kroon* recommended lactate of zinc for young patients, especially where the digestion was poor.

We shall now consider the evidence for the use of bromides, borax, and luminal.

* T. Kroon, "Epilepsie en hare behandeling," Diss., Amsterdam, 1859.

Duncan Gibb used a bromide salt for irritability of the throat in epileptics, and incidentally noted the influence on the fits. Sir Charles Locock tried bromides in menstrual epilepsy, and also got encouraging results. From the evidence supplied by these two observers, bromides came into general use, more especially after Radcliffe, and Hughlings Jackson in 1864 introduced the drug into the National Hospital for Epileptics and Paralytics.

It is very difficult to estimate the number of practically chronic epileptics who derive an extraordinary degree of benefit from the use of bromides. Patients come to a clinic with a history of long-established fits, and bromide is prescribed. They continue to take the drug for some time, but as no fits occur they stop the medicine, and the clinic sees them no more. Inquiry quite a long time after shows that they have remained free from fits for long periods after having stopped taking bromides. These cases do not, of course, comprise all the cases of epilepsy, but it is surprising how often the above history would apply. The cases we do see again are those which do not react well to treatment. As a matter of fact, such cases, because they are not lost sight of, form the basis for statistical records culled from hospital and dispensary lists.

From the available statistics the following figures are offered.

Turner finds that bromide is successful in stopping the fit in 23·5 per cent. of the cases. Binswanger gives practically the same figure. At present it is impossible to regard these figures, or any available figures, as an accurate description of the action of bromide alone. Along with the bromide the patient receives directions more or less minute as to a hygienic method of life. Whether the bromide figures would be so good, if no effort were made to order the patients' lives, is not very probable. As regards the numbers who are alleviated by the use of bromides, Biro gives the figure at from 30 to 40 per cent. of the cases. Some confusion exists as to whether the actually stopping of the fits or the moderating of their severity should be included in the same statistical category.

Certainly the various authorities agree that as a general rule the severe type of fit benefits more from bromides than the mild form, while the least effect is seen in psychical disturbances and myoclonic shocks. From the point of view put forward earlier in this book, such a conclusion is not surprising, since the psychical disturbances, absences, and atypical phenomena are not to be regarded as regular discharges, but atypical phenomena due to some particular form of intoxication. Or it may be due to an ordinary form of intoxication acting on an organism specially predisposed, probably one with an hereditary tendency towards epilepsy or mental disturbances.

Certainly, all statistics regarding epilepsy are at best vague. This is due to the large proportion of cases which drift in and

out of clinics leaving practically no trace. It is a very great pity that more conjoined effort is not made to keep in touch with every case of epilepsy. Certainly more time should be allowed for examination and an effort should be made to interest the friends and relatives in the rationale of the treatment.

The Effect of Bromides. Mode of Action.—Salkowsky* noted that carbolic or strychnine convulsions were lessened by bromides. This was explained by Schultze† as due to the influence of bromides in diminishing metabolism in nerve cells.

Toulouse‡ introduced the idea that if patients were given a salt free diet the bromide given medicinally would be more active, and smaller doses would be effective. This he explained on the grounds that if common salt were denied to the tissues, they would utilise the bromide to maintain their correct osmotic ratio. Laudenheimer§ and von Wyss‖ also maintained that the retention of bromide is favoured by abstention from chlorides. In other words, the theory is that the chloride ion and the bromide ion are interchangeable. Abstention from chlorides alone would have no therapeutic value, but conjoined with the administration of bromides secures a more active assimilation of the bromide and concurrently a decrease of the irritability of the ganglion cells (Voisin, Hondo, Meyer, van der Velden.)

According to this theory, poisoning with bromides, or an overdose of bromides, would be rectified by free administration of ordinary domestic salt. Where the use of large doses of bromide has continued over a long period, symptoms of retention, due to breakdown of the heart and kidneys, appear. Acute bromism can be cured by large doses of common salt, but this is fraught with danger in patients who are accustomed to a certain amount of bromide. Chronic bromism may be treated by inducing diuresis.

Von Wyss, as a result of a series of experiments, ascribes the comparatively larger quantity of bromide in the brain to the greater quantity of water in that organ. The kidneys are but ineffective filters of bromide. If excess of chloride or iodide be administered, the kidneys excrete 50 per cent. of the excess during the first day, whereas with an excess of bromide only 6 per cent. is excreted.

It has, therefore, to be admitted that a salt free diet is a distinct advantage when bromide is being administered. Unfortunately, experience shows that it is not a very practical method. Certainly with an intelligent and docile patient a salt free diet may be attained and smaller doses of bromide be efficacious in keeping the patient free from fits. If however any error occurs, the result

* Salkowsky, *Pflügers Archiv. f. d. ges. Physiol.*, 1872, vol. v.
† Schultze, *Zeitschr. f. Biologie*, 1883, vol. xix., p. 311.
‡ Toulouse, *Semaine médicale*, 1904, No. 42, p. 362.
§ Laudenheimer, *Neurolog. Centralblatt*, 1910, p. 461.
‖ Von Wyss, *Arch. f. experiment. Pathol. und Pharmakol.*, vols. lv. and lix.

may be even dangerous, for the patient is immediately exposed to the risk of having a fit or series of fits, the addition of common salt having the effect of minimising the quantity of bromide retained by the tissues.

Previous to 1914 I had four or five varieties of special bread baked by a large baking firm. These breads contained no ordinary salt, but had known quantities of either bromide, borax, or oxide of zinc. When the war began the baker, in spite of protests from me, stopped preparing the bread. The result was that a great number of my patients, who had been having one or other of these special breads, began to have fits. Some of them even became as bad as they were when treatment started. These patients were exposed to two adverse circumstances—the withdrawal of the drug, and the sudden addition of common salt.

Apart from the danger of a sudden change from a diet free of salt to a diet containing ordinary salt, one has to consider the effect lack of ordinary salt has on the appetite. Patients with heart or renal complications do not do well on the salt free diet, neither do the very obese (Kinberg). As a result of long experience I do not attempt the salt free diet, but advise that very highly salted articles of food should be avoided. In some articles of food, such as bread or soup, one can quite easily use a bromide salt such as sedobrol (Ulrich) instead of ordinary salt. This modification is frequently quite enough, and is, in many cases, well tolerated by patients of all types.

In a good many patients it has been found beneficial to restrict the amount of food taken. The sense of satiety is often little developed, or atrophied, in epileptic patients, hence they are liable, if uncontrolled, to overeat themselves. It is probable, therefore, that this explains the result of Weeks, Renner, Allen, and Wishart,* who experimented in groups of patients with periods of partial and complete fasting. In many of the patients the fits decreased in number and even ceased eventually.

Drawbacks to the Treatment with Bromides.—Patients differ greatly in their tolerance of bromide. Some will take 20-gramme doses, while others cannot tolerate 4 grammes. The weak and fragile patient rarely tolerates bromides well.

The first sign of intolerance is as a rule acne, which appears first on the forehead and back; a little later a foul breath and intestinal disturbances follow, accompanied by lack of appetite, ataxic symptoms, and mental somnolence. The first and very troublesome symptom of acne is probably due to diminished peripheral resistance to organisms. Sometimes much help may be got from frequent baths and the utmost cleanliness of the patient. He should avoid handling the affected areas as much as possible.

As a result of my own experience, I consider that if one does

* Wishart, *Archiv. of Neurol. and Psych.*, 1923, p. 683.

not get the desired result with 3 or 4 gramme doses of bromide larger doses will only give a temporary improvement. Therefore I hardly ever give large doses.

In cases of well-established, but not inveterate epilepsy, it is (p. 340) often beneficial to combine rest in bed with the exhibition of moderate doses of bromide, particularly where the results of this drug with a well-regulated mode of living have been disappointing. Where this is impossible, then cut down the bromide still further, and try such drugs as borax, zinc, veronal, hyoscine, nitro-glycerine, and mercurial iodide.

Where one has to deal with inveterate cases, the conditions are different. Here the patients, in many cases, take very large doses of bromide, and if one cuts down the doses, fits become very troublesome. Here one has to balance the advantages and disadvantages and do the best one can. The case is always difficult, for if one cuts down the bromide, the patient has fits, and also he is likely getting quite enough bromide to keep up the acne, which is probably giving him a great deal of trouble. Gowers always held that in such a case arsenic, in the form of Fowler's solution, should be given with the bromide. This practice I also follow, with the precaution of never permitting a patient to take arsenic for longer than a few weeks in case of toxic symptoms arising from the accumulation of the drug in the tissues.

Where the acne has developed into a pustular condition, then Ulrich advises that a paste made of ordinary salt and zinc oxide should be applied as a compress.

There is no doubt that, both among medical men and laymen, bromide is a drug with a bad reputation. There is not, I think, sufficient evidence to justify this reputation, but there is no doubt that most of the cases one sees where bromides have been used over a period of years do present very serious mental deterioration. Among all my chronic patients I have known but two cases where bromides had never been taken, although the fits had continued for ten and twenty years. Certainly these two cases did not show anything like the mental deterioration common to the patients of this standing who have taken bromides. I have a suspicion that the rapid change of great fits into petit mal is often nothing but a transformation due to the premature use of bromide.

Whatever may be the essential reason for the distressing mental symptoms, all physicians should realise that the steady dosing of any patient with $2\frac{1}{2}$ or 3 grammes of bromide daily is a very serious matter. Certainly we have progressed sufficiently to know that it is erroneous to double the dose of bromide where the smaller dose does not give good results. I need not point out how wrong and unscientific was the old habit of giving a certain

dose of bromide to every epileptic in an institution; and yet this used to be done quite regularly.

The dosing of any patient with bromide is a matter for great care. Each case must be watched; only with individual attention to the merits of cases can we hope to do patients real and lasting benefit.*

Preparations of Bromide in Use.—Some time ago it became fashionable to consider that potassium bromide had a bad effect on the heart, so ammonium bromide was prescribed instead. This opinion was not, I think, based on any accurate or scientific evidence, but was none the less very generally accepted. Later it was suggested that the combination of peptone and bromide might be successful, so a preparation called bromipine was used. At the present time there is a craze for gelodurate capsules (Pohl). Jödicke† praises them because they are not acted on by the gastric juices, and so there seems less risk of gastro-intestinal trouble. Personally, I never, or practically never, use these passing forms of bromide, but administer either the potassium or sodium salt.

Occasionally one meets cases which do not react in the usual way to bromides. This is especially the way in the case of those suffering from atypical fits. In such cases smaller doses of bromide may even increase the number of fits.

Borax.—Gowers introduced the use of borax. It has been used fairly generally, and is certainly one of the recognised methods of treatment in epilepsy. The Danish school of physicians use it very freely, even up to 8 grammes daily (Lange).‡ Such a dose seems rather dangerous, for with smaller doses such symptoms as eczema, diarrhœa, sickness, loss of weight, and even albuminuria may arise. Féré and Erlenmeyer investigated the results got with borax. With a daily dose of 1 to 3 grammes, Féré found improvement in 9·1 per cent. of his cases.

The action of borax is probably due to its aseptic properties as exerted through the gastro-intestinal tract. Jödicke, who only used it occasionally, found that it reduced the omental fat; it is, therefore, worth trying with stout patients.

Personally I only use it with bromide, the maximum dose being 1 gramme daily. With such a dose it is very rare to get any untoward symptom such as eczema or diarrhœa. Most effective mixtures are found to be: boracis, 13; brom. kal., brom. nat.,

* Gillès de la Tourette taught that a permanent dilatation of the pupils indicated that the correct dose of bromide was being used. This observation is not confirmed by other observers.

† Jödicke, *Zeitschr. f. d. ges. Neurol. u. Psych.*, 1913, vol. xviii., p. 248.

‡ Lange, " Hospital Tidende," 1896.

āā 40; aq., 1,000, and boracis, 28; brom. kal., brom. nat., āā 31; aq., 1,000. One or two tablespoons a day; rarely more.

Luminal or Phenyl-Aethyl-Barbituric Acid.—This substance which is a modification of veronal (an ethyl group being replaced by a radical) has become more generally used in epilepsy during the last ten years.

In its action, luminal is a sedative, but varies a good deal with different patients. For example, in one case of a young medical student who suffered from severe infrequent fits, a dose of 200 milligrammes daily was associated with mental apathy and some intestinal disturbances. On the other hand, Koog* records a case of a girl, in whom apathy was produced with a dose of 60 milligrammes. Jödicke found that a daily dose of 300 milligrammes was often very useful, *but certainly* found that the tendency to irritability increased. Perhaps this irritability is compensatory, and depends on the suppression of the fits. It is more frequently found with luminal than with bromide or borax. It is interesting to note that this writer suggests that a fit by its association with the condition of phagocytosis may act as a de-intoxicant of the system.

Bikeles and Uyszewski† did not find any evidence to show that the irritability of the cortex of the dog decreased with luminal, but they certainly found that the animal was not so prone to fits. Albertoni found that the lability of the cortex for the faradic current was diminished by luminal. There is a certain amount of disagreement as to the general effects of luminal.

J. Grinker,‡ after using the drug on 200 cases, found that the best results were got with patients who had severe fits. This result is also found with other drugs. C. Juarros,§ G. Maillard, and P. Meignaut‖ praise luminal for the good effect they found it had on the psychical condition. They also think that there are no cumulative effects. This would require more investigation before it could be generally accepted. They direct that the dose of luminal should be reduced every half year by 100 milligrammes. Recently Willcox,¶ has given a serious warning to the effect that prolonged use of barbituric hypnotics may cause serious and palpable alterations in the white matter of the spinal cord. In mental asylums in this country status epilepticus and death have been found to follow the sudden stopping of luminal. In the case of idiosyncrasia scarlatinous exanthemes, with high fever and desquamation of the skin, death has occurred with luminal.

* Koog, *Journ. Amer. Med. Assoc.*, September, 1922, p. 782.
† Bikeles and Uyszewski, *Ned. Tijdschr. v. Geneesk.*, 1919, vol. ii., p. 1868.
‡ J. Grinker, *Journ. Amer. Med. Assoc.*, September 2, 1922, p. 788.
§ C. Juarros, *La Medicina Ibera*, 1921.
‖ G. Maillard and P. Meignaut, *Presse médicale*, 1923, p. 522.
¶ Willcox, *Lancet*, 1927, vol. i., p. 1034.

Zinc oxide (see p. 341).

Among other drugs, which sometimes give good results, are nitro-glycerine (sol. nitro-glycerine 1, aqua 1,000 parts), belladonna, and veronal. In cases where bromide and borax cannot be used, these drugs are worth trying. Flechsig's bromide-cure I have found of no value. It is regrettable that so little critical observation is brought to bear on a new treatment. All sorts of drugs and combinations of drugs, including even camphor bromide (which, as has been shown, is the drug which inevitably causes fits), are exploited and administered practically blindfold. No attempt is made to establish an hypothesis as to the possible effect of the new drug.

Resource may be made to cannabis indica, the drug so much abused by the Mohammedan population of the world. The effect of this drug is generally known: the dreamy delights it evokes have been a matter of history since the days of Herodotus. It is a very unstable drug, and uncertain in its action. For these reasons it is not a very dependable medicine. Hugenholtz,* Reynolds, and Gowers, however, recommend it in epilepsy. Gowers gives details of a peculiarly refractory case of epilepsy which was much improved with cannabis indica when other drugs had failed. Sachs recommends its use in cases where headaches are a tiresome symptom.

Schussny† advocates extreme caution in the use of the drug, since he found disturbing symptoms after a very small dose.

In my own cases I do not use cannabis indica alone, but I find it a very useful adjuvant where a patient is in a very excitable condition, or condition of charge.

In such cases I give it in this form: Tinc. cannabis indica, 5; pot. brom., 20; gum. arabic., q.s.; aq., 1,000. The dose of cannabis indica may be doubled. It is well to remember that the herb is only active for a year, while the extract loses its potency in three.

Nitro-glycerine has already been mentioned as a drug which is sometimes of value in cases of petit mal. I have had satisfactory results with it in my own cases. Gowers also recommends it.

Extract U.M.G., No. 50, J. P., Patient aged 2 years. Child was breast-fed. During the first year of life he fell out of a baby-chair on his head. Within the next six months, fits began. During these fits there was slight deviation of the head to the left side, foaming at the mouth (slight), convulsions of hands and feet. The pupils were much dilated; the corneal reflex is absent. After the fit the little patient was obviously dazed. During the next year the fits increased in number, so that latterly there were one or two a day. Myoclonic shocks were frequent and troublesome.

---

* Hugenholtz, *Pharmaceutisch Weekblad*, 1908, No. 40.

† Schussny, *Therapeutische Monatshefte*, 1887, No. 5.

The child had no fits previous to the accident. The mother had eclamptic convulsions an hour after confinement with this child. On June 4, 1906, a very weak preparation of nitro-glycerine was given (0·5 nitro-glyc. in aq. 500), in doses of a teaspoonful thrice daily. The myoclonic convulsions stopped at once (see Appendix A, No. 1, p. 414). After a few days headaches, hitherto rather troublesome, also disappeared. Later the appetite improved, and the irritability passed away. The patient went on with the drug for three years. In 1915 he came home from school one day faint and sick; he also had albuminuria. At this time he was five weeks in hospital, then was discharged, recovered. In 1916 he was out at a party with his parents, when he had a severe fit. This fit was not associated with the use of alcohol. After this fit until 1923 he had no fits. He is now an intelligent artisan, and apparently normal in every way. (Compare description of fit on p. 420.)

In epileptics who have a defective circulation, and are of weak physical calibre, nitro-glycerine is very useful when associated with bromides. Where it is used with a bromide, it is well to add acid hydro-bromide diluted to render the solution sour.

Where a patient complains of pain from the biting of the tongue when in a fit, it is often beneficial to paint the tongue lightly with tincture of myrrh.

I have confined this consideration of drugs to those with which I have had experience. I am well aware that other methods are under consideration directed to the function of internal secretion, or the effect of anaphylactic shock,* but these are still *sub judice*, and I can say nothing about them from personal experience.

§ 7. Treatment of the Inveterate Cases.

Psychical effect. Mercury treatment. Example of a case where the improvement was permanent.

This class forms a goodly percentage.

So long as epilepsy is only treated after the increasing frequency of fits bring the patient to the consulting-room, this class will always be large. Among these cases one not infrequently finds quite a number of patients who have managed to preserve a fairly good psychical condition in spite of long-continued fits. Where this is the case, both the physician and the patient may take courage. With intelligent collaboration from the patient much may be done therapeutically to mitigate the disorder. Sometimes a patient when seen at first is practically continually in a stuporous condition, because the fits are occurring so frequently that he has no chance to recover from one before he is plunged into the next prodromal period (Case 8, p. 319). Even in these cases it is possible to achieve something. If a free period can be

* The observations of M. Cohen and H. Lichtig (*Journ. of the Amer. Med. Assoc.*, 1924, p. 1107), on a number of patients, show that the anaphylactic shock can play only a very small part in the genesis of the epileptic fit

induced the patient may recover to the extent that psychically he is able to collaborate with his physician. In cases of hystero-epilepsy, which have become chronic, a partial recovery may allow of a psychical analysis being made, which may in turn lead to a clearing up of the condition at least in part (Freud, Jelliffe, E. Jones, and Stanford Read).

It is obvious that this partial recovery, or the production of a fit-free period, is more quickly attained, or more likely to be attained, in a special home or hospital, where the patient is in the best hygienic conditions and under trained observation.

As a rule, these chronic cases are best sent to bed for complete rest—that is, after the first few days when the character and symptoms of the case are being watched. Very often the characteristics and symptoms of the case are totally different from the descriptions given. It is therefore well to have the patients going about as usual in the sanatorium for the first few days, so that skilled observation may determine what the symptoms, prodromal and otherwise, really are. During this period, and probably for longer, it is well to isolate the patient from his friends and relatives. Great attention must be paid to the normal functions, and while the patient is in bed daily massage should be administered. Prodromal treatment (p. 353) may here produce excellent results.

As far as possible cut down drugs, but do it cautiously. Later on, when the patient is up, graduated exercises and some form of mental activity should be begun, but under careful observation and only when the fits are not so frequent.

Great attention must be paid to the diet sheet and the proper functioning of the bowels, while careful watch must be kept for any contributory cause, such as intestinal parasites. Over and over again surprisingly encouraging results are got in chronic cases when put under a hygienic routine of life.

Where patients show no improvement under such a régime, further treatment must be begun. The iodide of mercury cure should now be tried. The method is very similar to the mercurial treatment used for lues. The cure starts with one to five iodide of mercury pills (50 milligrammes) daily. All other drugs, so far as at all possible, must be stopped. This goes on for probably one, two, or more weeks, great care being taken for the proper hygiene of the mouth. About this time the typical oral symptoms appear, softening and hæmorrhages from the gums, accompanied by diarrhœa and vomiting. The temperature rarely goes up. The dose of mercury must now be cut down until the symptoms clear; when the dose is increased, and so on. Usually all epileptic symptoms disappear, but reappear in a few weeks. While the patient is taking the cure he is usually only able to take fluids,

but so soon as he improves I usually begin with bread, into which zinc oxide or a compound of bromide or borax is baked.

I have records of patients who have had this treatment some fifteen years and more ago, but owing to the difficulty of tracing the cases I cannot yet present a complete summary of the treat- and the results, but this I intend to do later. At present I may say that in one of ten cases of mixed grand mal and petit mal the fits were stopped for periods of several months. In one case out of fifteen or twenty, fits were completely stopped. Good results were not infrequently got with children; one case is here given in detail.

Case No. 9, Av. W., 8 years old. Is one of seven (three miscarriages). *Complaints.*—"Fainting" fits for four years. Patient had many "fainting" fits each day in which she fell down, but had little or no convulsions. Severe headaches associated with hyperhidrosis, nausea, sometimes vomiting and pain in the stomach. Enuresis during the night; this had always been troublesome.

The patient was a full-term child; had no infantile disorder, but had infantile convulsions. When three months old, she had a tumour on the head, which was cauterised. At the age of 3 she awoke suddenly one night in a violent convulsion, in which she squinted badly. At this time she was very ill for two days and had diplopia. Shortly after this the patient began to have the fainting fits. Different treatments were tried, all unsuccessfully.

Family History.—Father was addicted to drink, while his brother was an epileptic, and had died in an asylum. Her mother's brother had apoplexy and died at the age of 26, while a sister died in confinement, complicated by convulsions (eclampsia).

The patient was particularly troubled with the fainting fits while lying awake in bed in the morning, and a little later when dressing. In the evening the fits began again. The patient had often had iron and bromide treatment, but with no result. In this case the hereditary history was bad and the home conditions unfavourable. She was placed in hospital and given complete rest in bed, and fed with bread containing varying doses of borax, bromide, or zinc oxide. This was followed, after two and a half months, by a very slight temporary improvement; the intervals between the fits were somewhat longer.

On January 31, 1906, the mercurial treatment was begun. The patient got three pills each day of iodide of mercury (25 milligrammes), and also potassium iodide. After a few days the pulse quickened from 80 to 90 or 100. As no mouth symptoms had started, the amount of mercurial iodide was doubled on February 6. Immediately after this increase she had very many fainting fits, and on the first day after she was sick and began to have trouble with her mouth; the pulse also ran up to 120 or 130. This was on February 7, and from this date she had no more fits (see Appendix A, No. 2, p. 416). On March 8 she was given bread containing zinc lactate (0·15 gramme), zinc oxide (0·2 gramme), potassium bromide (2·0 grammes), and bicarb. sod. (2·5 grammes). After an interval of several months she had another course of mercury. In 1922 she came up for examination. She was now the mother of three healthy children, never had fits, but sometimes had headaches.

As this patient might be regarded as a case of pyknolepsy, I add the case of an older patient who had had fits over a longer period.

Case No. 10, P. S., 25 years old. Typist. *Complaints.*—(1) Fits over a period of ten years. These were worse in the morning before breakfast,

and were preceded by myoclonic shocks. The convulsions were worse on the left side of the body, and were associated with biting of the tongue and enuresis. These fits used to occur twice a month, but gradually increased to three per week. For three and a half years the patient used Uten, a quack medicine (see p. 421), which certainly produced some improvement, diminishing the number of fits, but it was supposed to have made him somewhat demented. (2) Myoclonic shocks were troublesome, occurring before and after a fit. (3) He had also attacks of giddiness or dizziness, in which he felt as if he would fall, but managed to support himself. During an attack of this type the hands were slightly convulsed, while consciousness was almost, if not completely, lost for a moment. After this the patient felt quite well. Patient's memory had been failing for some time, and he was often subject to fits of dejection. He was also worried by the recurrent dislocation of the left arm. Headaches were not troublesome, and came on only after a fit.

As regards his past history no facts were forthcoming earlier than the age of 13, when he had typhoid fever. At 14 he went to work in a printing office, where he bore heavy weights on his head. When he was 15, he fell down one day in a severe fit. Two months later he had another, and so on, until he had three fits each week. A short time after the first fit myoclonic shocks and dizzy fits began. Enuresis was a very troublesome symptom.

In his family history the one important fact was that his father drank, but only moderately.

When the patient was seen he had fits both during the day and night, but they were worst in the morning and evening. Before a fit he felt worn out, and had myoclonic shocks as a prodromal symptom. Myoclonic shocks also troubled him apart from the fits. Analgesia was well marked and general. Mentally he was rather demented. This, as indicated, was supposed to be due to the drugs he had to take. When examined on January 2, 1907, he was a sturdy-looking man. There were no objective symptoms, save scars.

He was admitted to hospital. The following is a description of a fit. September 10, 1907, patient had violent shocks for several days. In the fit itself the face turned to the left, the eyes opened, while the corneal reflex was absent. Both arms and legs were straightened in line with the trunk and the fists doubled. After the stiffness came an attack of shivering, particularly marked in the left leg, which performed vigorous treading movements. Enuresis followed. Ten minutes after the fit, a pin prick was felt on the right leg or arm, but not on the left. This patient was given two months' treatment in bed with the usual course of drugs,* but no improvement followed. He was then put on the mercurial treatment (three pills daily, containing 50 milligrammes of mercurial iodide). After two or three weeks he had diarrhœa, while his mouth began to give trouble. The fits and myoclonic shocks both ceased (compare Appendix A, No. 3, p. 418). After stopping the mercury, the patient was put on a cannabis indica and potassium bromide mixture, which was continued for a number of years. He remained free from fits for some time, but had one on his wedding night in June, 1908.

Up to 1918 he was kept under observation, and was free from fits, but took prophylactic courses (p. 333). When last heard of he had had no fits for ten years, and very rarely a myoclonic shock. He lived carefully, avoiding any form of intemperance. Mentally he was in excellent form and had built up a good business, while domestically he was happy, and was the father of a healthy child.

