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ESSAYS AND ADDRESSES ON DIGESTIVE AND NERVOUS DISEASES AND ON ADDISON'S ANÆMIA AND ASTHMA

ARTHUR F HURST
M.A., M.D., OXON., F.R.C.P.


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ESSAYS AND ADDRESSES ON DIGESTIVE AND NERVOUS DISEASES AND ON ADDISON'S ANÆMIA AND ASTHMA

ORATIONS & ADDRESSES

By

SIR JOHN BLAND-SUTTON,

Consulting Surgeon to the Middlesex Hospital

Illustrated.

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ESSAYS AND ADDRESSES ON DIGESTIVE AND NERVOUS DISEASES AND ON ADDISON'S ANÆMIA AND ASTHMA

BY

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PREFACE

One of the medical officers at the Seale Hayne Military Hospital related the following story at our last anniversary dinner. He told us that, shortly after he had joined us, I came into his room and watched him treating a case of hysterical paraplegia. After a couple of minutes I called him aside and told him he could scarcely hope to cure the patient by the antiquated method he was using. Very much surprised, he answered that he had carefully read what I had written on the subject and was employing the treatment I had recommended, to which I answered that the article he quoted was written long ago—nearly a year, in fact—and was hopelessly out of date.

I have much the same feeling when asked for reprints of my papers. They always seem to be out of date. I like to believe that this is evidence of the scientific spirit, which is never content to leave a question as settled, but is always ready to modify views, however strongly held, in the light of further evidence. Perhaps I am wrong ; it may really be the first sign of the advent of senility.

Whichever view is correct, my object in republishing the essays and addresses in this volume is to put on record my present views on various subjects, in which I have been specially interested during the last ten years. They have all been revised and expanded, and though, perhaps, I shall regard them as already out of date by the time they appear, they certainly express the opinions I held when the last proofs were corrected.

I should like to take this opportunity of saying how much I am indebted to the large number of friends who have worked with me whilst the questions discussed in these essays and addresses were being investigated. The majority of them are referred to by name in the various papers, but I wish to record again my thanks to my colleagues and assistants at Guy's Hospital and New Lodge Clinic during

the last three years, and especially to J. F. Venables, J. A. Ryle, F. A. Knott, P. J. Briggs, J. J. Conybeare, J. H. Ryffel, R. D. Roberts, T. Turner, R. D. Passey, J. R. Bell, A. C. Hampson and J. W. Shackle. I am also indebted to the Editors of the *British Medical Journal*, *Lancet*, *Quarterly Journal of Medicine*, *British Journal of Surgery*, and *Practitioner*, for permission to reprint papers originally published by them and for the use of some of the illustrations. Mr. C. J. S. Thompson, Curator of the Wellcome Historical Museum, has kindly provided me with a photograph of the old print from which the illustration of the ibis in the act of giving itself an enema is reproduced.

ARTHUR F. HURST.

NEW LODGE CLINIC, WINDSOR FOREST,
June, 1924.

CONTENTS

PAGE

Diagnosis of the Nervous Disorders of the Stomach and Intestines 1

Gastric Diatheses :

(i.) The Hypersthenic Gastric Diathesis . . 19

(ii.) Achlorhydria and its Relation to other Diseases. 42

Addison's (Pernicious) Anæmia and Subacute Combined Degeneration of the Spinal Cord . . 53

Achalasia :

(i.) Achalasia of the Cardia (so-called Idiopathic Dilatation of the Œsophagus or Cardiospasm) 110

(ii.) Pelvi-rectal and Anal Achalasia (Hirschsprung's Disease ; so-called Congenital Idiopathic Dilatation of the Colon) 123

The Sins and Sorrows of the Colon . . . 135

Ulcerative Colitis 150

Chronic Appendicitis and Appendicular Dyspepsia . 169

Cholecystitis and Gall-stones in the Light of Recent Research 186

Asthma 217

The Hysterical Element in Organic Disease and Injury of the Central Nervous System . . 235

Contractures—Localised Tetanus, a Reflex Disorder, or Hysteria 262

Index 301

DIAGNOSIS OF THE NERVOUS DISORDERS OF THE STOMACH AND INTESTINES.*

No more appropriate subject than the diagnosis of the nervous disorders of digestion could have been chosen for discussion at this meeting of the British Medical Association. For it was here in Cambridge that Gaskell did his pioneer work on the autonomic nervous system, and it is here that Langley has for so many years carried out his remarkable investigations, which have added such a wealth of detail to the foundations which had been so truly laid. And one of the earliest clinical contributions to the subject came from the pen of our revered President, Sir Clifford Allbutt, the Regius Professor of Physic in the University of Cambridge, who, in 1884, chose " Visceral Neuroses " as the subject of his Goulstonian Lectures.

For a discussion on such a wide subject as the diagnosis of the nervous disorders of the stomach and intestines to be profitable it is essential to keep to facts. Much of the traditional teaching dates from a time when knowledge of the physiology and anatomy of the stomach and intestines was very rudimentary, and clinical methods of examination were much less accurate than they are now ; but it has kept its place in text-books of medicine in spite of the failure of modern research to confirm it.

An attempt must first be made to gain a clear conception of what is meant by certain terms, such as functional, neurosis, psychoneurosis, neurasthenia, and hysteria. A functional disorder is one which does not depend upon organic change ; it may be either biochemical or nervous in origin. Functional disorders of nervous origin, the only ones with which we are concerned to-day, are of two kinds—the

* The opening paper read in the Section of Medicine at the annual meeting of the British Medical Association, Cambridge, June 30th, 1920. (Reprinted from the *British Medical Journal*, October 2nd, 1920.)

neuroses, which are independent of mental processes, whether conscious or subconscious, and the psychoneuroses, which have a psychical cause. This distinction is of fundamental importance, as the psychoneuroses alone are amenable to psychotherapy.

Neurasthenia has generally been classified as a neurosis. But it really depends upon definite, though evanescent, organic changes in the central nervous system and in the suprarenal and possibly other endocrine glands, which result from mental and physical exhaustion and chronic intoxications. It is therefore an organic and not a functional disorder. As, however, the somewhat ill-defined condition, which has in the past been known as nervous dyspepsia, has been regarded as often, if not always, caused by neurasthenia, the relation of neurasthenia to the nervous disorders of digestion requires discussion.

The psychoneuroses can be broadly classified under the headings of hysteria and psychasthenia. Before the war I should have classed the tics separately, but I am now convinced that they are really hysterical. By hysteria I mean a condition in which symptoms are present, which have been produced by suggestion and are curable by psychotherapy. During the war my fellow workers and I gathered together a great deal of evidence, which appeared in the "Seale Hayne Neurological Studies," to show that in the absence of gross hysterical manifestations there is no underlying condition to which the name of hysteria can be given. We have confirmed Babinski's observations that Charcot's physical stigmata are invariably a result of suggestion on the part of the observer, and, what is more important, we are firmly convinced that although certain psychological conditions, such as an abnormal degree of suggestibility, predispose to hysteria, they are not essential parts of it, and that hysteria may occur in individuals with a perfectly normal mental make-up. When this is once realised, it becomes clear that absence of the mental characteristics, which lead to an individual being labelled as neurotic, does not in any way exclude the possibility of the digestive or other disorder from which he is suffering from being hysterical, any more than it can be assumed that symptoms in a neurotic girl

are not due to organic disease. It follows that a diagnosis can only be made from the nature of the symptoms and the results of physical and laboratory methods of examination.

I. Nervous Disorders of the Stomach

Nervous Dyspepsia. Atonic Dilatation of the Stomach. Hyperchlorhydria and Hypochlorhydria

The traditional description of the nervous disorders of digestion depended upon false ideas of physiology and anatomy. It was, for example, assumed that a certain degree of tone and a certain activity of peristalsis were normal, and that a normal stomach secreted juice of a certain strength. Any divergence from these standards, which were as a matter of fact often very vague, was regarded as evidence of disordered function. Such a condition as atonic dyspepsia, due to atonic dilatation of the stomach caused by deficient tone associated with deficient peristalsis and secretion, and acid dyspepsia due to hypersecretion were described, whilst the more scientific writers talked of hypochlorhydria and hyperchlorhydria as clinical entities. In addition to the motor and secretory neuroses, a sensory neurosis was recognised, in which indigestion was supposed to result from hyperæsthesia of the gastric mucous membrane. But my own investigations, which have been confirmed by numerous radiographers both in England and abroad, and the recent chemical investigations by fractional test meals, carried out by Reyfuss and Crohn in America and Ryle and Bennett at Guy's Hospital, have shown that such great variations occur in the muscular tone, peristalsis and secretory activity of the stomach in normal individuals that it may well be doubted whether what is generally regarded as atonic dilatation, hyperchlorhydria, and hypochlorhydria do not really fall within the normal limits. This being true when the diagnosis is supported by an x-ray examination and gastric analysis, what can one say of the cases in which the diagnosis is made in their absence ? I have seen so many doctors, who believed that they had atonic dilatation of the stomach but were found with the x-rays to have hypertonic stomachs, and I have seen so

many cases, in which the symptoms pointed to hyperchlorhydria but achylia was actually present, that I am quite certain that it is utterly impossible to form a reliable estimate of the muscular or secretory activity of the stomach from a consideration of the symptoms alone. The investigations I carried out with several Guy's students some years ago proved, moreover, that the theory of gastric hyperæsthesia has no basis in fact, as the mucous membrane of the stomach both in health and disease is entirely insensitive to tactile, thermal and painful stimuli and to hydrochloric acid up to the maximum strength in which it could conceivably be present in the gastric juice.

The discovery of variations from the average normal tone, peristalsis and secretion in individuals with digestive symptoms is therefore no evidence that these variations are in any way responsible for the symptoms. The atonic dilatation and hyposecretion, which are supposed to be the cause of the dyspepsia of the exhausted neurasthenic, exist as a rule only in the imagination, as there is not the smallest evidence to show that true neurasthenia in any way affects the motor or secretory functions of the stomach. I can well believe that an exhausted individual, who happens to have a stomach, the tone, peristalsis and secretion of which are below the average, will be more likely to suffer from indigestion than a man with an average normal stomach. His condition may be correctly described as neurasthenic dyspepsia, and he may benefit from treatment directed to increase the motor and secretory activity of his stomach, but it must be remembered that the neurasthenia is not the cause of the deficient tone and secretion, and that in the absence of the neurasthenia there would be no digestive symptoms, although the deficient tone and secretion would still be present. Exhaustion may be the exciting cause of a different group of gastric symptoms in a man whose stomach is of the hypertonic, hypersecretory type, and these symptoms may be the herald of an attack of duodenal ulceration. But the hypertonus and hyperchlorhydria are congenital and not caused by the exhaustion or by the duodenal ulcer which may ultimately develop ; they simply predispose to a certain form of indigestion—the acid dyspepsia or hyper-

chlorhydria of the text-books, which occurs as a result of various conditions, one of which is exhaustion.

It is clear from what I have said that there is little justification for retaining such terms as atonic dilatation of the stomach, hyperchlorhydria, hypochlorhydria, atonic and acid dyspepsia as descriptions of clinical conditions. But we can separate two varieties of neurasthenic dyspepsia, which can only be recognised with certainty with the aid of the x-rays and gastric analysis,—the asthenic, occurring in an individual with a stomach with less than the average tone and secretion, and the hypersthenic, occurring in one with a stomach with more than the average tone and secretion.

Hysterical Vomiting

Hysterical vomiting has long been recognised, but the old view of the nature of hysteria led to the belief that it was a comparatively rare condition, which only occurred in neurotic females who showed the so-called hysterical stigmata. I had begun to realise already before the war that this was too narrow a conception, but it was not until I saw the large numbers of otherwise healthy soldiers suffering from this condition that I realised how common it really was, and my experience during this last year has fully confirmed my expectation that it would prove equally common in civil practice. Hysterical symptoms result from suggestion : the suggestion which gives rise to hysterical vomiting is vomiting. Whether this is emotional in origin or due to gastric irritation, reflex action or toxæmia, auto-suggestion leads to its aggravation whilst the primary cause is still present or to its perpetuation after the latter has disappeared. To the auto-suggestion is almost invariably added the hetero-suggestion involved in treatment by dieting, drugs and other measures, which have been continued longer than necessary owing to want of recognition of the hysterical element in the case. Hundreds of gassed soldiers continued to vomit after the gastritis caused by the swallowing of irritant gas dissolved in the saliva had completely disappeared. We ultimately came to the conclusion, summarised by Captain W. R. Reynell in the " Seale Hayne

Neurological Studies," that whenever vomiting persisted for more than a month after gassing it was certainly hysterical. In the same way vomiting caused by acute indigestion from food poisoning or food excess may continue after the irritant has been expelled from the stomach, and the persistent vomiting of young women, which was formerly regarded as due to gastric ulcer and more recently to chlorosis, is most frequently of this nature. The reflex vomiting of phthisis and chronic appendicitis are often greatly exaggerated by the addition of an hysterical element, and when vomiting persists after the removal of a chronically inflamed appendix, the condition is generally hysterical and not the result of hypothetical adhesions. During the past year I have seen three young women with hysterical vomiting, in whom the organic basis was found with the x-rays to be chronic partial obstruction of the duodenum by the superior mesenteric vessels ; in these cases also relief of the underlying condition by duodeno-jejunostomy does not always cure the vomiting. An individual, who has once been seasick and on his next trip across the channel lies down in the saloon with a basin by his side directly he gets on board, will certainly succumb to the mass suggestion afforded by his vomiting neighbours as soon as the ship sails. I knew an old lady who invariably vomited in the train from London to Dover *en route* for the Continent but on no other railway journey, and I am told that the inhabitants of a certain small island much visited by tourists assemble on the quay to meet the boat from the mainland and always vomit in sympathy with the passengers if the crossing has been rough.

The most important of all forms of hysterical vomiting, which has led to the death of many mothers and of still more unborn infants, is the so-called " pernicious vomiting of pregnancy." I have not yet seen a case in which immediate recovery did not follow psychotherapy. We have proved conclusively that the disturbed metabolism is due to starvation and dehydration and is not an indication of some obscure toxæmia.

I was recently asked to see a woman in the fourth month of pregnancy, who since the third week had been unable to retain even fluids. She was extremely emaciated, her tongue was

dark and dry, and her pulse rate was 160. Large quantities of diacetic acid were present in her urine, and the ammonia index, which measures the degree of acid intoxication, had risen from the average normal of 5 to 28, although 10 is the limit generally regarded as an urgent indication for emptying the uterus. I was convinced from past experience that the condition would prove to be hysterical, although arrangements had already been made to terminate the pregnancy. On cross-questioning her, I discovered that when she began to vomit her father had said to her, " You will have a bad time of it, as your mother was sick all the time she was carrying you." I explained to her how this remark had acted as a suggestion, and how she would be able to retain ordinary food directly she was given it, as she would eat it with enjoyment instead of drinking milk, which she disliked, as a matter of duty. She accepted this explanation at once, and when I returned later in the afternoon she was eager to put it to the test by having some tea and buttered toast. She took this in my presence and kept it down without difficulty. She had more solid food for supper, and next day she had a good breakfast and steak for dinner. She had vomited a little in the early morning, but with this exception she remained perfectly well. She took an ordinary diet and gained 16 lb. in weight in four weeks ; the ammonia index rapidly fell to the normal for pregnant women, and diacetic acid disappeared from the urine. There was a slight return of vomiting in the morning during the third week, but this was quickly controlled by further psychotherapy, and a healthy infant was born at full term.

The diagnosis in cases of this kind is easy, as in the absence of obvious organic disease such as appendicitis, vomiting, which begins early in pregnancy and does not cease in the usual way at the end of six or eight weeks, is always hysterical.

It should be remembered that severe pyloric obstruction is the only purely gastric disease which causes persistent vomiting. If this can be excluded, and if there is no fever, no headache, and nothing pointing to organic disease elsewhere in the abdomen, the vomiting is probably hysterical.

Flatulent Dyspepsia and Aerophagy

We are, I think, too often ready to accept a patient's own diagnosis. He says he is suffering from flatulence, and we treat him with diet and antiseptic drugs for "flatulent dyspepsia." But when we look more closely into the matter, we find that the condition is almost invariably a psychoneurosis and can be rapidly cured by psychotherapy, although there may be a small organic basis requiring other treatment.

A patient with so-called flatulent dyspepsia complains of a feeling of fullness in the upper part of the abdomen, which he at once assumes is due to flatulence, by which he means an accumulation of gas, and which he probably assumes is a result of fermentation. But careful investigation has shown that fermentation very rarely occurs in the stomach, which empties itself too rapidly and secretes a juice which is too acid for any appreciable amount of bacterial activity to occur. Only in cancer of the pylorus, in which gastric stasis and deficient acidity are present together, can severe flatulence be really due to fermentation. In the absence of the characteristic symptoms suggesting this condition, which would call for further investigation with the stomach-tube and x-rays, a complaint of flatulence can be assumed at once to be due to something else than fermentation.

Aerophagy is the only common cause of flatulence. The patient feels some slight discomfort in his stomach, which he thinks is due to wind, and which he hopes he will be able to "disperse" by eructation; as there is really no excess of gas present, the attempt proves unsuccessful, but results in the swallowing of air. After half a dozen or more attempts have been made without success, air being swallowed on each occasion, the stomach becomes so distended that an attempt is at last successful. Aerophagy is a psychoneurosis. In severe cases it persists long after the primary gastric discomfort has disappeared. It may then be regarded as a visceral tic, and, like all hysterical symptoms, it can be readily cured by pure psychotherapy.

The gas brought up in aerophagy is odourless and tasteless.

There can be little doubt that aerophagy is present if eructation is frequently repeated, and no doubt at all if it occurs six or more times in rapid succession, as fermentation could not conceivably give rise to such a large quantity of gas. Eructation occurring before breakfast in the absence of pyloric obstruction is always due to aerophagy, as there is nothing in the stomach from which gas could be produced. The diagnosis can be confirmed by means of the x-rays, with which it is easy to watch the whole process of aerophagy (Fig. 1).

Occasionally a patient complains of flatulence, but says

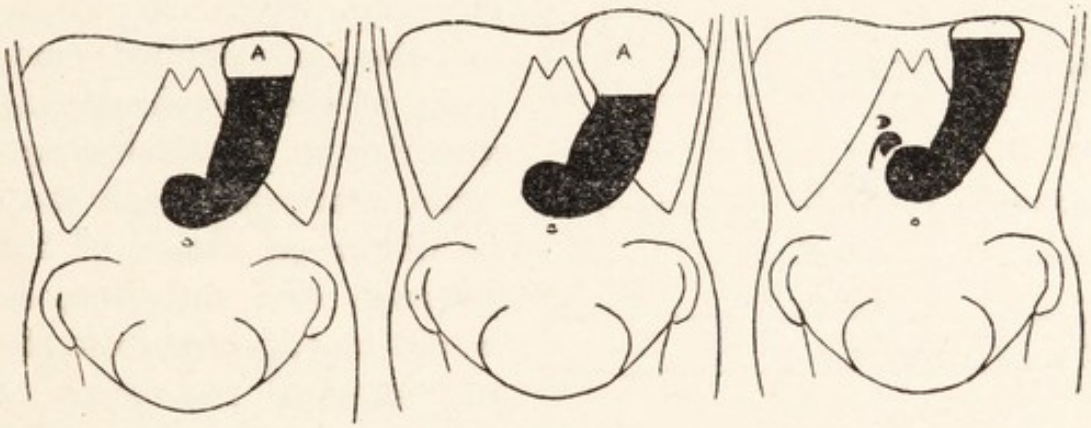


FIG. 1.—Effect of aerophagy.

Hypertonic stomach with closed pylorus and normal quantity of gas (A) in fundus.

Stomach distended with swallowed air (A).

Increased intragastric pressure has resulted in belching of air and forcing of pylorus.
D = duodenum.

that he never brings any wind up, although he is much troubled with abdominal distension. It may at once be concluded that he is suffering from pseudo-flatulence, as if excess of gas is in the stomach it can always be brought up without difficulty. In cases of doubt, the absence of any accumulation of gas can be confirmed with the x-rays. Pseudo-flatulence may be caused by spasm of the diaphragm ; a sensation of great distension is suddenly experienced, and the abdomen becomes so enlarged that the clothes have to be loosened. The distension disappears as suddenly as it came without eructation or passage of flatus ; it also disappears under an anæsthetic and on firmly compressing the whole of the abdomen for some minutes. The x-rays not only

demonstrate the absence of excess of gas in the stomach, but also show the low position of the diaphragm and the absence of respiratory movements. This condition of hysterical spasm of the diaphragm was not uncommon in soldiers, especially after dysentery or colitis.

Psychasthenic Gastric Symptoms

It is now recognised that many cases formerly regarded as neurasthenic are not really suffering from the result of exhaustion, their condition being of psychical origin and more accurately called psychasthenia. Though the chief symptoms are psychical, the uncontrolled emotions of the psychasthenic give rise to physical symptoms, amongst which may be disturbed action of the stomach and intestine, as would be expected from the physiological researches of Pavlov and Cannon, which have recently been extended by the observations on normal men at Guy's Hospital by Bennett and Venables, who demonstrated the effect of various emotions suggested during hypnosis on the curve of gastric acidity (Fig. 2).

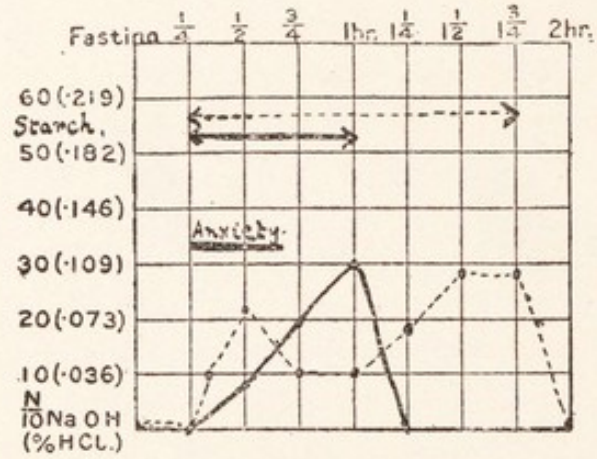


FIG. 2.—Effect of hypnotic suggestion of danger on the emptying rate and secretion of free hydrochloric acid.

Continuous line = normal curve; broken line = experimental curve.

After an initial rise, perhaps due to suprarenal stimulation, secretion is seen to be inhibited and evacuation is delayed (T. I. Bennett and J. F. Venables).

The most common psychasthenic gastric symptoms are a vague feeling of uneasiness or sinking in the epigastrium, anorexia and nausea; occasionally hysterical vomiting occurs as a complication. These physical symptoms may be a source of much distress to the patient, and not infrequently he consults a doctor about them without mentioning his more important mental symptoms unless pressed to do so. It is consequently of the greatest importance to get the patient's confidence and to learn every detail of his history—what worries he has, how he sleeps, whether he has night-

mares, and whether he has any phobias or obsessions. If the symptoms do not correspond with any organic disease and no physical signs of disease are found on ordinary examination, and if the mental symptoms of psychasthenia are present, the digestive symptoms can generally be assumed to have the same origin, and no good can be done by further concentrating the patient's attention on his abdomen by test meals or x-ray examinations, although there is no doubt that the depressing emotions which are the cause of the symptoms inhibit to some extent both the secretory and motor functions of the stomach.

The only treatment required is psychotherapy ; diet and drugs are useless, as the physical symptoms are merely the expression of a psychical disorder, which cannot be cured except by psychical means.

II. Nervous Disorders of the Intestine

Constipation

It is comparatively rare for a patient to consult a doctor on account of constipation without having already attempted to cure himself with aperients. But no accurate diagnosis can be made until it has been ascertained whether the patient is really constipated at all. In my experience the symptoms generally ascribed to auto-intoxication caused by intestinal stasis are in most cases really produced by purgatives. They lead to the absorption of excess of toxic material, partly by hastening the half-digested contents of the small intestine into the cæcum, where fermentation and putrefaction are consequently increased, and partly by causing the contents of the transverse, descending and pelvic colon to be fluid instead of solid, so that absorption of toxins takes place throughout the length of the bowel instead of in the cæcum and ascending colon alone.

In spite of his probable protests the patient should be instructed to see what happens if no drugs are taken for a week, an effort being made to open the bowels each morning. In most cases he quickly loses his abdominal pain and his so-called toxic symptoms. The bowels are often opened daily, in which case a diagnosis of *hysterical pseudo-constipa-*

tion can be made—hysterical because the patient had suggested to himself as a result of faulty education combined with the reading of pernicious advertisements that he was constipated and required aperients to keep himself well, whereas a little psychotherapy, in the form of explanation of the physiology of his bowels and the origin of his symptoms and persuasion to try to open his bowels each morning without artificial help, results in a cure. In many cases, however, the patient does not succeed in opening his bowels, although he may feel more comfortable than when he was taking drugs. A further abdominal and rectal examination should now be made. If no sign of organic disease is present, and if, as is generally the case, no accumulation is felt in the abdomen, the rectum will be found to be filled with fæces, which are in some cases stony hard, but in others quite soft, proving that there is no delay in the passage through the intestines. In spite of this the patient has no desire to open his bowels, although a normal individual would feel an urgent call to defæcation under such conditions. In 1908 I first described this condition of inefficient defæcation and called it dyschezia, to distinguish it from true intestinal stasis, in which there is delay in the colon.

The majority of cases of dyschezia, which is the commonest form of severe constipation, are of nervous origin. They are caused by neglect to respond to the call to defæcate owing to laziness, insanitary conditions of the w.c., or false modesty. The rectum gradually dilates, so that an increasing quantity of fæces is needed to produce the adequate internal pressure required to give the sensation of fullness, which is the natural call to defæcation, and finally the sensation is lost completely. But the patient is still capable of emptying his rectum if he tries. He has, however, so convinced himself that he cannot get his bowels open unless he takes enemata, or such enormous doses of aperients that the fluid fæces practically act as enemata, that he finally suggests to himself that his rectum is powerless to act by itself, true hysterical dyschezia being thus produced. In many cases no treatment is required beyond explaining to the patient the nature and cause of his condition and persuading him to make an effort to empty his rectum, which he must realise

is really quite capable of doing its work, but occasionally it is also necessary to re-educate his rectum with graduated enemata.

In severe cases it is advisable to examine the intestinal functions with the x-rays, a barium meal being given after the patient has discontinued taking his aperients. The time table I gave twelve years ago for the passage of food along the alimentary canal was nothing more than the average taken from numerous records obtained with the x-rays, but it has unfortunately often been regarded as representing the normal standard, the slightest variations from which indicate the presence of intestinal stasis. The fallacy of this has often been pointed out, as the normal limits are very wide, but I still frequently see patients who have been advised to submit themselves to colectomy or other drastic treatment as a result of an x-ray examination which showed a somewhat slow passage, which was, however, well within the normal. It is therefore necessary once again to describe briefly what evidence is required in order to diagnose stasis in different parts of the intestinal tract.

Ileal stasis should only be diagnosed if no trace of barium has reached the cæcum six hours after the opaque meal, or if a considerable quantity of barium-containing chyme is still in the end of the ileum nine hours after the meal, if the stomach is known to have emptied itself in three hours. If most of the barium is still in the cæcum and ascending colon at the end of twenty-four hours, they are the seat of stasis, even if a little has passed to the more distant parts of the colon, but a faint shadow of the cæcum is often visible in normal individuals even three days after the meal. If the splenic flexure is reached in twenty-four hours, and the greater part of the barium is in the transverse colon at the end of forty-eight hours, there must be stasis in the transverse colon. Lastly, if at the end of twenty-four hours the greater part of the barium has collected in the pelvic colon or rectum or both, and in spite of this no desire to open the bowels is felt, dyschezia can be diagnosed.

Apart from dyschezia the only common form of constipation of nervous origin is that resulting from anorexia. Anorexia is a common symptom of both neurasthenia and

psychasthenia, and the deficient stimulation of the intestine which it causes generally leads to a slow passage through the whole colon. Intestinal activity is also likely to be inhibited by depressing emotions in psychasthenia. There is, however, no evidence to show that the nerve exhaustion of neurasthenia has any influence on the bowels. I am convinced that no such thing as atonic constipation exists, for tone and peristalsis are independent functions ; and whereas deficient peristalsis is a common cause of constipation, the x-rays have proved that atony of the colon is a rare condition, generally organic in origin, and not necessarily associated with any disturbance in peristalsis.

Intestinal Hypochondriasis

When a patient himself complains of auto-intoxication and intestinal stasis, gravely discusses the question of kinks and adhesions, and produces a diary in which every stool he passes is minutely described, the diagnosis of intestinal hypochondriasis is obvious. The medical profession is, I fear, largely responsible for this common nervous disorder, as these terms are employed too thoughtlessly, for the conditions they refer to are all rare and can only be diagnosed after a most thorough investigation. If this proves negative, the patient must be taught that his auto-intoxication is a result of drugging, that intestinal stasis in moderation is a virtue, as it promotes digestion and absorption of his food, and that we all have kinks and adhesions, and so long as they remain in the abdomen and do not get on the brain they do not really matter. No man knoweth his own bowels ; what is a good action for one is a poor thing for another, and the sufficiency of a stool should be judged by the comfort felt after it has been passed and not by its size, its shape or its consistence. He alone is happy and devoid of that most trying of the nervous disorders of the bowel—hypochondriasis—who follows Sir James Goodhart's admirable advice, to do as the dogs do and never look behind him.

Nervous Diarrhœa

When a patient complains of frequent actions of the bowels, his stools must be examined before a diagnosis of

diarrhœa can be made. What is called diarrhœa by the patient is often the frequent passage of small scybala, and the most common cause of this is dyschezia, the condition being due to rectal retention with overflow. The passage of a little mucus with hard lumps of fæces is of no importance, as mucus is the natural lubricant of the bowel and is secreted whenever hard fæces are retained in the rectum or pelvic colon. But if mucus or blood is present with soft or liquid stools, colitis, either primary or secondary to a growth, can be diagnosed with certainty. When, however, in a case of chronic diarrhœa, neither mucus nor blood is present, and achlorhydria and the toxæmia of Graves's disease can be excluded, the possibility of a nervous origin requires consideration.

The colon is not in constant activity like the stomach and small intestine, and its movements are very rarely seen during an x-ray examination. Its whole motor activity is confined to a small number of powerful peristaltic waves each day, which travel along the greater part of its length. In 1913 I found, with Alan Newton, that this " mass peristalsis " very rarely occurs except as a result of the gastro-colic reflex excited by taking food into the stomach. It is exaggerated in certain individuals to such an extent that, in addition to passing a solid stool on getting up in the morning, they have diarrhœa after breakfast and also after their other meals. This nervous diarrhœa is a pure neurosis, but not a psychoneurosis, and can only be overcome by the regular use of minute doses of drugs which have the power of damping down the reflex. In most cases, however, it becomes exaggerated owing to the patient's absorption in his fear that he will have diarrhœa at inconvenient moments. A dinner party becomes an impossibility for him, and he gradually becomes more and more of a recluse. At this stage psychotherapy is required to overcome the psychical element which has developed on the top of the neurosis.

The bowels seem to be so little under voluntary control that I doubted for a time whether nervous diarrhœa could ever be regarded as hysterical. But Captain C. H. Ripman had a soldier under his care at Seale Hayne Hospital with severe nervous diarrhœa of nearly two years' duration, which

he cured at a single sitting by direct suggestion under hypnosis. As there was no doubt about its origin as a result of suggestion, it fulfilled the conditions required for a diagnosis of hysteria, having been caused by suggestion and cured by psychotherapy.

But a diagnosis of hysterical diarrhœa is not enough. The ultimate object of diagnosis is to gain a basis for rational treatment. It is therefore necessary in each case to discover what is the nature of the suggestion which has caused the diarrhœa. Careful cross-examination will generally reveal some definite cause. In most cases the original attack of diarrhœa was emotional in origin, over-activity of the bowel being one of the rarer of the many physical symptoms of emotion. When diarrhœa has once resulted from an emotion, any repetition of the emotion, even in a much slighter or modified form, or anything reminding the patient either consciously or subconsciously of the event which gave rise to the emotion, is likely to suggest a recurrence of the diarrhœa. This pure psychoneurosis may also occur as a complication of the exaggerated gastro-colic reflex I have already described, the bowels becoming so much a plaything of the patient's emotions that any important engagement, and not merely engagements for meals, and finally excitement of any kind, will lead to diarrhœa.

Muco-membranous Colic

Muco-membranous colic is a condition, in which constipation is associated with the constant or intermittent passage of membranes of coagulated mucus and with attacks of pain. I do not speak of mucous colitis, for there is no colitis without mucus, nor of muco-membranous colitis, because this condition is nervous and not inflammatory in origin ; these expressions should therefore be discarded. The accumulation of hard fæces in the colon of individuals with an irritable nervous system may lead to reflex spasm of the intestinal muscles and reflex secretion of mucus. The latter remains so long in contact with the mucous membrane before it passes on that it has time to be coagulated and form thin membranes, which are passed either with the stools or separately.

But it is not sufficient to find these membranes in the stools of a constipated patient to diagnose muco-membranous colic, as they may also be passed in certain organic diseases, the most common of which is a growth of the pelvic colon. A careful investigation of the abdomen is therefore necessary, and this should include a sigmoidoscopic examination, as many cases of cancer of the pelvic colon can be diagnosed in no other way. If no growth is discovered, the mucous membrane is generally found to be perfectly healthy in appearance ; there is no colitis present at all beyond the slight catarrh caused by the irritation of retained fæces, and corresponding with this the membranous shreds of mucus are found microscopically to contain few, if any, leucocytes. When, therefore, muco-membranous colic is not associated with organic disease, it may be regarded as a neurosis, and as it is most likely to occur in exhausted individuals, whose nervous system has become abnormally irritable, treatment is required for the exhaustion and for the constipation. Unfortunately there is a great tendency for the neurosis to develop into a psychoneurosis, and here again we are, I fear, ourselves largely to blame. So long as the patient does not know she is passing mucus she is comparatively well, but when she once knows, and still more when a course of Plombières treatment has made her a connoisseur in fæces, a mental element is added, which it is often difficult to remove. I know of few sadder spectacles than the bedridden young woman, the only child of a widow whose life is devoted to keeping up her daughter's reputation as an intestinal martyr. But get her away from her parent, her purges and her Plombières, and she will soon be free from her psychoneurosis ; the muco-membranous colic, the pure neurosis, may still be present, though it requires but little treatment beyond wholesome neglect.

In these introductory remarks I have endeavoured to describe how the more important nervous disorders of the stomach and intestine can be recognised. At the same time I have shown how much would be gained by boldly discarding the traditional teaching in so far as it was founded on theory and not on facts. This discussion will, I think, be most fruitful in results, if it leads to a satisfactory classifica-

tion of gastric and intestinal neuroses based on observed facts, as this alone will give us the data required to diagnose when a disorder of digestion is nervous in origin, what is the nature of the underlying nervous condition, and to what disturbances in function it has given rise.

GASTRIC DIATHESES.*

Two Lectures

Delivered at the Hôpital Saint Michel, Paris, in October, 1922.

I. THE HYPERSTHENIC GASTRIC DIATHESIS

AND THE PATHOLOGY, PROPHYLAXIS, AND TREATMENT OF DUODENAL ULCER

THE doctrine of diatheses, never as popular in England as in France, has during the last quarter of a century come to be regarded with increasing disfavour in both countries as a result of the progress of scientific medicine. Professor Chauffard has, however, shown how well a modernised conception of diatheses may fit in with the results of the most recent bio-chemical research in connection with the pathology of gall-stones, a subject which he has made so peculiarly his own. He writes : " L'hérédité ne peut être qu'une transmission de terrain, d'aptitudes nutritives ou réactionelles, . . . qu'il fait que chacun de nous apporte et conserve sa *personnalité humorale.*"

A similar conception of diatheses may, I believe, be applied to certain other diseases, and I wish to-day to show how it throws a new light on the pathology of duodenal ulcer, and thereby opens out new hope for the prophylaxis and successful treatment of this condition, when once the presence of the underlying diathesis has been recognised.

Here in Paris it is with special pleasure that I approach the subject of ulcer. I have gained more knowledge about the disorders of digestion from surgeons than from physicians, as my visits to Moynihan in Leeds and to the Mayos in America and my association in London with my surgical

* Reprinted from the *Lancet*, 1922, ii., 1369 ; 1923, i., 111. The original lectures in French were published respectively in the *Journ. de Méd. de Paris*, xli., 840, 1922, and the *Arch. des Mal. de l'Appareil Digestif*, xiii., 747, 1923.

colleagues have shown me how many lessons may be learnt by the study of the "pathology of the living," as revealed during operations performed on carefully investigated cases. But there is one exception; for I look back upon the three months, fifteen years ago, when I had the privilege of attending the clinic of Albert Mathieu, as the finest introduction to gastro-enterology that any young physician could wish to have. From that time I read everything which emanated from Mathieu's pen with the greatest care, and perhaps in no direction was his teaching of more value than in connection with gastric ulcer. His death removed from us one of the Masters of Medicine, a man whose name throughout the world occupies a position in gastro-enterology which ranks with that of Charcot in the annals of neurology.

The Normal Stomach

Fifteen years ago C. J. Morton and I [1] examined a number of healthy medical students with the x-rays after they had eaten some porridge mixed with bismuth oxychloride. We were surprised to find how greatly the shape and position of the stomach varied in different individuals. In the erect position the umbilicus was situated about half-way between the lesser and greater curvature in the majority (Fig. 3); but in some the greater curvature was above and occasionally considerably above the umbilicus (Fig. 4), whilst in others the lesser curvature was below the umbilicus (Fig. 5). The high position of the greater curvature in the former group appeared to be due to hypertonus, as the upper level of the gastric contents was also unusually high; its low position in the latter group was due to hypotonus. In most cases peristalsis was more active and the evacuation of the stomach more rapid in the hypertonic stomach than in the average one, and still more so than in the hypotonic one. In spite of this none of the individuals examined complained of any digestive symptoms, so that both the hypertonic and hypotonic stomach could be regarded as normal variations from the average type found in the majority of healthy men.

These results have recently been confirmed by the much more extensive observations of Moody, Van Nuys and

Chamberlain,[1a] who examined 600 healthy young adults, men and women being in equal numbers. They found that the average position of the greater curvature when standing is 2·5 cm. and 4·5 cm. below the interiliac line in men and women respectively. What may be called a hyper-

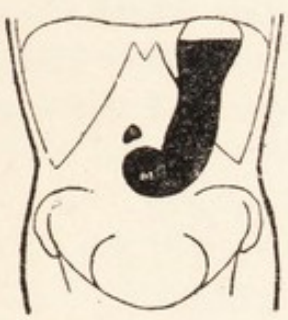


FIG. 3.—Average normal stomach.

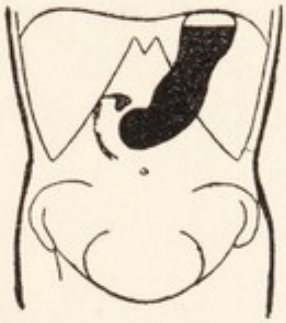


FIG. 4.—Hypertonic stomach in healthy man without symptoms.

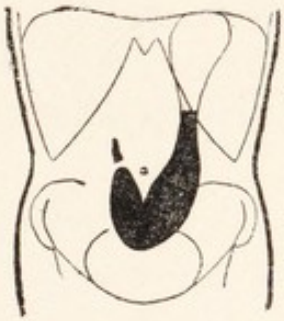


FIG. 5.—Hypotonic stomach in athletic young man without symptoms.

tonic stomach was found in 17 per cent. of men and 7 per cent. of women; a hypotonic stomach was found in 3·6 per cent. of men and 15 per cent. of women. The position and tone of the stomach did not in any way depend upon the muscular development of the individual.

Employing the fractional test-meal devised by Rehfuss [2]

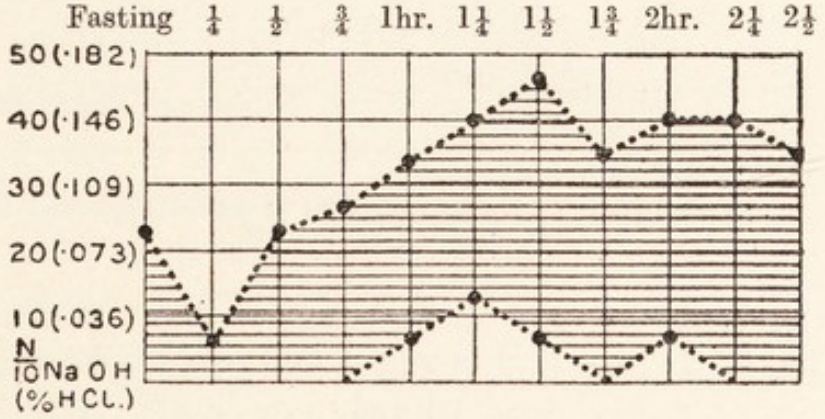


FIG. 6.—The shaded area represents the limits of free HCl in 80 per cent. of 100 healthy students (Bennett and Ryle).

of Chicago in 1914, J. A. Ryle and T. I. Bennett [3] examined a hundred healthy students at Guy's Hospital in order to form a normal standard, with which the results obtained in pathological cases could be compared. The thin tube with metal bulb introduced by Einhorn for obtaining the contents of the duodenum was at first employed, but we now use an

improved form designed by Ryle, which has the advantage of having a rubber instead of a metal bulb. The tube is swallowed by the fasting patient first thing in the morning. All the resting juice is removed, and a meal of gruel is then eaten. Specimens are withdrawn every quarter of an hour until all starch and sugar have disappeared. The total acidity and the free hydrochloric acid of each fraction are estimated and plotted as curves. Fig. 6 shows the extent of the variations in the free acid in 80 per cent. of the hun-

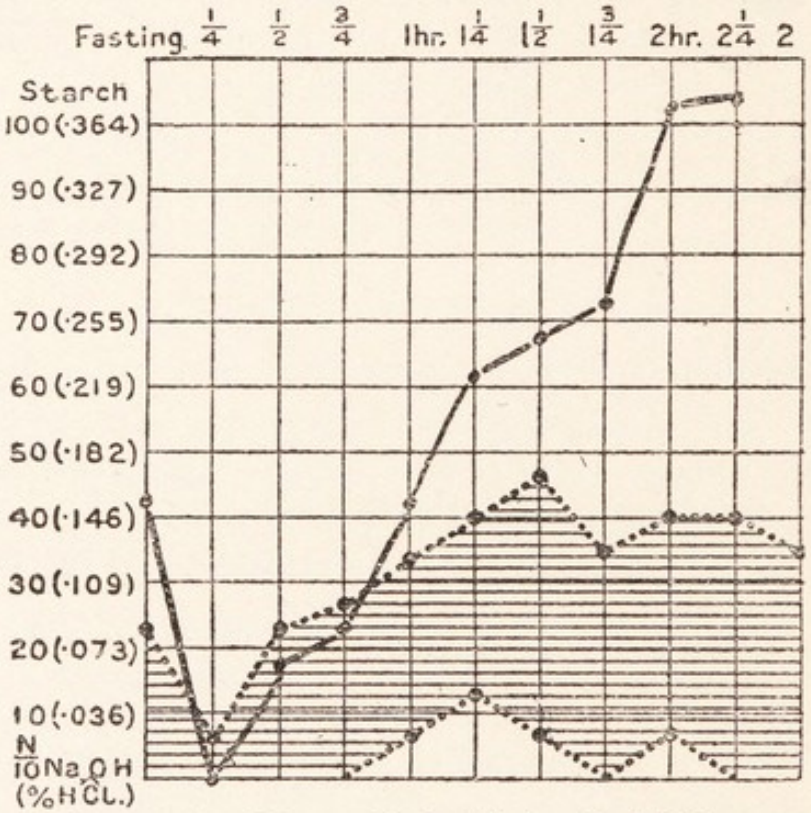


FIG. 7.—Constitutional hyperchlorhydria in a healthy young man. Continuous line, free HCl.

dred normal students. In the remainder it was above or below this, 10 per cent. showing a definite hyperchlorhydria (Fig. 7), and 4 per cent. showing complete achlorhydria, although no digestive symptoms of any kind were or ever had been present.

THE HYPERSTHENIC GASTRIC DIATHESIS.

The recent investigations of Campbell and Conybeare have shown that a large proportion of healthy men with hyperchlorhydria have also hypertonic stomachs. These are the

individuals, who have what I would call the hypersthenic gastric diathesis, an inborn variation from the average normal, which manifests itself in hypertonus of the stomach with active peristalsis and rapid evacuation, and hyperchlorhydria with digestive hypersecretion. This condition is much more common in men than in women, and is often present in several members of the same family. It is compatible with perfect health, and is not associated with any special features in the other functions of the body. Although no doubt caused by an unusual degree of tonic activity of the vagus, it is strictly localised to that part which controls the activities of the stomach, and is not accompanied by a slow pulse or other signs of general vagotonia.

By retaining a Ryle tube in his stomach

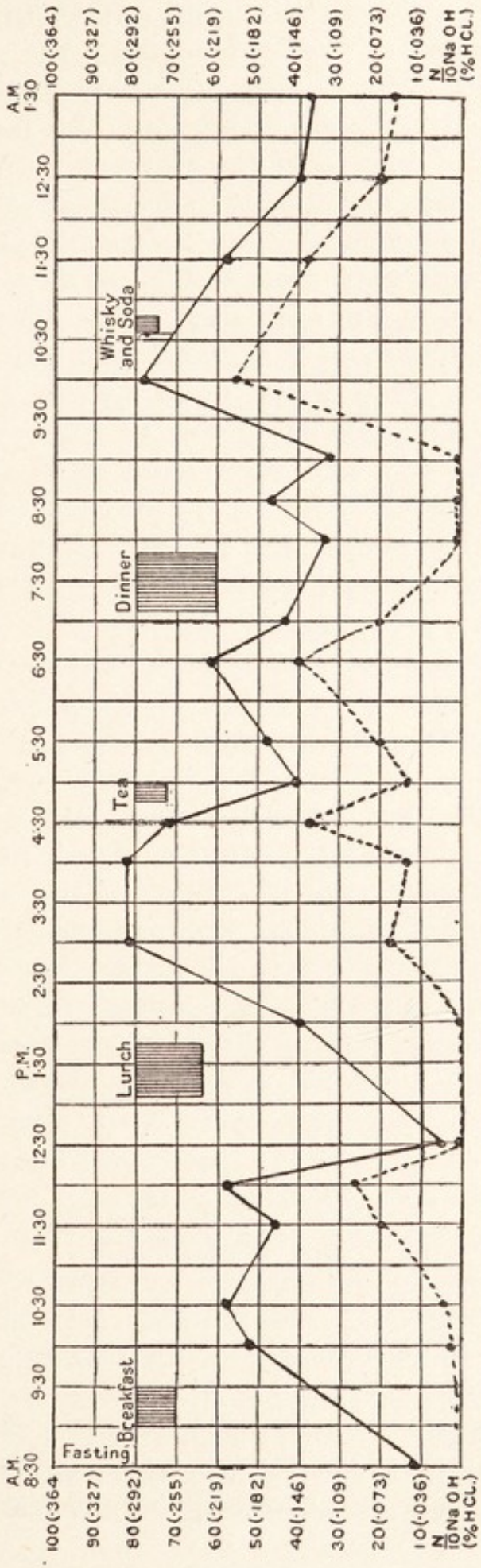


FIG. 8.—Free HCl ·····, and total acidity ——, estimated half-hourly throughout the day whilst ordinary meals were being taken. (Dr. T. I. Bennett.)

from early morning until late at night, Bennett found that it contained food throughout the day, except for a brief period before lunch, when ordinary meals were taken at the ordinary times (Fig. 8). The last traces of the evening meal do not leave the stomach until the early hours of the morning, and if a late supper is taken, food is still present until an hour or two before breakfast. The hypersthenic stomach just described is, on the other hand, empty for several hours each day. If meals are taken, for example, at 8.30 a.m., 1 p.m., and 7.30 p.m., the stomach will be empty from about 11.30 a.m. to 1 p.m., from 5 p.m. to 7.30 p.m., and 11.30 p.m. to 8.30 a.m., a total of five hours in the day and eight hours in the night, in contrast with perhaps an hour in the day and four or five hours in the night in people with the average normal stomach.

So long as food is present in the stomach the quantity of free hydrochloric acid is kept low by the dilution of the gastric juice with the food and drink, and by partial neutralisation with the alkaline salts and proteins of the food. In most people a little gastric juice is continually secreted during the few hours in which the stomach is empty, but Carlson has shown that this is deficient in hydrochloric acid unless a more abundant secretion, rich in acid, is called forth by hunger ; but with meals of the ordinary size taken at the ordinary times it is rare for actual pangs of hunger to occur. In individuals with the hypersthenic gastric diathesis, however, there are several waking hours in which the stomach is empty, and in these the continuous secretion of gastric juice is probably more abundant as well as more acid than in most normal people. Many such individuals are habitually hungry already three hours after meals, and may for this reason form the habit of taking a little food or drink at such times. If they take food, the free acid will be diluted and partially neutralised for a time. If they drink whisky or a cocktail it will be only very slightly diluted, and not neutralised at all, and a further secretion of juice may actually result.

In the absence of food little peristalsis occurs in the stomach unless the individual is hungry. It is clear, therefore, that in the average normal man undiluted gastric juice

rarely enters the duodenum, and when it does its acidity is low, but in people with the hypersthenic gastric diathesis the undiluted juice leaves the stomach for several hours out of each twenty-four, although those who take the precaution of never going for more than about three hours without food considerably reduce the number of these hours. As hyperchlorhydria and hypersecretion, as well as hypertonus and hypermotility, form a part of this diathesis, any undiluted gastric juice which reaches the duodenum is more acid than that which occasionally reaches it—but for a much shorter total duration—in the average individual.

The Essential Predisposing Cause of Duodenal Ulcer

The x-rays have modified our conception of the anatomy of the duodenum. The "duodenal bulb" formed by the first part of the duodenum, and separated from the stomach by a clear area corresponding to the pyloric sphincter, has obviously a quite different function from that of the rest of the duodenum. During an opaque meal taken in the erect position it is always filled and therefore always visible; the rest of the duodenum is only visible for occasional moments after an additional quantity of chyme has been evacuated from the stomach, when some of the contents of the duodenal bulb overflow and are carried by a rapid peristaltic wave into the jejunum, the peristaltic wave appearing to originate not at the pylorus but at the junction of the bulb with the second part of the duodenum. It is a significant fact that duodenal ulcers almost always occur in the bulb and not in the other parts of the duodenum.

The x-rays show that on lying down the duodenal bulb is much less constantly filled than on standing up. Hence, during the few hours of the night in which undiluted gastric juice may sometimes leave the stomach in the average normal individual, there is no tendency for it to accumulate in the duodenal bulb. But in a man with the hypersthenic gastric diathesis there are several hours in every day, during which the mucous membrane of the duodenal bulb is continually in contact with the undiluted and exceptionally acid juice

secreted by his gastric mucous membrane. But even this results in no harm except under certain conditions, so that



FIG. 9.—Hypertonic stomach in case of duodenal ulcer.

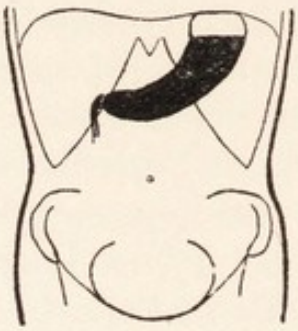


FIG. 11. — Hypertonic stomach in man with duodenal symptoms of one week's duration.

such a man may go through life without ever having the slightest digestive disturbance. The diathesis, however, renders the individual liable under certain conditions to

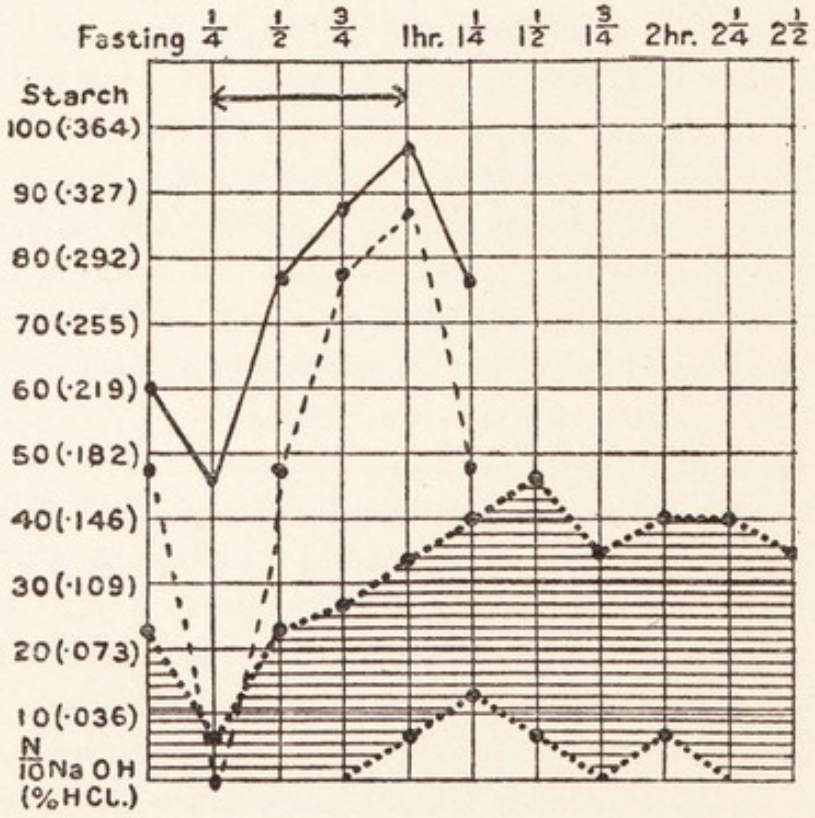


FIG. 10.—Case of duodenal ulcer, showing hyperchlorhydria and rapid evacuation. Continuous line, total acidity; dotted line, free HCl.

develop duodenal ulcer. I believe, moreover, that a duodenal ulcer cannot develop in anybody who has not this

diathesis, which might therefore receive the alternative name of "duodenal diathesis." For in almost every case of duodenal ulcer in which no functional or organic pyloric obstruction has developed the stomach presents these peculiar motor and secretory features, which are quite indistinguishable from those seen in healthy individuals with perfect digestion but with the hypersthenic gastric diathesis. The hypertonus, active peristalsis and rapid evacuation, first recognised by A. E. Barclay [4] as characteristic of duodenal ulcer (Fig. 9), and the hyperchlorhydria and digestive hypersecretion with the characteristic climbing curve (Fig. 10), which the researches of Crohn,[5] Ryle,[6] and others have shown is generally present, are found in just as marked a degree in cases in which

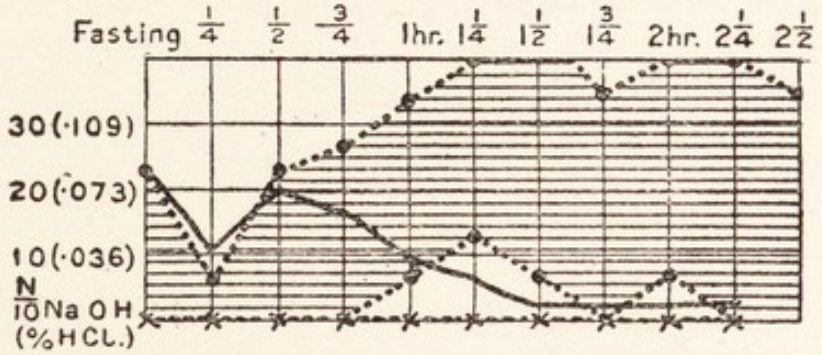


FIG. 12.—Achlorhydria after gastro-enterostomy (J. J. Conybeare). Continuous line, total acidity; dotted line, free HCl.

the symptoms have only been present for a short time as in those in whom it has been present for many years, so long as no secondary pyloric obstruction has developed. One of the most extreme examples of hypertonus I have ever seen (Fig. 11) was in a man who had had very suggestive symptoms of duodenal ulcer for a single week. Moreover, the motor and secretory functions remain unaltered when all symptoms have disappeared for years, and it is certain that no active ulceration is present. Even after a gastro-enterostomy has been performed for a duodenal ulcer, whether pyloric obstruction is present or not, the stomach retains its old characteristics. A gastro-enterostomy leads to more rapid drainage of the stomach, and at the same time ensures the entry of the alkaline contents of the duodenum by the stoma. The result is that the acid gastric contents are more or less completely neutralised unless the secretion of hydrochloric

acid remains excessive. When continuous hypersecretion is secondary, as in cases of pre-pyloric ulcer causing obstruction, the operation results in its disappearance. But when hyperchlorhydria is primary, as in cases of duodenal ulcer, it persists, and the alkaline duodenal contents are insufficient to neutralise the excessively acid gastric juice. Thus, J. J. Conybeare [7] has found that in most cases in which the operation has been performed for conditions other than

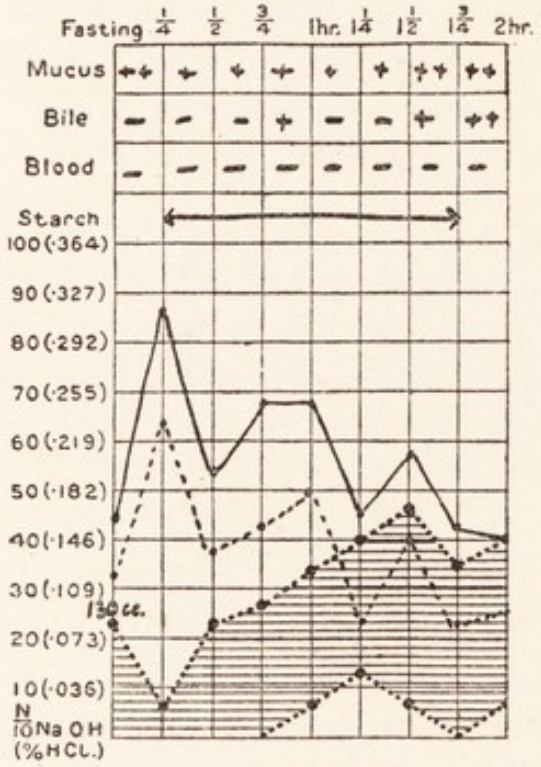


FIG. 13.—Jejunal ulcer two years after gastro-enterostomy for duodenal ulcer: hyperchlorhydria and hypersecretion persisting.

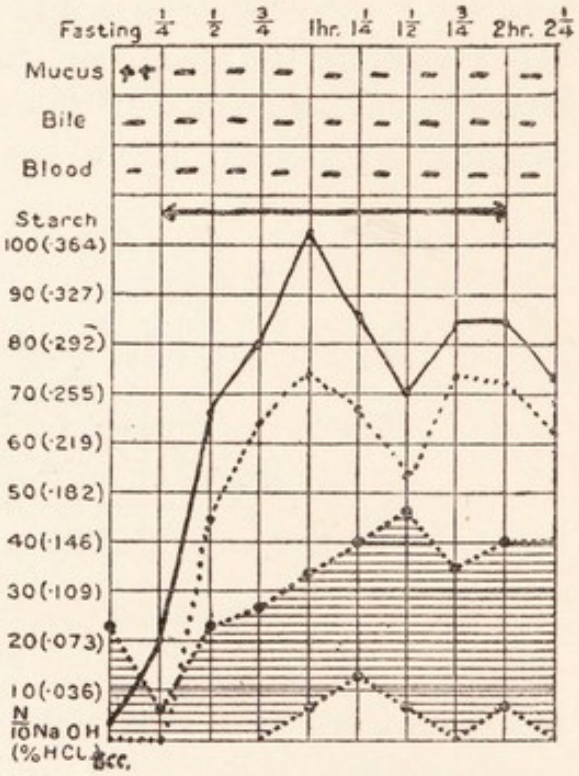


FIG. 14.—Same case as Fig. 13; a year later: hyperchlorhydria persisting after gastro-enterostomy undone, jejunal ulcer excised, and duodenal ulcer healed.

duodenal ulcer, even if extreme hypersecretion was present, there is an almost complete absence of free hydrochloric acid throughout digestion (Fig. 12). But if a duodenal ulcer has been present, free hydrochloric acid is still found, often in considerable excess, though less than before the operation (Fig. 13). When, however, the gastro-enterostomy is undone on account of the development of a jejunal ulcer, the hyperchlorhydria is found to be as high as ever (Fig. 14). This is doubtless the reason why in the large majority of cases in which a jejunal ulcer develops after a gastro-

enterostomy, the operation was performed for a duodenal ulcer.

Gastric and Duodenal Ulcer as Family Diseases

I have seen several cases in which two or more brothers and sisters have suffered from gastric ulcer or from duodenal ulcer, and still more in which brothers and sisters of a patient with a gastric or duodenal ulcer have had symptoms of a similar character, but so much less severe that it seemed doubtful whether actual ulceration was present.[8] In one family the father and two out of nine children were dyspeptic, and four others had typical symptoms of duodenal ulcer, one dying from a perforation (Family B.); in another (Family M.) the mother and all three sons and one grandson had duodenal ulcer.

Family B.

Mother.—No indigestion. Now seventy-five and well.

Father.—Died of chronic Bright's disease at seventy-seven; always dyspeptic and gouty; used to take vast quantities of tr. rhei. co. (neat) and said to have "gouty dyspepsia."

Children :—

1. Male; *dyspeptic;* very atypical.
2. Male; died of perforated *duodenal ulcer* at thirty-five years. Very long and typical history.
3. Female; always *dyspeptic;* not typical duodenal ulcer.
4. Male; typical *duodenal ulcer;* symptoms for years.
5. Male; occasional attacks typical *duodenal ulcer;* pain in winter.
6. Male; very fit; 6 feet in height and proportionately big.
7. Male; typical *duodenal ulcer.*
8. Male; athlete of exceptional power; very fit.
9. Female; no symptoms.

Family M.

Father.—Suffered from attacks of diarrhœa. Died of sudden heart failure at seventy-four.

Mother.—Died at seventy-eight. All her life had *duodenal ulcer*—typical hunger-pains, for which she took alkali and food between meals.

Children :—

1. Male; fifty-five. Several attacks typical *duodenal ulcer,* beginning when forty-five.
2. Male; fifty-two. *Duodenal ulcer* since forty. Confirmed by operation. Gastro-enterostomy when forty-nine, followed by *jejunal ulcer.*

3. Male; forty-five. *Duodenal ulcer* since thirty-seven. Perforated July, 1915, and again in July, 1916.

Two sisters, fifty-six and fifty, with no gastric symptoms.

A third sister died in 1886, aged seventeen, from supposed perforation of appendix, but no operation.

Grandchild.—Male; twenty-seven, son of (1). Typical *duodenal ulcer* since 1917, when on military service in France.

I am indebted to Dr. J. A. Ryle for the histories of the following family.

FAMILY H.

Father died of bronchitis and mother of cancer of breast.

1. Daughter died in 1904, aged thirty-eight, after operation for *retro-peritoneal abscess* and peritonitis.

2. Son died in 1919, aged forty-five, after gastro-enterostomy for *duodenal ulcer.*

3. Son, now forty-two, was operated on in 1907 for *duodenal ulcer.*

4. Daughter died in 1910, aged twenty-two, after operation for *perforated gastric ulcer.*

5. Daughter suffered from *indigestion* and died suddenly when twenty-nine.

6. Son, aged twenty-two, was operated on for *duodenal ulcer.*

As a perforated ulcer is very often mistaken for a gastric ulcer, No. 4 may really have had the former. Both No. 1 and No. 5's deaths may quite possibly have been also due to perforated duodenal ulcer.

A medical man with a duodenal ulcer belonged to a family, in which so many individuals suffered from a sinking sensation requiring frequent meals for their relief, that they habitually spoke of the "family sinking." His mother required frequent meals during the day, and a younger brother and sister both felt marked sinking about two hours after meals, which was only relieved by food. His father and elder sister and a younger brother were not troubled in this way, but several cousins had the characteristic "family sinking."

It is an interesting fact that I have never myself seen one member of a family in whom the presence of a gastric ulcer was proved and another in whom a duodenal ulcer was certainly present. This affords additional evidence that the types of stomach which predispose to the development of gastric and of duodenal ulcer respectively are congenital, and either one or the other may exist in several members of a

family. Dowden [9] has reported an interesting example of inheritance of both the gastric and the duodenal ulcer diatheses. He operated upon a father and son with duodenal ulcer, one of which had perforated, and on a daughter with gastric ulcer, and uncle on the mother's side with duodenal ulcer. The mother had a gastric ulcer operated on by another surgeon.

The Essential Exciting Causes of Duodenal Ulcer

Rosenow [10] has shown that when cultures are made from the deeper tissues of gastric and duodenal ulcers, the streptococci, which can often be isolated, are generally specific, as animals inoculated with them intravenously develop in a large proportion of cases hæmorrhages in the gastric or duodenal mucous membrane, which may later form acute and even chronic ulcers, lesions in other situations being comparatively rare. Moreover, streptococci isolated from infected tonsils or teeth in such patients give rise to similar lesions, whereas those isolated from septic tonsils or teeth in patients suffering from cholecystitis and appendicitis generally give rise to cholecystitis and appendicitis respectively, and comparatively rarely to gastric or duodenal lesions.

These remarkable results explain the important part played by dental and tonsillar infection in the production of ulcers, but they do not explain why gastric ulcers occur in some cases and duodenal ulcers in others. Thus the specificity of the infection is for ulcer in general, and not as a rule for gastric or duodenal ulcer in particular, as it is exceptional for the relative frequency of the experimental production of lesions in the stomach and in the duodenum to vary according to the situation of the ulcer in the patient from whose teeth, tonsils, or ulcer the streptococci were isolated.

Gastric or duodenal lesions developed in 9 per cent. of animals inoculated with streptococci from the infected teeth or tonsils of individuals otherwise healthy or suffering from diseases other than ulcer, cholecystitis or appendicitis. They also developed in 11 per cent. of animals inoculated with streptococci from cases of appendicitis, and in 29 per cent. from cases of cholecystitis. As none of these patients had

a gastric or duodenal ulcer, it may be assumed that they differed from those patients with gastric or duodenal ulcer in whom similar streptococci were isolated in being constitutionally less liable to develop chronic ulcers. Thus in most people the minute areas of necrosis in the gastric or duodenal mucous membrane, which are caused by hæmatogenous infection conveyed from the teeth, tonsils, appendix, or elsewhere, rapidly disappear under ordinary conditions; either no symptoms occur at all, or acute ulcers develop, which quickly heal, though they may occasionally give rise to hæmatemesis or even perforation. These acute ulcers are exactly analogous to those which may be produced in the duodenum in uræmia and by the toxins absorbed from burns. But in the presence of the peculiar conditions, which I have described as characteristic of the hypersthenic gastric diathesis, a minute area of necrosis in the duodenal mucous membrane is unlikely to heal. It will be digested by the acid gastric juice, with which it is in contact for several hours during the day and intermittently during the greater part of the night. Not only will healing fail to occur, but a chronic ulcer may develop.

The specific streptococci isolated from infected teeth or tonsils in cases of ulcer do not lead to any gastric or duodenal lesion when given by the mouth, even in very large doses. It seems clear, therefore, that apical infection of the teeth, which can only be recognised with the aid of the x-rays, is of more importance than pyorrhœa alveolaris, and that infection from the latter is, like the former, conveyed primarily by the blood rather than through the swallowing of infected material from the mouth. When, however, an ulcer has once formed, secondary infection of its surface may occur, so that bacteria derived from pyorrhœa alveolaris, particularly when swallowed during the hours the stomach is empty, may help to keep active the primarily hæmatogenous infection.

Secondary Exciting Causes of Duodenal Ulcers

A chronic ulcer is more likely to develop if the individual with the hypersthenic gastric diathesis, whose duodenum has been affected as a result of some focal infection, also habitually irritates it in other ways. An average man who eats too

rapidly without chewing his food, who is careless about his diet and frequently indulges in food containing mechanical and chemical irritants, which do not lose all their irritating properties during their stay in the stomach, will either not suffer at all in spite of his carelessness, or at most will develop a moderate degree of chronic gastric and duodenal catarrh. But if he has a hypersthenic stomach, the duodenal irritation will become more pronounced and will hasten the development of a chronic duodenal ulcer under the conditions already described. Alcohol in the form of whisky, cocktails and *apéritifs*, even when taken apart from meals, is diluted by the food which is almost continuously present in the stomach in most people, but in those with a hypersthenic stomach it is likely to reach the duodenum in an almost undiluted form, especially if it is taken shortly before lunch or dinner. It is then likely to act as a serious irritant, and I have seen many men in whom excessive indulgence in alcohol seemed to be directly responsible for the formation of a duodenal ulcer, although if they had not possessed the hypersthenic gastric diathesis nothing more than chronic gastritis would have developed.

I have already pointed out that this diathesis is more common in men than in women, this being the chief cause of the much greater frequency of duodenal ulcer in the former. But an additional cause is, I believe, to be found in the effect of excessive smoking, common in men but very rare in women, which stimulates the secretory and motor functions of the stomach, and thus leads to an exaggeration of the hyperchlorhydria and hypertonus already present in an individual with the hypersthenic gastric diathesis. R. D. Roberts has shown that smoking a pipe during the first and fourth quarters of an hour of a fractional test-meal accelerated the evacuation of his stomach from one and three-quarter hours to one hour. He also found a slight but definite reduction in the secretion of hydrochloric acid during periods of not smoking.

Diagnosis

The symptoms of duodenal ulcer must be familar to all, but I should like to say a few words about the differential

diagnosis. It is, I believe, impossible to recognise at what point in the history of a case actual ulceration appears. An operation has been performed on patients with the typical symptoms and the motor and secretory characteristics of the duodenal diathesis, and nothing abnormal has been discovered. This is due, I believe, to the fact that the diathesis may itself give rise to symptoms, perfectly healthy individuals with it being more liable to feel hungry three hours after meals than the average person. If over-worked or worried this hunger becomes distressing; it may be accompanied by faintness and nausea; it may wake him at night, and may even amount to pain. The patient can then be regarded as suffering from that form of nervous dyspepsia which is associated with hunger pain. Or if the accessory exciting causes of ulcer are present without the primary infective or toxic cause in individuals with this diathesis, similar symptoms will develop, but I doubt whether actual ulceration ever occurs under these circumstances, although the symptoms may be identical. The reflex dyspepsia which results from cholecystitis, cholelithiasis, and chronic appendicitis tends to assume the same characteristics if it occurs in an individual with the duodenal diathesis. In such cases actual ulceration may later occur as a complication of the primary disease, owing to secondary hæmatogenous infection of the duodenum.

For these reasons the claim that it is possible to diagnose duodenal ulcer from the anamnesis alone is exaggerated, and even the association of hypertonus, rapid evacuation and hyperchlorhydria with the characteristic symptoms proves nothing more than the presence of the duodenal diathesis, which has painted the nervous, irritative or reflex dyspepsia in its own colours. Only manifest or occult hæmorrhage, or the recognition of definite deformity of the duodenal bulb with the x-rays, proves that actual ulceration has occurred (Figs. 15, 16, 17 and 18). In their absence the exciting causes of the dyspepsia must be removed and the general dietetic and hygienic measures I shall presently describe should be taken in order to prevent the development of an ulcer, but no strict treatment with diet and alkalies is necessary, and surgery is only required for the



FIG. 15.—Normal duodenal bulb. (Dr. P. J. Briggs.)

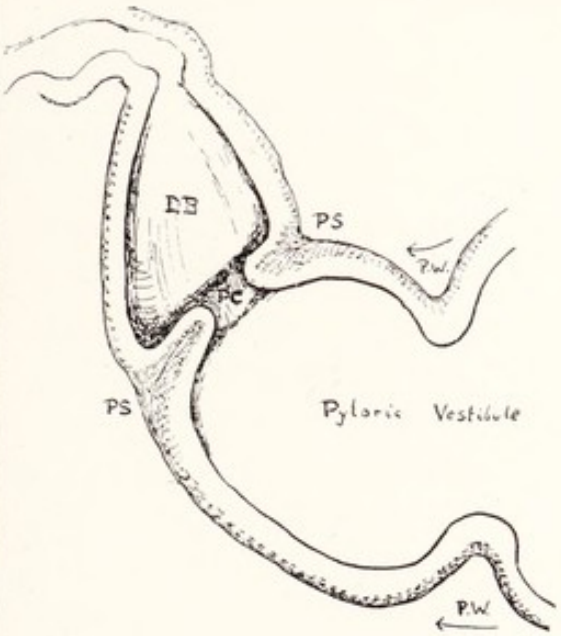


FIG. 16.—Diagram of section through pyloric vestibule, and duodenal bulb, DB., corresponding with radiogram of Fig. 15. Pyloric sphincter, PS.; P.W., peristaltic wave moving towards pylorus.



FIG. 17.—Very deformed duodenal bulb in a man of thirty-one, with fourteen years' history of duodenal ulcer. (Dr. P. J. Briggs.)

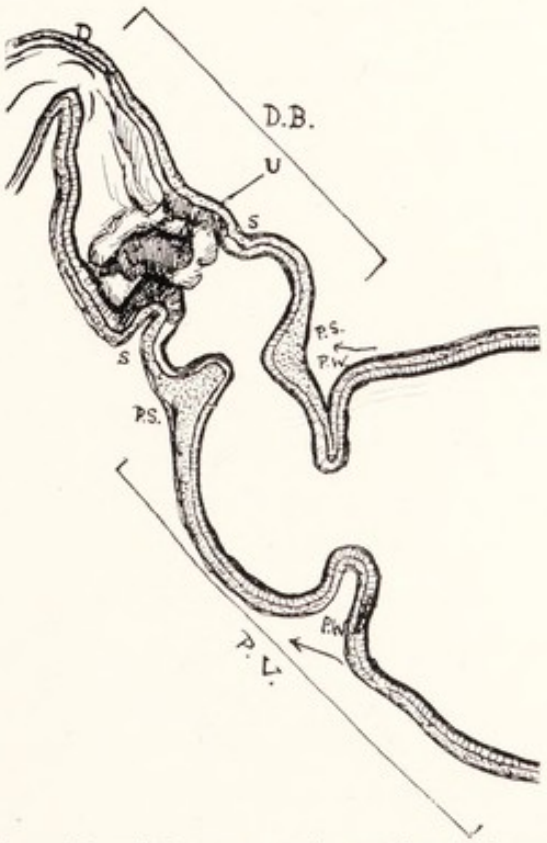


FIG. 18.—Diagram of section through pyloric vestibule, P.V., and duodenal bulb, D.B., corresponding with radiogram of Fig. 17. Ulcer (U) with spasm (S., S.) in duodenal bulb, separated by pyloric sphincter (P.S., P.S.) from pyloric vestibule and by acute angle at D from descending part of the duodenum. P.W., P.W., is a peristaltic wave in pyloric vestibule, which has almost reached the sphincter.

removal of such exciting causes as a chronically inflamed appendix.