Although I have used the mercurial treatment for more than a hundred cases of chronic epilepsy, I have never found any permanent damage done to either the teeth or mouth of a patient.

* Different kinds of bread containing up to 5 grammes bromide salts, or 100 milligrammes zinc oxide, 120 milligrammes zinc lactate, borax 1 gramme, or combinations.

With proper supervision and care it is a method which should always be considered, and, if possible, tried in cases of severe chronic epilepsy.

§ 8. The Prodromal Treatment and Prophylactic Measures in Epilepsy.

In all cases look for possible cause. Watch for prodromal symptoms. Seek the causes of relapse. Note the condition of the tongue. Use medical remedies with continual supervision, varying dose where indications for doing so occur. After the arrest of the disease the patient must be under observation probably for years at increasing intervals.

It is soon noticed that prodromal symptoms are more easily elicited from intelligent patients, but in almost all cases such symptoms may be got by careful search. Until proved otherwise almost any variation in a patient's manner of life might be followed by a fit; or it may be a manifestation of the condition of charge, so that we might consider these signs for practical purposes the prodromal symptoms. Where a patient is brought into an institution where proper nursing is available, it is almost always possible to establish the sequence of events which are associated with the fit. Needless to say, this is not easy, but it is in most cases possible. The dictum " There are no fits without prodromal symptoms " is a good rule, and one which ought to be ever before the mind of the doctor and nurse treating epilepsy.

The importance of recognising prodromal symptoms is that preventive treatment can be at once started. It often happens that putting a patient to bed or administering such a drug as cannabis indica or giving an enemata or the combination of these measures may ward off a fit. Not infrequently one meets with patients who find out on their own account some method, probably a somewhat unusual one, to prevent the attack; such a case was referred to on p. 303.

To the ancients we owe the advice, to put a bandage around the extremity in which the fit starts in order to prevent a threatened attack. Experienced neurologists have confirmed this, although it must be admitted that genuine fits rarely start in one extremity. Probably the fits referred to in the advice were Jacksonian fits. Regarding these focal fits the therapeutic effect of bandage need not give rise to astonishment. Bubnoff and Heidenhain have shown that subliminal currents applied to the cortex, too weak to cause a convulsion, will do so if some stimulation is applied to the proper extremity, even by blowing over it. This can be looked upon as a proof, that the irritability of the cortex is influenced by stimulation of the skin of the region involved.

If this observation held good in an authentic case of genuine epilepsy (demonstrated by autopsy), it would not merely have a therapeutic, but also a pathogenetic value. For in that case we should have a direct argument to the effect that the motor cortex plays a part in the genuine epileptic fit.

Where one has to deal with a long-established case of epilepsy, the conditions are more difficult. Here the conditions which

produce a fit may be many and varied and extremely slight in degree. As has been frequently shown, each fit paves the way for the next; so, on a patient who has had many fits, the smallest deviation may produce a fit.

In such a case the great desideratum is to establish a gap between the fits so as to give some opportunity for the natural resistance to be re-established. If possible, the conditions connected with the first appearance of the fits must be ascertained. Frequently the first fits coincided with some peculiar circumstances, overstrain, or alcoholism, and, in women, the incidence of the premenstrual period (pp. 284, 339). Precautions should be taken to prevent the patient being exposed to the same conditions, or, where this is not practical, precautions at special times must be observed.

The more one sees and studies epilepsy, the more convinced one becomes that the idea that the epileptic fit comes as a bolt from the blue is wrong. Certainly the fit is a surprise to the lay friends and relatives, but that is because they lack the necessary training for observation of such cases. If a careful and thorough examination is made of such a supposed "bolt from the blue" case, one will certainly find a chain of symptoms, slight in themselves, but important when taken as a whole. Such symptoms are general malaise, headache, irritability, myoclonic shocks, gastro-intestinal disturbances, and hyperhidrosis. These are all danger-signals, and indicate the weakening of the physiological resistance. What actually precipitates the fit may be a very slight matter—a fright, a slight injury, rise of temperature, or gastro-intestinal disturbance.

A very important point to remember is, that although the fits may be arrested, the patient is still, potentially, an epileptic. This is not sufficiently appreciated, hence the idea that any treatment for epilepsy is palliative, not curative. Both the patient and the doctor must be on guard for the reappearance of any prodromal symptoms, while the treatment and mode of life found to arrest the fits must never be relaxed, at least not in the first years after arrest of the fits.

It is a helpful point to note that, after a long cessation of the fits, the prodromal symptoms may reappear, but they give a longer warning before the fit, and so allow of prompt and effective treatment where the case is carefully watched.

P. Clark* pointed out this very fact, stating that at least half the relapses could be prevented by proper after-care. Here an after-care helper, as suggested in Chapter XV., can do much good. In order to prevent even a day's discontinuance of the medicaments, I insist on the patients asking for a fresh bottle, when the bottle is half emptied. The regular use of such drugs as have been ordered

* P. Clark, *Amer. Journ. Med. Sciences*, October, 1920, p. 582.

must never be interrupted, except where the patient has a rise in temperature. Here the dose must be diminished. One point about the treatment of epilepsy always offers difficulty, and that is the administration of the long after-care period. This period is of utmost importance, but naturally it cannot be carried out in an institution. The patient is, from a lay point of view, well; he is able to work, and with the care and treatment he does not have fits, and yet he must have after-care if he is not to relapse. Much is done by putting the patient on a definite régime of life and by correct medication, but a careful watch is necessary for untoward symptoms. It is here that a course of training for relatives of epileptics would be so helpful (p. 333). When epilepsy is treated ideally, such a course will be arranged, and relatives will attend as naturally as they now do special courses for the relatives of the deaf mutes.

As this is not yet possible, the best thing to do is to arrange that an experienced nurse accompanies the patient to his home, and there instructs the relatives on the procedure. Where the case is also removed from the immediate care of the specialist, the family doctor must have special directions.

Even with this arrangement the treatment of the case is difficult. At those periods in the treatment where it is of the utmost importance that patients should adhere strictly to all details, both as regards drugs and hygienic procedure, patients frequently become unreliable and careless. Epileptics are often not very tractable, and much of the examination necessary for an accurate knowledge of the patient is unsuitable for relatives or even nurses to carry out.

One cannot, for example, get reports as to a segmental distribution of sensation for pain, whether it is variable, and other associated neurological data, but some points can be recorded. The condition of the tongue, the temperature, condition of the pupils, mental attitude, and changes in the mental attitude are all suitable for lay attendants to record. The condition of the tongue is particularly important (p. 262). It generally happens that the fits stop some time before the tongue clears, so a clean tongue is a very favourable sign. My own observations are in agreement with those of Agostini, who considered that the condition of the tongue was as good an index of the gastro-intestinal metabolism as the chemical examination of a test meal.

The administration of medicaments is peculiar to each patient. Whichever drug is selected—bromide, borax, luminal, or zinc oxide—the dose has to be found for each patient. This takes time and careful judgment. Here, again, is a matter which must be carefully explained to lay relatives: the drug must be taken regularly as prescribed. Any irregularity in the use of the drug is, of course,

dangerous, not only in case of relapse, but also to life itself. The drug prescribed for an epileptic must be taken by him as regularly as he takes food. Besides the regular dose, which must be as small as possible, special administration of the drug is necessary at certain times—for example, as soon as prodromal symptoms appear. The outline of this method is given elsewhere, so it need not be repeated here, but a careful note must be kept of the dose and times of administration. Such additional dosage is necessary at such times as the menstrual period, or where the patient is to be exposed to special fatigue or strain. The menstrual period is one which often requires special precautions, and it is my custom to increase the dose gradually, by stages several days before the period, during the period, and gradually diminish it for two or three days after the period. (Refer to section on Menstruation, Chapter VI., p. 235.)

It will be found that the majority of patients tend to stop attending the doctor as the condition improves. This is really one of the difficulties in the treatment of epilepsy. The patient and his relatives naturally think that the fits have stopped, and that with the use of the standardised dose of a drug they can get on quite well. The patient, if he be intelligent enough, or his friends, must be warned against such a course. All epileptic patients must be examined regularly, and reports of their progress examined, so that the drug or drugs may be properly given, and, when suitable, diminished and withdrawn. This withdrawal should be applied very slowly—*i.e.*, by 10 milligrammes of luminal, or ¼ gramme of bromide in the three months. In addition to the medicinal and hygienic methods of treatment, the importance of healthy outdoor exercise must not be forgotten. As soon as possible, a patient should be encouraged to co-operate with others in outdoor games, congenial work, religious duties, and general activity. It need not be said, that in most cases where the patients are children, such activities must be begun under the supervision of a nurse. It is important that the nurse gains the confidence of the patient, so that she may exercise the necessary control over his actions as pleasantly as possible.

§ 9. **Treatment of Status Epilepticus.**

From my own experience I have found that status epilepticus almost always follows upon such an error as the complete cessation of the taking of bromide or luminal, when the patients have been long accustomed to these drugs. It is highly probable that the accumulation of different toxins combined with the hyperexcitability of the *subcortical* convulsive centres, brought on by the number of preceding fits, is the true cause of this complication.

(Irritability of cortex not found in Cat 203, which yet displayed status epilepticus, p. 132.) The question may naturally arise why such a phenomenon as an epileptic fit, which is essentially a physiological phenomenon, should degenerate into so distinctly a pathological condition as status epilepticus. The pathological nature of this condition is such, that it is recognised as being dangerous to life itself.

It will be recalled that a severe and complete fit in a well-nourished animal brought about its own cure (p. 243 footnote). How it does this is not exactly known. (It is recognised that the blood-sugar is increased by a fit; probably this increase is due to the accompanying condition of asphyxia. This may be an important indication for further research, p. 282.) Further, it was shown that in badly fed cats, bromide of camphor induced atypical fits, while in weak and starved animals fits induced by insulin are also atypical. Neither of these fits, however, act as the severe and complete fits in well-fed animals.

The results got from experimental work raise the question whether the same condition is met with clinically—that is, that status epilepticus only occurs after the weakening of certain organs, such as might result from long-standing epilepsy. (A parallel condition exists in insulin experiments, where there is an absence of glycogen in the liver, and status epilepticus does supervene.) It can certainly be said that cases of primary status epilepticus are rare; personally I have never seen such a case in genuine epilepsy. In my opinion, both experimental and clinical evidence show that the well-nourished organism recovers rapidly from a complete severe fit.

It is highly probable that if the proper degree of care necessary for each case of epilepsy were given, status epilepticus might never occur. Where a patient has a series of fits and does not recover consciousness in the intervals, for this is characteristic of status epilepticus, his life is certainly in danger.

It is, therefore, obvious how necessary and important prophylactic measures are. It must be impressed upon the household of a patient, who is receiving bromide salts regularly, that the intermission of the drug is fraught with the gravest danger.

I have found the prolonged anæsthesia, with ether or chloroform, of great value in interrupting and stopping such a series of fits as occur in status epilepticus.

In a sense, the treatment of status epilepticus must follow on parallel lines to the general treatment of epilepsy. It has been shown that in the general treatment of epilepsy the object is to prevent the stimuli which are associated with fits, so that the patient may have a long period free from fits. In status epilepticus the object is the same; one must prevent or hinder the stimuli which induce so easily the phenomenon of repeated fits.

Experience shows that this is best done by placing the patient in a perfectly quiet, darkened room; by administering enemata to empty the rectum and colon, and the administration of bromide chloral, or better still, dormiol, per rectum (dormiol 10 parts, water 150 parts, three tablespoonfuls in $\frac{1}{3}$ litre of water given per rectum) (Hoppe).* Amylene hydrate (Alt) is also good. Both these drugs are very useful for assisting the narcotic effect of the ether and carrying the patient into the condition of sleep.

P. Jardine† recommends lumbar puncture, especially in cases of eclampsia in the pregnant woman. He considers eclampsia to be a form of status epilepticus; this view seems very probably correct (p. 240). It is found that status epilepticus occurs fairly often in institutions for chronic epileptics. Jödicke‡ recommends perfusion with saline infusion or with Donath's solution: Cal. sulph., 0·2; cal. chlor., 1·0; sod. chlor., 6·75; cal. carbon. pur, 0·4; sod. phos. cryst., 3·1; aq. ad 1,000. He also recommends venesection and the removal of 100 to 500 grammes blood. These methods seem to me to be good.

P. Clark and T. B. Prout§ recommend the following prescription to be given at the beginning of status epilepticus: Tinc. opii desdor., gtt., 5; pot. brom., 1·5; chloral. hydr., 1·2; liq. morph. sulph. (U.S.), 30. While waiting for the effect of this dose, anæsthetise the patient with ether.

Bourneville made the observation that in such case the temperature rises post-mortem, and records a case where it reached 41° C.

Ross,‖ working with cases at Sonyea, also recorded a post-mortem rise in temperature to 102° F.

It is noticed that after the condition of status epilepticus, should the patient recover, he will be free of fits for a long time.

Here is evidence that the condition of status epilepticus has the same effect as a single severe complete fit on the toxins. It dissipates them and puts the patient into a better condition. It would seem, therefore, that the danger to life is not so much due to the fits themselves as to complications arising from weakness of the heart and pulmonary symptoms.

It is recommended that great care be taken to prevent the occurrence of the condition of decubitus.

The diagnosis rests on the record of the case. Probably there are no cases where there is not a long history of epilepsy.

* J. Hoppe, *Münch. med. Wochenschrift*, 1902, No. 17.
† P. Jardine, *Lancet*, 1907, p. 1432.
‡ Jödicke, *Deutsch. med. Wochenschrift*, 1912, No. 19.
§ P. Clark and T. B. Prout, *Journ. of Nervous and Mental Diseases*, 1905, p. 64.
‖ Ross, *Epilepsia*, 1909, vol. i., p. 218.

§ 9. **Prognosis.**

Mortality. Chances of remissions. Chances of permanent disappearance of symptoms. Age. Marriage. Climacteric. Mentality. Symptoms of degeneration. Final course.

The immediate danger to life of an epileptic fit is not great, except in regions such as Holland, where numerous opportunities occur of a patient falling into water and so being drowned. At the same time, experience teaches that the life of an epileptic patient is comparatively shortened.

Amman's statistics* are probably the best because they are compiled in Switzerland, where the census of epileptics has been carefully made, and the registers accurately kept. It is shown from these figures that if, when the statistics relating to the mortality amongst very young children is excluded, the mortality rate amongst epileptics is higher than normal and that it reaches its highest point between the ages of 25 and 30 (Ganter).

The greatest danger to life occurs where a patient turns over on to his face in a nocturnal fit, and so is suffocated with his own saliva. To prevent this happening, the patient should be given a horse-hair pillow, covered with a double layer of coarse canvas. The family, in each case of epilepsy, should be instructed to have a responsible person sleeping on the same floor, preferably next door to the patient. This must be kept up for years after the disorder has evidently been arrested. It must never be forgotten that grave danger is incurred should any interruption occur in the dose of bromide or luminal, which the patient may have been accustomed to over a long period.

Severe or dangerous wounds are so comparatively rare in epilepsy, that the conclusion is come to that the patients themselves must be warned, either by prodromal symptoms or by a brief aura just before the fit, and have learned to place themselves so that they do not suffer injury during the fit.

It is seen more particularly in large institutions that many patients die of pulmonary tuberculosis. This may be explained as due to a combination of circumstances. The development of almost complete analgesia, the danger of choking if a fit occurs during a meal, and the results of prolonged bromide medication together, may reduce the normal defences for the pulmonary system and lay the patient open to infection.

There is no need to take a gloomy or distorted view of the future of a patient who has had but a single epileptic fit. This is especially the case where one has succeeded in establishing the chain of unfavourable circumstances, which broke down the

* Amman, "Erkrankung und Sterblichkeit an Epilepsie in der Schweiz," Diss., Zurich, 1912, and *Epilepsia*, 1914, vol. v., p. 54.

natural resistance. If care be taken that these different unfavourable phenomena be avoided, the patients may, in many cases, be guaranteed against a repetition of the fit. At the same time, the grave significance of the fit must never be lost sight of. It marks a very serious event in the patient's life. It is the breaking-down of the natural physiological resistance. It must never be forgotten that the characteristic of the disorder is that it is self-perpetuating. A fit, therefore, should be a turning-point in the life of a patient. The normal physiological resistance has been broken down once, and it will, unless care is taken, break down more readily the second time. Even after a considerable lapse of time, one cannot say that the breakdown has no further significance. In a sense, a patient who has had but one fit never gets over it; he must always be careful and on guard against any strain. Always remember that more especially after a fit (compare p. 339) a comparatively minor cause, as compared with the first, may induce a second fit. Such a cause might be a slight form of intoxication or some psychical disturbance. Schroeder van der Kolk very justly says: "The first fit passes without proper use being made of it" by the physician.

If the malady be untreated—that is, if myoclonic shocks and fits are untreated—what is the course of the disease?

Experience teaches us that the symptoms may completely disappear; indeed, this is of more frequent occurrence than one would be inclined to think. It must, however, be recalled that, as has been explained more fully elsewhere in this book, the process of myoclonic shocks to myoclonic fits is a reversible one.

It is impossible to say why such cases show these spontaneous remissions. In too many cases such a remission is termed a cure; but here lies a distinct danger. It has been shown that a remission from therapeutic measures must be regarded as a temporary condition maintained by care. This natural or spontaneous remission must be treated in the same way. The patient has had a breakdown; he is liable to have another. At the same time, where a patient comes with the history that some relative has had epileptic fits which also underwent spontaneous remission, it makes the immediate prognosis more favourable. It is entirely a delusion that the prognosis is affected favourably by the occurrence of the climacteric, the establishment of the menstrual function, or by marriage (see p. 329).

The facts which do influence the prognosis favourably are that the condition has not lasted long, and that the mentality is unimpaired. One finds the first factor referred to by different authors in various ways. Herpin, for example, puts the limit at which a favourable diagnosis can be given as 100 fits. Gowers,

Binswanger, Turner, and other writers consider that if the disorder has lasted but two to five years the prognosis may be favourable.

One of the most favourable symptoms is that the disorder has manifested itself in complete severe fits complicated only by myoclonic shocks and headaches. Where abortive or atypical fits occur, the prognosis is not so good. This is in accordance with the views expressed elsewhere in this book that myoclonic shocks and fits are in a sense physiological phenomena, while atypical discharges may be looked on as pathological processes. Although it is true that the occurrence of a few fits in a year may be arrested by a proper regulation of the patient's life, yet experience teaches that caution is needed in giving the prognosis in such a case. Indeed, I have seen cases where a patient who has more frequent fits, may have, in reality, a better prognosis than a patient with but rare and probably nocturnal fits. This is because the patient with the more numerous fits takes more care and follows out the directions with great exactness.

From the point of view of the prognosis in epilepsy, those cases which occur after infantile convulsions are less hopeful. This is particularly the case if the patients were backward mentally before the fits appeared. Such cases frequently show a dull or subnormal type of mind before the recognition of epilepsy; they are backward children at school and subject to fits of temper, while they may have shown signs of psychical or moral defect. Further, the prognosis is influenced favourably where the patient is, apart from his epileptic disorder, normal. Here one can get intelligent co-operation. Sometimes one has to persuade the patient of the seriousness of the malady, particularly where the fits are very few and nocturnal, before the co-operation is attained.

According to some authors, the prognosis is not so good where the disease occurs between the ages of 6 and 14 years. It certainly seems to be the case that after the age of 40 the epileptic fits sometimes tend to be arrested, while the tendency to dementia increases.

Féré points out correctly that epilepsy, where the fits are limited to one side, has a more favourable course than ordinary epilepsy. It is less complicated with psychical symptoms, and is more often arrested. Epilepsy associated with organic lesions has, as would be expected, an unfavourable prognosis; this is more particularly the case where paralytic symptoms are present.

The psychical symptoms, should they appear in the course of the epileptic disorder, are to be considered as serious, for they influence the prognosis unfavourably. There is abundant evidence

to show that epileptics who escape psychical complications may hold high and responsible positions in the State.

Should, however, psychical symptoms appear repeatedly, the patient is of necessity relegated to a different social plane.

It must, however, be said that even in cases where everything is unfavourable, where there are atypical discharges, mental defects, organic changes and psychical complications which appeared early in the case, a comparatively successful result may be got from therapeutic measures (p. 397). The influence of epilepsy or insanity in the hereditary history does not seem to influence the prognosis unfavourably. Gowers and Turner both show statistical data to confirm this.

In a case of epilepsy, much depends upon the relations between the physician and the patient. If the physician can imbue the patient with enthusiasm for his own recovery, and demonstrate to the patient how much interest he (the physician) takes in the case, and how much care he takes of the conduct of the case, the best basis is established for a successful issue to the treatment. The household of the patient must also be imbued with this enthusiastic belief in the possibility and probability of relieving the patient. They must understand that the régime, as ordered, is not fanciful or haphazard, but carefully considered, and it must be followed out exactly. It is often seen with epileptic patients that an improvement occurs after a thorough, careful, systematic, and skilled examination of the patient.

It must not be forgotten that epilepsy is the happy hunting-ground of the quack. It is the disease *par excellence* for the exploitation of all sorts of cures, from the quack remedy to the old family prescription. Certainly one cannot deny that one both hears of and sees cases that have improved after taking remedies of the most fantastic type.

It is probable that an important percentage of epileptic patients arrive at a lunatic asylum. These include cases which were treated at one stage with good results, and also, of course, those who showed psychical complications. When the stage of final dementia is reached, not only the myoclonic phenomena, but also the epileptic fits sink into the background. At times a condition is reached when no reactions occur after stimuli of any kind.

These patients may show contractures, atrophic and contorted extremities, towards the end of life. These conditions may be explained, as for those occurring in other forms of dementia, as due to the lack of cerebral inhibition on the flexion reflexes.

Much, of course, depends on the standard of nursing how far these deformities may go.

Finally, it must be remembered that an epileptic patient is a

source of danger to himself, his immediate surroundings, and to society as a whole.

The question whether epileptics are by nature of their disorder outside ordinary social life largely depends on the special features of the given case. Persons who are subject to occasional epileptic fits need not be excluded. This follows from Turner's statistics (Turner, *loc. cit.*, p. 260). He estimates, from his statistics on all epileptics, that the risk of sudden death, as a result of a fit, is 5 per cent.; from accidents during a fit, 12 per cent. The outlook for patients with moderate frequency of fits must be judged from the points already dealt with. In some walks of life there is a much better chance for such patients than in others. Further, the possibility exists that if proper care be taken under experienced physicians the disorder may be arrested.

From the recent paper by S. Wilson* on the subject I gather that he supports the later and more optimistic views on the subject. From Chapter XII. it will be gathered that, according to this view, the *less severe* cases should specially be encouraged to start treatment with a period of (special) hospital observation.

* S. Wilson, *British Medical Journal*, 1927, vol. i., p. 221.

CHAPTER XIII

PATHOLOGICAL ANATOMY

In the Ordinary Sense there is no Question of the Development of a Pathological Anatomical Condition in Conjunction with the Genesis of Epilepsy. Conditions generally found in Chronic Cases and those showing Psychical Deterioration. Relative Significance of So-called Encephalitis.

It is quite evident, from the preceding pages, that there can be no question of a definite pathological anatomical condition developing in conjunction with ordinary genuine epilepsy.

At the same time the question may arise whether in those cases where psychical changes occur, or where psychically abnormal conditions were present before the fits, whether histological changes may not be found. These changes might at least resemble those found in other types of long-standing psychoses.

In whatever way the question is put, it is one which has attracted much attention, and repeated efforts have been made for almost a century to establish some evidence of changes in the brain associated with epilepsy. Unfortunately these researches have been made on cases which were unfit clinically for epileptic research (p. 194). In this connection Binswanger very justly says that the examination of the brain in cases of incipient and arrested epilepsy has either been neglected or negative in result.

Under the influence of the pathological school of Bichat, Bouchet and Cazauvieihl in 1825 found certain changes in the cornu ammonis in some old asylum cases of epilepsy. These results were verified by Meynert in some of his cases, and he propounded the question whether these changes might be the cause of epilepsy. It must be remembered that at that time the cornu ammonis was supposed to have a motor function. At the present time the work of Edinger would show that it is related with the olfactory centres.

Although the examination of the brain in epilepsy was continued, changes were less and less frequently recorded. Féré recorded only 1 in 20 cases, and Robertson 1 in 30. Barthez and Rilliet, Bourneville, and Brissaud* investigated the changes in the cerebral cortex which occur in tuberous sclerosis so often associated with epilepsy. It is interesting to find that the changes

* Brissaud, *Arch. internat. de Neurol.*, 1880, vol. i., p. 669.

in the cornu ammonis, still recorded in pathological anatomy, have tended to disappear as one of the etiological factors in epilepsy. At the same time, Alzheimer,* in 1907, reported that he found changes in this area in 50 per cent. of his bad cases of epilepsy.

Foville and Schroeder van der Kolk† found vascular changes in the medulla; this was confirmed later by Echeverria. Schroeder van der Kolk considered that these changes—*i.e.*, the enlargement of the capillary vessels—to be a result, not the cause, of the disorder. Virchow emphatically denied the existence of any such changes. Probably because of the respect given to the opinion expressed by Virchow, or because the medulla was mistakenly considered to have little significance in epilepsy, the description of changes in this area gradually disappeared from the literature.

In the latter part of last century more and more attention was directed to the role played by the cerebral cortex in epilepsy. It is, therefore, not surprising to find that Voisin found numerous changes in the ganglion cells. This observation was verified by Claus and van der Stricht who, however, thought that the first changes in this region were vascular.

Marinesco and Sérieux,‡ and also Sala, found similar changes, but thought that they were due to the malady and not the cause. Chaslin§ and Bleuler found changes both in the cells and glia—*i.e.*, so-called "edge gliosis." They thought that the glial tissue was increased between the pia mater and the outer tangential fibres. In many cases they found it impossible to localise the increase of the glial tissue, and the impression arose that in epilepsy there was an increase in the glia or a general gliosis (Maewski, Emich, Karowski, Colucci). The problem now arose whether the undoubted changes in the ganglion cells were primary and associated with a secondary increase of the glia (Alzheimer, Bloch, Marinesco, Bleuler), or whether the increase of the glial tissue was primary, and the ganglion cell changes secondary (Cotard and Chaslin). The high standard of the workers precludes the possibility of there being any mistake due to artifacts. It is noticeable that none of these writers give it as their opinion that these changes in the ganglion cells and glia were the cause of epilepsy. Most of them, like Tramer,‖ state that they do not admit the relationship as cause and effect, but suggest that there may be a parallelism between these changes and mental deterioration. This last suggestion is most significant, and speaks volumes.

* Alzheimer, *Allg. Zeitschr. f. Psychatrie*, 1907, p. 465.

† J. L. C. Schroeder van der Kolk, "Verhandel. d. koninkl. Akad. v. Wetensch. te Amsterdam," 1858, vol. vi., p. 166.

‡ Marinesco and Sérieux, *Roumanie médicale*, 1899.

§ Chaslin, *Arch. de méd. expérimentale et de l'Anatomie pathologique*, May, 1881.

‖ Tramer, *Schweiz. Archiv. f. Neurol. u. Psych.*, 1918, vol. ii., p. 236.

The problem which offers the greatest fascination is whether any evidence can be found in the brain, and, if so, what it is, in *cases of incipient myoclonic epilepsy*, or in *cases of severe fits with no other symptoms* which have lasted for a shorter or longer period and in which *treatment succeeded in arresting the disorder*. Can any evidence be got in the brain, and, if so, what is it ?

The problem is not nearly so interesting where, after a long course of epileptic fits, dementia has supervened, or where chronic cerebral abnormalities exist, possibly due to the fits or to certain psychical changes or to long continuance of certain drugs.

Still less interesting in this connection are those cases which have always had some degree of mental defect.

An interesting and recent piece of research on this point was done by A. Jakob.* He examined the brain in three cases: the first, a case of tuberous sclerosis; the second, a neglected imbecile, with heteroptosis in the grey matter (this has been shown by Polak to exist in epileptics and in other abnormal conditions); the third, a person who from birth was psychically abnormal, and never able to speak properly. In this case the brain was microcephalic, probably due to an encephalitic process. He also examined the brains in two cases of genuine epilepsy. Here the results were negative.

Although Jakob's discussion on tuberous sclerosis along with the work of Bielschowsky and Perusini is interesting, at the same time it is only the finding of this condition in early or arrested cases of epilepsy which should be regarded as of great significance.

It is particularly important that in all cases the clinical history should be recorded with great accuracy—otherwise, anatomical observations become of little value.

This research also shows that in real organic cerebral epilepsy the first fit may be called forth by some acute infection such as measles, or inoculation with some specific organism, as has been shown, may also occur in genuine epilepsy.

Turner, Bevan Lewis, and Roncoroni leave the question open, but seem to be of Kraepelin's opinion that epilepsy is more likely to develop where the brain has a structural defect than in a normal brain. Such structural defects would be manifest as changes in the ganglion cells or glial elements.

Reference must finally be made to Gerstmann's work. In the same way as Ranke and Alzheimer he examined the brains of epileptic cases and found the persistence of the Cajal fœtal cells in the molecular layer of four out of six epileptic cases.

In two cases of alcoholism associated with epilepsy these cells were not found. He also found large atypical cells in the brains

* A. Jakob, *Zeitschr. f. d. ges. Neurologie u. Psychiatrie*, 1914, vol. xviii., p. 2.

of idiots, and considered that they indicated abnormalities in the process of development which might expose the patient to epilepsy or some abnormal psychical condition. Gerstmann further considered that the accumulation of ganglion cells round the vessels in the brain were related to the senile plaques described by Redlich.

The question whether certain groups of patients have any particular histological abnormality is dealt with by some writers. Tramer found that in the brain of spastic cases certain changes in the Betz cells occurred with fair regularity. He did not find anything characteristic of myoclonic epilepsy. Volland also found no regular cortical change in myoclonic epileptics, but he found karyolytic and tigroid abnormalities in the cells of the anterior horn of the spinal cord. He found these changes so regularly that he was inclined to consider that there might be some relationship between them and myoclonia.

G. Lafora, working in Cajal's laboratory, found an extraordinary number of corpora amylacea in the spinal cord of a myoclonic case. Such changes I have also found in a case of paralysis agitans (1905). (This was a patient of Dana.)*

Joffroy, Dubief, and Borgerini also found corpora amylacea in the cord in cases of paralysis agitans, but in older cases than mine. Such a change was also recorded by Bielschowsky, Spielmeyer, Westphal, Sioli, Pilotti, and Weiman in encephalitis epidemica and "athetose double." These results are worth remembering, for it has been shown by Bertet and Joliet that after section of the spinal cord poisoning with carbolic acid indicates the existence of an autonomic motor centre in the cord. The same is the case where the animal is poisoned with bromide of camphor.

The negative results got by Marshall Hall where section of the spinal cord stopped hæmorrhagic convulsions, Quincke's case of chronic chorea in a dog where section of the spinal cord stopped choreic convulsions, and the case of Gallerani and Lussanna where sections of the cord stopped clonic convulsions following the administration of chinconidine, cannot be regarded as having the same value as the positive results. It must be mentioned that Ramsay Hunt † found in cases of static epilepsy (this is not a rare complication in Friedreich's disease) atrophy of the nucleus dentatus and of the tractus spino-cerebellaris.

Finally, it must be admitted that very poor anatomical results have been got by experienced and skilled investigators, many of whom started with the idea that genuine epilepsy was, in most cases, an organic malady (Marchand, M. de Fleury).‡

We know that with long-standing epilepsy, associated with psychical changes, cortical cells decay while the glial elements

* C. Dana, *American Jnl. of the Med. Sciences*, November 9, 1899, p. 502.
† Ramsay Hunt, *Brain*, 1923, p. 507.
‡ M. de Fleury, *Revue de Médecine*, 1923, p. 271.

increase (Chaslin, Bleuler, Alzheimer, Jakob). It would also appear that changes in the cornu ammonis occur more frequently here than in other psychoses. We know as a result of operations that quite frequently in focal epilepsy nothing is found except a milky appearance of the pia mater (Tillmann, Kramer, Volland, Muskens). With the exception of *one case* by Claus and Van der Stricht, we have *no* information about the changes in incipient or arrested epilepsy. It is not a matter for wonder. therefore, that Marinesco and Bouché called the results of anatomical investigation "negative." Burlureaux styled them as extensive as they were unimportant. It is a fact that many authors agree with Binswanger, and do not consider as proved that genuine epilepsy is due to an organic alteration.

Huntington's chorea is looked on by many as being related to myoclonic epilepsy. Anatomical examination has here again

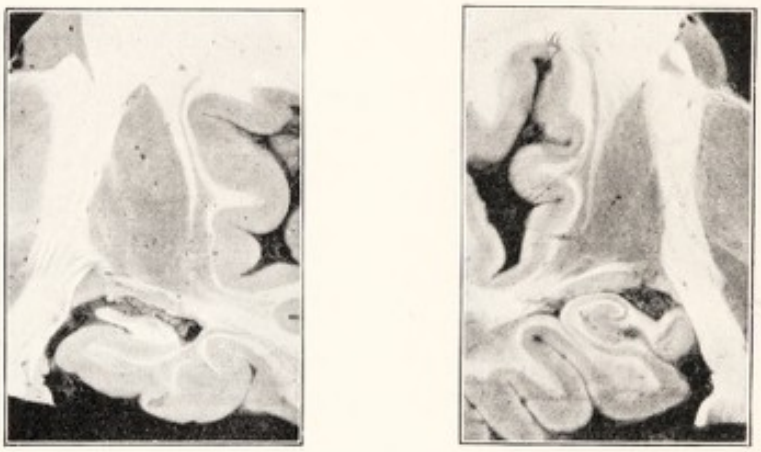


FIG. 44.—ON THE LEFT SIDE NORMAL AMMON'S HORN; ON THE RIGHT SIDE THE CONVOLUTIONS ARE ATROPHIC.

given very little result. Facklam, Kéraval, and Raviart found changes in the Rolandic convolutions (Rossi and Gonzalez found similar changes in myoclonia). Jelgersma and Vogt found changes in the corpus striatum, while Gezelle Meerburg also found, in addition, changes in the cortical ganglionic cells.

Attention must be called to the discrepancy between the great importance assigned by neurologists to encephalitic cicatrices and the rarity with which such lesions are described anatomically.

This is evident from the foregoing review, and it is also apparent in the Annual Reports of Autopsies in the Craig Colony, especially those given by J. F. Munson. A case of epilepsy is, however, reported by Mingazzini,* where there was a lesion (?) in the Rolandic convolutions, and Kogerer reports a cicatricial lesion in a case of lepto-meningitis.†

This discrepancy may be due to encephalitic lesions incurred

* Mingazzini, *Beitr. zur pathol. Anat. u. Psych.*, 1920, vol. lix.

† Kogerer, *Zeitschr. f. d. ges. Neurol. u. Psych.*, vol. xix., 1920.

early in life being repaired. In youth the power of anatomical regeneration may be considerable.

On the other hand, one is led to believe that in some cases of severe infantile convulsions, and in certain cases of slight hemiplegia (compare pp. 222 and 225), there may be no anatomical lesion, but the symptoms may be due to metabolic alteration.

To my friend, Dr. A. Gans, I owe the privilege of publishing some photos which show the changes usually described, especially

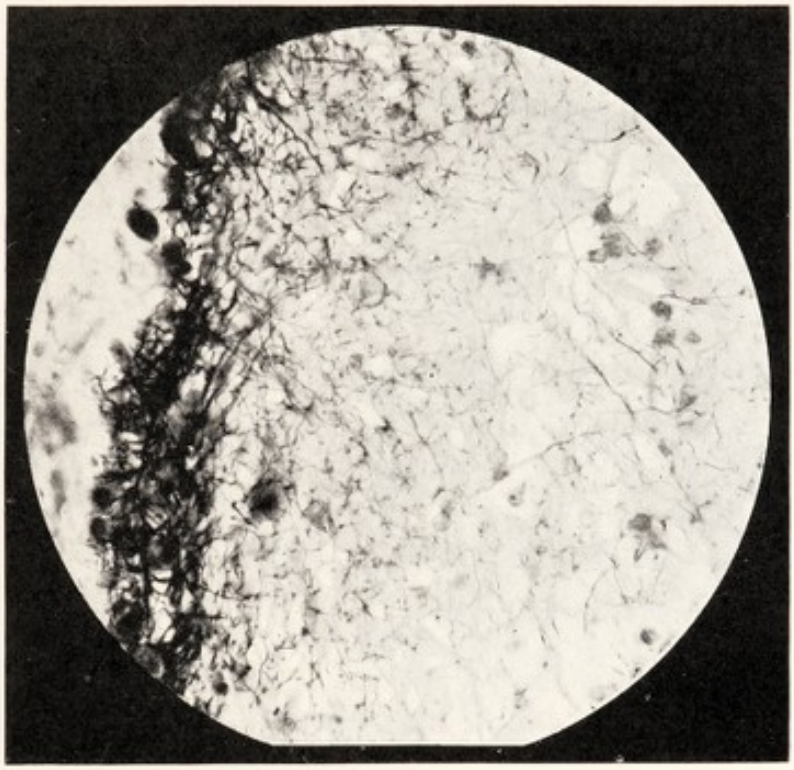


FIG. 45.—THE SO-CALLED "RAND-GLIOSIS" OF AN EPILEPTIC DEMENT.

the sclerosis of the cornu ammonis (Fig. 44, p. 368), and of the "rand-gliosis" (Fig. 45).

Fig. 44 shows on the left side the normal configuration, and is taken from the case of a patient who suffered from dementia præcox and who died in his sixty-fifth year. The right half is a macrophotograph, taken from an epileptic woman who suffered from epilepsy from early youth. She was not very demented, and shortly before her death she worked in the sewing-room. In addition to the sclerosis of the cornu ammonis, one is also struck by the absence of the normal structure in the hippocampus.

Fig. 45 is taken from an epileptic woman of 56 years, who became very demented, and suffered from contractures in later years. The dark-stained corpuscles are corpora amylacea.

CHAPTER XIV

TRAUMATIC EPILEPSY AND SURGICAL TREATMENT

§ 1. The Frequency of True Traumatic Epilepsy in Civilian Practice.

In a classification of the various forms of epilepsy, traumatic epilepsy forms a separate group. At the same time there are many points of resemblance between ordinary epilepsy and the traumatic variety, both as regards the etiology, general symptoms, course of the disease, therapeutical measures, and the final stage. It must be conceded that under this heading there are often included many cases which are open to criticism as cases of genuine traumatic epilepsy.

Such criticism is always expected, for the compilation of cases of traumatic epilepsy is always attended by data which cannot be absolutely verified. The case when seen at first may bear a scar on the skull due to an injury; here one depends on someone's story, but whether the fits and the injury are correlated is another matter. Further, a patient may show many severe scars on the head, but they may all be caused by the injuries he has received when falling in fits. The mere fact of a severe scar on the scalp is no proof at all that the fits are in any way connected with an injury (p. 276).

The following is a list selected from 2,000 of my own cases:

	Males, 1,000.	*Females*, 1,000.
Trauma of head	107	42
Trauma with scars	28	10
Trauma with defect of skull	6	2
Fall or blow on other part of body ..	82	26
Loss of consciousness, accompanying fall or blow	6	1

These figures, which show that the occurrence of trauma on the head is two-and-a-half times more common in men than in women, and about three times more common with a permanent scar or defect of the skull, seem to me to be very suspicious and to put one on guard. It is interesting to note that neither Turner nor any other authority on epilepsy has found similar figures. It is highly probable that such a list of cases with traumatic etiology compiled from the histories of cases should be regarded with suspicion. It certainly is the case that one cannot depend upon

any history as to the importance of a cranial injury. Patients who naturally enough wish to associate the malady with an injury are very prone to find a cranial scar, and to supply the history of an injury to suit.

In both cases the patient may be perfectly honest in his intention, but the data he supplies may probably be quite wrong.

Even a physician may be led astray in diagnosing the presence of a tangible scar. Taking these facts into consideration, I maintain that the diagnosis of traumatic epilepsy can only be made where an X-ray photograph, or an actual operation, or a post-mortem examination, demonstrates beyond doubt that a local lesion has affected the skull and involved the brain.

It is inevitable that if genuine traumatic epilepsy be considered in this restricted sense, civilian practice affords a comparatively small number of cases. On the other hand, such cases as one does get allow of great opportunities for diagnosis and for the formulating of prognosis. So far as I have dealt with this class of case I have found very encouraging results, even where the condition has lasted for many years. Where the diagnosis is made, and the appropriate local treatment adopted, the result may be, and often is, most satisfactory, even where the disorder has been present for very long. This is in contrast to the relatively rare cases where one gets a really satisfactory and permanent recovery in ordinary epilepsy which has persisted for very many years.

§ 2. Traumatic Epilepsy with a Cranial Depression due to Trauma in the Motor Zone.

CASE 1.—*Depression of the calvarium over the left parietal area. This was caused by a fall from the third storey of a house on to a clothes prop, when the patient was but three. As a result she had very many fits each day. She had been previously operated on three times, but with no improvement. In two later operations the brain was exposed and the bony splinters removed, with no result. Later the area of hyper-excitable cortex was removed and the patient had no more fits. She has remained well for the ensuing seventeen years.*

Miss T. (Medical attendant: Dr. H. Vos) fell at the age of 3 on to a clothes prop from the third storey of a house. As a result of this fall she had a trauma, which left a depression on the left side of the calvarium over the parietal region, and was operated on the same day in the University Hospital. She immediately began to have unilateral epileptic fits. When 13 years old in 1899, she was operated on again in the Binnen-Gasthuis (Professors Winkler and Rotgans), with a temporary improvement. Some years later Professors Winkler and Rotgans operated again (scars still visible, see Fig. 53), but again unsuccessfully. In 1908 she came to me and I put her in the O. L. V. Hospital, and recommended that another cranial operation be tried. This suggestion was not followed out, because it was felt (K. Bowman) that as the fits were now bilateral and were very

numerous further operative treatment was inadvisable lest "the condition might get worse."

The patient now began to show psychical changes.

A year later she was brought back to see me through the agency of a charitable institution.

Examination of Patient : Family History.—No history of any nervous disease.

On examination of patient's shaven head a well-marked star-shaped scar was seen inside the scar of the Wagner flap over the left parietal region.

It was noticeable that the right hand was very backward in development as contrasted with the left. Tested with the dynamometer, the right hand registered 42, while the left registered 62. Testing of the right hand showed that the finger-nose test was perfect. She could recognise small objects placed in the right hand, her eyes being shut. There was no disturbance of tactile or painful sensations, but she was unable to

FIG. 46.—ON THE SKULL IS SHOWN A HORSESHOE-SHAPED SCAR OF THE WAGNER FLAP USED IN THE SECOND OPERATION IN THE BINNEN-GASTHUIS.

Within this scar is another scar, which was caused by the original injury and the operation which was performed immediately after.

recognise passive movements, bending and stretching, of the right index finger.

Sensations of passive movements of the joints of the hand were in other respects normal. The deep reflexes were found normal on the left side, exaggerated on the right.

In my first operation (Dr. Oidtmann assisting with Dr. Philips as anæsthetist) the Wagner flap and deformed piece of bone left from the earlier operations were removed. There was no improvement, the fits continued as they had done for years. After six weeks a second operation was performed. This time the dura mater was freely exposed, and a macerated opening found in it. Just inside this opening two small splinters of the vitreous lamina were found lying on the cerebral cortex; these were removed (see Fig. 47). No improvement followed this operation.

A final operation was performed. The brain was exposed as before, and with a bipolar electrode and a weak faradic current stimulation was applied over this part of the cortex. It was found that epileptic fits were

induced by stimulation of certain definite areas of the cortex. These areas were carefully removed with a spoon to a depth of 4 millimetres, and the wound closed. This operation was performed fifteen years since, and the patient has remained well and has had no more fits. She married, has healthy children, and has no mental incapacity whatsoever.

Case 2, M., age 42. (Medical attendant: Dr. van der Plaats.) Family history seemed negative as regards nervous disease, except that a brother had myoclonic nocturnal shocks associated with obstinate constipation.

The patient had (in 1905) epileptic fits which persisted for seventeen years. These fits developed after an injury to the head, caused by compression between two iron rods. A depression accommodating two fingers was present over the right parietal area. Five years after this injury the fits began. Besides the fits the patient also has severe myoclonic shocks, which affected both sides of the body. Latterly the patient was troubled with indigestion and constipation. Further, before a fit, he was dull and tired, hands and feet were cold, the tongue coated, the breath foul, he was constipated, while mentally he became irritable. These symptoms persisted for several days before a fit.

There were no disturbances of sensation, and only very slight unilateral symptoms. With drugs and prophylactic treatment he remained free of fits for twelve years, but in 1916 the fits began again. The patient had now had the malady for almost thirty years (seventeen years with fits, twelve years respite by means of drugs and care), and psychical symptoms

FIG. 47.—PHOTOGRAPH SHOWING THE TWO BONY SPLINTERS OF THE VITREOUS LAMINA LYING IN THE OPENING OF THE DURA MATER.

These splinters had lain there for over twenty years and caused thousands of fits.

began to appear. He had post-epileptic fits of temper, and manifested certain changes in general character.

The patient was sent by me to a psychiatrical and neurological clinic with the request that an operation should not be undertaken without notifying me. Unfortunately this request was not complied with, and a general surgeon operated, removing part of the skull. The patient developed pneumonia but recovered. The fits still continued, but the patient refused to be operated on again, dementia supervened, and he died in 1923. There was no autopsy.

§ 3. Traumatic Epilepsy with Compression of the Skull not involving the Motor Areas.

CASE 3.—*Fracture of the skull, when patient was three, involving the right frontal area. At puberty she was troubled with headaches, while convulsions began which involved particularly the left hand, but were not associated with loss of consciousness. On the ulnar side of the left arm there were disturbances of the tactile sensation and appreciation of pain. Patient was operated on, after which she had no fits for thirteen years.*

G. (Medical attendant: Dr. J. J. Brouwer). Patient fell, when three, from a second storey to the ground, alighting on

a stone; this caused a fracture of the right frontal area (see Fig. 50). At first the wound gave no trouble. Her family history contained no significant data.

She came under my care in 1909, when the history was that for

FIG. 48.—CASE 3: SHOWS HYPERALGESIC LINES (HORIZONTAL) AND HYPERÆSTHETIC LINES (VERTICAL) ON THE SIDE OF THE HAND, PARTICULARLY NEAR THE LITTLE FINGER.

Disturbances also occur about the shoulder.

six months she had had headaches and latterly convulsions, characterised particularly by movements of the left hand (see Fig. 49). In this movement the fingers were rapidly flexed

FIG. 49.—CASE 3: PHOTOGRAPH DURING A CONVULSION.

and extended; the whole phenomenon consisted of small rapid movements. The patient was not unconscious and watched the process, but could not prevent it. The ulnar fingers were more involved than the radial.

During a convulsion the face was congested, while the eyes filled with tears; the pupils were dilated, while movements of the mouth appeared just as the fit subsided. The patient had curious subjective symptoms associated with these fits; sometimes she was nauseated, at other times she complained of disagreeable odours, or she was sleepy, or had diplopia. She was somewhat incapacitated in the use of the left hand, especially for rapid movements, such as piano-playing, neither was she able to do heavy work with it. There was hypalgesia and hyperæsthesia of the ulnar side of the left hand (Fig. 48, p. 374). Patient was operated on (Dr. McLeod acting as assistant). Patient almost

FIG. 50.—CASE 3: SHOWS THE FRONTAL AREA WITH THE POSITION OF THE SCAR.

The backward direction in which the plexus of enlarged veins was directed is shown in white.

collapsed under the anæsthetic, and had to have artificial respiration applied.

When the skull was opened, it was found that the dura mater was firmly attached to the scar in the bony skull. At the point of greatest compression due to the injury, a number of enlarged dural veins were seen, but no pulsations were present. When the cortex was faradised through the dura at a point 2 centimetres backwards from that point where the dura and bony skull are adherent, epileptic fits were elicited.

A week later a second examination of the patient under an anæsthetic showed no pulsations in those veins, but they were clearly seen as three enlarged veins, about the size of an ordinary

lead pencil. These veins ran backward from the point of greatest pressure (due to the fracture) to the point at which stimulation with the faradic current elicited a fit.

The whole area was washed with a warm, weak solution of corrosive sublimate. After this operation in 1910, until 1923, the patient had no fits, while the disturbances of sensation also disappeared.

Epitome.—It is important to note that in this case the point at which the dura and the bony skull were adherent was not the point at which the convulsion could be elicited. Three enlarged veins passed from this point to a point about 2 centimetres backwards; stimulation of this point elicited convulsions. The enlarged veins served as a link between the locus of irritation and the irritable zone.

CASE 4.—*This patient exhibited focal convulsions and physical symptoms for a period of five years after a blow on the head. He was operated on twice, but with no result, finally an operation removing the Wagner flap and the layer of fascia which had been inserted resulted in his complete recovery.*

J. v. D. (Medical attendant: Dr. Dito), age 25 years, was a sailor; later became a florist. He was healthy as a child, only having had measles. There was no history of infantile convulsions. He became a stoker, and confessed that he drank a good deal. While sailing on the Argentine coast some seven years ago he got a severe blow from the windlass on the right side of the head. He was unconscious for a week, and during that time had no medical treatment beyond the first-aid bandaging. He was taken to the British Hospital in Buenos Ayres, where he was operated on, and the pieces of broken bone were removed. When he recovered he was not allowed to resume work as a stoker, but received a sum of money from the firm (4,000 guilders) to start a bicycle shop, but he failed in this enterprise.

He next tried to enter the Army, but was rejected on account of his psychical symptoms, bad temper, and general unreliability. He tried the sea again, but had to give it up because of severe headaches. Later he married and a child was born.

When he began to have fits, they occurred first during sleep. The fits soon increased in number, and the patient would have a series of eight or ten fits each day.

When examined at the clinic he displayed a type of fit which had lasted over the past eighteen months. These fits started with a staring expression, when the patient stared straight in front and evidently did not hear any question being put to him.

Sometimes these attacks of staring were isolated from any other phenomenon and might occur six times a day. When an

actual fit supervened, the twitching began at the left corner of the mouth, and gradually spread as a convulsive movement over the left side, then passed to the right. Such fits always occurred in series, indeed the patient's condition resembled status epilepticus.

After a fit followed a curious psychical condition in which the patient seemed in a dream, but was at the same time troublesome and resistive; three men were sometimes required to restrain him. Dizziness was a troublesome feature, but less so than at the beginning of the illness. As regards his physical health, the patient stated that *he had always been constipated, but latterly he had become much worse.* Psychically he had changed a great deal. He was

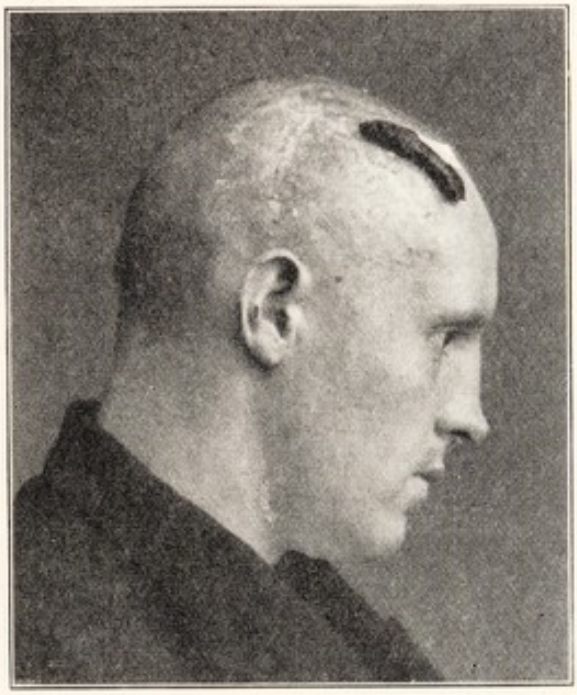


FIG. 51.—CASE 4: AFTER OPERATION.

Half of the original piece of bone (Wagner flap), which was attached to the dura mater, is placed *in situ* on the head. Below it is the original scar; over the scar the skin wound is seen.

very bad-tempered and violent. In the family history it was found that his father had drunk, and his mother and sister had both suffered from chronic headaches. His eldest brother had a severe convulsion at the age of three, but afterwards he was quite healthy.

According to the report on the case given by Dr. van Campen in *Ned. Tijdschr. v. Geneesk.*, 1923, vol. ii., p. 1281, an operation was performed, 23.12.22. In this operation an exostosis was removed and a Wagner flap formed. After this operation the patient made no improvement. A second operation was thereupon performed, in which a piece of fascia lata was transplanted under the Wagner flap.

It may be noted that when the patient came under my treatment the series of fits were so severe that it had been necessary to place him in the Wilhelmina Hospital, and the note from this hospital to the Board of Labour was to the effect, "Not much can be expected from an operation, and it would be better to wait some time before doing anything."