Treatment of Duodenal Ulcer

It is first of all essential to eradicate completely any foci of infection which may be present. Not only should pyorrhœa alveolaris be thoroughly dealt with, but all the other teeth, however healthy they may appear to be, should be x-rayed, and the discovery of apical infection should lead to their immediate extraction. The tonsils should be carefully examined. If they show evidence of chronic infection they should be enucleated, and chronic nasal or naso-pharyngeal catarrh should be treated by appropriate measures. If there is evidence of chronic or recurrent appendicitis the appendix should be removed ; although it is of interest to inspect the duodenum in order to confirm the diagnosis of ulcer, a gastro-enterostomy should not be performed unless the ulcer has led to definite pyloric obstruction, as a medical cure should be as complete as a surgical cure without incurring the slight danger of the operation, the not inconsiderable danger of jejunal ulcer, and the other more frequent, but less serious, unpleasant sequels of gastro-enterostomy.

The patient should remain warm in bed throughout the treatment, but he should get up every day to have a bath and to open his bowels, the difficulties with which are greatly reduced if a bed-pan can be avoided.

Throughout the treatment the mouth should be kept absolutely clean, and the tongue frequently scraped with a wooden spatula if any fur accumulates on it.

The object of treatment is to reduce the secretion of gastric juice as much as possible, and to keep the hydrochloric acid in the stomach completely neutralised throughout the day and, what is almost invariably neglected, throughout the night. The evidence is conclusive that free hydrochloric acid prevents an ulcer healing, whatever additional factors may have contributed towards its production in the first instance. At the same time as much food as possible is required to maintain the patient's nutrition, especially when he has lost much weight, though this is much less often the case with duodenal than with gastric ulcer. Finally, the food should

be as unirritating in its mechanical and chemical characteristics as possible.

These are the commonly accepted principles of treatment, but several years ago I realised how inadequately they were carried out by the various methods in use both in England and abroad. I tried in various ways to fulfil these principles more satisfactorily, but it was not until I read a paper by Sippy of Chicago just before the war, that I realised how far short of perfection my improved methods still remained. I had the good fortune to meet Dr. Sippy during a visit to America in 1919, and my present method of treatment, though differing considerably from his, has been much modified as a result of his teaching.[11]

From 7 to 10 ounces of milk or junket are given every fourth hour from 8 a.m. to 8 p.m. inclusive. Every fourth hour from 10 a.m. to 10 p.m. a feed consisting of the same quantity of arrowroot, cream of wheat, or potato, artichoke or other vegetable purée is given. Red currant, apple or other fruit jelly or fruit juice may be added to some of the feeds and cream to others.

To each milk feed 15 grains of sodium citrate, which combines with the lime in the milk and consequently prevents the formation of irritating clots by the rennin of the gastric juice, dissolved in 1 to 4 drachms of emulsion of magnesia, are added ; the latter contains 5 grains of oxide of magnesia to the drachm. This has the advantage over sodium bicarbonate in having four times its neutralising power, in causing no distension of the stomach with carbon dioxide, which is evolved when it reacts with the hydrochloric acid, in having a mild aperient action, and in producing a very much smaller secondary increase in secretion after the initial neutralisation than sodium bicarbonate, which Crohn has shown by the fractional test meal to be the most powerful stimulant to the secretion of gastric juice in existence.

Immediately before the milk feeds half to one ounce of olive oil is taken. This inhibits the secretion of gastric juice ; at the same time it supplies a digestible and absolutely unirritating food of very high nutritive value in a concentrated form. Immediately before the remaining feeds from 5 to 10 minims of tincture of belladonna, which has a similar

inhibiting effect, is given, as oil before each feed sometimes gives rise to nausea and is more than can generally be digested (Fig. 19).

An hour after each feed a powder containing 10 grains of prepared chalk and 30 grains of bismuth carbonate is taken in a little water. The former has two and a half times, the latter only one-third, the neutralising power of sodium bicarbonate, but neither gives rise to any secondary hypersecretion, and they neutralise the acid so slowly that the carbon dioxide set free is dissolved in the gastric contents as rapidly as it forms. At 7 a.m. half an ounce of bismuth carbonate, shaken up but not suspended in 5 to 10 ounces of water, is swallowed, and the patient then lies on his right side so that the powder may form a protective covering to the ulcer; at the same time it neutralises any acid present, and calls forth a local secretion of protective mucus.

Sippy has not referred in any of his publications on the treatment of ulcer by complete neutralisation to the toxæmia which may result. In a recent paper from the Mayo Clinic, Hardt and Rivers [12] describe the toxic symptoms which occasionally develop in cases in which it is impossible to neutralise the acid completely. The patient is at first unduly introspective and nervous. He then complains of difficulty in taking his milk. After a time headache, nausea and vomiting occur. The patient becomes apathetic and drowsy, and in one of their cases death ensued. In every instance the urea in the blood became greatly increased, and albumin and casts appeared in the urine. In some there was evidence of kidney disease before the symptoms developed, and in the fatal case definite chronic nephritis was found.

I have met with three similar cases in private patients, though none in hospital, during the last three years. In one case the patient had only one kidney, and this was affected with pyelitis. In the other two patients a moderate degree of pyloric obstruction was present and there was an extreme degree of hypersecretion. In one of these death occurred, in spite of the early cessation of the alkaline treatment. The urea content of the blood was greatly increased in all three cases.

It is impossible at present to say what is the cause of the toxic manifestations. But it seems clear that no case in which the kidneys are diseased should be subjected to the full alkaline treatment, and the same is true when partial pyloric obstruction is present, in spite of Sippy's advocacy of the treatment in such cases. If any suspicious symptoms develop, a blood-urea estimation should be made and the treatment discontinued until it is ascertained whether it is excessive, in which case the treatment should be modified.

For ulcers associated with renal disease treatment by diet, olive oil and belladonna in the manner I have described, with only small doses of alkalies, may give sufficiently good results, but if pyloric obstruction is present, even in a mild degree, it is probably wise to recommend gastro-enterostomy without further delay.

Ten to fifteen minims of tincture of belladonna are given at 10.30 p.m., or in severe cases atropine sulphate is injected subcutaneously in order to inhibit the nocturnal secretion of gastric juice ; the largest dose which does not produce unpleasant dryness of the mouth should be given, beginning with one-hundredth of a grain. One or two additional feeds should be kept at the patient's bedside during the night, so that he can have some food, followed by an alkaline powder, without delay if he wakes.

If the patient is constipated the dose of magnesia should be increased, and if the bowels are not opened on two consecutive days an enema should be given. If diarrhœa occurs, the dose of magnesia should be reduced.

The strict treatment just described should be continued until for three weeks the patient has had no spontaneous pain and no trace of tenderness has been present, and a fortnight has elapsed since any occult blood has been found in the stools and the x-rays have shown any evidence of active ulceration. The pain and tenderness generally disappear within forty-eight hours ; the other signs of healing appear considerably later, the exact time depending upon the size and age of the ulcer and its proximity to the pylorus.

The diet can now be rapidly increased until at the end of a week everything is allowed, with the excep-

tions presently enumerated in discussing how to prevent recurrences.

Prevention of Recurrences

When the ulcer has healed our duty is only half done, for the patient has the hypersthenic gastric diathesis, and will certainly develop another ulcer very soon if the conditions which gave rise to the original one are not modified.

It is therefore necessary to give him definite written instructions as to the precautions he must take in order to

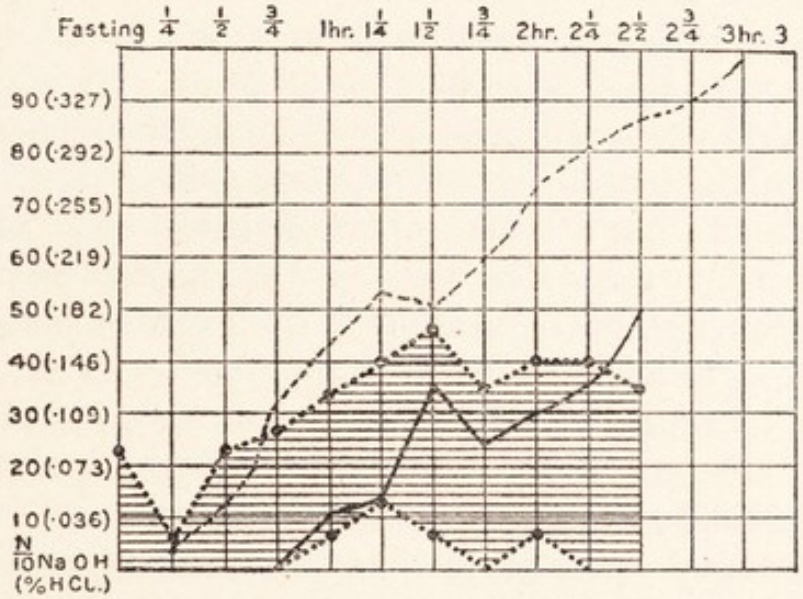


Fig. 19.—Effect of belladonna on curve of free HCl. Dotted line, hyperchlorhydria without treatment; continuous line, effect of 15 minims Tinct. Belladonnæ taken before test-meal. (R. D. Roberts.)

avoid the accessory exciting causes. He must understand that he has this peculiar duodenal diathesis, which makes it essential for him for the rest of his life to obey the instructions, if he wishes to avoid a recurrence of his duodenal ulcer. He must eat slowly and chew thoroughly. Alcohol is only allowed in small quantities in a dilute form during meals. Excess of salt, vinegar and other condiments must be avoided. Fruit is only allowed if it is ripe, and all pips and skins are removed; this is true whether it is taken raw or cooked, and currants, raisins and lemon peel in puddings, cakes and jam must be avoided. Vegetables are only allowed as purées, and salads should be prohibited. Tough

meat, high game and over-ripe cheese are forbidden. Plenty of butter and cream are invaluable, as their fat inhibits the secretion of gastric juice and delays the evacuation of the stomach. In long-standing cases, especially if the patient is thin, some olive oil should be taken before each meal. Smoking is only permitted in strict moderation on account of its stimulating action on the secretion of acid. The patient should be told that his stomach empties rapidly, and that the uneasy sensation he may have experienced two or three hours after meals, even before actual hunger pain developed, was due to this. He must therefore take small intermediate feeds, which have the effect of diluting and partly neutralising the gastric juice which would otherwise pass into the duodenum in a pure form. In addition to breakfast, lunch and dinner, he should take something on waking, in the middle of the morning and on going to bed, and he should have tea at about five o'clock. The exact hours of meals should be regulated in such a way that he never allows himself to get actually hungry or uncomfortable, and he should then keep strictly to these times, and not regulate the hours of his meals by his other appointments, but regulate the hours of his appointments by his meals. This is particularly important in medical men, who are more liable than any other profession to develop duodenal ulcer, owing, I believe, to the irregularity of their meals and their tendency to eat quickly and to smoke excessively. The nature of the intermediate feeds is immaterial; milk is suitable if the patient is at home, but if he has to be at his business some plain chocolate or biscuits will do equally well.

The patient should be told that if he has a recurrence of symptoms he must at once report himself, and that the recurrence will prove to be either his own fault or ours. It is generally his, because he has not followed instruction with sufficient care. It is occasionally ours, because the precautions we have laid down have been insufficiently strict; it is then necessary to determine, if possible, what led to the return of symptoms, and to make whatever additions to our instructions may appear to be necessary. A considerable experience has shown me that it is rare for a

duodenal ulcer to recur if the rules I have laid down are followed. I therefore advise operation very rarely—only when secondary pyloric obstruction is present or when there are repeated relapses in spite of every precaution. The latter indication, however, is purely theoretical, as since the war I have not seen a single case in which this occurred in the absence of pyloric or duodenal obstruction.

I am further persuaded in this course because, as the years pass, the number of patients I see who are suffering from jejunal ulcer and from other unpleasant sequels of gastro-enterostomy steadily increases. The result of the operation may be unsatisfactory from the beginning; more commonly only after months and sometimes even years do these sequels appear. It is a remarkable fact that during the last two years the number of private patients who have consulted me for symptoms which have followed a gastro-enterostomy performed for duodenal ulcer by various surgeons, many of whom may be ranked among the most skilful and experienced in Great Britain, is almost as great as the number of those suffering from an actual ulcer of the duodenum.

Much as we owe our surgical colleagues for the advances in our knowledge of the symptoms and diagnosis of duodenal ulcer, which have followed their investigations in the operating theatre into the "pathology of the living," I am convinced that duodenal ulcer should still be regarded as a medical and not a surgical disease. Recognition of the diathesis which predisposes to it, and of the primary and accessory exciting causes which lead to its actual development, should encourage us to think more of its prevention than its cure; even if we are only consulted when it is too late to talk of prevention, we should no longer remain content with the treatment of the active ulcer, but should regard the prevention of recurrence as a matter of equal importance.

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II. ACHLORHYDRIA AND ITS RELATION TO OTHER DISEASES *

In my first lecture I attempted to show how the "hypersthenic gastric diathesis," one manifestation of which is hyperchlorhydria, predisposes to the development of duodenal ulcer. To-day I propose to speak about its direct antithesis—the "achlorhydric gastric diathesis," in which the mucous membrane of the stomach, owing to some obscure congenital deficiency, secretes no hydrochloric acid. Some authors have denied the existence of primary or constitutional achlorhydria, believing that all cases are secondary to chronic gastritis. Though I am convinced that this view is incorrect, the matter is not one of fundamental importance, as the physiological and pathological results of achlorhydria are identical whether the condition is primary or secondary. I shall therefore have to discuss the results of the acquired condition at the same time as that of the congenital abnormality. An understanding of the pathogenesis of achlorhydria is, however, important, as it enables us to decide whether in a given case the condition is likely to be permanent and what treatment is likely to be most satisfactory. But the effects of achlorhydria on digestion and on the body as a whole are largely independent of its cause, as the same sequels may occur whether it is primary and congenital, secondary to chronic gastritis or other local disease, or a sequel of a gastro-enterostomy or gastrectomy.

* The relation of achlorhydria to Addison's anæmia and subacute combined degeneration of the cord, which was considered at length in this lecture, forms the subject of a separate address (p. 53).

Achlorhydria or Achylia Gastrica

When I speak of achlorhydria I mean a condition, in which no free hydrochloric acid is present when fasting and in which none appears throughout the period of digestion. The introduction of the fractional test-meal has greatly increased the accuracy with which this can be recognised. We have found that it is not at all uncommon for free hydrochloric acid to be completely absent from the gastric contents an hour after a meal, and yet to be present in small quantities, and occasionally even in large quantities, at some other period of digestion. Thus, out of 662 consecutive fractional test-meals performed at New Lodge Clinic, complete achlorhydria was present in seventy-eight (11·8 per cent.) cases; free hydrochloric acid was absent from the one-hour fraction in forty-nine (7·4 per cent.) additional cases, in thirty-three of which it was also absent from the resting-juice and from the three-quarter hour fraction, although free acid was present at other times during the test-meal—fifteen times in normal amount and twice actually in excess. In the additional 7·4 per cent. of cases the old-fashioned one-hour test-meal would have led to a diagnosis of achlorhydria, whereas the fractional method showed that free acid was actually present either in subnormal, normal or even excessive quantity, but that its first appearance was delayed. Thus the frequency of what is diagnosed as achlorhydria is much less than the old method would indicate. This is particularly well seen in the case of cancer of the stomach, in which achlorhydria is found in about 80 per cent. of cases by the old method (Hayem and Lion), but in only about 50 per cent. by the new (Hartman).

The discovery of complete achlorhydria does not necessarily indicate that no gastric juice containing hydrochloric acid is secreted, as small quantities of acid may be completely neutralised by the alkaline saliva and food, the alkaline juice secreted in the pyloric vestibule, and the regurgitated bile, pancreatic juice and duodenal secretion. Moreover, in most cases of achlorhydria some pepsin is present in the gastric contents. Achlorhydria is therefore not synonymous

with achylia gastrica, which is rare in comparison. Achlorhydria has the same effect on digestion whether it is due to actual achylia or not, and as it is also more readily recognised, for practical purposes a diagnosis of achlorhydria is sufficient, and the term should be employed in preference to achylia, unless actual investigations have proved that no trace of hydrochloric acid or pepsin is secreted by the gastric mucous membrane.

Chronic Gastritis as a Complication of Primary or Constitutional Achylia Gastrica

In recent years the view that achylia gastrica, including that which is associated with Addison's anæmia, is always due to gastritis has been upheld by Faber.[1] But sometimes no trace of the round-celled infiltration he regards as characteristic of the condition is found *post-mortem*. Faber has himself recorded such a case, in which death occurred from phthisis, and two similar ones have been described by Permin; in order to explain these exceptions, Faber suggested the existence of a functional achylia due to the intoxication and fever. He believes that atrophy of the gastric mucous membrane is generally due to the chronic gastritis, its extent depending upon the duration of the latter, but that it has no specific relation with Addison's anæmia, as he has often found it very well marked in old people with no trace of anæmia. Weinberg injected formalin into the stomach immediately after death in eleven fatal cases of Addison's anæmia. In three severe atrophy of the mucous membrane was present, in two slight atrophic changes were found near the cardia and little or none in the rest of the stomach, and in three there was no trace of atrophy anywhere. Very slight and scattered round-celled infiltration was present in all, but this is frequently found in the stomach of people with normal gastric secretion and even with hyperchlorhydria. It was found by Faber himself in sixteen out of thirty cases of gastric ulcer. It is clear, therefore, that the pathological changes in the stomach in achylia gastrica are often so slight and patchy, large areas with normal glands being present, that there can be no question

of the achylia being due to actual destruction of all the secreting tubules.

The origin of the gastritis can, I believe, be best understood by a consideration of the functions of the gastric juice. Quite apart from its specific activities, the gastric juice softens any hard and dry particles of food which reach the stomach as a result of insufficient mastication, and dilutes such chemical irritants as alcohol which may reach it in a too concentrated form. The achylia gastrica, which is an inborn error of function unconnected with any organic change in the stomach, is thus likely sooner or later to be complicated by chronic gastritis. As it frequently gives rise to no symptoms of any kind, the individual receives no warning that he must be exceptionally careful to chew his food thoroughly, to avoid mechanical and chemical irritants in his diet, and to avoid swallowing very hot or very cold food or drink. By the time that obvious symptoms have developed, and still more so by the time that death occurs from some secondary or independent disease, the gastric mucous membrane shows obvious changes. This, I believe, is the true explanation of the pathological observations of Faber and others, who have found evidence of chronic gastritis and often of atrophy of the mucous membrane after death in most cases of achylia.

I believe that it is much more common for gastritis to be secondary to achylia than for achylia to result from gastritis. When gastritis is primary—as it undoubtedly is in the achlorhydria of alcoholics, which is often associated with cirrhosis of the liver—recovery frequently occurs if the source of irritation is removed. Thus I have several times observed a return to the normal gastric secretion after alcoholic patients have been deprived of all alcohol and kept on a light diet for a few weeks. On the other hand, the majority of cases of achlorhydria, in which no obvious primary source of irritation is present, show no change in their gastric contents, even after prolonged treatment with careful diet and suitable drugs, although all symptoms may have disappeared for a long period. Thus a lady who consulted me in 1913 for nausea was found to have complete achlorhydria. She lost her

symptoms on taking hydrochloric acid. In 1920 she consulted me for nervous symptoms ; she had had no nausea or other digestive disturbance for seven years, but complete achlorhydria was still present. In her case I feel convinced that the achlorhydria was a congenital abnormality, and any sign of inflammation or atrophy which might be discovered on microscopical examination of her gastric mucous membrane would, I believe, be due to the permanent loss of the protection from mechanical and chemical irritants normally afforded by the softening and diluting action of the gastric juice. Dr. Max Einhorn related to me the case of a man who consulted him in 1892 on account of severe "dysentery" with loss of over 40 lbs. in weight. He was found to have achylia gastrica. In less than two years he gained 60 lbs. in weight and recovered completely from the "dysentery." Once a year, for twenty-eight years, he attended Einhorn's post-graduate lectures, and complete achylia was always present, but no gastro-intestinal symptoms of any kind returned, and he died in 1921 at the age of eighty-two from prostatic disease.

Primary achylia gastrica does not depend upon any anatomical peculiarity, as fragments of gastric mucous membrane, which I have had removed during an operation for appendicitis in patients with this condition, have generally looked perfectly normal and have always shown the usual number of healthy-looking oxyntic cells. It must, therefore, be due to an inborn deficiency in the functional capacity of glands, which appear to be structurally normal.

The Digestive Functions of Gastric Juice

The specific functions of the stomach are two-fold—digestive and antiseptic. The digestive function consists in the chemical and physical preparation of the food which reaches it from the mouth for digestion in the intestines. The antiseptic function consists in partial destruction of organisms originating in the mouth, nose or naso-pharynx, or introduced in food or drink.

The chief digestive function is the partial conversion of proteins into simpler bodies by the action of pepsin, which is

only active in the presence of free or organically combined hydrochloric acid. The other ferments of the gastric juice are of comparatively little use, but the softening action of the hydrochloric acid on connective tissue, which was first emphasised by Adolf Schmidt, is an important function, as it disintegrates meat and permits the gastric and pancreatic juice to act upon the protein and fat. As the secretin formed by the action of hydrochloric acid on the prosecretin present in the duodenal mucous membrane was shown by Bayliss and Starling to be an important stimulant of pancreatic secretion, it might be expected that achylia gastrica would lead to achylia pancreatica. This is not, however, the case ; presumably the psychical and the other chemical stimuli of pancreatic secretion are sufficiently powerful to cause an adequate flow of juice in the majority of cases.

In the absence of the normal gastric secretion food enters the duodenum in much the same state as that in which it is swallowed. If the individual eats slowly and chews thoroughly, any mechanical and thermal irritation the food might exert will be prevented in the mouth, and any chemical irritants it contains will be diluted by the saliva, so that it is not likely to damage seriously either the gastric or intestinal mucous membrane. But if it is bolted, or if mastication is inefficient owing to want of teeth, the food will have the same deleterious effects on the duodenal mucous membrane as that which I have already mentioned in connection with the stomach, though the rest of the intestine will be protected by the diluting action of the bile and the pancreatic and intestinal juices. The saliva cannot, however, in any way compensate for the loss of the softening effect of the hydrochloric acid on connective tissue and the digestive action of pepsin on proteins. Consequently in all cases of achlorhydria much completely undigested food will reach the duodenum. Although pancreatic digestion is in most cases sufficient to do the work of the gastric juice in addition to its own, protein digestion in the intestine will be considerably delayed, and a larger quantity than normal is likely to reach the cæcum in an incompletely digested state, so that there will be a plentiful supply of only slightly altered protein available for bacterial decomposition in the colon.

Achlorhydria is frequently latent, being discovered accidentally in people with no obvious digestive symptoms. When symptoms occur, they are due chiefly to the irritation of the small intestines by food inadequately prepared in the stomach. To this is often added irritation of the colon by products of abnormal bacterial activity, owing to the supply of incompletely digested proteins being excessive and to the excessive number of bacteria likely to reach it because of the absence of the normal antiseptic action of the gastric juice. The most common symptom is consequently diarrhœa, which tends to occur in attacks of moderate severity over a period of many years. Although it generally resists all other forms of treatment, it stops immediately if a little hydrochloric acid is given with meals. The next most common symptom is nausea, which is quite independent of attacks of diarrhœa.

Intestinal Dyspepsia following Gastro-Enterostomy

Nine years ago [2] I described the digestive symptoms which may follow a gastro-enterostomy apart from the development of a gastro-jejunal or jejunal ulcer. They are of a precisely similar nature to those caused by primary achlorhydria, being due to the passage into the jejunum of food which has not undergone the necessary mechanical and chemical preparation in the stomach owing to its rapid evacuation, and to the absence of free hydrochloric acid, which frequently follows the operation unless it is performed for a duodenal ulcer, when the hyperchlorhydria generally persists (Conybeare).[3]

Association of Achlorhydria with Appendicitis, Cholecystitis, Pancreatic Disease and Dysentery

The majority of people with pyorrhœa alveolaris are none the worse for the large quantity of infective pus they are constantly swallowing, as the bacteria are to a large extent destroyed by the antiseptic action of the hydrochloric acid of the gastric juice. But out of each hundred normal people about four have constitutional achylia gastrica (Bennett and

Ryle [4]), and presumably the same proportion of otherwise healthy individuals with pyorrhœa alveolaris, or chronic infection of the tonsils, nose or naso-pharynx, have achylia. So long as the mucous membrane of the stomach and intestines is intact and no abnormal degree of stasis occurs in any part of the alimentary canal, the bacteria, which gain access to the stomach and owing to the loss of the antiseptic action of the gastric juice pass in undiminished numbers into the intestines, do not invade the mucous membrane. But the large number of organisms constantly present in all parts of the alimentary canal may seriously aggravate any pathological condition already present. It has, for example, been shown by Rosenow that appendicitis and cholecystitis are probably always secondary to hæmatogenous infection, and that the same streptococci isolated from the teeth or tonsils of a case of appendicitis or cholecystitis, which give rise to inflammation of the appendix or gall-bladder when injected into the veins of animals, have no such effect when introduced in large quantities into the lumen of the appendix or gall-bladder respectively. When, however, the mucous membrane of the appendix is once damaged, or the free flow of its contents is impeded by the presence of a fæcolith or a stricture or kink following a previous attack of appendicitis, secondary infection from the lumen may occur and give rise either to an attack of acute appendicitis or to chronic appendicitis. The same thing may happen in connection with the gall-bladder after its mucous membrane has once become damaged. I have long been struck by the comparative frequency of achlorhydria in patients suffering from chronic appendicitis, and T. G. D. Bonar [5] has recently found that 33 per cent. of sixty-five cases operated upon for this condition at Guy's Hospital had very little or no free hydrochloric acid in their stomachs throughout the course of a fractional test-meal. I believe that the hyperchlorhydria which was present in 55 per cent. of Bonar's cases must be a reflex result of the appendicitis, but I cannot see how the achlorhydria can also be secondary. It seems more probable that primary achylia gastrica predisposes to chronic appendicitis by helping to maintain or to aggravate an infection which is primarily hæmatogenous, by

permitting access into the lumen of the appendix of excess of oral streptococci, which in a normal individual would have been destroyed to a large extent by the gastric juice. The proportion of patients with gall-stones who have achlorhydria (49 per cent.) and hyperchlorhydria (23 per cent.) was also found by Bonar to be greater than normal, and I believe that this is due, as in the case of appendicitis, to the former predisposing to ascending infection, whilst the latter is a reflex result of the primary gall-bladder disease.

Chronic pancreatitis and carcinoma of the pancreas are generally associated with achlorhydria, but I have seen normal gastric secretion in one case of the former, in which death followed rupture of the gall-bladder, and in two of the latter, in which the pancreas was almost completely destroyed by growth. I have already pointed out that achlorhydria does not lead to pancreatic achylia in spite of the absence of the stimulus to secretion normally produced by secretin, but there does not seem to be any reason why the latter should cause achlorhydria. The association is more probably due to the pancreatitis, which is, perhaps, the common precursor of carcinoma of the pancreas, being caused by an ascending infection from the duodenum, which becomes infected owing to the absence of free hydrochloric acid from the stomach.

Both the *Amœba histolytica* and *B. dysenteriæ* are destroyed by dilute hydrochloric acid. Consequently individuals with absent or deficient gastric secretion are particularly likely to become infected with both forms of dysentery. Strauss [6] found achlorhydria in twenty-one and hypochlorhydria in nine out of 100 cases of bacillary dysentery, the deficient gastric secretion having probably predisposed to the infection rather than resulted from it. It seems not unlikely that exhaustion, exposure and insufficient food led to a diminished gastric secretion in many of the soldiers in Gallipoli and Mesopotamia, quite apart from the fact that about 4 per cent., or 6,000 out of the whole Gallipoli army, would in any case have had constitutional achlorhydria. This may have been one reason why such an enormous proportion developed one or both forms of dysentery. Whilst acting as a member of the Medical Advisory Board of the Mediterranean Expedi-

tionary Force in 1915, I suggested that the troops on the Peninsula should be provided with a palatable drink containing 0·1 or 0·2 per cent. hydrochloric acid instead of water as a prophylactic measure against dysentery, but the proposal was rejected on the score of administrative difficulties. Knott [7] has shown that this strength of acid would be sufficient to destroy *B. typhosus* as well as *B. dysenteriæ* present in water or food, so that an acid drink is a method of prophylaxis which might well be adopted in any future campaign in a country where typhoid fever and dysentery are prevalent.

Achlorhydria and Rheumatoid Arthritis

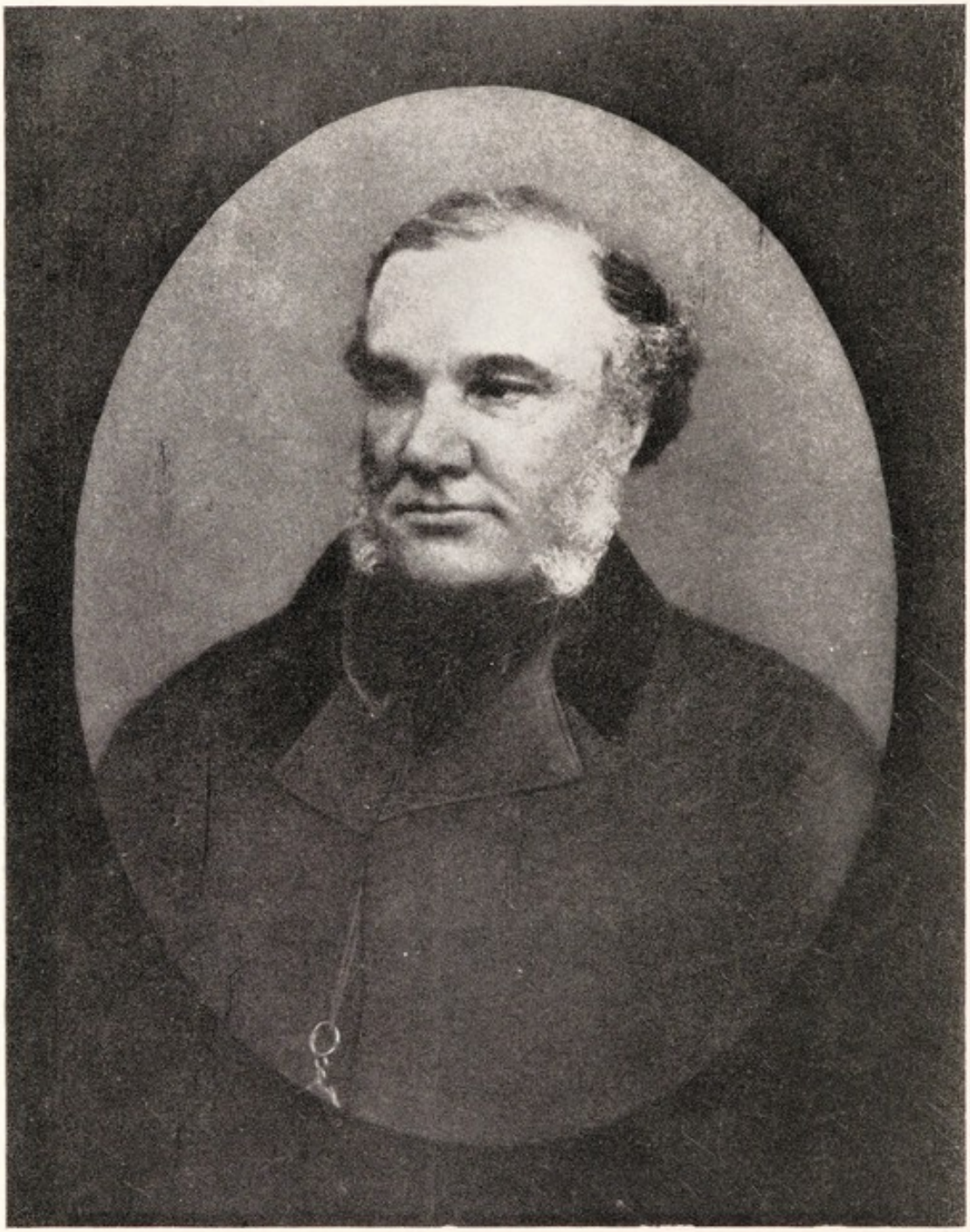
Rheumatoid arthritis is, I believe, invariably secondary to focal infection. In most cases this is primarily in the teeth, the removal of which will lead to the rapid cure of most early cases of the disease. Not infrequently the tonsils are also infected and require removal, and occasionally other foci, such as the nasal sinuses, require treatment. But in some severe cases, though temporary improvement follows the removal of these foci, the disease is not completely arrested. It is then usual to find that the intestines are also infected, presumably from swallowed organisms, the intestinal infection being secondary to that in the mouth. A remarkable proportion of these cases have complete achlorhydria. Thus Woodwark and Mackenzie Wallis [8] found a diminution or absence of free hydrochloric acid in nine out of ten cases of rheumatoid arthritis. Faber [1] found achylia gastrica in fifteen out of sixty-five cases, or 23 per cent., of "chronic polyarthritis," and Kahlmeter [9] twenty-seven out of fifty, or 54 per cent. Coates and Gordon,[10] in a series of twenty cases of definite rheumatoid arthritis investigated at the Royal Mineral Water Hospital at Bath, found achlohydria in fourteen and hypochlorhydria in three. Among fifteen consecutive private cases of rheumatoid arthritis under my own observation, examined by the more accurate fractional method, achlorhydria was present in three, hypochlorhydria in five, and a low normal curve of secretion in three. About four out of every 100 patients who develop rheumatoid arthritis presumably have con-

genital achylia gastrica. They are extremely likely to develop intestinal infection secondary to their oral sepsis; the treatment of the latter alone cannot then lead to their cure. If, for example, ten out of the 100 patients referred to do not recover after the oral sepsis has been eradicated, four of them—or 40 per cent.—are likely to have achlorhydria. The latter is, of course, not an essential predisposing factor in the development of secondary intestinal infection, but it is certainly a very powerful predisposing cause. A test-meal should therefore be given in all cases of rheumatoid arthritis, and, if achlorhydria is found, full doses of hydrochloric acid should be given, as well as sour milk and perhaps a vaccine prepared from streptococci isolated from infected teeth and the intestinal contents.

Kahlmeter also found achlorhydria in no less than six out of sixteen cases of acute rheumatic fever, so that its great tendency to recur, even after tonsillectomy, may possibly also depend in some instances on a chronic intestinal infection.

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Thomas Addison

Thomas Addison, M.D.
Born 1792; died 1860. Physician to Guy's Hospital, 1824 to 1860.

ADDISON'S (PERNICIOUS) ANÆMIA AND SUBACUTE COMBINED DEGENERATION OF THE SPINAL CORD*

History and Nomenclature

A very peculiar disease, which will doubtless be viewed in different lights and receive different appellations.

Combe, 1822.

In 1822 Combe[1] of Edinburgh published an excellent description of a case, which the clinical history and post-mortem examination show must have been an example of what is now known as pernicious or Addison's anæmia. No other cases had been recorded when Thomas Addison,[2] physician to Guy's Hospital, in a paper on "Anæmia and Disease of the Supra-renal Capsule," read before the South London Medical Society, in March, 1849, referred incidentally to a "remarkable form of anæmia," which he had regarded in recent years as a "subject of earnest inquiry and very deep interest." Six years later his classical description of the disease appeared in his monograph "On the Constitutional and Local Effects of Disease of the Supra-renal Capsules." He introduced the subject by giving the following "brief narrative of the circumstances and observations by which I have been led to my present convictions.

"For a long period I had from time to time met with a very remarkable form of general anæmia, occurring without any discoverable cause whatever; cases in which there had been no previous loss of blood, no exhausting diarrhœa, no chlorosis, no purpura, no renal, splenic, miasmatic, glandular, strumous, or malignant disease. Accordingly, in speaking of this form of anæmia in clinical lecture, I, perhaps with little propriety, applied to it the term 'idiopathic,' to distinguish

* An abstract of this paper was given as an address to the Northampton Branch of the British Medical Association on March 25th, 1923, and published in the *British Medical Journal*, 1924, I., 93.

it from cases in which there existed more or less evidence of some of the usual causes or concomitants of the anæmic state.

"The disease presented in every instance the same general character, pursued a similar course, and, with scarcely a single exception, was followed, after a variable period, by the same fatal result. It occurs in both sexes, generally, but not exclusively, beyond the middle period of life, and so far as I at present know, chiefly in persons of a somewhat large and bulky frame, and with a strongly-marked tendency to the formation of fat. It makes its approach in so slow and insidious a manner, that the patient can hardly fix a date to his earliest feeling of that languor which is shortly to become so extreme. The countenance gets pale, the whites of the eyes become pearly, the general frame flabby rather than wasted; the pulse perhaps large, but remarkably soft and compressible, and occasionally with a slight jerk, especially under the slightest excitement; there is an increasing indisposition to exertion, with an uncomfortable feeling of faintness or breathlessness on attempting it; the heart is readily made to palpitate; the whole surface of the body presents a blanched, smooth and waxy appearance; the lips, gums and tongue seem bloodless; the flabbiness of the solids increases; the appetite fails; extreme languor and faintness supervene, breathlessness and palpitations being produced by the most trifling exertion or emotion; some slight œdema is probably perceived about the ankles; the debility becomes extreme, the patient can no longer rise from his bed, the mind occasionally wanders, he falls into a prostrate and half-torpid state, and at length expires; nevertheless, to the very last, and after a sickness of perhaps several months' duration, the bulkiness of the general frame and the amount of obesity often present a most striking contrast to the failure and exhaustion observable in every other respect.

"With, perhaps, a single exception, the disease, in my own experience, resisted all remedial efforts, and sooner or later terminated fatally. On examining the bodies of such patients after death, I have failed to discover any organic cause of such serious consequences."

Since Addison's time all cases of his "idiopathic anæmia" admitted to Guy's Hospital have been carefully analysed, and the results have been recorded in our *Reports* successively by Wilks,[3] Taylor,[4] Pye-Smith,[5] Hale-White,[6] French,[7] and, finally, in 1922, by Campbell and Conybeare.[8]

In 1871 Biermer[9] of Zurich published a paper on "Progressive Pernicious Anæmia." Under this heading he included "a number of different forms of anæmia which have certain characteristic features in common, a spontaneous origin without clear etiology being one of the rarities." A careful study of Biermer's work shows conclusively that he added nothing new to our knowledge of the disease described by Addison twenty-one years earlier beyond pointing out the frequency of retinal hæmorrhage. On the other hand, he added much confusion by including under a single name both Addison's "idiopathic anæmia" and a great variety of other conditions. The designation "Biermer's anæmia," which is employed in Germany, Scandinavia and Switzerland, is therefore quite unjustified. The name "pernicious anæmia," having been introduced by Biermer for an entirely different purpose, is equally unsuitable, as well as being most undesirable on account of the depressing significance it has for the sufferer who receives this description of his disease. As the investigations of the last twenty years have shown that the disease is almost certainly due to infection of the intestinal tract, the original name of idiopathic is no longer correct. Addison's description of the disease is so admirable that I am convinced that no more suitable name could be devised than Addison's anæmia, as William Hunter[10] first suggested in 1909. Patients should be told that they are suffering from Addison's anæmia rather than from pernicious anæmia, but until the new name has become universally adopted by text-books on medicine, it is perhaps desirable in papers published on the subject to refer to "Addison's [so-called pernicious] anæmia" in order to avoid confusion with Addison's disease.

The Blood in Addison's Anæmia

It is interesting to recall that all the early investigations on Addison's anæmia were carried out before the introduc-

tion of any modern hæmatological methods. Neither Addison nor Biermer had any knowledge of the nature of the changes in the blood, though the condition was, of course, recognised as an anæmia, and as early as 1855 Wilks had shown at Guy's Hospital that there was no increase in the number of white corpuscles present. In 1858 Leared [11] described at the Pathological Society of London the red blood corpuscles as being "very variable in size, many of them being of an oval shape," but this appears to have been an isolated observation, which was not repeated until two Swiss physicians, Quincke [12] and Eichhorst,[13] independently published their work on the microscopical changes in the blood in Addison's anæmia in 1876. Quincke drew special attention to the irregularity of their shape, which he called poikilocytosis, while Eichhorst laid chief stress on the presence of very small corpuscles. The following year, Mackern and Davy,[14] two students at Guy's Hospital, carried out a very thorough investigation of the blood in a case of Moxon's; they found that the red corpuscles were reduced in number, variable in size, some being larger and others smaller than normal, and of great diversity in form, some being oval and others spindle-shaped. They found also that the corpuscles did not form the usual rouleaux. Similar observations were made the same year by Byrom Bramwell[15] in Edinburgh.

So far as I have been able to ascertain, the first blood count and the first estimation of hæmoglobin in a case of Addison's anæmia at Guy's Hospital were made in 1879 with the recently introduced apparatus of Gowers, which was a modification of that originally devised by Malassez in 1872. But the conclusions to be drawn from such examinations were first formulated by Laache[16] of Copenhagen in his monograph on anæmia published in 1883. In it he gave an account of his remarkable investigations on the blood of nine cases of Addison's anæmia, and concluded that the disease is characterised by the fact that the red cells, though reduced in number, contain a normal or even excessive amount of hæmoglobin, in contrast to other forms of anæmia, such as chlorosis, in which the corpuscles were abnormally pale. Hayem[17] of Paris had come to a similar

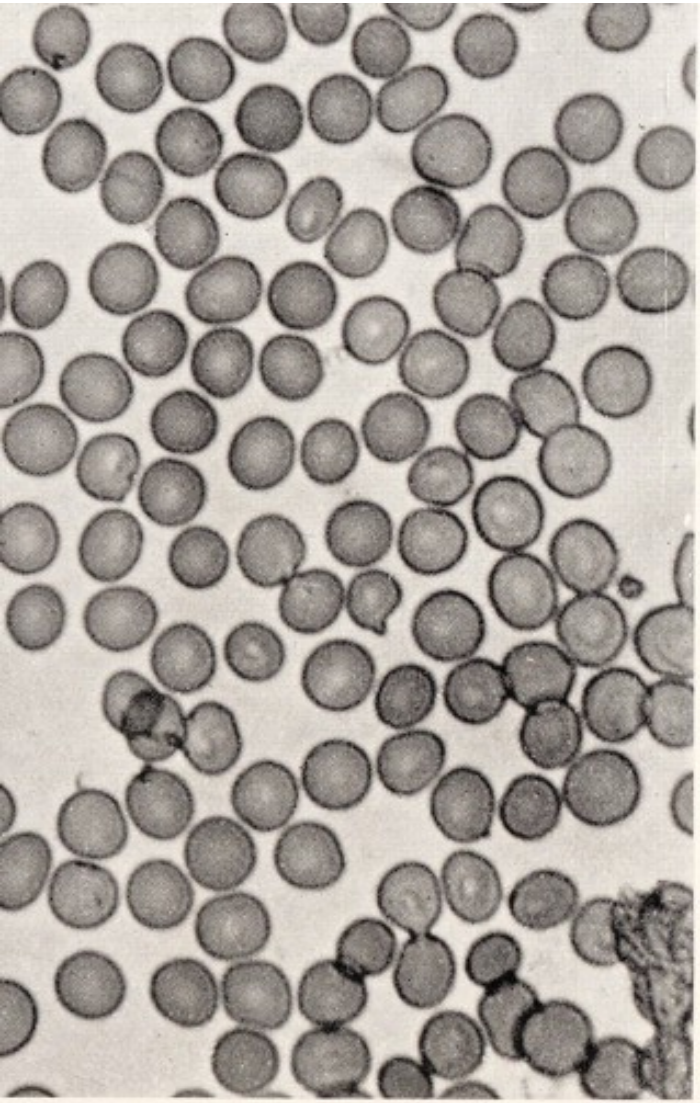


FIG. 20 (*a*).—Blood film from a healthy man. Mean diameter of red corpuscles. (M.D.) 7·4 μ.

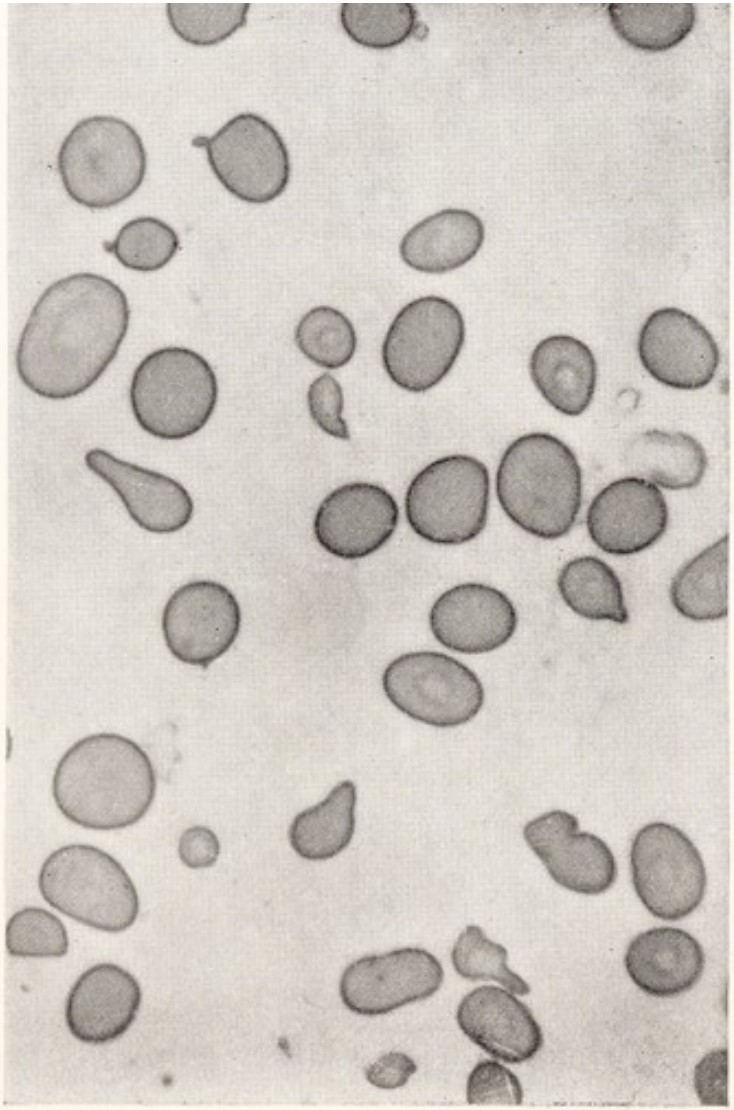


FIG. 20 (*b*).—Blood film from case of Addison's anæmia during phase of acute hæmolysis, showing megalocytosis, anisocytosis and poikilocytosis. M.D. 8·27 μ.

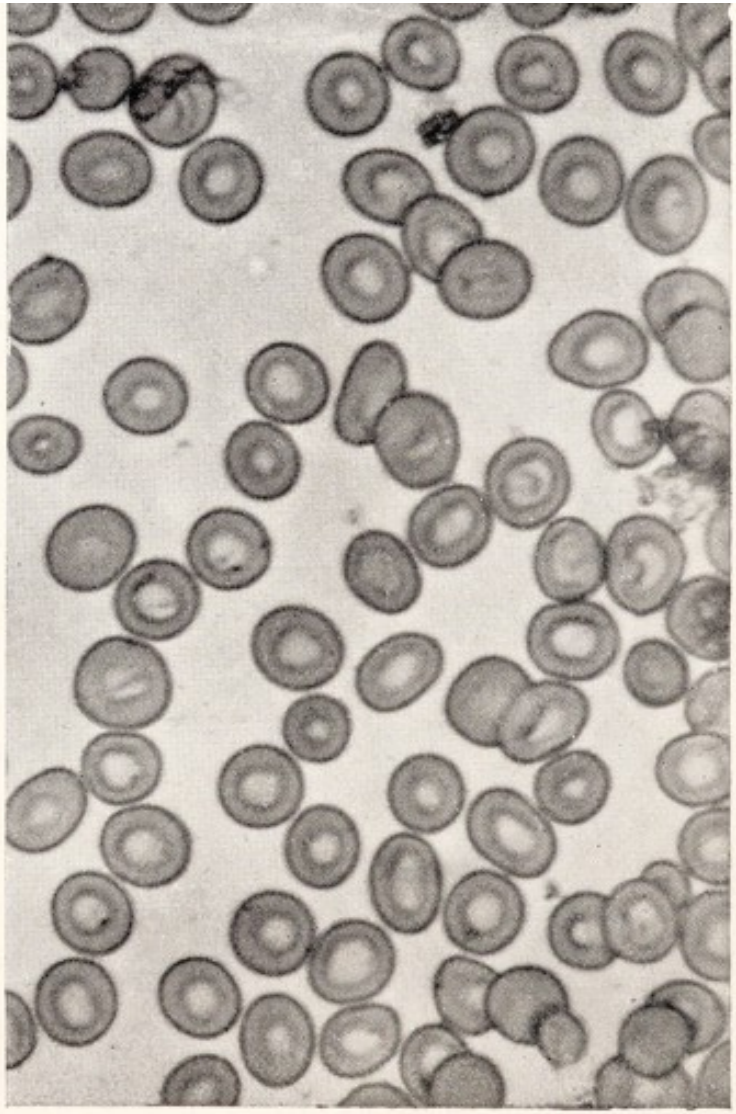


FIG. 20 (*c*).—Blood film from case of Addison's anæmia during remission of hæmolysis, showing persistent megalocytosis. M.D. 8·86 μ.

FIG. 20.—(After A. C. Hampson and J. W. Shackle.) The magnification is the same in the three micro-photographs.

conclusion seven years earlier as a result of his examination of the blood of a single case.

Between 1880 and 1892 Ehrlich [18] carried out his important investigations, as a result of which he concluded that the presence of nucleated red cells, and especially of megaloblasts, was an essential feature of Addison's anæmia. He was also the first to draw attention to the diminution in number of the leucocytes. Valuable as his work was, it had the unfortunate effect of directing attention exclusively to the blood-picture in the diagnosis of the anæmia, the clinical features of which had been so well described by Addison.

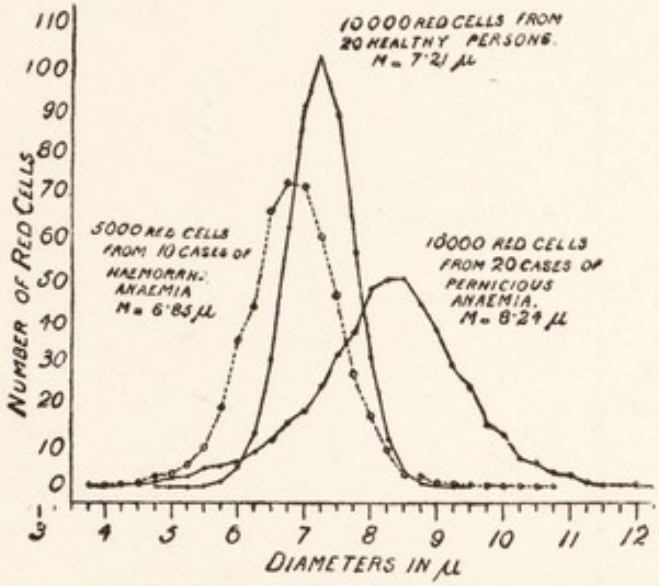


FIG. 21.—Curves showing size of 10,000 red corpuscles from twenty healthy individuals, compared with curves of 5,000 cells from ten cases of hæmorrhagic anæmia and 10,000 cells from twenty cases of Addison's anæmia respectively (C. Price-Jones).

The most characteristic changes in the blood in Addison's anæmia are now recognised as being the great inequality in the size of the red corpuscles — the anisocytosis—caused by the presence of microcytes and megalocytes, as Laache emphasised as long ago as 1883, and the increase in their average size in spite of the presence of some cells far smaller than the smallest found in normal blood. The megalocytosis is present in the very earliest stages and almost always during remissions, even when there is little or no actual anæmia present (Fig 20).

Price-Jones [19] has introduced an extremely valuable graphic method of recording the size of the blood-corpuscles. Five hundred cells are accurately measured and the number of each size is charted, the size being shown horizontally and the number vertically. The middle curve in Fig. 21 represents that obtained by him from the measurement of 10,000 cells of twenty normal individuals, reduced for comparison to the size of a curve of 500 cells. It will be seen that the total

variation in size of the corpuscles is not great. The diameters of 10,000 cells measured by Price-Jones in twenty cases of Addison's anæmia and those of 5,000 cells in ten cases of anæmia secondary to hæmorrhage are shown in the same figure. In Addison's anæmia the whole curve moves to the right and has a very wide base, owing to the presence of very

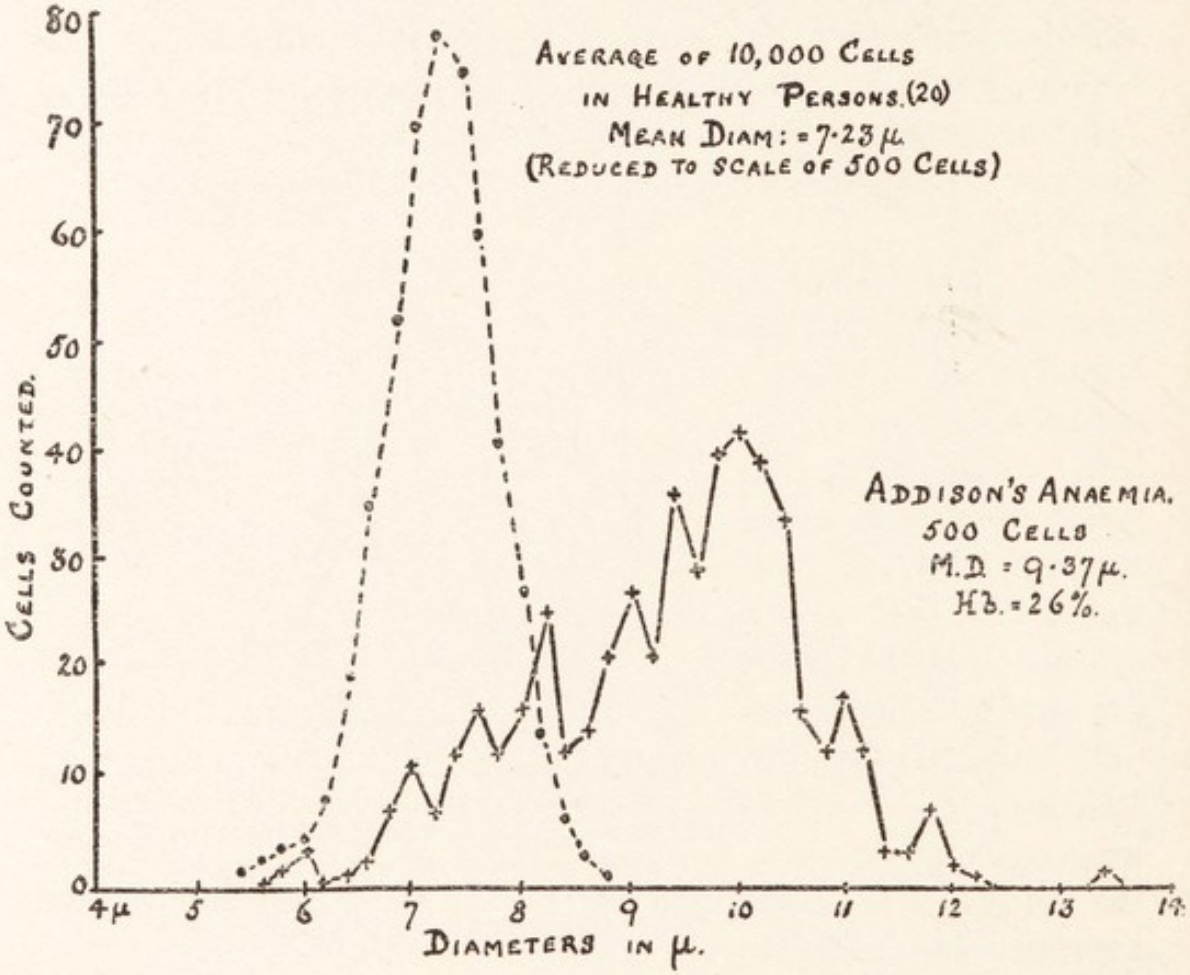


Fig. 22.—Price-Jones' cell-distribution chart in case of Addison's anæmia, showing characteristic megalocytosis, anisocytosis and irregular curve, Hb, 26 per cent.; red cells, 1,440,000 per cub. mm.; C.I., 0·9 (A. C. Hampson and J. W. Shackle).

small microcytes and very large macrocytes. Fig. 22 is a typical chart made for me by J. W. Shackle and A. C. Hampson from a case of Addison's anæmia, superimposed on the normal curve they obtained by measuring 10,000 cells in twenty healthy individuals, which is almost identical with Price-Jones's normal curve. It shows the characteristics I have mentioned, and in addition the irregular form always seen with Addison's anæmia, which is in striking contrast

with the uniform curve obtained with normal blood, and with the curve in secondary anæmia, in which the highest point moves to the left, the curve is comparatively uniform, and the total variation in the size of the cells is not much greater than normal. These characteristics were seen in every one of sixty-eight observations in thirty-three cases of

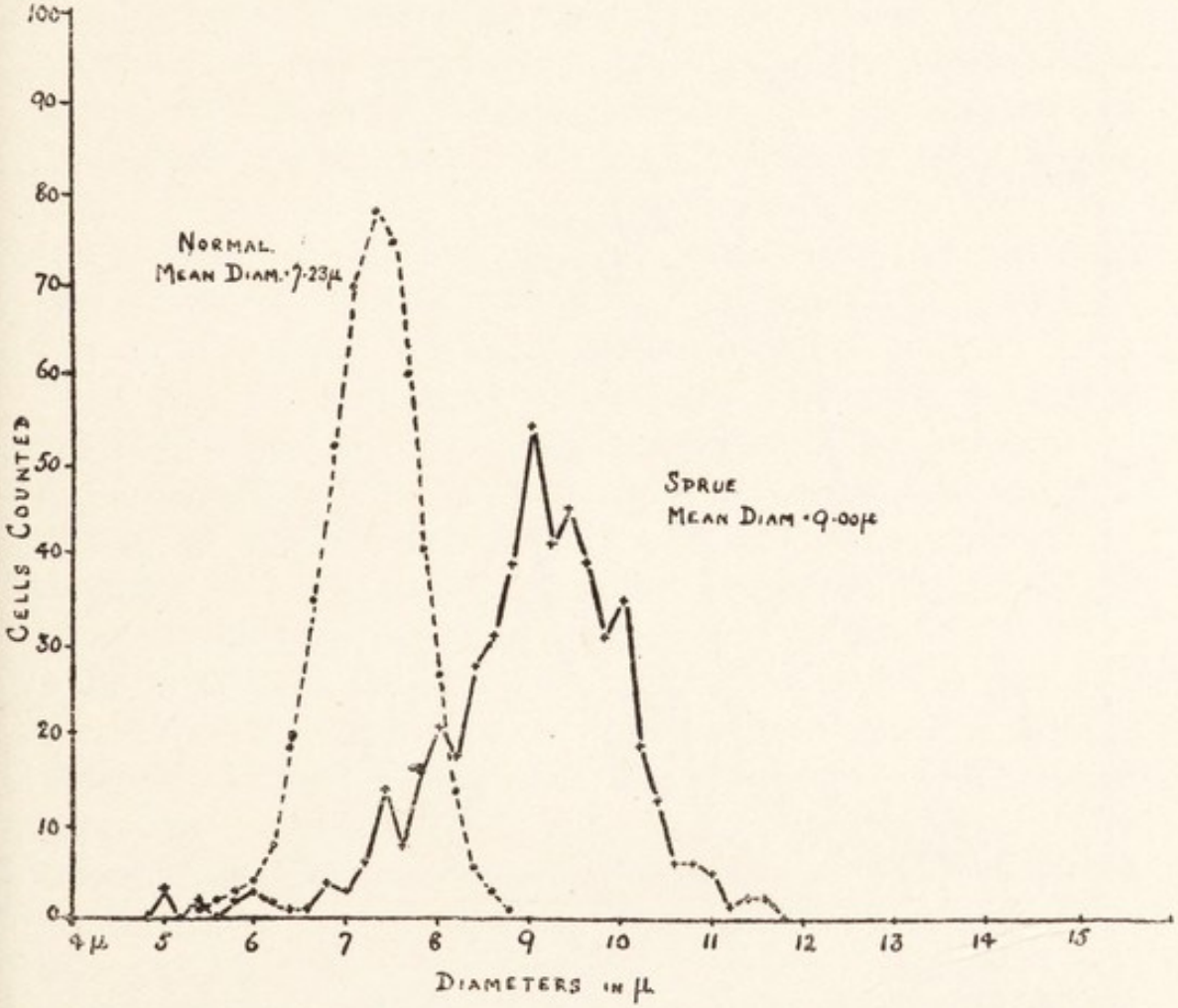


Fig. 23.—Typical megalocytosis in a case of sprue with low hæmoglobin percentage (A. C. Hampson and J. W. Shackle).

Addison's anæmia charted by Price-Jones, and in twenty cases charted by Shackle and Hampson.[20]

Shackle and Hampson obtained precisely similar curves in the very closely allied anæmia associated with sprue (Fig. 23), and Passey and Carter Braine[20B] in that associated with infection with the tapeworm, *Dibothriocephalus latus*. With these exceptions, they have been found in no other disease.

These cell-distribution curves are very laborious to make,

but they are of the greatest value in diagnosis in doubtful cases, as the characteristic curve is present in Addison's anæmia before the patient is actually anæmic, and also during most remissions, and they give a useful graphic record of the progress of each given case (Fig. 24).

Price-Jones found that the diameters of the red cells vary in Addison's anæmia between 3·75 μ and 13·9 μ with an

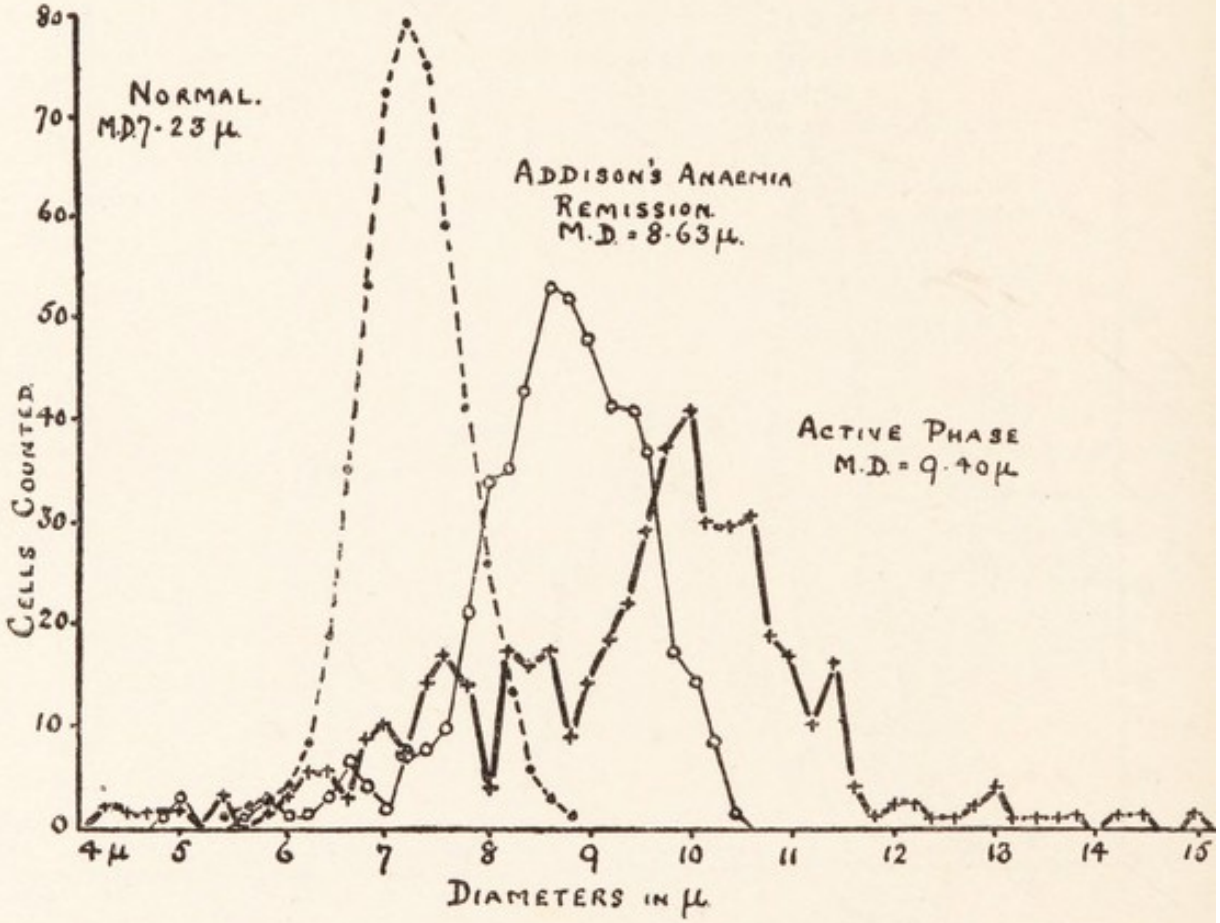


FIG. 24.—Addison's anæmia in active stage (Hb, 20 per cent.; red cells, 800,000 per cub. mm.; C.I., 1·25), and during remission (Hb, 96 per cent.; red cells, 4,440,000 per cub. mm.; C.I, 1·08). The latter shows persistent, but less marked, megalocytosis, and less anisocytosis with a less irregular cell-distribution curve (A. C. Hampson and J. W. Shackle).

average of 8·31 μ instead of between 4·75 μ and 9·5 μ with an average of 7·24 μ, as in healthy individuals. The irregular curves and the anisocytosis are, as Price-Jones points out, probably due to the presence of the three types of cells in the blood. (1) Large cells arising from abnormal stimulation of some parts of the marrow. These are the characteristic megalocytes, the abnormal stimulant being, I believe, the same toxin as that which causes the hæmolysis, or, at any rate,

one produced by the same intestinal infection. (2) Normal sized cells resulting from the normal activity of the healthy portions of the bone-marrow. (3) Small cells resulting from over-stimulation of the remaining part of the bone-marrow as a result of the anæmia caused by the abnormal destruction of red cells. These cells are identical with the microcytes present in the anæmia caused by hæmorrhage, which result in a low mean diameter of the cells in such cases.

Nucleated red corpuscles, and especially megaloblasts, which have generally been regarded as of great importance in diagnosis, are much less characteristic of the disease. They are never present throughout the illness, and very rarely either in the early stages, when diagnosis is most important, or during remissions. A prolonged search is often required to find a single megaloblast, and in some cases they are not discovered at all. The same is true of polychromasia and punctate basophilia. The presence of these abnormal types of corpuscle is evidence of an unusual degree of regenerative activity in the bone marrow in response to a toxæmia; they are consequently found in other severe toxic anæmias, such as lead poisoning.

In most cases the number of white corpuscles is reduced. This is due to diminution in the number of polymorphonuclear cells formed by the bone marrow, possibly owing to the over-growth of the red cell-producing tissue crowding out the leucocyte-producing tissue, which is, perhaps, also affected by the direct action of the toxins. The lymphocytes form in the lymphatic glands and elsewhere in normal numbers; consequently the leucopenia is accompanied by relative, though not absolute, lymphocytosis. Naegeli has drawn attention to the constant diminution in the numbers of hyaline cells. Eosinophil cells may also be reduced in number, and ½ to 1½ per cent. of the white cells may be myeloblasts. In a very severe and typical case under my care a large carbuncle developed. It was interesting to observe that the bone marrow was still able to respond to this stimulus, as a leucocytosis of 19,000 cells per cent. developed, with 39 per cent. polymorphonuclear cells, 15 per cent. large lymphocytes and 42 per cent. small lymphocytes.

Blood platelets are much reduced in number; clotting

is therefore slow, as thrombokinase is mainly derived from the platelets.

In the exceptional cases, in which an early diagnosis is made owing to the presence of subacute combined degeneration of the cord or of Hunter's glossitis suggesting the possibility of Addison's anæmia, or when the discovery of achlorhydria in a case of gastric or intestinal dyspepsia is followed as a routine measure by a complete blood examination, the blood-picture generally presents some at any rate of the features which are characteristic of the fully developed disease, even if the degree of anæmia is very slight or actually non-existent. The most important of these is the megalocytosis, which Price-Jones has shown is quite independent of the degree of anæmia.

Thus in one of my cases of subacute combined degeneration of the cord the patient had achlorhydria ; he did not look pale, and on December 12th, 1922, his red corpuscles numbered 5,600,000 per cubic millimetre, his hæmoglobin percentage being 83. But although the colour index was only 0·74, the average size of his red corpuscles was increased from the normal of 7·24 μ to 8·86 μ, and well-marked anisocytosis was present, the Price-Jones chart of his red cells being quite typical (Fig. 25). Nine weeks later, on February 25th, 1923, the hæmoglobin percentage had fallen to 46, and the red corpuscles count to 2,500,000 per cubic millimetre ; the serum was yellow, and van den Bergh's test, which was negative at first, gave an indirect positive reaction. After this, however, steady improvement occurred, and by April 8th the hæmoglobin percentage had risen to 86 and the red corpuscle count to 4,400,000 per cubic millimetre. This case is, however, unusual in showing such marked anisocytosis in the absence of anæmia, as Price-Jones has found that the anisocytosis generally varies with the percentage of hæmoglobin.

By examining the blood of every patient with achlorhydria, Schaumann discovered an early case, in which the hæmoglobin percentage was still 93. But the colour index was 1·6, megalocytes were present, and increased bile pigment was present in the blood. Three weeks later the hæmoglobin percentage had fallen to 67, and in four weeks

to 59, the colour index being 2·5 and 2·2 respectively. At the same time megaloblasts had appeared.

Sometimes Addison's anæmia appears to be preceded by anæmia of an ordinary non-megalocytic type. Thus Zadek [29] records the case of a man of twenty-six, with achlorhydria, who had 2,700,000 red corpuscles per cubic millimetre and

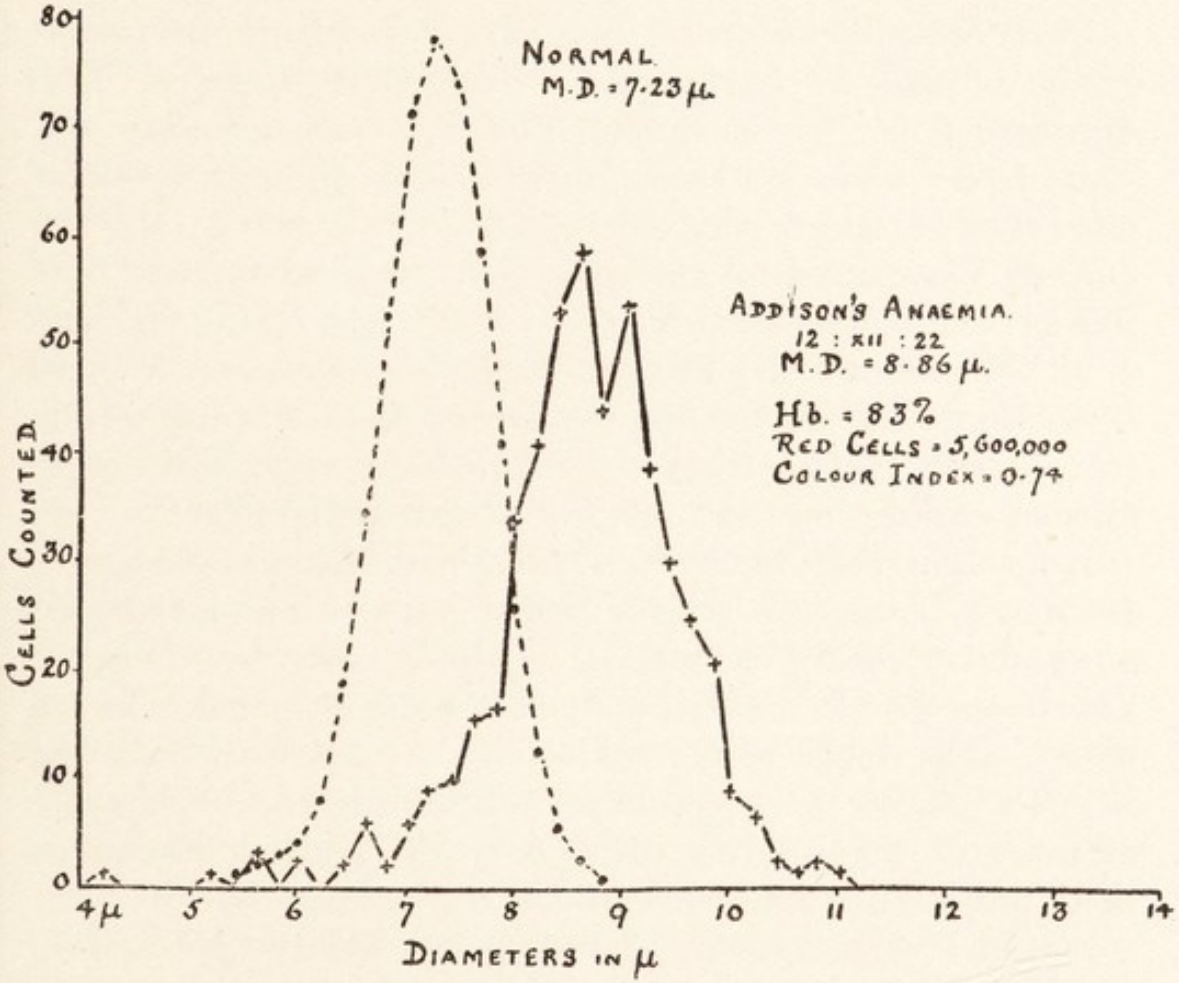


FIG. 25.—Subacute combined degeneration of the cord, with 5,600,000 red corpuscles per cub. mm., and colour index only 0·74, but the typical megalocytosis of Addison's anæmia. Complete achlorhydria was present (A. C. Hampson and J. W. Shackle).

40 per cent. hæmoglobin, the colour index being 0·74. There were no abnormal red cells, the blood-picture being thus quite definitely not that of Addison's anæmia. But nine months later the figures had fallen to 1,042,000 red corpuscles and 25 per cent. hæmoglobin, the colour index being now 1·25. The serum was gold yellow, and many normoblasts, megalocytes, microcytes and poikilocytes were present. The tongue was sore and the spleen enlarged. The case was now typically one of Addison's anæmia, which was

doubtless already present six months before, but at that time the bone marrow had not yet responded to the toxæmia which was causing the hæmolysis with the hyperchromatic anisocytotic reaction, which gives the characteristic blood-picture.

The Cause of the Anæmia

In 1876 Quincke discovered that the viscera contained excess of iron in fatal cases of Addison's anæmia. The significance of this remained, however, obscure until ten years later, when William Hunter began his long series of observations, which resulted in the definite proof that the anæmia was caused by excessive blood destruction, and that this led to the deposition of excess of iron-containing pigment in all the viscera. He found that the liver always contained more than the spleen, and concluded that the hæmolytic toxin was absorbed from the alimentary tract and consequently exerted its most marked action on the liver.

It has long been known that the blood serum in Addison's anæmia is definitely yellow, whilst that in non-hæmolytic anæmias is nearly colourless. Hijman van den Bergh [21] has shown that this colour is due to excess of bilirubin in the blood. The depth of the colour and the degree of van den Bergh's "indirect" reaction for bilirubin in the blood are a measure of the activity of hæmolysis. During remissions there may be no excess of bilirubin in the blood at all.

Ziegler [22] and Kanner [23] have shown that the production of bilirubin from hæmoglobin under normal conditions only takes place in the hepatic cells. From these some passes through the Kupfer's cells of the liver into the blood, any excess over that required to keep its concentration in the blood at the average normal point being excreted in the bile. In Addison's anæmia excessive hæmolysis occurs in the liver, and also in the spleen and possibly other situations. Consequently hyperbilirubinæmia results, and excess of bilirubin is found in the bile obtained through a duodenal tube (Gorke [24]); the quantity of stercobin excreted in the fæces in twenty-four hours is always excessive (Ryffel [25]) and may reach four times the normal (Eppinger and Chamass [26]). Just as the kidneys in diabetes do not excrete sugar until the

concentration in the blood has reached the leakage point, which is considerably higher than the normal concentration, so in the presence of excessive hæmolysis a considerable degree of hyperbilirubinæmia develops before the leakage point is reached and bile pigment appears in the urine. This only occurs in unusually acute hæmolytic crises, which are sometimes observed in the course of Addison's anæmia.

The characteristic lemon-colour of the skin in Addison's anæmia is a less intense yellow, and is of a different tinge to that of even very slight obstructive jaundice in spite of the high concentration of bilirubin in the blood. Only when the hyperbilirubinæmia exceeds the leakage point and bile appears in the urine in the acute hæmolytic crises just referred to does actual jaundice with discoloration of the conjunctivæ occur. Van den Bergh has shown that bilirubin is altered in certain of its properties after excretion in the bile, so that any bilirubin which is reabsorbed can be distinguished from that which has never left the blood stream. It is thus possible by means of van den Bergh's reaction to distinguish hyperbilirubinæmia caused by hæmolysis from that caused by reabsorption of bile in obstructive jaundice, even if the latter is so slight or the examination is made at such an early stage that no bile has yet appeared in the urine and jaundice has not developed. The lemon-yellow colour of the skin in Addison's anæmia is probably caused by staining with bilirubin, which has not yet undergone the changes in its characters which excretion into the bile brings about. Bilirubin reabsorbed after these changes have occurred leads to the skin and conjunctivæ becoming stained the familiar colour of ordinary jaundice.

Achlorhydria in Addison's Anæmia

Since 1886, when Cahn and von Mehring [27] first drew attention to the absence of free hydrochloric acid from the gastric contents in a case of Addison's anæmia, it has gradually become recognised that the association is almost, if not quite, invariable. Thus Ewald,[28] using the old-fashioned test-meal, found achlorhydria in every one of seventy-five cases; Zadek [29] obtained the same result in his fifty cases, and,

according to Weinberg [30], it was present in every one of the 105 cases of Addison's anæmia in Martius' Clinic at Rostock between 1900 and 1917. Levine and Ladd,[31] using an Ewald test-meal and obtaining samples of the gastric contents whilst fasting and every three-quarters of an hour afterwards, found free hydrochloric acid only three times in a series of 108 cases. In one of the exceptions the blood and symptoms were typical of Addison's anæmia and the diagnosis was confirmed post-mortem, but in the two others the diagnosis remained doubtful even at the autopsy.

Recent investigations with the fractional test-meal have shown that the absence of free hydrochloric acid invariably persists throughout the whole period of digestion. In other conditions, such as cancer of the stomach, it is not at all uncommon to find a small quantity of free acid and occasionally even a large quantity in one or more of the fractions, when the resting juice and the contents removed at the end of three-quarters of an hour or an hour, or both, contain none, but this is never the case in Addison's anæmia. Complete achlorhydria was present in every one of my twenty-two cases examined by the fractional method, as well as in every one of sixteen cases of subacute combined degeneration of the spinal cord.

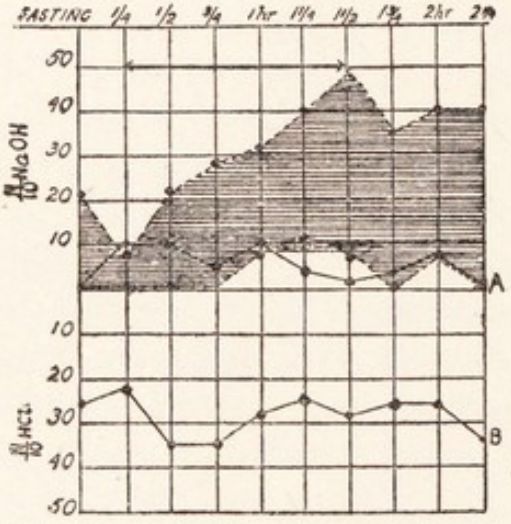


FIG. 26.—Fractional test-meal in case of Addison's anæmia. A = total acidity; B = amount of N/10 HCl required to produce free acid.

It is clear, therefore, that before a case can be diagnosed as Addison's anæmia in spite of the presence of free hydrochloric acid in the gastric contents, the clinical and pathological features must be subjected to special scrutiny. Thus the clinical history of the much-quoted case of Sophie Herzberg's,[32] in which free acid was said to have been present in a fatal case of Addison's anæmia, was not at all characteristic. The colour index was 0·8 on the only occasion when the hæmoglobin percentage and the number of red corpuscles were both estimated. The illness began in the middle of May, and the

leucocyte count steadily rose from 7,700 per cubic millimetre, when first enumerated on November 5th, to 14,000 on November 15th, and 70,000 on November 22nd, death occurring on November 27th. This high leucocytosis makes the diagnosis of Addison's anæmia extremely improbable. Herzberg's other six cases all had achlorhydria and leucopenia. In the only one of his thirty-five cases in which free hydrochloric acid was present, Faber [33] himself expressed doubt as to the accuracy of the diagnosis, the anæmia being not improbably really secondary to a severe hæmorrhage. Weinberg has reviewed all cases, in which sufficient clinical details were available, and in which Addison's disease was diagnosed in spite of the presence of free hydrochloric acid in the gastric contents, and concluded that in every instance the diagnosis was doubtful. The following case under my care, reported by J. W. Shackle, is of special interest from this point of view.

Fatal case of "idiopathic" hæmolytic anæmia with normal-sized red corpuscles and without achlorhydria.—Ellen C., aged sixty-one, was admitted into Guy's Hospital on October 13th, 1922. Three months before admission she became unable to walk even a short distance owing to increasing general weakness and shortness of breath.

On admission she was very weak and had a definitely lemon-yellow colour, which became more obvious the last few days of her life. The hæmoglobin percentage was 44 and the red cells numbered 1,769,000 per cubic millimetre, the colour index being 1·24. The leucocytes numbered 7,875 per cubic millimetre, and of these 78·7 per cent. were polymorphonuclear, 18·3 per cent. lymphocytes, 2 per cent. hyaline and 1 per cent. eosinophile cells. There was no anisocytosis or megalocytosis (Fig. 26A) and no nucleated red cells were seen, but poikilocytosis was present.

The tongue was clean and moist and had never been sore. The tonsils were not inflamed or enlarged; the teeth were carious, and there was some pyorrhœa. There were no digestive symptoms. The liver and spleen were somewhat enlarged. A test-meal showed the presence of free hydrochloric acid in the stomach.

The reflexes were normal, and there was no sign of degeneration of the central nervous system. No retinal

abnormality was observed. The Wassermann reaction was negative.

Van den Bergh's test for excess of bile pigment in the blood gave a negative direct reaction and a positive indirect

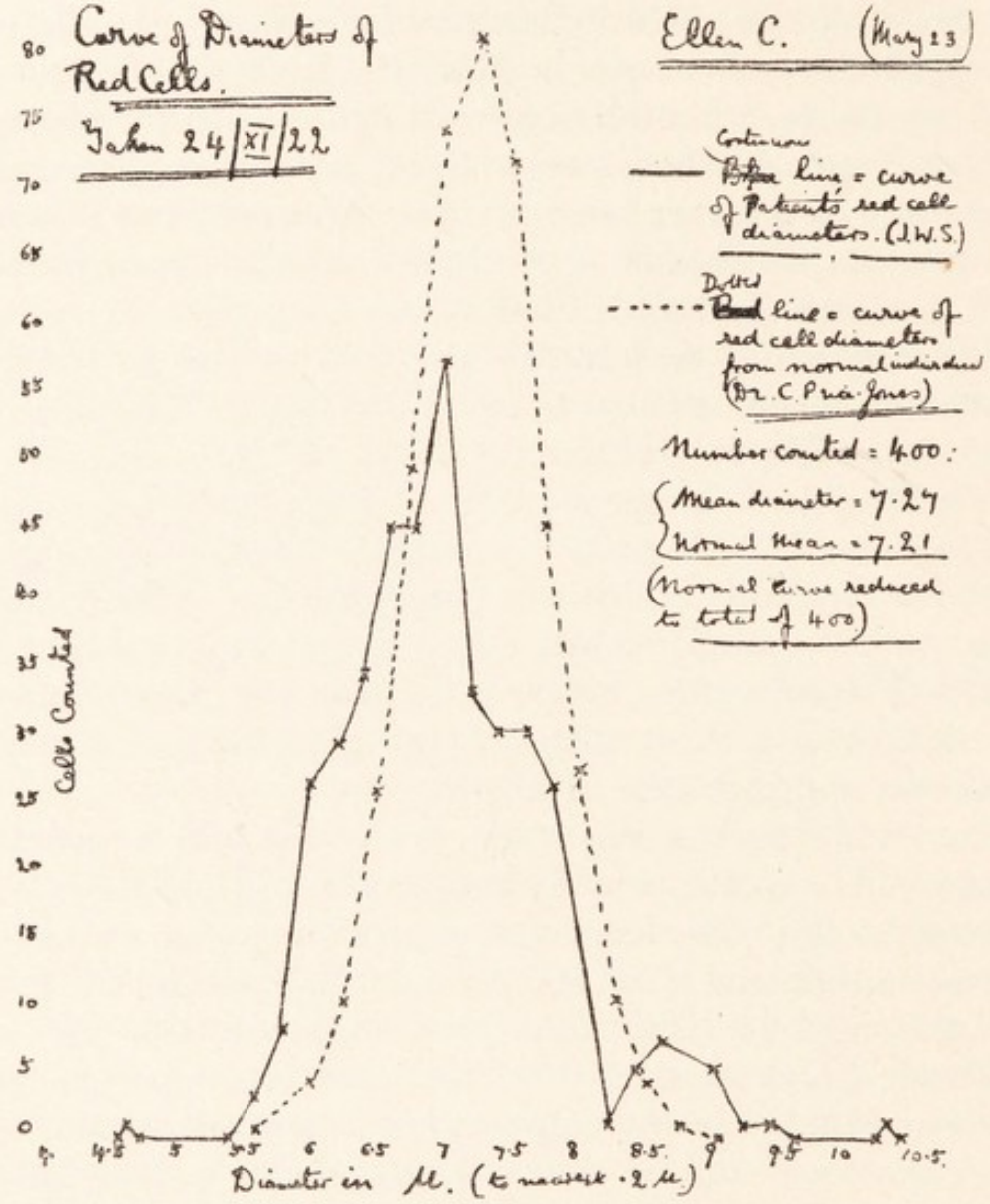


FIG. 26A.—Cell-distribution curve in a case of septic anæmia (J. W. Shackle).

one, indicating an excess caused by blood destruction and not biliary obstruction.

The temperature on admission was 98·8°, but from October 21st to November 4th pyrexia was present, the temperature rising on October 25th to 102°. On November 30th a second bout of pyrexia developed, which lasted till death on December 6th.

The post-mortem examination revealed no neoplasm or

septic focus of any kind. The heart showed evidence of fatty degeneration, but no signs of endocarditis. The liver was somewhat enlarged; both the liver and the kidneys gave the Prussian-blue reaction, though somewhat slowly. The spleen was slightly enlarged and was soft in consistence.

The bone marrow of the humerus was found to be converted into the "red currant jelly" type. A smear from it showed that the normal fat cells were largely replaced by masses of cells, a large percentage of which were normoblasts, there being also numerous neutrophil and eosinophil myelocytes.

The colour of the skin, which was definitely lemon-yellow during the last few days of life, the positive indirect van den Bergh's reaction, and the Prussian-blue staining of the liver and kidneys post-mortem, prove that the anæmia from which this patient died was hæmolytic in origin. As no other cause of death was found and the red marrow was greatly hypertrophied, the post-mortem examination would certainly point to Addison's anæmia as the diagnosis. But although the colour-index of the blood was high, the size of the red corpuscles, when accurately measured on two different occasions, differed so fundamentally from what Price-Jones has always found in Addison's anæmia that he came to the conclusion that the anæmia was undoubtedly not Addisonian. The constant absence of megaloblasts and the discovery of a very few normoblasts in only two of the numerous films examined pointed in the same direction. If the presence of hydrochloric acid in the gastric contents had been the only evidence against Addison's anæmia, it might have been regarded as proving that the rule that achlorhydria is always present is not absolute, but has very rare exceptions. When, however, it is associated with a blood-picture quite unlike that of Addison's anæmia, it can certainly be regarded as an additional strong argument against that diagnosis. The same may be said about the absence of soreness of the tongue and of nervous symptoms, though, as these are not present in more than about 80 per cent. of cases, neither by itself would be of great importance.

The unusually high pyrexia and terminal leucocytosis suggest the probability that the anæmia might have been secondary to a hæmolytic streptococcal septicæmia, which

would lead to post-mortem changes indistinguishable from those of Addison's anæmia. The case would then fall into the group of cases described by Hunter as "septic anæmia," a condition which he regards as quite distinct from Addison's anæmia.

Gastric analysis may give information of real help in diagnosis, the presence of free hydrochloric acid in any fraction of a test meal being a decisive point against the diagnosis of Addison's anæmia, whereas the discovery of achlorhydria would considerably strengthen the probability of such a diagnosis being correct. At the autopsies on the only cases in Campbell and Conybeare's Guy's series, in which a diagnosis of Addison's anæmia had been made in spite of the fact that free hydrochloric acid was present in the stomach, no evidence of hæmolysis was present; one patient was found to have infective endocarditis, and the other, who died of pneumonia, had the microscopical changes in the spleen typical of Hodgkin's disease.

In seven of Levine and Ladd's cases, in which the possibility of Addison's anæmia was considered but the diagnosis had finally to be rejected, five had free hydrochloric acid in the gastric contents; the remaining two were cases of bothriocephalus anæmia and sprue respectively, and in both of these diseases achlorhydria is known to be common.

There is abundant evidence that the achlorhydria precedes the development of the anæmia and is not secondary to it, as some authors have suggested. There is generally a more or less long history of digestive disturbance, of the type which may result from uncomplicated achlorhydria, preceding the first symptoms of anæmia. One of my patients, for example, had suffered for fourteen years from intractable diarrhœa, which completely stopped directly he was given hydrochloric acid after our diagnosis of Addison's anæmia had led to the discovery of his achlorhydria.

In a paper published in 1913 Faber [33] brought forward the first conclusive proof that the achlorhydria is primary and not a result of the anæmia. He described three cases, in which the blood was normal with a hæmoglobin percentage of 100, 95 and 90 respectively, when he discovered the

presence of achylia. Ten, seven and three years later typical Addison's anæmia began to develop. More recently he has published another case in which achylia had been found thirteen years before, and Bie [34] has reported one in which Faber had discovered achylia twelve years before the onset of anæmia. Since Faber's first publication, Cobet and Morawitz [35] have reported a case in which achylia was known to exist seven years before the anæmia; Kuttner,[36] one in which it had existed five years; Charles Hunter,[37] one in which it had existed two years; and Levine and Ladd, cases in which it had existed six years and one year respectively before the anæmia. Lastly, Dr. J. F. Wilkinson of Melbourne has told me of a case in which achylia was present ten years and another three years before the first symptoms of anæmia appeared.

If achlorhydria were secondary to the anæmia, or even if it were secondary to gastritis produced by the same toxin which caused the anæmia, cases would occur in which normal gastric secretion could be observed giving place to hypochlorhydria and finally to complete achlorhydria as the disease progressed. Such a sequence of events has been observed in cancer of the stomach and phthisis. Thus Permin [38] gave test-meals in 658 cases of phthisis, and found that achlorhydria was present in 23 per cent. in the first stage, 34 per cent. in the second, 47 per cent. in the third, and in 75 per cent. of those who died within six months of the examination. In contrast to cancer of the stomach and phthisis, achlorhydria is found in all cases of Addison's anæmia at whatever stage of the disease the examination is made, and no case has been recorded in which either a normal secretion or even hypochlorhydria has been discovered at one period and achlorhydria on a later occasion. It was present, for example, in early cases in which the hæmoglobin percentage had not fallen below 90, 85, 85 and 80. One is forced to conclude that the achlorhydria precedes the development of the anæmia.

The achlorhydria persists when the anæmia has almost or completely disappeared either spontaneously or as a result of treatment. Thus in three Guy's cases it was still present when the hæmoglobin percentage was 85, 82 and 80

respectively, compared with 45, 38 and 23 respectively some months or years before (Campbell and Conybeare [8]). Levine and Ladd [31] found it with the hæmoglobin at 82, 104, 85, 87, 88, 85 and 90, although at one time it had been 33, 35, 28, 35, 28, 22 and 48. Still more remarkable is the case of a man, who was in the London Hospital seventeen years ago for typical Addison's anæmia with 700,000 red corpuscles per cubic millimetre and complete achlorhydria. The achlorhydria is still present, though for years he has been perfectly well; when shown recently before the Medical Society of London by Maitland-Jones,[39] his red corpuscles numbered 5,200,000 per cubic millimetre. In a case of Zadek's [29] achlorhydria was present with a hæmoglobin percentage of 108, the red corpuscles numbering 5,402,000 per cubic millimetre, though at his worst, four years before, the figures had been 23 and 610,000 respectively.

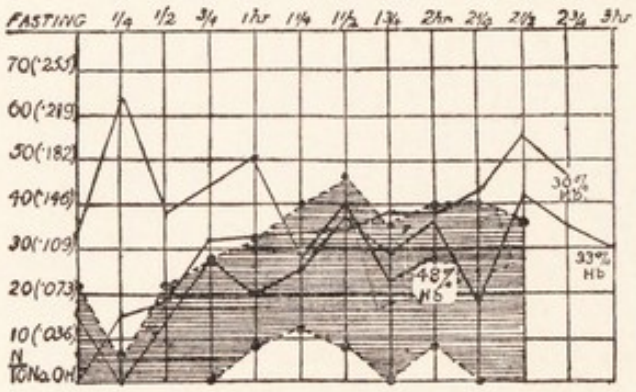


FIG. 27.—Curves of free HCl in cases of hæmorrhagic anæmia with hæmoglobin percentage of 30, 33 and 48 respectively.

The achlorhydria is thus far more constant than any other symptom, not excluding the anæmia. Even the anisocytosis and megalocytosis may in rare instances disappear completely during remissions and after apparent recovery, though the achlorhydria persists.

There is no constant change in the gastric secretion in any other form of anæmia. Thus fractional test meals in four consecutive cases of gastric or duodenal ulcer, complicated by severe secondary anæmia due to hæmorrhage, gave curves of exactly the same form as would have been expected in the absence of hæmorrhage; the percentage of hæmoglobin was 30, 33, 48 and 49, figures which are quite as low as one would expect to find in an average series of cases of Addison's anæmia when first examined (Fig. 27). In two cases recorded by Campbell and Conybeare [8] of hæmorrhagic anæmia caused by rectal hæmorrhage with a hæmoglobin percentage of 44 and 42 respectively, and in two cases of chlorosis with

a percentage of 25 and 48, the curves of gastric secretion were normal. Campbell and Conybeare also report a fatal case of Hodgkin's disease, in which the hæmoglobin percentage was 25 and 17 on two occasions three months and three weeks respectively before death ; a test-meal given the same day as the first count and again a week after the second showed that free hydrochloric acid was present, though in small quantities. It is obvious, therefore, that anæmia does not cause achlorhydria.

There is, I believe, nothing specific about the achlorhydria which is an essential predisposing cause of Addison's anæmia. It is in most cases caused by constitutional and congenital absence of gastric juice—achylia gastrica — in which no hydrochloric acid and very little or no pepsin are secreted, but it may also be caused by acquired achylia, and by any condition in which such acid as is secreted is at once completely neutralised.

(1) *Constitutional Achylia Gastrica and the Familial Occurrence of Addison's Anæmia*

In a monograph published in 1897 Martius [40] expressed the belief that the majority of cases of achylia gastrica are primary or constitutional, and that comparatively few cases are secondary to some local disease such as gastritis or cancer. The contrary view has been defended by Faber [33] of Copenhagen, who has repeatedly maintained that achylia is almost always secondary to chronic gastritis, and that no such condition as primary or constitutional achylia exists. In 1916 Martius returned to the subject and brought forward further evidence in favour of his view, about the correctness of which I do not think that there can now be any further doubt. Thus fragments of mucous membrane, which I have had removed during an operation for appendicitis in patients with achlorhydria, have generally looked perfectly normal and have always shown the usual number of healthy living oxyntic cells.

Constitutional achlorhydria is probably due to an inborn deficiency in the functional capacity of structurally normal gastric glands. In favour of this view is its occurrence in

different members of the same family. Thus Albu [41] discovered it seven times in more than one member of a family. It was the cause of chronic diarrhœa in a woman, whose son, aged seventeen, and daughter, aged fourteen, were both found by Udaondo [42] to have achylia as well, although they had no digestive or other symptoms. Jung [43] found it, associated with absence of ferments, in a brother and sister ; the former had no symptoms, but the latter had suffered from dyspepsia for years. It was present in both of two sisters, who consulted me at different times for slight digestive symptoms ; their brother had a normal curve of acidity.

There is some evidence to show that the constitutional incapacity of the gastric glands to secrete hydrochloric acid is congenital. Thus it was already present in 4 per cent. of the 100 medical students examined by Bennet and Ryle,[44] the age of the majority being about nineteen or twenty. Albu has observed achylia gastrica in thirty-one children less than ten years old, the youngest being only four, and among the families of patients with Addison's anæmia examined by Weinberg [30] were children aged three, four, five, six and ten (two) with achylia. The children in Albu's series had been brought to him on account of anorexia, feeble development or diarrhœa. In one of them achlorhydria was still present when he was examined seventeen years later. On the other hand, the children examined by Weinberg were quite healthy, and their gastric secretion was only investigated because one or other parent had Addison's anæmia and achlorhydria.

Congenital achylia gastrica is undoubtedly the inherited factor in the cases of familial Addison's anæmia, which have been recorded with increasing frequency since Gulland [45] first drew attention to the subject in 1907. He referred to three fatal cases occurring in middle life, the father of each patient having died of the same disease. In a later publication with Goodall,[46] he states that " it is quite common to get a history of one other case in a family. In one of our cases the patient's father, paternal uncle, brother and sister had all died of the disease ; in another, the patient's father, uncle and sister had died of it." In 1910 Gilbert and Weil [47]

described the case of two brothers, aged forty-five and forty-two, who died of Addison's anæmia. The following year Patek [48] described a family in which two brothers, aged thirty-five and forty-two, a sister, aged forty-five, a female cousin on the paternal side and probably a paternal uncle died of Addison's anæmia. In every case the blood-picture was typical, and in the only one in which a post-mortem was performed the diagnosis was confirmed. The two remaining sisters in the family had suffered from moderately severe anæmia of a secondary type. Dr. Patek informs me that they are now in 1923 quite well, but the grown-up daughter of one of them has developed anæmia of a secondary type.

Bartlett [49] in 1913 recounted the history of a family living in Vermont, in which the father died at forty and a son at twenty-four from anæmia, but there was no blood examination. As no other obvious cause of death was found post-mortem, it seems quite likely that their deaths were due to Addison's anæmia. Two other sons out of a total of five children died at the age of thirty-five of typical Addison's anæmia with sore tongue and digestive symptoms, the diagnosis being confirmed hæmatologically and by post-mortem examination.

In 1913 Matthes [50] reported the occurrence of three cases in one family, and in 1914 Roth [51] described the case of two brothers who died of Addison's anæmia, one at the age of forty-five, the other at fifty-nine. In 1922 Faber [33] described the case of a man with Addison's anæmia, whose three uncles had died of the same disease.

Levine and Ladd [31] investigated the family history of 143 cases diagnosed as pernicious anæmia at the Peter Bent Brigham Hospital in Boston and obtained a definite history of the disease in other members of the family nine times, or in 6·3 per cent. of cases ; in two others there was a family history of fatal anæmia of uncertain nature, and in forty-one a history of cancer or tuberculosis or both, either of which may possibly have been diagnosed in some instances erroneously when Addison's anæmia was really present. In Cabot's [52] series of cases the disease occurred once in two sisters and once in a brother and sister.

Schauman [53] has seen seven examples in Finland of two

or more members of the same family who suffered from Addison's anæmia in the absence of all evidence of bothriocephalus infection. A remarkable family history was described in 1922 by Mustelin,[54] a former assistant of Schauman's, in which a woman of sixty-nine, her daughter of forty-four, and the latter's daughter of twenty-five, all came under his observation with complete achlorhydria and the typical blood-picture and tongue of Addison's anæmia.

Hastings Gilford [55] has recently recorded the case of a woman of sixty-five who died of Addison's anæmia ; two of her first cousins were said to have died from the same disease. Twelve years before he had observed a brother of twenty-six and a sister of twenty, in a family of ten brothers and sisters, who died of Addison's anæmia, from which an uncle of sixty-three had also died ; since then another brother had died at the age of thirty-five from the same disease. Dr. T. Houston of Belfast tells me he has seen a number of examples of familial Addison's anæmia. In one family the father, son and two daughters died of the disease ; the daughters, who were typical cases, were actually examined by him. Three sisters of one family and two brothers of another, who were all seen by him, died of typical Addison's anæmia. Tscherning [56] has recorded the cases of a man of fifty-eight, his brother of fifty, and their sister of forty-eight, who all suffered from Addison's anæmia. He also refers to Klein's account of three cases in a family. Decastello [57] records the histories of three sisters and their brother, who all died from rapidly fatal Addison's anæmia, the diagnosis being confirmed in two of them by autopsies.

Minot [58] has recorded a remarkable family, in which a brother and two sisters died of Addison's anæmia between the ages of sixty-one and sixty-three. An uncle, an aunt and a male cousin on their mother's side died of the same condition.

Panton, Maitland-Jones and Riddoch[59] have described the case of a man with an unusually chronic form of Addison's anæmia, associated with achlorhydria and a typical blood-picture. One of his mother's two brothers and one of her five sisters died of the same disease, and another of the sisters had an enlarged spleen, was yellow, and died at an early age.

I have myself seen a typical case of Addison's anæmia in a woman of thirty, whose mother died of the same disease.

Still more important are the cases in which various members of the family of a patient with Addison's anæmia are found to have achlorhydria, though apparently in perfect health. Martius [40] found achlorhydria in the three children of a man who died of Addison's anæmia, and in the only child, a boy of ten, of another man who died of the disease. The three-year-old daughter of a third patient had achlorhydria, whilst her eight-year-old sister had hypochlorhydria. His assistant, Queckenstedt,[60] found that one of the four children of a patient who died of Addison's anæmia had achylia and the other three hypochlorhydria. Weinberg has since examined the gastric contents of twenty-two children and two sisters of twelve patients with Addison's anæmia and achylia gastrica in Martius's Clinic. Nine of the children and one sister of seven of the twelve patients had achylia. The most striking history was that of a man with Addison's anæmia, who had four children ; of these a boy of ten, a boy of six and a girl of four had achylia. At this early age it is obvious that the abnormality must have been constitutional and congenital and not acquired. In another case a daughter of thirty-four and a son of thirty-one had achlorhydria, the third child, a daughter of thirty, having normal gastric acidity. Among Schauman's seven examples of Addison's anæmia occurring in more than one member of a family was one in which a woman, her mother and sister and the latter's daughter suffered from Addison's anæmia, whilst another sister had achylia gastrica but no anæmia. Faber [33] records a fatal case of Addison's anæmia in a man whose father had died of the same disease. Both his sister and he had achylia ; the sister suffered from severe non-Addisonian anæmia, from which she completely recovered.

A lady of fifty-four recently came under my observation for pyelitis. Hearing that her sister had died at the age of thirty-six of Addison's anæmia, we gave her a fractional test-meal, although she had never had digestive symptoms except a prolonged attack of diarrhœa some years before. We found she had complete achylia. This was doubtless a familial abnormality, predisposing to Addison's anæmia in

her sister and perhaps to the diarrhœa in herself. The daughter of a man with Addison's anæmia, who consulted me on account of diarrhœa and general unfitness, was found to have achlorhydria, but no blood abnormality. On the other hand, the daughter of another man and the daughter of a woman, who both died of Addison's anæmia, had normal gastric acidity.

The majority of people with constitutional achylia gastrica are probably none the worse for it, beyond being subject to attacks of indigestion, and especially nausea and diarrhœa, which quickly improve with the administration of dilute hydrochloric acid. Some probably pass through life without even suffering from these comparatively slight symptoms. In others the achylia probably predisposes to the development of cholecystitis, pancreatitis, appendicitis and rheumatoid arthritis. In a small proportion of cases the other factors appear which lead to the development of Addison's anæmia.

According to the statistics of the Registrar-General for 1921, about 9,000 per million of the population in Great Britain over the age of twenty die annually, and of these sixty-five, or 0·7 per cent., die of Addison's anæmia. The number of cases erroneously diagnosed as Addison's anæmia is probably no greater than that of cases in which the disease is mistaken for some other condition such as cancer. If it be accepted that about 4 per cent. of all adults have constitutional achylia, it is also presumably present in 4 per cent. of those who die. As the proportion of cases in which the achlorhydria, which is followed by Addison's anæmia, is acquired and not constitutional is probably very small, it follows from these statistics that about one in six, or 16 per cent., of individuals with constitutional achylia ultimately develop Addison's anæmia.

Addison's anæmia was present in twenty-two, or 11 per cent., of 207 cases of achylia gastrica, excluding cancer and phthisis, examined by Faber. In addition to these, fifteen had a hæmoglobin percentage between 65 and 80, and twenty-two below 65, making a total of 18 per cent. with anæmia of a non-megalocytic type. Weinberg found that, apart from cases of actual anæmia, a small proportion of

patients with achlorhydria and normal or slightly supra-normal hæmoglobin had a slight reduction in the number of red corpuscles, so that the colour index was over 1, and many megalocytes, with very slight poikilocytosis and occasionally even a few normoblasts. This may represent the earliest stage of Addison's anæmia, and such cases may perhaps be regarded as examples of a latent form of the disease, from which at any moment the fully-developed condition may develop.

(2) *Chronic Gastritis and Atrophy of the Gastric Mucous Membrane, and their Connection with Achlorhydria and Addison's Anæmia.*

Samuel Fenwick [61] in 1877 observed that the mucous membrane of the stomach was markedly atrophied post-mortem in some cases of Addison's anæmia. A similar atrophy was observed in five cases of cancer of the stomach and in sixteen out of fifty-five cases of cancer in other situations. He thought it possible that some cases of Addison's anæmia might be caused by the imperfect secretion of the gastric juice, which he concluded would result from atrophy, but in the majority of cases no such atrophy was present. Austin Flint had already in 1860 suggested that the disease might be due to "degenerative disease of the glandular tubuli of the stomach," resulting in such a reduction of the amount of gastric juice that the assimilation of food becomes inadequate to the wants of the body. In my lecture on gastric diatheses I showed that the changes described by Fenwick, and in later years studied in greater detail by Faber and others, are really secondary to the mechanical and chemical irritation which is the natural sequel of constitutional achylia gastrica (p. 44). They have thus no direct relationship with Addison's anæmia.

(3) *The Achlorhydria of Alcoholic Gastritis and Cirrhosis of the Liver*

I have seen one case of alcoholic cirrhosis of the liver associated with Addison's anæmia. The patient had symptoms of chronic gastritis, and a fractional test-meal showed

that complete achlorhydria was present. A similar case, in which the existence of cirrhosis of the liver and Addison's anæmia was confirmed post-mortem, was reported by Roth [51] in 1914. In my experience cirrhosis of the liver is generally accompanied by complete achlorhydria, secondary in all probability to alcoholic gastritis, as I have watched the return of a normal curve of secretion during treatment by careful dieting and complete abstention from alcohol. It is probable, therefore, that when Addison's anæmia develops in a patient with alcoholic cirrhosis of the liver, the achlorhydria, which is an essential factor for its development, is secondary to the alcoholic gastritis and is not primary and constitutional. If the patient could be persuaded to abstain permanently from all alcoholic drinks, the return of normal gastric acidity would render the prognosis unusually hopeful.

(4) *Achlorhydria following Gastro-enterostomy and Gastrectomy*

In one of Campbell and Conybeare's Guy's series of cases Addison's anæmia followed the performance of a gastro-enterostomy, and Sir William Willcox tells me that he has observed a precisely similar case. Except when performed for duodenal ulcer, this operation is frequently followed by complete achlorhydria, owing to the rapid drainage of the stomach and the neutralisation of the gastric juice by the alkaline fluids entering through the stoma from the proximal loop of jejunum (Fig. 12, p. 27) (Conybeare [62]). Achlorhydria acquired in this way probably provided the essential predisposing cause for the development of the anæmia.

Hartman [63] records the case of a man, fifty-eight years old, who had his whole stomach excised by W. J. Mayo for carcinoma. At that time his red corpuscle count was 5,520,000 per cubic millimetre. He did very well for about a year, but then became progressively weaker and more anæmic. Twenty months after the operation his red corpuscles numbered 2,000,000 per cubic millimetre, the hæmoglobin percentage was 53, and the colour index 1·3; there was slight anisocytosis and poikilocytosis. A year later he was still weaker, and his blood showed similar but

more severe changes. This patient, within two years of being completely deprived of gastric juice by the removal of his stomach, had thus developed the blood-picture of Addison's anæmia, which Hartman also regards as invariably associated with achlorhydria. He suggests that the characteristic picture of Addison's anæmia might have been discovered, if a blood examination had been performed on Moynihan's [64] patient, who died from severe anæmia of less than twelve months' duration three years and eight months after complete gastrectomy for cancer without any abnormality being found at the autopsy. Dr. J. R. Bell tells me of three other cases of Addison's anæmia, which followed the artificial achylia produced by total gastrectomy performed for cancer in Vienna.

(5) *The Achlorhydria of Cancer of the Stomach*

In 50 per cent. of cases of cancer of the stomach complete achlorhydria is found with the fractional test-meal, and oral sepsis is, of course, not uncommon in this disease. The conditions required for the development of Addison's anæmia and subacute combined degeneration of the cord may therefore be present in cancer of the stomach, as in the following case of mine, recorded by R. L. Wakefield.

Addison's anæmia with subacute combined degeneration of the spinal cord secondary to cancer of the stomach.—A man, aged fifty-two, was admitted into Addison Ward on August 3rd, 1922, for progressive weakness in the legs and arms, and pains in the chest and abdomen. In October, 1921, he had begun to have a sensation of " pins and needles " in his hands and forearms, and he found that his limbs were getting weak. In December he began to get indigestion with pain from one and a half to two hours after meals. The pain was partially relieved by food and extended over the whole of the abdomen and chest. The bowels at this time acted normally. He vomited occasionally and twice noticed a little blood in the vomited material.

In June, 1922, the weakness and " pins and needles," which had been almost confined to the upper limbs, now appeared in his feet and legs. There was also some unsteadi-

ness in walking. He found that exertion gave him pain in the region of his heart and made him short of breath. Between June and his admission in August his weakness became more marked, and for some months he steadily lost weight. Since March, 1922, his tongue had been painful and ulcerated.

On admission the patient's complexion was a pale lemon-yellow colour. His cranial nerves showed no abnormality. His knee jerks and ankle jerks were normal and equal ; the plantar reflexes were extensor. The abdominal reflexes were difficult to obtain. Vibration sense was absent in the left leg and diminished in the right. The " shooting test " was performed badly with the right fingers and left toes. There was no astereognosis. The patient could differentiate hot from cold tubes, but pin-pricks and the touch of a blunt object on the fingers seemed to him the same. He was able to appreciate the touch of cotton wool everywhere except on the soles of his feet. His muscles were flabby and feeble, but his grip was fairly strong. The blood and cerebro-spinal fluid gave a negative Wassermann reaction, and the latter contained no excess of cells.

His tongue was fissured and sore, and several small ulcers were present. His teeth were very septic, and there was universal severe pyorrhœa alveolaris. The tonsils were normal.

A fractional test-meal showed complete achlorhydria with blood, pus and mucus in each specimen ; the gastric contents had a very foul smell. The x-rays showed a hypertonic rapidly emptying stomach with no irregularity in outline. The fæces gave a strong guaiac test and a well-marked hæmatoporphyrin spectrum. A doubtful tumour was felt high up in the epigastrium. The spleen was enlarged and firm. The liver was slightly enlarged. The urine was dark in colour and contained no abnormal constituents. The bowels were regular. The systolic blood pressure was 88 mm. Hg. and the diastolic 55 mm. Hg. The heart was normal.

The following table shows the number of red and white corpuscles, hæmoglobin percentage and colour index at different dates.

Date.	Hæmoglobin percentage.	Red Cells, per cub. mm.	Colour Index.	White Cells, per cub. mm.
14.9.22	31	1,500,000	1·03	4,700
18.9.22	24	—	—	—
20.9.22†	30	1,250,000	1·2	5,330
25.9.22†	32	—	—	—
29.9.22	20	1,200,000	0·83	4,675
30.9.22	36	—	—	—
5.10.22	20	—	—	—
19.10.22	30	1,300,000	1·15	—
21.10.22	28	—	—	—
	25	—	—	—
23.10.22†	36	—	—	—
	35	1,500,000	1·16	—

† After transfusion.

On October 9th Dr. Price-Jones reported that the blood film presented the typical picture of Addison's anæmia. A transfusion was performed on September 18th and 23rd and on October 21st.

A diagnosis of subacute combined degeneration of the cord with Addison's anæmia and hæmorrhagic gastritis or possibly carcinoma of the stomach was made. As no improvement followed removal of the septic foci in the mouth, the administration of hydrochloric acid and arsenic, and transfusion repeated on two occasions, Mr. R. P. Rowlands was asked to operate on October 24th in order to remove the spleen if no growth was found. A large inoperable neoplasm was, however, discovered in the cardiac half of the stomach with large and hard glands near the lesser curvature, and there was pus in the peritoneal cavity. The patient died ten days later.

At the post-mortem the heart was surrounded by a great deal of bright yellow fat. The stomach showed a large fungating mass occupying more than half of the mucous surface. Many hard nodular glands were found on the greater and lesser curvature. The liver showed one nodular lump on its surface, and the pancreas contained several secondary deposits. The spleen was soft and enlarged, 18 cm. long, with its capsule thickened. The ribs on section showed an extraordinary development of the red marrow. None of the viscera gave a definite Prussian-blue reaction.

Dr. C. P. Symonds found the typical changes of subacute combined degeneration in the spinal cord.

Clinically there seemed no doubt that this was a case of Addison's anæmia. The patient had the characteristic lemon-yellow colour, his blood-picture was typical, he had a sore tongue, van den Bergh's test gave an indirect positive reaction, complete achlorhydria was present, and he showed well-marked symptoms and signs of subacute combined degeneration of the spinal cord. The only unusual feature of the case was the presence of a considerable quantity of blood in each fraction of the test-meal on both occasions on which one was given. I have never before seen such an occurrence in Addison's anæmia. One possible explanation was that the chronic gastritis, which is frequently associated with the achlorhydria, had taken on an acuter hæmorrhagic form. Another possibility was that this case was an example of the condition, which J. R. Bell and I had been led to anticipate might occur from our investigations on the pathogenesis of subacute combined degeneration of the cord, the results of which were about to be published in *Brain* [72] at the moment when this patient came under my observation. We had shown that this disease is always associated with achlorhydria, which we regarded as the essential predisposing cause both of the nervous degeneration and of the Addisonian anæmia which probably always accompanies it. We had failed to discover any report of an actual case of cancer of the stomach associated with subacute combined degeneration of the cord, although several writers had referred to the occurrence of such an association as an alternative to the more common one with Addison's anæmia. We suggested that, should future observations definitely prove the existence of this association, it would probably be found only to occur among the 50 per cent. of cases of cancer of the stomach, in which complete achlorhydria is present throughout the period of digestion.

In this case the presence of a severe anæmia was as obvious as that of subacute combined degeneration of the cord, and the anæmia was certainly of the Addisonian type, and not of the secondary type commonly seen in cancer of the stomach. There is no reason why the existence of cancer

of the stomach should exclude the possibility of Addison's anæmia being also present, and the discovery of a growth of the stomach at the exploratory operation and its confirmation after death in a patient with Addison's anæmia and subacute combined degeneration of the cord simply confirm what we had regarded from purely theoretical considerations as a rare but quite possible association.

It will in the future be of great interest to examine the blood of patients with inoperable cancer of the stomach in order to see how often during the last stage an Addisonian type of anæmia is added to the earlier secondary anæmia, whether this only occurs when achlorhydria is present, and whether under these conditions any signs or symptoms of subacute combined degeneration of the cord can be discovered. It is only natural that both the anæmia and nerve signs should escape observation in the large majority of cases, as when the diagnosis of inoperable cancer has once been accepted it is not likely that careful hæmatological and neurological investigations will continue to be made.

Degeneration of the Spinal Cord in Addison's Anæmia

Lichtheim[65] in 1887 described three cases of Addison's anæmia with spinal cord symptoms. A post-mortem performed on two of them showed degeneration of the posterior and lateral columns. His clinical and pathological observations were soon confirmed by Minnich [66] and Nonne [67]; the latter author before long came to the conclusion that his original idea that the degeneration of the spinal cord was secondary to the anæmia must be incorrect, and that both conditions were the result of some chronic intoxication.

In the last twenty-five years spinal cord symptoms have been recognised in Addison's anæmia with increasing frequency as they have become more systematically looked for. Thus in 1918 Woltmann [68] found "indisputable evidence of the destruction of nervous parenchyma" in 80·6 per cent. of 150 cases which were subjected to a detailed neurological examination at the Mayo Clinic. This corresponds closely with my own experience and with the figures

obtained by Minnich, who discovered degenerative changes in 77 per cent. of the spinal cords of a consecutive series of fatal cases of "pernicious" anæmia.

I believe that no definite line can be drawn between Addison's anæmia accompanied by changes in the spinal cord and subacute combined degeneration of the cord accompanied by anæmia. The difference is simply one of degree and depends upon whether a hæmolysin or a neurotoxin is the more active. If either toxin is first produced alone, there is more time for it to give rise to marked changes; thus when Addison's anæmia is rapidly fatal, there may be no time for nervous symptoms to develop, or, if they do develop, they may be trivial in comparison with those observed in cases in which the nervous degeneration has progressed for many months without any anæmia. There appears to be no essential difference between the clinical symptoms or the pathological changes in the spinal cord except in their severity, whether the nervous degeneration or the anæmia predominates.

Nature of the Anæmia Associated with Subacute Combined Degeneration of the Spinal Cord

In some of the nine cases, reported by Risien Russell, Batten and Collier [69] in 1900 in their classical description of subacute combined degeneration of the cord, no anæmia was recognised throughout the disease; in others it developed towards the end, whilst in others it preceded the manifestation of nervous symptoms by many months. But repeated examinations of the blood "failed to reveal the alterations found in pernicious anæmia," the changes being those "characteristic of secondary anæmia." The red corpuscles were generally normal in shape, nucleated cells were only found in one case in very small numbers, and no megaloblasts or microblasts were present.

In 1904, however, Byrom Bramwell [70] described a case in which the nervous symptoms developed three years before the anæmia was obvious, but the blood finally presented all the typical features of Addison's anæmia. After death excess of iron was found in the liver, and there was a great

increase in the red bone marrow; the spinal cord changes were typical of subacute combined degeneration. Eleven years later he brought forward further evidence pointing to the anæmia being of the Addisonian variety in subacute combined degeneration of the cord, even when it did not at first conform to type. In one case rapid changes occurred in the blood during the last fortnight of life, the colour index slowly rising in consecutive investigations from 0·8 to 2·3.

In his latest article on the subject, published in 1921, Collier [71] came to conclusions entirely different from those in his earlier writings. He states that a careful investigation of the blood changes at various stages of the disease and of the post-mortem findings in a large series of cases has proved beyond any possible doubt that the blood changes in every case are identical with those that are met with in the various stages of Addison's anæmia, and that the typical post-mortem picture of the disease occurs quite frequently in subacute combined degeneration.

Our experience entirely agrees with that of Bramwell and Collier. The anomalous results obtained on examination of the blood in many cases are due to the fact that the blood-picture, which is generally regarded as characteristic of Addison's anæmia, is only present when the anæmia has attained a moderately severe degree. In the early stage, in which a diagnosis is rarely made in uncomplicated cases of Addison's anæmia, but is that which is most frequently present when a case of subacute combined degeneration first comes under observation, the colour index is often under 1, and nucleated red corpuscles are rarely seen. But in all but two of our cases megalocytosis and anisocytosis were present, and Price-Jones's curve was typical of Addison's anæmia whenever it was charted. Moreover, the blood serum was abnormally pigmented, and van den Bergh's indirect reaction for bilirubin was positive. The two exceptions were early cases, and, as thorough treatment was at once instituted, it may be hoped that a hæmolysin will never be formed in sufficient quantity to cause anæmia.

The lemon-yellow colour, which Collier observed in many cases before he came to the conclusion that the anæmia was of the "pernicious" type, and which has been present in

most of our cases, affords just as good evidence of hæmolysis as the Prussian-blue reaction obtained in the liver and other organs after death. This reaction, although present in almost all cases of typical Addison's anæmia, cannot always be obtained in subacute combined degeneration, because the blood destruction has not been sufficiently severe and prolonged.

Achlorhydria in Subacute Combined Degeneration of the Cord

I have had the opportunity of investigating sixteen cases of typical subacute combined degeneration of the cord, the first ten in association with J. R. Bell,[72] by the fractional method of gastric analysis. In all of the sixteen free hydrochloric acid was completely absent throughout the period of digestion. The test was repeated in three of the cases with the same result.

As long ago as 1898 Faber [73] had observed a case in which an ordinary test breakfast showed achylia; the nervous symptoms had preceded the onset of typical Addison's anæmia by several months. In 1919 Barker [74] found complete achlorhydria in two cases, presumably after an ordinary one-hour test-meal. Quite recently Vanderhof [75] of Richmond, Virginia, has published valuable confirmation of our results. He found complete achlorhydria in every one of twenty-nine cases of subacute degeneration of the spinal cord which he had the opportunity of investigating. Dr. J. F. Wilkinson tells me that he discovered achlorhydria in a patient who consulted him for digestive symptoms a year before the first signs of subacute combined degeneration of the cord appeared, and Szlapka [76] has recently described a similar case in which the interval was two years.

For purposes of control gastric analyses were made by J. R. Bell in a series of typical cases of disseminated sclerosis and tabes dorsalis. In ten consecutive cases of disseminated sclerosis achlorhydria was never found, the curves of acidity being the same as would be likely to occur in a series of ten normal people. Of eleven consecutive cases of tabes dorsalis one was found to have achlorhydria; the remainder

had curves which fell within normal limits, though in three cases it was somewhat high. As 4 per cent. of normal individuals have achlorhydria, the single case in this series is probably of no importance (Table I.).

TABLE I.

Relative Frequency of Achlorhydria (tested by fractional method) in Various Conditions

	Number of Cases.	Achlorhydria.		Low Acidity.	"Normal" Acidity.	High Acidity.
		Number.	Percentage.			
Normal (Bennett and Ryle) . . .	100	4	4	1	87	8
Various medical diseases (New Lodge Clinic and Guy's) . . .	762	86	15	81 (10·6 per cent.)	405 (53·1 per cent.)	166 (21·3 per cent.)
Carcinoma of the stomach	23	13	56·5	6	4	0
Addison's (pernicious) anæmia . . .	24	24	100	0	0	0
Subacute combined degeneration of the cord	16	16	100	0	0	0
Tabes dorsalis . .	13	1	7·7	4	5	3
Disseminated sclerosis .	10	0	0	2	7	1

The diagnosis may be greatly helped by gastric analysis. The presence of free hydrochloric acid in any fraction of a test-meal is a very strong point against the diagnosis of subacute combined degeneration, whereas the discovery of achlorhydria greatly strengthens the probability of such a diagnosis being correct. In three recent cases, which presented features very suggestive of subacute combined degeneration, a normal curve of gastric acidity was discovered. Each eventually proved to be suffering from syphilitic disease of the spinal cord.

It is interesting to note that cases of subacute combined degeneration occur with a family history of Addison's anæmia. Thus the father, paternal grandfather, paternal uncle and brother of a male patient of mine with subacute combined degeneration of the cord and achlorhydria, who died of typical Addison's anæmia, also died of Addison's anæmia, but fortunately his three children had normal gastric secretion, so that there is no reason why they should inherit the disease. The grandfather of a man of forty-three, suffering from subacute combined degeneration of the cord

and achlorhydria but no anæmia, died of Addison's anæmia, and Willson [77] has recorded the case of a woman with subacute combined degeneration of the cord whose two maternal aunts died of Addison's anæmia.

Oral Sepsis and Glossitis in Addison's Anæmia

In 1900 Hunter introduced the now familiar term "oral sepsis" to describe the infective condition of the mouth, which is an undoubted factor in the pathogenesis of numerous diseases, and demonstrated for the first time the extreme importance of its association with Addison's anæmia. Improved methods of investigation and especially radiography have only confirmed the views he expressed nearly a quarter of a century ago. It has sometimes been said that the occurrence of Addison's anæmia in edentulous patients proves that the association with oral sepsis is not invariable, but the vast majority of edentulous patients are only edentulous because they have had severe oral sepsis, and the latter may have laid the foundations of the disease before the teeth were extracted, even if a considerable interval elapsed before its presence became obvious. Moreover, there are other sources of sepsis, such as the tonsils and nasal sinuses, which may in exceptional cases provide an alternative primary focus of infection. I have never myself seen a case of Addison's anæmia or subacute combined degeneration of the cord, in which definite evidence of oral and in exceptional cases pharyngeal sepsis could not be found on careful investigation.

The sore tongue, which is now widely recognised as a very common symptom of Addison's anæmia, was first observed by Barclay in a case he reported in 1851, two years after the publication of Addison's earliest description of the disease. No further notice was taken of this symptom, however, until William Hunter described it in 1889, and in the thirty-four years which have since elapsed he has repeatedly directed attention to it as an essential feature of the disease, which he has seen in every case—150 or more—of which he has full records.

Most other observers have not found the sore tongue with such remarkable constancy. Thus Levine and Ladd saw the typical tongue in eighty-two and a suggestive appearance in twenty-four of their 143 cases of Addison's anæmia, making

a total of 83 per cent., but this percentage would probably have been considerably increased if every case had been watched from the onset until the end. I have, however, myself certainly seen more than one fatal case, in which a sore tongue had never been present, and in which the appearance of the tongue remained perfectly normal throughout the illness.

Hunter believes that the characteristic glossitis is not produced by ordinary oral sepsis, but that when once it is contracted it is greatly aggravated by infection spreading from septic teeth to the neighbouring part of the tongue. The glossitis may be the focus, from which the intestines are subsequently infected if the teeth are removed before the disease has developed, as there is often a history of recurrent attacks of soreness of the tongue before the onset of symptoms due to the anæmia. Thus in two patients of Schauman's the glossitis preceded the discovery of anæmia by five and ten years respectively.

The patient complains of soreness of the tongue, which is increased by highly seasoned food and by hot food and fluids, so that he cannot eat or drink anything which is not cold. The soreness may amount to actual pain. Red patches appear, especially at the tip and edges, and small vesicles may form. In severe cases the whole tongue may present an appearance described by Hunter as resembling raw beef. The glossitis varies greatly in degree from time to time, and the acute inflammation with its accompanying soreness may disappear completely for long periods, being sometimes present only for a few days or weeks at a time. In quiescent intervals evidence of past glossitis may be afforded by fissures and by smooth patches, from which the papillæ have more or less completely disappeared. Hunter has pointed out that the tongue lesions are least obvious when the anæmia is most severe, as the patient has insufficient blood to cause redness ; on the other hand, they may be very obvious when the patient is comparatively well.

Familiarity with the characteristic features of the glossitis of Addison's anæmia may make it possible to diagnose a case before symptoms of anæmia have appeared.

A lady consulted me on account of soreness of her tongue,

which she had had for two years, together with recurrent diarrhœa. The condition was so suggestive of Hunterian glossitis that a complete investigation of her blood was carried out, which showed that she had 62 per cent. of hæmoglobin and 3,140,000 red corpuscles per cubic millimetre, with an increase in their average size from the normal of 7·23 to 8·87 μ, well marked anisocytosis and poikilocytosis; a few nucleated cells were found. Van den Bergh's test gave a positive indirect reaction, and complete achlorhydria was present. There is no doubt that the patient was suffering from Addison's anæmia, the first symptom of which was glossitis, as the diarrhœa was secondary to the achlorhydria and probably preceded the development of the specific intestinal toxæmia.

Dr. R. D. Passey has told me of the case of a lady of fifty-eight, whom he first saw in July, 1922, on account of severe glossitis of one year's duration. On account of the typical appearance of the tongue he examined her blood, although there was no symptom of anæmia. He found she had 85 per cent. hæmoglobin and 3,400,000 red corpuscles per cubic millimetre, the colour index being thus 1·2. The average size of the red corpuscles was much increased, and nucleated cells were found. Leucopenia with relative lymphocytosis was present. She had already had a good many septic teeth removed in November, 1921, and again in July, 1922, with temporary benefit, and the remainder were removed on Dr. Passey's advice. A streptococcal vaccine was prepared from the teeth, and each injection was followed by a slight exacerbation of the glossitis. When seen in April, 1923, she was better than she had been since the onset of her illness; the glossitis had nearly disappeared, and the hæmoglobin percentage was 88, but in February, 1924, it had again fallen to 70.

Similar cases have been recorded by Schauman and Naegeli.[78] It is thus probable that, although there may be a history of soreness of the tongue before the onset of other symptoms, an early examination of the blood would show that hæmolysis was already occurring, and that the characteristic megalocytosis was present.

According to Hunter, the glossitis is quite specific and

occurs in connection with no other disease. It is interesting to note that, according to Schauman, it never occurs in bothriocephalus anæmia, which is also hæmolytic and shows identical changes in the blood, but which is associated with achlorhydria in only 50 per cent of cases instead of in 100 per cent. as in Addison's anæmia. Becker, however, has recently reported that glossitis was not uncommon in the cases of bothriocephalus anæmia observed by him. I have seen glossitis identical in appearance with that occurring in Addison's anæmia in at least four cases of severe but not hæmolytic anæmia, in two of which the anæmia was found to be secondary to a growth of the colon, so I cannot regard the presence of a sore tongue in an anæmic patient as conclusive evidence that the anæmia is of the Addisonian type.

The Evidence of Intestinal Infection in Addison's Anæmia and Subacute Combined Degeneration of the Cord.

In 1889 Hunter suggested for the first time that Addison's anæmia is due to excessive destruction of blood, caused by the absorption of hæmolytic poisons from the alimentary tract. He thought that these poisons were produced in specific lesions affecting particularly the tongue and stomach, but also the intestine. His own later investigations and those of many other observers have confirmed his main thesis, that a hæmolytic toxin is produced in the digestive tract. But whatever we may conclude as to the significance of the specific glossitis he described, there seems little doubt that any gastritis present is secondary to the achlorhydria, which is a constant predisposing factor and is in most cases constitutional and congenital in origin. The observations which I shall now describe show, I believe, that a definite infection of the intestine with a hæmolytic streptococcus is present in Addison's anæmia, but Faber and Bloch,[79] using improved methods to prevent post-mortem changes, found that it is not, as was formerly believed, associated with any inflammatory or atrophic lesion of the intestinal mucous membrane. The infection gives rise to a mild degree of pyrexia in at least 70 per cent. of cases.

Streptococci are almost invariably present in the sockets of septic teeth, whether the individual is otherwise healthy or not. But so far as our observations go, the *Streptococcus longus pyogenes* is rarely found in the contents of the duodenum removed during life with an Einhorn tube, except in Addison's anæmia and in subacute combined degeneration of the cord. In four normal individuals and in eight cases of infective jaundice from Gallipoli, which C. J. Martin and I investigated in Lemnos in the autumn of 1915, no streptococci were present. Among ninety-one patients suffering from various other conditions the duodenal contents, the majority of which were examined by F. A. Knott, contained a *S. longus* in only nine instances, and in these they were generally very scanty and slow-growing. In nineteen of the ninety-one cases achlorhydria was present, together with very severe oral sepsis in about six, and slight pyorrhœa alveolaris in several others, but in spite of this no streptococci were found. In sixteen of the twenty cases of Addison's anæmia and in all of the nine cases of subacute combined degeneration of the cord which we have investigated the *S. longus* was found on cultivation of the duodenal contents. In the four exceptions, but in no other case, hydrochloric acid had been given in large doses before the duodenal contents were obtained, so that it is not improbable that streptococci were originally present in the duodenum. The likelihood of this is increased by the fact that in the only two cases, in which a second examination has been made after treatment with acid in patients who were originally found to have *S. longus* in the duodenum, no streptococci could be isolated. In the last fourteen positive cases F. A. Knott has investigated the hæmolytic power of the streptococci : he found that they were hæmolytic in thirteen ; the fourteenth was a case of subacute combined degeneration of the cord with achlorhydria, but a perfectly normal blood-picture. The streptococci found in the duodenum in non-anæmic cases were never hæmolytic.*

* In an additional case Knott confirmed the discovery of a hæmolytic *S. longus* in the duodenal contents obtained by a tube by isolating the same organism in fluid obtained by puncture during an operation for appendicectomy. No cocci were found in the puncture fluid obtained in four other patients not suffering from Addison's anæmia.

The contrast between the 8·7 per cent. of 103 controls, in which streptococci were found, with 86 per cent. of twenty-nine patients with Addison's anæmia and subacute combined degeneration of the cord, or 100 per cent. if only those are included who had not previously been treated with large doses of hydrochloric acid, is so striking that it is, I think, fair to conclude that an infection of the intestine with a long streptococcus is an essential factor in the pathogenesis of these diseases. That the streptococcus itself is the organism, which produces the toxin responsible for the nervous disease as well as the anæmia, appears very probable from the fact that in two of my patients with subacute combined degeneration of the cord each injection of an autogenous vaccine, made from a *S. longus* isolated from the socket of an infected tooth and from the duodenum respectively, gave rise after an interval of some hours to a temporary aggravation of the sensation of pins and needles in the hands and feet, which was followed eventually by the almost complete disappearance of the symptom.

A small number of observations on the bacteriology of the duodenum have been published since the first communication by Bell and myself on the subject, and they confirm our results. Thus in fourteen normal individuals examined by Bogendorfer [80] the duodenal contents, though not sterile, contained neither the colon bacillus nor streptococci. In four out of six patients with hyperchlorhydria examined by Gorke [81] the duodenal contents were sterile, and in the remaining two a very small number of organisms were found. On the other hand, in seven cases of achlorhydria examined by Gorke and eleven by Bogendorfer large numbers of bacteria were always present; in the majority of cases these included *B. coli*, but a *S. longus* was not found. In the only two cases of Addison's anæmia investigated a hæmolytic streptococcus was isolated by Bogendorfer in addition to the bacteria found in the other cases.

I believe that achlorhydria is an essential predisposing cause of Addison's anæmia and subacute combined degeneration of the spinal cord, because the loss of the antiseptic action of the normal gastric juice alone makes it possible for the bacteria, which reach the stomach from the mouth when

oral sepsis is present, to infect the intestine. But the association of oral sepsis with achlorhydria only leads to the development of Addison's anæmia when the sepsis is due to infection with a special streptococcus, which produces hæmolytic and neurotoxic poisons after it has established itself in the small intestine.

In addition to the bacterial toxins it is possible that others are produced by the action of the organisms on the proteins, which reach the duodenum in a completely undigested form owing to the absence of the normal digestive activity of the gastric juice.

In whatever way the poisons are produced, it is probable that one of them is specially toxic for the blood and leads on absorption to a hæmolytic form of anæmia, and that another is specially toxic for nervous tissues and leads to combined degeneration of the spinal cord. In most cases the former toxin is the dominant one, but in a small minority of cases the latter is the more important. Although one or other may appear to be present alone in the early stages, it is rare for the hæmolytic toxin and still more rare for the neurotoxin to continue to be produced without the other throughout the course of the illness. In the only case I have seen of subacute combined degeneration of the cord with absolutely normal blood, the duodenal *Streptococcus longus* was found by Knott to differ from that found in all the other cases by being non-hæmolytic. Presumably it would have subsequently developed hæmolytic properties and anæmia would have resulted, if steps had not been taken to eradicate the infection.

Remissions

One of the most remarkable features of Addison's anæmia is the frequency of remissions. They occurred in 83 out of 101 cases in the London Hospital series analysed by Maitland Jones. The most common number was two, but there were occasionally as many as five or six, the average duration being six months.

During remissions the patient feels perfectly well. A slightly lemon-yellow colour may still be detected in his skin, but he no longer looks abnormally pale. His spleen is

generally still palpable, and gastric analysis shows that complete achlorhydria is present. Symptoms due to subacute combined degeneration do not disappear, though they may become much less severe. The tongue often shows evidence of former glossitis.

In the large majority of cases the blood-picture is still abnormal. The colour index often remains over 1, though the number of red corpuscles may be normal or over normal, and the hæmoglobin percentage may exceed 100. Thus in six such cases reported by Brösamlen [82] the hæmoglobin percentage varied between 96 and 112, and the colour index between 1·3 and 1·7. Some megalocytes are still seen, but microcytes and poikilocytes are very few or completely absent[19]. This corresponds with the fact, to which Price-Jones has drawn special attention, that the increase in the average size of the corpuscles is independent of the degree of anæmia, but the anisocytosis varies directly with it. Little or no basophilia is present, and no normoblasts or megaloblasts are found. The blood serum may still be slightly more yellow than normal, but van den Bergh's test for excess of bilirubin is generally negative. In one of my cases, in which the red corpuscles numbered 740,000 per cubic millimetre and the hæmoglobin percentage was 18 in October, 1921, the red corpuscles numbered 5,730,000 per cubic millimetre and the hæmoglobin was 110 per cent. in February, 1924, the colour index being 0·97. But there was still typical megalocytosis, though no other morphological abnormalities were present.

In exceptional cases the blood-picture is perfectly normal or shows nothing more than a slight anæmia of a secondary type. Zadek [29] has reported four cases of this kind, in which the colour index was one or less than one, no megalocytes or other abnormal cells were present, and the colour of the blood serum was normal. In one case the red corpuscles number 5,400,000 per cubic millimetre and the hæmoglobin percentage was 108; in the other cases slight anæmia of a secondary type was present.

In remissions, in which the blood-picture is normal except for the presence of megalocytosis and in which the colour of the blood serum is normal, the continued presence of

large cells is probably due to permanent changes in the bone marrow caused by the toxæmia in the acute stage of the illness. In the remissions, in which the blood-picture is quite normal, the bone marrow must have recovered completely from the effects of the toxins which caused it to produce abnormal cells. Unfortunately these cases tend to relapse almost as surely as those in which blood destruction and pathological activity of the bone marrow have never ceased.

Zadek has shown, by examining a specimen of bone marrow removed from the middle of the tibia, that the changes which are always found in this situation in fatal cases of Addison's anæmia are present during life in the active stages of the disease. He has discovered, however, that during remissions the red marrow with its preponderance of megaloblasts is replaced by normal yellow marrow, containing mainly fat cells with a few normocytes and only a very small number of megaloblasts. This is true whether the remissions are associated, as is usual, with a blood-picture which is still abnormal or, as occurs in exceptional cases, with a blood-picture which is normal in every detail. For example, in two cases of fully developed Addison's anæmia the marrow was dark red and contained thirty-nine and fifty-nine megaloblasts and eighteen and thirty-three normoblasts respectively per 1,000 normocytes, whereas in two cases in the stage of remission with abnormal blood-picture and in two with a normal blood-picture the marrow was yellow and contained only an occasional megaloblast and no normoblasts at all. In the post-mortem on a patient with Addison's anæmia, who died of an acute intercurrent disease during a remission, Zadek found that the bone marrow was yellow.

It is clear, therefore, that Ehrlich's theory that Addison's anæmia is a primary megaloblastic degeneration of the bone marrow, denoting a reversal to an embryonic type of blood formation, is incorrect. The changes which occur in the marrow are partly caused by a specific poison, which acts upon the bone marrow and may perhaps be identical with the hæmolysin, and partly by an attempt to compensate for the prolonged and excessive blood destruction, being analogous to the changes which occur in anæmia following severe hæmorrhage. Sometimes in the early stages and in

rare cases during remissions, the blood-picture shows none of the changes which result from the reaction of the bone marrow to the toxæmia, athough some anæmia may be present, which van den Bergh's test shows is hæmolytic in character. The characteristic features of the blood in Addison's anæmia are due to the reaction of the bone marrow to the toxæmia, and the stage when it appears and its degree at any period depend upon the varying power of reaction of the marrow in different individuals. Remissions are caused by partial or complete cessation of the toxæmia, and not, as has often been maintained, by the megaloblastic regenerative activity of the marrow, which Zadek's observtions on the bone marrow have shown is no more manifest during remissions than it is in normal individuals. The occurrence of remissions in which the blood-picture is perfectly normal confirms this view.

I believe that the partial or complete disappearance of toxæmia which results in remissions is brought about by the development of a certain degree of immunity towards the infection, this originating either spontaneously, or more commonly as a result of treatment, which has led on the one hand to a diminution of the virulence of the infection and on the other to greater resisting power of the patient. The almost inevitable relapse occurs because the infection has not been completely overcome, and because the achlorhydria—the essential predisposing cause—is permanent and unaffected by the general improvement. A remission can only pass into complete recovery if the intestinal infection is annihilated, and the primary source of infection is completely eradicated. The achlorhydria then no longer matters any more than it does in the large majority of other individuals who have constitutional achylia gastrica. Remissions in Addison's anæmia are thus strictly analogous to those in duodenal ulcer, in which the predisposing hypersthenic stomach is also constitutional. But however long a remission lasts, the patient is never altogether free from the danger of a recurrence, as the achlorhydria is permanent, and reinfection may occur or a long dormant infection may become active again. Thus McPhedran [83] has recorded a case in which a patient died from a recurrence after a remission of seventeen

years, and Stockton [84] has reported a case of fatal recurrence twenty years after the onset of symptoms and eleven years after apparent recovery in a man in whom achlorhydria persisted throughout the whole period.

Prophylaxis and Early Treatment

As everybody with achlorhydria can be regarded as liable under certain conditions to develop Addison's anæmia, whenever the former is discovered in the course of a routine investigation of a patient suffering from digestive or other symptoms, he should be advised to take hydrochloric acid in adequate doses for the rest of his life. At the same time all oral sepsis should be eradicated, and the patient should be instructed to have his teeth thoroughly examined and, when necessary, treated every six months. This will not only probably make him safe so far as Addison's anæmia is concerned, but also cure any digestive symptoms, such as nausea or chronic diarrhœa which may be present, and diminish the special liability he has to develop such conditions as rheumatoid arthritis, acne rosacea, appendicitis and cholecystitis.

Familial Addison's anæmia is due to familial achylia. It is, therefore, worth considering whether it would not be wise to examine the gastric contents of the other members of the family of patients with the disease, and, if achylia is found, advise them to take the precautions I have just described.

The prospect of eradicating the infection, which causes Addison's anæmia and subacute combined degeneration of the cord, is, of course, much more favourable in early cases than when the disease is well-established. Early diagnosis can only be made if in every case in which achlorhydria is discovered, in every case of sore tongue or of recurrent glossitis, and in every case of paræsthesia affecting the feet and hands, a thorough examination of the blood and central nervous system is made, and in the two latter conditions a test meal is given. It should be remembered that the examination of a blood film for megalocytosis is far more likely to lead to an early diagnosis than a simple blood count and hæmoglobin

estimation, and that the criteria upon which many hæmatologists depend for a diagnosis of Addison's anæmia are only present in the more advanced stages when treatment is much less hopeful. It should be remembered also that in subacute combined degeneration of the cord with achlorhydria but normal blood, early treatment can be regarded as prophylaxis, in the absence of which anæmia is almost certain sooner or later to develop.

Treatment

(*a*) *The Intestinal Infection*

The most important part of the treatment of Addison's anæmia and subacute combined degeneration of the cord is to overcome the intestinal infection and so arrest the development of the neurotoxic and hæmolytic poisons. Oral sepsis should be thoroughly dealt with, as Hunter first demonstrated in 1900. Every tooth which shows the slightest sign of infection on expert clinical examination should be condemned. An x-ray photograph should be taken of all the remaining teeth, however healthy they may appear, and the least evidence of apical infection or periodontitis should lead to their removal. In most cases every tooth will have to be extracted. If the tonsils are infected they should be enucleated ; it should be remembered that infected tonsils are not necessarily large, and that severe infection in flat tonsils may be hidden behind the anterior pillars of the fauces. Chronic nasal catarrh and infection of the nasal sinuses should also be looked for by an expert rhinologist and, if discovered, thoroughly treated.

As the removal of infected teeth or tonsils is sometimes followed by an acute hæmolytic crisis and aggravation of the nervous symptoms owing to the sudden absorption of large quantities of toxin from the raw surfaces left by the operation, it is wise to give two or three injections of streptococcal vaccine prepared from the teeth or tonsils before removing them.

The achlorhydria should be corrected by the administration of large doses of dilute hydrochloric acid. The dose usually given is quite insufficient. As M. E. Shaw was the

first to show on a number of cases of mine, anything less than a drachm of dilute acid given as a single dose during a fractional test-meal does no more than barely neutralise the alkaline gastric contents for a quarter of an hour

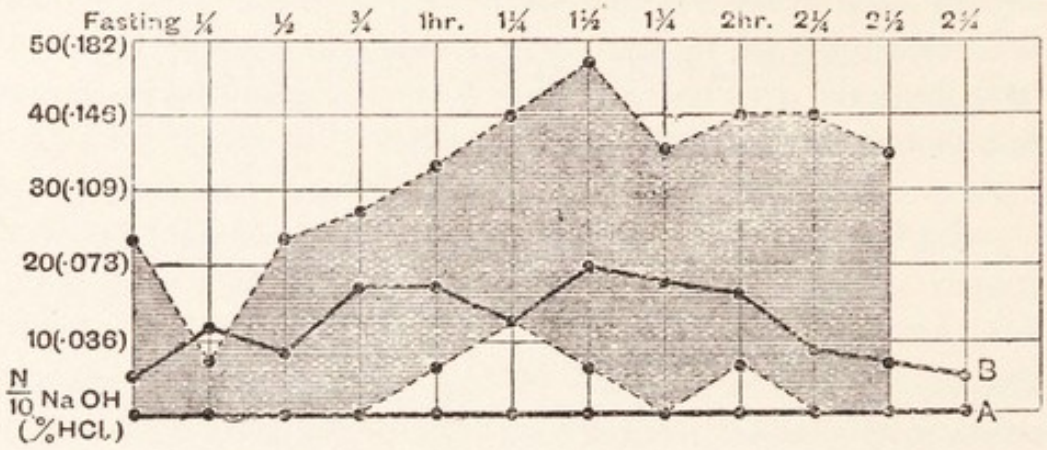


FIG. 28.—Fractional test-meals to show free HCl in a woman with subacute combined degeneration of the spinal cord. A, without addition of HCl—complete achlorhydria; B, with addition of ℥jss dilute HCl in ℥ij water.

(Fig. 28). At least 1½ drachms are required to produce anything like the normal acidity throughout the period of digestion of an ordinary meal. In practice it is difficult to take more than 1½ or two drachms with each meal, and the

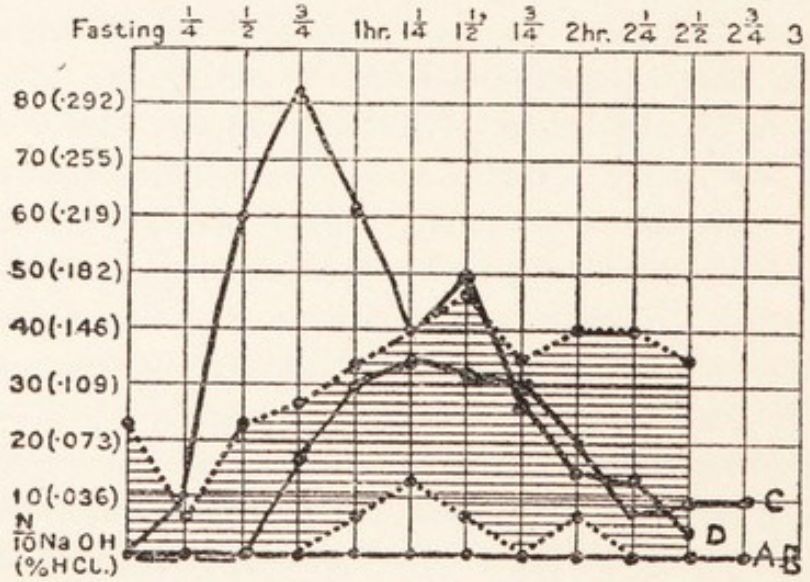


FIG. 29.—Fractional test-meals to show free HCl in man with Addison's Anæmia. A, without addition of acid; B, with addition of ℥i dil. HCl to meal (complete achlorhydria persisting); C, with ℥jss dil. HCl (normal curve); D, with ℥ij dil. HCl (hyperchlochydria).

results obtained with these doses are quite satisfactory (Fig. 29), any digestive symptoms which may have been present disappearing at once. The dilute acid should be given in the proportion of 1 drachm to 5 or 6 ounces of

water ; this makes a strength which is rather less than that of normal gastric juice, but Knott has shown that it completely destroys cultures of *Streptococcus longus* in less than fifteen minutes. As pepsin is also very deficient or absent, a grain should be added to each drachm of dilute acid, so as to improve the gastric digestion. About 6 drachms of the acid should be mixed with a pint and a half of water, which is then sweetened with sugar. With the addition of orange juice or a mixture of orange and lemon juice it makes a very palatable beverage. A little wine can also be added if the patient likes. About one half-pint (2 dr. dilute HCl) should be drunk just before and during lunch, another half-pint before and during dinner, and the rest fasting in the morning about an hour before breakfast. This early dose is probably the most important, as the acid can then act on the bacteria in the stomach and duodenum in a concentrated form undiluted by food. If there is any difficulty in taking the acid, it may be diluted by the addition of more water. The patient should continue to take it without intermission for the rest of his life, as, even if the intestinal infection appears to be overcome, the achlorhydria remains permanently in the large majority of cases.

Milk, which has been soured with an active lactic acid bacillus, should also be given for an indefinite period. It is best taken between meals so as not to be rendered inactive by the hydrochloric acid. Most patients can manage half a pint three times a day without difficulty. Though this remedy has lost much of the popularity it had a few years ago, there is no doubt that it is a most efficient means of rendering the intestine a less suitable culture medium for most pathogenic bacteria. Faber [33] has reported very satisfactory results from the use of kephir, a similar preparation which he first used in 1914, when a woman of sixty-eight with typical Addison's anæmia of five years' duration, who had failed to respond to treatment with arsenic, rapidly improved when on her own initiative she began to take kephir. Her blood quickly became normal, and she had remained perfectly well when Faber reported her case eight years later.