When the patient was examined after the foregoing operation there was some stiffness of the left leg. The left index finger and thumb were ataxic and astereognostic. Over the back of the thumb there was hyperalgesia. The left foot showed some disturbances of sensation after the second operation. Babinsky's reflex was present in the left foot. Knee reflexes were exaggerated on both sides. The optic disc on the right side showed some dilatation of the veins.

Another operation was decided on which I performed on 20.9.23. At this operation a fluctuating horseshoe-shaped piece of bone was found; this was removed with considerable difficulty (see Fig. 51). Under the bone was found the remains of the layer of fascia, placed there in the preceding operation. When the dura mater was opened, no pulsations were visible, and there were no traces of any injury or any traces of the earlier operations. Stimulation of this area with a minimal current (current too weak to produce a contraction when applied to muscle) showed that violent convulsions could be elicited over quite a wide field. The impression received was that the fluctuating piece of bone and the resulting increase of local pressure had caused a hyper-excitability of the cortex. The dura mater was carefully sutured and the wound closed. After this operation up to now (December, 1927) the patient had no more fits, neither had he the curious staring attacks. He has since resumed work.

Epitome.—From the standpoint of technique, it is interesting to compare this case with Case No. 1 of this series. In this case also a Wagner flap was made, while in both instances the dura mater was unopened (in the earlier operations). In the second case, as in the first, no improvement followed the earlier operations. In the first case because the bony splinters which had penetrated the dura mater were not found. In the second case the surgeon, supposing that the fits were due to some mechanical friction, placed a layer of fascia beneath the Wagner flap. This supposition was purely theoretical, and there is no evidence that such a type of friction would exercise any influence on the production of convulsive phenomena.

§ 4. Traumatic Epilepsy without Fracture of the Skull, the Injury not being sufficiently severe to cause Fracture.

CASE 5.—*Patient fell on her head while bicycling. Some years later symptoms of paralysis appeared in the right arm which disappeared spontaneously. About eighteen months later, Jacksonian convulsions began and were fairly frequent.*

Patient was operated on, when encephalitis serosa was found. After the operation the symptoms disappeared, and the patient recovered.

Miss V. (Medical attendant: Dr. Vrydag), age 26 in 1907. In 1899 she fell from her bicycle and was unconscious for a short time. After she recovered somewhat she vomited repeatedly. In 1905 symptoms of a nervous type appeared in the right leg and arm. The limbs became numb and paralysed so that she dropped articles she attempted to hold. Convulsions of the right half of the face also appeared. These symptoms cleared up spontaneously and apparently depended on some local affection of the left hemisphere.

In 1907, after influenza, stiffness was noticed in the left hand. Four months later the left arm was paralysed, while the patient also had three Jacksonian convulsions on the left side of the body. These symptoms also cleared up, but shortly after more serious and persistent symptoms began. Jacksonian convulsions, involving the right side of the tongue and causing disturbances of speech, were very prominent. At the end of July of 1907 there was facial paralysis, while the deep reflexes were exaggerated. The general condition of the patient went rapidly from bad to worse during the next few weeks. She now had as many as thirty to sixty violent convulsions a day, which involved both sides of the face, but were most marked on the right side. The muscles of the tongue, soft palate, and pharynx were paralysed. It was impossible to feed the patient, and she lost weight steadily. The evening temperature was slightly raised.

It was extremely difficult to localise a site for operation owing to the condition of the tongue and pharynx, and the fact that the patient was left-handed. It was, however, decided to make an exploratory opening over the left hemisphere. It was appreciated that there was a certain amount of risk in operating—indeed, Drs. Winkler and Posthumus Meyes thought it was highly probable the patient would succumb.

An opening was made through the bony skull over the left hemisphere from 8 to 9 centimetres in length. The dura mater was found in a condition of great tension and was anæmic in appear-

ance. No pulsations were visible, since the cerebral tension was so high.

As rapid decompression might have been fatal, a superficial incision was made in the dura mater. A week later the dura was opened and the pia mater was seen to be purplish in colour, while the veins were much distended. A quantity of clear sub-arachnoid fluid was exuded. It was found that stimulation of this discoloured area with a weak faradic current elicited fits of the same character as those which had tormented the patient. This part of the cortex was washed with a warm solution of corrosive sublimate (1 in 5,000).

For a few months after operation there were some functional symptoms, a legacy from the miserable time the patient had had, and some astereognosis of the left hand. These symptoms all cleared up, and the patient kept perfectly well until she died of some intercurrent malady in 1923.*

Epitome.—The local findings and the latter course of this case led us to conclude that this was a case of traumatic encephalo-meningitis. If this be so, this is the first case where the diagnosis of serous encephalo-meningitis was made "in vivo durante operatione."†

CASE 6.—*Patient had a fall when in his sixth year and developed Jacksonian convulsions of the left leg and a certain degree of paralysis. For two years prior to operation he was unable to work, and was unsuccessfully treated for his malady in several institutions. Finally, he was operated on, when a cerebral swelling was found. After this operation patient remained free from fits up to the present time, ten years later.*

J. V. (Medical attendant, Dr. J. Koetser), age 26 years. Chauffeur. When in his sixth year he fell and struck his head a severe blow against a lantern. A scar still remained over the temporal area, while at the time of the injury the patient bled profusely. There was no depression of the skull. At first the patient complained of headaches, but in a few months convulsions began in the left leg. Sometimes he was able to abort such an attack by holding the leg perfectly still. The headaches continued, but the convulsions were not troublesome from the ninth to the fifteenth year. The fits then returned, were much more severe, and involved the whole body. He went to the neurological department in the Binnen Gasthuis, and had treatment for six weeks. He did not improve. When discharged, he asked if an operation might help him. He was told that an operation would do him no good.

* Dr. Vrydag, A case of traumatic encephalo-meningitis serosa.

† Muskens, *Epilepsia*, 1910, vol. ii., p. 364; Dehmel, *Langenbecks Arch.*, 1923, vol. cxxv., p. 565.

He went to other neurologists, but the drugs he got did him no good; he made no progress, and was unable to work.

When he was 18, twelve years after his injury, he came to my clinic. After consultation with his medical attendant an operation was decided on (Dr. Steen van Ommeren acting as my assistant). When an opening was made over the site of injury it was found that the cerebrum protruded through the opening (cerebral hernia). It was found to be a case of one of the various forms of pseudo tumour of the cerebrum (Rebizzi).* At first the patient suffered severe pain, due probably to the tension on the approximated edges of the dura mater. After a week or so there was evidently some readjustment of pressure, and this symptom stopped. The patient remained perfectly well and free from fits after the operation, and was able to earn his living as a coachman. He occasionally suffers from slight headaches, but these are associated with exposure to cold. As a prophylactic he has continued to take a daily dose of a bromide-borax mixture during the ten years which have elapsed since the operation.

§ 5. Traumatic Epilepsy where there is no Fracture of the Skull or External Wound. The Fits are Unilateral and are associated with Psychical Symptoms.

CASE 7.—*Patient had leptomeningitis after a blow on the head. For thirty-six years after the injury he had fits—at first focal, later general, in character. He developed a curious dreamy psychical condition at times, which was accompanied by kleptomania.*

In the exploratory operation the cortex was hyper-sensitive to the faradic current, therefore in a very irritable condition. After the opening of the dura mater the patient remained free of fits.

V. V. (Medical attendant: Dr. Coopmann), age 50. A teacher of the piano. His father's sister was in Meer-en-berg because of fits, while a brother of his father committed suicide, being an epileptic.

Patient's father drank, and when under the influence of drink threw a hammer at the patient, then aged 14, which struck him on the left fronto-parietal area. This area had remained painful and tender to the touch. Shortly after this injury the patient began to have fits. At first they started in the right arm, but later on they spread over the entire body and became frequent. When seen thirty-six years after the accident, he had developed status epilepticus.

Very early in the course of the malady he displayed psychical symptoms. When this dreamy state came on, he was impelled

* R. Rebizzi, " Pseudotumore cerebrale," Mantova, 1916.

to steal money or jewels—*i.e.*, became a kleptomaniac. However, he grew up and married, but was unable to earn his living, and depended on his wife who kept a boarding-house. This boarding-house did not do well, probably because of the unpleasant symptoms displayed by the patient. On one occasion he stole 700 guilders from a boarder. He then disappeared, and was only found after twelve days wandering in a public garden in the Hague, without his coat and with no money. He seemed to have recovered so far, for he begged and got money from a passing stranger to take him to Amsterdam. When he reached Amsterdam he wandered about half a day looking for his house. He was eventually brought home by his daughter who chanced to meet him. Next day he recovered, but had no memory as to where he had been or what he had done with the money.

During the long period of thirty-six years the patient wandered from clinic to clinic, where he was treated with practically no benefit. The question of an operation was never suggested to him. When he came to my clinic I found that he practically always had a headache. *He said his tongue was always coated, but became worse if he were constipated for several days.* He complained of a disagreeable smell, which he referred to his nose.

On examination I found that he had a tender or painful area in the left fronto-parietal region. This spot was not always precisely the same. There was tremor of the right hand which sometimes persisted in sleep. Stereognosis was defective in the right hand, while the right underarm was insensitive to a prick, and to tactile stimulus on the radial half. He limped with the right leg.

Patient was operated on 10.5.23. An opening was made in the area of injury, the left fronto-parietal region. The dura mater was much thickened, and when opened showed a plexus of enlarged veins. The pia mater was milky white and there was an abundance of serous fluid. The cortex over the site of injury was tested with a very weak faradic current, and it was found possible to localise a portion of the cerebral cortex about the size of a two-shilling piece (guilder), stimulation of which induced convulsions of the right arm and a complete fit. The area was carefully and thoroughly washed with a weak warm solution of corrosive sublimate (1 in 5,000), and the wound closed in the usual way. When the patient came out of the anæsthetic, he remarked that for the first time for thirty-six years he did not have a headache.

The patient went on well, had no headaches and no fits, and until 1925 seemed in every way cured.

It is noteworthy that in this case the patient had a family history of epilepsy.

After the patient was well for about eight months, he began to teach the piano again, and gave concerts in some of the hospitals. As he recovered, he was able to give a very interesting account of his psychical condition before he was cured.

He described the process he passed through as follows:

He had headaches, was dizzy, while myoclonic shocks and great and small fits formed a background to his everyday life. After a series of these events, probably augmented by digestive upset and the taking of drugs, he began to feel an irresistible desire to get away.

He described this sensation as not so much desire, but the uncontrollable instinct he had to obey a call to get away from his surroundings. He was not sure but thought that the dull and shabby circumstances of his daily life may have been the stimulus urging him to make a change. He simply had to get away, and to do so begged, borrowed, or stole without compunction. In this way he had gone to Paris, Brussels and Düsseldorf, where he gave recitals while in this dreamy state, and was quite well known. On one occasion he went to Rotterdam, and actually got a position as organist at 100 guilders a week. Of course he never kept his contract, but passed on oblivious of the whole concern. He was a good musician, and played well even when in this dreamy exalted state. The difficulty was that he was inclined to play a particular type of music—*i.e.*, voluntaries at unsuitable places and times, and the other members of the orchestra could not follow him. This used to lead to his dismissal.

In personal manner he had a certain charm and impressed strangers favourably.

A curious physical symptom he always displayed, was copious perspiration both in summer and winter, when he was working or when he was idle. It is interesting to note that this symptom also disappeared after the operation, while the patient considered he played with a firmer touch.

After three years of good health after the successful operation the patient went away to the provinces. Against my advice he tried to get a post as organist, and to do so played before large audiences in crowded churches. Symptoms of gastro-intestinal disorder appeared, such as constipation, congestion and headaches—in fact, all his earlier symptoms were repeated.

Eventually he had one of his dreamy attacks, when he took some money. This particular attack of dreaminess lasted ten days, but he had a slight respite in that period, for he was able to send a note to his wife, giving his exact address, and asking her to come for him. When he again followed his exact rule of hygienic living these symptoms disappeared and did not return.

This last " attack " demonstrated the connection between the gastro-intestinal disturbances and the incidence of the dreamy states. It also shows that an operation can only eliminate one factor in the condition: collaboration of an abnormal cerebral condition and gastro-intestinal disturbance appeared to be necessary to induce this dreamy state.

§ 6. Doubtful Traumatic Epilepsy. Cases in which the Presence of a Scar is Doubtful, and the Association of the Fits with an Injury not definitely established.

CASE 8.—*Patient had an injury to the head, after which she had numerous epileptic fits. The fits started in the left side of the face or the left arm, and were so frequent that status epilepticus was displayed. In these fits she bit her tongue. Alongside these undoubtedly epileptic fits were certain hysterical symptoms. Patient was operated on; three incisions were made in the dura. After this operation she made a complete recovery;*

five years later she had had no fits at all. Some hysterical symptoms did linger, and became evident when she was emotionally excited.

G. B. (Medical attendant: Dr. Premsela), age 15. Her mother died from the effects of some nervous and mental disorder. A brother had epileptic fits, while her father, who was a shipwright, could not climb to heights because of dizzy fits.

When patient was 9 she fell downstairs on her head. She was unconscious for half an hour and later had persistent headache.

Later an iron rod fell on her head, and a movable scar remained at the site of injury. For two years she had fits, which started on the left side of the body. In these fits, she bit her tongue and dropped any article she chanced to be holding. Besides these severe fits she had numerous slighter fits, and was much troubled with headaches. Her doctor was much concerned over the display of status epilepticus, and considered the case as one requiring special treatment.

An operation was performed in 1918. An opening was made over the right parietal region. During the operation patient had a fit, this probably accounted for the fact that it was very difficult to produce a fit by direct stimulation of the cortical area. No tangible lesion was found; three incisions were made in the dura and the meningeal vessels tied. After this operation the patient had no more fits. The only untoward symptom was a hysterical outburst under the strain of a domestic quarrel.

CASE 9.—*Patient fell down the stairs and struck his head against a metal rail. This caused an injury to the right frontal bone. Later he developed fits, which began on the right side of the face, and were associated with vaso-motor disturbances. Patient was operated upon.*

Twelve years after the operation the report was that he had practically recovered.

F. v. d. H. (Medical attendant: Dr. Ekermann), age 10. Patient, when brought for examination, complained of fits, which occurred generally after falling asleep, especially if he had been excited. These fits were associated with intense congestion of the face, which became purple. The fit began on the right side of the face; then it involved the hands and feet, and the patient fell down in convulsions. Consciousness was not always entirely lost. The fit, with the congestion, lasted in all about five minutes.

Immediately after a fit the patient had distinct inhibition of speech. Latterly the fits had come on almost every evening. Headaches had also been a troublesome symptom ever since his

injury; at times he was quite free from them, but at others he was distracted with the pain for days at a time. Occasionally he had convulsions of the right side of the face alone, but this symptom the patient considered to be under his control.

The past history of the case showed that the birth had been slow, and during the pregnancy the mother had been in trying circumstances. As a child patient had measles, pneumonia, whooping cough and scarlet fever. As a young child he had screaming fits during the night if he had a fright during the day.

Four years before the date of examination he fell downstairs and injured himself, as has been described. He lost a lot of blood at the time, while the scar over the right canthus remained painful for some time; two years after the injury convulsive movement were seen on the right side of the face, and a little later the epileptic fits began. In the family history little could be elicited beyond the fact that his mother's family was tubercular. His mother showed asymmetry of the face, the right side being abnormal.

When examined the patient was a small, badly nourished child. There was a scar on the right fronto-parietal region, and another horizontal scar just below the line of the hair on the right side of the forehead. This was from an accidental injury got when fighting with another child. The whole region in the neighbourhood of these scars was painful when percussed and at times was reddened. When asked to show his teeth, the patient seemed to contract the muscles on the two sides unequally; the left side was exposed before the right. There was nothing else to be made out.

For a time general medical treatment was tried, but with no improvement, and an operation was decided on. Unfortunately, the notes and X-ray photographs of the operation have been lost.

In 1923, however, thirteen years after the operation, information was got about the patient. He was now an officer in a mail steamer sailing to India. The history he gave was that one year after the operation he had a slight fit, but no more followed. The headaches also stopped. Occasionally he said he experienced some pain at the site of operation, and sometimes when he awoke after sleep he was dizzy and had to grasp some steady article for a moment. Six months before this report the patient said he felt as if he were to have a fit; this was after a very exhausting day, but nothing happened.

CASE 10.—Refer to Case 10, p. 399.

In cases of this type, instead of a lesion after a trauma, as was expected, a slowly growing tumour has been found. Probably the tumour is in no way associated with the injury. In such a case the diagnosis traumatic epilepsy should be made with the greatest caution.

Certainly I have repeatedly had cases showing no definite scar, no abnormality of the bone on palpation and no specific lesion with an X-ray photograph. The cases in this group would require further investigation, but this I hope soon to be able to supply.

If all my earlier cases were re-examined carefully, I consider it highly probable that a good number would be found belonging to this group.

§ 7. **Epitome.**

These histories constitute an integral report of my cases of traumatic epilepsy, with the exception of two. These two cases were both associated with injury to the bones of the skull. In one case treatment with drugs (this should always get a good trial) succeeded in stopping the fits; while in the second case the symptoms were too slight to require organised treatment.

It must be remembered that in civilian practice one meets with very many cases of epilepsy supposed to be traumatic. Some of these are genuine cases, others are due to tumour, which is in all probability quite independent of any injury, while the great majority are cases of ordinary epilepsy. Considering first the locus of the trauma, it is evident that those involving the parietal region in the area of the motor zone are the most frequent. This is also found to be the rule in traumatic epilepsy acquired during the war (Delorme, Makins, Béhague, Redlich, Billet, Lenormant).*

In addition to such cases, however, Cases 2, 3, and 9 show the trauma in quite another part of the head.

It is possible that the investigation of the ponto-medullary convulsive centres and the irritability of the motor cortex, as described in the second part of this book, may throw some light on this matter. It would appear that there is an interdependence between the cerebral cortex and the medulla oblongata in reacting to the faradic current.

Further, it would appear that this interdependence is present between both the motor and non-motor areas of the cortex and the medulla (compare p. 174, l. 36 and p. 176). Consideration of the nine cases of traumatic epilepsy just described shows how various were the conditions present. In three cases a local serous meningitis was found with adhesions. Further, in one case splinters of bone were found beneath a macerated opening in the dura mater (No. 1) (compare cases by Clüsz and Ohnstedt,† and Volland). In another case (No. 6) swelling of the brain was found. In two cases (Nos. 1 and 4) it seemed highly probable that the Wagner flap formed at earlier operations was strongly irritant to the cortex,

* 30me Congrès de Chirurgie de Strasbourg, 1921, p. 23.
† Ohnstedt, " Annals of Surgery," 1892.

the first fits in such cases probably being due to adhesions. In another case (No. 3) a plexus of veins joined the injury in the bone to the cortex. Stimulation of these areas produced fits similar to those experienced by the patient. The plexus of veins apparently acted as a conductor of the irritation from the bone to the cortex (see Zeller's case). In two cases (Nos 5 and 7) serous meningitis was present, of short duration in one case, while in the other it was chronic. As regards the question of predisposition, two cases (Nos. 4 and 7) had alcoholic parents (fathers), while in four there was a family history of epilepsy.

Notwithstanding such differences in the cases under consideration, is it possible that the same mechanism may be responsible for all the cases ?

In an attempt to answer this question, one must keep in view the curious unanimity of symptoms in all the cases. Certainly there were slight degrees of paresis and disturbances of sensation peculiar to some of the cases, but on broad general lines the symptoms may be classified as follows:

1. All the patients had fits.
2. Headaches were present in cases Nos. 1, 3, 4, 5, 6, 7, 8, 9.
3. Psychical disturbances in Nos. 1, 2, 3 (slight and fugitive), and in Nos. 4 and 7 (heavy and dreamy).

For further information regarding the latter heavy dreamy types of psychoses, refer to Chapter II., § 5, pp. 305 and 318, where it is shown that an hereditary history of mental disorders seems to be not infrequently associated with the appearance of psychical changes in cases of traumatic epilepsy. It is possible, however, that the psychical changes are really due to some gastro-intestinal abnormality or insufficiency Such a condition may have been of long-standing, as in cases Nos. 3 and 4, or it may rather be a result of the cerebral injury, as in cases Nos. 1 and 7. In all these cases gastro-intestinal disturbances were prominent.* It seems very probable that a closer connection exists between psychical symptoms and gastro-intestinal disturbances than was previously supposed.

The question arises whether the fits and headaches were due to the adhesions formed between the cortex and the dura mater. It seems possible that these adhesions might exert a certain irritation, since at each systole the contents of the skull are pressed against the dural coverings.

Certainly, in the case where splinters of bone (No. 1) had

* It is interesting to note that in cases of epilepsy following on infantile encephalitis gastro-intestinal disturbances occur as frequently as in ordinary cases of genuine epilepsy. Further, occasional convulsions are very often associated with gastro-intestinal upset (p. 224). Heredity plays a part in infantile convulsions of both types.

penetrated below the dura mater, there was no doubt that the irritation had produced thousands of fits.

Further, in the single case where there was disturbance of sensation over the ulnar region (Fig. 48, p. 374), a plexus of veins was found extending over that part of the cortex, which experience has shown to be associated with segmental disturbance of sensation in this area. Compare the diagram of the post-central convolutions (Fig. 52).

From the history of cases Nos. 1 and 4, and also from the case recorded by Redlich,* there can be little doubt but that a fluctuating Wagner flap is an extremely irritating factor. It is probably made worse if a layer of fascia has been transplanted beneath it.

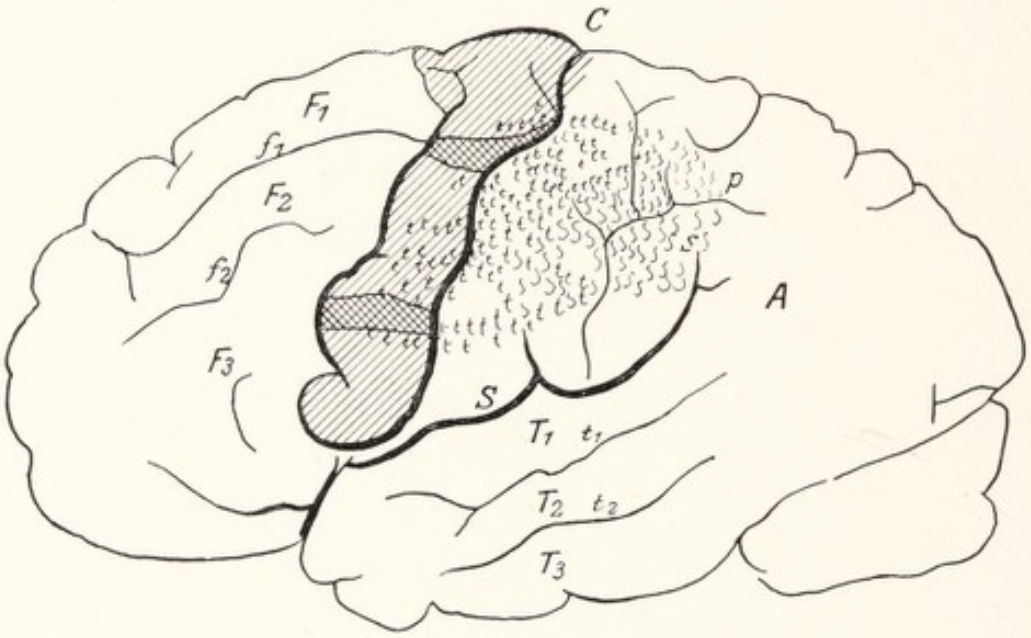


FIG. 52.

A projection of segmental alteration of sensation as compiled from a series of cases (*Ned. Tijdschr. v. Geneesk.*, 1912, p. 84, and *Neurologisches Centralblatt*, 1912, p. 958). *t.t.* indicates superficial sensation; *s.s.* indicates deep sensibility.

As a matter of fact, these theories practically ignore the possibility of some factor influencing the vasomotor supply to the cortex It must be recalled that Biedl, Cushing, and Sargent observed blanching of the pia mater when the cortex was stimulated with the faradic current or when adrenalin was applied to the cortex. Leriche† and Kennedy‡ both record cases where they have reason to believe that they saw contraction of the pial veins while the fit lasted during operation in traumatic epilepsy.

The whole matter of the vasomotor innervation of cerebral vessels is a question, which recently has lost much of its actuality, since the work of

* Redlich, *Allgem. Zeitschr. f. Neur. u. Psych.*, 1919, vol. xlviii., p. 17.
† Leriche, *Presse Médicale*, 1920, vol. xxvi., p. 645.
‡ Kennedy, *Arch. of Neurology and Psychology*, 1923, p. 608.

Krogh and Dale has made it probable that the capillaries are no longer to be regarded as merely passive channels of exchange between the blood and tissues, but as active organs, possessed of nerves and muscles. D. Fraser* considers these novel propositions as an expected support for A. E. Russell's theory, that the epileptic fit is a result of cortical vaso-constriction. Also E. Weber† has confirmed by means of Sherrington's oncograph the existence of a vasomotor centre in the medulla oblongata, reacting on impulses from above, from below and from the sympathetic. Gaskell thought to have demonstrated motor nerves in the cerebral arteries.

It is important to note that after the experience of the war Claude, Redlich, Friedrich, and Martin all condemn the use of artificial coverings or plates in cranial operations, while Sargent‡ speaks with reserve on the use of celluloid.

Leyton and Sherrington§ found that, after ablation of portions of the brain when collodion dressings were used, convulsions appeared. These convulsions ceased if the dressings were removed. They considered that the convulsions were caused by the traction exerted on the cortex due to drying and shrinkage of the dressings. In this connection reference may be made to the work of Luys, who proved that a certain degree of mobility was characteristic of the cranial contents. Sargent also refers to Gavon's work. According to Gavon, the mobility of the cranial contents may be estimated as from 3 to 9 centimetres.

This is in accordance with the opinion of Horsley, who never used any covering to isolate the cortex from the meninges. As a disciple of Horsley, I have never seen any untoward results follow an aseptic cerebral operation.

Reference must be made to the theory of Béhague and P. Marie, who consider that traumatic epilepsy is largely due to changes in the production and character of the cerebro-spinal fluid. One is willing to grant that very little is known about the influence of the changes in the pressure of the cerebro-spinal fluid induced in cerebral operations, yet there does not seem sufficient evidence in favour of this theory to allow of its acceptance.

A diagnostic method of great importance is the use of the faradic current. Much experience is required before the method can be used with success, but where the needful experience has been gained it is invaluable. It is a method which, as Horsley pointed out, is only suitable as a last resort; but as a last resort, if used with skill and knowledge, it is invaluable.