Finely powdered or granulated charcoal absorbs gas in the

intestines, and is the best remedy I know for intestinal flatulence. It also makes the foulest stools almost odourless. It seems reasonable to suppose that it may also absorb some of the hæmolysin and neurotoxin produced in Addison's anæmia. I therefore give a large tablespoonful of charcoal first thing in the morning and last thing at night.

In a further attempt to overcome the infection which is responsible for the disease, I advise the administration of an autogenous vaccine prepared from streptococci isolated from the patient's own duodenum, or, failing that, from a dental or tonsillar streptococcus. It should be given over a long period in doses so regulated as not to give rise to any general, hæmolytic or nervous reaction.

The important part played by the spleen in the hæmolysis of Addison's anæmia was proved by Hunter, who demonstrated the large amount of free iron it contained in fatal cases, and showed that splenectomy increased the power of animals to resist poisoning with such hæmolytic toxins as toluylendiamine. Hijman van den Bergh [21] confirmed this by finding that blood, removed from the splenic vein during splenectomy or after death in Addison's anæmia, contained more bilirubin than the blood in the general circulation—in one case actually three times as much. In four out of his six positive cases the splenic blood contained hæmoglobin, which was always absent from the peripheral blood; in some cases methæmoglobin, hæmatin and certain unknown pigments were present in the splenic blood, though absent or present in smaller quantities in the peripheral blood; these substances possibly form intermediate stages in the formation of bilirubin from hæmoglobin, as just the same series of pigments is found in hæmorrhagic exudates and in hæmatomas.

It would, therefore, seem natural that splenectomy should prove useful in Addison's anæmia, as it undoubtedly results in the removal of one of the sites of blood destruction. The results obtained in Addison's anæmia by splenectomy have not in the past been sufficiently good to warrant the general adoption of the operation as a method of treatment. I think, however, that this is due to splenectomy having been tried independently of other treatment. When employed in

addition to the other methods I have described, I believe it may prove to be of great value. Two patients of mine, who had shown no improvement for several weeks, and whose hæmoglobin percentage would rise to 20 or just above after each transfusion, only to drop again to 15 a few days later, had their spleens removed by Mr. R. P. Rowlands and Mr. L. Bromley respectively. Though they had been delirious and extremely prostrate, they at once felt better after the operation, and the condition of their blood rapidly improved, so that both were able to leave hospital a few weeks later, and they have now been able to follow their ordinary occupations for over a year, although they are both still very anæmic. All who had seen them during the weeks before the operations agree that the improvement in their condition must almost certainly have been due to the splenectomy.

(*b*) *Symptomatic Treatment*

If the production of hæmolytic toxins is arrested, the blood shows spontaneous improvement. This may be greatly accelerated by symptomatic treatment. The frequent remissions, which are generally regarded as very characteristic of the disease, were hardly everob served before 1877, and are almost certainly due to a great extent to the use of arsenic, which was first employed in that year by Byrom Bramwell.[15] In the majority of cases Fowler's solution given by mouth proves quite satisfactory, but occasionally some preparation, which can be injected into the muscles or direct into the blood, proves more efficacious.

Direct transfusion of blood was tried by Thomas Bryant in a case of Addison's anæmia at Guy's Hospital in 1879. I am convinced of the great value of this method of treatment, which generally requires repetition, often on several occasions. Experience shows that in many cases it not only adds a quantity of healthy blood with normal red corpuscles to that already circulating, and in this way produces an immediate rise of 5 to 10 per cent. of hæmoglobin, but it also frequently initiates a steady rise in the percentage, when this has been stationary or actually falling. Ryffel suggests that this is due to the extra quantity of oxyhæmoglobin stimulat-

ing to increased activity the hypertrophied red bone marrow, which has been comparatively inactive as a result of the poor quality of blood circulating through it, but I think that healthy blood may perhaps also contain some hormone, which has a specifically stimulating action on bone marrow. It may also be due in part to the introduction of antibodies into the circulation, which increase the individual's power of dealing with the infection which causes the anæmia. For this reason either fresh blood or defibrinated blood should be used in preference to citrated blood, which Adrian Stokes has shown is deprived of most of its bactericidal properties by citration.

On the assumption that the favourable effects of transfusion are due to the stimulating action of normal blood on the bone marrow, and to the assistance it affords in overcoming the intestinal infection, rather than to the mere addition of about 5 per cent. of hæmoglolin to that already present in the circulation, it occurred to me that the repeated injection of small quantities of blood might be equally or more effective than an occasional massive transfusion. In six cases, in which 20 or 25 c.c. of fresh blood have been injected intravenously with an ordinary serum syringe on alternate days, very promising results have so far been obtained. If this method proves effective, it will have the great advantages of being so simple that any practitioner can carry it out, that the same donor can be employed on each occasion instead of only every three months, and that the treatment can be continued without difficulty for an indefinite period.

It might have been supposed that the cessation of toxæmia would not lead to any improvement in the nervous symptoms corresponding to that in the anæmia, although the progress of the spinal degeneration would be arrested. But I have several times seen considerable improvement result, not only in the sensory symptoms, but also in the ataxic paraplegia, quite apart from the result of treatment by re-education and exercises. This is probably due to the fact that the nervous tissue may be thrown out of action as a result of the toxæmia, but be still capable of recovering if no more toxins are produced, this being what happens in various

acute infective conditions involving the central nervous system. The degree of improvement which may follow suitable treatment depends therefore upon the amount of actual destruction of nervous tissue which has already occurred. Similar favourable results have been recently reported by Vanderhof [75] as a result of removing foci of infection and giving large doses of hydrochloric acid.

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ACHALASIA

PART I

Achalasia of the Cardia (so-called Idiopathic Dilatation of the Œsophagus or Cardiospasm)*

Dilatation of the œsophagus without organic obstruction was first described by Hannay,[1] who published a detailed clinical history and pathological report of a case in 1833. In 1882 Mikulicz [2] suggested that it was due to spasm of the cardia, and in recent years the term "cardiospasm" has almost entirely replaced the earlier designation of "idiopathic dilatation of the œsophagus." It is clear, however, that this name is equally incorrect, and that the dilatation and hypertrophy of the œsophagus are due to achalasia or absence of the normal relaxation of the cardia. For the word "achalasia" I am indebted to Sir Cooper Perry, who coined it for me, as it was obvious that the word "cardiospasm" and the erroneous idea it conveys would never be discarded unless some less cumbersome expression than "absence of relaxation" was devised. Since I introduced it in 1915, it has been adopted by most writers on the subject, including Keith and Greig.[3]

Pathology

Zenker and Ziemssen,[4] in 1877, and Morell Mackenzie,[5] in 1884, suggested that the condition was due to "diminished contractile power" or "general weakness" of the muscular coat of the œsophagus. This theory did not, however, explain the hypertrophy, which is always present and which indicates that the œsophagus must have made violent efforts to overcome some obstruction; it is to the failure of these

* Reprinted, with additions and corrections, from the *Quarterly Journal of Medicine, VIII.*, 300, 1914.

that the dilatation must be due. As no organic obstruction is ever found, the cardiac orifice after death being of normal size and admitting the passage of a finger without any difficulty, it is clear that the obstruction must be functional. Since the suggestion was first made by Mikulicz that the functional obstruction is due to a spasm of the cardiac sphincter, nearly all writers have adopted this view, and the condition is now generally known as cardiospasm. As the symptoms may be present without intermission for many years before death, it is obvious that a considerable degree of hypertrophy of the cardiac sphincter would result from the long-continued spasm. The rapidity with which hypertrophy develops in a spasmodically contracted sphincter is well seen in hypertrophic pyloric stenosis of infants, and it is inconceivable that a spasm of the cardia could last as many years as the spasm of the pylorus last weeks without giving rise to hypertrophy. In none of the specimens I have seen, however, and in none of recorded autopsies has there been any hypertrophy of the cardia, the normal state of which has been in striking contrast with the hypertrophy of the œsophagus itself. In a patient of mine, upon whom Mr. R. P. Rowlands recently operated, it was quite obvious that the exposed cardia was no thicker than normal, and it offered no resistance to the passage of a large mercury bougie. Considerations of this sort led Rolleston,[7] in 1895 to suggest that the dilatation of the œsophagus might be due to "a failure in the co-ordinating mechanism by which the cardiac sphincter is relaxed during swallowing," and he suggested that "paralysis or continued inhibition of the longitudinal muscular fibres of the œsophagus would allow dilatation of the tube to occur, and at the same time by interfering with the opening of the cardiac sphincter would induce hypertrophy of the circular muscular coat."

In 1910, without knowing of Rolleston's view, I came to a somewhat similar conclusion. On watching the process of swallowing with the x-rays, the barium-containing food is seen to pass very quickly down the œsophagus to the cardia, where there is a momentary pause, the lower extremity of the shadow ending as a fine point which corresponds to the cardiac orifice of the stomach (Fig. 30 (a)). A moment after-

wards the food is seen to pass on into the stomach, and, where the shadow ended before as a fine point, a shadow almost as wide as the œsophagus itself is now seen (Fig. 30 (b)). The obvious explanation is that when a peristaltic wave has carried the food to the closed cardia, the latter widens owing to active relaxation of the circular muscle-fibres, which surround it and form the cardiac sphincter. It has been stated that there is no definite thickening of the muscle at this point corresponding to the sphincters at the pyloric and ileo-

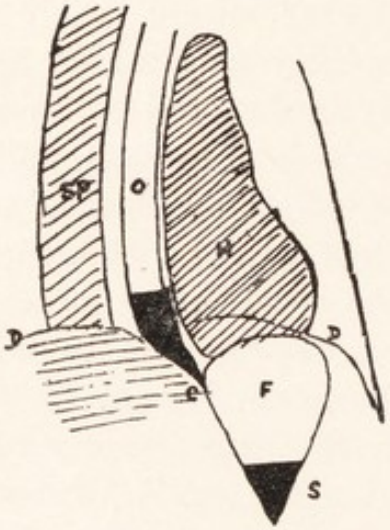


FIG. 30 (a).–X-ray appearance of œsophagus in right antero-lateral position when a mouthful reaches the cardia; an earlier mouthful has already entered the stomach.

O, œsophagus; C, cardia; F, fundus; S, barium-containing food already in stomach; SP, spine; H, heart; D, D, diaphragm.

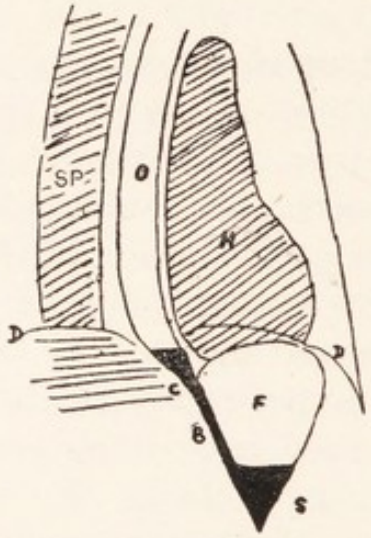


FIG. 30 (b).—X-ray appearance immediately after Fig. 30, the cardia having relaxed, so that a stream of barium-containing food, B, runs down the inner wall of the fundus through the relaxed cardia, C, to join the food already in the stomach, S.

cæcal orifices, but Sir Arthur Keith has demonstrated to me that this is incorrect and that a true cardiac sphincter does in fact exist. My x-ray observations are confirmed by experiments on animals, which show that the cardia relaxes when each peristaltic wave passing down the œsophagus in the act of swallowing reaches its lowermost end, just as the pyloric sphincter relaxes when each gastric peristaltic wave reaches it. Cannon [8] has shown that section of the vagi in animals below the origin of the recurrent laryngeal nerves prevents the normal relaxation and leads to the accumulation of food in the œsophagus,

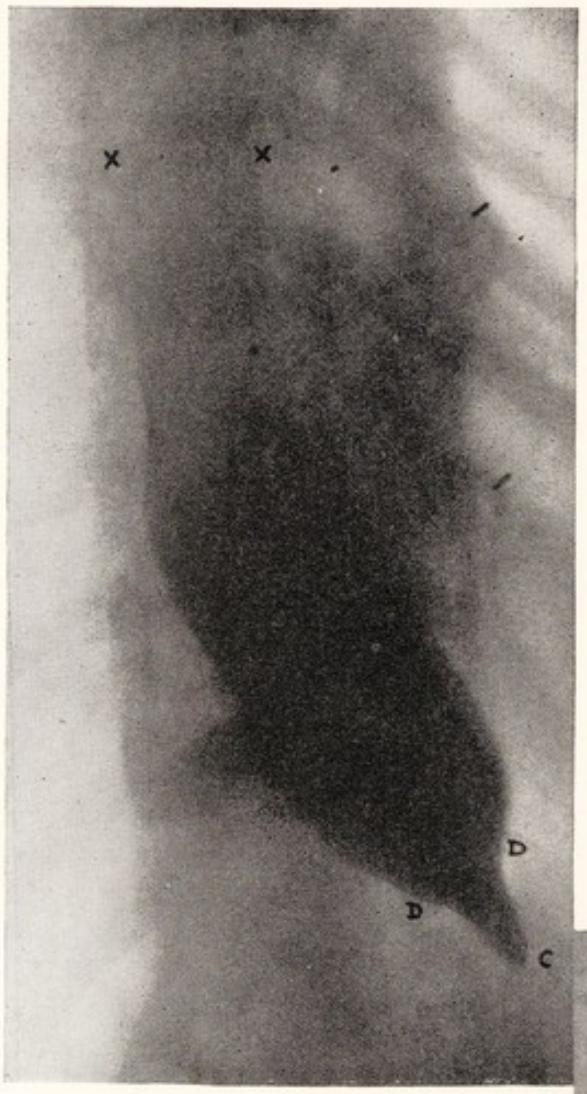


FIG. 31 (*a*).—Skiagram by Dr. Lindsay Locke, showing the dilated œsophagus, filled with opaque meal. XX, upper surface of column of fluid supported by the closed cardia, C. DD, narrowing of dilated œsophagus caused by unyielding fibrous tissue, where it passes through the diaphragm.



FIG. 31 (*b*).—Skiagram by Dr. Lindsay Locke, taken directly after Fig. 31 (*a*), showing the mercury tube, MM, passing through the cardia into the stomach.

which consequently becomes dilated. I believe that under certain conditions a similar phenomenon occurs in man: there is an absence of relaxation—achalasia (*a*, not; *χαλάω*, I relax)—so that the œsophagus continues to end as a blunt point (Fig. 31 (a)). Consequently food stagnates in the œsophagus, which dilates as more and more collects in it; the distension of the œsophagus acts as a powerful stimulus to peristalsis, which is not only excessively violent, as is easily seen with the x-rays, but continues at intervals throughout the day, instead of occurring only in single waves as each mouthful is swallowed. This is the cause of the hypertrophy.

The powerful peristaltic waves are unable to overcome the obstruction offered by the closed cardia, because the dilatation of the œsophagus is so great that they are insufficiently deep to obliterate its lumen; they cannot, therefore, appreciably increase the pressure exerted on the cardia, their mechanical effect being dissipated in the form of an axial reflux stream. On the other hand, I have found that the weight of an india-rubber tube filled with mercury is sufficient to cause it to drop without the slightest difficulty through the cardia into the stomach, the actual passage through the cardia being often inappreciable to the hand which holds the mercury bougie. With the aid of the x-rays I have several times watched it pass directly into the stomach, as if it met with no resistance at all (Fig. 31 (b)). This would be quite impossible if the obstruction was due to spasm: the resistance offered to the introduction of the finger, for example, when the anal sphincter is in a condition of spasm is very considerable, and considerable force is required to overcome it. Moreover, the tube can be withdrawn with equal ease: it is not gripped, as it would be were a spasm present, and as the finger is gripped when it is withdrawn from a spasmodically contracted anal sphincter. I have seen one case of combined achalasia and cardiospasm, an officer, thirty-three years old, who had had all the symptoms of achalasia for three years, but the mercury tube met with some obstruction when introduced and was tightly gripped when withdrawn. This only occurred on the first two occasions, the contrast afterwards, when the cardiospasm had disappeared,

being very striking; the achalasia was also rapidly cured. The cardiospasm was probably caused by secondary œsophagitis.

In the majority of cases of achalasia of the cardia no obvious cause can be discovered either during life or after death. The symptoms in two of my patients developed during military service—one whilst on ordinary duty at the front in France, the other, a Dublin Fusilier, whilst being subjected to ill-treatment in a German prison on account of having refused to join Casement's Irish brigade. In a few cases an ulcer or carcinoma of the stomach has been present, the achalasia being then due to reflex inhibition of relaxation, just as achalasia of the ileo-cæcal sphincter may be a reflex result of appendicitis. In others inflammation or ulceration of the lower end of the œsophagus has been found with the œsophagoscope or at the autopsy; this is generally due to irritation by the decomposition products of food retained in the dilated œsophagus. A primary peptic ulcer in the immediate neighbourhood of the cardia would probably give rise to a true spasm, just as an ulcer involving the pyloric and anal canals gives rise respectively to pylorospasm and anal spasm. One of my patients had mitral stenosis and a very dilated left auricle; the latter was probably the source of the reflex inhibition of relaxation. In rare cases achalasia may be due to a lesion of the vagus, degeneration of which was discovered in one case by Krause; this may also have been the cause in a boy in whom achalasia developed after whooping-cough (Rolleston [7]), and in a man of sixty-three under my care, who had no knee-jerks or ankle-jerks, but a negative Wassermann reaction and no other evidence of nervous disease.

Keith [6] has shown that Auerbach's plexus, where the vagal nerve fibres end in cells situated between the circular and longitudinal muscular coats of the alimentary canal, consists mainly of nodal tissue, similar to that in the heart, and only to a small extent of nerve cells and fibres. The nodal tissue, the branching cells of which appear to become continuous with processes of certain groups of muscle cells and with the branched process of ganglionic cells, is specially developed at the sphincters. It seems likely that the majority of cases of achalasia of the cardia

are caused by progressive organic disease involving Auerbach's plexus in this situation, the condition being strictly comparable to heart-block.

The lower two-thirds of the œsophagus are generally most dilated. The dilated œsophagus may be able to hold as much as a pint, and its circumference may exceed 6 inches, but owing to the resistance offered by the border of the œsophageal aperture in the diaphragm, there is comparatively little dilatation here and in the intra-abdominal portion of the œsophagus. The œsophagus may be lengthened as well as dilated; it then runs a somewhat tortuous course through the thorax. In one of my cases the x-rays showed that a pouch had developed in connection with the lower end of the dilated œsophagus.

Achalasia of the cardia may begin at any age: the age at onset in a series of my own patients was twenty-four, twenty-five, twenty-six, thirty, thirty-six, forty, forty-eight, forty-eight, sixty-three and sixty-five, and cases have been recorded which began at eight and at seventy. Eight of my patients were males and four females, but among all the published cases the sexes are equally affected.

Symptoms

The condition generally develops gradually, a slight attack lasting for a day or two being followed by a period of freedom for a few days or even several weeks or months; other attacks then occur at gradually shorter intervals, until finally the condition becomes permanent. In the intervals between the early attacks the patient feels perfectly well, and I have been unable with the x-rays to detect anything abnormal in the act of deglutition. The attacks often begin in the morning, and the patient realises he is going to have one from the difficulty he experiences in swallowing saliva when he wakes. He feels as if the food "sticks"; he often recognises that the obstruction is beneath the lower end of the sternum, but sometimes the sensation is felt in the upper part or middle of the chest. The patient realises that food "won't go down"; it feels as if "the passage is closed," and the food "fills up" or "blows out" the chest. Some-

times actual pain is produced, and in one case a slighter pain was felt at the same level behind. The patient may notice gurgling in the chest, as if "gas was bubbling through water." Salivation occurs in almost every case. The saliva is frothy and contains much mucus, and large quantities may be rejected; thus one patient of mine spat out 10 ounces during a single night.

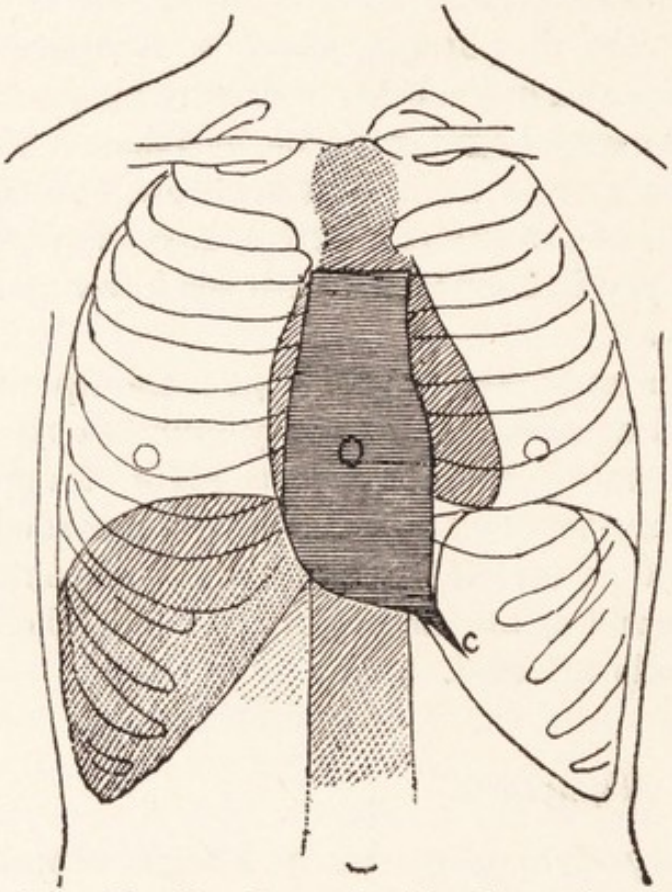


FIG. 32.—Drawing of dilated œsophagus, O, caused by achalasia of the cardia, C. It is filled all day with an eight-inch-high column of food. Anything more which is is eaten increases the weight of the column and opens the cardia. Food then enters the stomach till the column is again eight inches high, when the cardia closes once more.

As a rule the patient voluntarily relieves his discomfort within a few minutes of finishing a meal by bringing up the greater part of what he has eaten, mixed with saliva. He can generally do this quite easily, but occasionally requires to produce a vomiting reflex by tickling his throat; in neither case is there any nausea. It is uncommon for the food to be returned quite involuntarily, but this may happen if a large quantity has been retained in a greatly dilated œsophagus sufficiently long for a certain amount of bacterial decomposition to occur, when the products may irritate the œsophagus and cause its contents to be rejected.

Most patients can swallow fluids more easily than solids, but one of my patients could retain solids more easily and always avoided drinking fluids with her meals. The food is retained most easily if it is swallowed extremely slowly.

The weight of the column of food in the dilated œsophagus after a meal is sufficient to force a small proportion of the fluid present through the cardia as a very narrow stream, but as soon as the height of the column falls below a certain point, generally about eight inches, or the individual lies down, the pressure becomes insufficient and the flow ceases. Consequently food stagnates in the œsophagus for an indefinite period, and a considerable quantity can be removed from it even after a fast of twenty-four hours (Fig. 32).

The œsophagoscope shows that the cardiac orifice is completely closed. The mucous membrane may be normal, but it is often red and inflamed, especially in the lowest part of the œsophagus, and there may be superficial erosions, which are probably in most cases secondary to the stasis.

The general health at first remains perfectly good, in contrast to what occurs in malignant obstruction of the œsophagus, and in spite of the fact that weight is rapidly lost ; thus one patient lost two stone in the three months following the onset, but felt otherwise as well as ever. After a certain amount of weight is lost, a condition of equilibrium appears to develop ; though only extremely small quantities of food reach the stomach, the patient loses no more weight, and though he is less strong than formerly, he may continue to live in this condition for many years and reach old age. Owing to the small quantity of food residue reaching the colon, the patient is naturally very constipated.

Diagnosis

The patient's description of his symptoms is generally so characteristic that a diagnosis of œsophageal obstruction can be made with a considerable degree of probability. This is confirmed most easily and with greatest certainty by means of an x-ray examination, the patient eating thick porridge mixed with milk and barium sulphate. It is most important that the examination should be made during an attack : several of my patients had previously been examined with the x-rays and had been told that nothing was the matter,

as no obstruction was found owing to the examination having been made during an interval. The possibility of achalasia should always be considered if the obstruction is found to be situated at the cardia.

When obstruction at the cardiac orifice has been diagnosed, it is next necessary to ascertain whether this is due to achalasia or to organic disease: the only organic disease which requires consideration is cancer, as non-malignant strictures are extremely rare, except as a result of caustic poisoning, when a history is generally obtainable, and the stricture is found to extend for some inches upwards instead of being strictly confined to the cardia. The intermittent character of the early attacks, the absence of all constitutional symptoms in spite of rapid loss of weight, the comparatively early age at onset with many patients, and, in cases in which an early diagnosis is not made, the long duration of the illness, point to achalasia rather than growth. The contrast between the perfectly normal œsophagus seen with the x-rays when an examination is made in the intervals between the attacks in the early stage and that seen during an attack is characteristic of achalasia, as very little variation is observed at different times in cancer. The even outline of the shadow and the localisation of the obstruction to the cardia in achalasia differ from the more irregular outline and the more extensive area of obstruction in cancer, but neither of these points is conclusive, as in very early cancer of the cardia the x-ray appearance may be indistinguishable from that of achalasia. The only conclusive evidence is the great ease with which a mercury tube passes through the cardia in achalasia in contrast with the complete obstruction offered to its passage by a growth. An ordinary bougie is less satisfactory, as it may impinge against the dilated lower end of the œsophagus immediately above the diaphragm, and it is therefore often difficult and sometimes impossible to pass one in achalasia. In cases of many years' standing the saccular lower end of the œsophagus may be so large that it reaches below the cardiac orifice: in one such case the mercury bougie was only passed after several unsuccessful attempts had been made, but the long history excluded a growth.

Prognosis

If the condition is recognised at the onset of symptoms, a permanent cure often results from treatment, but if treatment is only instituted when the condition has become continuous and the œsophagus greatly dilated, cure, as distinct from mere relief of symptoms, is less likely to be obtained. Thus Myer and Carman[9] have shown that patients treated by Plummer's method have to eat slowly and chew thoroughly in order to avoid a return of symptoms, as the dilatation of the œsophagus persists. In very acute cases death has occurred at an early stage, but more often the patient survives for a considerable period, even for twenty or more years, although in the absence of treatment only a small quantity of food ever reaches his stomach.

Treatment

The simplest and most effective treatment is by means of a mercury tube. The tube has a rounded end with no holes in it, its diameter being 24 gauge ; it is advisable, however, in the first examination to pass a tube of 20 gauge before using the larger one. It is filled with mercury, the upper end being closed. A string is attached to the upper end to prevent the possibility of its dropping into the stomach, and two circles are marked on the bougie at distances of 16 and 17 inches respectively from its lower extremity. The tube drops through the cardia ; it requires no pushing and can be easily managed by the patient himself. It is kept in position for a few minutes on each occasion at first, but later it can be withdrawn directly after it has entered the stomach. The lower extremity should not pass more than an inch beyond the cardia, which is situated, on an average, 16 inches from the teeth, as otherwise indigestion may result from irritation of the stomach. The patient feels relieved and realises that " the passage is clear " as soon as it is withdrawn. It should be passed immediately before meals : the food then enters the stomach without difficulty. In very early cases the tube may only need to be passed once : in my first case an ordinary bougie was passed the day after the symptoms commenced, and it was never

necessary to pass it again. Generally, however, the tube has to be passed before each meal at first ; then it can be passed once a day, and gradually less often, till finally it can be discarded entirely, even if symptoms have been present for as long as seven years, or it only requires to be passed at rare intervals when the patient feels that some slight obstruction is returning.

I have only had a single case in which no lasting improvement occurred, and in which the patient had to continue to use the mercury tube every day for years. A trial was made of the treatment devised by Russell in 1898, and more recently improved by Plummer,[10] which has been rendered superfluous in most cases by the introduction of the mercury tube. The patient slowly swallows 3 yards of silk thread in the afternoon and another 3 yards the following morning ; sufficient reaches the intestine to prevent its withdrawal when it is pulled tight. A tube is threaded over the silk through the cardia, which is then forcibly dilated by the inflation of a bag attached to the tube. Unfortunately this proved equally unsuccessful, so that the patient still had to use his mercury tube every day. I therefore asked Mr. R. P. Rowlands to divide his cardiac sphincter in exactly the same way as the pyloric sphincter is divided in Rammstedt's operation for the hypertrophic pyloric stenosis of infants. This was done on February 5th, 1924. In the short time which has since elapsed (June, 1924) the patient has been able to swallow food without feeling any obstruction, and it seems likely that the operation has cured the condition which had been present for seven years.

Waterbrash and the Morning Sickness of Alcoholics

The condition called waterbrash, the *vomissement pituiteux* of French authors, and certain associated phenomena can be most satisfactorily explained as due to a special form of achalasia of the cardia.

At a certain interval after a meal, which varies in different cases, but is fairly constant for each individual, an uncomfortable sensation of constriction, which may amount to

severe pain, is felt deeply beneath the lower end of the sternum. This may be accompanied by profuse salivation, which was so great in one of my cases that pain was felt in the jaws, doubtless owing to the capsule of the parotid glands being stretched by the hyperæmia of the unusually active glands. Occasionally the substernal discomfort or pain disappears spontaneously after a more or less long interval, but more frequently relief only occurs on vomiting a few mouthfuls of clear fluid, which is generally described by the patient as being like water (waterbrash), though it sometimes contains a good deal of mucus. The fluid is never sour in uncomplicated cases, but it may taste slightly salty or sweet. The vomiting is rarely accompanied by much straining, and the fluid may even rise into the mouth without any effort at all; it is rarely preceded by nausea. It is sometimes repeated two or three times at intervals of ten to twenty minutes.

It is clear that the fluid must come from the œsophagus and not from the stomach, as even when the previous meal was large and has only been finished within an hour, no food is present in the regurgitated material, which is alkaline in reaction, and has all the characters of pure saliva, although it is quite obvious that the stomach must still contain a considerable quantity of food mixed with gastric juice. That this is the case is sometimes proved when a few mouthfuls of gastric contents, recognised by their acid taste and reaction, and by the presence of partially digested food, are vomited as a result of straining immediately after the alkaline fluid has been brought up. Moreover, the volume of saliva vomited each time is generally between 60 and 120 c.c., which appears to represent the amount of fluid which the undilated œsophagus can retain without rejecting.

The vomiting is sometimes preceded by an obviously excessive flow of saliva, but more frequently no abnormal salivation is recognised by the patient, the saliva accumulating in the œsophagus without the patient being aware of its presence. The accumulation of fluid in the œsophagus is clearly the cause of the discomfort or pain felt beneath the end of the sternum.

Waterbrash may persist for years without any other

evidence of indigestion, but it is generally associated with some form of functional or organic gastric disease, and I have seen well-marked waterbrash in several patients with duodenal ulcer. It occurs particularly in conditions associated with gastric hypersecretion, probably because they also give rise to reflex hypersecretion of saliva, but Mathieu has observed it at the onset of gastric carcinoma.

The œsophageal origin of the fluid was first suggested by Mathieu,[11] but he thought that the accumulation was a result of cardiospasm, which was due to a reflex from the stomach produced by its irritating contents or by some lesion which also caused excessive salivation.

It seems to me more likely that when the flow of saliva is moderately excessive, it runs down the œsophagus without the patient's knowledge and without the aid of actual swallowing: the cardia is naturally closed, and the fluid therefore collects above it in the lower end of the œsophagus. Cannon [12] has shown that the presence of free hydrochloric acid in the stomach tends to inhibit the relaxation of the cardia. Hence gastric hypersecretion, which is the chief cause of excessive flow of saliva, tends at the same time to prevent the relaxation of the cardia. The food does not accumulate in the œsophagus, as the cardia relaxes during swallowing: thus I have never seen any stasis of the food in the œsophagus on examining a case with the x-rays. When obvious salivation occurs and the patient makes repeated deglutition acts, the cardia might be expected to relax; but by this time an excessive quantity of hydrochloric acid has accumulated in the stomach and inhibits the relaxation of the cardia, even when the swallowing acts cause peristaltic waves to reach the lower extremity of the œsophagus.

It is possible that the morning vomiting of alcoholic individuals is due to a similar process, although it is accompanied by more violent vomiting efforts. In this case the fluid consists of saliva mixed with a considerable proportion of pharyngeal and œsophageal mucous secretion, as catarrhal pharyngitis and œsophagitis are frequently associated with the catarrhal gastritis of alcoholic patients. As there is no gastric hypersecretion in alcoholic gastritis, reflex inhibition

of relaxation would not occur, the accumulation being due to excess of fluid running down the œsophagus during the night without the aid of actual deglutition. When the vomiting is violent the stomach may empty itself later, the fluid then brought up being bile-stained and sometimes faintly acid in reaction.

In some cases slight regurgitation of the gastric contents into the œsophagus may occur before the accumulation of saliva is ejected, so that the vomited material contains a small proportion of the gastric contents.

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PART II

Pelvi-rectal and Anal Achalasia (Hirschsprung's Disease; so-called Congenital Idiopathic Dilatation of the Colon)

Hirschsprung [1] of Copenhagen, in a paper read at the Berlin Society for the Study of Children's Diseases in 1886, described two cases of fatal constipation associated with dilatation and hypertrophy of the colon. They were good examples of what is now generally known as Hirschsprung's disease, although an account of two cases had been published forty years earlier by von Ammon.[2] The condition has also been described as megacolon and congenital idiopathic dilatation of the colon, but in my opinion pelvi-

rectal achalasia, or in some cases anal achalasia, is the most appropriate name for the disease.

It is only in recent years that its comparative frequency has been recognised. Thus Hale-White [3] could only find records of twelve cases in 1897, to which Crozier Griffith [4] added twelve in 1899, but in 1908 Finney [5] was able to collect 206 papers which had been published on the subject, and the literature during the last fifteen years has been even more extensive.

The disease occurs almost eight times more frequently in boys than in girls, but cases seen after the age of fifteen are equally distributed among males and females.

Pathology

In about half of the cases—ten out of nineteen at Great Ormond Street Hospital—the lower limit of the dilatation is at the pelvi-rectal flexure, where the movable pelvic flexure joins the fixed rectum at an acute angle. From this point upwards there is a rapid enlargement, the maximum diameter being generally about 4 inches higher. In the remaining cases the dilatation begins at the sphincter ani, and the normal narrowing of the pelvi-rectal flexure is obliterated. In about one-third of the cases the enlargement is confined to the pelvic colon or rectum and pelvic colon ; in the others varying lengths of large intestine are dilated, but the dilatation, which is often enormous, is always greatest in the pelvic colon, and diminishes as it is traced towards the cæcum, the small intestine being always spared.

The muscular layer of the dilated intestine is always hypertrophied, the thickness in some cases being a quarter of an inch. The hypertrophy is most marked in the circular fibres, but the layer of longitudinal fibres is always thickened and shows but little evidence of division into the normal bands, and the *muscularis mucosæ* is also hypertrophied (Finney [5]). The mesocolon and the peritoneum covering the intestine are thickened, the former containing unusually large blood vessels, lymphatics and lymphatic glands. The mucous membrane is always thickened from chronic inflammation and is often ulcerated.

At least nine different theories have been advanced as to the pathogenesis of the disease, but the majority do not account for the invariable presence of hypertrophy and the frequent observation of peristalsis in the dilated colon. Most authors follow Hirschsprung in regarding the condition as a result of a congenital developmental abnormality. Others, including Hawkins,[6] ascribed it to a congenital neuro-muscular defect. But the hypertrophy can only be the result of the increased work which the intestine has to do in in order to overcome some obstruction. Peristalsis occurring in a hypertrophied colon could not fail to evacuate it, if there were no obstruction to the passage of its contents.

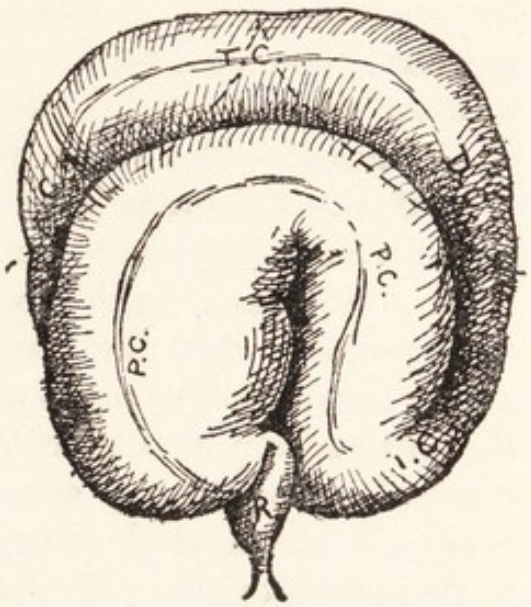


Fig. 33.—Drawing of the colon shown in Fig. 37, to show its position before removal from the body, with secondary kink between the dilated pelvic colon, P.C., and rectum, R. T.C., transverse colon. D.C., descending colon.

I believe that the obstruction is due in the group of cases, in which the dilatation begins at the pelvi-rectal flexure, to achalasia, or absence of active relaxation, of the circular muscle fibres at the pelvi-rectal flexure, when at the commencement of defæcation a peristaltic wave passes down the pelvic colon and reaches the flexure in the process of emptying the pelvic colon into the rectum. The obstruction leads to the accumulation of fæces and gas in the pelvic colon, which gradually becomes dilated; the excessive activity of the muscular coats in the attempt to pass on the fæces leads to hypertrophy. This may at first be sufficient to overcome the obstruction, but sooner or later the compensation breaks down and the dilatation becomes progressively greater. In the group of cases in which the rectum is dilated a similar condition of achalasia affects the sphincter ani, which fails to relax when the peristaltic wave, which should evacuate the rectum in the process of defæcation,

reaches it. In both varieties the condition of the colon is thus strictly comparable to the dilated and hypertrophied œsophagus, which I have shown is caused by achalasia of the cardia.

In those cases in which the rectum is not involved, the colon, when once dilated, as Perthes [7] was the first to point out, and as was clearly demonstrated at the operation on my first case, produces a kink by overhanging the undilated part below. The greater the distension of the pelvic colon, the greater is the obstruction (Fig. 33) ; thus when it is distended by pressure on its proximal part at an operation or post-mortem, the obstruction is seen to become exaggerated, whereas emptying the pelvic colon into the descending colon diminishes it. The obstruction would thus be maintained, even if the achalasia were to disappear. The absence of any obvious obstruction post-mortem is easily explained, as there is no organic stricture, the secondary kink being only demonstrable when the parts are in position. A laparotomy allows the dilated colon to rise out of the abdominal wound ; the obstruction is thus often relieved for the moment, and many surgeons have consequently failed to discover its existence at an exploratory operation. I have been able to demonstrate this valvular mechanism with the sigmoidoscope in two cases, and Bensaude and Sorrel [8] have seen it on four occasions. The achalasia theory accounts for the fact that the intestinal contents can be passed through a tube introduced into the dilated colon per rectum, especially if the secondary kink is rendered less acute by the adoption of the knee-elbow position, which causes the loaded pelvic colon to fall towards the diaphragm, whereas without the aid of a tube little or nothing is evacuated in spite of the strong peristaltic contractions of the hypertrophied and dilated intestine. In severe cases the kink prevents the passage of the tube until it is abolished during a laparotomy by pulling the dilated colon upwards. The secondary kink also accounts for the rare cases, one example of which I have seen, in which the patient can empty his distended intestine by defæcating in some unusual position, such as when leaning over the back of a chair, as by this means the kink may temporarily disappear.

In the cases in which the rectum as well as the pelvic colon is dilated this valvular mechanism does not occur. The condition is then due solely to achalasia of the anal sphincter, which for some reason does not relax when the peristaltic wave carrying the fæces from the pelvic colon through the rectum reaches it. The dilated and hypertrophied colon, which may result from obstruction due to fæces or to organic disease, whether this is congenital narrowness of the anus, as in Treves's [9] case, or an anal ulcer leading to spasm of the sphincter, as in Fenwick's [10] case, cannot be properly regarded as examples of this disease.

Symptoms

There is generally a history of constipation, dating either from birth or from the first few months of life. At an early stage the bowels cease to act spontaneously, and drugs gradually lose their effect, until an evacuation can only be procured by means of an enema. Very rarely the bowels are opened daily, but the quantity passed is never sufficient, and large accumulations of fæces are always found in the distended colon. The stools are generally soft or even semi-liquid, and at operations and after death the intestinal contents are found to be similar in character. In less severe cases, and especially in young children, scybala may be passed. In the late stages, if secondary colitis and stercoral ulceration are present, attacks of pseudo-diarrhœa may occur.

Soon after the onset of the constipation, the abdomen, which is generally normal in size at birth, gradually becomes enlarged owing to distension of the colon with gas and fæces, the size varying from time to time according to the frequency with which an evacuation is obtained. It gives a resonant note on percussion, but dull areas are present over fæcal accumulations. By examining the patient with the x-rays after a barium meal it is possible to recognise where the stasis begins, and if a barium enema is also given the exact extent of the dilatation can be discovered. My experience agrees with that of Bensaude and Sorrel,[8] who observed that in cases with well-marked toxic symptoms there is

generally delay in the passage through the whole colon, but in those in which no toxic symptoms have occurred the delay is confined to the dilated pelvic colon. In pelvi-rectal achalasia the rectum is generally empty, but in anal achalasia it is full of fæces and there is no pelvi-rectal flexure separating its lumen from that of the dilated pelvic colon.

Sooner or later an attack of complete obstruction generally occurs, no fæces being passed for such long periods as two or three months, though momentary relief sometimes follows the evacuation of small quantities of gas. The abdomen becomes enormously distended and tense ; it is then painful, and the pressure on the diaphragm may cause severe dyspnœa, cyanosis and palpitation. The outline of the distended colon is seen, and peristalsis is generally visible. Albuminuria and œdema of the legs, penis and scrotum are sometimes observed. Vomiting may now occur, and the patient become exceedingly emaciated ; death finally results from exhaustion, from general peritonitis secondary to perforation of a stercoral ulcer, or from some intercurrent disease, especially of the lungs. An attack of complete obstruction can often be relieved by enemata, or by the passage of a rectal tube into the dilated colon ; this permits the escape of gas and fæces under high pressure, but similar attacks are very apt to recur.

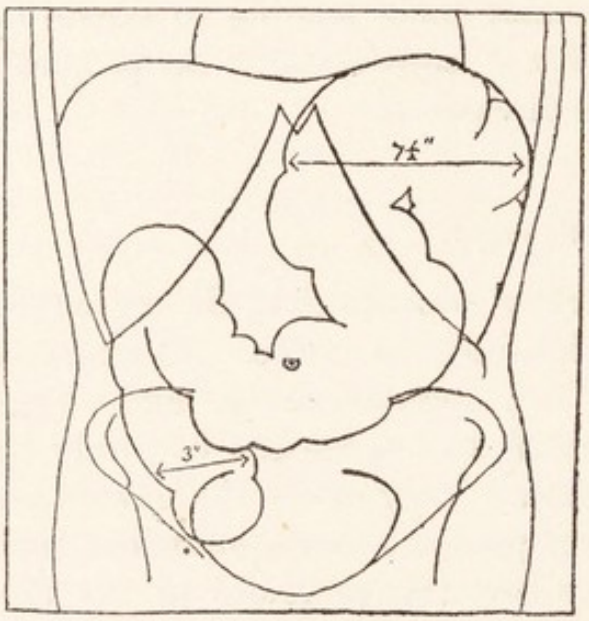


FIG. 34.—Megacolon due to pelvi-rectal achalasia in a man of forty. No symptoms beyond constipation since childhood. Bowels opened every four or five days with a four-quart enema. The hepatic flexure was reached in six hours and the pelvic flexure in twenty-four hours but no further progress was made at the end of seventy-two hours.

Death may occur in the first year of life, but more frequently between the ages of three and eight. In a few cases adult life is reached. In two of my cases the patients were forty (Fig. 34) and thirty-five (Fig. 35) respectively, and

had never suffered from anything worse than chronic constipation, and in another, a boy of nine (Fig. 36), the condition was accidentally discovered during a routine examination on account of slight general unfitness and a mild degree of constipation.

Latent Megacolon from Anal Achalasia.—Mr. B., aged thirty-five, 6 feet 7 inches in height, and weighing 15 stone, had always enjoyed good health and was a noted athlete. Whilst in England and on the East African coast, where he is an official, and where the climate is not very trying, he is perfectly well, his bowels being opened twice a day. He has to make frequent expeditions into the interior, where the heat is very great, and he perspires excessively; at the same time his meals are irregular, and he is unable to obtain green vegetables, so that, although he rides for five or six hours a day, he at once becomes constipated. When his bowels have not been opened for four or five days he takes gr. iv. calomel in the evening and an ounce of salts in the morning; a normal stool results without any pain. He consulted me in order to know what steps he should take in order to keep his bowels regular whilst on his expeditions.

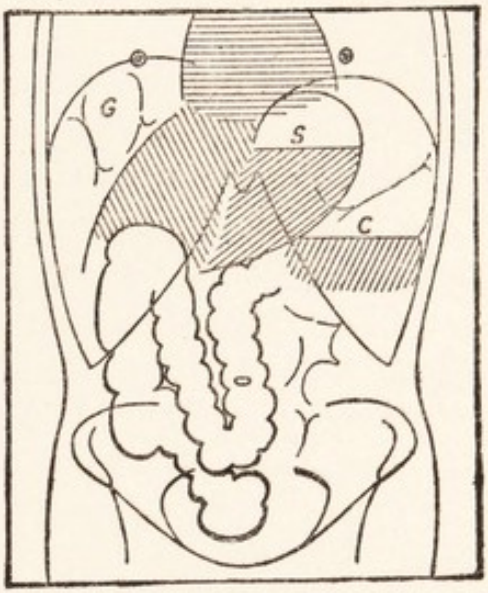


FIG. 35.—Latent megacolon with gas-containing coil, G, above the liver, in a case of anal achalasia; S, upper surface of contents of stomach; C, upper surface of contents of a dilated coil of colon.

An x-ray examination showed that his colon was abnormally long and dilated, but the chief dilatation was beyond the middle of the transverse colon. The exact anatomical relations could not be made out, but an enormous dilated sac of colon pushed up the left side of the diaphragm and contained semi-fluid fæces, the upper surface of which could be distinguished distinct from and below that of the gastric contents (Fig. 35). A part of the dilated colon was also above the liver, so that the gas-containing bowel could be clearly seen under the right dome of the diaphragm.

A similar condition was observed in the boy of nine already referred to, the distribution of the dilatation being almost exactly the same in the two cases (Fig. 36). A finger inserted in his rectum passed straight through a normal anal canal into an enormously dilated sac, and a sigmoidoscope could be introduced its entire length without meeting the slightest resistance. In spite of this remarkable condition there was no intestinal stasis.

These are apparently cases of anal achalasia, in which the hypertrophy of the intestinal musculature has produced compensation.

The following case is a typical example of the more severe form of the disease, as it occurs in young adults.

Megacolon in a woman of twenty-two. Death after colectomy.—Edith G., aged twenty-two, was admitted under me on September 27th, 1907. She had been constipated and had a large abdomen as long as she could remember. For the few weeks before admission she had become steadily more constipated and her abdomen more distended. She became dyspnœic and complained of abdominal pain, but she did not vomit. On admission she had been absolutely constipated for three days; her abdomen was tympanitic and enormously distended; the diaphragm was pushed up so far that the liver dullness extended from the third to the fifth space, and the heart dullness began in the first space. Some soft fæces were found in the rectum, and an enema was given with a copious result, but the distension was unaffected. A diagnosis of volvulus was made, and Mr. R. P. Rowlands operated. The other abdominal contents were completely hidden by the enormously distended colon, the muscular coat of which was greatly hypertrophied and the vessels much enlarged. The small intestine was normal. No volvulus was present, but the dilated pelvic colon was found to have folded over the rectum so that a kink was produced. By pulling the pelvic colon upwards, it became possible to introduce a tube from the rectum into it, and a large quantity of gas and fluid fæces was evacuated. The gas reaccumulated very rapidly; a rectal tube kept permanently in the pelvic colon gave relief, but it was frequently blocked and the distension returned.

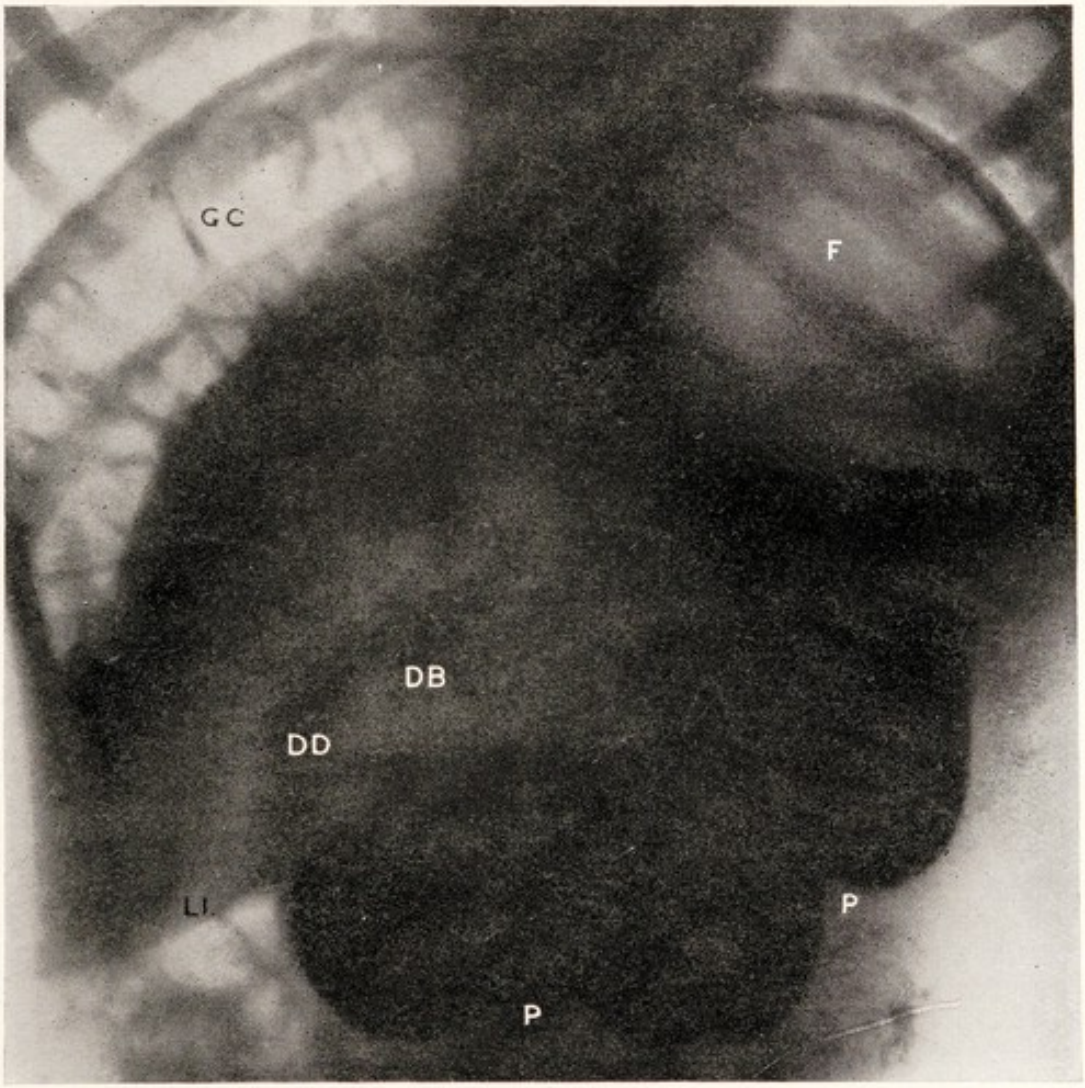


FIG. 36.—Anal achalasia in a boy of nine, leading to megacolon, part of the gas-containing hepatic flexure (GC) having passed behind and above the liver so as to be directly under the diaphragm. F, fundus. P.P, peristaltic waves of normal stomach. DB, duodenal bulb. DD, descending part of duodenum. (Radiogram by Dr. P. J. Briggs.)

As no improvement occurred in the patient's condition, it was decided to remove the dilated colon. The operation was performed on October 9th, but the patient died from shock

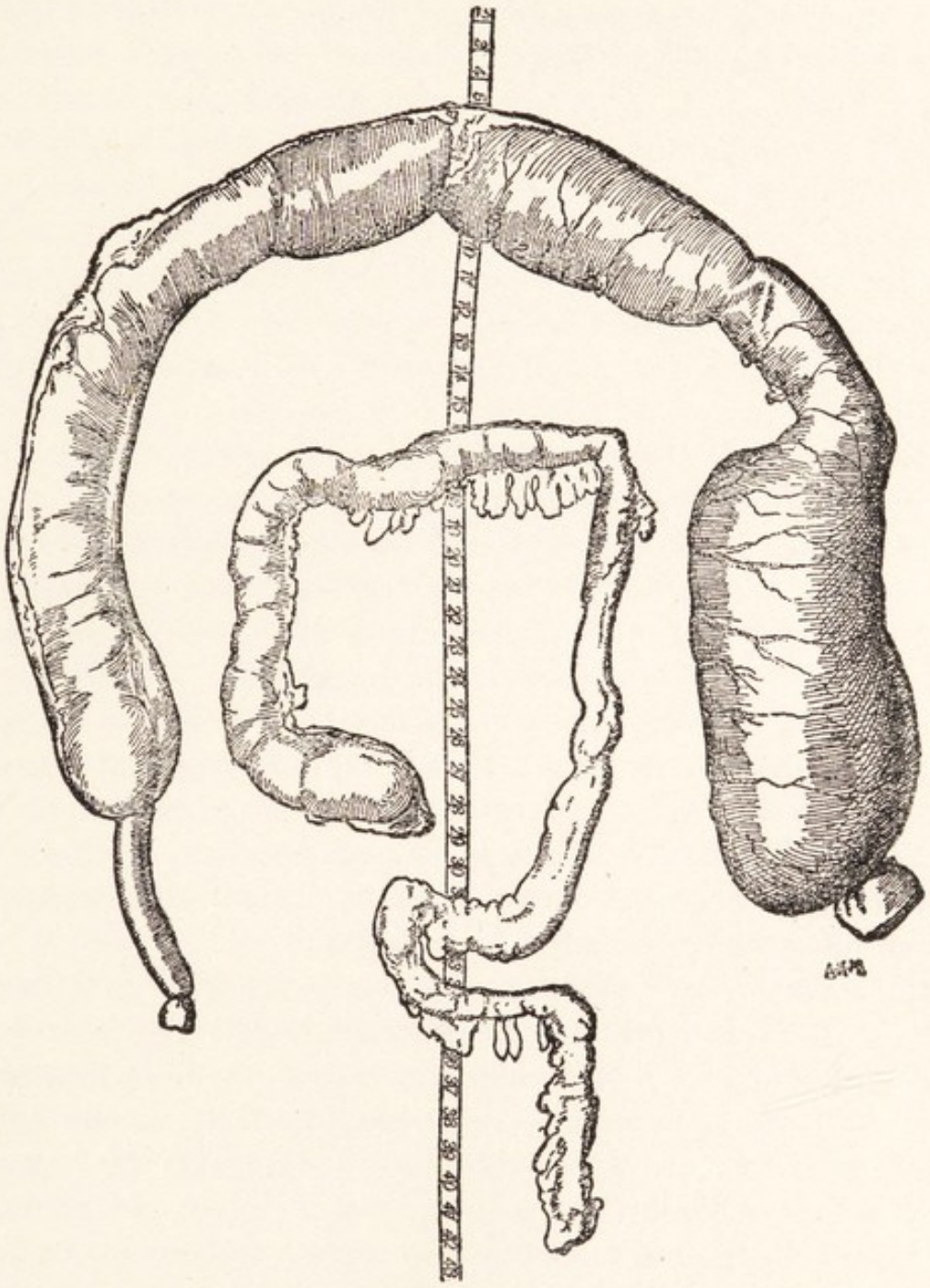


FIG. 37.—Drawing from a photograph of a normal colon and the colon removed by operation in a case of pelvi-rectal achalasia.

the following day. Fig. 37 is drawn from a photograph of the colon by the side of a normal colon.

Treatment

(*a*) *Anal Achalasia.*—All cases of anal achalasia ought to be cured, or at any rate kept in a satisfactory condition of

health, by non-surgical means. A rectal tube should be inserted into the dilated rectum every day and the colon washed out thoroughly. This can be done without any difficulty. It is generally necessary as a preliminary measure to empty the colon digitally. Thus in two of my cases a large and very hard mass of fæces had collected in the rectum, where it was acting as a kind of ball-valve which prevented the evacuation of the rest of the colon. It required to be broken up and removed bit by bit under an anæsthetic before the colon could be emptied. Five pounds of fæces were removed by this means in one case; the fæcal ball itself weighed a quarter of a pound and measured $2\frac{1}{4}$ inches in diameter.

It is obvious that no short-circuiting operation could be of any use and that colectomy is out of the question, as the obstruction is at the anus. The only possible operation would be a colostomy, but the results are extremely unsatisfactory, and I feel convinced that daily lavage, if carried out with sufficient thoroughness, should prove satisfactory in every case. In some it is possible to dispense with the treatment after a time, but it is doubtful whether the colon can even contract down to a normal size and whether the anal achalasia ever disappears, so that the patient will always remain liable to attacks in which the fæces have to be removed by lavage.

(*b*) *Pelvi-rectal Achalasia.*—In early cases of pelvi-rectal achalasia, such as in one of my series, and the second of the series published by Bensaude and Sorrel, medical treatment can cure the condition. Any impacted fæces should be removed and the colon thoroughly emptied by repeated irrigation. Abdominal massage and exercises are of value, as they help the emptied colon to regain its normal size, and they strengthen the stretched abdominal muscles. But the most important point in the treatment is to keep the colon as far as possible free from distension with gas and fæces. If, after the initial irrigations, castor oil does not act, glycerine enemata should be tried, and if they fail, an attempt should be made in the knee-elbow position to pass a rectal tube beyond the kink, so that flatus can escape and the bowel can be irrigated. It is, however, often first necessary

to manipulate a sigmoidoscope beyond the kink into the pelvic colon, the patient being in the knee-elbow position; an india-rubber tube is then passed through the sigmoidoscope, which is carefully withdrawn, leaving the tube in position. If the distension returns rapidly, the tube should be retained continuously.

When, as is sometimes the case, non-operative measures do not give relief, or it is found impossible to introduce a tube into the distended colon owing to the secondary kink at the pelvi-rectal flexure, a laparotomy should be performed. On pulling the distended colon upwards, a tube can be passed into it from the anus and the colon emptied; it is then generally advisable to make an anastomosis between the undistended rectum and the terminal ileum or, preferably, the lower end of the dilated part of the colon. It is, however, exceedingly difficult to do this, and it may even be quite impossible owing to the small size of the rectum and to its situation deep in the pelvis. Even if the primary operation is successfully performed, in most cases the whole of the dilated colon subsequently requires to be excised. A colostomy is only indicated as a temporary measure if there are urgent symptoms of obstruction, as the dilated bowel is so large and heavy that it is very liable to tear away from the abdominal wall and give rise to peritonitis by leakage: the mortality of the operation in pelvi-rectal and anal achalasia is consequently extremely high, eleven out of fourteen cases collected by Mummery [11] having died.

My own experience of surgical treatment has not been happy. In addition to the case already described in detail, in which death followed colectomy, a boy of five died from shock a few days after ileo-proctostomy had been performed. But a girl of twenty, who required a colectomy after an ileo-proctostomy had proved ineffectual, was very much better, though not completely cured, when I last saw her nearly two years after the first operation. I have also had the opportunity of observing the excellent results obtained from an ileo-proctostomy performed by Sir Arbuthnot Lane on a boy of sixteen for pelvi-rectal achalasia.

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THE SINS AND SORROWS OF THE COLON*

An Address delivered before the Harrogate Medical Society on November 26th, 1921.

THE sins of the colon are its diseases. But I sometimes wonder whether it is not more sinned against than sinning, for what with attacks from above with purges, attacks from

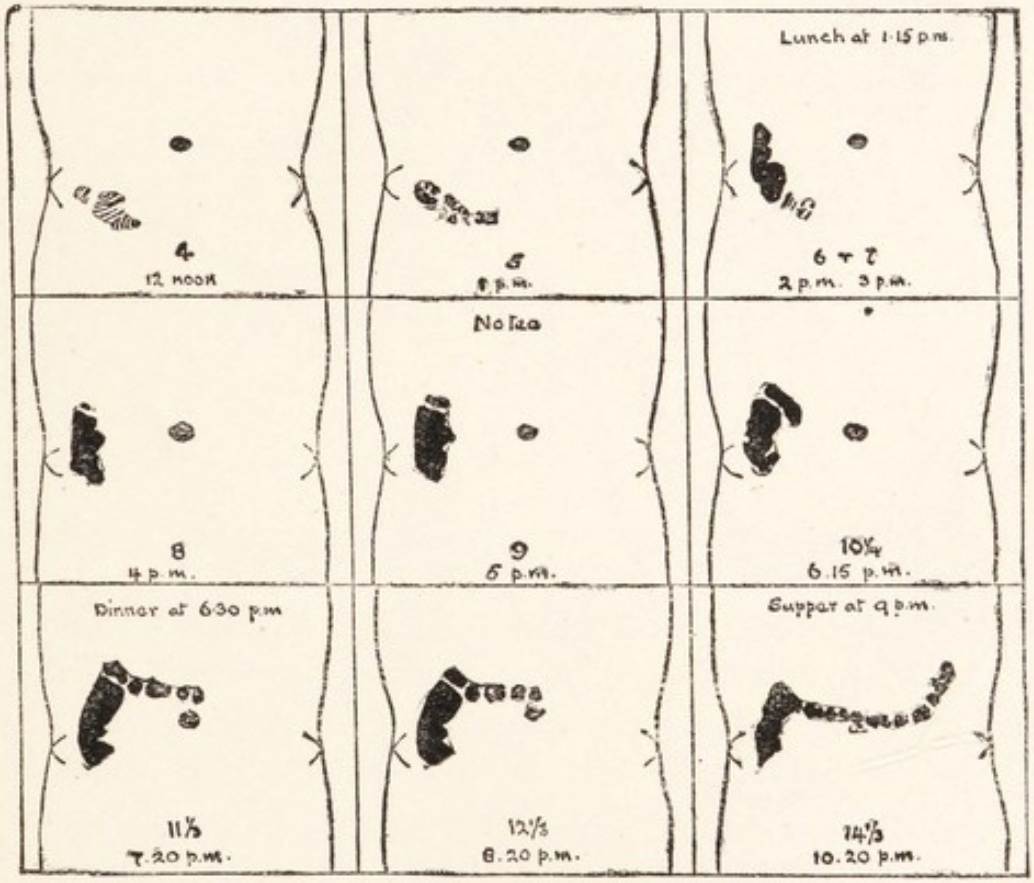


FIG. 38.—Hourly tracings to show effect of meals on the movements of the colon. The opaque meal was taken at 8 a.m.

below with douches, and frontal attacks by the surgeon, its sorrows are numerous and real. I believe that a more thorough appreciation of its normal anatomy and physiology, and the routine employment of the various methods of examination, which modern science has made available, are required in order that its sins may be recognised at such an

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early stage that treatment may lead to their complete and permanent relief.

The Motor Functions of the Colon

Like all other hollow organs the motor functions of the colon depend upon tone and peristalsis, which are mutually

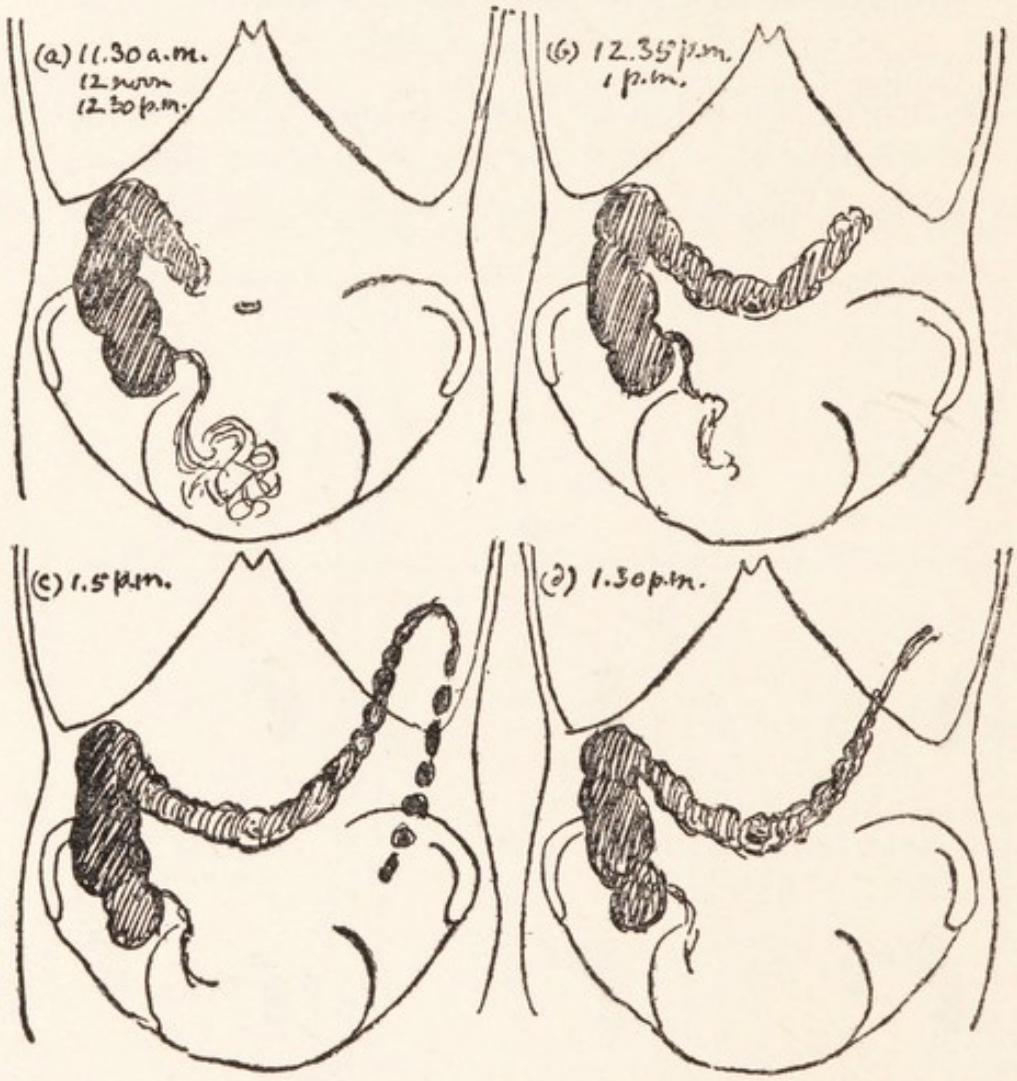
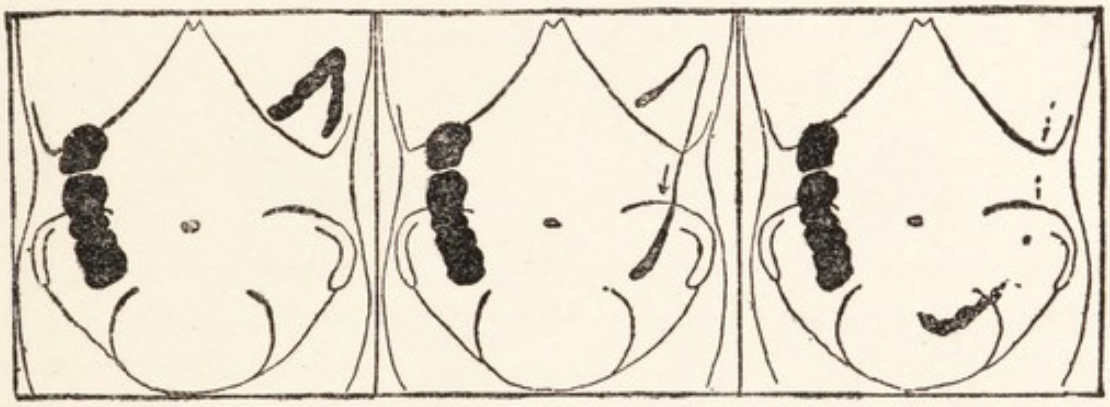


Fig. 39.—Tracings taken to show effect of dinner, finished at 12.30 p.m. and followed by a slight desire to defæcate at 1 p.m., on the colon movements. Opaque meal taken at 7 a.m.

independent. An atonic stomach or colon is often referred to as if it were one in which peristalsis was deficient, but peristalsis is often very active in the presence of hypotonus and may be weak or irregular in the presence of hypertonus. The tone of the colon depends largely upon the bulk of its contents; it varies continually according to the amount of fæces and gas present in each segment at the moment. Owing to this the internal pressure is normally constant and

only rises when its tone or the volume of its contents is pathologically excessive, pain being then produced. As the cæcum and ascending colon contain large quantities of semi-fluid fæces during the greater part of the day, their tone is less and their lumen is consequently much greater than that of the rest of the large intestine, especially the descending and iliac colon, which are generally empty and consequently in a state of tonic contraction, which more or less obliterates their lumen. Thus it is quite normal to find a large and splashy cæcum, when the iliac colon can be felt in the left iliac fossa as an almost solid cord.

Anybody who has made frequent x-ray examinations after a barium meal must have been struck by the remarkable



(*a*) (*b*) (*c*)

FIG. 40.—Mass peristalsis of colon, provoked by the sight and smell of food in a patient who felt sick with hunger.

contrast afforded by the continuous peristalsis of the stomach and the continuous peristalsis and segmentation of the small intestine on the one hand, and the completely motionless colon on the other. On comparing the appearance of the colon every hour through the day, I was struck by the fact that it only changed materially after those hours in which a meal had been taken (Figs. 38 and 39). By making a screen examination at intervals of a quarter of a minute during the later part of a meal and immediately after, Alan Newton and I [1] were rewarded by seeing on several occasions "mass peristalsis," which E. G. Slesinger and I had already in 1907 seen during defæcation, and Holzknecht [2] had subsequently observed in the course of a routine examination. It is now recognised as being the only movement of importance occurring in the colon (Figs. 40 and 41). Two or three

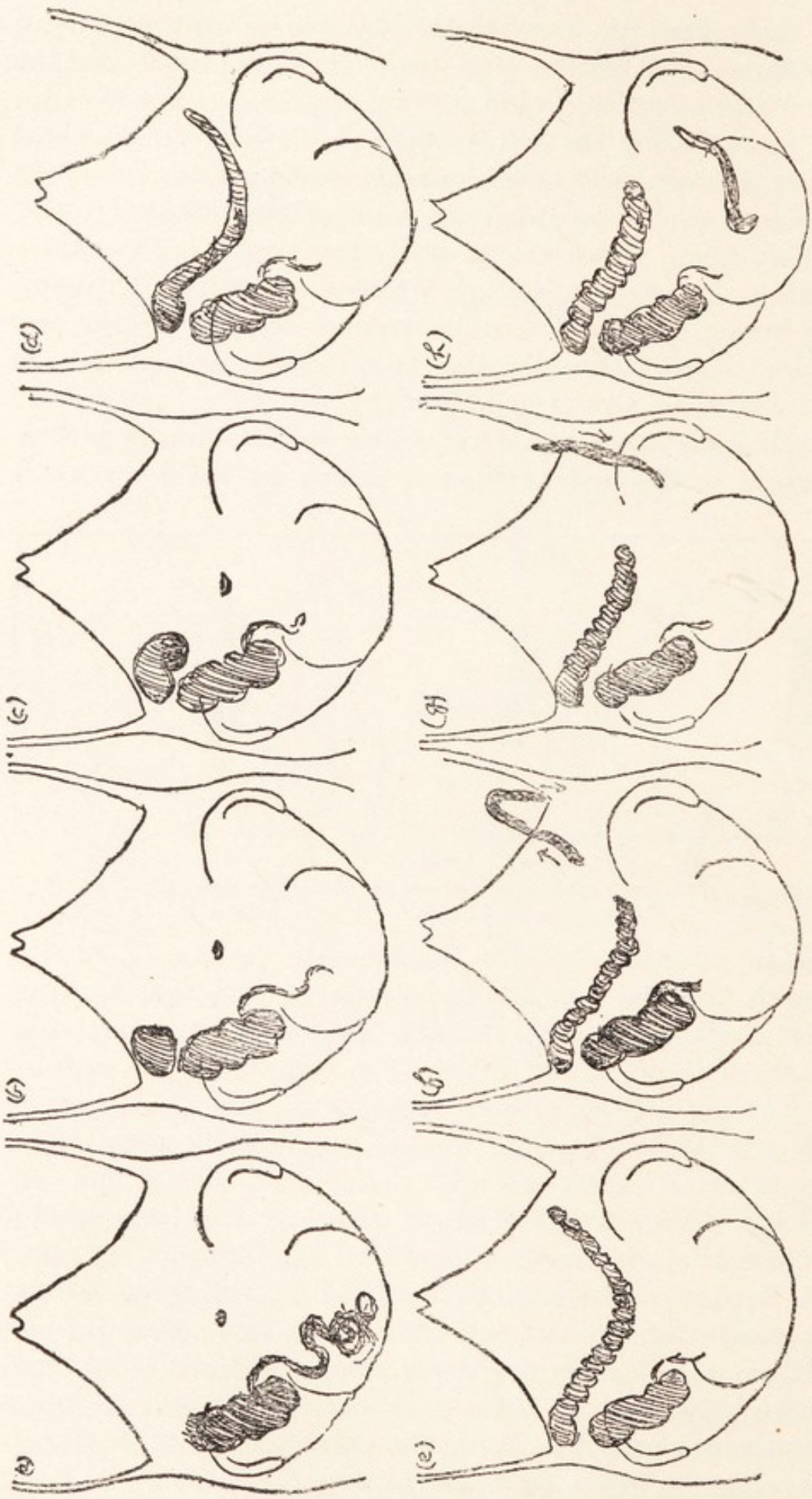


FIG. 41.—Tracings showing mass peristalsis occurring immediately after luncheon at 12 noon, an opaque meal having been taken at 7 a.m. An interval of five minutes occurred between the series (*a*) to (*e*) and the series (*e*) to (*h*).

times a day a powerful peristaltic wave moves rapidly along a considerable length of the bowel, carrying all the contents before it. The chief stimulus to this movement is the gastro-colic reflex, which follows the entrance of food into the empty stomach. After all of the soluble material and most of the water have been absorbed from the intestinal contents, they are carried from the cæcum and ascending colon by mass peristalsis to the pelvic colon, where they remain until the first peristaltic wave of the following morning occurs, either as a result of the stimulus of getting up and dressing or of breakfast. They are then carried into the previously empty rectum, where they give rise to the desire to defæcate, which is followed by the normal reflex process of defæcation. Consequently during the greater part of the day the cæcum, ascending colon and pelvic colon are more or less full, but the rest of the colon is generally empty.

The Radiology of the Colon

No attempt should be made to treat a case of constipation which does not quickly respond to simple treatment until an x-ray examination has been carried out. This should not be done until the patient has discontinued the use of aperients for forty-eight hours, but, if necessary, an enema can be given the day before and again in the early morning of the day on which the examination begins.

By no other means is it possible to compare the position of the colon in the erect and horizontal postures, to determine whether adhesions are present, which fix its different segments to each other or to neighbouring structures, and to discover how quickly the intestinal contents traverse the bowel and how long their residue remains in each segment. It is, however, useless to carry out such an investigation unless it is realised that the rate for the passage of the intestinal contents varies within wide limits in healthy individuals, and that the position and mobility of the cæcum, ascending and transverse colon are also subject to considerable variations. It is not pathological for the cæcum to drop into the pelvis in the erect position, and a powerful forward in the Guy's fifteen of 1907, who had never had a day's indigestion

or constipation, was only one of several perfectly healthy individuals I have seen with the greater curvation of the stomach over two inches below the umbilicus, and the transverse colon reaching almost to the bottom of the pelvis.

Ptosis of the colon hardly ever gives rise to symptoms by causing kinks, and stasis in the colon must be considerable before it can be regarded as of real importance.

It is an interesting fact that since I gave an account of the first patients with constipation ever investigated by means of the x-rays in a paper read before the Royal Society of Medicine in 1907, more than half of the severe cases which have been sent to me have suffered from pure dyschezia, or inefficient defæcation, the passage through the intestines having been normal in rate. In this condition the only treatment required is re-education of the act of defæcation by a proper attention to the hygiene of the bowels, together with the use of graduated enemas in resistant cases. In the remaining cases stasis in the proximal part of the colon was most common ; it is comparatively rare for the whole of the large intestine to be involved. An accurate diagnosis will show what form of treatment by diet, drugs, massage, which should be given on the first occasion under the x-ray screen so that the exact manipulations required can be observed, exercise, and, in the case of general colonic stasis, intestinal lavage is indicated in each individual case.

Radiography after an opaque meal rarely reveals the presence of a growth in the early stage ; in all suspicious cases a barium enema should be given, as this is often arrested at the seat of the tumour, but I have seen several patients in whom this method also failed to show anything abnormal, although a growth was discovered by other means or subsequent events showed that one was present.

Colitis and "Colitis"

Colitis is inflammation of the colon. But the term "colitis" is very frequently applied in the absence of any evidence that the colon is inflamed. I am convinced that the loose employment of the word is an important factor in the development of many cases of severe hypochondriasis.

Colitis should never be diagnosed unless positive evidence of its presence is obtained by examination of the stools and by means of the sigmoidoscope. Under normal conditions the mucous membrane of the colon is kept moist by the secretion of mucus, which renders the onward passages of the fæces more easy. Like all other mucous membranes, it reacts to mechanical and chemical irritation by the secretion of excess of mucus, in order to protect its delicate lining epithelium from injury. Consequently the presence of hard fæces in the normal colon calls forth a secretion of mucus. If the fæces accumulate in the rectum, the mucus is unformed. If, however, the mucus is produced in the pelvic colon or more proximal part of the large intestine, and a thin layer of mucus remains in contact with the mucous membrane sufficiently long, a slowly acting ferment, mucinase, which is present in the mucous membrane, causes it to coagulate, much in the same way as fibrinogen forms fibrin when blood coagulates. A membrane of coagulated mucus is produced, and this is subsequently passed in the form of shreds, or occasionally as tubular casts of the part of the colon in which it was produced. Microscopical examination of this mucus may demonstrate the presence of desquamated epithelial cells, but there are no pus cells or other signs of inflammation, and the sigmoidoscope invariably shows that the mucous membrane is perfectly healthy. The names "mucous colitis" and "muco-membranous colitis" commonly applied to this condition are therefore incorrect. When pain caused by spasm of the colon coexists, as it often does, the term "muco-membranous colic" might be used, but in the absence of pain the condition should not be regarded as any more pathological than the presence of a little unformed mucus with scybala, which have been retained rather longer than usual in the rectum.

When mucus is present with soft or fluid fæces, colitis is more likely to be present. But inquiry must first be made as to whether an aperient has been taken, because the mucous membrane also protects itself from chemical irritation by drugs by the production of mucus. Thus the existence of colitis can only be inferred from the discovery of mucus, if the fæces are unformed and no aperient has been taken.

More important than mucus is the presence of pus in the stools. This always indicates that some organic pathological condition exists. In cancer and in ulcerative colitis the pus can generally be recognised by the naked eye. If, however, it comes from the more proximal parts of the colon, it is likely to be intimately mixed with the fæces and the mucus, both of which should be examined microscopically, especially if the latter is unformed and opaque instead of transparent.

In the absence of hæmorrhoids bright red blood in the stools is of equal significance. If no mucus or pus is present it probably comes from a rectal polypus, but if mucus and pus coexist acute hæmorrhagic colitis, ulcerative colitis, dysentery or cancer is almost certainly present.

Unless abdominal or digital examination of the rectum reveals the presence of a growth with certainty, a sigmoidoscopic examination should be made in every case, in which the symptoms and the appearance of the stools suggest the presence of colitis or a growth.

The Sigmoidoscope

The sigmoidoscope is one of the most valuable of all instruments used in the investigation of disease, and yet it is rarely employed except by surgeons, especially those interested in diseases of the rectum. In my opinion every physician and every practitioner should familiarise himself with the sigmoidoscope. With a little practice it can be introduced with perfect safety into the bowel of women as well as men without an anæsthetic and without causing anything more than a moderate degree of discomfort. An anæsthetic makes it impossible to assume the knee-elbow position, in which the passage round the pelvi-rectal flexure can be negotiated in almost every case without inflation, which is a matter of great importance, as inflation not only causes pain, but may also be dangerous when the wall of the colon has become thinned by ulceration.

It is no more justifiable to treat colitis without first inspecting the mucous membrane of the colon with the sigmoidoscope than it is to treat a sore throat without looking at the pharynx. I have seen numerous cases, which had been

treated for months as "colitis," in which the sigmoidoscope revealed the presence of a growth. It must be remembered that the pelvi-rectal flexure, the most common place in the colon for the development of cancer with the exception of the rectum, is beyond the reach of the finger introduced per anum, and a growth here and in the lower six inches of the pelvic colon, which are also accessible to inspection with the sigmoidoscope, is often impalpable from the abdomen, although it can sometimes be felt through the front wall of the rectum or by bimanual examination.

With the sigmoidoscope, too, the various forms of colitis can be recognised, the absence of any inflammation in muco-membranous colic can be demonstrated, the diagnosis between amœbic and bacillary dysentery can be made, and the process of recovery in colitis and dysentery can be watched. The symptoms of ulcerative colitis and dysentery, like those of gastric and duodenal ulcer, disappear under treatment long before the ulcers have healed. We have the great advantage in treating the former that the sigmoido-scope makes it possible to determine when the cure is really complete, and no case should be allowed to pass from active treatment until the sigmoidoscope has demonstrated that the mucous membrane is perfectly healthy. By this means alone can disappointing relapses be prevented. Only when the sigmoidoscope comes into its own, will the surgeon see most cases of cancer of the pelvic colon and upper part of the rectum at the early stage, in which alone a radical cure by operation is still possible.

The Use and Abuse of Purgatives

If the fortunes made from purgative pills had been devoted to the institutions which treat the victims of their abuse, the financial problem of the voluntary hospitals would have been solved. About £10,000,000 were expended in 1921 on patent medicines, the majority of which contain purgatives.

I have already pointed out that the stools should be inspected and the x-ray examination performed whilst no aperient is being taken. It is interesting to observe how large a proportion of patients, who are supposed to be the

victims of toxæmia from intestinal stasis, feel better whilst these examinations are being carried out. The fact is that symptoms result far more frequently from the artificial diarrhœa produced by purgatives than from intestinal stasis. Purgatives often cause abdominal pain, intestinal stasis very rarely. Bacterial decomposition is very active and excess of toxins is produced and absorbed in the colon when its contents are kept fluid by the use of purgatives, but the reverse is the case in the semisolid or solid contents of the colon in intestinal stasis.

On several occasions when I have been asked to decide whether the operation of colectomy, which had been recommended for "intestinal stasis," should be performed, I have found that all the symptoms disappeared on giving up purgatives and adopting some more rational treatment. It is sad that the description Gulliver gave the Houyhnhnms of the habits of his fellow countrymen is as true to-day as it was in 1727: "They take in at the orifice above a medicine, equally annoying and disgustful to the bowels, which relaxing the belly drives down all before it; and this they call a *purge*." I do not say that an aperient should never be used, but when required, one should be chosen and a dose should be found which result in the passage of a single formed stool each morning.

Intestinal Lavage

The mythical origin of intestinal lavage should be of interest in Harrogate, where many thousand Plombières douches are administered every year. Pliny (A.D. 77) tells how the Egyptians learnt to wash out their bowels from observing the habits of the ibis: "He washes the inside of his body by introducing water with his beak into the channel, by which our health demands that the residue of our food should leave." It is cruel to deprive the ibis of his claim to this epoch-making discovery, but the truth must be told: the ibis does not give himself a Plombières douche, but after washing his beak in water he oils it in his preen-gland, which is situated near the anus, in preparation for preening his feathers.

In the seventeenth century the enema reached the height



Sic homines édocuit

of its popularity. It is recorded that Louis XIV. received several thousand intestinal douches in the course of his life, and that the pious Duchess of Alva treated her sorely ill son with enemas of an emulsion of religious relics. Unhappily they failed to save him.

The last twenty years have seen a remarkable revival in the popularity of the intestinal douche, a popularity which has led at times to its indiscriminate use for conditions in which it is not suitable. It is a valuable remedy, but its precise indications require to be defined, and it should be properly administered.

In the first place, intestinal lavage is of use when it is necessary to remove retained fæces from a colon, which on account of its irritable or inflamed condition ought not to be further irritated by the use of aperients. Muco-membranous colic comes under this category. The fluid used should be of a non-irritating character, or a condition of catarrhal colitis will be added to the hypertonic and hypersecretory condition already present, just as the inhalation of irritant fumes produced by the burning of the powders used in asthma causes catarrhal bronchitis to be added to the simple hypertonic and hypersecretory condition of the bronchi, which is alone found in uncomplicated asthma. I had thought at one time that the Harrogate sulphur water used for intestinal lavage might sometimes act as such an irritant, but I have found by actual experiment on the healthy mucous membrane of the colon that it is no more irritating than normal saline solution. It would be interesting to know whether it owes to its radio-active or other constituents any healing properties not possessed by the latter.

There is a real danger that a course of intestinal lavage in cases of this kind might lead to constipation by making the patient too dependent upon them. For this reason patients should attempt to get their bowels open naturally each morning before they receive their douches ; if this is impossible, they should take paraffin together, when necessary, with the minimal dose of senna required to produce a stool.

Secondly, intestinal lavage is of great value in the treatment of the severer forms of colitis, and especially of ulcerative colitis. Antiseptic and astringent drugs can be

applied by this means directly to the mucous membrane in any required strength, without becoming diluted in the stomach and small intestines and without irritating them. The drug I have found most valuable in the local treatment of colitis is tannic acid, ½ to 2 grains to the ounce.

It is of great importance that the douche should be properly administered. Nurses are always taught to pass the tube as far into the rectum as possible, and they are rarely satisfied unless twelve or more inches have been introduced. Until comparatively recently I understand that this was the practice not only in Plombières, but also in Harrogate and the other English spas in which the treatment has been employed. But the pelvi-rectal flexure, where the freely movable pelvic colon joins the fixed rectum at an acute angle, is 4½ inches from the anus, and it is a physical impossibility to pass a rubber tube beyond the flexure, except sometimes in the knee-elbow position or through a sigmoidoscope which has been manipulated past it. This was proved long ago by Sir James Goodhart in the post-mortem room, and in 1908, and again more recently, I demonstrated the same fact with the x-rays, which show that the tube turns back when the flexure is reached and then curls up in the rectum (Fig. 42). The end of a tube passed in the usual way must therefore rub against the mucous membrane of the rectum, and when twelve or more inches of stiff tubing are introduced into the rectum it is obvious that a considerable amount of damage may be done. This explains the observation I have frequently made, that in cases of severe colitis treated by douching through a tube introduced in the ordinary manner, the sigmoidoscope shows a pelvic colon either healed or nearly healed, whereas the whole of the rectum, which has been rubbed every day with the tube, is still acutely inflamed. The tube should therefore be introduced not more than two inches beyond the anus. The fluid should be run in slowly at a pressure not exceeding twelve inches of water, and not more than a pint and a half should be used. The x-rays have shown that a barium enema of a pint and a half of fluid, introduced at a pressure of twelve inches through a tube inserted two inches beyond the anus, invariably reaches the cæcum, whatever position is

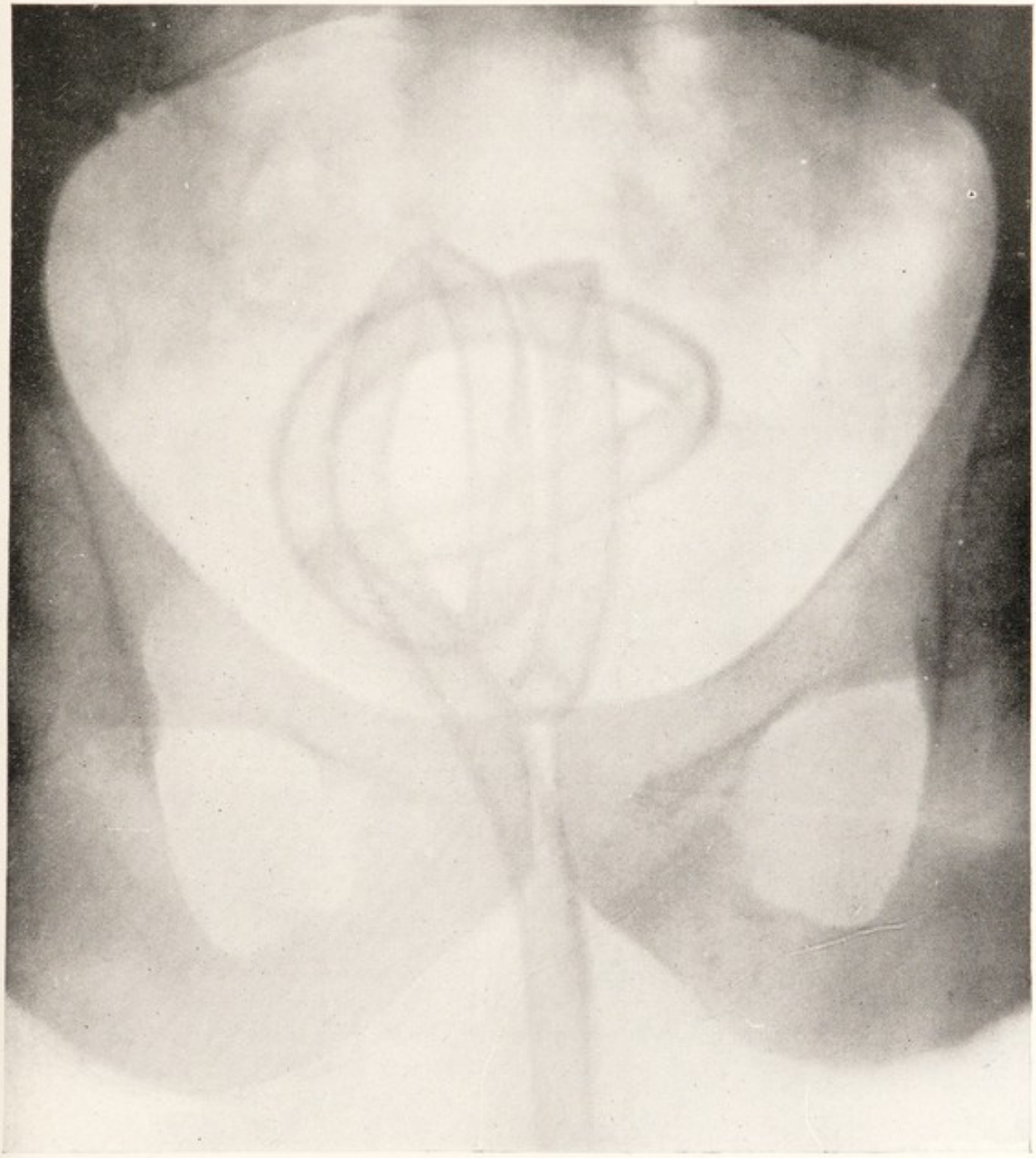


FIG. 42.—Skiagram by Dr. P. J. Briggs, showing rubber tube coiled in rectum after insertion in the ordinary manner for giving a so-called "high enema."

assumed by the patient, unless organic obstruction is present. I believe that de Graaf was correct when he wrote in his monograph, *de Clysteribus*, in 1668, that the usual ritual of lying in a series of positions during the administration of the douche has not the slightest effect. There is no doubt, however, that the knee-elbow position, by making the pelvi-rectal flexure less acute, allows the fluid to pass more readily into the pelvic colon and so prevents the over-distension of the rectum, which otherwise may make it difficult for the patient to retain the fluid for twenty or thirty minutes, as is advisable in the severe forms of colitis.

The Surgery of the Colon

Apart from the treatment of cancer of the colon, diverticulitis, and other causes of acute and chronic obstruction, the indications for surgery in diseases of the colon are few.

At one time I believed that appendicostomy or cæcostomy should be performed in every case of ulcerative colitis of any severity, as Lockhart-Mummery has so persistently urged. But since I discovered that anti-dysenteric serum has such a remarkable healing effect on most cases of the disease, I believe that it will in the future only be necessary to perform the operation in the exceptional cases in which no improvement follows the intravenous injection of large doses of serum (*vide* page 160).

I have always held that intestinal stasis only requires surgical interference in very rare and neglected cases, in which prolonged medical treatment fails to relieve local and general symptoms of real severity. In the fifteen years I have been interested in the subject I have only recommended five patients to undergo an operation for this condition—three times short-circuiting and twice partial colectomy. One patient died, one was completely and permanently cured, and the remaining three were benefited to a varying extent. Short-circuiting or excision of the part shown by the x-rays to be affected should be performed in preference to complete colectomy. The statistics of Guy's Hospital show that the mortality in total colectomy for intestinal stasis is about 16·5 per cent. The ultimate

results of the operation would require to be extremely good to justify such a high mortality, considering that with the exception of one case recorded by Lockhart-Mummery [3] intestinal stasis has never, so far as I know, proved fatal. I have come across an occasional brilliant result, but much more frequently the patient is either no better or is actually worse, and sometimes very much worse, than he was before the operation. It is a surgical aphorism that no operation should be performed on the stomach in the absence of a demonstrable lesion, and I look forward to the time when a similar aphorism will be applied to the colon. I have been appalled in the past to see how lightheartedly colectomy has been recommended for comparatively trivial symptoms, before any serious effort had been made to treat them by other means. But it is satisfactory to note that the operation, which reached the height of its popularity shortly before the war, is gradually becoming obsolete. I was told in 1919, during my visit to Cleveland, Baltimore, and the Mayo clinic, that after an unsatisfactory trial colectomy was now no longer practised for intestinal stasis, and in contrast to the forty colectomies performed at Guy's in 1914, only one was performed in 1920 and not one in 1921.

A Diagnostic Clinic for Harrogate

I have endeavoured to show how the treatment of diseases of the colon should never be undertaken before a thorough investigation has been carried out. I have not referred to various other examinations of equal importance—such, for example, as that of the secretory functions of the stomach by a fractional test meal, which may reveal the presence of achlorhydria, one of the most common causes of chronic diarrhœa and a powerful predisposing factor to infection of the bowel.

These investigations require team-work. Each physician practising in a health resort like Harrogate should have at his disposal a diagnostic clinic, into which his patients could be admitted for ten days or a fortnight whilst he investigates them by the usual clinical methods, inspects their stools, and, when necessary, makes sigmoidoscopic examinations,

whilst his radiological, biochemical and bacteriological colleagues carry out such examinations as he may direct. At the end of this period he will be in a position to advise what treatment is required during the remainder of the patient's visit.

If possible, the physicians should have no financial interest in the nursing-home side of the clinic. Patients should receive two accounts, one from the clinic and one from the physician. The latter should be an inclusive one, fixed beforehand, which should cover every examination which may be required. A certain proportion of the physician's fee should be paid to a central fund, out of which the radiographer and pathologists receive their salaries, which would thus be proportionate to the amount of work they are called upon to perform.

During the past year I have been associated with a clinic run on somewhat similar lines. Investigations have been carried out by clinicians, pathologists and a radiographer, working as a team, and I can assure you that my work has been more interesting, less fatiguing, and more satisfactory from my own and from my patients' point of view than it ever was before. I believe that the future of medicine lies largely in the development of team-work in diagnostic and treatment clinics. In this direction Harrogate has a great opportunity. It should lead the way in establishing spa treatment on a sound scientific basis, so that those earlier days will sink into oblivion when spa treatment meant the application of spa water to the skin, the stomach and the bowel, whatever was the matter with the patient, and Guy Patin's criticism of mineral waters, "I do not believe much in these, they never cured anybody, and I never believed that they would," was justified. Harrogate will then maintain its position as the Mecca for the sins of the colon, and will be free from any suspicion of reproach as adding to its sorrows.

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ULCERATIVE COLITIS*

History

Simple ulcerative colitis appears to have been first recognised by Sir Samuel Wilks[1] at Guy's Hospital in 1875. He pointed out that severe ulceration was occasionally found in the colon of individuals who had never been abroad, and that, although it was indistinguishable anatomically from dysentery, it must yet be a distinct disease, as the latter was accompanied by characteristic constitutional disturbances and was probably due to malaria. A study of eight cases dying at Guy's Hospital was published by Hale-White[2] in 1888, and of twenty additional cases by Cameron and Ripman[3] in 1910. These authors followed Wilks in regarding ulcerative colitis as distinct from dysentery, but believed that in most cases it was a secondary manifestation of some general toxæmia, such as that caused by granular kidney, rather than a specific and primary intestinal infection. Saundby[4] in 1906 and Hawkins[5] in 1909 had, however, published good clinical descriptions of the disease, which they both regarded as probably due to a dysenteric infection.

In a report on an epidemic of "idiopathic ulcerative colitis," which resulted in 118 deaths in the Lancaster County Asylum in 1898, Gemmel[6] expressed his belief that this condition, which had always been well known in asylums, was really dysentery. Vedder and Duval,[7] working under Flexner in 1902, proved that epidemics of "dysentery" occurring in institutions in America were caused by the *B. dysenteriæ*, and two years later Eyre[8] showed that asylum dysentery in England was also caused by this organism. As the *B. dysenteriæ* is likely to be so enormously outnumbered by the *B. coli* in the stools, the isolation of the

* Reprinted, with additions, from *Guy's Hospital Reports*, lxxi., 26, 1921; and a note contributed to the discussion on "Ulcerative Colitis" at the Proctological Sub-section of the Royal Society of Medicine, May, 1923.

former, except at the onset of acute cases, is extremely difficult.

So far as I am aware no bacteriologist has yet succeeded in isolating a dysentery organism from the stools in the sporadic disease as it occurs in England, but Dudgeon [9] has isolated a Flexner bacillus from material obtained from the surface of an ulcer through a sigmoidoscope in two cases.

During the last fourteen years Lockhart Mummery [10] has made several important observations on ulcerative colitis as a result of his investigations with the sigmoidoscope, the use of which has entirely revolutionised our knowledge of the disease.

With the exceptions I have mentioned, very little has been written on ulcerative colitis in England and in America ; and in no text-book on medicine, so far as I am aware, is there an adequate description of the disease from a clinical standpoint. A review of the Continental literature is equally disappointing ; the only valuable contributions I have been able to find were written by Mathieu [11] in France and Adolf Schmidt [12] in Germany.

Ætiology

Ulcerative colitis is a condition, which occurs sporadically in England and in other countries in which dysentery is not epidemic. Young adults are most frequently affected, and the disease is equally common in men and women. It is undoubtedly infective in origin, and from the very close similarity it bears to bacillary dysentery it would seem probable that the unknown organism which causes it must be closely related to the *B. dysenteriæ*. There is generally no evidence connecting ulcerative colitis with oral sepsis or appendicitis, but I have seen the condition complicated by secondary infection from the teeth in one case, and from a tubal abscess in another.

Ulceration of the colon also occurs in rare cases of uræmia, probably as a result of the excretion into the large intestine of toxins which cannot be excreted by the diseased kidneys, and in mercurial poisoning. The rectum and pelvic colon may be ulcerated as a result of infection with gonococci, tubercle bacilli, streptococci or other organisms introduced

per anum or invading them from neighbouring organs. None of these conditions should be included under the name of ulcerative colitis. The ulceration of the colon which occurs in typhoid and paratyphoid fever is also, of course, distinct, but the pathology of dysentery requires consideration in any discussion on sporadic ulcerative colitis.

Morbid Anatomy

Sigmoidoscopic examinations at different stages of the disease and *post-mortem* investigations show that the primary change is an acute inflammation of the mucous membrane of the colon. Patches of localised necrosis then occur, and the gradual separation of the necrotic tissue leads to superficial ulceration. The edges of the ulcers are not undermined and the floor is formed by the submucous or muscular coat, the ulcers tending to spread superficially rather than deeply. When healing occurs, new mucous membrane forms; owing to the superficial nature of the ulcers, very little scarring occurs and strictures rarely develop. When the sigmoidoscope is passed after complete recovery from ulcerative colitis or bacillary dysentery, nothing more is seen than some slightly depressed and puckered areas in the mucous membrane, which may be somewhat paler and smoother than normal. I have found by means of the sigmoidoscope that the appearance of the colon in the sporadic ulcerative colitis observed in England is indistinguishable from that of the colon in bacillary dysentery, thus confirming the *post-mortem* observations made by Wilks fifty years ago.

Symptoms

The onset is sometimes acute with severe diarrhœa and fever. More commonly it is subacute or insidious, the first symptom noticed generally being the passage of blood and mucus with or without diarrhœa. Even in cases which appear to begin acutely a history can often be obtained of slight intestinal irregularity with the occasional passage of mucus or blood for several months, and sometimes even for two or three years, before the onset of severe symptoms.

Diarrhœa is always present sooner or later. As many as fifteen stools may be passed in the day, but in the earlier stages the bowels are only opened between two and six times. The largest number of stools is generally passed in the morning, and it is common, as in other forms of diarrhœa, for one or more loose stools to be passed shortly after each meal, especially after breakfast. The fæces are generally fluid, but rarely watery. Sometimes the first stool passed in the day is almost solid, the others being more or less fluid. The bulk of each stool is small, especially when many are passed. When the pelvic colon and rectum are alone involved the stools may be solid, though they are rarely hard ; in other cases diarrhœa alternates with constipation. Both naked eye and microscopical examinations show that the food is well digested, except in the comparatively rare cases in which the lower end of the ileum is involved as well as the colon. Undigested starch and, less frequently, undigested meat fibres are then found ; in such cases the stools are pale and very offensive, and much flatus is passed. The pus and blood cause the fæces to be alkaline, unless excessive bacterial decomposition of starch occurs owing to the simultaneous presence of enteritis.

The distinctive feature of ulcerative colitis is the passage of blood, pus and mucus in each stool, and often also alone without any fæces. In quiescent periods they may appear to be absent, but chemical and microscopical examinations show that this is not the case. Blood may be passed in large quantities alone, but it is generally mixed more or less intimately with the mucus and pus. It is generally bright and red, and never produces black tarry stools, such as are seen in cases of gastric and duodenal ulcer. It is mostly fluid, but small clots are often present, and occasionally a single elongated dark red clot is passed alone. The mucus is unformed, and may be clear or opaque owing to the presence of pus ; membranes are never passed. In most cases small collections of pus are easily recognised with the naked eye in addition to that mixed with the mucus and fluid fæces, but occasionally pus is only found on microscopical examination ; in rare cases there is an unexplained preponderance of eosinophile cells. The amount of pus compared with

mucus gives an approximate measure of the severity of the case.

Abdominal discomfort is generally, but not always, present; actual pain is rare, except immediately before defæcation, when severe colic often occurs; this disappears as soon as the bowels are opened, especially if flatus is also passed. Tenesmus is unusual and only occurs if the anal canal is involved. The abdomen is sometimes slightly distended, but in many cases it is retracted. Tenderness is often completely absent, even in severe cases, but pressure over the colon may cause discomfort. If the tenderness is considerable, the inflammation has generally spread to the peritoneum and local peritonitis is present; this is most commonly observed in the right iliac fossa (*perityphilitis*) and left iliac fossa (*pericolitis sinistra*). A moderate degree of muscular rigidity is often present in severe cases, especially when there is any local peritonitis, but it is rarely sufficient to prevent the cæcum and iliac colon from being palpable. They are almost always freely movable, and the impression of "thickening" which is sometimes given is generally due to hypertonus of the muscular coat and not to inflammatory infiltration; corresponding with this, the diameter of the palpable part of the colon is generally less than normal. I have on a number of occasions been able to verify this at operation, the tender and apparently thickened colon being perfectly normal in its external appearance and showing no true thickening on direct palpation, although in some cases the peritoneal surface is abnormally red.

Micturition is sometimes unduly frequent and may cause pain.

Digital examination of the rectum is only painful in the rare cases in which the anal canal is inflamed; in such cases spasm of the sphincter ani resists the introduction of the finger and grips it after it is introduced. The thickened mucous membrane and the ulcers are readily felt when the rectum is involved.

A sigmoidoscopic examination should always be made. An anæsthetic is never required, as the passage of the instrument does not cause pain unless the anal canal is inflamed; in such cases a cocaine sempule should be introduced a quarter

of an hour before. If the sigmoidoscope is carefully introduced under visual guidance without inflation and only as far as it goes without difficulty, there is no danger, the few cases in which perforation has occurred having all apparently been due to its blind passage. The mucous membrane is bright red, thick and sometimes slightly granular. It bleeds very readily when touched. Its surface is covered with blood-stained, purulent mucus, some of which should be removed on a sterile swab for bacteriological examination. Superficial ulcers are invariably present, but in early cases they may be so small that they are difficult to recognise. More frequently they are of larger size and are sometimes so extensive that only small islets of mucous membrane are left, which may feel like small flat polypi on rectal examination, the floor of the ulcers being mistaken for the surface of the mucous membrane. The ulcers are always superficial with irregular edges ; the thick mucous membrane is not undermined. The floor of the ulcers appears greyish-yellow when the blood and mucus are wiped from their surface. In some cases the sigmoidoscope shows that the rectum or the rectum and lower part of the pelvic colon are alone inflamed, as normal mucous membrane is found higher up.

The x-rays give some indication of the extent of the inflammation. When the small intestine is not involved the cæcum is only reached after the normal interval of three or four hours. The shadow of the ulcerated colon is mottled and often abnormally narrow owing to spasm ; if the cæcum and proximal colon are normal in appearance the ulceration is probably confined to the distal part of the colon. In a very severe case, in which the sigmoidoscope showed that the healing of the ulcers had resulted in narrowing at the pelvi-rectal flexure, a barium enema showed very clearly the extent and degree of the stricture. The whole of the pelvic colon had been converted into a thick-walled narrow and shortened tube, although the patient's condition was in every way satisfactory and the mucous membrane of the colon was quite healthy.

The general condition of the patient varies considerably in different cases. In acute cases and in acute exacerbations of more chronic cases, irregular fever is generally present.

Apart from this the patient has often a good appetite and resents any restriction in diet. There is no gastric ulceration, and gastric analysis shows nothing abnormal. The constant diarrhœa leads to progressive emaciation and weakness, but in slight cases the patient may feel so well that he is unwilling to undergo treatment in bed. The loss of blood leads to secondary anæmia, which may be severe ; the amount of hæmoglobin is often only 50 per cent. of normal, and may fall to 20 per cent. ; numerous nucleated red corpuscles may be present.

Complications

The symptoms which indicate that the inflammation has spread to the peritoneal coat of the colon have already been mentioned. The evidence is not, however, conclusive, as I have seen the walls of the cæcum thick and the peritoneum obviously acutely inflamed in a case in which tenderness was completely absent. General peritonitis is very rare and is not due to perforation, but to direct spread of infection through the wall of the colon. Localised abscesses are still more unusual. In spite of the severity of the inflammation, I have only twice seen a stricture follow healing of the ulcers.

Thrombosis of the femoral vein is said to be not uncommon, but I have never seen it myself. Occasionally multiple arthritis develops ; though septic in origin, suppuration does not occur. The condition is strictly analogous to the arthritis which may follow bacillary dysentery. Multiple peripheral neuritis has also been observed.

Diagnosis

The passage of bright blood by rectum may be due to a number of causes, which can only be distinguished from each other by thorough examination of the stools and the use of the sigmoidoscope. The association of blood in the stools with pus and mucus indicates the presence of ulcerative colitis or a growth of the pelvic colon or rectum.

In addition to the form of ulcerative colitis described above, I have occasionally met with cases in which the sigmoidoscopic appearance corresponds with Hale-White's descrip-

tion of post-mortem specimens of the condition he called *follicular ulceration*. The whole surface of the mucous membrane is granular owing to the swollen condition of the lymphoid follicles. The degree of inflammation, as shown by redness, swelling and liability to bleed when touched, is obviously less than is generally the case in ordinary ulcerative colitis and bacillary dysentery. The apices of many of the follicles are more or less denuded of epithelium, thus giving rise to follicular ulceration. Hale-White described the condition as always secondary to some other disease, the symptoms of which were so much more prominent that the colitis could not be diagnosed during life, but I have seen it occur as an independent condition, and also in cases of growth of the colon, an association first described by Lockhart Mummery.

A growth can be excluded by rectal and abdominal palpation, and by the sigmoidoscope. Even if the growth is too high to be reached by the instrument its presence is rendered very probable when the accessible part appears normal, and blood, mucus and pus are seen coming from the inaccessible part of the colon.

If the patient has been in the East the possibility of dysentery should be considered, and even in the absence of such a history it is possible that a patient may have become infected by a dysentery carrier living with him. Mucus obtained direct from the surface of an ulcer during the sigmoidoscopic examination should, therefore, always be examined bacteriologically, and the agglutinating power of the patient's serum should be tested against various strains of *B. dysenteriæ*. I have already pointed out that the sigmoidoscopic appearance of the mucous membrane in bacillary dysentery and ulcerative colitis is identical. Amœbic dysentery is, however, so distinct that a definite diagnosis can easily be made by the use of the sigmoidoscope alone. Small, round, red elevations are seen on the otherwise normal-looking mucous membrane, corresponding with the collection of broken-down material in the submucous tissue caused by the invasion of *Entamœba histolytica*. In the centre of each elevation is a depressed yellowish ulcer, corresponding to where the submucous abscess has broken

through the mucous membrane. The fact that a patient has never been out of England does not exclude the possibility of amœbic dysentery, as I have seen three cases arising at home, in which the diagnosis was made from the sigmoidoscopic appearance, and in which rapid and permanent recovery followed treatment with emetine.

Prognosis

Very acute ulcerative colitis may cause death in a few weeks. More commonly the condition becomes chronic with periodical acute exacerbations, and thus approximates to the ordinary form of ulcerative colitis, in which the onset is insidious and the course very prolonged. Death generally results from cachexia owing to the prolonged diarrhœa and constant loss of blood, and very rarely from general peritonitis.

The more severe the diarrhœa, the more serious is the prognosis, as it indicates that the whole or greater part of the colon is involved. Evidence of participation of the ileum in the inflammation is of serious import, as the toxæmia is likely to be more profound. The severity of the local conditions varies more with the quantity of pus than with that of blood in the stools, but severe recurrent hæmorrhage is a very serious symptom. The extent of ulceration can only be accurately determined with the aid of the sigmoidoscope.

Treatment

If a sigmoidoscopic examination is always made when a patient passes blood or mucus in his stools or is suffering from diarrhœa, the cause of which is not obvious, ulcerative colitis can often be recognised at such an early stage that it is still readily amenable to medical treatment. No case can be regarded as cured until a further sigmoidoscopic examination has shown that all ulceration has disappeared and the mucous membrane is no longer inflamed. The appearance seen with the sigmoidoscope gives an indication of the condition of the whole of the colon, as the pelvic colon and rectum are generally affected in the earliest stage both in bacillary dysentery

and ulcerative colitis, but not in amœbic dysentery, which generally affects the cæcum and ascending colon first and most severely. When, therefore, the rectum and pelvic colon are found to be normal as a result of treatment, it can be assumed that the mucous membrane of the rest of the colon is also healthy. Symptoms frequently disappear weeks or even months before healing is complete, especially if the patient is kept in bed ; this is the cause of the very common relapses after apparent cures, but if all the ulcers have really healed and the mucous membrane is no longer inflamed there is very little tendency to recurrence.

The patient should be kept warm and recumbent in bed until no blood has been passed for a week, the bowels are not opened more than twice a day, and no ulceration and no inflammation can be seen with the sigmoidoscope. But he should continue under strict treatment till the mucous membrane appears to be perfectly normal, and he should be careful about his diet and keep his stools soft with saline aperients or liquid paraffin for at least an additional year, when the newly-formed mucous membrane may be assumed to have overcome its original vulnerability to mechanical irritants.

The stomach is almost invariably unaffected, and it is also rare for the small intestines to be inflamed. As digestion is usually almost complete by the time the cæcum is reached, the diet is consequently of less importance than might be expected. If the food is thoroughly chewed a light mixed diet is permissible, and if, as is often the case, the patient has lost weight, two or thee pints of milk should be given in addition. The food must be thoroughly masticated. Everything which could irritate the colon mechanically should be prohibited ; vegetables are only allowed if they have been passed through a fine sieve, and no fruit except in the form of jellies should be given. Tough meat, porridge and wholemeal brown bread are prohibited. At one time I always prescribed milk, which had been soured with a reliable lactic acid-producing bacterial culture, but I do not think it exerted any obvious effect on the course of the disease. Pyorrhœa alveolaris and other sources of sepsis in the mouth, nose or pharynx should be removed, as they may aggravate the

condition by leading to secondary infection of the ulcerated colon.

Treatment with Anti-dysenteric Serum

I was much struck in Salonica by the extremely good results obtained in acute bacillary dysentery with large doses of polyvalent anti-dysenteric serum injected intravenously. I have tried the same treatment in two chronic cases. In one the patient was so ill that appendicostomy had to be performed at the same time ; death occurred after a temporary rally, but the patient had been very ill for four years, and on his discharge from a military hospital three years before he had not been expected to live for more than two or three weeks. In the following case, however, the improvement was so striking that there is no doubt that all cases of chronic bacillary dysentery should be treated in this way.

Bacillary dysentery of two years' duration ; intravenous injections of anti-dysenteric serum ; rapid recovery.—Henry W., aged thirty-five, whilst serving in Salonica, had an attack of acute dysentery in December, 1918. He was admitted into hospital : bacteriological examination of the stools was negative on the first two occasions, but on the third Flexner's *B. dysenteriæ* was isolated. Up to this time he had been treated with emetine, but it had aggravated his symptoms. He was now put on starvation diet, given sodium sulphate in large doses, and had daily lavage of his colon with potassium permanganate solution. He was discharged from hospital in March, 1919, and sent to England. There was now no blood in his stools, but he still had a tendency to diarrhœa. Severer symptoms appeared in June, 1919, but in two months he was again better. In March, 1920, the old symptoms returned and gradually got worse. His stools became increasingly frequent and loose, and blood and mucus were invariably present in them. By September he was passing as many as seven stools a day, and on September 12th he passed half a pint of bright red blood. He was admitted to Guy's Hospital under my care on September 13th, 1920. His stools consisted of bright red blood, mucus and pus, which was easily recognised by the naked eye. Small quantities of liquid fæces were present in some, but not

all, of the stools. Nothing abnormal was found in his abdomen, and there was no tenderness or rigidity. On rectal examination numerous ulcers could be felt. He was sigmoidoscoped the day after admission, and innumerable shallow, irregular ulcers were seen, the surfaces of which were covered with purulent mucus. The intervening mucous membrane was swollen and very red, and bled directly it was touched. A swab taken from the surface of an ulcer during the sigmoidoscopic examination showed the presence of an aberrant type of Flexner's *B. dysenteriæ*.

The patient was given intravenous injections of polyvalent anti-dysenteric serum, beginning with 40 c.c. on September 21st, the dose being increased by 10 c.c. each day until he received 100 c.c. on September 27th and 28th. The Lister Institute polyvalent serum was used, as on my return from the East in 1916 I had supplied the Institute with a collection of cultures obtained from Salonica cases to be used in the preparation of its polyvalent serum. In addition to the serum treatment he was given colon douches of albargin solution and charcoal by mouth. By October 1st the stools were semi-solid and contained neither blood nor pus and very little mucus. On October 7th a second sigmoidoscopic examination showed that every ulcer had healed and that the mucous membrane was now only very slightly inflamed. Small depressed whitish areas were seen, which presumably represented scars of the healed ulcers. By October 11th the stools were normal and no dysenteric organism could now be isolated. Full diet was allowed, the bowel irrigations were stopped, and the patient was allowed up. When a further sigmoidoscopic examination was made on November 11th, the mucous membrane looked perfectly healthy except for indistinct scars. The patient was discharged on November 6th feeling perfectly well, and in spite of his restricted diet he had gained almost exactly a stone in weight during the eight weeks he was in hospital. I saw him again on December 6th; he looked and felt perfectly well, and nothing abnormal could be seen with the sigmoidoscope.

The remarkable result obtained in this case encouraged me to try the effect of the same treatment in a very severe case of

sporadic ulcerative colitis, which was under my care at the same time. No dysenteric organism was found in the stools, and the patient's blood did not agglutinate any of the common strains of dysenteric bacilli, but recovery was even more rapid and complete than in the case described of bacillary dysentery.

Acute ulcerative colitis cured by anti-dysenteric serum.—Cedric D., aged twenty-one, had several attacks of diarrhœa in the summer of 1919. A few weeks after the onset he noticed blood and mucus in his stools. His motions gradually became more loose and frequent, and his general health deteriorated. He was kept in bed after August, 1920, and was given olive oil enemata and a very light diet. No improvement occurred, and early in September he was given injections of emetine, as it was suggested he might be suffering from amœbic dysentery. His condition was, however, greatly aggravated by this, and he passed much more blood, pus and mucus, and had almost continuous nausea. I first saw him on October 1st, 1920. He was very emaciated, had a high temperature, and complained of a moderate amount of pain ; there was some general abdominal tenderness. He passed as many as a dozen stools in a day, each of which contained blood, pus and mucus. He had lost 3 stones in weight during the previous six weeks. He was very pale and looked ill. The sigmoidoscopic examination showed that the colon was in exactly the same condition as in the case of bacillary dysentery just described. As he was so ill, I recommended that an appendicostomy should be performed without delay. The appendix was, however, very adherent ; the stoma did not prove satisfactory, and considerable quantities of fluid fæces escaped from the opening. The colon was washed out continuously for forty-eight hours through the stoma with saline solution and afterwards with albargin, but the patient's condition became steadily worse. A bed-sore developed on his sacrum, and there seemed little doubt that he would die soon if nothing more was done. Sigmoidoscopic examination on October 11th showed that no improvement had occurred. Very large quantities of blood were passed by rectum ; on October 12th a blood count showed 2,700,000 red corpuscles per cubic millimetre, and the

hæmoglobin percentage was 34. The patient's condition was so grave that it became necessary to transfuse him. On October 14th he was given 500 c.c. of his father's blood ; the beneficial effect was immediate. From October 18th onwards he was given intravenous injections of polyvalent anti-dysenteric serum, beginning with 40 c.c. and increasing the dose every day by 10 c.c. until 100 c.c. were given on October 24th. By October 21st blood had already disappeared from the stools, which rapidly became more solid, and by October 26th no mucus was present. On October 23rd, *five days after the first injection of serum*, a sigmoidoscopic examination showed that the mucous membrane was already entirely free from ulcers ; very slight scarring was observed, and the colour was slightly redder than normal. At a further examination made on November 1st the mucous membrane was found to be perfectly healthy. He was given full diet from October 31st, and was allowed up on November 2nd. A blood examination on November 5th showed that the red corpuscles now numbered 4,360,000 per cubic millimetre, and the hæmoglobin percentage was 72. The patient felt and looked entirely different. He was discharged on November 17th, having gained a stone in weight in four weeks. His stools were now quite normal. The appendicostomy opening had not been used since the serum treatment began, but it was not quite closed on discharge. He had a slight recurrence in July, 1921, which rapidly responded to treatment with serum, and when last seen, in July, 1923, he was completely fit.

I have now treated about ten cases with anti-dysenteric serum. The results have been remarkably satisfactory. They are not due simply to the use of horse serum, but are definitely specific. In one severe case I tried the effect of large doses of ordinary horse serum ; no improvement resulted, but the administration of anti-dysenteric serum after a week's interval had the usual rapidly favourable result. I generally begin with an injection of 40 c.c. intravenously ; this is followed on consecutive days by injections of 60, 80, and 100 c.c. The four injections are often sufficient, but it is sometimes necessary to repeat the maxi-

mum dose two or three times. A considerable reaction often occurs; the patient's temperature rises, and a profuse erythematous rash appears. The joints may become swollen and painful. But these symptoms generally last only a few hours and never longer than a few days. They seem less likely to occur if 15 grains of calcium lactate are given three times a day the day before and during the days of treatment. No anaphylactic symptoms have been observed, even in patients who have previously had serum, but care was always taken to desensitise the latter by very small preliminary injections, and the same precautions would be necessary in any patient who was subject to asthma. The improvement is generally as rapid as that in cases of amœbic dysentery treated with emetine, and of acute epidemic bacillary dysentery with intravenous anti-dysenteric serum. In one case, in which appendicostomy had been performed some months earlier, improvement was incomplete. A secondary streptococcal infection had apparently become grafted upon the original dysenteric infection, as complete recovery only took place after the removal of the teeth, this being followed by a temporary severe local reaction. An attempt to treat the patient with a vaccine prepared from streptococci isolated from the stools had to be given up owing to the violent reaction which followed the injection of only a quarter of a million bacteria.

Dr. John Fawcett and Dr. J. A. Ryle,[13] obtained an equally satisfactory result in one case under their care. The treatment failed in two others, but in both of these they recognised the ulcerative colitis as being of a hypertrophic character, quite different from the ordinary type, so that in all probability it was caused by a different infection. One of these patients died shortly afterwards from perforation, which rarely, if ever, occurs in the usual form of ulcerative colitis, and in the other an appendicostomy, which was subsequently performed, led to no further improvement. Jerwood [14] has also reported a case in which the patient was "incontinent, very weak, wasted, and quite determined to die," and in which rapid recovery followed treatment with anti-dysenteric serum.

So long as any blood is passed the stools should be kept

watery by repeated drachm doses of sodium sulphate ; by this means irritation of the mucous membrane by the decomposition products of retained blood and pus is prevented.

It is always advisable to examine the stools bacteriologically and to test the agglutinating power of the blood serum against the different organisms found. In my experience, however, vaccine treatment has generally very little effect, doubtless because of the extreme difficulty of discovering the organism which is really responsible for the colitis. If it can be identified with certainty vaccination may be tried in addition to, but never as a substitute for, other treatment.

When the patient is very ill as a result of long-continued loss of blood from the colon, all treatment is likely to fail unless his general condition improves. Transfusion of blood is of remarkable value in such cases, a patient who was almost moribund before sometimes recovering sufficiently to be able to stand vigorous treatment, which ultimately results in cure.

If complete recovery does not rapidly follow the injection of anti-dysenteric serum, the colon should be irrigated every day. Ten years ago, after having tried a considerable number of astringent and antiseptic drugs in the local treatment of ulcerative colitis, I came to the conclusion that the best was albargin, a preparation of silver nucleinate, which Rogers had found the most effective in dysentery. During the war albargin became increasingly difficult to obtain, and the English stocks were finally exhausted towards the end of 1915. I then tried silver nitrate again, but it caused too much pain, and I finally employed tannic acid as the best substitute for albargin, the strength being gradually increased from gr. $\frac{1}{2}$ to gr. 2 to the ounce. This proved more effective than plain saline solution and much less painful than silver nitrate.

When albargin again became obtainable after the war, it appeared to me to be less effective and to cause more pain than formerly. The Council on Pharmacy and Chemistry of the American Medical Association have recently issued a report [15] which explains this, as they find that all the silver

in albargin, as now supplied from Germany, is in the form of silver nitrate, and that the product possesses no properties which it does not share with the latter. In view of this there seems no doubt that tannic acid is the most suitable preparation for the local treatment of ulcerative colitis. A weak solution of flavine (1 in 10,000, increasing up to 1 in 2,000) may be tried as an alternative, as suggested by Gordon Watson.

In order that the fluid should reach the surface of the ulcers the colon should be as empty as possible before it is injected. The treatment should therefore be given, whenever possible, after the bowels have been opened naturally ; if in the later stages of treatment there is a tendency to constipation, sufficient liquid paraffin should be given to make this occur. In any case an injection of a pint and half of warm water should be given about half an hour before the tannic acid, in order to clear away the remaining fæces, blood and mucus ; this should only be retained for about five minutes.

A pint and a half of the tannic acid solution should be run in very slowly at a pressure of not more than 12 inches of water, through a tube introduced only just beyond the anal canal. The patient should be in the knee-elbow position with the thighs perpendicular to the bed, the back as concave as possible and the shoulders resting on a pillow ; in this way the natural obstruction at the pelvi-rectal flexure is much reduced. Consequently fluid runs more easily out of the rectum into the pelvic colon ; the rectum does not get distended, so that the urgent desire to evacuate the fluid, which generally occurs if the patient is in the usual lateral position, does not occur.

I have found with the x-rays that fluid injected in this way invariably reaches the cæcum, so that the whole of the ulcerated mucous membrane is treated, as the ileum is rarely, if ever, affected. The fluid should be retained for gradually longer periods up to an hour. If the tube with its attached funnel is kept in position, there is rarely any difficulty about this, as the patient can allow some of the fluid to escape temporarily if he finds it difficult to retain.

Intestinal antiseptics given by mouth have very little, if any, effect ; if sour milk is given, they would probably

diminish or totally prevent its activity. When the diarrhœa is particularly severe opium or its alkaloids may be required.

The administration of large doses of charcoal leads to the absorption of gas and a great diminution of any colic which is present, as the latter is almost invariably caused by intestinal flatulence. At the same time, if the stools are offensive, which is not very common in ulcerative colitis, they become odourless. Possibly bacterial activity is reduced and toxins are absorbed by the charcoal, as the general condition of the patient appears to benefit considerably when it is given. Half an ounce of very finely powdered animal charcoal should be taken in milk or arrowroot, sweetened with a little sugar, the last thing at night, and in severer cases two or three times a day.

Until three years ago I was inclined to advise appendicostomy in all cases of any severity. But since I have used large intravenous doses of serum I have only found it necessary to advise appendicostomy in a single case, and I have only occasionally had recourse to antiseptic injections. There must, however, be cases, such as the two under the care of Dr. Fawcett and Dr. Ryle, to which I have already referred, in which the pathology was different, and in these serum would be useless. The question of operation would then require consideration. The only radical surgical measure would be excision of the affected part of the bowel, but this is rarely, if ever, possible, as the ulceration almost always extends to the rectum, so that complete excision is impossible. For the same reason short-circuiting operations are useless; they are also very dangerous, as the distal segment is inflamed.

The ideal operation is appendicostomy, or, if the appendix has already been removed, a valvular cæcostomy, which allows the introduction of fluid through a catheter, but not the escape of fluid fæces. The colon should be washed out continuously for forty-eight or seventy-two hours with saline solution introduced drop by drop through a catheter, and allowed to escape from a bed-pan, upon which the patient lies. The pan is fitted with a side tube, which allows its contents to run into a receiver on the floor. After this the colon is washed out with plain water once a day, and when all the fluid has passed, the tannic acid solution already

mentioned is introduced and allowed to escape when the patient wishes. The treatment is otherwise the same as without operation, but, if serum has proved ineffective, improvement is generally more rapid, and complete recovery is likely to occur in about half the time. The stoma should not be allowed to close until the sigmoidoscope has shown that the mucous membrane has completely healed. Although it would be reasonable to expect that washing the colon out from above would be more efficacious than from below, the operation is not, however, always followed by satisfactory results. In one case, at any rate, the patient appeared to be going steadily downhill until the opening was allowed to close and treatment from below was substituted, and in two others no improvement occurred until anti-dysenteric serum was injected into the veins.

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CHRONIC APPENDICITIS AND APPENDICULAR DYSPEPSIA*

We cannot doubt that, as advancing knowledge brings us better means of investigation, and so enables us to discover and distinguish structural changes, of which we now can only observe the functional results, the aggregate of maladies called dyspepsia must undergo successive subtraction, tending more or less completely to its total subdivision into special maladies.—BRINTON, 1844.

THE first suggestion that chronic inflammation of the appendix may cause dyspeptic symptoms appears to have been made as long ago as 1896 by Rutherford Morison.[1] Three years later Ewald [2] drew attention in Germany to the same subject in an article on "appendicitis larvata." But it was not until 1910, when Moynihan [3] introduced the term "appendix dyspepsia," that the frequency of the condition became widely recognised in England and in America, where a paper on the subject was published about the same time by Graham and Guthrie [4] from the Mayo Clinic.

The importance of chronic appendicitis as a cause of gastric symptoms is now firmly established. But it is interesting to recall the reception which Moynihan's original article met with on its appearance in the *British Medical Journal* in January, 1910. Sir Anthony Bowlby [5] complained of the vagueness of the clinical picture which had been drawn, and predicted that "one result of Mr. Moynihan's paper will be that many 'dyspeptic' people will undergo operations for the removal of the appendix, and the great majority of them will be none the better." The following week Sir Clifford Allbutt [6] wrote in reference to the same article: "May we not ask ourselves if there is not something in it—perhaps a great deal—immature, fragmentary if you please, yet with a core of important truth?" The twelve

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years which have since elapsed have shown the wisdom of both writers. Few will now deny that there is " a great deal in it," that Sir Berkeley Moynihan's paper contained such a valuable " core of important truth " that it may be regarded as almost epoch-making. But every physician and surgeon of experience must agree that Sir Anthony Bowlby's fears were to some extent justified, and that numerous dyspeptic people—though certainly not " the large majority "—who have had their appendix removed for supposed appendix dyspepsia have been none the better for it.

My chief object in writing this paper is to draw attention once again to the great value of the x-rays and of Bastedo's inflation test in the diagnosis of chronic appendicitis for appendix dyspepsia. I would, indeed, go so far as to say that no operation should be performed for this condition until the diagnosis has been confirmed by these means. If this practice became the rule, it would, I believe, be very rare for an appendix to be removed unnecessarily.

Symptoms

The gastric symptoms which may result from chronic appendicitis are probably caused by the reflex stimulation of the motor and secretory nerves of the stomach. The vomiting of acute appendicitis is obviously reflex in origin, and I shall presently describe how an ocular demonstration of the appendicular-gastric motor reflex can sometimes be obtained with the x-rays in chronic cases. The gastric hyperchlorhydria, which Bonar [7] has shown occurs in 88 per cent. of cases of chronic appendicitis with gastric symptoms, is doubtless of similar reflex origin. The sensory symptoms probably result from the combined effect of these motor and secretory disturbances on the activity of the stomach.

Chronic appendicitis may give rise to gastric symptoms, which are either the sole manifestation of the disease, or are accompanied by constant discomfort or short attacks of pain in the right iliac fossa. Epigastric pain, which may radiate downwards to the umbilicus or below, and occasionally towards the right iliac fossa, occurs after meals. The time of its onset is very irregular. Most commonly it occurs

immediately after meals, but occasionally it is delayed for two or three hours. The early onset after meals is doubtless due to the gastro-colic reflex, which Newton and I[8] found is the chief stimulant of peristalsis in the colon, and the contraction of the colon may be accompanied by contraction of the appendix, and both may pull upon any adhesions which may be present in connection with the appendix. It is, at the most, only slightly relieved by alkalies, and food very rarely gives even momentary relief. It is aggravated by exercise to a greater extent than is the case with the pain of gastric and duodenal ulcer. The degree of discomfort varies from time to time ; it is rarely completely absent, and may sometimes be sufficiently severe to compel the patient to stay in bed. Nausea is common and is often present in the absence of vomiting. It is sometimes produced by pressure on the abdomen, especially over the appendix, and it may also follow exercise. Vomiting may occur, especially immediately or soon after food, and when the pain is severe, but it gives much less relief than in gastric ulcer. Heartburn and acid regurgitation are uncommon.

Hæmatemesis is often said to be a symptom of appendicular dyspepsia. The truth is that the appendix, like the teeth and tonsils, may act as a focus of infection which may give rise to acute ulcers of the stomach or duodenum. These are accompanied by no symptoms in the majority of cases, but erosion of a blood vessel may occur and cause hæmatemesis, and in rare cases such an ulcer may perforate. If the hæmatemesis is preceded or accompanied by gastric symptoms, they are not due to the acute ulcer, but to reflex appendicular dyspepsia. Under certain conditions the acute ulcers, which result from infection in the appendix or elsewhere, may become chronic, but much more often they heal rapidly, owing to the absence of the essential predisposing conditions which constitute the "ulcer diathesis," in the absence of which a chronic ulcer is unlikely to develop.

Tenderness is generally more marked in the right iliac fossa than in the epigastrium, even when there is no spontaneous pain in the former situation. Occasionally the localised tenderness can only be discovered when pressure is exerted directly over the appendix after it has been rendered

visible with the x-rays. In many cases pressure in the right iliac fossa leads to no local pain, but to discomfort in the epigastrium, which is sometimes accompanied by nausea, exactly simulating the spontaneous symptoms. In pelvic appendicitis there is generally no abdominal tenderness, but a localised area of tenderness can be found per rectum, and the appendix itself can sometimes be felt; it is generally very tender, but pressure in all other directions produces no pain.

Constipation is commonly present. In rare cases there may be chronic diarrhœa, but more frequently a form of pseudo-diarrhœa occurs, in which frequent small stools are passed owing to the irritation of the rectum caused by a chronically inflamed appendix situated in the pelvis. Pelvic appendicitis may also lead to irritability of the bladder with frequent micturition, and in women to dysmenorrhœa.

X-rays in the Diagnosis of Appendicitis

The radiography of the appendix is a comparatively new field of investigation. Béclère,[9] in 1906, appears to have been the first to obtain a radiogram of the appendix. In 1911 Grigorieff[10] stated to a congress of physicians in Moscow that the appendix becomes filled with opaque material in all cases in which its lumen is in full communication with that of the cæcum. In 1913 George and Gerber[11] claimed that the appendix could be seen in 70 per cent. of their patients, and in the following year[12] I drew attention for the first time in England to the great value of the x-rays in the diagnosis of disease of the appendix. Since then numerous important contributions to the subject have been published, amongst which may be mentioned those of Spriggs[13] in 1919 and Redding[14] in 1921.

In my opinion no operation for chronic appendicitis is justifiable unless the diagnosis has been confirmed by means of the x-rays. The x-ray evidence is both direct and indirect; the former concerns the examination of the appendix itself, and the latter is concerned with the effect of chronic appendicitis on the rest of the alimentary canal. The sign of greatest importance is the direct determination of appendicular tenderness (*vide infra* (1) (*c*)); this by itself is sufficient



FIG. 43.—Appendicular dyspepsia cured by removal of dilated, tender and chronically inflamed appendix. (Dr. P. J. Briggs.)

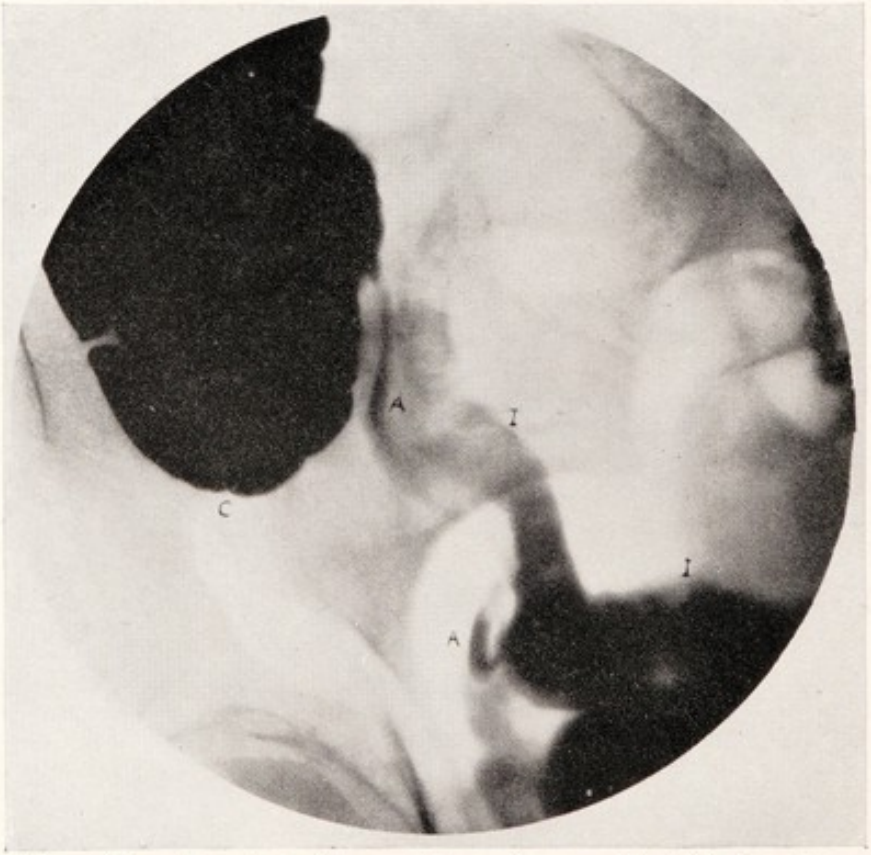


FIG. 44.—Chronic inflammation of appendix (A) hanging into the pelvis, with secondary ileal stasis. Terminal ileum (I) well filled twelve hours after opaque meal, owing to reflex achalasia of ileo-cæcal sphincter, as no adhesions were found at the operation. C, cæcum. (Dr. P. J. Briggs.)

to enable a definite diagnosis to be made in a large majority of cases.

1. *Direct Evidence*

(*a*) *The Shadow of the Appendix.*—The appendix is much more frequently visible in normal individuals than has generally been supposed, if proper means are taken to look for it. The examination should be made between six and twenty-four hours after the barium meal. A small diaphragm is used, and the cæcum and ileum are pushed from side, to side in an attempt to move them out of the way of the appendix, if the latter is not seen without doing this. In some cases the patient should turn gradually on to his right side, so as to obtain lateral views in case the appendix is situated behind the cæcum. It can be seen more or less clearly in at least 80 per cent. of normal individuals. It is visible with equal frequency in chronic appendicitis, when its shape and size and the rate of filling and emptying can be investigated (Fig. 43). Equally important is the discovery of its position in relation to the cæcum and terminal ileum, and the position of the cæcum in the abdomen. This often throws light on cases in which anomalous symptoms have resulted from the appendix being situated in the pelvis (Fig. 44), behind the cæcum, unusually high—when the symptoms may simulate those of gall-stones or duodenal ulcer, or even on the left side.

There is no diagnostic significance in the absence of an obvious shadow of the appendix. On the other hand, I have seen the appendix quite clearly in a patient who had an appendicular abscess opened abroad; she did not know whether the appendix had been removed, and its discovery with x-rays made it justifiable to advise operation for recurrent pain in the right iliac fossa. In a second case the x-ray examination showed that the appendix was still present and very tender, although the patient's parents had been clearly given to understand by an Austrian surgeon that he had removed it during an acute attack fourteen years earlier. Its subsequent removal by Mr. Warren Low was followed by permanent relief from abdominal attacks, which had become increasingly frequent during the last

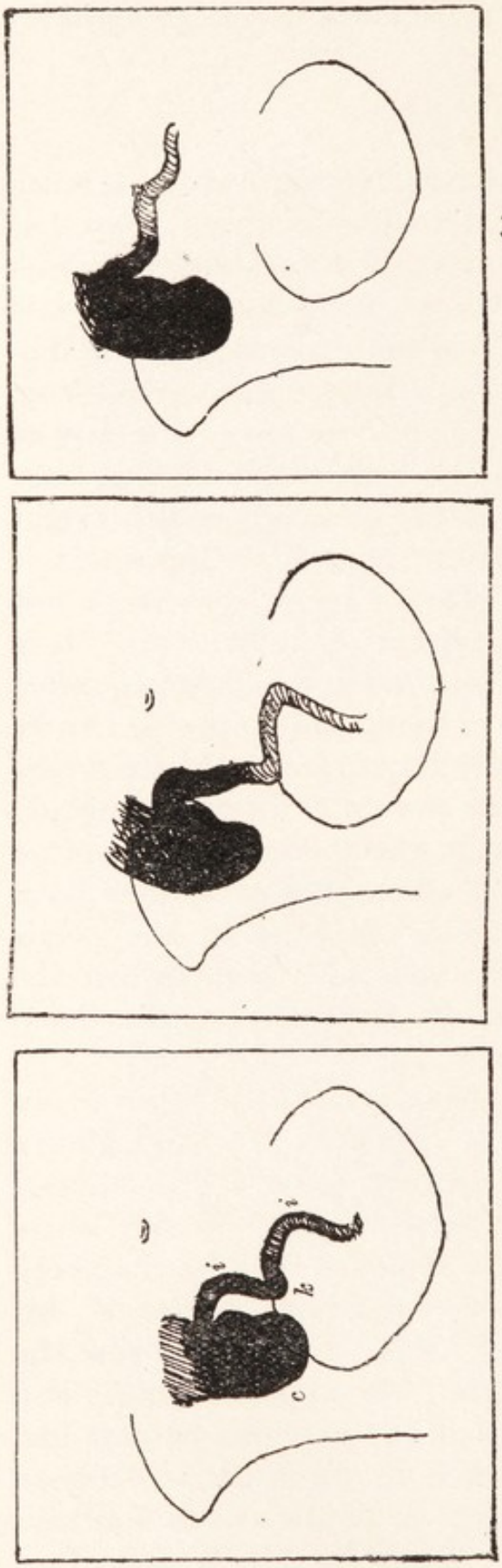


FIG. 45.—(*a*) Apparent ileal kink (*k*) at brim of pelvis; *c*, cæcum; *ii*, end of ileum. (*b*) Cæcum raised by pressure of fingers; "kink" still present. (*c*) Disappearance of "kink" after inflation of the colon.

seven years. In another case an inflamed appendix had been removed from a patient suffering from severe rheumatoid arthritis; the latter rapidly disappeared after the operation, but some months later the symptoms gradually returned. An x-ray examination showed that the stump of the appendix was still present, and that barium remained in it at least seventy-two hours longer than in the cæcum. As the stump was exceedingly tender, and was also the only fixed point of the whole bowel, a further operation was clearly indicated.

(*b*) *Adhesions in the Right Iliac Fossa.*—The presence of adhesions in connection with the appendix, terminal ileum and cæcum, whether to each other or to the surrounding parts, can be recognised by deep palpation during a screen examination. Great care is required to avoid diagnosing adhesions by

this method of examination when they are not present, but adhesions of any importance are not likely to be missed. If the cæcum is in the pelvis it can often be drawn into the right iliac fossa by manipulation under the screen. When this cannot be done, it is impossible to determine whether adhesions are present, as the cæcum and appendix are too deep to be palpated satisfactorily, unless the colon is distended with air or the bladder is not emptied for ten or twelve hours before the examination. If the appendix is adherent to the pelvic wall or to a pelvic organ other than the bladder, it does not rise under these circumstances.

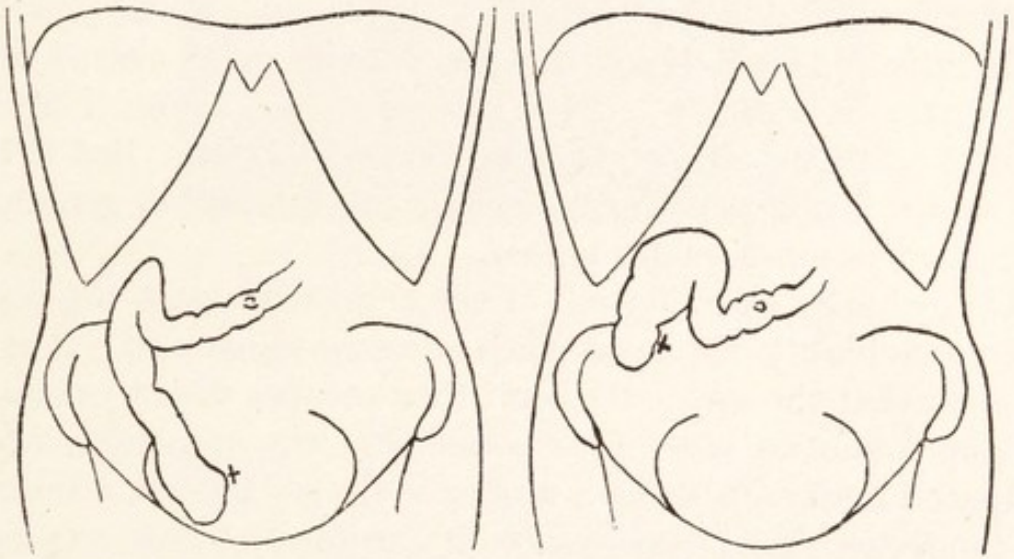


FIG. 46.—Chronic appendicitis associated with a very moveable cæcum. The appendix was not visualised, as its mouth was obstructed, but the point of maximum tenderness (+) maintained the same position in relation to the cæcum, in whichever direction the latter was moved.

Sometimes the ileum appears to be fixed where it crosses the pelvic brim ; but by manipulation the whole loop can be raised out of the pelvis, and the apparent adhesions and kink disappear. On one occasion (Fig. 45) I saw what looked like a typical ileal kink, the ileum being fixed where it passed over the brim of the pelvis ; no amount of manipulation had any effect upon it, but on inflating the bowel in carrying out Bastedo's inflation test for appendicitis, the distended pelvic colon lifted the last part of the ileum completely out of the pelvis, and palpation now showed that there were no adhesions and no kinks. Before a diagnosis of an ileal kink can be made with the x-rays the colon should therefore be

inflated, if palpation has failed to separate the apparent adhesion.

(*c*) *Tenderness of the Appendix.*—The x-rays have demonstrated that in chronic appendicitis tenderness is confined to the whole or more frequently to some part of the appendix itself, the part apparently corresponding to an inflamed area or to the position of one or more concretions (Fig. 47). When the cæcum and appendix are pushed aside by one hand, pressure upon the appendix with the other shows that it is still the maximum point of tenderness, whilst pressure over the original point of tenderness now causes no pain; this proves that true visceral tenderness and not referred tenderness is being demonstrated. If typhlitis is also present, as in infections with the *Entamœba histolytica*, the cæcum may be tender in addition, and in rare cases the ileum, if firmly bound down by adhesions, may be also tender. But if the appendix is the primary source of the disease, it generally remains the most tender point.

On ordinary examination of the right iliac fossa the parts are unavoidably displaced when pressure is exerted; it may happen that the appendix itself thus escapes direct pressure. I have found on several occasions that the appendix, when palpated under the screen, was exceedingly tender, although no tenderness had been observed immediately before on pressing in the right iliac fossa without the guidance of the x-rays.

In most instances the appendix is quite impalpable, and it would therefore be impossible without the x-rays to be certain whether the appendix itself was the seat of the local tenderness. Even when it is not filled with barium, and is therefore not visible with the x-rays, local tenderness in a situation, which from its relation to the cæcum and termination of the ileum is likely to be that of the appendix, is strong evidence in favour of appendicitis (Fig. 46).

(*d*) *Concretions and Foreign Bodies.*—The right iliac fossa should always be examined with the x-rays before the barium meal is taken, as in rare cases a concretion, and still less frequently a foreign body, can be seen in the appendix. Spriggs has pointed out that in many cases the barium passes round a soft concretion, which then gives the appearance of a vacuole (Fig. 48).

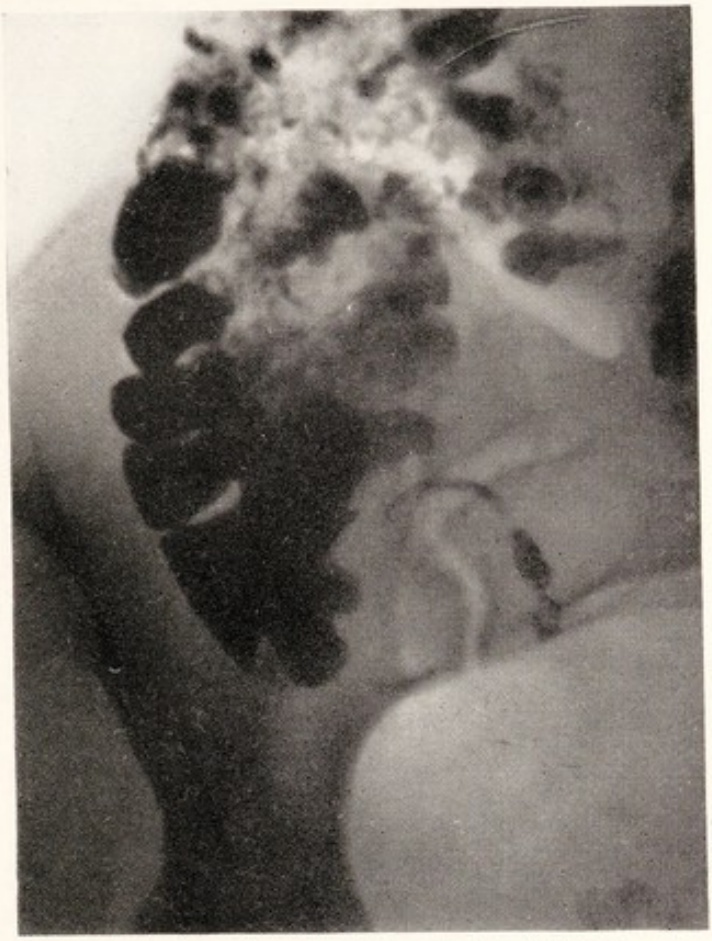


FIG. 47.—Tender appendix, forty-eight hours after opaque meal. When removed it was found to be chronically inflamed and contained pus. (Dr. P. J. Briggs.)