Reference may be made here to Case 1. It is a case which is essentially a scientific experiment supplying very valuable data. The patient was operated on three times at intervals of six to eight weeks. At the first

* D. Fraser, " Clinical Studies in Epilepsy," Edinburgh, 1925.
† E. Weber, *Centralblatt f. Physiol.*, 1921.
‡ P. Sargent, *Brain*, 1921, p. 316.
§ Leyton and Sherrington, *Quarterly Journal of Experimental Medicine*, 1917, vol. ix., p. 1660.

operation the whole bony covering over the motor area as well as the Wagner flap made at an earlier operation were removed. There was no improvement in the fits. At the second operation the dura was carefully explored, and in the old aperture pieces of bone were found and removed. The result was again very disappointing. At the next operation the cortex was examined by the faradic current and the exact limitations of the hyper-sensitive area worked out. This hyper-sensitive area was removed to the depth of a few millimetres. The result was that the fits were arrested, and after nineteen years no untoward symptom had returned.

From the available statistics it is shown that lesions of the parietal region are most frequently associated with traumatic epilepsy. Lesions of the frontal region come next, but are not much behind (Béhague). If a lesion in the occipital region is associated with traumatic epilepsy (as in the cases of Henschen and Kunz), hallucinations of light are more troublesome than the actual fits.

It must be emphasised that in all my cases of traumatic epilepsy the operation is but part of the treatment. The cases are all treated as genuine epilepsy so far as prophylaxis is concerned. A very exact and careful régime is drawn out, both for the method of life and for the diet. Great care is taken that digestive disorders do not arise and that constipation is avoided. Drugs, where necessary, are administered under supervision, and a careful watch is kept so that any disturbing factor is avoided. The after-treatment in a case of traumatic epilepsy, which has been operated on, is as important as the after-care in ordinary epilepsy where the fits have been controlled by a course of treatment. No apology is made for the reiteration of this point, for it is one of extreme importance. As Clüsz puts it, an operation merely removes one of the conditions which facilitates the development of chronic epilepsy.

§ 8. **Genuine Epilepsy after Encephalitis with Symptoms of Defect, Paresis, and Athetosis.**

§ 9. **Genuine Epilepsy not preceded by Encephalitis. There are no Symptoms of Defect, while the Fits are doubtfully Focal.**

Under these two headings I classify some fourteen or fifteen cases which I have seen and treated. In no case has the treatment been followed by permanent or completely successful results. In these groups operative treatment should be resorted to only as an extreme measure, and only undertaken by specialists. I have tried the operative procedure advocated by Kocher, in which an opening is made in the bony skull, the dura mater opened and a small portion of it removed (compare p. 110). I have also tried Horsley's method, where a portion of the cortex, demonstrated by a weak electric current to be hyper-sensitive, is removed. In one

case, when I used Horsley's method, there had been long-standing paresis of the hand; a really considerable improvement followed the operation. After either operation the course of the malady in some cases seemed to be retarded. At the same time neither operation can be regarded as very satisfactory. I have, therefore, come to the conclusion that an operation should only be undertaken in picked cases, and should only be performed by surgeons with wide experience in cerebral surgery.

To these two groups belong my two fatal cases. One of these was a marasmic patient who had little natural resistance. The other patient died from hæmorrhage, which could not be controlled. This case occurred many years ago, when the operative procedure had not reached the standard of excellence of the present day.

From my experience of cases belonging to these two groups I must agree with Krause, Tillmann, Alexander, and Volland that in many cases the pia mater is curiously milky in appearance. Further, it was found that uni-polar or bi-polar stimulation of the cortex with a weak current frequently caused fits. One cannot, however, conclude from this that the epileptic fits are due merely to a peculiar hyper-sensitivity of the cortex. On the contrary, this hyper-sensitivity of the cortex over a wide field may be the result of a series of fits. In Part II. I have pointed out that the occurrence of generalised fits should be considered as a function of the lower centres.

Sherrington and Leyton, who investigated the faradic irritability of the motor centres in apes, concluded that the response got from groups of cortical points was at least partly due to facilitation. Further, they found considerable evidence of reversal of response and of deviation (different results were got at different times upon stimulating the same cortical point). This fact they explained as demonstrating the increasing lability of these centres.

In the course of their experiments they exposed the cortex of two monkeys who had focal fits. In one they found that stimulation with a minimal current over a very wide cortical area induced the fits. In another case* (*Macacus fuliginosus*) the animal had numerous fits which started in the left corner of the mouth, and were associated with loss of consciousness. It was found that with artificial stimulation the fits never spread beyond the facial muscles, although ordinarily they did so. This is explained as being due to a quantitative discrepancy between an otherwise normal stimulus and the threshold, and may be a very frequent deviation in man.

* C. S. Sherrington, *Brain*, 1919, vol. xli., p. 78.

§ 10. Operative Treatment in Cases of Epilepsy.

"The result of operation can only be definitely pronounced on after a lapse of ten years. As regards general prognosis, much depends on the type of case. In the foregoing description which is subdivided into paragraphs, the prognosis becomes less favourable from paragraph 2 to paragraph 6. In all cases of operation the after-treatment is of utmost importance. As a rule the starting-point for traumatic epilepsy is the cortex, while the myoclonic type, as well as the generalised convulsion, starts in the ponto-medullary centres. The psychical symptoms in traumatic epilepsy may be regarded as a separate pathological entity; an endeavour will be made to explain this."

If the proposal put forward in § 1 that traumatic epilepsy as a diagnosis (in civilian practice) be limited to those cases where there is evidence of a direct connection between the development of the epilepsy and a tangible injury to the skull, the reader will admit that there is good reason for a favourable prognosis. The cases are of course few (only four), but in all good results were obtained. Further, from the evidence afforded by the histories of these cases (see §§ 2 and 3), it is shown that favourable results may be got, even where the malady has lasted many years, and where the fits have lost their focal character and become general. Further, the fact that unsuccessful operations have been performed does not prejudice the case, as is shown in Cases 1 and 4.

In the five focal cases, described in §§ 3 and 5, there was great diversity in the local findings. In Cases 4 and 7 lepto-meningitis was present, associated with compression and changes in the vessels. These cases showed psychical symptoms. Case 5 had serous meningitis, while Case 6 was associated with "swelling of the brain." Three of these cases did excellently, having no fits at all during the ensuing ten years. Two cases have been too recently operated on for definite conclusions to be drawn, but so far they are doing well. It may be mentioned that they both are requested to visit the weekly clinic, and are kept under close and careful observation with regular prophylactic treatment.

In my opinion the mechanism involved at first in traumatic and cortical epilepsy is quite different from that concerned with the initial stages of genuine, especially myoclonic, epilepsy. In the case of traumatic epilepsy there is not so regularly a preliminary stage which probably lasts for years, in which the symptoms are persistent headache and myoclonic shocks, and certainly these shocks, if present, will not be bilateral. Neither is there the same degree of compensation in the symptoms (compare p. 211). It is well known that in genuine epilepsy a severe fit will compensate for or replace both the headaches and the myoclonic shocks. In traumatic epilepsy such compensation

does occasionally appear, but not to the same degree. Further, the development of dementia, so frequent a sequel to the long-standing genuine epilepsy, is not common in the traumatic form. Certainly changes in the character, temper, and outlook of the patient do occur in traumatic epilepsy, but dementia is not so prone to occur. In both forms, gastro-intestinal disturbances are usual.

To sum up, chronic epilepsy might be described as the disastrous consequence of a too frequent functioning of a useful reflex, which causes a secondary hyper-excitability of the ponto-medullary centre and cortex. Whereas traumatic epilepsy might be described as the result of tangible changes in or near to the cortex cerebri, the result of which is to produce a pathological hyper-excitability of that portion of the cortex which is in turn associated with purely focal discharges. Later the ponto-medullary centres are involved, and the fits may become bi-lateral. Although the origin of the two forms of epilepsy is quite different, yet there is an intrinsic relationship between the two, while the possibility of transition from the traumatic to the genuine form has to be admitted.

So in Case No. 1, after twenty-five years of focal fits, bilateral fits developed, and finally psychical changes. In Cases Nos. 1 and 7 myoclonic shocks* appeared many years after the beginning of the malady. These myoclonic shocks were more marked in one limb than in the others; this is a feature not so often seen in the myoclonic shocks of genuine epilepsy. Gastro-intestinal disturbances are common in both types of epilepsy. Indeed, sluggishness of the gut is so frequently a symptom with all epileptics that one is sometimes inclined to wonder whether it is in itself a prodromal feature. Certainly it was a constant symptom in some patients before their trauma, and the question suggests itself whether this gastro-intestinal defect is a predisposing factor for the development of traumatic epilepsy should the patient sustain a cranial injury. In other words, is sluggishness of the gut a predisposing factor for the development of traumatic epilepsy, given the cranial injury ?

Whether there is something in this suggestion or not, it must be admitted that in genuine cases of idiopathic epilepsy an increased irritability of certain parts of the cerebral cortex has certainly been demonstrated. This irritability seems to be an important factor in the occurrence of fits.

Experiments carried out on animals, where the motor cortex

* F. Kennedy's case (*Arch. of Neurol. and Psych.*, May, 1923, p. 367), and Oppenheim's case, referred to by this author, show that even a typical myoclonic characteristic (occurrence of acustico-motor discharge) may supervene in epilepsy, undoubtedly caused by an old local cortical lesion (cortical hæmorrhage durante partu).

and medulla are both exposed, demonstrate that the irritability of the cortical and medullary centres increases and decreases simultaneously. We know that in epilepsy these two sets of centres co-operate, and it seems conceivable that if either of these centres be exposed to undue irritation, it will influence the other set—*i.e.*, the cortical centre would infect the medullary, or *vice versa*, and a liability to discharges or fits result. In this way the slow merging of traumatic epilepsy into the genuine disorder might be explained. On the other hand, in certain cases of genuine epilepsy the motor cortex acquires a very high degree of irritability.

Some investigation has been made into the nature and function of the reticular nuclei of the subcortical centres, but, so far, no anatomical connection has been proved to exist between the motor cortex and the nucleus reticularis.

The psychical symptoms described as occurring in traumatic epilepsy are essentially a separate phenomenon, and not to be regarded as belonging to the clinical picture of this malady. At least they do not form a symptom, as is so frequently the case with *genuine epilepsy*, where the psychical symptoms are due to intoxication of the patient. Where psychical symptoms do appear in traumatic epilepsy they really indicate that the disease is taking on the genuine form. Gastro-intestinal disturbances are usually present, and the patient comes under the malign influence of auto-intoxication. Also there is usually an hereditary tendency to psychical illness. In some rare cases, as in Case No. 1 of this series, where psychical symptoms appeared, not associated with gastro-intestinal disturbances, one is inclined to agree with J. Wagner,* who explains such cases on the grounds that the injury has itself produced a cerebral disturbance, which results in psychical symptoms. Such cases are rare and it is worth while noting that, when they do occur, there is generally a family history of either epilepsy or some form of psychical instability.

The after-treatment of cases of traumatic epilepsy which have been operated on has to be carried out with the same care and thoroughness as in the case of genuine epilepsy. Here also all sources of irritation, physical or mental, have to be avoided. The history of such cases as those recorded by Herpin and Binswanger show how a relapse may readily occur, even after a successful operation, if the patient does not observe the utmost care in his mode of life. In both those cases alcohol induced the relapse. Here it is interesting to recall that Nielsen† found the age-curve in symptomatic and idiopathic epilepsy running remarkably parallel.

* Wagner, *Jahrbucher f. Psychiatrie*, 1889, p. 97.
† Nielsen, *Journ. Am. Med. Assoc.*, 1925, p. 1255.

As regards the optimum time for operation, there is considerable diversity of opinion. Gowers states that operation should be undertaken only where there is a clear evidence of cranial trauma—*i.e.*, where the fits have involved first one side of the body and then the other side, and where there is a signal symptom.

This dictum can at present be accepted only with reserve.

A focal commencement or signal symptom is sometimes found in genuine epilepsy (see p. 144).

Gowers and Féré both consider that local tenderness of the skull, if persistent, is a definite indication for operation.

This opinion is sound and a safe guide so far as it goes. It seems to me that Gowers and Turner both place too much confidence upon the influence of an hereditary history of epilepsy as a contra-indication for operation.

Further, it does not seem justifiable to deny the connection between traumatic epilepsy and a trauma, although months elapse between the injury and the beginning of the fits. In Case No. 4 of this series five years intervened between the trauma and the epilepsy. In Case No. 5 years also intervened, but during that period the patient was tormented with headaches. Tuffier records a case with a four years' interval.

Further, the existence of long-standing epilepsy is not a contra-indication. This was shown in Case No. 1, where epileptic fits had occurred for twenty years; also in Case No. 7, where the patient had had epileptic fits for thirty-six years.

It must be taken into consideration that during this long period many factors (pp. 93 and 354) have influenced the case, such as alcoholism, irregular modes of life, further injury or shock, and probably, most important of all, the establishment of gastro-intestinal disorders.

§ 11. Indications for Operation in Traumatic and Focal Epilepsy.

From a consideration of the experience of traumatic epilepsy in civilian practice, it seems to me that an operation is decidedly indicated where there is a cranial injury with a tangible or visible lesion of the skull. Where the case is not so urgent as Case 4, resource should first be made to dietetic and drug treatment under the care of a competent nurse. Operation is also indicated in those cases where focal fits have followed trauma of the skull, although there may be no external evidence. This is especially the case where an injury to the skull is followed by loss of consciousness, while headaches remain as a permanent and very tiresome symptom. Even in those cases where the symptoms

do not appear immediately on the injury (as in Case 4) operation is not contra-indicated.

There are other cases which cannot be included in those groups, but which may be favourable subjects for operation, given good conditions for the operation. Such cases are those where the focal fits have been of long-standing, and where psychical symptoms begin to appear. If such cases have not yielded to the drug treatment, then an operation should be considered. The good conditions required are that the operation should be performed by a specialist in cranial surgery, that the condition of nursing should be perfect, and the patient otherwise strong enough to react after operation.

Further, it is pointed out that the occurrence of myoclonic shocks, as in Cases 1, 2, and 4, do not contra-indicate an operation. Myoclonic shocks have certainly been classed as one of the typical symptoms in genuine epilepsy, but, occurring in a case of this type, they merely indicate that the hyper-sensitivity of the focal cortical centres has spread to the ponto-medullary centres.*

The fact that the disease has lasted a very long time is no contra-indication to operation, neither is the presence of a hereditary history of epilepsy (this is in contradiction to the view of Sachs and Gessler), or the presence of psychical symptoms, if the general mental condition be not too far deteriorated.

There is no doubt that there has been an inclination among some surgeons to operate too readily on all cases showing unilateral convulsions or fits (Tillmann, Auerbach, Eguchi). Some have also operated in cases of cerebral infantile paralysis (Sachs and Volland).

Other operations have been advocated by surgeons and practised to some exent, such as puncture of the corpus callosum (Reinicke). After this operation I have never seen any real improvement. Jonesco advocates an operation involving the sympathetic centres, and claims that such an operation diminishes the irritability of the central convolutions. I have never performed such an operation, neither can I conceive of it being really efficacious.

It must be remembered that all cases which have been operated on must be treated with the same care as to drugs and diet as if they were cases of genuine epilepsy, where, of course, operation is not possible.

Attention would be called to Volland's report on cases suitable for operation. He seems to me to go too far when he postulates

* The case recorded by Fragnito does not altogether belong to this group. In his case there was a progressive local lesion of the Rolandic convolutions, while the muscles involved showed first myoclonic movements and later paralysis (*Rivista Italiana di Neuropathologia*, 1920, vol. xiii., p. 229.

the theory that where the patient recollects a prolonged loss of consciousness in early youth, he at the same time recalls an encephalitic process.

Operations in cases of encephalitis have to be decided on their respective conditions and symptoms.

In conclusion, it must not be forgotten that spontaneous recoveries or partial recoveries do occasionally occur, more especially where a patient is mentally well.

§ 12. **Prognosis.**

The reason for the depressing results recorded in the literature. The operation in suitable cases should be performed in stages.

In the last thirty years thousands of cases of alleged traumatic epilepsy and focal convulsions must have been operated on. It is therefore a matter for serious regret that out of all this number only some twenty-five cases of, at least partial cure, have been recorded by Clüsz. These twenty-five cases had all remained free from fits for a period of five years. The reasons for this very poor and depressing result have been dealt with in the preceding section, but it would be emphasised that even at the risk of making the list of successes still shorter, no case should be regarded as arrested until at least seven or ten years have passed with no signs of a fit (p. 334). Under this rule, the only cases of mine which could be regarded as arrested are Nos. 1, 3, 5, 6, and 9. It must be also recalled that Braun's patient had a fit after twenty years. Such a case indicates how important is the after-treatment, and how thoroughly and *continuously* it must be kept up. The threshold of tolerance can eventually be raised, but the treatment must be continuous, else it will break down.

It has been shown in the preceding sections that excellent results may be got in traumatic epilepsy with a cranial defect, even where the case is of long-standing and psychical symptoms have appeared. This was recognised by Echeverria.* Where the trauma has only left a superficial scar the prognosis is not so good, but where the whole diagnosis rests on a cranial injury, which has left no trace except on the memory of the patient, the prognosis is doubtful. Further, where symptoms of genuine epilepsy, such as myoclonic shocks, are superadded to the focal or unilateral fits, the prognosis must be guarded. In doubtful cases, which cannot reasonably be expected to improve, and where the patient's general health is good, I consider that an operation should be tried. As has been shown in the histories of cases, the operation may be performed in stages, beginning with a superficial

* Echeverria, *Archives générales de Médecine*, 1878, p. 673.

operation involving the opening of the dura mater, and progressing to the removal of a part of the cortex.* Where the operation is competently performed, there is no danger of fresh symptoms appearing or complications arising (p. 10, l. 28),

Perhaps the most important factor in determining the prognosis where an operation is to be performed is the surgeon who performs it. In this connection the research made by L. P. Clark† on the records of post-mortem examination carried out on epileptic patients operated on before being admitted into hospitals for chronic cases is interesting. These records show the "lamentable failure of the average surgeon" in such cases. In some cases it was evident that the dura had not been opened, the removal of exudate between the bony skull and the dura being deemed sufficient. As a result, Clark concludes: "The physician should get the neuro-surgeon to do this work." It is important to find that this opinion is also held by others.‡

§ 13. **Epilepsy in Cases of Tumour Cerebri.**

It is well known that epileptic fits are frequently associated with tumours situated in any region of the brain. In many instances the fits are explained as being due to increased intercranial pressure. In some cases there are doubtless other factors, such as the production of toxic materials from the tumour itself. In other cases the condition is analogous with that found in cases of trauma, where an injury elsewhere than in the motor centres may produce traumatic epilepsy (p. 390). In Part II., Chapter V., p. 185, l. 30, evidence is given of the functional correlation, not only between the ponto-medullary centres and the motor cortex, but with other cortical fields. The important significance of this evidence in explaining the presence of epileptic fits in association with traumata or tumours situated in non-motor areas of the brain is obvious.

A case which came recently under my care illustrates the effect of increased ventricular pressure on the production of Jacksonian epilepsy. In this case the tumour blocked the right ventricle first, with the result that there was dilatation of the right hemisphere. Jacksonian epilepsy limited to the muscles on the left side of the face and permanent paresis of some of the muscles in this region developed. When the case progressed and the tumour

* This also is shown in Friedrich's case, where extirpation of a section of the cortex gave a permanent cure. This case was published eighteen months after the operation (*Monats. f. Psych. u. Neur.*, 1909, vol. xxvi., p. 134.

† L. P. Clark, *Journ. Amer. Med. Assoc.*, 1924, vol. i., p. 770.

‡ Brouwer, *Nederl. Tijdschr. v. Geneesk.*, 1924, vol. xi., p. 1340.

became larger, both lateral ventricles were converted into one chamber (Fig. 53). The fits now ceased, but the patient died from the effect of the formation of a pressure-cone and consequent strangulation of the medulla.* In 1909 I called attention to this alteration in position of the cranial contents, due to changes in pressure, and pointed out that it was a frequent cause of death. This observation was later confirmed by Cushing.

CASE 10.—*Patient suffered for many years from headaches. For a somewhat shorter period fainting fits and focal convulsions*

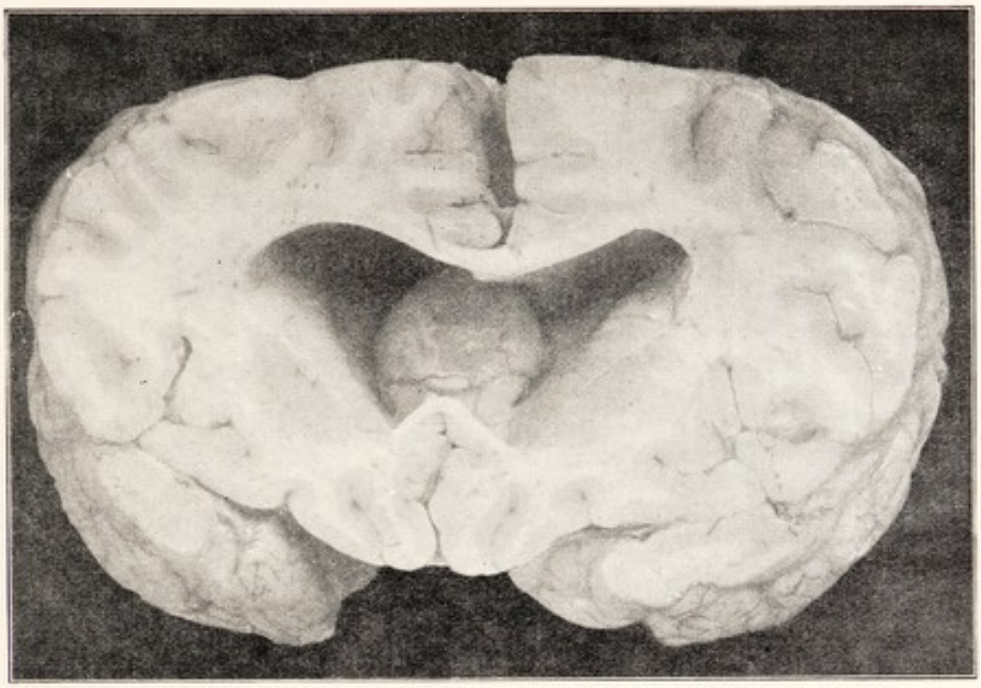


FIG. 53.—CASE 10: CROSS-SECTION THROUGH BRAIN.

In the middle note the tumour about the size of a nut. The clinical symptoms and the well-marked inflammatory changes in the right ventricle indicated that this tumour had blocked the foramen of Munro, and isolated the right lateral ventricle.

located at the left corner of the mouth had been present. He also had periods when he did not see well. After years of this modified form of the malady a complete epileptic fit occurred. Later his gait became unsteady. Repeated operation failed to give relief, and the patient died. Post Mortem: A tumour was found resting on the optic thalamus rather to the right side of the middle line. The right foramen of Monro was blocked first, and caused the dilatation of the right ventricle seen in Fig. 53.

Case W. D., age 39 (Medical attendant, Dr. M. H. Cohen). Patient was by profession a traveller. There was no history of epilepsy or insanity in the family. His father died from pneumonia, while the mother, who

* L. J. J. Muskens, *Epilepsia*, 1909, vol. i., p. 224.

was 71, had had an apoplectic seizure four years previously. Patient had an injury to his head, but it was not associated with complete unconsciousness. Headaches began to be very troublesome after this injury, and when very severe were accompanied by vomiting. In a period of ten years he had about twenty-five fits, which all began with convulsive movements at the left angle of the mouth. These fits were not always accompanied by loss of consciousness, but were frequently followed by indistinct or hazy vision. In the later months of the disease the patient had a staggering gait; the left leg frequently lagged.

Objective Symptoms.—The reflexes were strongly exaggerated on both sides. There was slight paralysis of the muscles at the left angle of the mouth; there was protrusion of both eyeballs, while the pupils were unequal.

Mentally he was liable to fits of dreaminess, and was frequently dazed. In his business he often made mistakes due to this condition of mental apathy and inattention.

On one occasion, late in the course of the disease, he was dazed for about two hours; then had a severe epileptic fit, after which he had a period

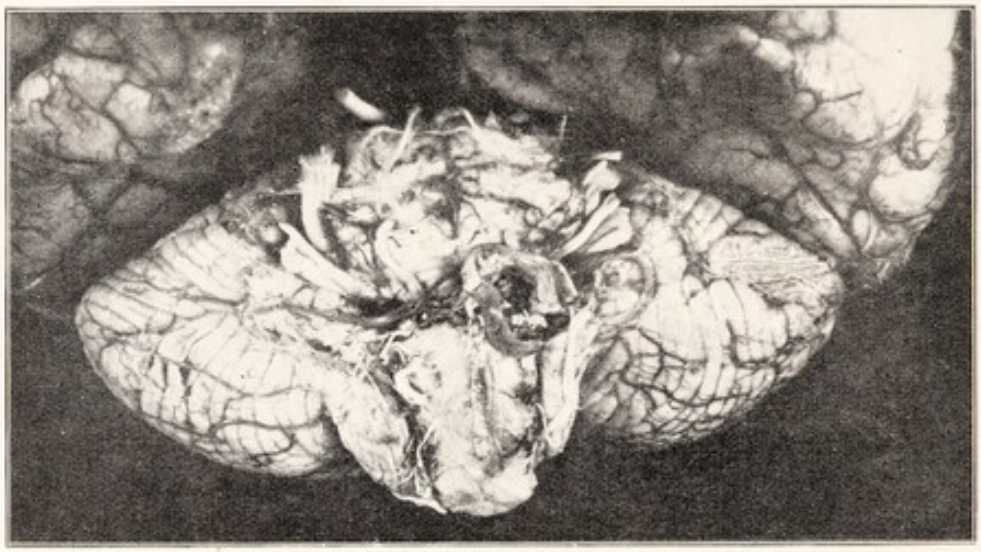


FIG. 54.—CASE 10: CEREBELLUM.

On both sides of the medulla the tonsils are seen to be sunk into the occipital foramen. The right is deeper than the left. Interference with the circulation of the cerebro-spinal fluid would be the cause of death.

of amnesia lasting for six hours. During this period he said and did indecent things.

An operation was performed in the hope of giving some relief. The dura mater was opened, and the presence of a hyper-sensitive area of cortex demonstrated by means of a weak electrical current over the fronto-parietal region. No improvement followed. After six months, during which the patient suffered great pain from headaches, the fronto-parietal region was again explored. A few days after this second operation the patient became comatose and died.