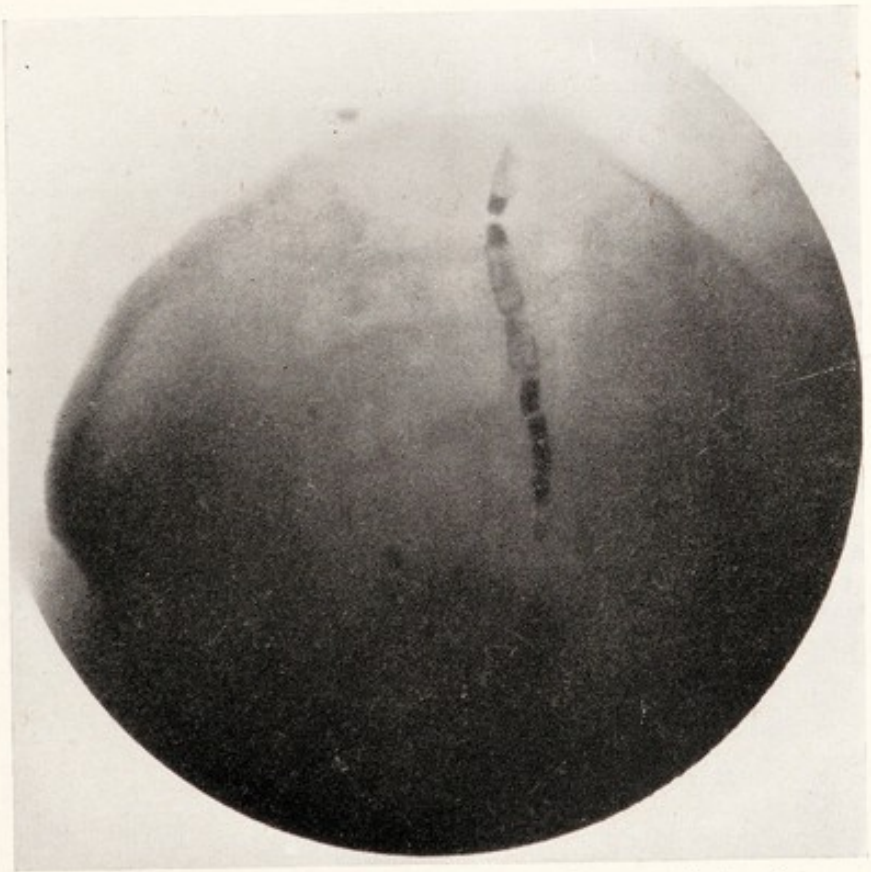


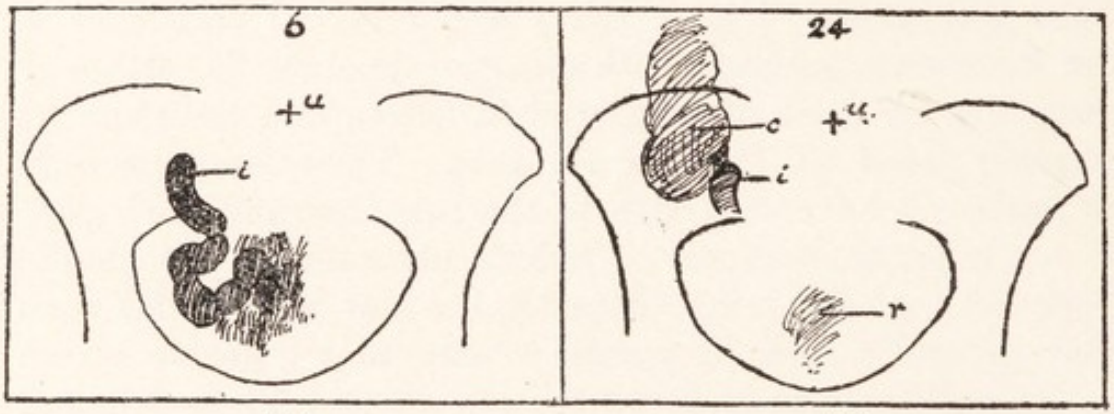
FIG. 48.—Chronically inflamed appendix containing fæcoliths, with barium still present forty-eight hours after opaque meal, when the cæcum and ascending colon are empty. (Dr. P. J. Briggs.)

2. *Indirect Evidence*

(*a*) *The Stomach: Spasmodic Hour-glass Contraction; Reversed Peristalsis.*—Chronic appendicitis may be associated with a spasm in the centre of the stomach. Indeed, chronic appendicitis is, after gastric ulcer, the most common cause of spasmodic hour-glass constriction of the stomach.[15] I have, on a few occasions, seen a spasm develop in the middle of the stomach when pressure was exerted over the appendix, and Mr. P. J. Briggs has seen the normal peristalsis become suddenly much more active under the same conditions; in most cases epigastric discomfort was simultaneously produced, occasionally without any accompanying pain in the right iliac fossa. I have twice seen reversed peristalsis in the stomach associated with chronic appendicitis, although there was no trace of pyloric obstruction, and the stomach emptied itself at the normal rate. These are the only exceptions I have met with to the rule that reversed peristalsis is pathognomonic of pyloric obstruction. It should be noted that the reversed peristalsis was less regular than that generally seen in pyloric obstruction. Feeble waves occasionally passed backwards from a point about 3 inches from the pylorus on the greater curvature at the same time as normal peristaltic waves started from the same point on their way to the pylorus. At the operation nothing abnormal was seen in either the stomach or duodenum. In one case the appendix was associated with an undescended cæcum and was, therefore, very near the pylorus; this fact may have been responsible for the abnormal gastric peristalsis.

(*b*) *Ileal Stasis.*—The normal stasis which occurs in the end of the ileum is increased in all conditions which lead to spasm or to inhibition of the normal relaxation (achalasia) of the ileo-cæcal sphincter. The most important of these conditions is appendicitis (Fig. 50). In the case of a middle-aged gentleman with symptoms of chronic appendicitis the stomach was empty six hours after the bismuth meal, but no bismuth was present in the cæcum, all of it having collected in the end of the ileum, though in the average normal individual the shadow by this time should have

reached the hepatic flexure (Fig. 49). The last few inches of the ileum could be clearly defined, as they were distended with chyme. Palpation under the screen showed that there were no adhesions, the whole of the ileum being freely movable. Twenty-four hours later some bismuth was still present in the last inch and a half of the ileum, and a little in the cæcum and ascending colon, all the rest having passed to the rectum, from which some bismuth-containing fæces had just been evacuated. It was clear, therefore, that the only stasis in this patient's alimentary canal was in the end of the ileum. Mr. R. P. Rowlands operated and removed an inflamed appendix full of pus, but found that the ileum was



(a) (b)

FIG. 49.—Ileal stasis due to reflex achalasia of the ileo-cæcal sphincter in chronic appendicitis. *i*, terminal ileum; *c*, cæcum; *r*, rectum; *u*, umbilicus.
(*a*) 6 hours after opaque meal; (*b*) 24 hours after opaque meal.

perfectly normal and was free from adhesions. The ileo-cæcal junction was not abnormally narrow, so that it was clear that the stasis could have been due to nothing else than achalasia or spasm of the ileo-cæcal sphincter.

(*c*) *Cæcal Stasis.*—Chronic appendicitis frequently causes stasis in the cæcum and ascending colon by giving rise to reflex inhibition of the normal mass peristalsis. In such cases the x-rays show that the cæcum and ascending colon are often abnormally large and unusually mobile.

The greater part of the opaque meal remains in the cæcum and ascending colon at the end of twenty-four hours and often after forty-eight or even seventy-two hours. The barium may pass through the rest of the colon at the normal rate, so that after twenty-four hours a small quantity may



FIG. 50.—Radiogram taken nine hours after opaque meal, showing ileal stasis with tender appendix. The appendix was chronically inflamed with a constriction between its proximal and middle thirds, corresponding with the gap in its shadow. There were no adhesions, the ileal stasis being due to reflex achalasia or spasm of the ileo-cæcal sphincter. (Dr. P. J. Briggs.)

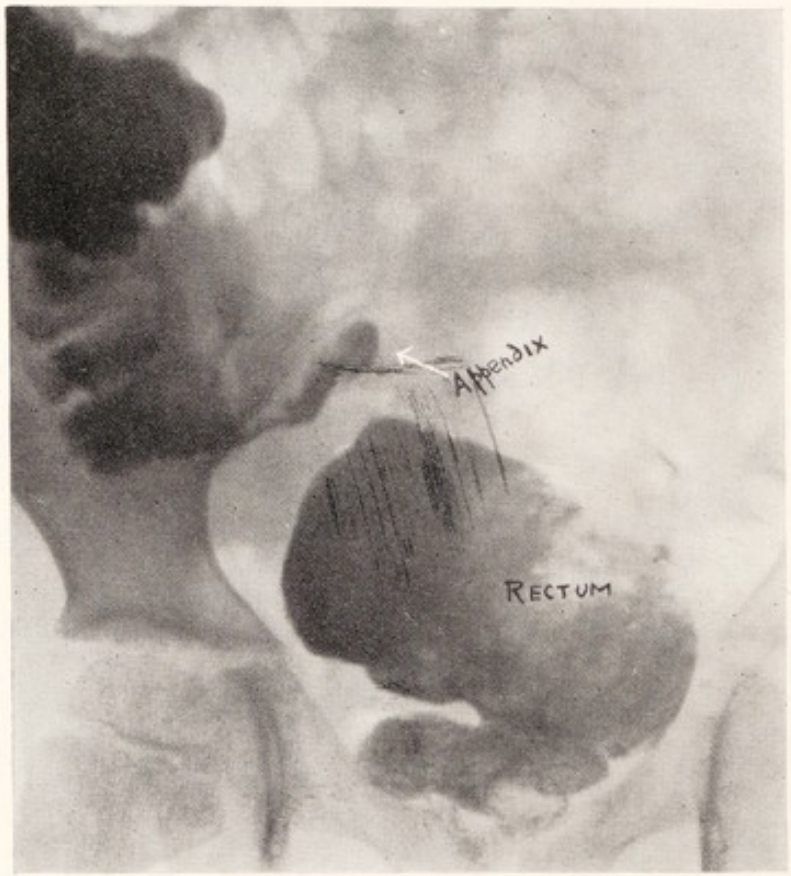


FIG. 51.—Dyschezia in a boy of ten, due to chronic inflammation of a tender pelvic appendix (Dr. P. J. Briggs.)

be seen in the neighbourhood of the splenic flexure or even in the pelvic colon, from which it may be expelled in the stool, although the greater part has not yet passed the hepatic flexure.

(*d*) *Rectal Stasis or Dyschezia.*—When the appendix hangs over the brim of the pelvis, or when the cæcum as well as the appendix is situated in the pelvis, chronic appendicitis may give rise to dyschezia (Fig. 51). In one such case the rectum was already distended with barium-containing fæces ten hours after the meal, though no desire to defæcate was felt ; the cæcum was still full, but the other parts of the colon were nearly empty. The appendix, which was clearly visible with the x-rays, was in close relationship with the rectum and was very tender on pressure ; it showed obvious signs of chronic inflammation when removed.

(*e*) *Enterospasm.*—Chronic appendicitis is the most common of the reflex causes of enterospasm. The x-rays generally show that the lumen of the colon is abnormally narrow in various short portions of its length, the exact position changing from one examination to another. The part most commonly affected is the proximal half of the transverse colon, and the contracted segment is generally shorter than what is observed in other forms of enterospasm. The constipation present in these cases is the result of interference with the normal peristalsis of the colon, and is not due to the mechanical obstruction offered by the contracted intestine, as the x-rays show that no delay occurs in the passage through the contracted segment, and that there is no dilatation of the bowel immediately proximal to it.

Bastedo's Sign

In a paper published in 1909 Bastedo [16] of New York described a sign, which he believes is of great value in the diagnosis of chronic appendicitis. In 1913 I published a paper [17] entirely confirming his observations. The test is simple to carry out, causes very little inconvenience to the patient, and is, in my experience, more reliable than any sign hitherto described, with the exception of the discovery with the x-rays of tenderness localised to the appendix.

The test depends upon the production of pain and tenderness in the right iliac fossa on inflation of the colon with air. For this purpose I use an ordinary rubber rectal flatus tube, which is connected with the nozzle of a Higginson's enema syringe. Bastedo recommended that the tube should be inserted 11 or 12 inches into the rectum, but, as a tube can very rarely be passed beyond the pelvi-rectal flexure, which is situated 4½ inches from the anus, there is no advantage in introducing it further than just within the ampulla of the rectum—about an inch and a half from the anus. After the tube has been inserted the patient lies flat on his back, and the pump is brought up between his legs. On now slowly pumping air through the tube the colon is seen gradually to distend, and after a certain quantity has been introduced an individual who is not suffering from appendicitis feels a diffuse discomfort in the lower part of the abdomen, but there is no pain unless an excessive quantity of air is introduced, in which case it is not more marked on one side than the other. There is also no tenderness. Patients suffering from appendicitis, however, generally experience pain in the right iliac fossa, even if the pain has hitherto been confined to the epigastrium or the neighbourhood of the umbilicus. In some cases the onset of pain is delayed until a few minutes, or even longer, after the air has been allowed to escape. In one of my cases, in which a diseased appendix was subsequently removed, pain was only felt some hours later. Whenever pain is produced, and in some cases in which no pain has been felt, well-marked tenderness is found in the right iliac fossa. When tenderness has already been observed in this situation, it is generally much increased by inflation, but it is also found in cases in which no tenderness has hitherto been noticed in spite of frequent examinations. In a number of instances I have observed a further exceedingly characteristic sign: the pain is referred to the epigastrium when pressure is exerted in the right iliac fossa after inflation, the epigastric pain being identical in character with that which formed the chief symptom of which the patient complained. Occasionally no pain was felt in the right iliac fossa on inflation, but the patient complained of epigastric discomfort and

sometimes nausea, identical in character with the symptoms which occurred spontaneously. When the examination is finished, the pump should be disconnected from the rectal tube in order to allow the greater part of the air to escape at once.

The test known as Rovsing's sign, although it had been employed by Dr. Lauriston E. Shaw for some years before Rovsing's first publication on the subject, in which pain is felt in the right iliac fossa on exerting pressure over the descending colon, has a similar significance to Bastedo's sign, as it appears to depend upon gas being pressed from the distal into the proximal part of the colon. It is, however, of limited use, as it is comparatively rare for sufficient gas to be present in the descending colon. After the colon has been inflated in the carrying out of Bastedo's test and the pain produced has disappeared, it can often be caused to return by pressing upwards along the descending colon, as in Rovsing's test.

In my own experience I have only obtained a positive Bastedo's sign in appendicitis, the appendix having always been found diseased at the subsequent operation, except in a few cases in which inflation of the colon gave rise to pain in the right iliac fossa, although the appendix had previously been removed. In such cases adhesions were probably present. In one such case Rost found a band passing from the side of the cæcum, which was otherwise abnormally movable ; in all probability the pain resulted from the pull of this band upon the distended and movable cæcum when the colon was inflated. In most cases in which the abdomen has subsequently been explored in spite of a negative Bastedo's sign the appendix has been found to be healthy ; in some cases disease has been discovered in the female pelvic organs, the gall-bladder, or the right kidney or ureter.

A negative response to the test does not definitely exclude appendicitis, but the probability of its presence is small in that case, and very clear evidence of other kinds is required before an operation for the removal of the appendix could be justified. If, however, it has been found impossible to visualise the appendix with the x-rays, the negative Bastedo test and the negative direct radiographic evidence

may both be due to chronic inflammation obstructing the mouth of the appendix or completely obliterating its lumen.

In my Goulstonian Lectures [18] I showed that the only stimulus to visceral pain is distension. On inflating the colon the pain eventually produced occurs no sooner in the appendix than in the rest of the colon so long as the former is not diseased, but if it is inflamed pain and tenderness are observed in the right iliac fossa. It is not yet clear to what extent adhesions binding down the appendix may be concerned in the production of the pain, but in some of my cases there were no adhesions, so that the chief factor in Bastedo's test is probably distension of the diseased appendix.

Treatment and the Question of Focal Infection in Chronic Appendicitis

Complete recovery should follow the removal of the appendix for chronic appendicitis, but it is not infrequent for the symptoms to persist for a time after the operation, especially in anæmic, neurasthenic or neurotic patients. It is best in such an individual to give a preliminary course of treatment before the operation is performed in order to improve the general condition, and it is important that the patient should have a sufficiently long rest afterwards instead of being allowed to get up in the usual way—often before the end of a fortnight.

Infected teeth and tonsils are so common that their association with appendicitis might be regarded as accidental were it not for the recent remarkable investigations carried out by Rosenow.[19] He has shown that intravenous injection of streptococci, and much less frequently of *B. coli*, isolated from a diseased appendix into rabbits produces appendicitis. He has also shown that streptococci, isolated from the teeth, the apices of which are infected, and from infected tonsils in cases of appendicitis, show a selective action on the appendix when inoculated into rabbits, appendicitis being produced in 68 per cent. of the animals, just as streptococci from the teeth and tonsils in cases of gastric or duodenal ulcer and in cholecystitis show a selective action on the

stomach or duodenum (60 per cent.) and the gall-bladder (80 per cent.) respectively. On the other hand, streptococci isolated from infected teeth or tonsils in the absence of disease of the appendix, stomach, duodenum and gall-bladder rarely cause appendicitis (3 per cent.), gastric or duodenal ulcer (17 per cent.), or cholecystitis (4 per cent.).

Rosenow has shown that the streptococci isolated from the appendix, teeth or tonsils in cases of appendicitis have no effect when introduced into the lumen of the normal appendix in spite of their specific action on the appendix when injected intravenously. Only when chronic inflammation has resulted in damage to the mucous membrane or in stasis in the appendix owing to the presence of fæcoliths, strictures or kinks from adhesions, is further infection from the lumen of the bowel likely to take place. Swallowed streptococci originating in pyorrhœa alveolaris and tonsillitis may then lead to secondary infection and recrudescence of inflammation which is latent or has died completely out, especially if the oral sepsis is associated with achlorhydria, which deprives the stomach of the normal antiseptic action of the gastric juice. Bonar [7] found achlorhydria in 33 per cent. of sixty-five cases operated upon for chronic appendicitis at Guy's Hospital, including both those with and those without gastric symptoms. Though the hyperchlorhydria which occurred in 55 per cent. of cases was probably a reflex result of the disease, I believe that the achlorhydria was not a result but a predisposing cause, individuals with constitutional achlorhydria being abnormally liable to develop appendicitis. Under the same conditions pathogenic strains of *B. coli* or streptococci in cases of colitis involving the cæcum may also lead to secondary appendicitis.

In spite of their specific affinity for the appendix the streptococci isolated in cases of appendicitis are culturally almost identical with those obtained in other diseases, and they soon lose their specific action on passage through animals. The not uncommon association of appendicitis with gastric ulcer and especially with duodenal ulcer, and also with cholecystitis, suggests that the streptococci may have a specific affinity for more than one organ or may in course of time vary in their specific affinities.

From these considerations it is clear that removal of the appendix in cases of chronic appendicitis may not lead to the complete disappearance of the patient's symptoms. The teeth should be x-rayed in order that any apical infection, which may occur in the complete absence of pyorrhœa alveolaris, may be discovered, and every septic focus in the teeth, tonsils and nasal sinuses should be eradicated—if possible before the abdominal operation is undertaken. In this way many of the disappointments due to the coincidence of colitis and early or latent cholecystitis, and to the recurrence of hæmatemesis from acute gastric or duodenal ulcers, should be avoided ; with the possible exception of the cholecystitis, no local surgical treatment carried out at the same time as the appendicectomy is likely to be of any use.

In slight and doubtful cases, in which an immediate operation is obviously unnecessary, no harm can be done by waiting to see whether the removal of foci of infection, together with the administration of dilute hydrochloric acid in adequate doses if achlorhydria is present, does not lead to complete and permanent recovery. I do not, of course, suggest any such delay if a definite attack of acute or subacute appendicitis has occurred, or in long-standing cases of unmistakable chronic appendicitis, but every surgeon will welcome the possibility of avoiding the necessity of operating on the doubtful cases, which so often are incompletely cured or whose state of invalidism may even be exaggerated by operation.

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CHOLECYSTITIS AND GALL-STONES IN THE LIGHT OF RECENT RESEARCH *

Some anatomists are apt to think too little of the effects of biliary calculi. They find them in the bodies of whose history during life they know nothing; and if there is in the bodies no evident mark of mischief from the stones, they are apt to suppose there has been none. What pain a patient may have felt from them cannot be guessed from viewing the body. A mere anatomist therefore knows but little of the effects of gall-stones. —THOMAS COE, M.D., in "A Treatise on Biliary Concretions," London, 1757.

THE present century has witnessed a remarkable development in our knowledge of the pathogenesis, symptomatology and treatment of gall-stones. The classical researches of Naunyn [1] of Strassburg between 1891 and 1905 laid the foundations for all subsequent workers on the subject. Since 1900 the bio-chemical investigations of Chauffard [2] and his associates in Paris, the bacteriological investigations of Rosenow [3] in Chicago, and subsequently at the Mayo Clinic, and the clinical discoveries which have followed the study of the "pathology of the living" by British and American surgeons, and especially by Moynihan,[4] have added so much to our understanding of gall-stones that the time is ripe for a review of the whole subject. Its importance can be best realised when it is remembered that in at least 10 per cent. of all people over the age of twenty gall-stones are found after death, so that there must be over four million people in England who have gall-stones now, or will have them before they die, and some 16,000 in Southampton alone.

Although the bio-chemical and bacteriological investigations have been carried out for the most part independently of each other, and have led to the formation of two entirely different views of the pathogenesis of gall-stones, I hope I

* An address delivered before the Southern Division of the British Medical Association at Southampton, on March 29th, 1922. An abstract appeared in *The Practitioner* for October, 1923.

shall be able to show that each is really complementary to the other, and that a combination of the two affords a satisfactory explanation of the clinical facts.

The results of the bacteriological investigations of Rosenow are already fairly well known in England, but far too little attention has been paid to the remarkable bio-chemical work of the French school. In his opening address on the "Diagnosis and Treatment of Cholelithiasis" in the Section of Surgery of the British Medical Association last July, Professor Rutherford Morrison remarked that, although the infective theory of the origin of gall-stones is still the most popular, there is sufficient against it to condemn it, and that doubts as to the etiology of gall-stones will not be dispersed until some satisfactory evidence is brought forward by the chemists. The bio-chemical investigations of Chauffard and his colleagues have, I believe, already to a great extent dispersed these doubts.

The Bio-Chemistry of Gall-stones Formation

A very large proportion of gall-stones are formed either for the most part or entirely of cholesterol. It is clear, therefore, that a proper understanding of their pathogenesis is impossible without a thorough knowledge of the physiology of the production and excretion of cholesterol.

Normal human bile contains 0·15 per cent. of cholesterol held in solution by the bile salts, which are themselves formed by the union of taurin and glycocoll with cholalic acid produced from cholesterol in the liver. Cholesterol is likely to be precipitated whenever the quantity to be excreted in the bile is increased or the amount of bile salts available for its solution is reduced. The former is the more important factor, though Chauffard believes that there may also in certain cases be a congenital or acquired functional incapacity of the hepatic cells to form sufficient cholalic acid. Thus normal individuals are able to take large quantities of cholesterol in their food without ill result, as a corresponding quantity of bile salts is formed by the liver, and the increase in the percentage of cholesterol in the blood and bile is only intermittent. Under certain conditions, the exact nature

of which is obscure, but which are apparently present in the majority of individuals who develop gall-stones, the liver is unable to form sufficient bile salts to dissolve all the cholesterol, so that some is retained, thus giving rise to permanent hypercholesterolæmia. The bile is then always saturated with cholesterol, which is consequently liable to be deposited in the form of gall-stones.

Graham and Judd [5] have drawn attention to the almost constant presence of a mild degree of hepatitis in cholecystitis ; no such change occurs in gastric and duodenal ulcer or in appendicitis. It gives rise to no obvious symptoms, but the liver is often slightly enlarged both in cholecystitis and cholelithiasis. A small piece removed at operation or after death shows a leucocytic infiltration of the interlobular or periportal sheaths, which may be accompanied by degenerative changes in the hepatic cells. The hepatitis is probably secondary to the cholecystitis, which precedes the formation of the gall-stones, and results from the close lymphatic connections between the liver and the gall-bladder. This hepatitis may well be the cause of the deficient power of the liver to form bile-salts.

The concentration of the bile varies directly with the concentration of cholesterol present in the blood ; this depends, of course, mainly on the absolute quantity of the substance present. Chauffard found over 0·2 per cent. cholesterol in the blood in all but three out of forty-six patients with gall-stones, the average normal being about 0·16 per cent. ; the percentage was generally between 0·3 and 0·4, but sometimes reached 0·5. The three exceptions were in cases complicated by infection with fever, which always lowers the percentage of cholesterol in the blood. These results have recently been confirmed by J. R. Bell of Melbourne, who has been investigating the subject in Sir Berkeley Moynihan's clinic. He has kindly let me see his still unpublished figures, which show that the average quantity of cholesterol in the blood of twenty-three cases of gall-stones, in which the diagnosis was confirmed at operation, was 0·21 per cent., and that of six cases of cholecystitis and cholangitis was 0·205 per cent., whereas in forty-two cases in which the gall-bladder was healthy the average was

0·16 per cent. In ten cases of duodenal ulcer and seven of chronic appendicitis, conditions in which the diagnosis from gall-stones may give rise to difficulty, it was 0·16 per cent. and 0·15 per cent. respectively. In eleven out of twenty-three cases of gall-stones and three out of six of cholecystitis it was 0·21 per cent. or more, but it reached this figure in only three out of forty-two non-gall-bladder cases.

Part of the cholesterol in the blood is produced in the body, the remainder being introduced in the food. The former originates in the corpus luteum and the cortex of the suprarenal glands, both of which are largely composed of cholesterol. Over-activity of these two organs is therefore accompanied by hypercholesterolæmia. Just before each menstrual period there is a slight but definite increase in the percentage of cholesterol in the blood for a day or two (Gonalous). This explains why, even in unmarried women, the rate of occurrence of gall-stones is greater up to the menopause age than in men. After this the rate is higher in men owing to the greater frequency of arteriosclerosis and granular kidney, which Rolleston and Moore [6] have shown predispose to gall-stones, and in which Chauffard, Laroche and Grigaut [2] have found hypercholesterolæmia, the result, apparently, of over-activity of the suprarenal cortex.

In pregnancy the great development of the corpus luteum is accompanied, as Chauffard, Laroche and Grigaut found in 1911, by well-marked hypercholesterolæmia; it reaches its maximum at the eighth month and does not disappear until about two months after parturition. Increased activity of the suprarenal cortex during pregnancy is an additional explanation of this hypercholesterolæmia. McNee[7] found in four women, who had died between the fourth and last months of pregnancy, that the percentage of cholesterol in the bile was increased from the normal of 0·15 per cent. to an average of 0·62 per cent. These observations explain why gall-stones are so much more common in women than men, and that among the women about 75 per cent. have had children. They also explain why in many instances the earliest premonitory symptoms date from pregnancy, often becoming more marked after each successive pregnancy. The symptoms

in one of my patients dated from a pregnancy in 1911; she was operated upon, and remained well until January, 1913, when a series of very severe attacks of biliary colic began four days after the birth of another child. Eight stones were removed from her gall-bladder in April, 1913, and she has remained well ever since.

The most important source of cholesterol in food is the yolk of eggs. Butter and cream, and liver, kidney, pancreas, and especially brain, contain a smaller quantity. Widal, Weil and Laudat have shown that the fat of food, apart from the cholesterol which may be present, also increases the quantity of cholesterol in the blood. Gall-stones occur less exclusively in the obese than has often been supposed, but there is no doubt that fat people are rather more likely to have them than others. This is, perhaps, due in part to deficient exercise, which may favour biliary stasis. But the consumption of large quantities of food containing eggs and cream is probably a more important factor. Chauffard relates the case of a thin and anæmic woman, who was given eleven eggs a day in an attempt to improve her nutrition; she had a typical attack of biliary colic at the end of six months, when she had consumed a total of 1,934 eggs, containing in all about 8 ounces of cholesterol.

I have been struck by the frequency with which patients suffering from gall-stone dyspepsia, in contrast with all other forms of dyspepsia, discover for themselves that they cannot take fatty food, especially eggs. Occasionally they develop an actual distaste for the latter, although in many cases they had previously liked them and sometimes had indulged in them somewhat excessively.

The influence of a diet rich in cholesterol also explains why gall-stones are much more common among Europeans than in Japan and Java, where, moreover, 50 per cent. of gall-stones are formed mainly of pigment and contain very little cholesterol.

Infection

Since Naunyn's time much attention has been paid to the rôle of infection in the pathogenesis of gall-stones. It has been usual to point to the supposed association with typhoid

fever as conclusive evidence in this connection, although typhoid fever is now so rare in England that it is most exceptional to find a patient with gall-stones who has had it. It might, however, have been expected that gall-stones would have been observed as a sequel of the typhoid and paratyphoid fever which attacked many thousands of British troops during the war, although, of course, the incidence was very small compared with that in the South African War owing to the efficacy of prophylactic vaccination. But I have not seen a single case of gall-stones in a soldier who had enteric fever during the war—a striking contrast to the number of cases of hepatitis which have occurred as a sequel of amœbic dysentery, although the latter cannot have infected so large a number of men.

Even in America and on the Continent, where typhoid fever is still comparatively common, the association with gall-stones is less definite than was formerly believed. It is true that Chauffard obtained a history of typhoid fever in 20·9 per cent. of eighty-six cases and in 19·25 per cent. of a second series of 161 cases, but the high figures lose almost all their importance when one learns that in 17·4 per cent. of a consecutive series of eighty-six patients without gall-stones, who were under Chauffard at the same time, a history of typhoid fever was also obtained.

The presence of typhoid bacilli in the bile, when gallstones occur in patients who have had typhoid fever, is not surprising, as they are almost invariably found in the gall-bladder during the acute illness and may remain there for long periods afterwards, the gall-bladder being often the seat of the continued infection in typhoid carriers. Even their isolation from inside a gall-stone is not conclusive, as Gilbert and Fournier showed in 1896 that bacteria can penetrate a sterile stone, which has been incubated in a culture of *B. coli* for a fortnight, so that this discovery does not exclude the possibility that the stone may have been present before the infection or that it only developed later and independently of it.

In spite of these facts cases are sometimes observed, in which the evidence that gall-stones may form during typhoid fever seems conclusive. The following is an instance of this.

A woman of twenty-four, who was under my care in 1910, had, since the birth of her only child three years before, occasionally suffered from a dull, aching pain in the epigastrium immediately after food, which was occasionally relieved by vomiting, but was never sufficiently troublesome to cause her to seek medical advice. On December 22nd, 1909, she was admitted into a fever hospital with typhoid fever on the twelfth day of the disease. Her temperature fell to normal on January 2nd. From January 14th to January 24th she had a relapse, in which the rash returned. On February 1st she complained for the first time of pain in the epigastrium and back, and she vomited. The gall-bladder was found to be enlarged and slightly tender. There was no jaundice or pyrexia. The pain persisted, and attacks of bilious vomiting occurred from time to time. On February 18th the temperature rose to 99·4° F., and the patient was admitted into Guy's Hospital under my care. Her temperature was 99·8° F., and her pulse-rate 120. She complained of constant pain in the region of the gall-bladder, from which it passed round the right side to the back. The upper part of the right rectus muscle was very rigid, but an enlarged and tender gall-bladder could be felt. There was no tenderness elsewhere. Deep respiration produced pain in the right side of the chest. Suppurative cholecystitis was diagnosed, and Mr. Philip Turner operated the same evening. There was no free fluid in the peritoneal cavity and no peritonitis except in the immediate neighbourhood of the gall-bladder, which was distended, tense, and adherent to the surrounding structures. The gall-bladder was opened, and after about four ounces of colourless, clear fluid had escaped, about half an ounce of pus was evacuated. About twenty-five facetted gall-stones were then removed from the gall-bladder. They varied in diameter from an eighth to a quarter of an inch, and consisted of slightly pigmented cholesterol. The clear fluid and the pus both contained a pure culture of *B. typhosus*, which was also isolated from the centre of some of the stones. The gall-bladder was drained, and the patient made an uneventful recovery. As this was the patient's first attack of typhoid fever, and the *B. typhosus* was found in the centre of the gall-stones, it seemed clear

that they must have been formed between the onset of the typhoid fever on December 12th and the operation on February 18th, a period of sixty-eight days.

Even if it be accepted as proved that typhoid fever is exceptionally the essential factor in the production of gall-stones, it does not necessarily follow that this is due to the infection of the bile with *B. typhosus*, as Chauffard has proved that the hypocholesterolæmia, which occurs during the febrile period of typhoid fever, is constantly followed during convalescence by an increase in the amount of cholesterol in the blood, owing to its excessive formation in the suprarenal glands. Moreover, the bile in fatal cases of typhoid fever contains a considerable excess of cholesterol, independently of the existence of cholecystitis and gall-stones. There is thus a bio-chemical factor comparable to that which makes pregnancy predispose to cholelithiasis. In the case just recorded, however, the stones almost certainly began to form in the period when hypocholesterolæmia was still present, so that the infection itself must have been the exciting cause.

Aschoff [8] has shown that pure cholesterol stones may form under aseptic conditions in the absence of any sign of cholecystitis, and it has since been abundantly proved that both the bile and the stones themselves are frequently sterile when a gall-bladder is removed by operation. Chauffard regards this as evidence that infection plays but a small part in the production of gall-stones. Rosenow has, however, found that infection is generally present, even when no bacteria can be isolated from the contents of the gall-bladder or from the surface of its mucous membrane. In such cases he cultivated streptococci, which were sometimes associated with *B. coli*, from its walls. According to Knott and most other observers, however, the presence of streptococci is most exceptional, though the *B. coli* is frequently found. Microscopical examination of the gall-bladder almost invariably reveals a certain degree of inflammation, even if it is not obvious to the naked eye. In those of my cases in which the bile, stones and wall of the gall-bladder were sterile Knott found evidence of old chronic cholecystitis, which suggested that an infection had originally been present but had since died out.

According to Rosenow, the streptococcus, which he believes

is associated with the large majority of cases of gall-bladder disease, is specific, just as those associated with gastric and duodenal ulcer, and with appendicitis, are specific. It generally reproduces the same disease when inoculated into animals, though it has no effect when injected directly into the lumen of the gall-bladder. Streptococci from foci of infection, such as the teeth, tonsils or appendix, which are present in the same patient as the gall-bladder disease, also give rise to cholecystitis in animals. It thus appears that a primary focus of infection is present as frequently in gall-bladder disease as in gastric and duodenal ulcer, and it is probably from this that the gall-bladder becomes infected by way of the cystic artery.

Rosenow found that the *B. coli* isolated from the gall-bladder in cases of cholecystitis was only rarely specific in the sense that the streptococcus was so often specific. It seems probable, however, that the *B. coli* also frequently leads to infection of the gall-bladder by way of the bile ; it passes from the colon by the portal vein to the liver, and is then excreted by the bile and infects the gall-bladder. In some cases it may also reach the gall-bladder as a result of an ascending infection. In a series of thirty-five cases at Guy's Hospital, in which the diagnosis of gall-stones was confirmed by operation, Bonar [9] found by means of fractional test-meals that achlorhydria was present in seventeen cases (49 per cent.) compared with the 4 per cent. which Bennett and Ryle found in healthy young men. In a similar series of twenty-two cases under Sir Berkeley Moynihan, Bell found achlorhydria in 32 per cent., and well-marked hypochlorhydria in an additional 18 per cent. Using an ordinary Ewald test-meal, Finger [10] found achlorhydria or hypochlorhydria in 45 per cent. of 115 cases, Rydgaard [11] in 47 per cent. of 158 cases, and Gatewood [12] in 45 per cent. of 192 cases in which the presence of gall-stones was proved at operation ; Gatewood's 45 per cent. include 30 per cent. with achlorhydria. The achlorhydria is probably the primary condition and acts by facilitating duodenal infection owing to the loss of the antiseptic action of the gastric juice ; an ascending infection with *B. coli* is consequently liable to occur under these circumstances. It is, however, unlikely to lead to chole-

cystitis unless the gall-bladder has already been damaged by a hæmatogenous infection with a streptococcus, *B. coli*, or *B. typhosus*, though these infections, if left to themselves, might have died out and given rise to no further trouble.

Biliary infection, as Naunyn first pointed out, leads to gall-stones by giving rise to cholecystitis, as a result of which epithelial debris and mucus collect in the gall-bladder. If for any reason excess of cholesterol is present in the bile, especially if catarrh of the bile passages leads to a certain amount of stasis, cholesterol is deposited on this foundation. The infection may become attenuated or die out completely so far as the contents of the gall-bladder are concerned, although its walls may remain infected, and from time to time a recrudescence of biliary infection may take place. The history of a case may be judged from the appearance of a section through the stone. Cholesterol stones correspond with uric acid and oxalate stones in the urinary tract, being the result of bio-chemical processes independent of infection, whereas the deposit of pigment is due to biliary infection, just as the deposit of phosphates on renal calculi is generally due to urinary infection. Pure cholesterol stones are not very rare. More often the centre is formed of cholesterol ; when this has reached a certain size, layers of pigment alternating with layers of cholesterol are deposited and the outside is often pigmented ; the pigment layers are formed during periods of infection, the final one having, perhaps, been the signal for the operation in which the stone was removed.

Biliary Stasis

Stagnation of bile must favour the development of gall-stones, both by allowing precipitation to occur when excess of cholesterol is present and by increasing the liability to infection. It is for this reason that stones almost invariably originate in the gall-bladder, in which the bile must always stagnate to a certain extent, and not in the ducts, in which there is a more or less continuous flow of bile. But when a stone has become impacted in the common duct, more cholesterol or pigment may be deposited upon it, and obstruction to the flow of bile by stones, growth or other conditions

may lead to the formation of small calculi even in the hepatic ducts.

Keith [13] in 1903 drew attention to the frequency of gall-stones in visceroptosis, this being clearly due to the liability of the bile ducts to become kinked when pulled upon by the peritoneal attachments to the right kidney, duodenum or pylorus on assuming the erect position, especially if for any reason pathological adhesions have formed between the gall-bladder and one or more of these organs. I have seen three cases of gall-stones, in which the liver had twisted round an antero-posterior axis and fallen into the right flank. A movable kidney may drag upon the bile-ducts and produce, according to Sherren,[14] typical attacks of biliary colic, indistinguishable from those produced by gall-stones. As the obstruction may eventually lead to the production of gall-stones, the two conditions not infrequently co-exist. The very mobile cæcum and ascending colon, which Waugh believes may give rise to symptoms simulating gall-bladder disease, is perhaps also a predisposing factor. The frequent weakness of the abdominal muscles following pregnancy, which results in an increased tendency to visceroptosis, may be an additional factor in the association of gall-bladder disease with repeated pregnancies.

Symptoms

It is probably rare for gall-stones to be present without any history of symptoms, most frequently in the form of continuous or intermittent dyspepsia. Abortive attacks of biliary colic, generally gastralgic in type, may occur independently or associated with gall-bladder dyspepsia. Typical attacks of acute colic are less frequent. They are commonly preceded by more chronic symptoms, the "inaugural symptoms" of Moynihan, and they rarely occur without any previous warning.

The "Inaugural Symptoms": Gall-bladder Dyspepsia.

In gall-bladder dyspepsia the patient complains of intractable indigestion. Discomfort or pain occurs at varying periods after meals. A characteristic feature of gall-bladder

dyspepsia is its extreme irregularity. In gastric and duodenal ulcer the pain begins, as a rule, with clock-like regularity a certain time after food. In gall-bladder dyspepsia, as in appendicular dyspepsia, the time of its occurrence and its severity vary greatly from meal to meal and from day to day ; it sometimes begins immediately after food, and at other times in the same patient it may not come until two or three hours after a meal, or it may only occur in the early part of the night, when it is much less completely relieved by taking food than is the case with the nocturnal pain of duodenal ulcer. In most cases the patient complains of what he calls flatulence, but this is really only a sensation of fulness, which is not associated with increased fermentation, and only with eructation when it gives rise to aerophagy by causing the patient to make repeated but futile efforts to belch in the hope of relieving his discomfort. In the majority of cases of simple dyspepsia, and in all cases of gastric and duodenal ulcer, more or less relief is temporarily obtained by means of alkalies, but they give little or no relief when the dyspepsia is due to gall-bladder disease.

Nausea is very common. It may occur on waking or be associated with vertigo, cold sweats, or headaches, in which case migraine may be simulated, though the headache is not unilateral. It may be relieved by breakfast, unless eggs are eaten, when it is often aggravated. It is sometimes followed by vomiting, which gives much less complete relief than in gastric ulcer.

Patients with ulcer generally lose all their pain in two or three days if put to bed on a strict diet, but improvement is less likely to follow in gall-bladder dyspepsia, which may, however, rapidly improve if yolk of egg, cream and other cholesterol-containing foods are excluded from the diet. Constipation is almost always present, but occasionally sudden, profuse, watery diarrhœa, lasting about half an hour, may occur at the onset of an attack of cholecystitis.

Abortive Attacks of Biliary Colic : " Biliary Gastralgia."

Many patients who suffer from gall-bladder dyspepsia and some who have no such symptoms complain of short attacks

of severe pain, which may occur at any time of the day or night without any obvious cause, such as an indiscretion in diet, although occasionally an attack is the direct sequel of the combined shaking and fatigue of a long railway journey, a drive in a motor-car on a bad road, or violent exercise. A patient of mine had a severe attack of biliary colic on two occasions immediately after spending two whole days in the train while travelling in America. Attacks may occur daily or at long intervals, or there may be a series close together followed by a long spell of freedom. The patient may shiver during an attack, although his temperature never rises greatly and generally does not rise at all. The shivering is occasionally accompanied by a sensation of "goose-skin," particularly in the epigastrium and right side of the upper part of the abdomen, and also by palpitation, various vasomotor disturbances and dyspnœa. When the pain is acute it is impossible to take a deep breath, the attempt producing a "catch" in the right side of the chest, which is very similar to what is felt in pleurisy. Jaundice does not often occur in these abortive attacks. It may, however, be present in some, though not in others, and it is generally evanescent and slight in degree.

Acute Biliary Colic.

Attacks of biliary colic most frequently result from impaction of a stone in the neck of the gall-bladder. They often occur in the night. The attack begins with extremely sudden acute pain high up in the epigastrium or in the region of the gall-bladder, or both ; it may pass through to the back or towards the tip of the right shoulder. The violent pain is accompanied by great restlessness, in marked contrast to the motionless state of a patient with a perforated ulcer or acute appendicitis. The patient moans and writhes without ceasing, and attempts to obtain some relief by bending forwards, flexing his right thigh and pressing upon his abdomen. He feels cold, but sweats profusely. Breathing is generally difficult, and crepitations or a rub may be heard at the right base, these being secondary to the biliary infection and not an indication of an independent intra-thoracic

condition. Nausea and vomiting almost always occur ; the vomiting may give some relief. Aerophagy is generally present. The pain commonly disappears with absolute suddenness. There is often slight albuminuria during an attack, and constipation is complete. The number of leucocytes per cubic millimetre may rise to 12,000 or 15,000, the increase being in the polymorphonuclear cells.

Jaundice occurs when a stone reaches the common bile duct. Hijman van den Bergh [15] has shown that the leakage point, at which bilirubin passes into the urine, is reached when its concentration in the blood rises from the normal of 1 in 250,000 to 1 in 50,000. About the same concentration is required to cause jaundice, but the appearance of a trace of bile pigment in the urine is, of course, much easier to recognise with certainty than the first trace of pigmentation of the skin or conjunctiva. Moreover, the pigmentation is somewhat slower to develop, and it remains for a time after all pigment has disappeared from the urine. The colour reaction described by van den Bergh makes it possible to recognise the presence of excess of bilirubin in the blood at a concentration lower than the renal leakage point, so that the presence of a very slight degree of biliary obstruction can be proved to exist in the complete absence of actual jaundice and of bile from the urine, or at a stage before these develop and still longer before any change is noticed in the colour of the stools.

The Passage of Stones

Gall-stones are only passed in a very small proportion of cases. It is important to distinguish gall-stones or biliary sand from the intestinal sand associated with muco-membranous colic, the pseudo-sand passed by people who have eaten pears or bananas, and concretions produced by drugs or resulting from the administration of large quantities of olive oil. The rarest form of stone to be passed is a very small rounded one, which has probably traversed the normal passage during an attack of colic ; as it may be the only one, a cure may result. More frequently facetted stones are passed ; even if large numbers are found, it is very unlikely that all have left the gall-bladder. One

or less frequently two or three large stones may be passed after traversing a fistulous communication between the gall-bladder and duodenum or colon. The fistula may develop very slowly without symptoms after chronic cholecystitis has led to the production of adhesions, but more often perforation occurs in an acutely inflamed gall-bladder, which may be distended with clear fluid or pus. When a large stone traverses the whole bowel, pain is generally produced at one time near the right iliac fossa, owing to impaction in the terminal part of the ileum. If it passes further, pain is later felt below the umbilicus and finally in the rectum, from which the stones may have to be dislodged by the finger.

When a stone passes through a fistula into the duodenum, acute intestinal obstruction may occur, as in a case which was under my care in 1909. A stout woman of fifty-one was admitted with acute intestinal obstruction, which had already been present several days. She had had previous attacks of abdominal pain, and the present attack was preceded by severe pain under the right costal cartilages. Her abdomen was tender and slightly distended, but not rigid, and fæces were found in the rectum. We thought from the history and appearance of the patient that the obstruction was probably due to a gall-stone. Mr. C. H. Fagge operated at once. The small intestine was dilated and the colon collapsed. As soon as he put his hand into the pelvis he felt two stones, which were movable in the ileum, and he subsequently found a third, which was impacted two inches above the ileo-cæcal sphincter. The stones were removed, but the patient had had obstruction for so long that it was not surprising that she died four hours later.

The Pain and Tenderness in Cholecystitis and Cholelithiasis

Patients with gall-bladder disease suffer pain or discomfort and tenderness in several situations. The discomfort after meals is generally in the epigastrium; less frequently it is just above and to the right of the umbilicus. The attacks of colic, whether abortive or fully developed, often begin in the same situations. In most cases they spread round the right

side of the chest to the back, the point of greatest pain and tenderness being over the gall-bladder itself, but in some cases the pain never leaves the epigastrium. The chief pain behind is generally at the angle of the right scapula. After the attack has passed, a dull ache often remains for a long period in the same situations, and tenderness may be present over the third to the tenth dorsal spines (Ryle), the muscles to their immediate right, and the end of the eleventh rib. Figs. 52 and 53, prepared with the help of Dr. J. A. Ryle, show

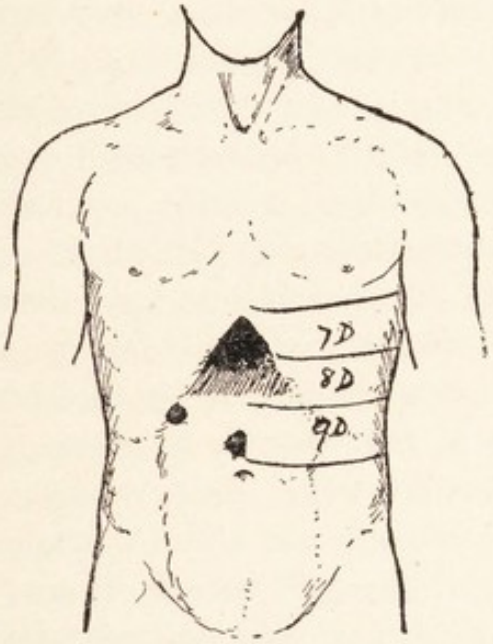


FIG. 52.—Areas of referred pain and tenderness in gall-bladder disease. 7D, 8D, 9D = cutaneous areas supplied by seventh, eighth and ninth segments of the spinal cord.

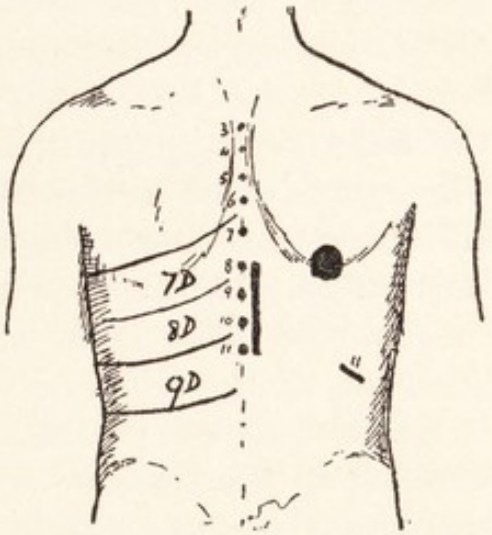


FIG. 53.—Areas of referred pain and tenderness in gall-bladder disease.

that all the tender and painful areas are in the distribution of the seventh, eighth and ninth dorsal segments. This is due to the fact that the gall-bladder and bile-ducts are supplied by nerve fibres coming from these spinal segments. The afferent impulses from the distended and consequently painful gall-bladder or bile-ducts produce an irritable focus in the spinal cord ; normal sensory impulses reaching this focus from the skin or muscles consequently become exaggerated and painful, so that pain may be felt and the skin and muscles become tender ; at the same time reflexes are produced which lead to rigidity of the upper part of the right

rectus abdominis muscle and the lowest intercostal muscles ; the tenderness and rigidity of the latter cause the impeded respiration and stitch in the right side of the chest. A pilomotor reflex may also occur and give rise to a goose-skin sensation.

The tenderness and pain in the region of the gall-bladder are true visceral tenderness and pain, as their situation alters with the respiratory movements and when the liver is in an abnormal position, as in the three cases already referred to. The gall-bladder tenderness is the most characteristic sign of cholecystitis ; it is most marked for some days after an attack of colic, whether abortive or severe, but is also often associated with gall-bladder dyspepsia in the complete absence of colic. It is best elicited with the patient lying relaxed on his back ; the fingers are then pressed beneath the right costal margin in the region of the gall-bladder. The pain is much increased when the fingers are brought into still more intimate contact with the gall-bladder by deep inspiration ; at the same moment the latter is brought to a sudden end. The pain produced in this way is in striking contrast to the absence of tenderness when deep pressure is exerted under the left costal margin or a very short distance to the inner or outer side of the gall-bladder under the right costal margin. Pressure on the gall-bladder often causes nausea, which may even occur in the absence of pain.

Occasionally the irritable focus spreads to the opposite side. In one of my cases the referred pain over the shoulder and at the angle of the scapula, as well as at the costal margin, were only felt on the left side, though the chief point of tenderness was over the gall-bladder itself.

The stomach is supplied by the sixth, seventh and eighth dorsal segments of the spinal cord, so that the situation of the pain and tenderness in diseases of the gall-bladder and stomach may be very similar, but the latter are more often left-sided. When the epigastric discomfort after meals is associated with cholecystitis it is probably due to a direct reflex from the gall-bladder affecting the movements and secretion of the stomach ; it is then often associated with

mid-gastric spasm recognisable with the x-rays and with hyperchlorhydria.

Radiographic Signs

Pure cholesterol gall-stones are too transparent with the x-rays to throw any shadow, but when much lime salts are present, especially in thin patients, they are sometimes visible, according to Case [16] actually in 50 per cent. of cases. The shadow must be distinguished from that produced by a renal calculus, a calcified tuberculous focus in a kidney, a calcified tuberculous gland, or a calcareous deposit in a costal cartilage. The distinction can be most readily made by means of stereoscopic skiagrams, and in the case of the kidney by the shadow being situated within that of the kidney itself. Moreover, in renal calculi a small shadow is clearer and smaller when the rays pass from the front to the back of the body than in the reverse direction, whereas the opposite is the case with a gall-stone. Renal calculi often have a characteristic shape. Calcareous glands are generally multiple and movable on manipulation.

Apart from the shadow thrown by the stones, an examination by means of the x-rays may be useful, as it sometimes shows that the pyloric end of the stomach or duodenum extends abnormally far upwards and outwards under the liver, from which it cannot be drawn by deep palpation, suggesting that the pylorus or duodenum is adherent to the gall-bladder ; this may, of course, be due equally well to an ulcer as to gall-bladder disease. The maximum point of tenderness is found immediately outside the shadow of the duodenal cap and not over the latter as in duodenal ulcer. There may also be indications of adhesions to the hepatic flexure. Occasionally a spasm is visible in the centre of the stomach, but this is of no great value in diagnosis, as an intermittent reflex gastric spasm occurs also in appendicits and with duodenal ulcer, in addition to the more permanent spasm observed in ulcer of the lesser curvature of the stomach. The x-rays, moreover, often furnish definite evidence of the presence of a gastric or duodenal ulcer, but gall-stones may, of course, be present at the same time.

Bio-Chemical Investigations

Gastric analysis is often of great help in the diagnosis from duodenal ulcer, as the hyperchlorhydria, which is typical of the latter, was only observed in 23 per cent. of thirty-five Guy's cases (Bonar) and 18 per cent. of twenty-two Leeds cases (Bell) confirmed by operation, whereas in 49 and 50 per cent. of cases respectively complete or almost complete achlorhydria, which never occurs in duodenal ulcer, was found.

The presence of occult blood in the stools is a further point in favour of the diagnosis of ulcer ; in the absence of the latter it may very rarely be caused by the formation of a fistula from the gall-bladder to the duodenum or hepatic flexure or by the development of cancer of the gall-bladder.

Estimation of the cholesterol in the blood sometimes affords additional help in diagnosis. The normal proportion is 0·15 per cent., and 0·3 per cent. or more in a suspicious case is an important point in favour of gall-stones against such other diseases as in ulcer or appendicitis. Bell has shown that with a percentage of 0·19 or more the odds are 3·3 to 1 in favour of gall-stones as against duodenal ulcer or other abdominal disease, and the odds increase with each addition of 0·01 to the percentage. On the other hand, with a percentage of less than 0·10 they are 2·6 to 1 against gall-stones. It is, however, necessary to add that these results have not so far been confirmed in a number of my cases examined by J. M. H. Campbell.

Examination of Bile and Duodenal Contents

During the last two years we have obtained a specimen of the duodenal contents and a separate specimen of bile for pathological examination as a matter of routine in all cases of suspected disease of the gall-bladder. Whenever an operation has subsequently been performed, the gall-bladder and its contents have been carefully examined so as to correlate the pre-operative findings with the pathological changes discovered after cholecystectomy. We have come to the conclusion that very valuable information can be

obtained by this method. We have very rarely failed to introduce the tube into the duodenum, and the proceeding is no more unpleasant for the patient than a fractional test-meal, Ryle's tube being used for both. The sterilised tube is swallowed up to the 23-inch mark, first thing in the morning, before the patient has had anything to eat or drink. The stomach is emptied and then washed out with sterile water ; the last washing is kept for bacteriological examination in order to exclude the possibility of contamination. The tube is then slowly played out up to the 28½-inch mark, which allows sufficient length for the duodenum to be reached. Samples are aspirated every quarter of an hour until the comparatively abundant, acid, turbid and colourless fluid present in the stomach is replaced by the very small quantity of neutral or alkaline, clear, and bile-stained fluid present in the duodenum. The pylorus is generally passed in less than half an hour, and more than an hour is rarely required. The first duodenal specimen is kept for examination ; the duodenum is then washed out with sterile water, and from 2 to 4 drachms of magnesium sulphate in concentrated solution are injected through the tube. Meltzer [17] discovered in 1917, that this results in the simultaneous contraction of the gall-bladder and bile-ducts and relaxation of the sphincter of the common bile-duct. Consequently an abundant flow of pure bile rapidly ensues. This is aspirated and the tube is then withdrawn.

The duodenal contents and bile have been examined microscopically and bacteriologically by Dr. R. D. Passey, and more recently by Dr. F. A. Knott, who has recently analysed with Dr. J. F. Venables the findings in 100 consecutive specimens of bile obtained by this method at Guy's Hospital and New Lodge Clinic, which included seventeen from proved and fourteen from probable cases of gall-bladder disease. In the absence of gall-bladder disease they very rarely contain any pus cells and still less frequently cholesterol crystals, but often a few columnar epithelial cells and a little mucus. The bile and duodenal contents are either sterile or contain a few staphylococci, most of which are dead. A few colonies may grow very sluggishly and probably represent the survivors of the swallowed bacteria, most of which are

killed by the gastric juice. The *M. catarrhalis* was never found, being apparently always destroyed in the stomach. In patients with achlorhydria, whether they have gall-bladder disease or not, numerous bacteria are found in the duodenum, including *B. coli*, but rarely streptococci unless the patient is suffering from Addison's anæmia or subacute combined degeneration of the cord, in which a hæmolytic streptococcus is almost always found.

In gall-bladder infections the bile and duodenal contents often contain pus cells. They were found by Venables and Knott in eight out of seventeen proved cases and ten out of fourteen probable cases of gall-bladder disease, together making 58 per cent., as compared with three out of twenty cases of Addison's anæmia, and three out of forty-nine cases of other diseases, together making only 8·7 per cent. Cholesterol crystals were found by Knott and Venables in the bile of eight out of seventeen proved cases and seven out of thirteen probable cases of gall-bladder disease, making together 50 per cent., but in not a single one of seventy cases in which there was no sign of cholecystitis or gall-stones. The bile contains bacteria, generally of a single variety, which is also present in the duodenal contents, often in pure culture. The most common infecting organism is a form of *B. coli ;* a streptococcus has only been found in exceptional cases. Thus, in the 100 consecutive observations carried out by Knott and Venables a *B. coli* was isolated from the bile in fifteen out of thirty cases of certain or probable gall-bladder disease, compared with twenty out of sixty-one other cases. Among the six cases of gall-bladder disease with achlorhydria it was found five times, compared with ten out of eighteen cases of Addison's anæmia and six out of nine other cases in which achlorhydria was present. The difference was much more striking in cases in which free hydrochloric acid was present in the stomach ; the organism was isolated in ten out of twenty-four (41·7 per cent.) gall-bladder cases, but in only four out of thirty-four (11·7 per cent.) other cases. A streptococcus, though constantly present in the duodenal contents in cases of Addison's anæmia, was not found in any of this series of gall-bladder cases. Whenever the gall-bladder has subsequently been removed at operation the

same kind of cells and the same bacteria have been found by Knott in its contents as were discovered in the bile obtained through the duodenal tube.

Prophylaxis and Medical Treatment

The additions to our knowledge of the clinical history of duodenal ulcer, which have resulted from modern surgery, together with the recent advances in radiological and biochemical investigations have made it possible to diagnose the condition with some degree of certainty, at a stage when medical treatment is so successful that surgical assistance is only required under exceptional circumstances. We have not yet reached as far as this in our knowledge of cholecystitis and cholelithiasis, but in the light of the clinical and pathological investigations I have described it is now possible to diagnose gall-bladder disease in many cases at a stage when it is still amenable to medical treatment. The various infections which give rise to infective or catarrhal jaundice, and the infection of the bile in typhoid and paratyphoid fever, even if complicated with cholecystitis, generally disappear spontaneously, and there is no reason why other biliary infections should not be curable under favourable conditions, and why simple infective conditions of the biliary tract should be less amenable to medical treatment than those of the urinary passages. Even crystals of cholesterol deposited on the walls of the gall-bladder or minute agglomerations of crystals—the basis of what may later become gall-stones—can be redissolved by the bile, if it contains any excess of bile salts over the quantity required to hold the cholesterol already dissolved in it. Moreover, frequent thorough evacuation of the gall-bladder may lead to the removal of such agglomerations, whilst they are still small enough to pass into the duodenum, especially if any catarrh of the ducts which might lead to partial obstruction is overcome by combating the infection which gave rise to it.

Thus a diet which renders the bile capable of dissolving more cholesterol, drugs capable of overcoming the biliary infection, and measures capable of preventing biliary stasis,

are likely to stop the formation of gall-stones if adequately employed at a sufficiently early stage. The excellent results obtained by J. Chauffard as a result of treatment by diet and biliary antiseptics has been abundantly confirmed by my own experience and by that of several other physicians and practitioners who have tried it since I first wrote about it nine years ago.[18] With the recent addition of a new method of providing adequate biliary drainage without operation the results are, I believe, likely to be still more satisfactory.

(i.) *Diet*

In order that no more crystals of cholesterol should be deposited, and that any already deposited in the gall-bladder may be redissolved, it is essential that the bile should not be in a saturated condition. A diet must therefore be chosen which contains a minimal quantity of cholesterol. With the exception of brain, the yolk of egg contains a larger percentage of cholesterol than any other food. A single egg contains about ¼ gram of cholesterol. No eggs should be allowed, and nothing made from the yolk of eggs. Butter should be used sparingly, as it contains 0·4 per cent. of cholesterol, compared with 2 per cent. in egg-yolk and brain. It may be spread thinly over bread and toast, but should not be used in cooking. Cream is also prohibited, but milk contains too small a percentage to be of any importance. Kidney, liver, sweetbread and brain are not allowed. As all animal fats increase the cholesterol percentage in the blood, quite apart from the cholesterol they contain, the fat of meat, and pork, goose and duck should also be prohibited. Anything likely to increase intestinal putrefaction, such as high game and ripe cheese, should be avoided. In my opinion women should avoid the yolk of egg during the last four months of pregnancy and the first two months after, even if they have never had any symptoms of gall-bladder disease, as there is no doubt that the hypercholesterolæmia at this time is a powerful predisposing cause of gall-stones.

(ii.) *Biliary Antiseptics*

If the bile obtained through a duodenal tube is sterile, any infection which is present must be confined to the walls of

the gall-bladder, so that it is unlikely any antiseptic excreted in the bile could have any effect upon it. If, however, organisms are cultivated from it, and this can certainly be done in the majority of cases, an attempt should be made to render the bile as strongly antiseptic as possible, in the hope that the further multiplication of bacteria in the gall-bladder should cease, and even that the infection should be overcome if the conditions are favourable. It is therefore worth while giving a trial to treatment by biliary antiseptics in most cases of chronic cholecystitis, whether gall-stones are present or not, and similar treatment should follow any operation performed on the biliary tracts, and should also precede it for a few days unless it has to be performed as a matter of urgency. It is also undoubtedly wise to give a biliary antiseptic as a routine measure in typhoid and paratyphoid fevers, as in these diseases the bile is always infected.

Salicylates and urotropine are the only two antiseptics which are excreted in the bile. Salicylates are true cholagogues, increasing the excretion of bile salts and cholesterol without increasing the concentration of the bile, which actually becomes more fluid. It has been proved conclusively that it exerts a definite antiseptic action on the bile, and it has the further effect of relieving general malaise and any local discomfort which may be present. It appears in the bile in half an hour and exerts its maximum effect in two hours. From 10 to 20 grains of sodium salicylate or aspirin should be taken three times a day for at least three months and then for a week in every month.

In 1908 Crowe [19] demonstrated on patients with biliary fistulæ that urotropine is excreted in the bile and that it acts as a biliary antiseptic. This was confirmed three years later by Chauffard in similar cases, and quite recently by F. A. Knott [20] in a series of investigations on patients of mine with cholecystitis, from whom specimens of bile were obtained by means of a duodenal tube. When urotropine is given for urinary infections it is usual to add acid sodium phosphate in order to be sure that the urine is acid, as it does not act unless formalin is set free in the acid medium. Bile is alkaline, so that any urotropine it contains must be in an unaltered state, and yet it has been proved experimentally that it

can act as an antiseptic in this fluid. Thus Knott has shown that the addition of urotropine to bile renders the latter antiseptic in spite of its alkaline reaction, although its addition to alkaline urine or cerebro-spinal fluid is without effect. He has proved that this depends in some way upon the presence of bile salts. It is obvious that the larger the dose of urotropine the more effective it is likely to be. The maximum dose which can be used depends upon the vulnerability of the bladder ; frequency of micturition with the passage of blood and bladder cells occurs with an over-dose, but by giving sufficient potassium citrate to make the urine alkaline, I have found that the amount a patient can take is greatly increased. This was first suggested to me by J. H. Ryffel, who pointed out that the irritation of the bladder depends to a great extent upon the formalin which is set free by the acid urine, and that there is no reason for keeping the urine acid when the drug is given for its action on the bile instead of on the urine. I generally give a single large dose of urotropine every night with enough potassium citrate to keep the urine alkaline. Beginning with 20 grains of urotropine and 60 grains of potassium citrate, the dose of the former is increased by 10 grains every night till the slightest sign of bladder irritability is felt or until the urine contains the first trace of blood. The dose is then reduced to what it was before the last addition was made, and the patient continues to take this for several weeks, the urine being still examined once a week to see that no blood appears. As a rule the patient is able to take the same dose for an indefinite period, but it is safest to give it only five days in each week. Different individuals vary greatly in the amount they can take, but it is generally possible to give as much as 60 grains and often 80 or 90 grains every night. Knott has demonstrated that urotropine given in this way completely sterilised the infected bile in several cases of cholecystitis under my care, pus cells which were present previously in the bile disappearing at the same time. The sterilisation was always accompanied by disappearance of tenderness, pyrexia and other clinical signs of cholecystitis.

Rosenow's work indicates how important it is to look for and remove foci of infection in the teeth, tonsils and nasal

sinuses as a part of prophylactic and medical treatment, and also before any operation is performed for gall-stones or cholecystitis, as otherwise a recurrence of the infection is very likely to occur. If the appendix is diseased, an operation should at once be performed for its removal, and the gall-bladder can be dealt with at the same time. An autogenous vaccine prepared from the *B. coli* or other organism isolated from the bile obtained under aseptic conditions through Ryle's tube may be tried. It seems not unreasonable to expect that it may prove to be as useful in helping to overcome a biliary infection as is an autogenous vaccine prepared from a urinary organism in cases of pyelitis and cystitis. Care must be taken to start with a small dose and only gradually increase it ; in one case general malaise with fever and vomiting occurred each time an attempt was made to increase the dose.

(iii.) *The Prevention of Biliary Stasis*

Stasis of bile in the biliary tracts and especially in the gall-bladder must be prevented as far as possible. Under ordinary conditions bile is secreted continuously, but collects in the gall-bladder until the first chyme enters the duodenum after a meal, when contraction of the gall-bladder, accompanied by relaxation of Oddi's sphincter, which normally keeps the mouth of the common bile-duct in the biliary papilla closed, results in a copious flow of bile into the duodenum. When the four ordinary meals are taken in the day, the stomach is never completely empty ; it is therefore doubtful whether the gall-bladder would empty itself any more frequently if two or three additional intermediate feeds were taken, as has often been recommended.

I have already referred to Meltzer's discovery that the introduction of a concentrated solution of magnesium sulphate into the duodenum has the same effect on the gall-bladder and Oddi's sphincter as acid chyme. This led Lyon [21] to recommend that the solution should be introduced directly into the duodenum through an Einhorn tube every day in cases of gall-bladder infection. J. F. Venables, working in New Lodge Clinic, has shown that, contrary to

the belief of Meltzer,[17] Lyon, Meakins [22] and other earlier observers, the same result is obtained equally well and very much more conveniently by taking the solution by mouth about an hour before breakfast. The duodenum remains empty for half or three-quarters of an hour, when there is a sudden rush of bile, just as abundant as that obtained by the direct method. From 1 to 4 drachms of magnesium sulphate in concentrated solution should be used, the dose depending on the condition of the patient's bowels. By this means the complete evacuation of all the biliary passages which are not actually obstructed can be assured at least once a day.

When visceroptosis is present, an efficient abdominal support should be worn, in order to prevent the biliary stasis which might otherwise result from kinking of the biliary ducts.

A moderate amount of exercise is useful, as it probably helps to prevent stagnation of the bile, by causing the diaphragm to contract vigorously whilst the abdominal muscles are contracted and by rhythmically squeezing the liver. But violent exercise and long railway journeys, and especially journeys in badly sprung motor-cars on rough roads, are likely to bring on attacks of colic.

(iv.) *Olive Oil, Belladonna and Hydrochloric Acid*

Olive oil has long been used in the treatment of gall-stones. It was first recommended because it was found that olive oil dissolved gall-stones *in vitro*, but nobody ever explained how the olive oil was going to reach the gall-bladder. The success of the treatment appeared to be proved when soft concretions somewhat resembling gall-stones were discovered in the fæces, although, if the oil was expected to dissolve the stones, it is not clear why they should be excreted in solid form. Ultimately it was discovered that the " stones " were really composed of calcium oleate and contained no trace of cholesterol or other constituent of bile.

There is, however, no doubt that in certain cases a table-spoonful of olive oil taken before meals does relieve gall-bladder dyspepsia. The explanation is that it is a powerful inhibitant of gastric secretion and gastric spasm, and relief

is therefore likely to follow its use in cases in which a test-meal shows the presence of hyperchlorhydria and the x-rays reveal evidence of hyperactivity or mid-gastric or pyloric spasm, which may, perhaps, be associated with spasm of Oddi's sphincter. In cases of this sort 5 to 10 minims of tincture of belladonna given before meals are also often very helpful.

On the other hand, in those cases in which achlorhydria is discovered, olive oil only aggravates the symptoms, but some relief may follow the use of a drachm of dilute hydrochloric acid given in 4 ounces of sweetened orange or lemon juice and water as a beverage at meals. By acting as an intestinal antiseptic it may also help to overcome any secondary biliary infection which may be present.

Although morphia injections are often required for the pain in severe attacks of biliary colic, they should never be given for minor attacks, and a patient should undergo operation long before there is any chance of his becoming addicted to the drug. I have seen two cases of severe morphinism develop in patients with gall-stones, and surgical removal of the cause of pain failed to cure the habit.

(v.) *Spa Treatment*

In view of the fact that thousands of patients supposed to be suffering from gall-stones are still sent every year to Vichy and Carlsbad, the question of spa treatment requires brief consideration. Formerly its object was "expulsive," and an attack of colic within the first fortnight of the "cure" was welcomed. It is now realised that even if a stone is passed, it is probable that others are still present, and the treatment given is of much milder character. Biscons and Rouzaud have made the interesting discovery that the hypercholesterolæmia generally associated with gall-stones disappears as the result of drinking the hot alkaline Vichy waters. There is no doubt, too, that the dietetic and other treatment is likely to improve the condition of obese patients.

A visit to Vichy may therefore be considered in the later stages of the medical treatment I have advised, and it is also

likely to prove beneficial during the weeks of convalescence after an operation on the biliary passages.

(vi.) *Surgery*

If the symptoms point definitely to the presence of gall-stones, an operation should be advised, unless on account of obesity or renal or cardiac complications the patient is a bad subject for operation. Under such conditions a trial should be given to the treatment just described, and an attempt should be made at the same time to improve the patient's health in case an operation has eventually to be performed. If the symptoms point to the presence of a form of gall-bladder disease, which may respond to medical treatment, an operation should only be advised if a thorough trial of the latter gives insufficient relief, if the patient is going abroad, where he would be unable to get skilled surgical help should an operation ever become necessary, or if there is evidence of the appendix being also diseased.

It is not for a physician to discuss details of surgical technique, but my experience fully confirms that of Moynihan, Rowlands, and those other surgeons who habitually perform cholecystectomy in preference to cholecystostomy. I should like to add that if a definite diagnosis of gall-bladder disease has been made, the gall-bladder should be removed, even if its external appearance is healthy, unless some other condition is found at the operation which adequately explains the symptoms. Such a gall-bladder may show macroscopic evidence of inflammation of its mucous membrane, or there may be a deposit of cholesterol crystals on its walls, but in some cases only microscopical and bacteriological examination reveals the presence of disease. I have several times seen cases in which an apparently normal gall-bladder was left at an explanatory operation, but in which the symptoms have persisted until its removal at a second operation.

It should be remembered that even in uncomplicated cases the operation is not entirely without danger. Three of my patients died within a week for no obvious reason. The danger is somewhat reduced by keeping the patient in bed

on a strict diet and giving biliary antiseptics for a week or two before it is carried out.

A patient who has had gall-stones removed by operation should be careful with his diet and continue with the magnesium sulphate, and perhaps from time to time take some salicylate and urotropine in order to prevent their re-formation in the gall-bladder if it has not been removed, or in the ducts after cholecystectomy, as the latter is followed by great dilation of the ducts owing to the resistance offered by Oddi's sphincter. This would be particularly important in the case of a woman becoming pregnant or in any patient developing typhoid fever.

Apart from true recurrences, the symptoms occasionally return within a few months of the operation. When this happens it is probable that all the stones were not removed ; when large numbers are present it is not at all easy to be certain that one or more may not have been left behind, particularly in the hepatic ducts. I have known this happen on several occasions. The patients were regarded as neurotic, but from my experience of these cases, if a thorough course of the medical treatment already described proved unsuccessful, I should certainly advise a patient to undergo a second operation, if the symptoms returned with their original severity within a few months of the first operation.

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Vide also J. F. Venables and F. A. Knott, F. A. Knott and Bowell, and W. E. Tanner in *Guy's Hospital Reports*, July, 1924.

ASTHMA*

I am extremely concerned at the return of your old asthmatic complaint. . . . It is very well worth your while to submit to any course of medicine or diet, to any restraint or confinement, in order to get rid of so troublesome and painful a distemper. . . . Notwithstanding this, which is plain sense and reason, I much fear that, as soon as ever you are got out of your present distress, you will take no preventive care, by a proper course of medicine and regimen ; but, like most people of your age, think it impossible that you ever should be ill again.—LORD CHESTERFIELD TO HIS SON. *Letter cclii., August 4th*, 1752.

SIR JOHN FLOYER, who published the first book in the English language on asthma in 1698, was himself an asthmatic. In spite of this he "panted on to ninety," as Dr. Johnson wrote in a letter to Bennet Langton on March 27th, 1784. Like Floyer, I also suffer from asthma, so I have the advantage, which few writers on the subject possess, of thirty years of observation on a single case.

The subject is one of special interest at present, as recent research in England, America and France has led to the explanation of many problems connected with asthma which had previously been obscure.

DEFINITION

Fifteen years ago I first defined asthma as the reaction of an over-excitable bronchial centre to blood-borne irritants and to peripheral and psychical stimuli. Recent investigations have shown that the chemical causes of asthma may, perhaps, act peripherally as well as centrally, so that a general over-excitability of the nervous control of the bronchi, including the nerve-endings in the bronchi as well as the bronchial centre in the medulla, probably exists. One part of the

* An address given before the Chichester and Worthing Division of the British Medical Association on February 16th, 1921. Reprinted, with additions and alterations, from the *Lancet*, 1921, i., 1113.

vagal nucleus controls the activity of the bronchi. Normally it is in a certain degree of tonic activity. When over-active, the broncho-motor fibres of the vagus cause the bronchioles to contract, and the broncho-secretory fibres cause the secretion of bronchial mucus to be excessive. This general over-activity is associated with congestion of the bronchial mucous membrane, analogous to what occurs in other organs when in a condition of functional activity. The engorged mucous membrane adds to the bronchial obstruction caused by the spasm of the circular muscle fibres, and consequently the mucus cannot be easily expelled. It is retained so long that it undergoes a process of coagulation, similar to the change which occurs in the formation of fibrin from fibrinogen, this being due to the activity of a ferment, mucinase, which is present in the bronchial mucous membrane. As the coagulated mucous casts of the bronchioles are slowly expelled along the spiral bronchi, they assume the characteristic features of the spiral mucous filaments, described by Curschmann of Leipzig in 1883. An exactly similar process occurs in the bowel in muco-membranous colic ; mucus is secreted in excess, and, owing to the associated spasm, it is retained abnormally long, so that there is time for the characteristic membrane to form as a result of the action of the mucinase of the intestinal mucous membrane.

The investigations of Huber and Koessler [1] on the morbid anatomy of six asthmatics, who had died in a paroxysm or from some other cause, confirm these views. They found definite hypertrophy of the muscular coat of the bronchi and bronchioles with hypertrophied mucous glands and hyperæmia of the mucous membrane.

Asthma and Anaphylaxis

Our knowledge of the chemical irritants of the bronchial centre and the bronchi is of recent origin. Much important work on the subject has been carried out by Freeman [2] of St. Mary's, Walker [3] of Harvard, Widal and his associates in Paris [3a], and Coke,[4] work which has thrown light on the hitherto inexplicable individual variations in the ætiology of asthma. The irritant is generally, but not

always, a protein to which the individual is abnormally sensitive. The nature of these toxic idiopathies, as they have been called by Freeman, is obscure, but they present many analogies to experimental anaphylaxis, and it appears probable that they are examples of congenital or acquired sensitiveness to certain proteins. In guinea-pigs bronchial spasm is one of the characteristic phenomena of anaphylaxis. Whether a man who is sensitive to a certain protein will be unaffected by exposure to a moderate dose of it, or whether he will develop asthma, an urticarial or eczematous rash, an acute gastro-intestinal attack, or even an attack of migraine or epilepsy, depends upon whether he is otherwise normal, or whether he has an irritable bronchial centre, an irritable skin, an irritable digestive tract, or the irritable foci in the brain, upon which migraine and epilepsy respectively depend.

Walker found that 52 per cent. of 400 cases of asthma, and Coke that the same percentage of 350 cases, gave positive reactions to the cutaneous tests, which Walker was the first to use on a large scale for recognising hypersensitiveness to proteins. My own experience, however, which dates from the autumn of 1919, has been very disappointing, as my colleagues and I have obtained a very small percentage of positive reactions with the dried proteins prepared in America by Walker's methods, and with the dissolved proteins prepared by three different firms in England. This has also been the experience of every other physician who has told me of the results of his tests with the cutaneous reactions in asthmatics, and Freeman has recently stated that in his experience cutaneous tests can only be usefully carried out in about 5 per cent. of asthmatics. It is difficult to understand this contradiction, but it is possibly due in part to the fact that Coke states that he does not usually compare his results with a control, in which the solvent is alone applied to the scratch : we have frequently found that apparently positive reactions have really been of no importance, as they have been no greater or even less than the reaction with the control.

Although cutaneous reactions are so rarely obtainable, I do not think that the frequency of a toxic idiopathy as a factor in asthma has been exaggerated by Walker or Coke. I am

inclined, indeed, to believe it occurs in over 50 per cent. of cases, but it is never the only factor, as one would gather from their writings, the irritable bronchial centre being the one thing common to every case of asthma.

The protein may gain access to the body by inhalation in the case of pollen, emanations from the hair and skin of animals, and dust containing vegetable matter; it is ingested in the case of a great variety of foods; and, lastly, the protein may be derived from bacteria, which have formed a focus of infection in the bronchi or nose and less frequently in the tonsils, teeth or intestines. The anaphylactic factor is most common in cases beginning in early life; thus 80 per cent. of those beginning in the first two years of life, 65 per cent. from two to fifteen, 50 per cent. from fifteen to thirty-five, 25 per cent. from thirty-five to fifty, and none beginning after fifty were of this type (Walker). The special liability in children is most marked with food proteins, and next with animal proteins; sensitiveness to bacterial proteins and, according to Coke, to feathers is equally distributed whatever is the age of onset up to forty.

Food

Goodale[5] in 1916 showed that extracts of wheat foods gave positive skin reactions in asthmatics who had attacks of asthma when they ate bread. Subsequently Walker, Coke and others investigated the question in connection with a great variety of foods. In sixty-eight out of Walker's 400 cases and eighty of Coke's 350 the patient was sensitive to food proteins. In more than half of these the protein was derived from cereals, in most instances wheat and oats, but occasionally rice or barley. Wodehouse has shown that different individuals are sensitive to different wheat proteins. In most cases the natural proteose of wheat is the most active and differs from the proteose produced artificially from the gluten of wheat. Heating, except to very high temperatures, does not affect the anaphylactogenic properties of wheat proteins.

Next to cereals come eggs among the foods which may cause asthma, and then potato, casein, and fish, especially

lobster, oyster, salmon, mackerel, cod and haddock. The proteins of beef, chicken and other forms of meat, cabbage, spinach, beans, tomatoes and other vegetables, and strawberries and other fruit are occasionally active, but generally in association with other food proteins. There are, indeed, few, if any, foods to which some individuals are not sensitive.

Only a small proportion of patients discover for themselves that the particular article of diet, to which they are shown to be sensitive by the skin reaction, gives them asthma, and in some cases eczema and urticaria as well. They have sometimes, however, a distaste for the food to which they are sensitive, especially in the case of eggs.

Pollen

Freeman has found as the result of the long series of investigations on hay fever he has carried out during the last ten years, that although a patient suffering from hay fever or hay asthma may be shown experimentally to be sensitive to a variety of pollens, grass pollen is the only one of much importance in England. It is always present in the air during the grass-flowering season from the middle of May to the beginning of August, except when recent rain has washed it away. It alone of English pollens is produced in sufficient amount, is easily disseminated by light wind, and is capable of producing a strong reaction. Daisy pollen, for example, only flies a few yards in contrast to grass pollen, which can fly many miles, and trees only pollinate for a few days instead of for several weeks. Coke, however, believes that the pollen of the pine and hornbeam is responsible for many cases of asthma and hay fever, in which attacks begin in the middle of April. In America conditions are very different, and Walker has shown the need for investigating the sensitiveness of each patient to a large variety of pollens. The majority of cases of hay asthma are associated with hay fever, which occurs, of course, still more frequently as an independent condition.

Animal Emanations

Hyde Salter[6] in 1859 was the first to recognise that asthma may be caused by emanations from animals. He

recorded cases of asthma brought on by the presence of cats, horses, guinea-pigs, rabbits, hares, cattle, sheep and deer. Horse, cat and dog asthma are the most common, the others being comparatively rare. Many patients are at once aware of the presence of a cat in the room from the development of asthmatic symptoms, which are sometimes associated with nasal catarrh and even urticaria. Trousseau described a case of a woman who had an attack of asthma directly her feather bed was shaken in her presence, and Salter had a patient who could not sleep upon a pillow stuffed with feathers. Sensitiveness to hen, goose and duck feathers is as common as that to horses and cats, and the experience of many asthmatics that they only get asthma in certain places or certain rooms in certain places is often due to the presence of feather beds, pillows or eiderdowns. In cases of horse-asthma this may be due to the horse-hair stuffing of mattresses or pillows. Goodale in 1916 found that an alcoholic extract of the hair of cats produced a skin reaction in patients suffering from cat asthma, the reaction apparently indicating that the individual was hypersensitive to the proteins contained in the extract. Wodehouse [7] found that the substance in the hair of cats and other animals which gave rise to the reaction was not the keratin, which forms the main constituent of hair, nor the proteins of their blood, but various other proteins which he isolated from the dandruff of the animal's skin. Freeman has shown that a slighter reaction is also produced by the flesh, serum, fæces, and nasal mucus in individuals who are sensitive to the dandruff, and that sensitiveness to a horse is associated with a lesser degree of sensitiveness to other members of the horse-tribe, such as the zebra, but to a very slight extent, as a rule, to the donkey.

Careful inquiry into the patient's history may lead to the discovery that attacks are caused by other animals, such as rats and mice, or by parrots, as in a case of Latham's. Lintz[8] recorded a case of mouse asthma cured by extermination of the numerous mice in the patient's house ; additional proof that the emanation of mice was the cause of her attacks was obtained by the occurrence of asthma, when a box containing a mouse was brought into her presence without her knowledge.

The quantity of specific protein required to cause an attack of asthma is, of course, exceedingly minute. The comparatively large quantity of foreign protein, introduced into the circulation when horse serum is used therapeutically, is sufficient to produce an attack in many asthmatics who are not otherwise liable to horse-asthma. Anti-diphtheritic or other serum ought, therefore, never to be given to an asthmatic without preliminary desensitisation. In the absence of this precaution death from anaphylactic shock has sometimes occurred. Out of twenty-two cases, collected from the literature by Lamson [9] in 1924, in which death was almost certainly the direct result of injecting serum into patients who had not been rendered sensitive by the previous administration of serum, ten, or 45·5 per cent., gave a history of asthma or hay fever.

Bacterial Toxins

It has long been recognised that asthma may be associated with infection of the bronchi, and less commonly of the nasal mucous membrane, teeth, tonsils and intestines. I have seen numerous cases in adults, which dated from a definite attack of pneumonia or bronchitis, and in children the onset may follow whooping cough or measles. The infection may give rise to the production of bacterial proteins to which the individual is abnormally sensitive, in which case the asthma is of anaphylactic origin, or the lesion produced may act as an irritant focus and give rise to reflex attacks of asthma. It was hoped that it might prove possible to distinguish between these two results of infection by testing the cutaneous reaction to the toxins of each organism isolated from the sputum or other infective material or to stock toxins obtained from various organisms; but a positive reaction is very rarely obtained even in the anaphylactic cases. Vaccination may lead to improvement in both classes, but this is likely to be more marked in the former. Our experience agrees with that of Eyre, who believes that the organism which most frequently has a specific relation with asthma is a bacillus of the Friedländer group; it is often found in the spirals coughed up during an attack. Possibly the products

of protein decomposition in the intestines may escape destruction or neutralisation in the liver when produced in excess by abnormal bacterial activity ; such substances as histamine are then likely to cause asthma in predisposed individuals.

Other Toxins

Asthmatics are occasionally sensitive to other proteins as well as those already referred to. Thus in one of Walker's patients an attack was always produced in the presence of a flax-seed poultice, and in another the attacks were caused by tobacco smoke, as in a case described by Floyer in 1726. The patients were found by the skin reaction to be sensitive to a protein of flax-seed and tobacco respectively. In other cases people become sensitised to a protein present in the dust produced in the performance of their trade. Cullen described the case of an apothecary's wife and Trousseau the cases of two apothecaries who were sensitive to ipecacuanha powder. A similar case, in which a chemist only began to have asthma after he had been able to manipulate the drug without trouble for years, has been recorded by Widal and his colleagues. He was only able to return to work in his shop after being desensitised by subcutaneous injections of ipecacuanha. Sensitisation of this kind undoubtedly explains many of the remarkable idiosyncrasies shown by asthmatics.

Some asthmatics show a similar hypersensitiveness to aspirin. According to Coke, this only occurs in individuals, who, having taken large doses without ill effect, discontinue taking the drug for some time and then begin again, when asthma results.

Reflex Causes

The most important peripheral stimuli which may affect an irritable bronchial centre and produce asthma reflexly arise in the nose, bronchi, stomach and bowel. There is a point on the mucous membrane of the nasal septum opposite the inferior turbinal, which appears to be specially rich in afferent nerve fibres which may influence the bronchial centre. Touching this with a probe may cause an asthmatic

patient to wheeze, and contact with a congested inferior turbinal may give rise to an attack of asthma. Congestion of the turbinal is most frequently caused by infection, but apart from this, contact may occur in individuals with a narrow nose or deflected septum, especially when the turbinal swells as a result of gravity on assuming the horizontal position, this being one reason why sleep is much less likely to be interrupted by an attack of asthma if the patient sits in a chair instead of going to bed.

I have already pointed out that the association of bronchial infection with asthma is due to either or both of two factors—sensitiveness to the toxin of one or more of the infecting organisms, and a reflex caused by the irritation of the bronchial mucous membrane by the infection.

Distension of the stomach with food may cause asthma, especially in the evening, quite independently of the nature of the food. Similarly distension of the rectum with fæces produces reflex asthma in patients with an irritable bronchial centre ; immediate relief follows defæcation. Distension of the stomach as a result of aerophagy and of the colon with gas produced by excessive fermentation are occasional reflex causes. Delagesière has described a case in which an attack of asthma could be induced by pressure upon a chronically inflamed appendix.

Hysterical and Emotional Asthma

In an individual with an irritable bronchial centre, but never apart from this, asthma may be caused by an idea or an emotion. Thus if a patient has had an attack under certain conditions, he will expect to have another if the conditions are repeated. When for any reason the conditions have altered, but without the patient's knowledge, he may yet be so convinced that an attack will occur that one is produced. Asthma caused by auto-suggestion in this way is truly hysterical, though in the absence of an abnormal bronchial centre no amount of suggestion could cause bronchial spasm and hypersecretion. Trousseau describes the case of a lady, who always had asthma in the presence of roses, and had an attack when she saw some artificial roses

which she thought were real. On my first visit to Salisbury in 1908 I had a very severe attack, which was repeated the following year, but I had no further attacks on numerous occasions in 1918 and 1919 when I revisited the city, as I had meanwhile become firmly convinced that my second attack was brought on solely by expectation, whatever may have been the cause of the first. Many patients who learn to rely on certain remedies are sure to become asthmatic if they discover that they have forgotten to take their powder, inhalation or injection with them. Some asthmatics have an attack with any little excitement, business worry or annoyance, but a severe fright is more likely to stop an attack than to cause one.

The Suprarenal Glands and other Internal Secretions in Asthma

The excitability of different nerve centres shows considerable individual variations. This is proved by the variability of the pupil reflexes, skin reflexes and deep reflexes. I believe that asthma is due to a condition, which is generally or perhaps always inborn and often inherited, in which the part of the vagus nucleus controlling the bronchi is more active than in the average man. In some cases it is very slightly so ; the individual may then never have an attack of asthma in his life or, as in several of my patients, only a few attacks under very special circumstances. In other cases it is very hypersensitive, and the asthma is more severe and constant.

The activity of the broncho-constrictor fibres of the vagus is normally balanced by the activity of the broncho-dilator fibres of the sympathetic nerve-supply to the bronchi. This is largely dependent on the constant secretion of adrenalin.

Physical and mental fatigue is a very common cause of asthma. Many asthmatics are always ill when they overwork, but recover at once on a holiday. Asthma is always worse in the evening than in the morning, and many patients can eat a large breakfast without any unpleasant symptoms resulting ; but the smallest dinner, consisting perhaps of no articles of diet which cannot be taken with impunity at

breakfast, is followed at once by wheeziness. And even if no food is eaten at night, asthma may develop, though less severely. If the patient sleeps in the afternoon he is often less asthmatic in the evening, or if he sleeps just before dinner he may be able to eat much more than would otherwise have been possible. As asthma is caused by over-activity of the bronchial muscles, it might have been expected that fatigue would result in their relaxation, and consequently in the relief of the asthma. But physical fatigue does not seem to influence involuntary muscles, and certainly it does not lead to the relaxation of the bronchial spasm. Crile has shown how extreme fatigue leads to exhaustion of the cells of the suprarenal glands. It is quite possible that the fatigue of each day is sufficient to cause a slighter degree of similar changes. The smallest diminution in the secretion of adrenalin would allow the over-activity of the vagal broncho-motor centre to have greater play, and asthma would result. These considerations appear to afford an adequate explanation of the production of asthma by fatigue.

A toxic idiopathy or hypersensitiveness to a certain protein, according to certain French authors, depends in part upon the fact that the protein has the effect of depressing the activity of the suprarenals. This effect may manifest itself in depression of one or all of their normal activities, the chief being in connection with the blood vessels, the alimentary canal and the bronchi. Acute and severe anaphylaxis produced by large doses of serum injected into an individual sensitised by a previous injection of serum affects all three. More commonly only those functions in which the adrenal control is specially important for the particular individual are affected. Thus an asthmatic will have an attack of asthma, and a man with a sensitive vaso-motor system will develop urticaria or other vaso-motor disturbances in the skin. A man who tends to have gastro-intestinal attacks owing to the abnormal irritability of his digestive tract will vomit and have diarrhœa and abdominal cramp owing to exaggerated peristalsis and relaxation of the cardiac, pyloric and ileo-cæcal sphincters ; this explains idiosyncrasies to shell-fish, eggs and other foods, which are manifested by acute digestive

disturbances. In some cases an attack of asthma will be accompanied by the vaso-motor changes, or alternate with them, or will be accompanied by the abdominal attack. In one of my patients an attack of diarrhœa is always preceded by a feeling of tightness in the chest, which may develop into definite asthma whilst the diarrhœa lasts, finally disappearing with it. Lastly, in some cases the idiopathy is manifested in an attack of hay fever.

It is a familiar fact that a severe fright may relieve an attack of asthma. A man in the middle of a severe attack was driving downhill when the brake refused to act ; he was in immediate danger of dashing into a wall which faced him at the bottom of the hill, but at the very last moment he succeeded in regaining control of the car ; when he drew up he found that he was breathing with perfect freedom. This was probably due to the stimulation of the sympathetic nerves and of adrenalin secretion caused by the fright. The stimulation of suprarenal secretion by asphyxia, which is perhaps the cause of second wind in runners, explains also the spontaneous relief or " second wind," which an asthmatic may experience if he continues his exercise after walking has brought on a moderate degree of dyspnœa.

Finally, the extraordinarily rapid effect of adrenalin injections in bringing relief to an acute attack of asthma in many individuals can best be explained by this theory. The dose required is less than that required to produce general symptoms, such as a rise of blood pressure and a rapid pulse, because adrenalin first acts upon any organ which is too much under vagal control at the moment. If any intestinal symptoms are present these are likely to be relieved at the same time.

In women asthma is occasionally most severe during menstruation or pregnancy, but more often pregnancy results in temporary freedom. It may also appear for the first time or become aggravated at puberty or at the menopause, and I have seen one case develop after an artificial menopause. In such cases disturbance in internal secretions probably results in increased sensibility of the bronchial centre in the medulla, and administration of dried thyroid gland, and occasionally ovarian extract, exerts a favourable influence.

Inheritance of Asthma

All writers have noted the frequency of a family history of the disease in asthmatics, a frequency which is much too great to be accidental. Thus in 39 per cent. of Salter's 217 cases there was a clear history of inheritance, and a family history was present in 46 per cent. of Coke's 350 cases. The important question arises: What is it that is inherited? I think that there is sufficient evidence to prove that it is sometimes an irritable bronchial centre, sometimes a toxic idiopathy, and sometimes both. When an individual whose father or mother is asthmatic develops asthma in the absence of any evidence of a toxic idiopathy, or has his first attack of asthma as a sequel of an infection or after he has acquired in adult life a toxic idiopathy, he must have inherited an irritable bronchial centre. If no toxic idiopathy is inherited or acquired in an individual who is a potential asthmatic as a result of having inherited a sensitive bronchial centre, he may transmit the tendency to his children without ever developing asthma himself. Thus the paternal grandfather and uncle and maternal grandmother and aunt but neither parent of one of my asthmatic patients suffered from asthma.

An individual may share with some of his relations an abnormal sensitiveness to a certain protein. Coke relates the case of a woman who was sensitive to milk, and had severe asthma throughout her two pregnancies. Both children were fed on cow's milk: the first had gastric symptoms for the first six weeks of its life, and the second died from asthma when six weeks old. Much more frequently a general tendency to toxic idiopathies is inherited. This may manifest itself in different members of the family as asthma, hay fever or digestive disturbances, depending upon the inheritance or acquisition of an irritable bronchial, nasal or digestive system respectively.

Treatment

Three things require consideration in discussing the treatment of asthma: (1) the irritable bronchial centre; (2) the chemical, reflex and psychical stimuli which may affect the centre; and (3) the attack itself.

1. *The Irritable Bronchial Centre*

Every asthmatic knows that the better his general health is the less liable he is to asthma. In other words, the irritability of his bronchial centre varies directly with the state of his health. For this reason he should avoid overwork and take adequate holidays. Nothing is likely to do him more good than a month in the Swiss mountains in the winter, where he will probably find that he can indulge in ski-ing, lugeing and skating with a vigour and freedom from respiratory distress he has not known for months. He should try to take some exercise in the open air every day, and a great deal more during the week-end. Slight dyspnœa is no contra-indication, as it often disappears on persevering with the exercise. Respiratory exercises carried out regularly every morning are useful in every case. Most important of all, he should try his best to avoid all possible causes of asthma, as the longer he remains free from it the less irritable the centre will become, until finally, after some years of inactivity, it may cease to respond at all to stimuli which in the past invariably gave rise to attacks. The best cure of asthma is not to have it. It is almost always possible to find some place where the patient does not get asthma, and no asthmatic child should be allowed to go to a school where he is more or less constantly asthmatic.

I have found that the irritability of the bronchial centre can be to some extent reduced by giving between 4 and 10 grains of caffeine citrate when the patient feels slightly asthmatic and fears that an attack will develop later, as, for instance, immediately after lunch and dinner or on going to bed.

2. *Chemical, Reflex, and Psychical Stimuli*

(*a*) *Toxic Idiopathies.*—When asthmatic attacks are caused by food proteins, all that is generally necessary is to exclude from the diet any food to which the patient is found to be sensitive. Long abstention probably results in desensitisation. If eczema or urticaria is present it often disappears at the same time. Desensitisation does not follow injection of the proteins or feeding in slowly increased quantities of

the food, but desensitisation to pollen can almost invariably be brought about by the subcutaneous injections of progressively larger doses of the pollen extract during the weeks preceding each hay-fever and hay-asthma season.

A patient can often free himself from asthma by simply avoiding any animal to which he has been shown to be sensitive, or in the case of feathers by avoiding feather pillows, mattresses and upholstery. In horse asthma it may also be necessary to avoid horse-hair mattresses and pillows. When an asthmatic is sensitive to horse dandruff in a dilution of 1 in 10,000 or more, desensitisation is necessary, as the dust of city streets contains sufficient of the protein to cause attacks. In such cases, and whenever avoidance of the animals is impossible or does not relieve the asthma, desensitisation should be undertaken with the specific proteins. Nothing but specific treatment is of any use; thus an individual who is sensitive to horse serum can be desensitised with the serum if it is necessary to give him some antitoxin, but this has no effect on his asthma, even if he happens to be also sensitive to horse-dandruff proteins.

Idiopathy to bacterial toxins can generally be overcome by vaccination in the ordinary way with organisms isolated from the patient's bronchial secretion or material obtained from other infective foci. In determining which organisms are most important intradermal reactions give some help, but even if no reaction is obtained an autogenous vaccine may prove very useful in curing chronic bronchitis or rhinitis which has acted as a reflex cause of asthma. The reaction is generally negligible if the injection is made at night and the patient takes 10 or 15 grains of aspirin at the same time. As, however, a severe reaction may occur in specially sensitive patients, the initial dose should be very small.

Lastly, the daily life of each patient should be investigated in every detail in an attempt to find some special toxic idiopathy, other than the familiar ones already described, which may be in part responsible for the asthma.

(*b*) *Reflex Causes.*—Bronchitis should be treated by autogenous vaccines and small doses of iodide taken for long periods. A careful examination of the nose should be made,

and any obvious source of irritation should be removed, but no operation should be performed unless it is very clearly indicated, as I have seen several cases aggravated by such operations, and one of the worst cases I ever saw was a man of fifty who had his first attack of asthma immediately after a hypertrophied turbinal had been removed. I have seen several cases in which mere cauterisation of a sensitive point on the septum in an apparently normal nose, as advocated by Francis, has produced marked improvement, though rarely, if ever, complete disappearance of all attacks. In many cases an autogenous vaccine prepared from the nasal secretion will do away with the need for local treatment by relieving the congestion which is secondary to infection, and in any case it is a useful preliminary measure in order to diminish the severe reaction which occasionally follows an operation. Apart from the Friedländer bacillus already referred to, the *B. septus* isolated from the nasal secretion, and pneumococci, *M. catarrhalis* and streptococci from the nasal and bronchial secretion are the organisms most frequently found in the rhinitis and bronchitis associated with asthma.

Asthma caused by a gastro-bronchial reflex can be avoided by eating hardly anything for dinner, which should be as early as possible, and nothing at all on going to bed, as the reflex only comes into play as the day advances and the patient becomes more tired. I have already pointed out how much benefit he may derive by sleeping or resting for half an hour before his evening meal. Regulation of the quantity of food is of more importance than its quality, except for any toxic idiopathies which may be present, but the food, especially in the evening, should be as digestible as possible ; no better guide to a suitable diet could be found than that given in Dr. James Adam's little book on " Asthma."

The intestino-bronchial reflex comes almost entirely from the pelvic colon and rectum, and regular habits and exercises to overcome dyschezia are generally sufficient to keep it in check. Aperients should be avoided as far as possible, but in some cases a weekly colonic douche is needed to prevent a fæcal accumulation from forming.

(*c*) *Psychical Causes.*—Psychotherapy is only useful in so far as explanation of the mechanism involved may lead an asthmatic to take a less hopeless view as to his chance of complete recovery. So long as he feels convinced that certain circumstances will inevitably cause an attack they will certainly do so. He should be persuaded to be optimistic about his condition, and hope and even expect that what has hitherto caused an attack will not necessarily do so in the future. In his "Practical Inquiry into Disordered Respiration," published in 1807, Robert Bree gives a most interesting account of how he cured his own asthma by psychotherapy on realising that he was "under the dominion of a disease established by habit."

3. *The Attack*

An attack of asthma can most readily be cut short by the subcutaneous injection of adrenalin, as first recommended in 1910 by Brian Melland.[10] The most efficacious dose is very much smaller than that generally given. In many cases a single minim of 1 in 1000 adrenalin chloride is enough, more than two minims being rarely required. But the injection should be given at the beginning of an attack, directly a patient wakes in the night, for instance, and not half an hour or an hour later, when it has reached its full development. The relief is so immediate that the patient often falls asleep within five minutes of waking in an attack. Such small doses give rise to no unpleasant sensations, such as frequently follow the injection of three or more minims, and the blood pressure does not rise at all. Consequently the treatment can be continued for long periods without any fear of ultimately causing arterio-sclerosis. It is the only form of injection which a patient should be allowed to use on himself ; if he has to depend on some one else giving the injection he will rarely receive it at the right moment.

For slight attacks and for the feeling of slight dyspnœa, which may persist throughout the day when severe attacks occur at night, a weak solution of atropine and cocaine may be applied to the nasal mucous membrane with an atomiser.

No patient should be given any of the numerous powders,

which are used by inhaling the fumes produced when they are burnt, as they invariably aggravate any bronchitis which may be present and may actually give rise to bronchitis in patients who have hitherto been free from it.

I have seen several patients who have only recovered from a prolonged attack of asthma, persisting for weeks or months, after they had been persuaded to get away from home, though sometimes a succession of places must be tried before one is discovered in which relief occurs.

Lastly, I wish to emphasise the fact that these remarks on the treatment of the attack should not make us forget that our chief aim must be to devise such a course of action for the patient that he will eventually have no attacks to treat.

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THE HYSTERICAL ELEMENT IN ORGANIC DISEASE AND INJURY OF THE CENTRAL NERVOUS SYSTEM

THE following paper, written with Major J. L. M. Symns in 1918, when I was in command of the Seale Hayne Military Hospital for functional nervous disorders, is reprinted from the "Seale Hayne Neurological Studies" (Vol. I., p. 113) without alteration. The experience of the five years, which have elapsed since it was published, has abundantly confirmed the views here expressed. I have seen numerous cases of organic nervous diseases, in which active psychotherapy has resulted in very rapid and very considerable improvement owing to the removal of the hysterical element which was present. The conclusions we drew apply equally well to organic disease of all kinds, and the recognition of a functional element in such conditions, for example, as rheumatoid arthritis not infrequently results in a bedridden patient being restored to a state of more or less activity. I have, therefore, added a short note on the application of these principles to cases of rheumatoid arthritis, in which active infection is no longer present.

It has long been recognised that hysterical symptoms may be grafted upon symptoms caused by organic disease. Our experience with soldiers during the past four years has led us to believe that this association is much more common than has generally been supposed. We would even go so far as to say that there are few symptoms caused by organic disease, which are not liable to be aggravated and perpetuated by suggestion, so that it becomes necessary in almost every case of impaired function to look for an hysterical element which can be removed by psychotherapy. We have often found that hysteria may account for a large proportion of the incapacity in a patient presenting such definite signs of

organic disease that it might very easily have been presumed that the entire condition was organic. We are consequently now in the habit of testing every case, in which it is at all conceivable that an hysterical element is present, by the only means which can yield the necessary information, namely, by observing the effect of psychotherapy. No other means are available, as on the one hand organic physical signs do not exclude the possibility of hysterical symptoms being present, and on the other hand our observations, as well as those of other investigators, have proved that the supposed stigmata of hysteria are not present until they have developed as a result of the unconscious suggestion of the observer, who may produce them in suggestible individuals suffering from organic disease just as easily as in those suffering from hysterical disorders.

Hysterical Exaggeration of Progressive Nervous Disorders

Disseminated Sclerosis

It is not an uncommon occurrence to find an extensor plantar reflex, ankle-clonus, exaggerated knee-jerk, and absent abdominal reflex in a patient, who seeks advice for some early symptom of disseminated sclerosis, such as impaired vision or unsteadiness of the hands, in spite of the fact that no symptom of paraplegia is yet present. These physical signs are accepted as absolute proof that the pyramidal tracts have become involved in the disease, and experience shows that sooner or later the legs will become weak and that severe spastic paraplegia will ultimately develop. The conclusion to be drawn from these facts is that *signs of organic disease of the pyramidal tract may precede the onset of symptoms.*

Many patients, especially women, suffering from disseminated sclerosis have a peculiar state of mind, often erroneously called hysterical, one feature of which is an abnormal degree of suggestibility. It is not surprising therefore that hysterical symptoms—symptoms produced by suggestion and curable by psychotherapy—may develop.

When the lesion to the pyramidal tracts in such a suggestible individual becomes sufficiently marked to cause some stiffness and weakness in the legs, the stiffness and weakness may give rise to the idea of paralysis, and hysterical paraplegia may rapidly appear. If the patient is seen at this stage it may be impossible to make an accurate diagnosis, for we are face to face with a case of hysterical paraplegia with all the physical signs of organic paraplegia, although only a very small proportion of the incapacity is a result of the organic lesion. Such a patient may be given a rest cure, or inunctions of mercury, injections of salvarsan, or one of the numerous other drugs which have from time to time been advocated for disseminated sclerosis by individual physicians, only to be rejected by others, who have employed them with less faith and, therefore, with less effect. The treatment, whatever its precise nature, is really a form of psychotherapy, and the hysterical paraplegia disappears, leaving behind the physical signs of organic paraplegia and the slight degree of weakness and stiffness which were present before the onset of the hysterical symptoms. This we believe to be the chief explanation of many, at least, of the periods of more or less spontaneous improvement, which form such a characteristic feature of disseminated sclerosis. It applies equally to the improvement of other symptoms, such as amaurosis ; the slight impairment of vision, which results from the earliest changes in the optic nerves, sometimes even before any change can be recognised in the discs, suggests a graver loss of vision to suggestible individuals, so that almost complete blindness may occur long before definite optic atrophy is present. The vision may greatly improve again either spontaneously or as the apparent result of some form of treatment, but really as a result of suggestion.

It is very common in disseminated sclerosis to obtain a history of temporary weakness of the legs or temporary blindness some months or even years before the true nature of the disease is finally recognised. The temporary symptoms have generally been regarded as hysterical, but the physician who sees the patient now is inclined to say that the old diagnosis was both incorrect and unjust, as the symptoms must really have been organic in origin and a part of the

disease from which the patient is obviously suffering at the present time. The truth is that the early symptoms were probably to a great extent hysterical, having been suggested by the very slight incapacity caused by the organic disease. The hysterical element disappeared, leaving the slight organic element behind. The early diagnosis of hysteria, though only partially correct and in one sense unjust, was distinctly to the patient's advantage if it led the physician to employ psychotherapy, which would cause the rapid disappearance of the hysterical symptoms.

No satisfactory explanation has ever been offered, which would adequately explain the remittent character of the symptoms of disseminated sclerosis, if they were entirely organic in origin. It is certain that a period of rapid deterioration corresponds with the rapid development of new areas of disease in the central nervous system, and that such a period may be followed by another of much slower progress during which changes may occur in the rapidly formed areas of disease, which result in their contraction, so that nervous tissue which was originally thrown out of action by compression recovers its functions. This probably explains the temporary paresis of one or more of the external muscles of the eye and some of the slighter variations in the degree of paralysis of the limbs and of the impairment of vision, but it is hardly conceivable that sufficient change should occur in the central nervous system to account for the conversion of complete paraplegia into very slight stiffness and weakness of the legs or of total blindness into slightly indistinct or even normal vision. Our explanation also makes it easy to understand why spontaneous improvement occurs more often in females than in males and in the neurotic than in less suggestible individuals.

The above ideas are represented diagrammatically in Diagram I. The vertical represents the degree of incapacity, the total height being 100 per cent. The horizontal represents time. The line AG^1 represents the gradual development of paraplegia in a case of disseminated sclerosis. When the time B is reached the degree of incapacity BB^1 is still so slight that it remains unnoticed, but it is sufficient to produce physical signs. When the time C is reached a certain

amount of stiffness and weakness is noticed, this being represented as CC^1. This may continue to develop with the advancing disease until at the point D the incapacity is DD^1. It is possible, however, that the slight impairment of function represented by CC^1 suggests a further degree of incapacity, with the result that the patient becomes completely paraplegic. The total incapacity DD^2 is then made up of an organic element DD^1 together with an hysterical element

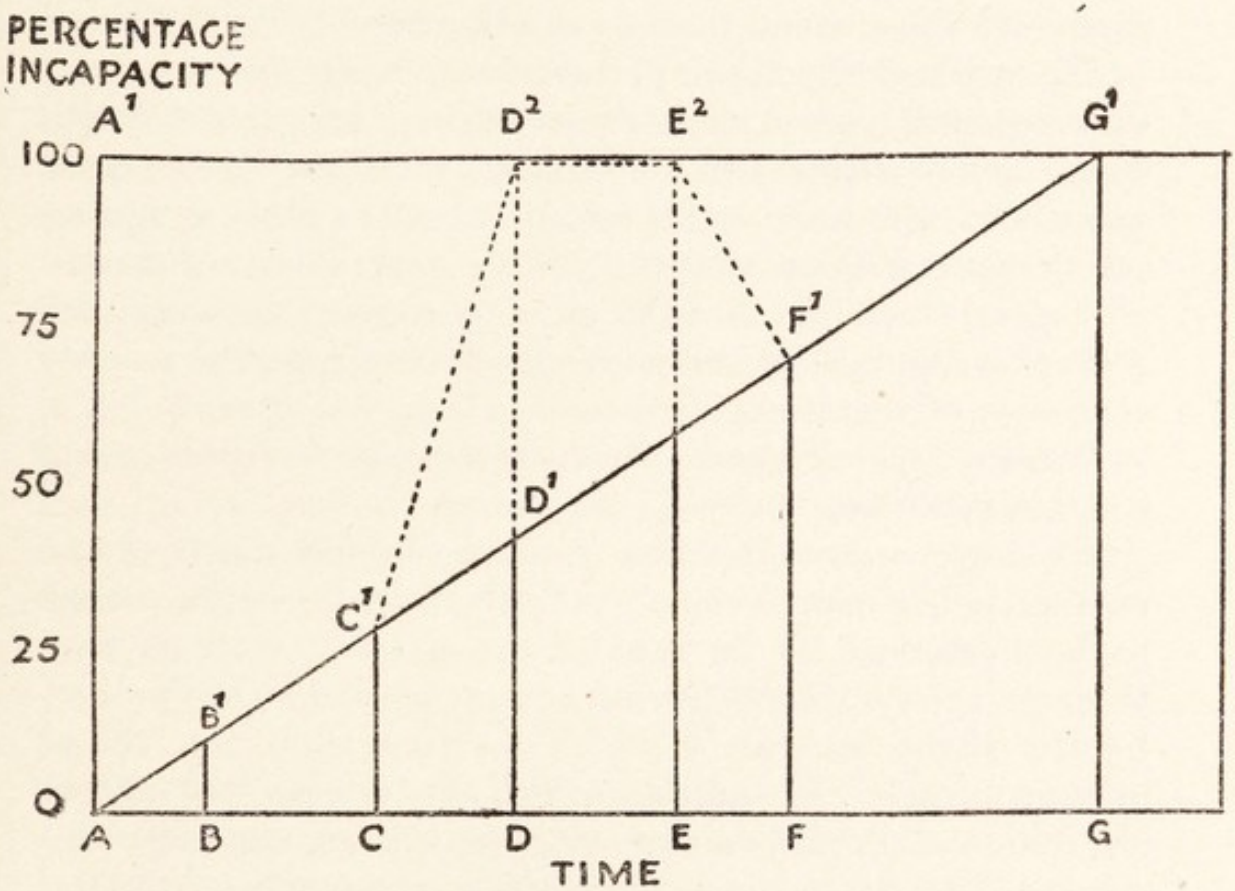


Diagram I.—Combined organic and hysterical incapacity in disseminated sclerosis.

D^1D^2. This condition of mixed organic and hysterical paraplegia may last until the point of time E, when, as a result of some counter-suggestion, the patient begins to improve and the hysterical symptoms eventually disappear, leaving him with the incapacity FF^1, which is somewhat greater than at the onset of the hysterical symptoms (CC^1), but very much less than the total incapacity. If the hysterical nature of the symptoms was at once recognised, the total incapacity DD^2 could have been reduced at a single sitting to DD^1.

Tabes

We have shown how disease of the lateral columns produces physical signs before any symptoms have developed, and how the earliest symptoms may be exaggerated as a result of the development of hysterical paralysis on the top of the organic incapacity. Exactly analogous phenomena may occur in disease of the posterior columns. It is very common to find lost ankle-jerks with feeble or lost knee-jerks and some impairment in the vibration-sense over the bones of the legs and sacrum in patients, who have sought advice on account of gastric or other crises, impaired vision, impotence or disturbances in micturition, which are due to early tabes, but who have so far had no ataxy or other symptom which would indicate that the posterior columns are diseased. It is clear, therefore, that the physical signs of disease of the posterior columns as well as of the lateral columns precede the onset of symptoms.

Physical signs of organic disease of the central nervous system are thus qualitative and not quantitative.

We have seen numerous cases, in which much of the incapacity in a man obviously suffering from tabes was proved to be hysterical by its rapid disappearance with psychotherapy, the symptoms having been suggested to the patient by the slight incapacity which resulted from the actual organic disease. In addition to this auto-suggestion, hetero-suggestion often plays a part, symptoms being unconsciously suggested by the medical officer in the course of his examination. It is, for example, very easy to suggest Romberg's sign, and we have now seen a number of cases in which a well-marked Romberg's sign was obviously hysterical. In some cases it was the only hysterical symptom present ; in others, like one reported by Lieut. S. H. Wilkinson, it was accompanied by hysterical paralysis, which had resulted from auto-suggestion.

The improvement in the gait of tabetic patients, which results from the methods devised by Frenkel, does not in our opinion always act solely by educating the patient to use his eyes to help his deficient muscle-sense and to make the most of such muscle-sense as he still has. The results

obtained are sometimes too rapid and too dramatic, and can scarcely be explained except as a result of suggestion, the inco-ordination being largely hysterical and the nature of the incapacity having been suggested by the slight degree of unsteadiness actually caused by the organic disease. One of us (A. F. H.) in 1913 saw a man with all the physical signs of tabes, who had been unable to walk for six years. He was brought in a chair to the Guy's Neurological Department at 9.30 a.m. After he had been examined, he was told that he would probably learn to walk again if he carried out certain exercises, which were shown to him. He continued to practise these, and by twelve o'clock he had improved to such an extent that he could walk the length of the room, and in a week he was walking about normally. This was regarded at the time as a triumph of re-education of the deficient muscle-sense, but the re-education must really have been re-education of the patient's mind—in other words, psychotherapy—as if the total inability to walk had been due entirely to organic change in the cord, it is inconceivable that the little muscle-sense still present could have been re-educated to such an extent in a single morning after lying dormant for six years.

Friedreich's Ataxy

We have not had the opportunity of investigating many cases of organic nervous disease during the war, as except for those caused by syphilis they are rare among soldiers. The following case, under the care of Captain W. R. Reynell, was a typical example of Friedreich's ataxy, and until recently we would have accepted all the symptoms as the result of the organic changes in the central nervous system without further discussion. We would have said that Friedreich's ataxy is one of those nervous diseases in which very little can be done, and that the patient could hope for no improvement, but would slowly and steadily get worse. We have little doubt that this opinion would have been shared by the vast majority of physicians. So convinced have we become of the enormous importance of looking for an hysterical element even in the most unlikely places that

Captain Reynell proceeded to treat the patient as if his incapacity was hysterical, although there was nothing in his mental or physical condition which gave any grounds for such an idea. The treatment was fully justified by the result, and instead of sending the patient home as a helpless cripple he has now been discharged from the Army in a condition, which will not prevent him from earning a living in some light occupation for a time, although, of course, the ultimate prognosis remains as hopeless as ever.

Hysterical ataxic paraplegia, associated with Friedreich's ataxy.—Pte. B., aged twenty-five, was a glass-fitter in civil life. Two years ago he gradually became unable to walk in the dark, but it was not until he was sent to France with a labour battalion in October, 1917, six months after joining the Army, that he had any difficulty in the daylight. He was stopped several times by the military police on suspicion of being drunk, as his gait was unsteady. After an attack of influenza in June, 1918, the ataxy was much exaggerated, and from this date he only went out in a bath-chair. The difficulty in walking then steadily increased up to the time of his admission to Seale Hayne Hospital on October 12th, 1918. Dr. W. H. Haupt informs us that the patient's father was a very heavy drinker and had infected his mother with syphilis, which had led to the perforation of her palate. His brother, aged twenty-seven, is a complete cripple and never leaves his home. Like the patient he was a glass-fitter, but eight years ago his hands became unsteady and he broke so much glass that he had to give up his work. Dr. Haupt reports that he has a humped back and lateral curvature of the spine, pes cavus, absent knee-jerks, extensor plantar reflexes, marked Romberg's sign, nystagmus, a peculiar hesitating, almost stuttering, speech, and intention tremor. He is very emotional, and laughs and cries at the least provocation. He is also very deaf. Dr. Haupt regards him as a typical case of Friedreich's ataxy.

Our patient's speech was slightly affected, and there were sudden changes of pitch, as in a voice that is breaking. On admission he could scarcely do anything owing to extreme inco-ordination, and he fell frequently when he tried to walk without assistance. He was very unsteady on standing,

and he fell immediately he closed his eyes. There was a slight but definite kyphosis, and the plantar arches were abnormally high on both sides. The knee- and ankle-jerks were completely absent on both sides. The plantar reflexes were difficult to obtain, but appeared to be extensor. When asked to pour water from a jug into a tumbler, definite incoordination in the arm movements was well seen, and much water was spilt. The Wassermann reaction was negative in the blood and cerebro-spinal fluid. A diagnosis of Friedreich's ataxy was made.

Treatment by persuasion and re-education was given, as it was suspected that the ataxic gait might be partly functional. He learnt to walk fairly well on the first day of treatment, and further improvement followed exercises practised for half an hour three times a day. A week after treatment was begun the gait was almost normal, and unsteadiness could only be detected when the patient changed his direction suddenly. The hands soon became so steady that he developed into a competent potter.

Hysterical Perpetuation of Regressive Nervous Disorders

Just as the physical signs of an organic lesion of the pyramidal tract may precede the development of paralysis due to the lesion and be associated with hysterical paralysis, which persists after the cure of the latter by psychotherapy, so may the physical signs persist after recovery from organic paralysis and be associated with hysterical paralysis, which develops as the organic symptoms disappear.

Injuries and acute diseases of the brain and spinal cord may result in changes which are to a great extent evanescent. The vaso-motor disturbances and microscopical changes in the nerve cells, such as chromatolysis and eccentricity of the nuclei, disappear entirely; inflammatory exudates and œdema also disappear entirely or leave only a trivial amount of permanent damage, and even hæmorrhages are absorbed to a great extent, the initial changes being thus very much greater than the permanent results of the lesion. The initial changes may, however, be sufficient to block the trans-

mission of nerve impulses and consequently to cause complete loss of function in the parts which receive their innervation from the affected portion of the nervous system. But the permanent results of the lesion may be so slight that no loss of function persists, although, corresponding with the converse conditions in disseminated sclerosis, the damage may be sufficient to give rise to the permanent presence of organic physical signs. This is seen, for example, in the hemiplegia and paraplegia following syphilitic endarteritis, which have been treated early and thoroughly, and in the spontaneous recovery in some cases of poliomyelitis.

In the majority of cases the gradual improvement in the actual lesion is accompanied by a corresponding functional improvement. Occasionally, however, especially among suggestible individuals, such as soldiers who are mentally and physically exhausted as a result of the stress and strain of active service, the patient may not realise that the lost functions are returning. The initial incapacity gives rise to the idea of permanent incapacity by auto-suggestion, often aided by the unconscious hetero-suggestion of the physician, and whilst a less suggestible man might recover the use of his paralysed limbs in a few days, the paralysis is perpetuated in the suggestible man by the development of an hysterical element, which has been produced by suggestion and which can be removed by psychotherapy. In such a case the paralysis remains complete, and although at first it is entirely organic in origin, the proportion of the organic to the hysterical element in its make-up becomes steadily less, and in some cases a stage is reached in which the incapacity is almost entirely hysterical and independent of structural change, although the latter may still be sufficient to give rise to physical signs. *A condition may thus occur, which is primarily organic, but is ultimately hysterical. Everything of organic origin may disappear, or the residual lesion may be sufficient to produce physical signs of organic disease without any loss of function or both physical signs of organic disease and some loss of function.*

These ideas can be represented diagrammatically in the same way as in the case of disseminated sclerosis. In Diagrams II., III. and IV., AA^1 represents the total in-

capacity resulting from the original wound or disease. This steadily improves, and when the time C is reached recovery may be complete (Diagram II.) or partial (Diagrams III. and IV.). The partial recovery may leave no obvious physical incapacity, but it may, as in Diagram III., leave sufficient residue to result in definite physical signs of organic disease represented by CC^1. In severer cases there may be some permanent incapacity, as represented by CC^1 in Diagram IV.

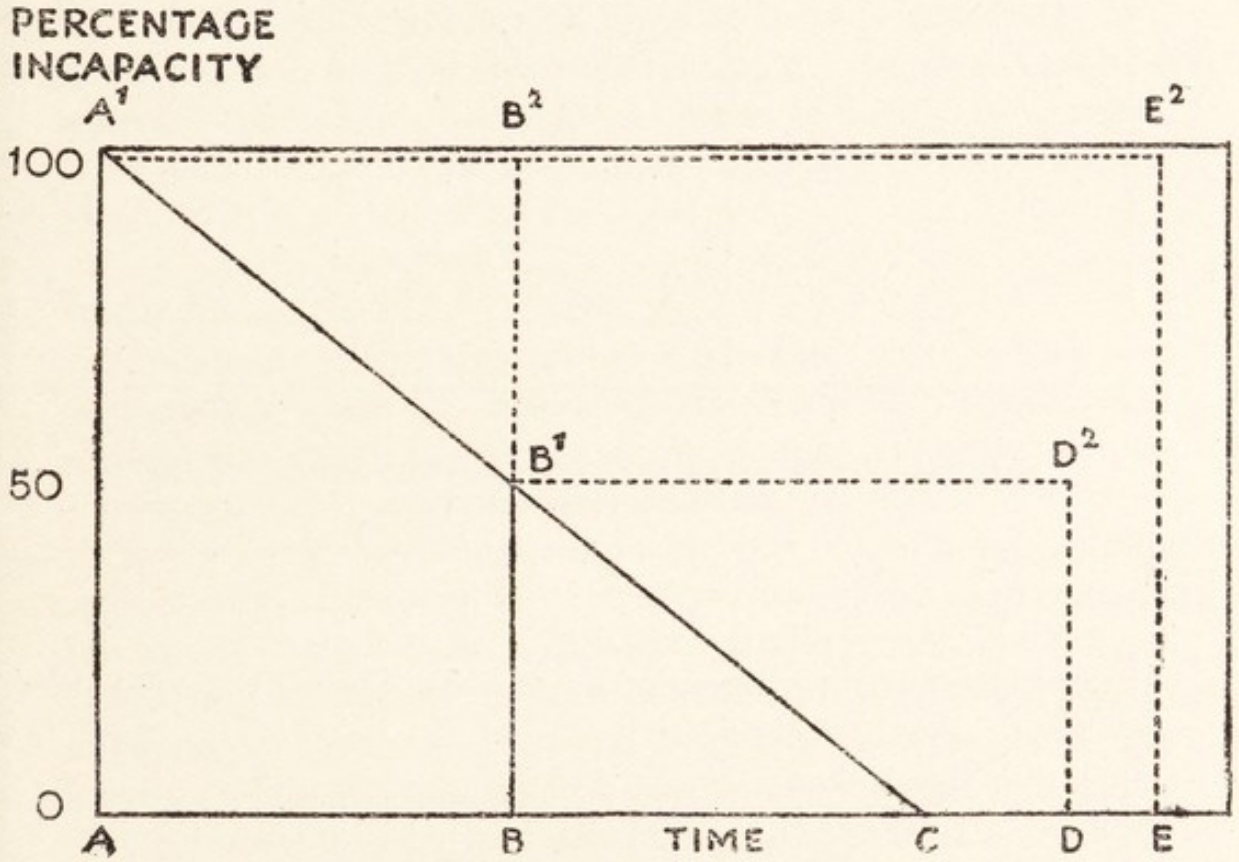


DIAGRAM II.—Hysterical paralysis associated with organic paralysis, from which complete recovery occurs.

In each case the steady improvement of the organic condition may be masked by a simultaneous development of hysterical symptoms, so that at the moment B the incapacity may be partly organic (BB^1) and partly hysterical (B^1B^2). If psychotherapy is employed at this moment the improvement represented by B^1B^2 takes place, the organic residue BB^1 remaining. If re-education is now constantly employed, steady improvement will occur. During the period BC the symptoms and finally the physical signs disappear (Diagram II.), the symptoms disappear but physical signs persist (Diagram III.), or some symptoms as well as the

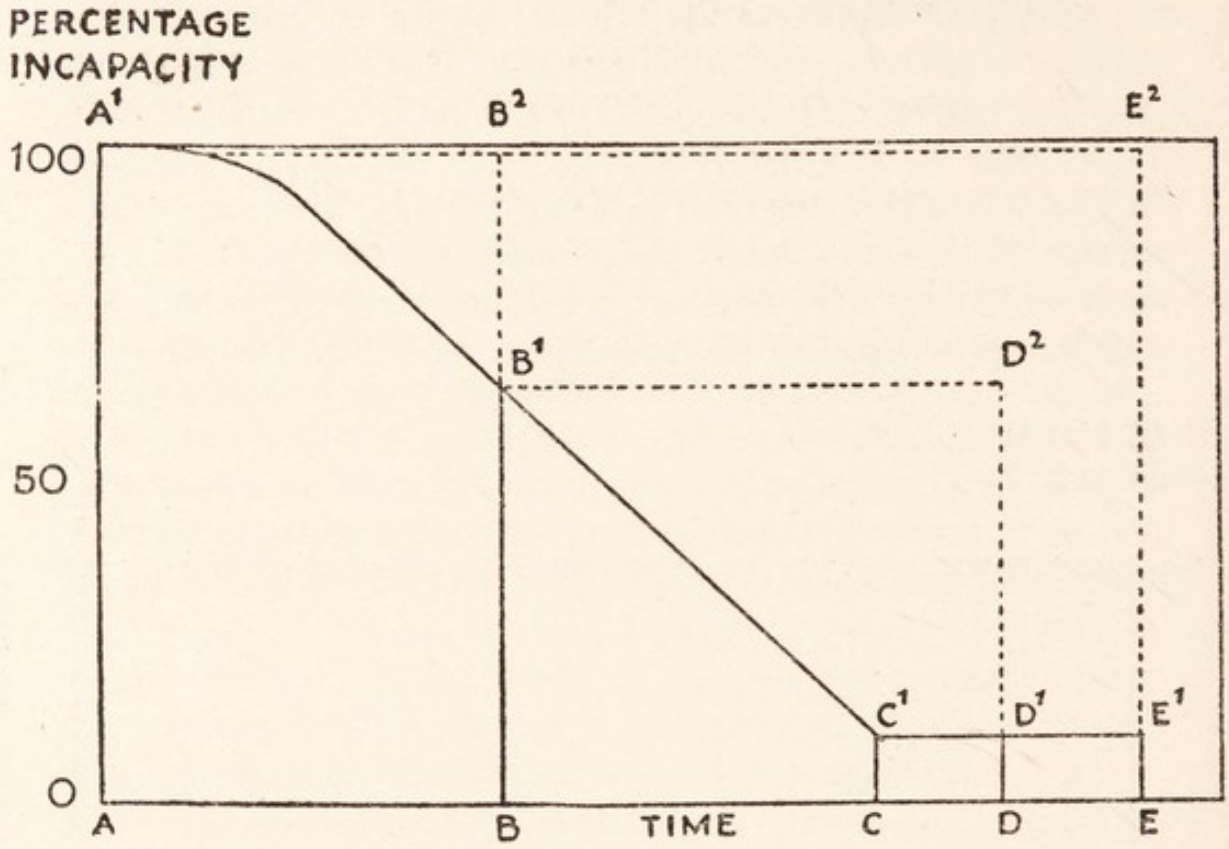


DIAGRAM III.—Hysterical paralysis associated with organic paralysis, which recovers incompletely.

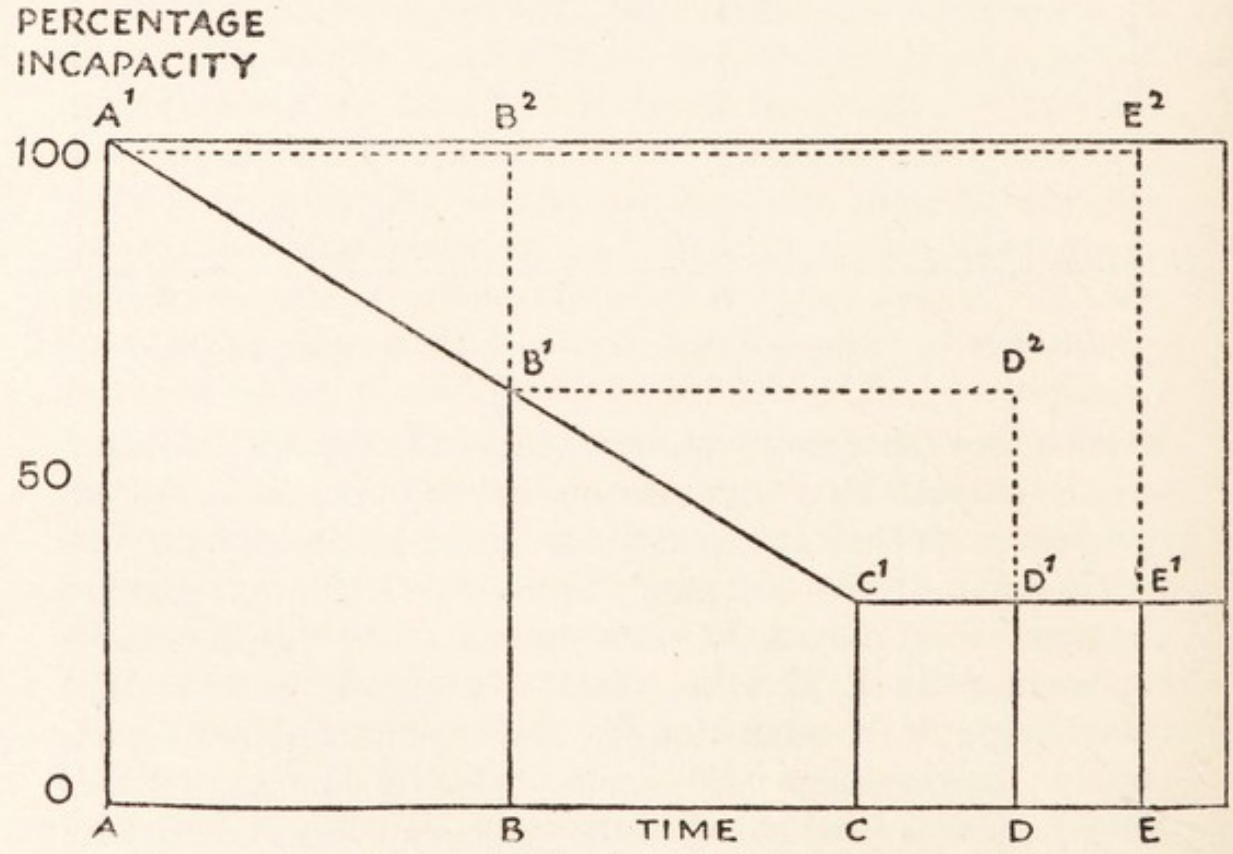


DIAGRAM IV.—Hysterical paralysis associated with organic paralysis, which recovers, but leaves organic physical signs.

physical signs persist (Diagram IV.). If, however, no re-education is given, the symptoms may again be perpetuated by the development of an hysterical element. In that case, at the period represented by D, when no further improvement can take place, the incapacity DD^2 in Diagram II. and D^1D^2 in Diagrams III. and IV. is hysterical, and can be rapidly removed by psychotherapy. If the partly hysterical nature of the condition is not recognised at all until later, when no further improvement in the organic residue is possible, as, for example, at the moment marked E, psychotherapy will result in complete recovery (Diagram II.), almost complete recovery although the physical signs will still be present (EE^1, Diagram III.), or incomplete recovery (EE^1, Diagram IV.).

The Symptoms and Signs of Organic Disease

The numerous symptoms and physical signs which are supposed to help in the diagnosis between organic and hysterical paralysis fall into three groups. The first group consists of the phenomena which afford visible and conclusive evidence of structural changes in the nervous system, such as optic atrophy and neuritis and abnormal cells in the cerebro-spinal fluid. Equally conclusive is the second group of physical signs—those which are entirely beyond voluntary control, such as the Argyll-Robertson pupil, the reaction of degeneration, and loss of knee- and ankle-jerks. The third group of signs consists in those which could be imitated more or less accurately by any one who had studied them, but which would not be likely to occur as a result of auto-suggestion or be simulated by an ordinary malingerer, as the individual would be unaware that such signs accompany the disease he believed or pretended that he had. The signs belonging to the last group lose much of their value in distinguishing organic from hysterical paralysis when the latter is a sequel of organic paralysis, as the characteristics of the hysterical paralysis are suggested by those of the organic paralysis. An ordinary individual, who develops hysterical hemiplegia, shows no paralysis of his platysma muscle (Babinski's platysma sign), because he is likely to be unfamiliar with the action of the platysma, and being

unaware of its existence continues to use it when the rest of the same side of the face is paralysed, but if the hysterical paralysis is a sequel of an organic paralysis, the characteristics of the latter, including paralysis of the platysma, are perpetuated (Fig. 54 (*a*), p. 250). Thus in hysterical hemiplegia and paraplegia, following organic hemiplegia and paraplegia respectively, most of the third group of physical signs, which are regarded as characteristic of organic disease, may persist. Being caused by suggestion, they are just as much a part of the hysterical condition as the paralysis itself, and like the latter they are completely removable by psychotherapy. Thus we have seen cases of organic paralysis followed by hysterical paralysis, in which the platysma, pronation and fan signs of Babinski, combined flexion of the thigh and pelvis (" Babinski's second sign "), ankle-clonus quite indistinguishable from that present in organic disease, Raimiste's and various other signs were present ; but the condition was none the less hysterical, as the paralysis together with these physical signs disappeared rapidly and completely under psychotherapy. The diagnosis of such cases may thus be extremely difficult, as *hysterical paralysis following organic paralysis may not only be associated with permanent physical signs of organic disease, such as the extensor plantar reflex, caused by the residual organic disease, but also with the accessory signs, which are supposed to indicate the presence of organic disease, but which may themselves be really hysterical, being produced by suggestion and removable by psychotherapy.*

Treatment

There is a widespread tendency to adopt a waiting attitude in the treatment of acute organic nervous diseases, which is sound if confined to the early stages, but becomes dangerous if it is continued for a longer period. The natural tendency of most acute diseases is towards recovery, but the functional capacity does not always tend to return *pari passu* with structural recovery, unless the physician makes use of psychotherapy in combination with re-education from the earliest possible moment. In organic hemiplegia following a head wound or an acute vascular lesion there is no reason

why passive movements should not be commenced a few days after the onset, and as soon as the patient's general condition permits he should be encouraged to attempt voluntary movements. When the hemiplegia is associated with aphasia, re-education of speech should be begun at the same time. Treatment of this kind, in which psychotherapy is preventative rather than curative, is extremely important and leads to a maximum of recovery in a minimum of time. The same is true in such conditions as acute poliomyelitis, in which there is often too great a tendency to rely upon mechanical means, such as massage and electricity, and to forget the psychical side.

The following cases are some of the more striking examples we have seen in soldiers of severe symptoms, which have followed organic injury or disease, being perpetuated as a result of the grafting of an hysterical element on the original organic incapacity. The first case is perhaps the most remarkable of all, as for two years the patient had been regarded by everybody who had seen him as suffering from incurable organic hemiplegia, but recovery with psychotherapy was almost complete.

Combined hysterical and organic hemiplegia of two years' duration following nephritis ; almost complete recovery with psychotherapy.—Pte. R., aged twenty-nine, reported sick on September 29th, 1916, when he noticed some œdema of his legs. Nephritis was diagnosed, and he was sent to a hospital. On October 1st he had several fits and was unconscious for a few hours. When he recovered consciousness he was suffering from severe right hemiplegia, involving the face, arm and leg, and he was also aphasic. He was transferred to England, and in July, 1917, as his urine was now free from albumen, he was transferred to a neurological hospital in London. His physician reports that on admission "there was complete right hemiplegia with late rigidity and aphasia, and also facial paralysis on the same side. Wassermann reaction negative. Complete anæsthesia on the right side, tactile and thermal. No sphincter trouble. All deep tendon reflexes much exaggerated, right greater than left, well-marked ankle-clonus right side ; plantar reflex indefinite :

tongue deviation to paralysed side. Later he developed spastic contracture of the right limbs." After a time he regained his power of speech with re-education. In May, 1918, a tenotomy was performed to overcome the flexion of his right knee. As this was not successful his leg was subsequently twice moved forcibly under anæsthesia. In August, 1918, he was transferred to another neurological hospital in London, as an attempt to gain him admission to the Star and Garter Hospital had failed.

There was still no improvement when he came under our care at Seale Hayne Hospital in October, 1918. The right leg and arm were totally paralysed and absolutely rigid, the elbow, wrist, and fingers being flexed, and the knee semi-flexed (Fig. 54 (*a*)). The right side of the face, including the platysma, was paralysed, but, as in ordinary organic hemiplegia, the upper part was only slightly involved (Fig. 54 (*d*)). The deep reflexes of the arm and leg were much exaggerated on the right side and slightly exaggerated on the left, and well-sustained, regular ankle-clonus was present. The abdominal reflex was absent on both sides. The plantar reflex could not be obtained owing to the extreme degree of spasticity.

The spastic paralysis was treated by persuasion and re-education, and in two and a half hours the patient was able to extend his leg and arm and move them slowly in all directions (Fig. 54 (*b*)). At the end of another hour he was able to stand by himself, and next day he was able to walk. This result was obtained without causing any pain to the patient, in spite of the extreme rigidity. The exaggerated deep reflexes and ankle-clonus remained unaltered, and an extensor plantar reflex was now obtained on the right side.

An attempt was next made to overcome the facial paralysis, and in ten minutes there was marked improvement. After forty-five minutes' treatment the facial paralysis had disappeared and the platysma was contracting normally (Fig. 54 (*e*)).

The patient is now (December, 1918) able to use his right hand for all ordinary purposes, *e.g.*, writing and needlework, and he walks with only a slight limp (Fig. 54 (*c*)).

Hysterical hemiplegia with persisting signs of organic disease

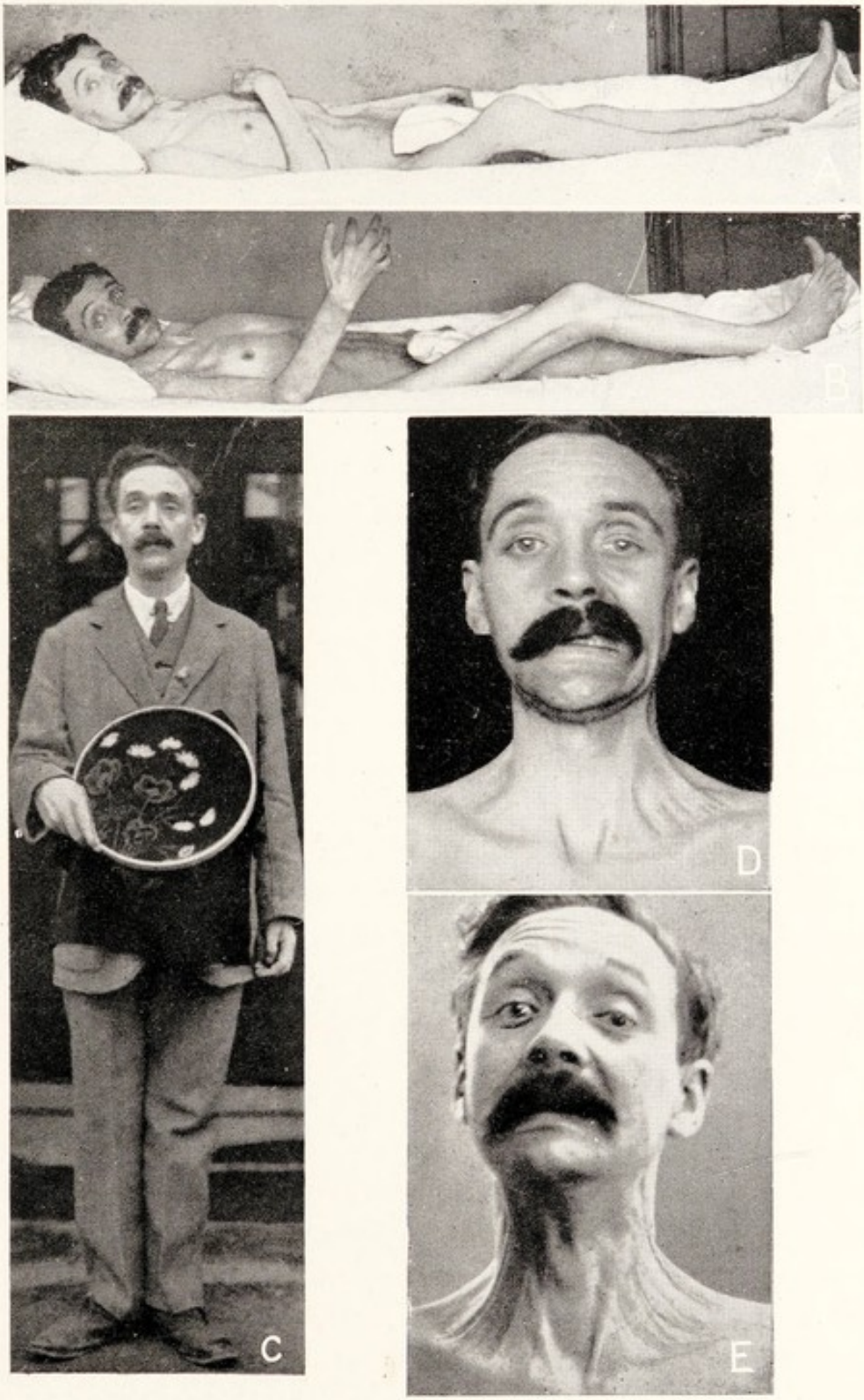


FIG. 54.—Combined hysterical and organic hemiplegia of two years' duration. (*a*) Before treatment. (*b*) After two and a half hours' treatment. (*c*) After six months' treatment. (*d*) Facial paralysis before treatment. (*e*) After forty-five minutes' treatment for face.

following concussion by shell explosion, cured by psychotherapy after persisting for eight months.—Pte. T., aged twenty-two, was admitted to Seale Hayne Hospital on June 20th, 1918, for hemiplegia of the left side, which developed as a result of being blown up by a shell eight months before. He could only stand with assistance and was quite unable to walk. There were definite signs of an organic nervous lesion ; the left plantar reflex was extensor, the abdominal reflex was absent, the ankle, knee, wrist and elbow-jerks were much exaggerated on the left side, and well-sustained ankle-clonus was present. In spite of this it was decided that the condition was probably to a large extent hysterical, and the patient was treated by vigorous persuasion and re-education. Within an hour he was able to walk and run, but it took five or six days to develop a normal walk and a natural carriage of the left arm, which was at first held in front of his left thigh. A fortnight later a distinguished neurologist, who was visiting the hospital, watched him playing billiards, and was asked to guess which had been the hemiplegic side, but the functional recovery was so complete that he was unable to do so, although all the signs of organic nervous injury were still present and had not altered when the patient was discharged from the hospital, feeling perfectly well, two months later.

Combined hysterical and organic hemiplegia of eleven months' duration, following gunshot wound of the skull ; great improvement with psychotherapy.—L.-Cpl. B., aged twenty-three, was wounded in the right parietal region in December, 1917, and was admitted to a general hospital in France with left-sided hemiplegia. Anæsthesia was noted over the left leg up to the knee and over the left hand and arm to a point just above the wrist. The report states that he could wriggle his toe and finger. On December 28th an operation was performed and a small crack in the skull was found ; some bone was removed, but no injury to the dura mater was discovered, and pulsation was normal. The bone was replaced and the wound sutured.

On April 3rd, 1918, when in hospital in England, the following report was made after a detailed investigation of his cutaneous sensibility. " Loss of sensation over the whole

of left leg up to the groin, and over the left side of trunk behind a line drawn from the anterior superior spine of the ilium to the middle of the arm-pit. Loss of sensation over the upper limb up to the arm-pit and on the outer surface as far as the acromion process. Sensation of heat corresponds with tactile sensation. No sense of joint movement in upper or lower limbs." On July 17th, 1918, he was transferred to Seale Hayne Hospital. The arm was rigidly extended at the elbow, the fingers were extended at the metacarpo-phalangeal joints, but flexed at the interphalangeal joints. The leg was rigidly extended at the hip and knee, and the foot was fixed in a position of extreme dorsi-flexion (Fig. 55 (*a*)). The deep reflexes were increased on the left side and well-sustained and regular ankle-clonus was present. The big toe did not take part in the plantar reflex, but the fan sign was present on the left side. The degree of rigidity was extreme, and the strongest effort was required to bend any joint.

The patient was treated by persuasion and re-education ; movement in all joints except the shoulder was obtained in one sitting of four hours without much discomfort to the patient. His temperature rose the next day and he developed pleurisy with effusion, which necessitated the postponement of further treatment for over two months. Psychotherapy was then continued, and he is now able to walk well (Fig. 55 (*b*)). He still has some spasticity, but is slowly improving.

Whilst in France limited anæsthesia was found associated with the hemiplegia ; eight months of treatment with electricity and massage only had the effect of making the paralysis absolute, and increasing the area of hysterical anæsthesia ; the aggravation of symptoms was clearly due to suggestion unconsciously applied by his medical officers. If the patient had been encouraged to move from the first, progress would have been steady and recovery would quickly have taken place.

At the present time (December 30th, 1918) there are no signs of organic disease, the ankle-clonus and increased deep reflexes having disappeared.

Syphilitic meningo-myelitis complicated by hysterical paraplegia.—L.-Cpl. M., aged twenty, reported sick on April 8th, 1916, with pain in the legs. A fortnight later he noticed

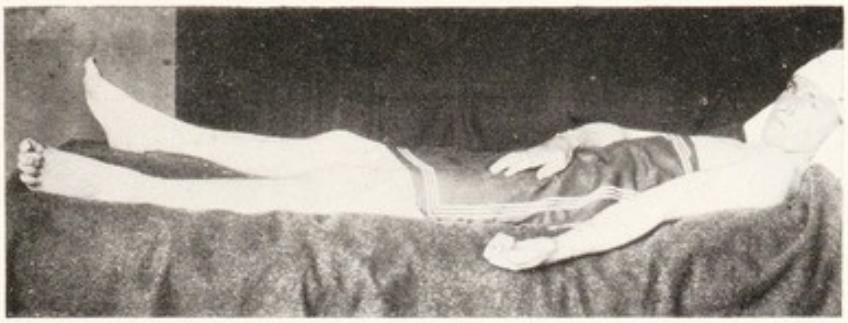


FIG. 55.—Hemiplegia following head wound. (*a*) Before treatment.



FIG. 55 (*b*).—Same case as Fig. 55 (*a*), after treatment.

weakness and became unable to walk. There was some loss of control over the bladder and rectum during May. On admission into hospital he was quite unable to walk, but the loss of power in the legs was incomplete. Sensation was normal. The knee-jerks and ankle-jerks were exaggerated and ankle-clonus was well marked. The abdominal reflexes were absent. The plantar reflex was examined on several occasions and was invariably flexor on both sides, but no doubt was felt by the consulting physician who saw him in France that there was organic disease affecting the lateral columns.

On reaching England the Wassermann reaction of the blood was found to be positive, and there was some tenderness of the spine. Iodides were given but no improvement occurred, so that the original diagnosis of syphilitic meningo-myelitis was discarded for disseminated sclerosis.

He came under our care for the first time in December, 1916. There were no physical signs of organic disease, and it was clear that the paraplegia was hysterical. With persuasion and re-education he rapidly recovered. He was then given intensive anti-syphilitic treatment until the Wassermann reaction was no longer positive.

The paraplegia was probably at first organic and due to syphilitic meningo-myelitis. The iodide doubtless led to recovery from the organic lesion, but the paraplegia was perpetuated as an hysterical condition, which only disappeared when treated by persuasion and re-education.

Hysterical paraplegia following organic paralysis due to concussion by shell explosion, cured by psychotherapy two months after the onset.—Pte. M., aged twenty-five, enlisted in September, 1914, and served for six months in France and a year in Salonica. He was very fit the whole time and was never worried by the shell fire. On November 22nd, 1916, he was blown up by a shell, and remained unconscious for four days with signs and symptoms of complete organic left hemiplegia with paresis of the right leg, and incontinence of urine and fæces. He began to answer questions on December 2nd, and complained of severe headache. His knee-jerks were then greatly exaggerated, especially the left, and the plantar reflex on both sides was extensor. The headache soon disappeared, and the paralysis gradually improved, but

he was still quite unable to walk when he reached Netley on January 24th, 1917. He had no recollection of anything between the fight in which he was blown up and the last few days in Malta. The right knee-jerk was 6, the left 7 (average normal 4) ; the left plantar reflex was still extensor, but the right was now flexor, and the left abdominal reflex was absent. The inability to walk was clearly hysterical, and it disappeared the day after admission as a result of persuasion ; with further re-education he soon learnt to walk without even a limp. When next examined, on February 2nd, the left plantar reflex had become flexor, and the left abdominal reflex was as brisk as the right ; but Babinski's second sign (combined flexion of thigh and pelvis) was still very definitely positive, and the knee-jerks were as before. The Wassermann reaction was negative. He was discharged to duty in April, the superficial and deep reflexes being normal and equal on the two sides, but Babinski's second sign was still present, though less marked. A striking point in this case was the disappearance of the extensor plantar reflex, which had persisted for sixty-four days, within nine days of the hysterical paraplegia being cured.

Hysterical paralysis associated with organic paralysis due to hæmatomyelia, the result of spinal concussion following shell explosion.—Pte. A. C., aged twenty-four, was blown 3 feet into the air, falling heavily on his face. He did not lose consciousness, and he is quite certain that his head was not doubled under him. He was unable to move for several hours, except that he managed to raise his face out of the mud in order to breathe. On being taken to hospital he remained quite helpless. His elbows were kept acutely flexed, as in a lesion of the fifth cervical spinal segment. His right arm and leg were completely paralysed, and only very feeble movements were possible on the left side. He had much aching and tingling pain in his limbs and a spasmodic pain in the calves. He had some retention of urine during the first day, and a catheter was passed on one occasion, but after this his bladder and rectum showed no abnormality. Though listless and suffering from headache, his mind was not confused, and his speech was normal. Knee-jerks were very weak, and no definite plantar reflex

was obtainable. By April 20th a slight degree of power had returned in the right arm; both arms were still painful. On May 12th it was noted that, although there was no anæsthesia, sensation to light touch was diminished up to the region of the clavicle. The headache had disappeared, and the pain in the limbs was less marked. Slight improvement in power occurred as a result of massage, but the muscles remained flabby and began to waste. By May 22nd the muscular tone had improved, the knee-jerks were now increased, ankle-clonus was elicited on the right side, and the plantar reflex was extensor on the right side, but normal on the left; both abdominal reflexes were absent.