Autopsy.—The two lateral ventricles were found fused into one large chamber. There was a tumour, the size of a walnut, resting on the optic thalamus, mostly on the right side. The right ventricle was accordingly more enlarged than the left (Fig. 53).

Epitome.—The autopsy demonstrates that the position of the tumour would at first cause blocking of the right ventricle. It is possible and probable that the attacks of fainting or local

convulsions were due to intermittent blocking of the foramen of Monro. The local convulsions were due to changes in pressure, and affected the most sensitive areas—the facial centres. When the increased intercranial pressure became uniform, these fits stopped. Death was caused by the displacement of the cerebellum (see Fig. 50).

It is not very generally known that a slowly growing tumour, located in the frontal part of the cerebrum, may simulate chronic epilepsy. In 1903 I had a case of a policeman who was treated as a case of genuine epilepsy. The treatment was so successful that for three years he had no fits. The only conflicting symptom noted at the clinical examination was that there was a slight difference in the knee reflex on the two sides. In 1907 the patient returned for treatment, but soon after died. It transpired that he had a large infiltrating tumour of the centrum ovale in the frontal brain. Another case was that of a woman of 23. She, too, had been treated as a case of ordinary epilepsy, and had no fits for a number of years. Eventually she returned for treatment, complaining of very severe headaches. On examination "choked disc" was found developed on both sides. When she died the autopsy revealed a psammoma of the choroid plexus.

Besides these I have records of some six or seven cases where the autopsy has demonstrated the presence of a cerebral tumour. One important diagnostic point which was evident in all the cases is that the loss of consciousness which accompanies a fit comes on later than in genuine epilepsy (Bonhoeffer). The headaches are also of a different character than those associated with genuine epilepsy, the character of which has been described earlier (pp. 214, 267, 291, and Chapter X.). Further, myoclonic symptoms have been rarely, if ever, observed in association with fits due to a tumour. Experience shows that tumours in the temporal region are most frequently accompanied by fits.

MacRobert and Feinier* maintain that where a tumour lies near the sylvian artery œdema is a usual accompaniment, and is very likely to produce fits.

Hughlings Jackson held that, just as epileptic attacks caused by tumours in the occipital region are ushered in by visual hallucinations, those of the temporal lobe ("uncinate attacks") are preceded by olfactory hallucinations.

In two cases of cerebral abscess occurring in patients who had lived for long periods in the East Indies, epileptic fits were present for years before the characteristic symptoms of local brain disease manifested themselves. One case had suffered from dysentery

* MacRobert and Feinier, *Journ. Am. Med. Assoc.*, 1921, vol. lxxvi., p. 500.

for ten years. Latterly he developed pulmonary abscesses and empyema, for which draining was tried with resection of a rib. In the other case the patient had been operated on for liver abscess.

Hartdegen and Bourneville found that tuberous sclerosis was, in some few cases, associated with fits of an epileptic character. From an examination of the literature of such cases it seems doubtful whether these malformations were the direct cause of the fits. It has not been definitely excluded that in these patients endocrine disturbances associated with alcoholism or menstruation did not bring about the generalised fits.

§ 14. Traumatic Epilepsy due to Injuries got in War.

It is interesting to find that support is got for the conclusions arrived at from a study of traumatic epilepsy occurring in civilian life in the history of traumatic epilepsy caused by injuries received in war.

The study of traumatic epilepsy among soldiers has been undertaken by both neurologists and surgeons, among whom may be mentioned the following: From among the German workers,* Redlich, Goldstein, Hauptmann, Aschaffenburg, Poppelreuter, Friedrich, Braun, Eiselsberg, Karplus, Borchardt and Eguchi, may be mentioned. In the French school,† Billet, Béhague, de Martel, Leriche are prominent; while among the English workers, Sargent, Gordon, Holmes, MacEwen, and Buzzard are outstanding.

Among the neurologists, Redlich and Béhague probably contribute the most valuable data, since they based their observations on an exact knowledge of epilepsy as a whole. The results which these observers offer are in strong support of the conclusions arrived at from the study of the foregoing cases of traumatic epilepsy in civilian life.

According to Redlich, it is rare to find psychical symptoms or the development of the characteristic epileptic psychoses in traumatic epilepsy (compare p. 308 and Chapter XIV., § 11). In only one case, where the mother of the patient was abnormal mentally, was there any definite psychical upset (Case viii. of Redlich). Perot, another writer, also points out that changes in temper and the dreamy mental conditions are of the same type as in ordinary or genuine epilepsy. Both these authors agree in suggesting that sufficient attention is not paid by some surgeons to the part played by splinters, adhesions of the dura, cysts or

* Redlich, *Zeitschr. f. die ges. Neurol. u. Psychiatrie*, 1919, pp. 1-110.
† 30me Congrès de Chirurgie, 1922, Strasbourg, pp. 23-205.

inflammatory change, while too much is done in the way of providing some artificial covering to a defect in the skull.

Horsley and Kocher pointed out twenty-five years ago that any artificial coverings to defects in the skull were a mistake.

Further, the observations already referred to of Leyton and Sherrington* on smaller apes are interesting. They found that after experimental ablation of parts of the cortex the collodion dressings caused epileptiform fits, which ceased after removal of the dressing.

As a disciple of Horsley, I never have found any necessity to alter his dictum.

From my experience with cases where an artificial covering has been used, I am not amazed to find Manasse and others recording that epileptic fits began after a peculiarly successful artificial covering had been contrived for a cranial defect.

As regards the frequency of epilepsy after gunshot wounds, it is interesting to find that most authors agree with Cestan and Béhague that 5 to 10 per cent. develop epilepsy.

Sargent and Holmes found only 5 to 6 per cent., but Turner† thinks this percentage too low.

All the observers agree that injuries in the temporal regions are most frequently followed by epileptic fits.

Béhague suggests that where a patient has had a cranial gunshot wound, and does not develop epilepsy within eighteen months, his chances of developing it later are about 4 in 1,000.

Certainly traumatic epilepsy received a great deal of attention during the war. It was evident that early in the war, at least, many of the neurologists and surgeons were not sufficiently acquainted with the problems of the disease to allow of their data being of much real value. For example, it would be argued that such a case could not be genuine epilepsy, but must be hysteria, because the fits were brought about by emotional disturbance! (compare p. 279). Further, it is noticeable that "War Epilepsy" —*i.e.*, epilepsy produced by the conditions of war, but not due to any trauma of the head—was less and less given as a diagnosis. It was found that such cases had either had previous epileptic manifestations (50 per cent. according to Bonhoeffer), or they had had infantile convulsions, or had a family history of epilepsy.

There is no doubt, however, that much valuable information was collected in the study of epilepsy during the war.

For example, it was shown that a disturbance of the frontal convolutions due to injury was sometimes associated with vesti-

* Leyton and Sherrington, *Quart. Journ. of Experim. Physiology*, 1917, vol. xi., p. 135.

† Turner, *Journ. of Neurol. and Psych.*, 1923, vol. iii., p. 307.

bular changes.* The association of segmental disturbances of sensation with certain cortical lesions was confirmed by several authors,† among whom was Goldstein.

The recurrence of non-traumatic epilepsy in men who had suffered long before from epileptic discharges, but were apparently cured, was a phenomenon which not infrequently occurred, and to which a great deal of attention was directed.

Reference is here made to the diagnostic method described by Von Jauregg Wagner, in which cocaine injections are used. If the patient be an epileptic, fits follow; but if not, it is a case of hysteria. It is a method reminiscent of the procedure described in classical literature, where slaves were exposed to smoke in order to discover if they were epileptics. As a method for use in ordinary practice, it is not of any importance. It may help to examine the "threshold," to find the "tolerance" against the fit (compare p. 93, l. 32; p. 285, l. 24; and p. 339, l. 41).

§ 15. Historical Note.

In a general review of the history of cranial surgery it is found that there are three periods in which operations on the skull have been practised. Such operations have been undertaken with different objects,

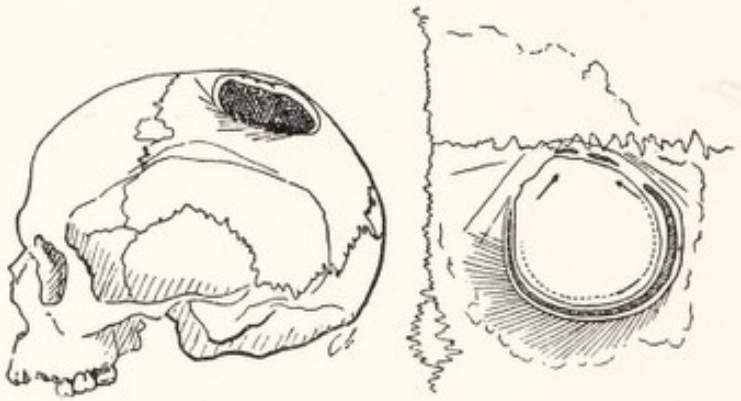


FIG. 55.—TREPHINE OPENING IN SKULL OF A NEOLITHIC MAN, SHOWING SCRATCHES OF THE SHARP INSTRUMENT ON THE EDGES OF BONE.
(After Chipault, *Chirurgie du Système nerveux*, 1894, vol. i.)

but the attempt to relieve traumatic epilepsy has been an outstanding objective. From prehistoric evidence, collected largely from Spain and France, it is clearly shown that prehistoric, especially neolithic man, did perform operations on the skull. The instrument was probably a specially prepared sharp stone, at least the marks found on neolithic skulls suggest this. Further, it is known that such openings were performed for therapeutic reasons, because such operations can be recognised in hydrocephalic skulls. Not only did neolithic man perform the operation, but the patients, at least in some cases, survived for long periods. This is demonstrated by the condition of the edges of the bony wound. In other cases

* *Brain*, vol. v., 45, p. 469.
† *Neurol. Centralblatt*, 1916, p. 831.

the peculiar sharp edge of the bone round the opening showed that the patient had not long survived.

These neolithic remains show rather curiously that the trephine openings were made not infrequently right in the middle of the sinus sagittalis —a site avoided, if at all possible, in modern surgery. Also no marks of trephining have been found on the hairless portions of the skull.

Apart from therapeutic reasons, neolithic man frequently trephined the skull in the dead. This was done to procure amulets or charms. The piece of bone removed was suspended on a cord and worn round the neck. Examples of such amulets, evidently after being used for long periods, have been found in Russia and on the borders of the River Rouge in the United States. After the neolithic period the art of trephining seems to have been lost. History affords very little reliable data, but, nevertheless, Hippocrates and Galenus described two forms of trephine.

The Renaissance saw a revival of the operation. This may have been due to the curious fortune of a nobleman who had visited many countries seeking for a physician to heal him of his epilepsy. Near Lyons he had a skirmish with some bandits, and received a severe cranial wound. When he recovered from this injury he found he was also cured of the epilepsy. Such a cure occurring in a prominent man attracted much attention, and trephining was taken up with enthusiasm. Indeed, at the beginning of the seventeenth century, surgeons, even in small towns in Holland, trephined fearlessly. Long lists of instruments were published, and it is evident from the medical literature of the time that no special care or training were considered necessary. Philip of Nassau was operated on seventeen times! It is not surprising that abuses occurred, and we find in the writings of Ambroise Paré an exposure of a "soi-disant" surgeon who undertook to cover a wound in a patient's skull with a golden ducat, but instead of doing so put the ducat in his own pocket.

In course of time the operation was gradually abandoned; even after the introduction of anæsthetics it did not come into favour. Indeed, in the middle of last century a Viennese celebrity is said to have declared that a man who dared to trephine his fellow man should himself be trephined for punishment. The immense progress which has been made in aseptic surgery in later years has brought the operation of trephining into quite a different field. With its revival are associated many English, American, and French pioneers, whose names it is not needful to recall here.

CHAPTER XV

A SYSTEM FOR THE PREVENTION OF EPILEPSY, AND FOR THE CARE OF EPILEPTICS

The Result of Investigations by the International League on the Incidence of Epilepsy in the Various Countries, and the Methods Adopted for the Care of Epileptics. The Voluntary Work done by Humane Institutions in Different Parts of the World, more especially in America. The Importance of a Central Institution in all Countries for the Treatment and Prevention of Epilepsy. Field Workers and their Work. Part of the Voluntary Treatment. The Treatment of Cases in their Own Homes. The Desirability of Collaboration between the State and Voluntary Institutions.

WHEN the International Medical Congress met in Buda-Pesth in 1908, the International League for the study of epilepsy was inaugurated. The first object of the League was to find out as far as possible the incidence of epilepsy in the different countries, and the various methods adopted for the prevention and treatment of this disorder. In the magazine of this League, *Epilepsia*, which was published from 1909 to 1914, reports appear bearing on these points.

It appeared from these investigations that America was the only country where a system could be said to exist. Two writers, Shanahan* and Munson,† supplied very interesting data regarding the co-operative efforts made by the Government and the various States and Municipalities for the treatment of epileptics and for the establishment of epileptic colonies.

Statistics and information were supplied for England by A. Turner;‡ for Hungary by J. Donath;§ for Germany by O. Hebold;‖ for Holland by Deenik,¶ Burkens, and Bonebakker;** for Sweden by A. Petren;†† for Denmark by A. Sell.‡‡ These reports were

* J. Shanahan, *Epilepsia*, 1912, vol. iii., p. 153; also 1913, vol. iv. p. 119.

† J. J. F. M. Munson, *Epilepsia*, 1912, vol. iii., p. 36.

‡ A. Turner, *Epilepsia*, 1910, vol. iv., p. 274; and 1913, vol. iv., p. 369.

§ J. Donath, *Epilepsia*, 1910, vol. ii., p. 217.

‖ Hebold, *Epilepsia*, 1909, vol. i., p. 235.

¶ Deenik, *Epilepsia*, 1910, vol. ii., p. 281.

** Burkens and Bonebakker, *Epilepsia*, 1910, vol. ii., p. 287.

†† A. Petren, *Epilepsia*, 1910, vol. ii., p. 400.

‡‡ A. Sell, *Epilepsia*, 1911, vol. iii., p. 78.

mainly prepared for National Commissions, which had been appointed to investigate the question in the various countries. It was evident from the reports that there was no lack of interest in the question, and the various countries keenly realised how important the whole matter was. In America, as has already been indicated, a system had been established, largely as the result of the work of a voluntary association, which had been in existence for forty years. In Europe, England, Germany and Holland had begun to establish some system for the treatment of epileptics.

It was quite evident from these reports that, with the exception of America, and in some parts of England, Germany and Holland, the only place for an epileptic patient was a lunatic asylum. This of course is most unsatisfactory. In very few of the countries was there the slightest provision for the treatment of incipient epileptics—indeed, it was evident that such a precaution had never been thought of. It was recognised by the League that in many countries there were practically no data regarding the incidence of the disease, and it was felt that one of the first objects should be the establishment of statistics. This branch of the investigation was badly interrupted by the war, and data were only available from Switzerland (Amman) and Holland.

Even the collection of the simple statistics relating to the number of persons suffering from epilepsy is not easy, for there is no exact or universal definition of what constitutes a "sufferer from epilepsy" (see p. 195 and Part III., Chapter IX.). Still, in countries such as Holland and Switzerland, this difficulty was got over by the fact that one physician could give the returns for a whole village or cantonment. The figures supplied showed that three to four out of a thousand inhabitants suffered from epileptic fits.

It was further evident from the reports that, with the exception of America, the various countries did practically nothing for the education of epileptic children. In the States the education problem had been tackled, and various institutions and schools had been started. The training of "field workers" had also been begun. These are women who have undergone a certain degree of training in an epileptic institute or colony, and are sent out to visit the families of the patients in order to ascertain facts regarding the family and the hereditary history. They also keep under observation patients who have been sent home after a term of treatment. The education of the epileptic child in England was begun, but the figures showed that only about one in twelve could be provided for. Data on this point are given by MacCallum* and MacDougall for England, and Weigandt and Berkhan† for Germany.

* McCallum, *British Medical Journal*, 1908, p. 611.
† W. Weigandt, *Psychiatr. neurol. Wochenschrift*, 1914, Nos. 27-29.

In Amsterdam in 1906 a Voluntary Workers' Association was formed, largely by the help and under the patronage of Mrs. van Deventer-Stelling for the after-care of epileptic patients when they left the hospital.

Although the war has hindered the work of the League, yet the investigations went so far as to show the great necessity for the establishment of some system for dealing with epilepsy and epileptics.

It was realised that the hope which inspired the early workers in America, that a proper segregation and isolation of epileptics would stamp out the disease, was Utopian. The view was at one time very generally accepted that epilepsy was almost always hereditary, but it has long since been realised that this is not so.

Although the theory that epilepsy is merely hereditary has been shown to be wrong, yet we must be grateful that it was at one time believed, for it produced many excellent schools and colonies for unhappy patients. At the same time, the gloomy view of the German School is not accepted. According to this school, any institution for epileptics would require to provide special accommodation for one-third of the patients who would be insane. It is regrettable that insanity should be so closely associated in the lay mind, and also at times in the professional mind, with epilepsy.

From a general consideration of the debates and discussions held at the annual meetings of the League, a general résumé is here given of what is considered desirable, and indeed needful, for the proper administration of epilepsy as a national problem.

1. It is desirable that a special central hospital should be established for every 6 to 10 million inhabitants. This hospital would deal only with epilepsy and would be the headquarters for consultation and research, as well as for treatment. Connected with this hospital, which should be in a metropolis, would be various clinics, laboratories and observation stations, which could also be used in medico-legal cases. There would be provision for the training of "field workers" (already referred to), and a special course of training with a qualifying certificate would be introduced. Facilities would be afforded for a regular course of instruction of relatives or friends of epileptics under treatment at home. The training of epileptic children would also come under the scope of this hospital, so far as it affected the course and progress of the disorder.

In some respects the National Hospital for Epileptics and Paralytics in London comes near this ideal, but there is a tendency to pay too much attention to paralytic conditions. Epilepsy always seems to suffer neglect if any attempt is made to associate

its treatment with any other malady, hence the need for hospitals solely for epileptics.

Where everything is favourable, the treatment of epilepsy is not easy. In such a hospital it would be necessary to arrange for patients to continue treatment under the physician—naturally a specialist—who sent him to hospital. Epilepsy is essentially not a disorder to be diagnosed and treated by one specialist and after a time sent into hospital and so automatically into another specialist's care. Where at all possible the specialist who begins the case must continue the treatment. In this particular the administration of this projected epileptic hospital would differ from the majority of hospitals. The experiment of permitting a patient in hospital to select his own doctor has been tried both in England and America, but it is not yet a general arrangement.

It is impossible for a medical man to deal with more than a certain number of fresh cases, more especially as patients have frequently to be advised as to occupation and supervised indirectly while in employment. This indirect supervision entails the instruction of employers of epileptics, while the medical adviser must also be prepared to give advice where the condition of the epileptic indicates that the employment must be changed. Much of this work could be done by lay-helpers who would follow up cases. In Holland such a system of after-care for epileptics has been in existence since 1904, and has done much good work.

2. For every 6 to 10 million inhabitants a colony for epileptics must be established. The Craig Colony in the State of New York is a model for any new colonies. There the patients live almost wholly in the open air, and enjoy both work and sport. Facilities would also be provided in such a colony for the study of the disorder.

3. For the demented, hopeless cases of epilepsy asylum accommodation is necessary. Whether it would be best to keep such cases apart from cases of general insanity, I cannot tell.

Such are the outlines of the scheme for the treatment of epileptics on national lines as conceived by the International League.

At the present time, when there is so much financial strain, one cannot hope to see such a scheme carried out. The immediate question before all who are interested in epilepsy is what can be done in the meantime to improve matters.

The need is probably more urgent than ever, for the strain and misery of the four years' war has increased the number of epileptics.

Apart from cases of traumatic epileptics, some authorities put the increase at thousands, others at tens of thousands (Claude).

There is no doubt that the conditions are peculiarly bad in the

southern countries of Europe, where there was practically nothing done for epilepsy before the war.

There is little doubt but that the general views on epilepsy have undergone modifications during the last years. Much of the recent work on the subject has favoured the conception of epilepsy as a disorder due to chemical metabolic changes. Epilepsy is essentially a reflex phenomenon, but this reflex, as the result of repetition, has become pathological. From the time of Hippocrates there have always been some who taught and believed that epilepsy was a reversible process and therefore curable (Schroeder van der Kolk and Herpin, etc.). In this book it has been the aim to show both clinical and experimental evidence in favour of this view.

A Consideration of the Best Methods of Dealing with Epilepsy from a Practical Standpoint.

1. Although the financial and other difficulties of the day make it impossible to carry out the full scheme as detailed, yet something might be done. It seems absolutely necessary that a central institution in a metropolis should be established. If we are ever to get away from the accumulation of chronic epileptic cases in our asylums, it is absolutely necessary that an institution should exist for the treatment of early cases. Such an institution would deal with the early cases as well as chronic cases where the mentality is normal, and also afford opportunities for physicians and nurses to learn the best methods of treatment. Doubtless such a hospital would be expensive, but it would be economical in the end. The very fact that such a hospital was established would be enough to stimulate the professional and lay interest in the disorder. The effect of a definite campaign against a specific disease is amply demonstrated by the work done in connection with tuberculosis.

2. As regards the establishment of colonies, the question would have to be settled after a survey of the cases requiring such treatment, and after due consideration of the cost. The colonies are doubtless desirable, but they are costly, and the alternative plan has been tried of boarding patients with pleasant families in suitable country homes. This would be like the "Familien Pflege" of the Germans, and the mental cases boarded out in Gheel in Belgium. Such a method associated with an organisation of field workers is good and is, of course, cheaper.

3. As regards the desirability of separate asylum accommodation for epileptics when they require asylum treatment, the matter is not so urgent. Gaupp, who reported on the methods used in Germany, where incurable insane persons were sterilised, suggested

that special measures might be introduced for the treatment of epileptics. This might be considered in extreme cases.

It is a curious fact that even in countries such as the United States, where epilepsy is treated as a serious national problem, practically nothing is done to ensure that incipient cases are properly treated. This is very remarkable, for Herpin and Schroeder van der Kolk and other workers have shown that, even with our present knowledge and methods of treatment, epilepsy in its early stages is a most hopeful disorder. The profession has long since realised that, if tuberculosis is to be treated successfully, it must be treated as soon as possible. In epilepsy we have not to fight an infection, we have merely to regulate, if one may so put it, an organism where the normal reflexes have gone astray. There is no doubt that popular prejudice lies at the root of this neglect. Both the profession and the laity have long regarded epilepsy as a hopeless disease. They may contemplate, indeed become enthusiastic over the establishment of colonies or homes for the unfortunate patients, but to organise a system, whereby the earliest manifestation would be regarded as sufficient to ensure prompt and correct treatment, is too revolutionary.

The old dictum, "Epileptic fits which have once occurred always recur. The condition is incurable. The fits come as a thunderclap out of a clear sky; they cannot be foreseen; they cannot be treated," is still the fixed belief of too many in the profession, and the older members of the profession influence the younger; and no doubt the fact that very few neurologists really devote much attention to epilepsy fosters the belief that even a specialist can do nothing. It is against this erroneous conception of epilepsy that the evidence of this book is directed, and it has been shown, both from the experimental and clinical aspects, that the various phenomena associated with epilepsy are reversible. For example, the physical symptoms, headaches, myoclonic shocks, exaggerated reflexes, and fits, may all disappear, may compensate one for another, or may alternate.

The psychical symptoms also appear and disappear. They may accompany, precede, or replace physical phenomena, or they may be replaced by physical phenomena. The mutability of all epileptic phenomena is one of the most characteristic properties of the disorder. Unfortunately, owing to the fact that epilepsy is so often brought for treatment when too long established, the general feeling in the professional mind is that it is a hopeless condition.

In spite of these discouraging facts, progress must be made. It is a great mistake to underestimate the educatability of the public. If even a few enthusiastic neurologists took up the matter,

and if even in one centre in a country epilepsy were properly treated in its earliest stages, the first step would be taken in the reformation. If the profession and public once grasp that epilepsy, in the majority of cases, is a curable disorder in its early stages, there would be no need to be anxious for the future of the campaign. Much can be done by intelligent propaganda, as witness the tuberculosis work and the cancer campaign in Belgium and Australia.

Such a reformation must begin in the medical profession. It is, therefore, obvious how desirable it is to establish a special epileptic hospital in each country where the proper treatment of epilepsy may be administered and taught.

APPENDICES

Explanation or Notice at Appendix

LISTS 1 and 2 (pp. 414-416)—designed after those in use in the National Hospital, Queen's Square—indicate the way in which notes are made during hospital observation. Note the absence of fits (p. 414) after June 1 and of myoclonic shocks (p. 415) after June 3—*i.e.*, on the fourth day after the prescription of sol. nitroglycerini—in patient No. 50 (p. 348). In the same way List 2 (p. 416) is an example of the effect of the iodide of mercury treatment, patient van W., No. 8 (p. 352).

Another case with iodide of mercury treatment is registered on List 3 (p. 418), but has been noted down on a policlinical list which is in use for outdoor patients. Here one finds that in the night of October 3, at 3 o'clock, the last fit of patient P. S., No. 10 (p. 351), occurred. All these lists are printed on strong paper, the clinical list offering space for 24 weeks, the policlinical ones for 24 months. With a horizontal line (—) the exact moment can be noted on which a discharge occurred, and equally also the shocks (p. 418), headache, etc., with a vertical line (|). This is made possible by dividing the diurnal period (8 a.m. to 8 p.m.) and nocturnal period (8 p.m. to 8 a.m.) in three parts, of 4 hours each. The divisional lines are drawn in slight blue lines. On p. 420 the notes of the nurse on the fit of patient J. P. (p. 348) are inscribed.

APPENDIX A

No. 1.

EXPLANATIONS OF TERMS IN TABLES

. . . . =shocks. — =fits. EII=Extra-Potio II. ▬ = severe fit. | =headache.
The number in the column (defæcation) gives number of times a day it took place. l =spoonful.

Name: J. P. (see p. 348). Address: 36, A-Street.
Admitted: April 8, 1926. Age: 2 years. Discharged: July 27, 1926.
Diagnosis: Myoclonic epilepsy, with severe series of fits, some time after fall from chair on head.

Date.		*Fits.*		*Fainting.*	*Disturbance of Sensation.*	*Treatment.*	*Extra-potio I.*	*Rest in Bed.*	*Temperature.*			*Pulse.*		*Tongue.*	*Pupils.*	*Defæcation.*	*Urine.*		*Body Weight and Notation.*
1909 *Month May.*	*Day of Week.*	*At Day.*	*At Night.*						8 *a.m.*	2 *p.m.*	8 *p.m.*	*M.*	*E.*				*C.c.*	*S.W.*	
30	Sun.	8 a.m. ═══ 8 p.m.	8 p.m. ═══ 8 a.m.		0	½ oxide of zinc bread and 1 to 3 tablespoonfuls of Extra-Potio I.	3 l.	▬	36·9		37·3			Coated		1			
31	Mon.	8 a.m. ═══ 8 p.m.	8 p.m. 8 a.m.				3 l.	▬			36·4			Slightly coated		4			
June 1	Tues.	8 a.m. ·˙· ·˙· 8 p.m.	8 p.m. 8 a.m.			Remains drowsy	2 l.	▬	37		37·3			Slightly coated		1			
2	Wed.	8 a.m. ·˙· ·˙· 8 p.m.	8 p.m. 8 a.m.			Stop Extra-Potio I. Instead: R Solut. nitroglycerini 0·5, aq. 500, 3×d. 1 teaspoonful	2 l.	▬			36·7			Slightly coated		1			2 l. pulv. liq. comp.

3	Thurs.	8 a.m. " " " " 8 p.m.	8 p.m. 8 a.m.			With dropping out of myoclonic shocks a quasi-choreic ataxy is noted while the child plays	2 l.				37·1			Better		3				
4	Fri.	8 a.m. 8 p.m.	8 p.m. 8 a.m.				2 l.				37·4		120	Coated		1				
5	Sat.	8 a.m. 8 p.m.	8 p.m. 8 a.m.				2 l.		37		37·1			Good		2				13·5 p.
6	Sun.	8 a.m. 8 p.m.	8 p.m. 8 a.m.			Vomits	2 l.		36·9		36·9			Coated		2				
7	Mon.	8 a.m. 8 p.m.	8 p.m. 8 a.m.			Convulsions in both arms	2 l.		37		37·3			Slightly coated		2				
8	Tues.	8 a.m. 8 p.m.	8 p.m. 8 a.m.			Milk dietary. Patient is put apart	2 l.		36·9		37			Coated		7				
9	Wed.	8 a.m. 8 p.m.	8 p.m. 8 a.m.		0	Vomiting. No appetite	2 l.		37		36·7			Coated						
10	Thurs.	8 a.m. 8 p.m.	8 p.m. 8 a.m.			Very troublesome	2 l.		36·9		37			Good						
11	Fri.	8 a.m. 8 p.m.	8 p.m. 8 a.m.			Behaves strangely	2 l.		37·4				142	Coated						
12	Sat.	8 p.m. 8 a.m.	8 a.m. 8 p.m.				4 l.													Weight.

APPENDIX A—*Continued* **No, 2.**

Name: A. v. W. (see p. 351). Address: B-Street.
Admitted: December 12, 1906. Age: 8 years. Discharged: April 8, 1907.
Diagnosis: Epilepsia minor, after years of enuresis nocturna, after encephalitis [?] in third year of life.

Date.		*Fits.*		*Fainting.*	*Disturbance of Sensation.*	*Treatment.*	*Rest in Bed.*	*Temperature.*			*Pulse.*		*Tongue.*	*Pupils.*	*Defæcation.*	*Urine.*		*Body Weight.*
1907 *Month Jan.*	*Day of Week.*	*At Day.*	*At Night.*					8 *a.m.*	2 *p.m.*	8 *a.m.*	*M.*	*E.*				*C.c.*	*S.W.*	
20	Sun.	8 a.m. — 8 p.m.	8 p.m. — 8 a.m.		0	Oxide of zinc bread + 4 spoonfuls of Extra-Potio I. Slept badly		37·2		36·9			Good		1			
21	Mon.	8 a.m. — 8 p.m.	8 p.m. — 8 a.m.			Pain in the stomach. Patient is dizzy		36·3		36·7		90	Slightly coated		1			
22	Tues.	8 a.m. — 8 p.m.	8 p.m. — 8 a.m.			Slept poorly		36·7		36·5		84	Slightly coated		1			
23	Wed.	8 a.m. — 8 p.m.	8 p.m. — 8 a.m.			Slept poorly		36·6		36·5		83	Slightly coated		2			
24	Thurs.	—				Slept poorly		37·1		36·9		88	Coated		1			
25	Fri.	—			0	Slept poorly. Bread with bromide and borax + 4 spoonfuls of Extra-Potio I.		36·3		37		90	Coated		1			
26	Sat.	8				Headache, slept poorly		37·6		37·1		90	Slightly coated		1			27·5
27	Sun.	11				Headache, slept poorly		36·3		36·7			Coated		1			
28	Mon.	45			0	Headache, slept poorly		36·6		36·2		82	Coated		1			

29	Tues.	19						36·2		36		86	Coated		1		
30	Wed.	14						36·9		36·5		82	Coated		3		
31	Thurs.	$\frac{-}{50}$			o	Stop medication. Pil. c. iodide of merc. 25 mg. No. 3 pro die + iodide of potass. 22·5:500, 1 tablespoonful a day. Vomited.		36·2		36·7		94	Coated		1		
Feb. 1	Fri.	20						36·9		36·5		88	Slightly coated		4		
2	Sat.	19						36·8		36·6		94			3		28·5
3	Sun.	22						36·1		36·7			Coated		1		
4	Mon.	15						36·6		36·4		110	Coated		2		
5	Tues.	22			o			36·5		36		128	Slightly coated		2		
6	Wed.	16				Vomited repeatedly		36·2		36·2		124	Coated		1		
7	Thurs.					Vomited. Pain in the mouth		36·1									
8	Fri.					D-bread contains: Lactat zinc., 150 mgr. Oxide zinc., 220 mgr. Bicarb. nat., 2·2 gr. Brom. kal., 1·9 gr. + 3 tablespoonfuls of Extra-potio II.		37·1		36·4		86	Coated		1		
9	Sat.				o	Two hours out of bed		36·6		36·4			Coated		1		28
10	Sun.	——				Two hours out of bed		36·6		36·2		80	Good		1		
11	Mon.					Two hours out of bed		36·2		36·3		104	Slightly coated		2		

APPENDIX A—*Continued* **No. 3.**

Name: P. S. (see p. 352). Age: 25 years. Address: C.-Street, The Hague Year: 1927.

1 C. bread per day.

Date, 1906.	*Day of Week.*	*Fits.* By Day.	*Fits.* By Night.	*Extra.*	*Defecation.*	*Body Weight and Notation.*
Aug. 25	Sun.	8 a.m. . . . 8 p.m.	8 p.m. 8 a.m.		1	
26	Mon.	8 a.m. 8 p.m.	8 p.m. 8 a.m.		1	Pain in stomach
27	Tues.	8 a.m. | 8 p.m.	8 p.m. 8 a.m.		1	Dizzy
28	Wed.	8 a.m. . . . 8 p.m.	8 p.m. 8 a.m.		2	
29	Thurs.	8 a.m. . . . 8 p.m.	8 p.m. 8 a.m.		1	0
30	Fri.	8 a.m. | 8 p.m.	8 p.m. 8 a.m.		1	Weight 57·3 kg.
31	Sat.	8 a.m. 8 p.m.	8 p.m. 8 a.m.		1	
Sept. 1	Sun.	8 a.m. 8 p.m.	8 p.m. 8 a.m.		2	1 D bread
2	Mon.	8 a.m. 8 p.m.	8 p.m. 8 a.m.		2	

Date, 1906.	*Day of Week.*	*Fits.* By Day.	*Fits.* By Night.	*Extra.*	*Defecation.*	*Body Weight and Notation.*
Sept. 15	Sun.	|			1	
16	Mon.	8 a.m. 8 p.m.			1	
17	Tues.				2	
18	Wed.				1	
19	Thurs.	8 a.m. . . . 8 p.m.	. . .		1	
20	Fri.	|			0	
21	Sat.				1	
22	Sun.	. . .	—		1	
23	Mon.				1	

Date, 1906.	*Day of Week.*	*Fits.* By Day.	*Fits.* By Night.	*Extra.*	*Defecation.*	*Body Weight and Notation.*
Oct. 6	Sun.				3	Stop pills
7	Mon.			E11	2	Sore throat
8	Tues.			3	5	Sore mouth
9	Wed.			3	2	Sore mouth
10	Thurs.			3	3	Sore mouth
11	Fri.			3	2	Sore mouth
12	Sat.	|		3	2	Sore mouth
13	Sun.	. . . . .	—	3	1	Sore mouth
14	Mon.			4	2	Sore mouth

3	Tues.				0	
4	Wed.	—			1	Tongue coated
5	Thurs.				1	
6	Fri.				1	
7	Sat.				1	
8	Sun.	... ...			0	
9	Mon.	...			1	
10	Tues.	..	—		1	Drowsy
11	Wed.	Innumerable fits.			1	
12	Thurs.				1	E bread
13	Fri.				1	
14	Sat.				1	

24	Tues.				2	3 pil. hg. pro die.
25	Wed.				2	Tongue coated
26	Thurs.				1	
27	Fri.				2	Weight, 56·4 kg.
28	Sat.				2	
29	Sun.				2	
30	Mon.				3	Mouth sore
Oct. 1	Tues.				2	Pain in stomach
2	Wed.				5	Mouth sore
3	Thurs.				5	Pain in stomach
4	Fri.				1	Vomited
5	Sat.				4	Pain in jaws

15	Tues.			3	1	Sore mouth
16	Wed.			3	2	Sore mouth
17	Thurs.			3	1	Pain in stomach
18	Fri.			3	2	Tongue coated
19	Sat.			3	1	Tongue coated
20	Sun.			3	2	
21	Mon.			3	1	
22	Tues.			3	2	
23	Wed.			3	1	
24	Thurs.			3	2	
25	Fri.			3	2	Weight 58·6 kg.
26	Sat.			3	3	

No. 4.

Name of Patient: J. P. (p. 348). Age: 2 years. Date: April 20, 1907. 7.30 a.m.

1.	*Condition before the Fit.*—Sleeping, awake, irritable, sleepy; temper day before (either depressed, or excited, teasing). Were there any other prodromes? Disturbances of sensibility? Constipation? Frequent passing of urine.	Patient has every day innumerable shocks and is very drowsy.
2.	*Warning.*—If present, describe the sensation, exactly where it starts and goes to. Hallucinations of smell and other senses.	Slept night before badly.
3.	*Commencement.*—Either suddenly or slowly.	Suddenly.
4	*Yelling.*	No.
5.	*Colour of Face.*—Red, blue, ordinary, pale.	Ordinary.
6.	*Movements, if Present.*—Stiffness followed by convulsions? What sort of movements? In which part of the body, face, arm, or leg? Right side or left side? Which part of body convulses first? Follow convulsions first rapidly, later more deliberately? Rotating, rolling, going in a circle, heading, fighting? Describe exactly.	Patient was on defæcation, fell suddenly forwards, so that I could just catch him. First I thought it was a myoclonic convulsion, but when patient was laid in bed, it appeared to be a fit. Convulsions of hands and legs simultaneously, eyes directed to the left, blinking with the eyes. The convulsions lasted longest in right hand and right foot. After the fit the face was directed to the right.
7	*Deviation of Head and Eyes.*—If present, to which side? Jerks of head and eyes? Quick to the right or to the left?	
8.	*Biting on the Tongue?*	No.
9.	*Involuntary Enuresis or Defæcation?*	Enuresis
10.	*Pupils, Reaction on Light?*—Cornea reflex.	During the fit patient reacted on nothing, and made a snoring noise afterwards. Pupils enlarged, cornea reflex absent.
11.	*Pulse and Respiration during the Fit?*	Pulse 110 per minute.
12.	*Duration of Movements.*	
13.	*Sensibility for Pain, after the Fit?*—Examine breast, hands, and feet. On which side pricking sensations are first felt?	
14.	*Symptoms after the Fit.*—Headache, dizziness, vomiting; weakness of arm or leg? Strange movements, plucking, smacking with the mouth, running about, rolling, falling to one side. If patient goes to sleep, for how long? How long after the fit pain is felt—for instance as a result of biting the tongue?	After the fit patient slept some hours; when waking up, he looked dazedly around and had shocks all day long.
15.	If present, what sort of equivalents? Is patient wandering or anxious? Curious behaviour, irritability, furious or immoral doings, extasis?	SISTER SIESTROP.
16.	Up to what moment before the fit patient can recall things clearly?	NOTE.—In the intervals between the individual fits, during a series of fits the cornea reflex was not always present, and the moving finger was not followed with the eyes.

APPENDIX B

Proprietary Remedies for Epilepsy

THE base of nearly all these proprietary remedies is bromide. Different samples of the same packing usually hold important differences in contents. Trouble is not taken to supply exact quantities in the packages, which in itself means danger for the patients. The analyses are supplied by Dr. Abrahams, of the Netherlands Society for the Investigation of Proprietary Remedies, from the annual publications of that Society.

	Volume.	*No.*
Anti-épileptique Uten Bromide of potassium, 12 per cent. Chalk Etheric oils Green aniline dye (Mrs. A. C. Alblas-Sorber).	XIX	II
Anti-épileptique Uten Green-stained potion of bromides Tinctura zingiberis (*Maandblad centrale gezondheidsraad*, December, 1913).	XXXIV	
Auxilium Orientalis Red-stained sugar Bromide of potassium	I	
Potio of Dr. Roland Bromide of potassium, 18 per cent. Green dye (M. J. van Pienbroek).	XXVI	2
Potio of Dr. Roland Bromide of ammonium, 10 Bromide of potassium, 40 Bromide of sodium, 55 Water to 620 (C. J. de Vogel).	XXXIII	3
Drukker's Potio Bromide of potassium, 10 per cent. Green dye (N. Keulemans).	XXXII	2
Liqueur Antiépileptique Fiévez Bromide of potassium Water Green dye (P. J. Kruysse).	IV	3
Potio of Malassina Bromide of potassium (C. van Guldensteeden Egeling).	IV	5

	Volume.	*No.*
Potio from the Schavonen-Apotheke in Frankfort Bromide of potassium Bromide of natrium (G. B. Schmidt).	XII	1
Parlaghy (Office Sanitas) Bromide of potassium	CIV	12
Potio of Niblett Strychnine Brucine (P. J. Kruysse). *Two dangerous drugs.*	I	4
Pills of Niblett Magnesia silicate White of zinc (P. J. Kruysse).	I	4
Cramp Powder of Dr. Stark Powder of valerianate Sugar (Council of Health in Karlsruhe).	IX	8
Cramp Tea of Dr. Stark Radix valerian Cortex rhamni frang. Flores arnicæ Roman camille Folia sennæ (Council of Health in Karlsruhe).	IX	8
Powder against Epilepsy (Old Family Prescription) Powder of Dictamus Powder of Zedoria (Dr. M. Greshof).	XXVII XXX	12 5
Powder against Epilepsy Radix zedoria Radix dictami (D. Bierhaalder).	XXII	3
Trench's Remedy Bromide of potassium Bromide of sodæ Bromide of ammonium	XXVIII	7
Vogelsang's Drug against Epilepsy Powder No. 1: Sugar Powder No. 2: Sugar (P. J. Kruysse).	IV	3

INDEX OF AUTHORS

A

Abadie, 202
Abrahams, 421
Adie, 315
Adrian, 30, 60, 83
Agostini, 245, 280
Albertoni, 6, 100, 107, 234, 377
Albrecht, 258
Alession, 280
Alexander, 11, 391
Allan MacDougall, 338
Allbutt, 4
Allen, 333, 345
Allende Navarro, d', 278
Allers, 280
Allocco, 202
Alt, 358
Alzheimer, 301, 312, 365, 368
Amantea, 286
Amman, 268, 270, 359, 407
Amsler, 234
Anfimow, 273
Anthéaume, 259
Arbuthnot Lane, 278
Ardin Delteil, 280
Armstrong, 280
Arrhenius, 270
Aschaffenburg, 216, 311, 402
Ashbey, 225
Atwater, 278
Aubinau, 202
Auboin, 216
Auerbach, 396
Aymes, 201

B

Babinski, 255
Baglioni, 34, 53, 102
Balint, 247
Banting, 282, 283
Barcroft, 278
Barenne, 90
Barnes, 303
Barthez, 364
Bastianelli, 193
Batelli, 10
Batti, 273
Baugh, 247
Bayliss, 87, 91
Bechterew, von, 6, 118, 202, 273, 308
Beck, 130
Beevor, 304
Béhague, 386, 402
Behnermann, 278
Belski, 288
Bemmelen (van), 5
Benedek, 258
Benedict, 273
Beriloff, 183
Berkhan, 407
Bernard, 38
Bernstein, 55
Bertet, 168, 367
Best, 258
Besta, 259
Betz, 368
Bevan Lewis, 366
Bichat, 364
Bickel, 280, 388
Biedl, 388
Bielschowsky, 366
Bignani, 193
Bigwood, 280
Bikeles, 130, 347
Billet, 386, 402
Billroth, 285
Binswanger, 5, 158, 191, 195, 219, 230, 235, 272, 284, 298, 303, 304, 364
Birk, 227
Biro, 372
Bisgaard, 257, 280
Bleuler, 365, 368
Bloch, 365
Blumreich, 239
Bödeker, 202
Boer de, 34
Boerhaave, 47, 200, 336
Bolk, 216
Bolten, 258
Bonebakker, 406
Bonell, 278
Bonhoeffer, 401, 403
Borchardt, 402
Borgerini, 367
Bossert, 227
Böttiger, 202
Bouchard, 258
Bouché, 124, 160, 368
Bouchet, 364
Bourichet, 317
Bourneville, 12, 90, 253, 257, 358, 364, 402
Bowditch, 73
Boyce, 9, 96, 121, 130, 139
Bratz, 280
Braun, 397, 402
Bregmann, 202
Bremer, 91

Breslauer, 190
Bressler, 202
Bressot, 316
Briche, 258
Bricon, 253
Brierre de Brismont, 236
Brissaud, 201, 365
Broca, 15, 34, 59, 66, 83, 98, 187
Brondgeest, 20, 66
Brown, 258
Brown, Graham, 3, 6, 30, 51, 64, 88, 96, 100, 174
Brown-Séquard, 5, 32, 100, 230
Brouwer, 374
Brouwer, B., 398
Bruce-Perbles, 259
Brühl, 259
Bruin, de, 224
Brunton, Lauder, 103, 218
Brush, 193
Bubnoff, 7, 120, 144, 286
Buchanan, 55, 90
Buck, de, 259, 280
Burch, 33
Burgé, 257
Burkens, 406
Burluraux, 369
Burr, 230
Buscaino, 280
Buzzard, 202, 402

C

Cadéac, 96
Caelius, 301
Caers, 249
Cajal, 367
Callum, Mc, 408
Calot, 287
Campbell, 283
Campen, von, 377
Campioni, 259
Carducelli, 288
Caro, 257
Carrière, 202
Casparie, 265
Cawson, 278
Cazauvieihl, 364
Celsus, 287
Ceni, 280, 287
Cérenville, 216
Cestan, 195, 403
Charon, 258
Chaslin, 365, 368
Chauffard, 202
Chauveau, 168
Cheyne-Stokes, 4
Chipault, 404
Chirée, 240
Chvostek, 227
Clan Thomson, 314
Clark, Pierce, 121, 191, 192, 202, 216, 245, 262, 278, 296, 314, 317, 354, 358, 398
Claude, 247, 258, 273, 307, 389, 409
Claus, 245, 259, 320, 324, 365, 368
Cleghorn, 368
Clingenstein, 287
Clüsz, 386, 390
Cobb, 42, 85
Cohen, 349
Collip, 283
Collier, 144
Collip, 282
Collucci, 365
Cololian, 280
Comby, 219, 224
Comsie, 268
Cooper, 83
Coopmann, 381
Cotard, 365
Crile, 278
Crinis, de, 247, 259, 280
Cuneo, 259, 280, 333
Curschmann, 239
Cushing, 388, 399
Cushney, 41, 98
Czerny, 207, 220

D

Dana, 253, 367
Darwin, Ch., 5, 199
Davenport, 268
Deenik, 406
Dehmel, 380
Delasiauve, 235, 239, 249, 336
Delmas, 239
Delorme, 386
Delteil, Ardin, 280
Deneffe, 12
Deventer-Stelling, van, 408
Dexler, 121
Dide, 258
Donaldson, 280
Donath, 240, 258, 280, 358, 406
Donders, 56
Doutrebente, 304
Dubief, 367
Dubini, 193
Dubois-Raymond, 80
Dumesnil, 287
Duncan, Gibb, 349
Durlacher, 240

E

Echeverria, 365, 397
Edel, 240
Edinger, 365
Eguchi, 396, 402
Eiselsberg, v., 402
Eisenberger, 53
Elliotson, 238
Elsberg, 277, 280
Emich, 365
Engelmann, 33, 41, 55
Erb, 220
Escherich, 227
Eussière, 202, 239

F

Facklam, 368
Falconer, 202
Falret, 299, 313
Fano, 69, 121
Farge, 202
Feer, 228
Feinberg, 202, 234
Feinier, 401
Felsen, 262
Féré, 121, 195, 216, 219, 222, 230, 238, 240, 255, 256, 259, 278, 300, 319, 361, 395
Ferenzi, 278
Ferranini, 202
Ferrier, D., 6
Fiessinger, 202
Filia, 236
Fischer, 54, 206, 258
Flatau, 192
Flechsig, 221
Fletcher, 283
Fleury, de, 259, 367
Follet, 202
Forbes, 30, 33, 56, 83
Ford, 222
Forel, 129
Fournier, 273
Fowler, 345
Fragnito, 396
Franck, 7, 44, 55, 96, 100, 113, 144, 191, 192, 242, 263, 300
Fraser, 389
Freud, 349
Freusberg, 14
Friedmann, 228
Friedreich, 200, 367
Friedrich, 398, 402
Frisch, 232, 253
Fritsch, 6, 144
Frölich, 34
Fuchs, 100, 191, 259
Fürstner, 253

G

Galde, 280
Galenus, 249, 405
Gallerani, 367
Gallus, 271
Gans, 369
Ganter, 359
Gaspero, Di, 259
Gaubius, 341
Gaucher, 275
Gavon, 389
Geitlin, 373
Gélineau, 315
Gerstmann, 307, 366
Gessler, 396
Gezelle Meerburg, 368
Gibb Duncan, 342
Gillès de la Tourette, 324
Gley, 278
Godart, 280
Godefroy, 262
Goldbloom, 280, 333
Goldflamm, 202
Goldstein, 402, 404
Goltz, 185, 308
Gonzalez, 202, 368
Goria, 202
Gorieri, 259
Gorn, 301, 202
Gotch, 16, 33
Gottlieb, 40, 167
Gowers, W., 125, 194, 219, 220, 224, 230, 232, 235, 239, 245, 249, 250, 274, 278, 285, 287, 298, 314, 324, 336, 338, 341, 345, 360, 395
Graham Brown, 3, 100
Grand du Saulle, Le, 300
Grandis, 56, 100
Gregg, 56
Grevenstuk, 281
Griffith, 83
Grinker, 347
Grünwald, 234
Gubler, 12
Gudden, von, 130
Guerini, 55
Guerri, 280
Guidi, 280
Guillain, 287
Gurber, 95
Gutti, 258
Gy, 202

H

Haig, 245, 280, 291
Halban, 287
Haldane, 258
Hall, Marshall, 168
Hallager, 257
Hallon, 287
Hamilton, 259
Hammet, 90
Handfield, Jones, 238
Hansen, 220
Harnack, 13, 101, 168
Harryman, 280
Hartdegen, 402
Hartenberg, 246
Hartmann, 259
Hauptmann, 284, 402
Hebold, 280, 407
Heidenhain, 7, 120, 144, 287
Heilig, 202
Heiman, 303
Heinrich, 280
Helmholtz, 54, 56
Henoch, 219, 226, 227
Henschen, 390
Hering, 34, 38
Hermann, 202
Herodotus, 348
Herpin, 218, 249, 250, 297, 336, 360, 394, 410
Hess, 3
Heubel, 9
Hill, 4, 49, 82, 120, 207, 276, 277

Hippocrates, 405, 410
Hitzig, 6, 10, 144
Hoch, 202
Hochheim, 13
Hochsinger, 219, 224
Hoesslin, 259
Hoffmann, 104
Hoffmann, P., 318
Högyes, 4
Holmes, Gordon, 150, 160, 286, 402
Holmes, Th., 328
Homen, 202
Hondo, 343
Hoppe, 280, 358
Horsley, 5, 8, 83, 96, 120, 389, 403
Houssay, 282
Huchard, 202, 288
Hugenholtz, 349
Hunt, 202, 206
Huntington, 368
Husemann, 91

I

Infeld, 287

J

Jackson, Hughlings, 5, 46, 47, 64, 82, 107, 188, 190, 255, 302, 307, 343, 398, 401
Jakob, 366, 368
Janet, 297
Jardine, 240, 358
Jauregg, 313, 404
Jelgersma, 216, 262, 303, 309, 368
Jelliffe, 202, 234, 251, 350
Jenner, 220
Jödicke, 259, 347
Joffroy, 367
Joliet, 168, 367
Jolly, 257
Jones, 350
Jones, Handfield, 238
Jonesco, 396
Jong, de, 281
Jordan, 30
Juarros, 338, 347
Juschtschenko, 258

K

Kalischer, 202
Karowsky, 365
Karplus, 13, 144, 292, 313, 402
Kato, 30, 53
Kaufmann, 281
Keeton, 61, 90
Kennedy, 280, 388, 393
Keraval, 368
Kersten, 258
Kinberg, 344
Klessens, 271
Kleyn, de, 150, 185, 191
Kocher, 396, 403
Koehler, 278
Koetser, 380
Kogerer, 368
Kompe, 287
Koog, 346
Koschewnikoff, 202
Kowalewski, 273, 291
Kraepelin, 366
Krainsky, 245, 257, 280
Kramer, 317, 369
Krantz, 257
Krause, 391
Krause, F., 7
Kreid, 13
Kries, von, 83
Kroon, 340
Krumbmiller, 259
Kumao Yamakami, 4, 278
Kunz, 390
Kussmaul, 3, 96

L

Lafargue, 202
Lafora, 367
Lafosse, 121
Lair, van, 200, 202
Lalage, 202
Lambrani, 202, 207, 291
Lambranzani, 258
Landeesen, 286
Landois, 239
Lane, 278
Lange, 346
Lange, C. de, 229
Langendorff, 16, 61, 277
Langley, 40
Laquens, 281
Lasègue, 313
Laudenheimer, 343
Lawson, 12, 44
Leblois, 287
Legros, 168
Lehmann, 254
Lejonne, 307
Lemoine, 285
Lemos, 254
Lennox, 280, 333
Lenoble, 202
Lenormant, 386
Lepage, 8, 185
Leriche, 388, 402
Leubuscher, 202
Levi, 202
Levy, 230
Lewis, 80, 277
Lewis, Bevan, 366
Leyden, von, 287
Leyser, 206
Leyton, 185, 389, 403
Lhermitte, 254
Libertini, 121
Liddell, 32, 67, 82
Lichtig, 349
Lier, van, 278
Locock, 342
Loewe, 280
Logan, 168, 185, 281
Lomer, 271
Loven, 84

Löwenhard, 278
Löwy, 13
Lucas, 30, 33, 53, 60
Luchsinger, 13
Luciani, 7, 107, 121, 144
Lugaro, 201, 202
Lugiato, 258
Lui, 258
Lundborg, 101, 192, 200, 202, 208
Lunwall, 259
Lussanna, 367
Luth, 198
Luys, 115, 389

M

Macdonald, 42
MacDougall, Allan, 407
MacEwen, 402
Mackenzie, R. I., 326
Macleod, 375
Macleod, J. J., 46, 121, 234, 258, 281
MacRobert, 401
MacWilliam, 207
Maes, 247
Maewski, 365
Magnan, 8, 30, 95, 103, 168, 245, 249
Magnus, 16, 20, 87, 150, 185, 191
Maillard, 347
Maillet, 202
Mainzer, 280
Mairet, 253, 280
Makins, 386
Manasse, 403
Mann, 227
Marburg, 215
Marchand, 257, 258, 320, 367
Marchi, 107
Marey, 32, 54
Marie, P., 202, 285, 287, 389
Marinesco, 201, 202, 365, 368
Marshall Hall, 3, 367
Martel, de, 402
Martin, 296, 389
Masoin, 278, 280
Matthaei, 40
Maxwell, 30
McGrugan, 61, 90
McCallum, 407
McCormick, 283
Meerburg, Gazelle, 368
Méglin, 341
Meignaut, 347
Meihuizen, 14
Meinert, 115, 367
Mendelsohn, 54, 80, 91
Menière, 288
Meunier, 96
Meyer, 13, 259, 280, 393
Meyes, Posthumus, 379
Meynertz, 202
Meyssier, 202
Michelson, 207
Mingazzini, 121, 253, 368
Minkowski, 168
Möbius, 202
Moeli, 273
Moleschott, 3
Molin de Teyssière, 202
Monakow, v., 193
Moniz, 202
Moore, 277
Morel, 303
Morgagni, 336
Morgan, 5
Morselli, 259
Mosso, 20, 66, 207
Mott, 202
Motte, de la, 238, 311
Müller Schürch, 273
Munnich, 56
Munro, 400
Munson, 368, 405
Muratow, 202
Murri, 202
Muskens, 32, 33, 34, 80, 98, 115, 147, 150, 192, 202, 219, 239, 247, 254, 259, 288, 368, 400

N

Naegeli, 259
Nagel, 61
Naumann, 228
Neri, Nerlinger, 238, 240
Nicoll, 326
Nielson, 394
Nieuwenhuysse, 259
Nikishawa, 185
Ninde, 316
Nobécourt, 259
Noble, 283
Noervig, 257, 280
Nolen, 234
Nonne, 293
Nothnagel, 5, 9, 158, 192, 254
Nouet, 320
Novi, 56, 100

O

O'Brien, 281
O'Connor Wright, 280
Oebeke, 144
Ogle, 277
Ohnstedt, 281, 386
Oidtmann, 372
Olmsted, 168, 185
Onimus, 7, 168
Opler, 287
Oppenheim, 257, 259, 393
Ormerod, 286
Osnato, 280
Owsjanninow, 4

P

Pagniez, 302
Paneth, 220
Papillon, 202
Paracelsus, 341
Parkinson, 55
Patch, 277

Pathault, 12, 90
Patrick, 230
Paukul, 54
Paulian, 254
Peiper, 262
Pellegrini, 258
Perbles, Bruce-, 259
Perrero, 202
Perugia, 259
Perusini, 366
Peterson, 285
Petren, 406
Pfaff, 280
Pflüger, 58
Philipson, 64
Piéron, 54
Pighini, 258
Pike, 5
Pilotti, 367
Piper, 57, 82
Pirquet, 227
Pitres, 7, 44, 55, 96, 100, 113, 144, 191, 253
Place, 54, 56
Poggio, 202
Polak, 366
Pohl, 346
Pollock, 150, 158, 234, 253
Poppelreuter, 402
Posthumus Meyes, 379
Pourtal, 201
Poynton, 221
Pratt, 30, 53
Prévost, 2, 10
Preyer, 207
Probst, 8, 174, 185
Prout, 202, 255, 358
Prus, 8, 144
Pugh, 258
Purkinje, 11
Putnam, 280

Q

Quincke, 168, 367

R

Rabot, 200, 202
Radcliffe, 341
Raecke, 301
Ramsay, Hunt, 201, 367
Randall, 286
Ranke, 366
Ranvier, 55
Raviart, 368
Ray, 83
Raymond, 202, 253
Raynaud, 216
Read, 351
Rebizzi, R., 381
Redlich, 191, 218, 239, 253, 262, 272, 284, 285, 315, 386, 389, 402
Reiher, 227
Reinicke, 396
Remak, 202
Renner, 333, 345
Reynolds, Russell, 191, 200, 201, 202, 260, 264, 348
Richet, 14, 15, 34, 54, 59, 67, 80, 83, 98, 187, 218, 253
Rilliet, 365
Rittershaus, 262
Rivano, 280
Robertson, 364
Robinowitch, 244
Robitschek, 202
Rochet, 249
Rockford, 291
Rodiet, 280
Roeber, 9
Roger, 201, 202
Rohde, 257, 259, 280
Roll, 277
Rollin, 262
Romanes, 5
Roncoroni, 259, 366
Rosenthal, 100, 259, 288
Rosett, 98
Ross, 358
Rossi, 130, 368
Rothmann, 8, 143, 185, 308
Rueff, 281
Russell, E. A., 253, 288, 389
Russell, R., 9, 96, 127, 130, 153
Russell Brain, 282

S

Sachs, 285, 396
Saito, 185
Sala, 365
Salkowsky, 343
Salomonson, Wertheim, 12
Samaja, 2, 10
Sanderson, 91
Sano, 14
Saquepée, 258
Sarbo, 191
Sargent, 388, 389, 402
Sauer, 259
Sauerbruch, 45, 196
Savory, 277
Schaefer, 53, 83
Schaefer, A., 57, 222
Schilling, 262
Schlecht, 259
Schott, 285
Schroeder van der Kolk, 5, 9, 47, 158, 191, 192, 219, 341, 365, 365, 410
Schroff, 4
Schuller, 215
Schultz, 258, 259
Schupfer, 192, 198, 202
Schussny, 348
Schwartz, 12
Schweigmann, 13
Seeligmüller, 202
Sell, 406

Seppilli, 202
Séquard, Brown-, 5, 32, 100, 230
Sérieux, 259, 365
Setchenow, 40, 64
Sewall, 82
Shanahan, 192, 338, 406
Sherrington, 16, 30, 32, 33, 38, 47, 50, 60, 64, 67, 73, 80, 87, 90, 98, 185, 389, 403
Simonelli, 202
Sioli, 367
Sloan, 61, 90
Slosse, 278
Söldner, 202
Solislohen, 253
Soltmann, 221
Sordelli, 282
Souques, 202
Spielmeyer, 367
Spitzer, 215
Spratling, 200, 262, 278, 312
Ssimonowitch, 305
Stanford, 350
Stannius, 38
Starling, 91
Starr, 202
Steen, van Ommeron, 380
Steffens, 292
Stephan, 14
Sterling, 192, 254
Stern, 254
Stewart, 5, 202
Stheeman, 220
Stier, 262, 285
Stoddart, 312
Stokes Adams, 277, 288, 318
Stokvis, 103, 218
Stookey, 277, 280
Strassmann, 202
Stricht, van der, 245, 320, 365
Strümpell, 202
Swieten, van, 285

T

Talma, 14
Tamburini, 273
Tarugi, 280
Tenner, 3, 96
Teyssière, Molin de, 202
Thiemich, 219, 220, 224, 227
Thom, 230
Thomsen, 259, 314
Thomson, 229, 257
Thomson, Clan, H.C., 314
Tigerstedt, 55
Tilanus, 287
Tillmann, 7, 368, 391, 396
Timme, 196, 253
Tintemann, 280
Tissot, 200, 239, 335, 341
Tod, 255
Tomaschewski, 305
Toulouse, 343
Tourette, 324
Tramer, 365
Tramonti, 280
Trasbot, 12, 90
Treadway, 150
Trepsat, 259
Trousseau, 227
Tuffier, 287
Türck, 9
Turner, 194, 216, 230, 238, 240, 250, 257, 272, 275, 278, 284, 318, 338, 343, 360, 363, 366, 395, 403, 407
Turnowski, 284
Turtschaninow, 9, 14, 101, 143, 150, 195, 202

U

Ulrich, 343
Uno, 278
Unverricht, 7, 113, 192, 193, 200, 202, 215, 309
Urstein, 311
Uspensky, 4
Uyszewski, 347

V

Valobra, 202
Vanlair, 7
Vaquez, 219
Veit, 202
Velden, van der, 343
Verga, 202
Verworn, 37, 90
Vidal, 4
Vidoni, 258
Virchow, 285, 365
Vogt, 195, 234
Voisin, 230, 245, 285, 343, 365
Volkmann, 54
Volland, 287, 367, 368, 386, 391
Vollmer, 258
Vorkastner, 311
Vos, 372
Vries, de, 287
Vrijdag, 379

W

Wagner, 202, 394
Wagner, von Jauregg, 313, 404
Wallenberg, 287
Waller, 16, 55, 91
Wallis, 326
Warren, 73
Webber, 211
Weber, 389
Weeks, 330, 333, 343
Weigand, 407
Weiman, 367
Weiss, 4
Wertheimer, 8, 185
Wertheim-Salomonson, 12
Westphal, 239, 287, 367
White, 202, 251
Wiedemann, 11, 49, 167
Wiersma, 207, 253, 262, 317

Wildermuth, 316
Willcox, 347
Williams, Roger, 328
Willis, 278
Wilson, 192, 247, 363
Wimmer, 254
Winkler, 287, 305, 379
Wishart, 333, 345
Wolfhügel, 277
Wuth, 258, 259
Wyllie, 206
Wyss, von, 343

Y

Yawges, 312
Yeo, 55

Z

Zander, 277
Ziehen, 191, 202
Ziemmsen, 277
Zimmermann, 259
Zuntz, 13, 239
Zwaardemaker, 16, 20
Zylberlast, 202

INDEX OF SUBJECTS

A

Abbreviated discharges, 213
Abortive epilepsy, 297
Abortive fits, 242
Absence, 296
Absinth, 8, 86, 95
Abstention from chlorides, 343
Accessory nerve, 177
Accumulation of toxins, 280
Acidity, 363
Acido-basic equilibrium, 280
Acne, 345
Acoustic reflexes, 23, 52
Adolescent epilepsy, 198
After-care, 392
After-discharge, 33, 39, 50, 62, 70, 184, 196
Albumen, 259
Alcohol poisoning, 195, 273
Alkalinity, 258
Alternative manifestations, 215, 287, 304
Amblyopia, 254
Amnesia, 301
Amylene hydrate, 358
Anacidity, 258, 280
Anæmia, 49
Analgesia (segmental), 63, 244, 262, 291, 312, 355
Aneurysma, 277
Anger convulsion, 228
Animal epilepsy, 1, 121
Anoxæmic fits, 4, 277, 283
Anti-social acts, 299
Anxiety, 278, 306
Apoplexy, 292
Arrest of epilepsy, 226, 353, 366
Arterio-sclerosis, 288
Artificial covering (of skull), 389
  respiration, 4
Asphyxia, 243
Asphyxial convulsions, 4, 276
Athetosis, 390
Atmospheric influence, 270
Atypical fits, 67, 193, 242, 266, 282, 295
Aura, 244
Auto-intoxication, 50
Automatic movements, 292-295
  stage, 44, 63, 244, 298
Automobile drivers, 393
Avalanche, 307

B

Babinski-sign, 255
Backwardness, 222
Bad days, 215
" Bahnung," 79, 274, 334, 360
Barbituric acid, 347
Bilateral fits, 151
Birds, 102, 121, 167
Blood-pressure, 244
  -serum, 280
  -sugar, 258
Borax, 345, 346
Breaking the fast, 213
Bromides, 342
Brown-Séquard convulsions, 6, 230

C

Camphor, 10
Cannabis indica, 348
Carbamide acid, 257
Carbolic acid, 195, 216, 286
Career, 331
Care of epileptics, 206
Catalonia, 311
Census of epileptics, 319
Central clinic, 229
Centres of myoclonic reflexes, 107
Centripetal connections, 158
Cerebellar nuclei, 188
Cerebellum, 9, 121, 130, 400
Cerebral pressure, 287
  swelling, 380
Cerebro-spinal liquor, 389
Chalk, 220
Charge, 187, 210
Childhood, 218
Chorea electrica, 193
Choreic dogs, 7
Chromaffine system, 258
Circulatory system, 252
Circus movements, 140, 254
Civilian praxis, 370
Classification, 194, 318
Climacteric epilepsy, 198, 360
Clinical history, 323
  observation, 246
Clocklike movements, 141
Clonic convulsions, 85
Coagulability, 259
Coated tongue, 263
Cocaine, 303, 404
Cod-liver oil, 223
Cold shivering, 32, 103
Colony for epileptics, 409
Compensation, 18, 33, 42, 47, 50, 210, 212, 217, 242, 305
Compression of skull, 373
Conductibility, 34, 42, 55, 57

Conduction of cerebral influx towards medullary centres, 249
Conjugate deviation, 174
Conjunctival reflex, 313
Consanguinity, 273, 328
Consciousness (loss of), 44, 93, 206, 252, 296
Conservation, 190
Constipation, 213, 257, 280, 377, 382, 390, 394
Continuity of treatment, 397
Conversion of reflexes, 167
Convulsive centres, 189
Corneal reflex, 313
Cornu ammonis, 365
Corpora quadrigemina, 146
Corpus striatum, 119
Cortex, 5, 96, 100, 120, 171, 180
  cerebelli, 126, 188
Cortical centres, 7
Cranial depression, 371
  injury, 393
Crime, 298
Cross-section of cord, 167
Crowded, 279
Cumulative effect of convulsant drugs, 91
Cyst, 46

D

Decerebrate animal, 80
Decreased irritability after a fit, 180
Delusional insanity, 299
Dementia, 45
Dementia præcox, 311
Depression, 248
Detoxicating effect, 30, 99, 210
Dietary, 339
Differential diagnosis, 288
Dilatation of pupils, 99, 103
Discharge, 18, 38, 41, 47, 49, 85, 210, 303
Discharging fit, 208
Dissociation of tracing, 97
Domestication, 199, 208
Dreamy state, 191, 246, 298, 303, 308, 312

E

Early epilepsy, 264, 316, 410
Eclampsia, 16, 240
  of children, 226
Ecstasies, 251
Edge-gliosis, 365
Effective dose, 29
Emotions, 233, 278
Employment, 409
Encephalitic process, 46, 196, 285, 364
Encephalitis, 4, 65, 217, 222
Encephalo-meningitis serosa, 381
Endocrine, 258
Endogenous poison, 194, 240, 306
Epilepsia, minor, 200
  procursive, 98
Epileptic character, 262, 321
  diathesis, 279
Epileptiform phenomena, 98
Epileptogenous drugs, 102
Epistaxis, 214
Equivalents, 302, 304
Ether anæsthesia, 59
Evolution of disorder, 242
Exciting causes, 272, 288
Excretions, 257
Exhaustion, 255
Exhibitionism, 299
Exogenous poison, 194, 306
Experimental epilepsy, 167
Extrasystole, 288

F

Facilitation, 107, 144
Fainting fit, 266, 296
Falling asleep, 42, 64
False reminiscence, 248
" Familien Pflege," 410
Family doctor, 340
Faradic stimulation, 143, 168, 174, 391
Fascicular contractions, 168
Fasting, 279, 333
Febrile disorder, 225, 231
Fever, 3
Fibrillar contractions, 168
Field workers, 407
Fillet, 141, 158
Fishes, 102
Fluctuating symptoms, 263
Focal convulsions, 376
Focus of epileptic phenomena, 102, 106, 193, 250, 394
Forced movements, 254
Forebrain, 112
Forensis, 315
Formatio reticularis, 127, 148, 151, 156
Fracture of skull, 379
  of spine, 287
Frequency of symptoms, 264
  of myoclonic convulsions, 202
Frontal animal, 165
Frontal headache, 291
Frontal pole, 161
Fugues, 299
Furunculosis, 315

G

Gastric contents, 263
Gastro-intestinal disturbances, 103, 220, 248, 254, 387, 393
Genuine epilepsy, 210, 225
Glittering glance, 300, 312
Grand mal, 197
Guinea-pigs, 5
Gynæcology, 286

H

Habit of fits, 289
Habitual forced movements, 229

Hæmorrhage, 3, 292
Hallucination, 50, 246, 303
Headaches, 211, 214, 242, 267, 291, 387
Hemilateral epilepsy, 305
Hiccough, 104
Hippocampus, 369
History of trephining, 404
Homolateral influence, 160
Hospital treatment, 409
Hygienic measures, 331, 336
Hyoscine, 345
Hypalgesia, 247, 374
Hyperexcitability, 61
Hypoglykæmic fits, 281
Hypophysis, 279, 315
Hysterical symptoms, 257, 260, 289, 291
Hystero-epilepsy, 203, 323

I

Improvement after fit, 47, 252, 279
Incipient cases, 194
Incomplete fits, 249
Increased irritability before a fit, 172
Indication to operation, 395
Individual treatment, 336
Infantile convulsions, 197, 210
  epilepsy, 234
Infectious diseases, 284
Infiltrating tumor, 401
Inflammatory lesion, 10
Inhibition, 64, 67, 87
Insuline, 46, 281
Insurance, 293
Intellectual aura, 305
Intermission of pulse, 288
Internal secretion, 349
International League, 407
Inter-paroxysmal symptoms, 246, 261, 313
Interrelation motor cortex and medullary centres, 191
Intestinal peristalsis, 280
Intoxication, 18, 218
  of subcortical centres, 250
Inveterate cases, 349, 395
Involuntary muscular contractions, 221
Iodide of mercury, 351
Irritability, 170

J

Jacksonian convulsions, 45, 289, 398
Jewish nation, 293

K

Kleptomania, 298, 306
Knee reflexes, 32, 73, 150

L

Lability of latency, 100
Laryngismus, 314
Latent period, 42, 54, 58, 73
Lead poisoning, 285, 307
Lengthening of latent period, 89, 97
Leptomeningitis, 368
Leucopenia, 259
Lightning-like contraction, 15
Local brain affection, 196
Localisation of myocolonic reflex, 6, 192
Loss of consciousness, 44, 195, 252, 292, 296, 316
Lumbar cord, 163
Luminal, 347
Lunatic asylum, 362, 407

M

Macacus, 338, 391
Marriage, 240, 327
Masturbation, 278, 314
Mechanism of discharge, 47
Medulla oblongata, 40, 126, 171, 176
Medullary centres, 144
Menière, 289, 293
Menopauses, 235
Menstrual epilepsy, 198
Menstruation, 235
  deterioration, 310, 315
Mental hospital, 269
  slowness, 211
Mentality, 316
Mercury treatment, 345
Metabolic changes, 254, 280
Method of experiments, 19
Midbrain, 147
Minor symptoms, 297, 314, 339
Molimina menstrualia, 235
Molluscs, 20, 102
Monakow's bundle, 139, 149
Monkeys, 195
Monobromide of camphor, 12, 15
Moribund, 284
Mortality, 359
Motor cortex, 139, 169, 186
  discharge, 303
  fit, 42, 265
  symptoms, 254
Murder, 312
Muscular exertions, 214
Mutability of epileptic symptoms, 411
Mutation, 199
Myoclonia, 199
Myoclonia symptomatica, 200
Myoclonic epilepsy, 200
  reflexes, 16
    in normal children, 219
    in physiological economy, 190
  shocks, 202, 396
  undulation, 201
Myotonic tracing, 92

N

Narcosis, 65, 86, 276
Nasal polypi, 286

National Committees of International League, 407
Neolithic man, 405
Neurasthenia, 290
Neuro-surgeon, 398
Night rest, 204
Nitroglycerine, 345
Nocturnal dreams, 300
fits, 217
Non-motor cortex, 184
Non-specific dyscrasic epilepsy, 275
Nosological value of symptoms, 264, 302

O

Obscuration of consciousness, 205
Occasional fits, 197, 223
Octopus, 20
One-sided fits, 107
Operative treatment, 393
Opisthotonus, 95
Organic lesions, 305
Orthopædic, 287
Outdoor games, 356
Ovary (removal of), 241

P

Pædiatrists, 232
Palæostriatal nuclei, 254
Palliative treatment, 354
Paradoxical condition, 31, 59
Paralysis agitans, 367
Paresis (general), 293
Passage of Jacksonian into generalised fits, 314
Pathological anatomy, 364
inebriety, 310
Pedunculus cerebri, 120
Permanent psychological state, 315
Petit mal, 102, 295
Phenol, 101
Phosphates, 227
Phosphorus, 280
Physiological principles, 334
tremor, 83
Pleural cavity, 216
Plucking movements, 260
Plumbism, 197
Pneumonia, 284
Pollakiuria, 257
Pontine centres, 182, 189
Ponto-medullary convulsive centres, 386
Poriomania, 299
Postaxial segments, 247
Post-epileptic headaches, 257
phenomena, 66
Post-paroxysmal paralysis, 255
phenomena, 254
psychisms, 260, 301, 306
sensory disturbances, 256
Posterior longitudinal fascicle, 153
nerve columns, 159
roots, 158, 169
Postural influence, 253
Potassium permanganate, 237
Præ-epileptic phenomena, 66, 243
Precipitation of toxins, 261
Predisposing factors, 271
Pregnancy, 29, 198, 235
Preludium, 249
Preparatory stage, 70
Prevention of epilepsy, 406
Procursion, 254
Prodromal period, 42
symptoms, 204, 272
treatment, 353
Prognosis, 359, 397
Prolapse, 259
Propaganda, 412
Prophylactic treatment, 291, 327
Protective roll of fits, 103, 229
Proteine-carbohydrate, 280
Pseudotumor, 381
Psychical prodromate, 248
Psycho-analysis, 350
Psychological change in animals, 22, 103, 215
theory, 216
Psychotechnical laboratory, 294
Pulsus alternans, 34
Punctiform hæmorrhages, 244
Pupils, 44, 49, 65, 253, 262, 292
Pyknolepsy, 314
Pyramidal tract, 139
Pyrexia, 103

Q

Quadrupeds, 121, 250

R

Rabot's myoclonia, 202
Rapidity of convulsions, 290
Rate of conduction, 56
Recovery, 47
Recruitment, 68
Recurrence of same type of discharge, 250
Reflex after-discharge, 43, 51, 62, 70, 76, 184, 189, 190, 196
epilepsy, 285
irritability, 36, 69
Refractory period, 31, 33, 36, 38, 49, 78, 81, 99, 157, 189, 242
Regional myoclonic convulsions, 61, 85, 191, 204
Reinforcement of reflexes, 39
Religious duties, 356
Remissions, 359
Removal of bony skull, 110
of dura mater, 110
Repetition of fits, 335
Respiratory spasm, 223
Resuscitation, 195, 286, 307
Retarded reflex movement, 165
Retrograde amnesia, 301
Retrogression, 254
Rhythm of convulsions, 81, 243
Rhythmic discharge, 82
Rickets, 220, 226

Rise of temperature, 233
Rudimnetary myoclonic reflex, 189

S

Salivation, 244
Santonine, 101
Scarlet fever, 222, 284
Scar of skull, 371
School children, 269
Scratch reflex, 6, 51, 100
Sea sickness, 229
Secretions, 257
Segmental distribution, 244, 247, 262, 291, 312, 355
Senile epilepsy, 198
Sense of satiety, 344
Sensibility (disturbance of), 244, 259
Sensitiveness to alcohol, 274
Sensoclonic reaction, 101, 208
Sensory aura, 308
Series of shocks, 206, 212
Sexes, 270
Shocks (myoclonic), 36
Signal symptoms, 395
Significance of symptoms, 242
Single convulsions, 52, 64, 201
Skull, 373
Sleep, 204, 207
Smoking, 279
Softening, 156
Solidungulates, 121
Spasmophily, 211, 218, 226
Spastic cases, 367
Spinal animal, 6, 80
cord, 2, 90, 169
" Spontaneous " myoclonic reflexes, 17, 36, 49, 68, 101, 157, 199
Start reflex, 41, 99
Stationary symptoms, 257
Statistics, 266
Status epilepticus, 23, 255, 357
Status neuro-oclonicus, 201
Stimulation, 182
Structural defect, 366
Strychnine, 9, 38, 55, 84, 90, 159
Stupor, 300
Substantia reticularis, 160, 193
Summation of stimuli, 40
Sunstroke, 285
Supranuclear connections, 193
Symptoms of charge, 191, 215, 217, 260, 262, 339
Synapse, 55
Syncope, 253
Systemic phenomena of after-discharge, 251

T

Tachycardy, 298
Tactile reflexes, 60
Tegmentum, 149
Temporal lobe, 299
Temperature, 13
Tendon reflexes, 150, 256
Terminal beats, 352
Terminology, 323
Tetany of children, 228
Theca, 109
Tobacco, 299
Tolerance, 29, 250
Tongue, 263
Tonic convulsions, 85, 171, 221
Tonisation, 174
Toxicology, 48
Toxic theory, 252
Tracings, 19, 82
Tram drivers, 293
Transitional fits, 242
Transition of reflexes to fits, 190
Traumatic epilepsy, 197, 275, 370
Treatment (continuity of), 397
Tuberous sclerosis, 364
Tumor cerebri, 398

U

Ubiquity of myoclonic reflexes, 188
Unconsciousness and loss of consciousness, 96, 195, 252, 293, 296, 317
Undressing, 261
Unilateral fits, 381
Urea, 217

V

Violence, 300
Viscosity, 258
Visual hallucinations, 305
Voluntary work, 406

W

Waking up, 204, 208
Wandering, 299
War injuries, 402
White matter, 120

X

X-ray photos, 385

Z

Zinc oxide, 337, 341
Zoological Gardens, 338

Printed in Great Britain for Baillière, Tindall and Cox, by Billing and Sons, Ltd., Guildford and Esher

WELLCOME LIBRARY INSTITUTE