On admission to Netley, on May 30th, he could move both arms and both legs, but they were very weak, the right side being worse than the left. Slight pain was still present in the hands and arms, but the pain in the legs had disappeared. There was marked wasting of the muscles of the upper limbs, especially of the hands, the atrophy and weakness of the right hand being severe. The right knee-jerk was 5 and the left $4\frac{1}{2}$ (normal 4); true ankle-clonus was present on the right side, and also, though less well maintained, on the left. No abdominal reflexes were obtained, and the plantar reflex was definitely extensor on both sides. The skin was much thickened over the palms of the hands and soles of the feet.

It seems clear that a hæmorrhage occurred into the cervical spinal cord at the time of the explosion, probably as a result of aerial concussion rather than of the concussion caused by falling after being blown into the air, as the patient is quite certain that the fall did not hurt him particularly, and that he could not put out his arms to save himself when in the air.

On June 11th the patient was still unable to sit up in bed, and there was no improvement in the condition of his arms and legs. As it seemed possible that some of the incapacity was hysterical in spite of the definitely organic basis, he was treated by very vigorous persuasion, and, although he would make no effort at first, at the end of five minutes he was sitting up in a chair, and at the end of a quarter of an hour he was able to stand and take a few steps with comparatively little support. During the next ten days he learnt to stand and walk with an almost normal gait

and without assistance. His condition must, therefore, have been largely hysterical and due to auto-suggestion, causing the perpetuation and exaggeration of symptoms, which were originally entirely organic and were still to some extent a result of organic changes in the spinal cord. Since then steady improvement has occurred both in the hands and legs; his gait is almost normal, and he can use his hands for all ordinary purposes, though there is still some atrophy and weakness of the small muscles. When discharged on October 23rd, the wrist-jerks were normal; the right knee-jerk was 7, the left 6, and slight ankle-clonus was obtained on the right side. The right plantar reflex was extensor, the left flexor. The abdominal reflexes had not returned.

Hysterical paraplegia following organic paraplegia due to a wound of the spine received seventeen months previously.—L.-Cpl. E., aged forty-three, was wounded in the back by shrapnel on September 27th, 1916. He immediately became paraplegic. A laminectomy of the sixth and seventh dorsal vertebræ was performed on October 10th, and a piece of shrapnel was removed, but no details about the operation are obtainable. He had incontinence of urine and constipation for several weeks. By the end of February, 1917, he could get about on crutches with difficulty. He was transferred from hospital to hospital before he was finally transferred to our care at Netley on March 20th, 1918. On admission he could only stand with the aid of crutches. The right knee-jerk was greatly exaggerated with response to the lower end of the tibia and slight spread to the opposite side; ankle-clonus was marked and sustained, but the plantar reflex was flexor. The left knee-jerk was exaggerated to a less extent, ankle-clonus was present, but not so well sustained, and the plantar reflex was flexor. With persuasion and intensive re-education he was walking in less than an hour. In a month his gait was normal, but rather heavy. The signs of organic disease remained unaltered. He was then discharged from the service, but was quite fit to follow his civil occupation.

Spinal concussion involving posterior columns associated with hysterical paraplegia.—Pte. W., aged thirty-two, was buried by a collapsing trench on July 30th, 1917; he was

fit in every way before this happened. When admitted to hospital in France he was unable to speak or move his legs, and it was found that he had no knee-jerks. His speech returned in a few days after stimulation with faradism, but he continued to stammer. On admission to Netley on August 28th he was still completely paraplegic and had a severe stammer ; both knee- and ankle-jerks were completely absent, and there was considerable rigidity of the legs. The plantar reflexes were normal. As a result of vigorous suggestion with the aid of faradism he was induced to walk on the day of admission, and with re-education his speech and gait slowly improved. At the beginning of January, 1918, the knee- and ankle-jerks were still absent and a slight Romberg sign was present, but he walked almost normally. The Wassermann reaction of the blood and cerebro-spinal fluid was negative, and no abnormal cells were found in the latter. It seems probable that the loss of jerks and the inco-ordination were due to the spinal concussion having involved especially the posterior columns, as in a fatal case described by Mott. The response to treatment by suggestion and persuasion shows that in spite of this the paraplegia was largely hysterical in origin, the paralysis due to the concussion being perpetuated by suggestion. The speech defect was, of course, entirely hysterical.

Hysterical incontinence, following concussion of spine, of eleven months' duration, cured by psychotherapy.—It is generally taught that incontinence of urine is never hysterical. But although the idea of incontinence is very unlikely to suggest itself to an individual spontaneously, it is not uncommon for the incontinence which is normal in babies to be perpetuated into childhood or even adult life as an hysterical condition. Several cases of this sort in soldiers at Seale Hayne Hospital were described by Captain J. W. Moore, M.C., U.S.A., together with one case of hysterical incontinence occurring as a sequel of the incontinence caused by the temporary organic changes resulting from concussion of the spinal cord. The following case, reported by Captain A. Robin, is of the same nature.

Gnr. E., aged twenty-two, went to France in June, 1917. In February, 1918, a 5·9 shell exploded close to him and he

was wounded in the back immediately to the right of the middle line about the level of the iliac crest. A foreign body was removed the same day in the C.C.S. On the following day, when being sent down the line by train, he had retention of urine and had to be catheterised. For the next three weeks a catheter was passed two or three times daily. Incontinence of urine had been present ever since and he had constantly worn a rubber urinal. He had had no pain and had experienced no desire to micturate. During the day he could with an effort pass a small quantity of urine at a time, but apart from this it continuously dribbled away, and he wet his bed every night. There was at first some constipation, but his bowels were now regular. He stated that his legs had felt weak for some time, but there was no definite paralysis.

He was discharged from the service, uncured, in September, 1918, and admitted to Seale Hayne Hospital on December 2nd as a pensioner. There were no physical signs of organic disease. The functional nature of the condition was explained to him, and he was kept in bed for a few days. There was at once distinct improvement, and by January 5th, 1919, the nocturnal incontinence had completely ceased. He was still lacking in confidence during the day when up, and at first slight dribbling occurred at times, but he at once gave up his urinal and soon did not pass urine more often than every three hours.

Partial hysterical blindness, following organic blindness caused by a wound in the occipital region, and associated with hysterical deafness.—In the following case blindness of a character generally supposed to be typical of organic disease was perpetuated as an hysterical symptom after the initial organic changes in the brain had disappeared.

Pte. W., aged twenty-two, was wounded over the right occipital region on June 7th, 1917. He was unconscious for five days and was then trephined. On admission to Netley, on July 6th, 1917, he was completely deaf in both ears, but as the vestibular reactions on rotation were normal the deafness was regarded as hysterical. It was noticed that he had difficulty in seeing and that he held anything he wished to read low down on the right side, although he volunteered no

complaint about this, and only spoke about his deafness. On further examination it was found that he was totally blind, except in the right lower quadrant of the field of vision of both eyes, the blindness being what might be expected to result from the wound over the lower part of the right occipital lobe near the middle line, which would be likely to involve the left lobe also to a less extent. An attempt was made at the end of August to cure the hysterical deafness by a pseudo-operation, the patient being told that a cut behind his ear would certainly restore his hearing. Nothing was said to him about his blindness, which was regarded as organic. The "operation" resulted in immediate improvement in his hearing, as it was now possible to carry on a conversation with him by shouting. Quite unexpectedly it was found that his vision was now absolutely normal, the blindness having been cured by the suggestive effect of the "operation." It must, therefore, have been due to perpetuation by auto-suggestion of the organic blindness, which was caused by concussion rather than destruction of the occipital lobe.

Mental symptoms and hysterical paraplegia, aphasia, and incontinence of five months' duration following a wound of the brain cured by re-education, persuasion and suggestion.—Pte. P., aged twenty-seven, was wounded in the left temporal region on December 6th, 1917. The dura mater was found to be torn and brain matter was escaping. A foreign body lying half an inch deep was removed and the wound was closed. On December 20th the patient had slight paresis on the left side of face, and on February 4th, 1918, he is reported to have had a fit. He was admitted to Netley on March 20th, 1918, after being in bed for seventy-three days in another hospital in England.

He was drowsy and listless and was unable to articulate. He was completely paraplegic and passed urine and fæces in the bed. There were, however, no signs of organic disease. He was at once made to get up in a chair and encouraged to take an interest in his surroundings. In a few days he became clean in his habits, and his speech gradually returned. A month after admission his mental condition was sufficiently clear to make it possible to treat the paraplegia by persuasion.

He improved slowly, and by May 24th was able to walk with a pseudo-spastic gait. The next day he was treated by direct suggestion by means of faradism, and in fifteen minutes was walking well and climbed two flights of stairs to see a friend. He has now returned to his old trade as a carpenter, and he is sound mentally as well as physically.

The Functional Element in Rheumatoid Arthritis

During the active stages of rheumatoid arthritis complete rest for every painful and tender joint greatly accelerates recovery, and fixation in a good position prevents deformity of fingers, wrists, knees and other joints. The irksome limitation of activity for weeks or months is worth while, as it may save the patient from becoming permanently crippled and perhaps bedridden at a later stage.

The active disease dies out eventually, sometimes only after many years, even if the foci of infection have not been treated. But with their complete eradication and with rest its course is comparatively rapid. When no pain and no tenderness are present, rest is no longer required. But patients, who have been long confined to bed on account of the pain involved in moving their limbs, rarely discover for themselves when the time for activity has arrived. I believe that there are thousands of people bedridden in their homes, in infirmaries, and in hospitals for incurables, who are really capable of taking up their beds and walking if they only knew it. When the active disease has died out, the fixity of the joints is very rarely due to bony ankylosis, and comparatively rarely to firm adhesions. It may be partly due to contractures, which ought never to have been allowed to develop, and which can generally be overcome by orthopædic measures. But in most cases it is mainly due to the prolonged inactivity having fixed the idea of incapacity in the patient's mind. His muscles are weak from disease, but they are not paralysed ; his joints are stiff, but they are not ankylosed. Yet he makes no attempt to move them. The incapacity is, in fact, largely hysterical, being caused by the suggestion of incapacity developing in the patient's own mind and often also in the minds of those in attendance upon him.

Explanation, persuasion and re-education, with the aid of manipulation and massage, which are, however, of quite secondary importance, often result in the recovery of the use of the limbs in a few weeks or even a few days. In September, 1919, a man came under my observation, who had been completely bedridden for four and a half years, with his knees fixed in a flexed position, and unable to use his deformed hands. There was no longer any active disease, and as a result of combined orthopædic and psychotherapeutic treatment he rapidly improved. When I showed him before the Clinical Section of the Royal Society of Medicine in February, 1922, there was no longer any limitation of movement in his knees, which looked perfectly normal; he could walk miles, and had been at work for two years. His hands still showed the typical deformity, but he could use them for all ordinary purposes.

CONTRACTURES—LOCALISED TETANUS, REFLEX DISORDER, OR HYSTERIA*

I AM reprinting the following paper, which was written in 1919 after four and a half years of war experience, because I believe that the principles laid down in it are as important in civil life as in the Army. For this reason, and because several of the cases described could have occurred equally well in ordinary peace time work, I have altered its original title of " War Contractures " to simply " Contractures."

The hysterical disabilities following injuries in civil life come particularly before the general practitioner, the surgeon and the orthopædist, but they are also seen by the physician interested in neurology. I am glad to find that Dr. J. A. Ross agrees with me that they are just as amenable to rapid and simple methods of psychotherapy as were similar cases during the war. It is important to lay stress on this point, as certain critics of our Seale Hayne methods, whilst reluctantly agreeing that they were successful among soldiers, predicted that they would have to be replaced by more elaborate psychological methods in civilians.

Hysterical contractures are far more common in civil life than is generally recognised. The success of the professors of manipulative surgery does not, I believe, depend entirely or even mainly upon their skilful manipulation. A large proportion of their patients are suffering from hysterical disabilities, and their success in such cases depends upon the atmosphere of cure in which they work, and their supreme confidence in their ability to bring about a cure by manipulation. The manipulation acts simply by suggestion on individuals, who are confident from what they have been told that their disability is about to be cured.

* Reprinted, with new introductory remarks, from the *British Journal of Surgery*, vi., 579, 1919.

From an early date in the war there was much controversy as to the nature of the frequent cases, in which contractures occurred as a result of injuries to the soft parts of the limbs, with or without the bones and joints being involved. The contractures were generally discovered when the dressings and splints were removed, but in some cases they were noticed directly after the infliction of the wound, and in others they only developed gradually several weeks later.

The War Office Committee for the Study of Tetanus circulated questions as to the frequency of muscular contractures after injuries among the "principal surgeons in England, especially those whose practices are among the large industrial classes, where injuries in civil life are common." Answers were received from about eighty surgeons, only one of whom had ever seen such a sequel of a wound. The result of the inquiry was remarkable, for I have seen frequent cases of contracture following injury in civil life ; and I have no doubt that, if the questions had been sent to neurologists and orthopædic surgeons, very different answers would have been obtained. In the following case, for example, the man was rapidly cured by psychotherapy of a contracture of the hand, which had developed after amputation of a finger five years before he joined the Army.

Hysterical contracture following amputation of a finger, of six years' duration, cured by psychotherapy in an hour.— Pte. W., aged twenty-six, had the third finger of his left hand amputated in April, 1912, for blood poisoning. Following the operation, all the fingers of the hand became rigidly flexed, but no treatment was given. He was admitted into the Army in April, 1917, in spite of his disability. He was employed on light work for the following eleven months, and was then admitted under us. He was treated by manipulation and persuasion, and in an hour there was complete relaxation of the fingers. Next day, under further treatment by persuasion and re-education, movement in all the joints was obtained. At the end of three weeks his hand was quite strong, and he was able to use it for all ordinary purposes. (Major J. L. M. Symns.)

Localised Tetanus Theory

Having received these answers, the Tetanus Committee came to the conclusion that the condition must be a new one, which had arisen as a result of some special circumstances arising in the war, and they ascribed it to localised tetanus, which had never been recognised in man before, but which undoubtedly occurs now that the routine administration of prophylactic injections of antitetanic serum has caused generalised tetanus to become comparatively rare. Most of the speakers at the conjoint meeting of the Sections of Surgery and Neurology of the Royal Society of Medicine with the Tetanus Committee, held as recently as February 14th, 1918, to discuss "Muscle Contractures following Injury," appear to have believed that localised tetanus is the explanation in the majority of cases.

Before the war the only form of localised tetanus which had been recognised was the so-called cephalic or head tetanus. A few cases had been recorded, in which the spasms began in the injured limb and remained most severe in it after generalisation occurred; but the first case of tetanus, in which the symptoms were strictly localised to one limb throughout the illness, was described in May, 1915, by Courtellement. Numerous observations on the subject have been published in France and England since that date, but even now many cases of localised tetanus probably escape recognition through want of familarity with the conditions.

Most cases of localised tetanus, which occurred before the middle of 1915, must have been diagnosed as traumatic hysterical contracture, and five out of the nine cases I have seen were at first regarded as hysterical. On the other hand, the contractures in at least two cases, which have been published as examples of local tetanus, must really have been hysterical in origin, as they developed immediately after the wound was received, although it is impossible for tetanus to develop until the bacilli introduced in the wound have had time to produce the toxin, which has then to travel to the central nervous system before it can give rise to symptoms.

In the early stages the diagnosis between localised tetanus and hysterical spasm may be extremely difficult. If the

contractures persist without abating for more than three or four weeks and do not disappear completely at the end of six or eight weeks, they are probably hysterical, even if they were at first due to tetanus. Spasms which begin immediately after the wound is inflicted cannot be due to tetanus ; they are generally reflex and protective in nature, but are often maintained after the first few hours or days by autosuggestion. A later onset is compatible with both tetanus and hysteria, and in both the extent of the contracture is often out of all proportion to the size of the wound. If the contracture persists in sleep, hysteria can be excluded. A general anæsthetic causes hysterical contractures to disappear more rapidly than tetanic contractures, which persist to some extent even under deep anæsthesia, although even hysterical contractures may still be present after consciousness is lost. If the muscles are of a wooden and unvarying hardness, tetanus is almost certainly present. An increase in the size of the muscle, possibly due to obstruction of its lymphatics, without tenderness or subcutaneous œdema, is conclusive evidence in favour of local tetanus. The continued tonic contraction in tetanus is generally accompanied by spasmodic and more or less painful contractions, which are often brought on by external stimuli. When there is any doubt as to the diagnosis during the first week, the condition should be assumed to be local tetanus, as it is never possible to say whether generalisation may not develop later. Early injections of antitetanic serum should prevent this, and they will do no harm if the spasms are not really due to tetanus. After contractures have persisted for a month, they should be regarded as wholly or in part hysterical in origin, and psychotherapy should be employed without further delay.

Reflex Theory

Babinski and Froment believe that many of the contractures which have hitherto been regarded as hysterical, or due to some obscure condition such as an ascending neuritis, as believed by Tinel, are really reflex in origin. They have summarised their views in the second section of their book,

published in 1917, on "Hystérie-Pithiatisme et Troubles Nerveux d'Ordre Réflexe en Neurologie de Guerre." This theory at first seems to offer a satisfactory explanation of many cases, the nature of which had hitherto remained obscure; but a critical investigation of the subject has convinced us that such reflex conditions never occur.

Babinski and Froment admit that reflex symptoms resemble hysterical symptoms in being quite out of proportion with the often trivial injury which gave rise to them, but state that they differ in being entirely unaffected by psychotherapy and in certain clinical features. Our experience showed, however, that the former distinction did not hold good, as rapid recovery always followed persuasion and re-education. The clinical features, which were believed by Babinski and Froment to exclude the possibility of hysteria, are discussed in a later section, where they are shown to be secondary to the impaired venous and lymphatic circulation, caused by the disuse resulting from hysterical paralysis and contracture.

There is no doubt that reflex contraction of the neighbouring muscles is not uncommon immediately after a wound is inflicted, the reflex being protective in nature, just as is the reflex contraction of the abdominal muscles in acute appendicitis or after perforation of a gastric ulcer. When, however, the symptom persists after the wound has healed, it is no longer due to any reflex action, but is the result of suggestion; the contracture is thus primarily reflex and subsequently hysterical.

Hysteria

Our own observations have led us to the conclusion that hysteria is invariably the cause in chronic cases, and that even when localised tetanus or a reflex spasm is present at the onset, any symptoms which persist are due to perpetuation by suggestion; they are thus eventually hysterical.

The matter is by no means of merely academic interest. If the contracture is due to localised tetanus, the proper treatment would be by injections of antitetanic serum. If the reflex theory of Babinski and Froment is correct, the patients can only be very slowly cured after months of treatment by physical methods. If, however, the contrac-

tures are hysterical in origin, they should be curable at a single sitting by psychotherapy.

When hysterical contractures are erroneously diagnosed as being due to localised tetanus or reflex action, the correct treatment will not be undertaken. Thus the popularisation of the idea of reflex symptoms by the publication of Babinski and Froment's book and its translation into English led to hysterical conditions being often diagnosed as reflex, with the result that they did not receive the benefit of psychotherapy, which would otherwise have cured them.

The following case, which was the first one I saw after reading Babinski and Froment's book, illustrates how an implicit belief in their teaching would have led us to neglect psychotherapy, without which the patient could not have been cured.

Hysterical contracture and paralysis of fifteen months' duration, at first supposed to be "reflex," cured by suggestion.—Pte. W., age twenty-one, received a slight wound in the hand in May, 1916. When the dressings were removed, his hand was found to be fixed, with the fingers semiflexed and the thumb adducted. Movements of the elbow and wrist were normal, but he could make no movements with the fingers or thumb. The wound soon healed, but the condition of the hand persisted in spite of massage and electricity. It had been supposed that the contracture was due to adhesions involving the tendons and palmar fascia. I first saw him in August, 1917, fifteen months after the wound was received. No improvement had occurred, the fingers and thumb being still flexed ; but it was found that the contracture could be slowly overcome by force. When a voluntary effort was made to move the fingers or thumb, the affected muscles were seen to contract, but no movements resulted, as the muscles opposing the desired movement also contracted instead of relaxing. There was no atrophy, and the electrical reactions were normal. The hand was swollen ; it was red when the room was warm and blue when it was cold, a considerable difference in temperature between the two hands being always present ; excessive sweating also occurred on the palm of the affected hand.

The condition would at once have been diagnosed as hysterical, had it not been that a recent study of Babinski and Froment's work on reflex paralysis and contracture led to the suggestion that this was an example of such a reflex condition, as the position of the hand was identical with that shown in one of the figures in their book, and œdema, vasomotor changes, and excessive sweating—which, according to them never occur in hysteria but are common in reflex disorders—were present.

As I wished to see how much relaxation occurred under anæsthesia, ether was given. The contracture relaxed more slowly than would have been expected in hysteria, this seeming at first to confirm the diagnosis of a reflex condition ; but as I still felt doubtful whether the condition might not be hysterical, I tried the effect of vigorous suggestion with the aid of electricity as the patient was coming round. With this treatment the muscles relaxed and all movements became possible. During the next few days treatment by re-education was continued, with the result that ten days later the patient was able to use his hand for all ordinary purposes. Simultaneously with the cure of the contracture and paralysis, the œdema, sweating and vasomotor disturbances completely disappeared.

Pathogenesis

The posture in hysterical contractures is identical with that which happened to exist at the time the contractures developed, and is in many cases that which was assumed immediately after the injury. Thus, if one or more peripheral nerves were damaged, the position corresponds with what would result from paralysis, or occasionally from irritation, of these nerves. In such cases, when the nerve recovers from the effect of the injury, which may be within a few hours if the latter is nothing more than slight concussion, or may be weeks or months if it is more serious, the abnormal posture and the inability to move are maintained as a result of suggestion.

In other cases the injury may lead to reflex spasm of the neighbouring muscles and inhibition of movement of the

whole limb, which is protective in nature, but which rapidly disappears as the condition of the wound improves. Apart from this reflex action, the patient more or less subconsciously assumes the position which gives most relief to the pain caused by his injury ; he keeps the affected segment of the limb rigidly in this position, and at the same time he often abstains from moving the limb as a whole, as this too would cause pain. Both the reflex and semiconscious local spasm and the general inhibition are liable to be perpetuated by auto-suggestion when the condition of the wound improves and the pain diminishes, the initial reflex and voluntary conditions merging insensibly into hysterical spasm and paralysis. The patient does not realise that the absence of voluntary effort on his part had the object of saving him from pain, but believes that it was due to "paralysis"—the direct result of his injury.

In some cases the injury itself places the limb in some abnormal position, and this is maintained owing to the pain, which the patient experiences when he tries to correct it, and to the reflex and voluntary spasm which oppose the efforts of the surgeon to replace it. This is particularly well seen in the hysterical contracture causing talipes equino-varus after the foot has been twisted into this position by an accident, whether this results in a simple sprain, tearing of ligaments, or a fracture.

Occasionally an hysterical contracture develops as a sequel of local tetanus. In such cases the posture is that caused by the contraction of the muscles, which are supplied by the anterior cornu cells of the spinal cord in the neighbourhood of the point of entry of the afferent nerve fibres connected with the parts immediately adjoining the wound, from which the tetanus toxin is absorbed. When at the end of three or four weeks the tetanic spasm gradually disappears, the contracture may persist as an hysterical condition. Apart from the history, this origin should always be suspected when the spasm involves a group of muscles, or the whole or a segment of a single muscle, which could hardly be thrown into action alone by voluntary effort. Thus in one such case the knee was fixed in a position of extension by spasm of the sartorius ; and in two others the knee was flexed and

the foot plantar flexed by a localised spasm of a small segment of the ham-strings and the calf muscles respectively. Contractures of this sort could not be imitated voluntarily, but the patient had become accustomed to them whilst the tetanus lasted, and the habit thus learnt was perpetuated without alteration when the tetanic spasm was gradually replaced by the hysterical contracture.

In many cases the posture is that in which the surgeon fixed the limb by means of splints or bandages when it was first dressed. The patient becomes so accustomed to the immobility of the joint, that when the splint or bandage is removed, he fails to realise that there is nothing to prevent the return of the normal functional activity. He makes a feeble effort to bend the joint, finds that it gives rise to pain without any obvious movement resulting, and gives up the attempt in despair, reconciling himself to the notion that the joint has become fixed as a result of the operation, and that no voluntary effort that he can make will have any effect upon it. A little manipulation, accompanied by a few words of explanation, could at this stage dispel the idea in five minutes, and months of disability would be saved. But too often the after-treatment is neglected, or the patient is ordered massage and perhaps diathermy and kataphoresis, which are given systematically by sympathetic nurses, with the result that the patient becomes more convinced than ever that there is something serious the matter, and that he will only get well with prolonged treatment, if, indeed, he will get well at all.

Hysterical contracture following an operation, cured by persuasion in five minutes.—Pte. H., age thirty, had the internal semilunar cartilage of his right knee removed on February 12th, 1918. I was asked to see him on April 5th, as he could still only walk with the aid of sticks, and was afraid to put any weight on his leg, his knee being kept quite stiff. By means of simple persuasion, which took only five minutes, he was taught to walk quite normally, no limp being perceptible. He walked back to his ward, leaving his sticks behind. He had not the complete range of flexion that he had in the other leg ; but he had quite enough to enable him to walk and run and to become once more an efficient soldier.

In cases of this kind the posture may alter from time to time if the splint is changed. Thus a man was wounded in the wrist, and his hand was bandaged with the fingers tightly clenched. Some weeks later the surgeon found that the hand had become contracted in this position. Under an anæsthetic the fingers were now fixed on a splint in a position of extreme hyperextension. Six months later his hand was still rigidly fixed in the new position. He came under the care of Captain A. Robin, who rapidly cured him by psychotherapy. As the posture is artificially produced by the use of splints, it may sometimes be one which cannot be imitated voluntarily ; but it is none the less hysterical, the patient having been trained to maintain the position whilst the limb was fixed.

In all these conditions the development of the hysterical contracture and associated paralysis is due to the fact that the patient fails to realise that there is no reason why the spasm should not relax and the power of movement return when the primary factor—nerve injury, protective reflex, conscious or subconscious antalgic spasm and inhibition of movement, localised tetanus, or fixation by splints or bandages—is no longer operative. The patient regards the contracture and inability to move as a direct result of his injury, and naturally ignores the intermediate cause, such as the pain or tetanus. If it had been pointed out to him, when the pain was disappearing, that his incapacity was due to the pain and only indirectly to the injury, and that there was, therefore, no longer any reason why it should be maintained, he would have made the necessary effort and the hysterical condition would never have developed. But not having been told this, and perhaps having been ordered treatment with massage or electricity at a stage when such treatment could have been of no real use, as recovery from any organic injury which may have been present at first was now more or less complete, the idea of incapacity was confirmed in his mind, and the original autosuggestion was fortified by the unconscious heterosuggestion of the doctor and the masseuse, with the result that the contracture and paralysis were perpetuated as hysterical conditions after the primary cause had disappeared.

From what has been said above, it is clear that contractures are always associated with more or less paralysis ; but the reverse is not the case, as uncomplicated hysterical flaccid paralysis is not uncommon. In many cases the paralysis is more extensive than the contracture, a contracture of the hand, for example, being sometimes accompanied by paralysis of the whole arm.

Etiology

Hysterical contractures and paralysis may result from injuries to the soft parts of the limb, with or without the bones and joints being involved. The commonest cause is a wound of the hand, foot, forearm or leg, the symptoms generally developing below and above the injury as well as in its immediate neighbourhood. In many cases no nerve is involved, but in others temporary concussion of one or more peripheral nerves or of the brachial plexus may have occurred, or they may have received some actual injury of a recoverable nature. The severity of the symptoms does not vary with the degree of infection or the extent of the injury, which is often trivial. They are very rarely associated with severe wounds, but we have seen a considerable number of cases in which hysterical contracture and paralysis have occurred in the hand after one finger has been amputated, and less frequently in the foot after the amputation of a toe. In other cases a severe injury to one finger has resulted in contracture affecting the whole hand. We have observed contractures and paralysis of exactly the same nature in the absence of actual wounds—as, for example, in fractures, dislocations, sprains and contusions. In a few cases the symptoms have followed some minor operation, such as for a ganglion of the wrist, varicose veins in the leg, or an abscess of the arm or leg. In one case it followed plating a fractured tibia ; three cases followed superficial burns ; two followed cellulitis ; and one case of flaccid paralysis of the arm followed anti-smallpox vaccination. Several cases of hysterical contracture and paralysis of one or both legs followed " trench foot " ; and we have seen seven cases in which the hysterical contracture appeared to be the sequel of localised tetanus.*

* In civil life hysterical contractures are not uncommon sequels of fibrositis, arthritis, and neuritis.

Hysterical monoplegia of seven weeks' duration following vaccination, cured in three-quarters of an hour.—Rfmn. D., age twenty-one, was admitted on August 12th, with paralysis of the left arm. He states that he was vaccinated on May 30th, and on June 28th, when at squad drill, he found that his left arm had suddenly become powerless. The limb was hanging useless by his side, and the hand and lower 4 inches of the forearm were blue and cold, the palm being mottled and purple. Persuasion for a quarter of an hour produced movements of the arm; in half an hour the colour and temperature were normal; and all movements of the limb, including the fingers, were perfect after three-quarters of an hour, though the hand-grip was not perfect until the next day. (Captain G. McGregor.)

Hysterical rigidity of knee of three months' duration following superficial cellulitis, cured in half an hour.—Pte. S., on October 4th, 1917, developed a large septic sore on the outer side of his right knee, which was incised a week later, a back splint being applied. The latter was removed on November 7th, when the knee was found to be rigidly extended. On December 28th free movements were obtained under an anæsthetic, but on the patient coming round, the knee remained fixed as stiffly as before. There was no improvement under massage, and on January 18th, 1918, he was sent to us as an out-patient. Within half an hour, by means of explanation, manipulation and persuasion, 30° flexion was obtained. He was instructed to perform exercises, but when seen again on February 18th very little further improvement had occurred. Another half-hour of similar treatment resulted in full flexion being obtained, and the patient was discharged a few days later. (Major J. L. M. Symns.)

Hysterical "main d'accoucheur" and anæsthesia following concussion of median nerve by gunshot wound of the forearm, cured by manipulation and persuasion in ten minutes after persisting for eight months.—Sergt. M. was wounded in the right forearm on April 10th, 1917, a compound fracture of the middle third of the radius being produced. When the splints were removed three weeks later, his hand showed a typical *main d'accoucheur* deformity, the fingers being rigidly extended and pressed together. Total anæsthesia was

present in the area supplied by the median nerve. As no improvement had occurred by November, an operation was performed, and the tendons and median nerve were freed from adhesions. This, however, aggravated the contracture, so he was transferred to us on December 21st, 1917.

Well-marked vasomotor disturbances, excessive sweating, and considerable atrophy of the soft tissues and nails were present. On the day of admission the hand was continuously but painlessly manipulated, the patient being persuaded at the same time that it would rapidly relax. In ten minutes complete relaxation was obtained and the deformity had disappeared. The fingers, which had not been moved voluntarily for eight months, could now move normally, but an area of total anæsthesia was still present. The anæsthesia was doubtless originally organic in origin, but as it now extended considerably beyond the area supplied by the median nerve, we thought that it must be hysterical. Suggestion with the aid of faradism for a few minutes on two occasions resulted in its complete disappearance. With the return of movement the vasomotor and secretory disturbances disappeared. A slight degree of wasting of the small muscles of the hand was now found to be present, but otherwise the hand was normal in every way. The patient was kept under observation for three weeks, and as there was no incapacity he then returned to duty.

Variety of Postures

In most cases a single segment of a limb is involved, the hand and foot being most frequently concerned. Very often, however, the whole or greater part of the limb is affected, but in such cases the contracture and paralysis are most severe in the immediate neighbourhood of the injury, although in rare instances the whole limb is completely paralysed and rigid.

Upper Limb

Hysterical contracture and paralysis of the hand give rise to three common types of posture. The fingers may be extended, in which case they are generally also adducted towards the middle finger, a *main d'accoucheur*

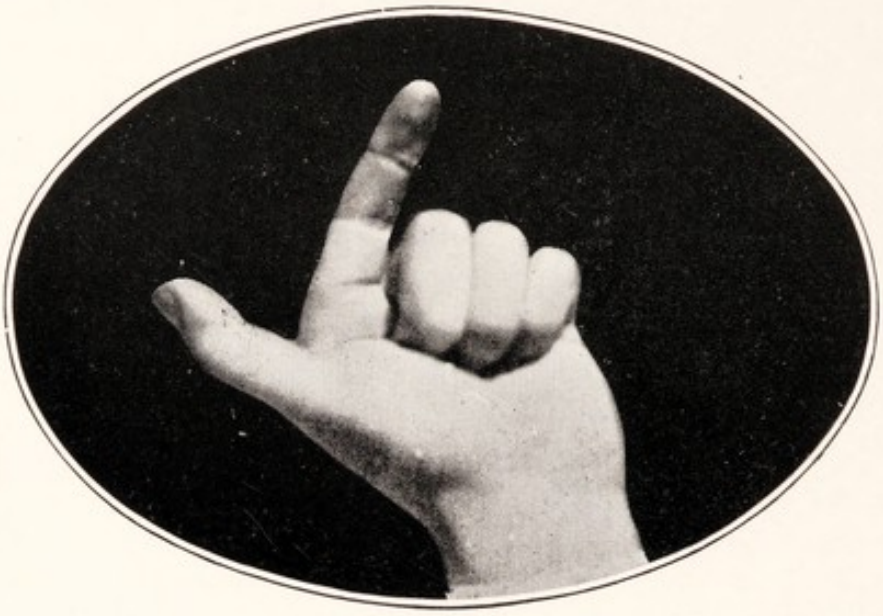


Fig. 56.—Hysterical contracture of hand persisting thirty-five months after wound near elbow.



Fig. 57.—Same hand as Fig. 56 after half an hour's treatment, showing depressions formed in palm by pressure of nails. (Capt. C. H. Ripman.)

resulting; in one case the fingers were abducted as well as extended. The other extreme is for the fingers to be clenched tightly into the palm of the hand; all the fingers may be involved; or only two or three, in which case one finger may occupy an intermediate position; in these cases the skin often becomes sodden with sweat owing to the impossibility of evaporation and the difficulty in washing; in one case, in which the position had been maintained for two and a half years, the nails of three fingers were found to have produced a depression about a quarter of an inch deep into the palm of the hand (Figs. 56 and 57). In the third variety, the hand takes up an intermediate position very similar to that assumed normally at rest. In the extended and clenched position the paralysis is always accompanied by more or less contracture; the intermediate position is that generally assumed in flaccid paralysis, but it may also be associated with contracture, though this is rarely severe. In most cases all the fingers are affected, but sometimes, especially when the condition has followed an injury of the hand or wrist, only those fingers most directly involved by the wound are implicated, the others being either normal or only comparatively slightly affected. Occasionally the fingers are in a position of extreme hyperextension, which may be so marked that it suggests that the condition cannot be hysterical in origin. In most cases of this sort, however, it is found that a patient has always been able to hyperextend his fingers, and a similar, though rarely so well-marked, hyperextension can be produced by voluntary action in the other hand.

When the wrist is involved, it is commonly in an intermediate position or flexed; in rare cases it may be fixed even to the extent found in the dropped wrist due to complete organic musculo-spiral paralysis. Hyperextension of the wrist is uncommon.

The hand is very frequently in a position midway between supination and pronation. When the contracture is incomplete, it is almost always possible to obtain greater movement in the direction of pronation than supination, inability to supinate the hand completely being very common.

When the elbow is involved, it is almost invariably flexed,

but I have seen two cases of extreme extension. The flexion is generally such as would correspond with the position of the arm when held in a sling.

When the shoulder is affected, the arm is generally held rigidly to the side. In incomplete cases, and when recovery is taking place spontaneously, it is often found that the elbow can be raised to the level of the shoulder, but it is impossible to raise it any further.

Lower Limb

In rare cases the toes alone are affected. One patient, who had been wounded in the thigh, developed a persistent flexor contracture of his toes, which disappeared as a result of psychotherapy after it had persisted for nine months.

In the commonest variety of hysterical contracture and paralysis involving the leg, the foot is extended in a position of talipes equinus. This is often associated with varus, which may be present alone. In some cases a very extreme degree of talipes equino-varus is present. These conditions may be due to simple flaccid paralysis, but there is generally some degree of rigidity, and in many cases the contracture is so extreme that not the slightest movements can be obtained in the joints by ordinary means.

Hysterical rigid talipes with paraplegia, tremor, and stammer of fourteen months' duration, cured in two days.—Sergt.-Major P., age thirty-two, was blown up in December, 1916, and remained unconscious for some days. He was paraplegic, stammered badly, and had a generalised tremor when admitted to a provincial hospital, where he remained for three months. He was then transferred to a hospital in London, where he remained for nine months. He was treated with massage and electricity, but very little improvement occurred. A piece of bone was removed from the left foot in October in order to correct some deformity, but no improvement resulted. At Christmas, 1917, he was sent to a convalescent hospital, from which he was transferred to us on February 14th, 1918. He stammered badly, and had a severe tremor involving both legs, which increased with every

voluntary movement, so that he was unable to stand, and could only walk a few unsteady steps with the aid of sticks, when further progress was prevented by the violence of the tremor. As no signs of organic disease were found, I told him that the treatment he would have the following day would cure him, and the presence in his ward of three men who had recently been cured of paraplegia helped to convince him that this was true. By 5 p.m. the next day, as a result of persuasion and re-education, he could talk slowly without any stammer, and he walked a quarter of a mile with a gait which was normal except for a limp due to left-sided talipes equino-varus.

As I could not at first overcome the deformity of his left foot by manipulation, I thought it might be due to some organic injury, especially as an operation had been performed upon it after a radiographic examination in London. Moreover, it was colder than the right foot and was always wet with sweat, whilst the right foot was dry, evidence which would be accepted by Babinski as excluding hysteria and suggesting a reflex origin. More vigorous manipulation, however, two days later, continued for an hour and a half, resulted in complete disappearance of the deformity, and the patient was now able to walk without any limp. It is obvious, therefore, that the talipes, like the paraplegia and stammer, was hysterical in origin.

The knee is frequently involved, extension and flexion being about equally common. Extreme flexion is rare, but rigid fixation in a position of semiflexion is often seen. Contractures in the position of extension are frequently so extreme that not the slightest movement can be obtained actively or passively until relaxation is produced by vigorous psychotherapy.

Hysterical stiff joint following gunshot wound of the knee, cured by persuasion.—Sergt. W., age twenty-three, sustained a gunshot wound on the outer side of his left knee on January 16th, 1918, which penetrated the joint. At the casualty clearing station the foreign body was removed, the joint was washed out, and the capsule closed. He reached a hospital in Scotland on January 30th, and on

February 20th he was allowed to get up, but the limb was still in a splint, and he had to use crutches. Four months later, according to his documents, adhesions of the knee-joint were broken down under an anæsthetic, and he was sent to a command depôt. He was admitted to Seale Hayne Hospital on August 20th, walking with the aid of a stick, with a very bad limp owing to inability to bend his left knee. Except for the scar of the incision on the outer side of the joint, the knee appeared normal, but he could only flex it to about 120 degrees. The stick was taken away, and with persuasion and re-education for half an hour complete flexion was obtained, and he walked with only a slight limp. The next day he was able to go up and down-stairs and walk on the level without a limp. (Captain G. McGregor.)

When the hip is involved, the limb is generally in a position of slight flexion, but rigid extension is sometimes seen. Adduction or abduction, and eversion or inversion, may be present.

Hysterical flaccid foot-drop, with inversion of the leg, following a gunshot wound of the right thigh a year before; rapid recovery with persuasion.—L.-Cpl. F., age twenty-three, was wounded by shrapnel in the outer side of the thigh on May 11th, 1917. A counter-opening was made, and a piece of metal removed. He began to get about on crutches in August, 1917, but always with his foot dropped and his leg turned inwards. On his medical case-sheet a specialist reports "there was some involvement of the right sciatic nerve." He was transferred to us on May 11th, 1918, with a spring attached to his boot to keep his foot up, and he could only get about with difficulty with the aid of sticks. It was explained to him that, having held his leg so long turned inwards and with his foot down, he had forgotten how to use his muscles. With simple persuasion and very little re-education he was able to walk quite well. At the end of four days he was put on horseman's work and physical drill, as he walked quite normally except for a slight tendency to allow his knee to turn inwards. With this exception he is now quite fit. (Captain S. H. Wilkinson.)

Trunk

A wound of the back may give rise to an hysterical spinal deformity, but this is much more frequently the result of simple bruising or so-called muscular rheumatism[1].

Hysterical spinal curvature following a wound of the back.—Pte. B. was wounded on March 21st, 1918. On admission in August he had a superficial scar, 3 inches long, running diagonally across his back opposite the third dorsal vertebra. He showed very marked kyphosis, which produced two deep horizontal folds across his epigastrium, below which the abdomen was round and prominent. His chest was also hollow from side to side, with very marked prominence of the points of his shoulders. He breathed very badly, with no abdominal movement, and very little expansion of the lower part of his thorax. He looked so pigeon-breasted, that the deformity was considered by some observers to be organic and due to adenoids, though he himself said he was absolutely straight until he was wounded. Unlike the majority of cases of hysterical spinal curvature, the curvature did not disappear on lying down. But with persuasion his body was gradually straightened out, his shoulders being pressed back until both the kyphosis and the side-to-side curvature together with the hollowing of his chest had disappeared. After prolonged persuasion he was able to move freely, and the depression of his epigastrium and the prominence of his abdomen with the horizontal furrows across his epigastrium disappeared. Three weeks later, being quite fit, he was sent back to duty. (Captain C. H. Ripman.)

Changes Secondary to Deficient Circulation

The normal circulation through a limb depends upon its active movements, the afferent nerve fibres from the muscles probably giving rise to localised reflex vasodilatation. If for any reason the arm is not moved in cold weather, the hand becomes shrivelled, white or blue, numb, painful and stiff. These well-recognised changes disappear at once with active exercise and on warming the limb, both of which restore the circulation. The tendency to disturbances of this kind is much greater in people with a poor circulation

than in those with a naturally good circulation. The former class know by experience that they must keep their fingers constantly moving in cold weather in order to avoid getting numb.

It is thus natural for the immobility caused by paralysis or contracture of a limb, whether organic or hysterical, to result in deficient circulation and the usual secondary changes. As, however, the paralysis is continuous, whereas the physiological inactivity referred to only lasts for a few minutes or at most for a few hours at a time, the secondary results are likely to become much more profound, especially in individuals with a poor circulation. Such deficient circulation is generally congenital, but in soldiers it is often acquired or aggravated as a result of exposure. Thus in all cases in which circulatory complications are severe the circulation in the normal hand is also feeble. The limb, especially its peripheral part, becomes cold and white or blue, and the diminished blood-supply results in a diminution in the volume of the hand, except in the cases in which œdema develops. Pressure on the skin with a finger is followed by a very slow return of blood to the part rendered anæmic.

When the venous and lymphatic stasis is very marked and the paralysis absolutely complete, œdema may occur, especially if the paralysis is accompanied by contracture in a position in which the veins and lymphatics are obstructed by the rigid muscles. The œdema is sometimes very considerable, and may give rise to the impression that there has been some injury of the blood-vessels (Fig. 58). This, however, is not the case, for with the return of voluntary movement the œdema disappears in the course of a few days as the circulation becomes once again normal.

The deficient circulation results in changes in the physiological properties of the paralysed muscles, even if the paralysis is entirely hysterical. Babinski and Froment have shown that under these conditions the muscles respond with abnormal slowness to galvanic stimulation. They proved that this is not due to permanent changes in the muscles by demonstrating that the response returns to normal when the limb is warmed ; and we have observed that this also occurs directly recovery takes place as a result of psychotherapy,

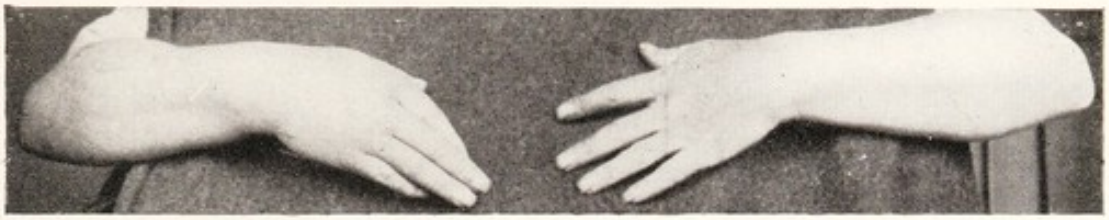


FIG. 58.—Hysterical contracture of right hand of fourteen months' duration, associated with severe œdema. Cured after two hours' treatment. (Capt. A. W. Gill.)

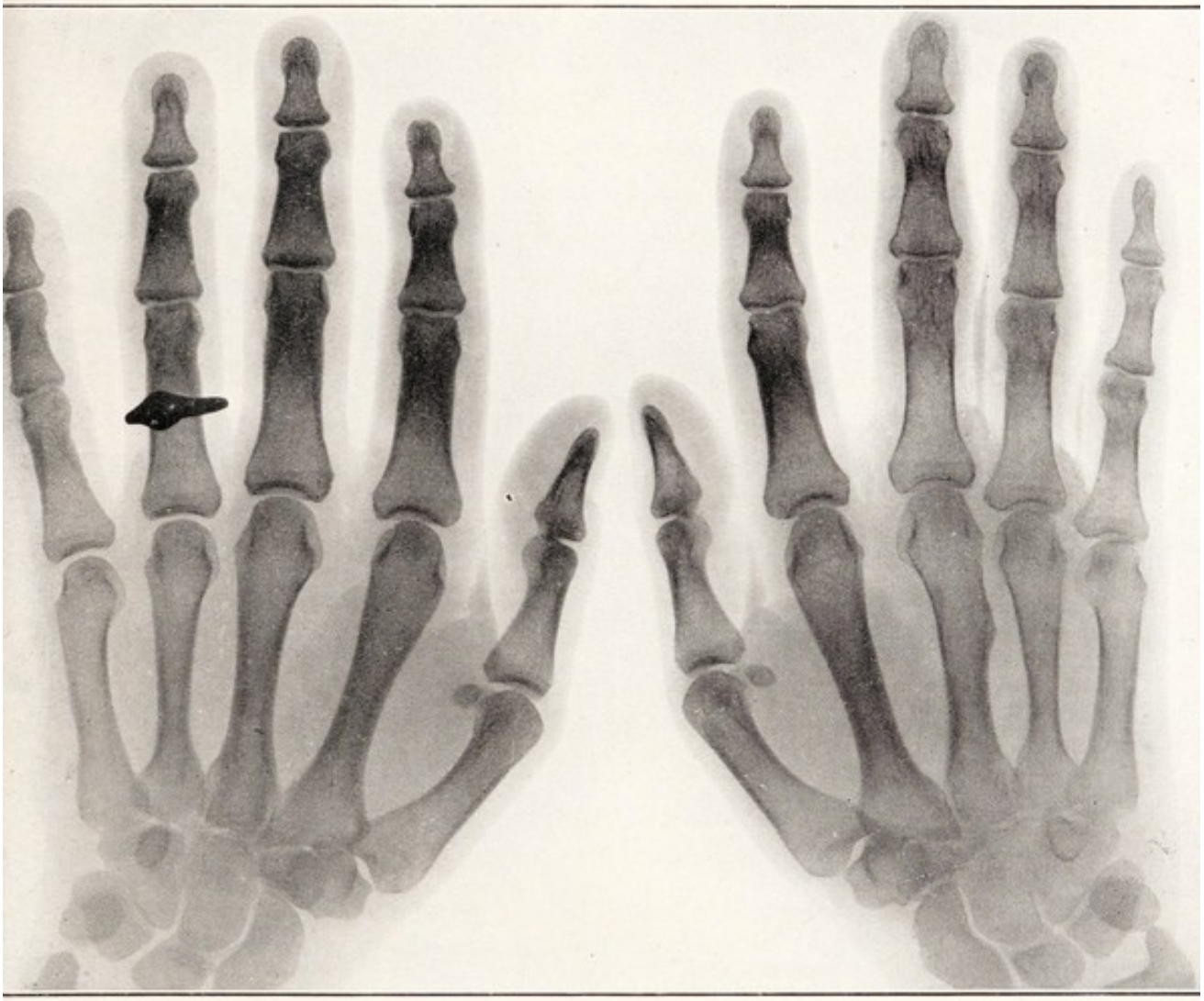


FIG. 62.—Skiagram of right and left hands, showing increased transparency of the bones of the right fourth and fifth fingers, and to a less extent the third finger, taken after recovery from a contracture involving the fourth and fifth fingers, with partial contracture of the middle finger, which had persisted for twenty months after wound of hand. The little and ring fingers also show atrophy of soft parts. (Major J. F. Venables.)

when the restoration of active movements gives rise to improvement in the circulation. Babinski and Froment also found that the muscles and sometines the nerves are abnormally irritable to mechanical stimulation, the response being unusually prolonged; in some cases these signs are only obvious when muscular relaxation has been produced by a general anæsthetic. Babinski and Froment observed that when the leg is involved, the ankle-jerk may disappear or be weaker than on the normal side, returning to normal on warming. This phenomenon is clearly due to changes in the muscles, analagous to those which give rise to the abnormal reactions to electrical and mechanical stimulation. The other deep reflexes are often increased, this being most obvious when the contracture is partially overcome under light anæsthesia; the changes are probably due to the increased tonicity of the muscles, which persists until anæsthesia is very profound.

More or less stiffness of the joints is generally present in cases of long standing, even in the absence of any muscular spasm. This may be so extreme that not the slightest movement is possible. It is most obvious in the joints of the hand, particularly at the metacarpo-phalangeal articulations. It has often been regarded as due to some organic change, as it is very well seen in cases of organic paralysis following injuries to peripheral nerves. In such cases so-called adhesions are often broken down under an anæsthetic, actual tearing being heard, and this is often followed by effusion round the joint. This has not unnaturally been regarded as evidence of organic change; but in all hysterical cases, and, I believe, in some cases of organic paralysis, the stiffness is not really due to any permanent organic alteration in the tissues. A considerable amount of relaxation occurs when the circulation is improved by immersion in hot water, and particularly by such means as radiant heat and whirlpool baths. In hysterical cases, even of many months' duration, directly the patient has been taught to contract his paralysed muscles and to relax any spasm which is present, the return of movement so improves the circulation that often in the course of a few minutes the condition of the joints and surrounding tissues returns to normal. As the condition of the joints is

exactly similar to what is seen in organic paralysis, I feel sure that in the latter case the condition is also often secondary to the deficient circulation ; and if instantaneous recovery from the paralysis were possible, the joints would return to their normal condition without any manipulation or breaking down of adhesions being required. As the stiffness is due to circulatory disturbances and not to any muscular spasm, whether hysterical in origin or not, it naturally persists under an anæsthetic ; and when the joint is forcibly moved, the surrounding structures which are torn are not abnormal fibrous tissue, but simply the normal periarticular tissue, which is temporarily in an abnormal condition owing to the deficient circulation. The injury to the normal tissues naturally results in effusion. This is a point of the greatest importance, as it follows that the apparent tearing down of adhesions and the production of inflammatory reaction do not necessarily mean that the condition is organic. When gas is used, or some other anæsthetic under which muscular relaxation is incomplete, any hysterical contracture which is present may also help to prevent free movement of the joint, as such a contracture, being quite independent of consciousness, only disappears under deep anæsthesia. Violent movements with incomplete anæsthesia may thus result in tearing of contracted, but otherwise normal, muscle fibres as well as of normal fibrous tissue.

By accurate measurement with a sphygmomanometer, Babinski and Froment found that the amplitude of the pulsation of the arteries in the affected limb is greatly diminished compared with that on the normal side. They found that this inequality disappears on warming, and Roussy and his colleagues[2], using exactly the same methods, noted its disappearance when the paralysis and contracture were cured by psychotherapy, proving that it is simply a result of the deficient activity of the limb.

Babinski and Froment found that the plantar reflex on the affected leg disappears, but reappears on warming the foot. They also describe some indefinite anæsthesia in the peripheral part of the limb, and the patient may complain of a varying degree of pain. These phenomena are additional results of the deficient circulation, being of exactly the same

nature as the numbness, pain and loss of plantar reflex observed in normal people, especially those with a poor circulation, if the limb is cold or " goes dead " in cold weather. Only if the anæsthesia is perpetuated by auto- or hetero-suggestion, after the return of the circulation on warming or after recovery from the contracture as a result of psycho-therapy, does it become hysterical. If a nerve was damaged at the time the injury was inflicted, genuine organic anæsthesia may be present at first. This disappears with more or less rapidity according to the severity of the injury; but, like the anæsthesia due to the coldness, it may be perpetuated by auto-suggestion, and sometimes by heterosuggestion if too frequent examinations are made by the medical attendant. We have shown [3] that anæsthesia of this kind may eventually be purely hysterical and curable instantaneously by psycho-therapy, although its extent corresponds exactly with the cutaneous distribution of the injured nerve, and although it had led to burns or other injuries which had not been felt.

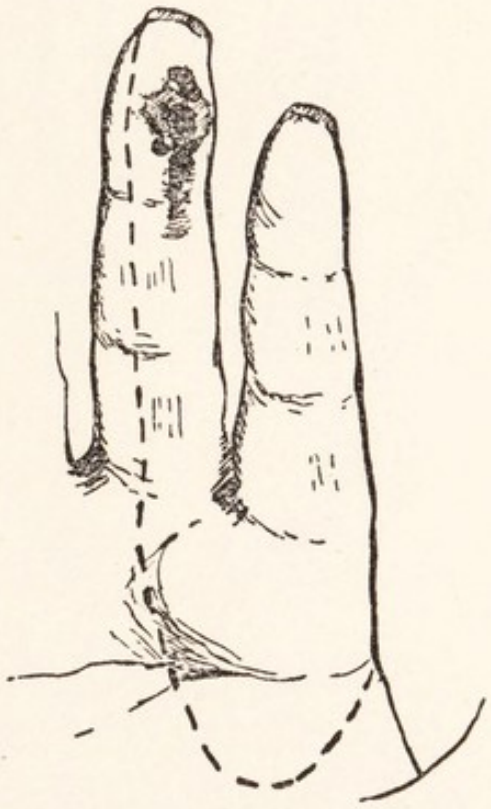


Fig. 59.—Hysterical anæsthesia in median nerve distribution, with unfelt accidental burn, cured by suggestion in a minute five months after injury to median nerve. (Captain A. Robin.)

Hysterical anæsthesia in distribution of the median nerve resulting in accidental burn, cured by suggestion in a minute, after persisting five months.—Pte. F., age thirty-six, received a penetrating wound of the right arm on October 4th, 1918, following which he had loss of muscular power of the hand, and anæsthesia of the area of skin supplied by the median nerve. The wound was excised at the casualty clearing station. He was admitted to Seale Hayne Hospital on February 20th, 1919, with an hysterical contracture of the

fingers, the fore-finger being rigidly extended and the hand being blue and cold. He had median nerve anæsthesia, and on the outer side of the second finger was an ulcerated area about the size of a shilling (Fig. 59), which he stated was caused by trying to hold a lighted match a few days previously. The contracture was cured by re-education and persuasion, and the next day the anæsthesia disappeared almost completely within a minute as a result of suggestion by means of faradism. With the restoration of the circulation and disappearance of anæsthesia the ulcer rapidly healed.

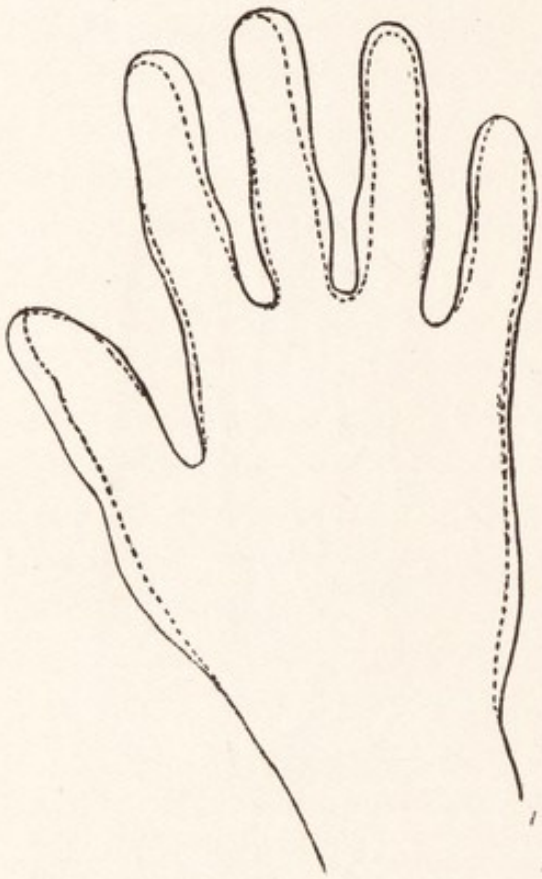


Fig. 60.—Tracing of hand (dotted) with hysterical contracture following wound of upper arm which had been present for sixteen months, superimposed on reversed tracing (continuous) of the other hand, showing atrophy of soft parts (Captain A. W. Gill).

The long-continued deficient circulation in hysterical paralysis also leads to malnutrition. Atrophy of the subcutaneous tissue occurs, with the result that the volume of the limb, particularly the tips of the fingers, greatly diminishes, and the increased blood-supply which occurs on warming the hand and on recovery from the paralysis only produces a comparatively slight increase in size, most of the loss of volume being due to actual atrophy. This is well shown in Fig. 60, which represents the tracing of a hand which had been hysterically paralysed for many months, superimposed upon the reversed tracing of the corresponding normal hand, and Fig. 61, which represents the first finger of a paralysed hand compared with that of the sound hand. The normal lines on the hands, especially the transverse lines on the dorsal aspects of the joints of the fingers, become less marked and may even

disappear. Owing to the diminished bulk of the fingers, the skin becomes too large for its contents and is thrown into longitudinal folds, especially over their palmar aspect. The muscles atrophy for the same reason, and also as a result of simple disuse, as their normal metabolism depends upon their activity. It is well known that the corresponding anterior cornu cells of the spinal cord atrophy from disuse after a limb has been amputated. It is exceedingly probable that this would also occur in hysterical paralysis, as the disuse may be just as complete. If post-mortem evidence of this were forthcoming, it would be an interesting confirmation of the far-reaching secondary organic changes which may follow disuse, even if this is purely functional as in hysteria.



Fig. 61.—Atrophy of index finger of left hand, compared with normal finger of right hand, resulting from hysterical contracture of left hand of eighteen months' duration, drawn after recovery from the contracture.

The x-rays show abnormal transparency of the bones, which is apparently due partly to deficient calcification and partly to absorption of the bony tissue, but we have never observed any definite alteration in their outline (Fig. 62, opposite p. 280). Although the joints occasionally appear to be enlarged, the x-rays show no change in the articular surface; this corresponds with the fact, pointed out long ago by Paget, that hysterical disorders of joints never give rise to any anatomical change as the result of pressure exerted in abnormal directions, however long the condition may persist. The enlargement of the joint may be due in part to œdema from deficient circulation, but it is more often simply apparent and due to contrast with the atrophy of the soft parts round the shafts of the bones. Lastly, the nails become thin, brittle and abnormally opaque, and they often show longitudinal grooves (Fig. 63).

Babinski and Froment rightly pointed out that the

phenomena I have just described as accompanying functional paralyses and contractures caused by minor injuries to limbs were not hysterical, because they were not due to suggestion and were, indeed, incapable of being suggested, and because they could not be removed by direct psychotherapy. Unfortunately Babinski and Froment went further, and concluded that the paralyses and contractures, which were associated with these non-hysterical phenomena, were therefore also non-hysterical and must be due to the same cause which gave rise to the latter. Although they were still uncertain as to their origin, they thought that the most likely explanation was that both the paralysis and contracture and the associated phenomena were reflex in origin, and corresponded with the atrophy and contracture in the neighbourhood of diseased joints, which Vulpian and Charcot long ago described as being due to reflex action.

We are, however, convinced that this explanation is incorrect, and that the paralysis and contracture are hysterical, and the associated phenomena are simply secondary to disuse. Cases of contracture, in which all the signs described by Babinski and Froment were present, have occurred in the absence of any wound, so that a reflex origin was excluded, their hysterical nature being subsequently proved by the cure which followed psychotherapy. Babinski and Froment had found considerable difficulty in curing paralyses and contractures of this nature by psychotherapy, which confirmed their opinion that they could not be hysterical. But our experience has been more fortunate, and we have not seen a single case in which psychotherapy failed to produce complete recovery. We have had cases precisely similar to every one of those of which photographs are reproduced in their book. The paralyses and contractures exactly fulfil the requirements necessary for a diagnosis of hysteria, being produced by suggestion and being curable by psychotherapy. The associated phenomena do not fulfil these requirements and are therefore not hysterical; but they are none the less the direct result of the hysterical symptoms, for when the paralysis and contracture disappear with psychotherapy, they disappear with them. The return of movement is always accompanied by an improvement in

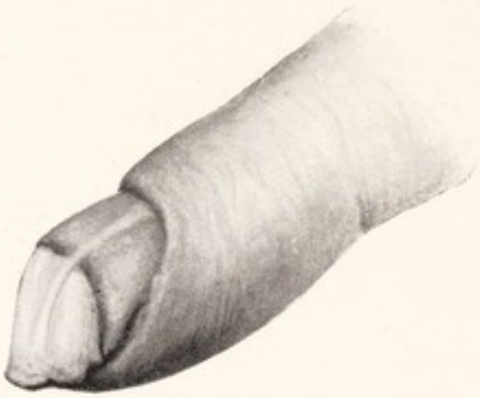


FIG. 63.—Improved nutrition of nail, drawn six weeks after sudden recovery with psychotherapy from hysterical paralysis which had lasted for over a year. (Capt. A. W. Gill.)

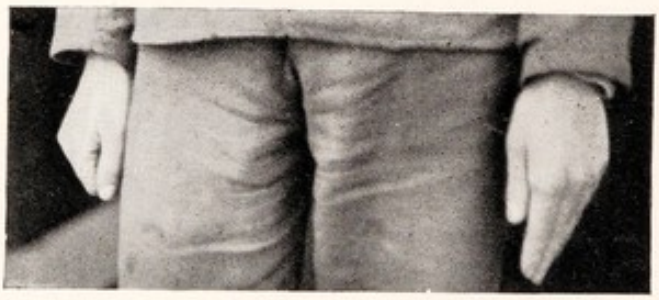


FIG. 64 (*a*).—Abnormal posture of left hand persisting after complete recovery at a single sitting from hysterical contraction and paralysis of sixteen months' duration, due to wound of left hand.



FIG. 64 (*b*).—Same case as Fig. 64 (*a*) after treatment by re-education.

the circulation, and the limb regains its normal colour and warmth. The electrical reactions and reflexes become normal at once, and the numbness and stiffness of the joints, however closely the latter may have simulated an organic condition, completely disappear. The only abnormal phenomena which are still present in the limb are the tendency to revert when at rest to the abnormal position, which I shall presently explain as a result of postural tone, and the persistence of the trophic changes, which naturally require a considerable time to disappear completely. As soon as the limb is used as much as it was formerly—which should occur immediately the first treatment is concluded—and the circulation is consequently restored, the supply of nourishment becomes normal again, and at the same time the active contractions of the muscles stimulate their metabolism so that they, together with the soft parts, the bones and the nails, gradually return to their original condition.

Fig. 63 shows very strikingly the change in the nutrition of the nail which follows recovery. The drawing was made about six weeks after the patient had been cured by psychotherapy from hysterical paralysis which had lasted for over a year. The new nail, which had grown since the cure of the paralysis, was in every way normal ; the distal part of the nail, which is seen in the picture to be white, rough and thin, in sharp contrast to the pink, smooth and thicker proximal portion, is what was left of the nail present before recovery took place. Three weeks later the last trace of the abnormal nail had been replaced by healthy nail.

The striking fact that the trophic changes are most obvious in winter, when the circulation is most feeble, and in individuals who have always had a poor circulation, is only what would be expected if our explanation of the secondary nature of these phenomena is correct ; it would be inexplicable if the reflex theory were accepted.

The excessive sweating which often occurs in these cases is less easy to explain. It may in part be a direct result of the cutaneous asphyxia when the circulation is unusually feeble. In cases of contracture, in which the hand is tightly flexed, it is in part due to the air in contact with the palm being kept warmer than that in contact with the palm of the

normal hand, and to the diminished evaporation which occurs in the enclosed space formed by the clenched hand. We have, however, observed in several cases, when recovery is incomplete and great efforts are being made by the patient to open and close the hand, that the actual secretion of sweat continues to be very excessive. In such cases it is possible that the intense nerve impulses, sent down from the brain to the centres in the spinal cord, spread from the motor nerve-cells to the neighbouring sympathetic nerve-cells which control the secretion of sweat. This would explain the fact that the sweating may occur, though to a less extent, in the normal hand.

Postural Length and Postural Tone

When hysterical paralysis, with or without contracture, has persisted for some months and psychotherapy leads to rapid recovery, it is often observed that, although the patient is able to perform every movement in a perfectly normal way at the end, perhaps, of an hour, he tends to maintain the abnormal posture, which was caused by the paralysis and contracture, directly his attention is withdrawn from the affected limb. A man, who as the result of a wound in the upper arm has developed hysterical monoplegia with contractures, resulting in the limb being carried with the elbow flexed and the fingers rigidly extended and crowded together in the form described as *main d'accoucheur*, may recover every movement of his elbow, wrist and fingers in a few minutes, and at the same time every trace of rigidity may disappear, but he will probably walk away from his treatment with his elbow flexed and his fingers still bunched together. Only if he constantly thinks of keeping his limb in the normal position does the latter gradually become adopted even when no attention is given to it (Fig. 64).

The abnormal postures produced by hysterical contractures persist after consciousness is lost when an anæsthetic is given; this is in part due to the fact, first observed by Babinski and Froment, that the contractures, which they regard as reflex in origin, are maintained until an advanced stage of anæsthesia is reached. But even after the muscular

spasm upon which the contracture depends has completely disappeared, the abnormal posture remains, however deep the anæsthesia may be, so that it is clear that some other factor besides the muscular spasm must be present. Babinski and Froment, in common with most other observers, assumed that this was fibro-tendinous or fibro-muscular retraction ; but the complete return to normal with re-education without any physiotherapy proves that this view must be incorrect.

Another striking fact about these conditions is the maintenance of the abnormal posture of the arm or leg during sleep. On the few occasions on which I have been able to investigate the question, I have found that hysterical contractures disappear during sleep, but in spite of this the abnormal posture is maintained, so that it is only by actually manipulating the limb that the absence of the spasm of the affected muscles can be demonstrated. The experiments of Ballet,[4] which he believed proved that hysterical contractures persist in sleep, really only proved that the abnormal posture persists. They consisted in fixing a paper band to the affected foot in such a way that any movement would tear it ; as it was not torn during the night, he concluded that the contracture had not relaxed. It is, however, much more probable that relaxation did occur, but the abnormal posture of the foot persisted, and no movement took place when the spasm disappeared.

After the hysterical contracture and paralysis have been cured, the abnormal posture is not only maintained during consciousness, but it also persists for a time during sleep and during anæsthesia.

From the above facts it is clear that some element is present which does not depend upon consciousness, but which has the effect of maintaining the abnormal posture during sleep and anæsthesia, both before and after recovery from hysterical paralysis and contracture. It is obvious that this factor has nothing to do with hysteria, as it is independent of consciousness, and is neither produced by suggestion nor cured by psychotherapy.

I believe that the explanation can be found in what Sherrington[5] has described as postural length and postural tone. Under normal conditions the position of a limb at

rest is maintained as a result of the tone of its muscles, the exact position depending upon the relative tone of the extensors and flexors. The fingers, for example, are normally slightly flexed, and remain so not only during the waking state, but also during sleep and during anæsthesia. Each individual muscle fibre has a certain degree of tone when at rest ; and as for the greater part of every twenty-four hours it is at rest, its anatomical structure adapts itself to this tone ; but it is capable of becoming shorter as a result of active contraction and longer as a result of active relaxation.

If, for example, the line AB in Diagram I. represents the length of a muscle fibre in the condition of extreme relaxation, and AC its length in extreme contraction, its normal "postural length," which depends upon its "postural tone," will be AD. It is capable of shortening from AD to AC on active contraction, and lengthening from AD to AB on active relaxation. If, as the result of continued contraction of the muscle—whether this is due to hysterical contracture,

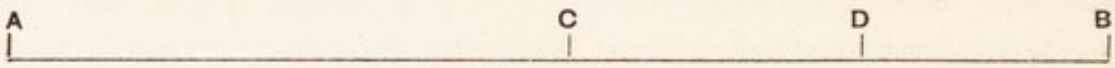


Diagram I.

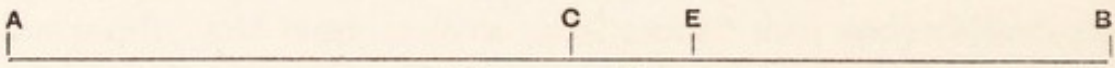


Diagram II.

organic disease, or tetanus—its postural length, which is represented by AE in Diagram II., is kept constantly shorter than that due to the normal postural tone, the structure of the fibre will adapt itself to this length. Consequently, when recovery takes place, although the fibre is now capable of full contraction to the length AC and full relaxation to the length AB, yet it will tend to return when at rest, both during consciousness and during sleep and anæsthesia, to the abnormally short length AE. When as a result of an effort of will the limb is kept in a normal position for most of the day, the structure of the individual muscle fibres gradually returns to normal, and the normal postural tone is regained.

If this explanation is accepted, it is clear that in addition to the treatment of the actual paralysis and contracture in hysterical conditions, the patient must be taught to keep his

limb in a natural position when he is not actually using it, and this can best be done by exercises in front of a looking-glass. Our observations show that the tone of a muscle adapts itself to new postures very rapidly, and in favourable cases a limb, which has been in an abnormal position for a year or more, returns to the natural one in the course of a few days.

The conception of postural length and postural tone of muscle has also considerable importance in the treatment of organic nerve injuries. A fundamental orthopædic principle is the prevention of the stretching of paralysed muscles, the tendency until quite recently being to keep them in a condition of extreme relaxation. Experience has, however, shown that better results are obtained with a less degree of relaxation. In cases of dropped wrist due to musculo-spiral paralysis, for example, the hand was formerly kept in a position of extreme hyperextension ; but recently it has been found that recovery is more rapid with only moderate extension. The change in practice has resulted from experience, and not from theoretical considerations ; but it is easy to understand why the most recent method of treatment is the best, as paralysed muscles, whether the paralysis is organic or hysterical, are likely to recover their normal activity most rapidly if they are kept at their normal postural length, so that when a return to voluntary power takes place, the structure of the individual fibres corresponds with the normal postural tone. The ill effects of allowing the paralysed muscle to be overstretched is probably not due, as has been generally supposed, to any injurious action upon its contractile power, but to the development of a new postural length, which results in the muscle, when it recovers its contractile power, working under the greatest possible disadvantage. At the same time the abnormally short postural length of the opposing muscle is extremely disadvantageous.

Abnormal Postural Length and Postural Tone in the Absence of Organic Disease and Hysteria

In our study of war neuroses we have been constantly adding to the conditions which we believe to be hysterical,

but which were formerly supposed to be organic in nature or due to some other functional condition than hysteria. I believe, however, that the conception of postural length and postural tone should result in the exclusion from hysteria of a group of cases, which has hitherto been regarded as hysterical. I have already spoken about the abnormal posture, which persists after the cure of hysterical paralysis and contractures as a result of psychotherapy. It is not at all uncommon for organic disease and injuries to result in abnormal postures owing to reflex action, the prolonged use of splints, the voluntary adoption of a posture with the object of relieving pain, or, in rare cases, local tetanus. When the primary condition has disappeared, the wound having healed or the disease having cleared up, there may be no contracture or paralysis left of either organic or hysterical nature, all movements being perfect and the patient being well able by voluntary action to return to the normal position. But owing to the long maintenance of the abnormal posture a new postural length of the muscles has developed, so that the limb tends, when at rest, to remain in the same abnormal position as it was whilst the lesion was still active. There is nothing hysterical about this, as it depends upon a structural though temporary change, and it is not produced by suggestion, although it is curable by re-education, which, however, acts in a different way to the psychotherapy required for hysterical symptoms, as it simply teaches the patient to maintain by an effort of will the natural position for a sufficient length of time to enable a new postural length of the affected muscles to develop. It is certain that many cases of abnormal posture, as well as some cases of abnormal gaits, are really of this nature and not hysterical. The diagnosis from hysteria can be made by the complete absence of any paralysis or contracture, and from organic disease by the rapidity with which recovery occurs with re-education.

Diagnosis

The diagnosis of an hysterical contracture depends primarily upon the incompatibility of the symptoms with

the injury. On careful examination it is generally at once clear that the exact form and extent of the contracture and paralysis cannot possibly be explained by the injury inflicted upon the affected muscles, or upon the nerves which convey motor impulses to them from the central nervous system. In some cases an injury to a nerve appears to be responsible for some of the paralysis present, but it is often found that the paralysis extends to muscles supplied by other nerves which could not have been injured. Moreover, an injury to a nerve cannot account for persistent spasm of the muscles it supplies, and still less for that of other muscles ; persistent muscular spasm resulting from injuries is thus invariably hysterical, unless the pyramidal tracts in the brain or spinal cord have been directly damaged. When a part of the condition is obviously hysterical, this should be cured, and an attempt made to cure the residual condition, however closely it may simulate the results of an organic lesion ; for the latter is often perpetuated as hysteria, and recovery of function may take place before the disappearance of the accompanying physical signs of organic disease, such as extreme muscular atrophy, loss of reaction to faradism, and abolition of the deep reflexes. I have already pointed out that vasomotor and trophic changes, which have in the past been regarded as conclusive evidence of organic disease, may be the result of disuse from hysterical paralysis, and that it is most important to recognise how impossible it is to distinguish by simple manipulation the stiffness of joints due to organic changes in the surrounding tissue from that due to local deficient circulation, quite apart from any associated muscular spasm.

According to Babinski, a further criterion for the diagnosis of the hysterical nature of the paralysis and contracture leading to an abnormal posture is the possibility of voluntarily imitating the latter with complete accuracy ; for, having been produced by suggestion, and being independent of any organic condition, it should be capable of reproduction by voluntary effort. Experience has taught us that this criterion, though often a valuable aid in diagnosis, may lead one astray, as there are certain exceptions to the rule. If the posture is due to the perpetuation by suggestion of a

position, which developed under circumstances which uncontrollably placed the limb in a position the patient could not voluntarily assume, its maintenance for a more or less prolonged period before the responsible circumstances ceased to be operative would be sufficient to train the muscles involved to continue to act in the same way, and would also lead to the development of postural lengths of the muscles, which would help to keep the part in the abnormal position, even after psychotherapy had resulted in a cure of the contracture and paralysis. Thus contractures developing after a splint or localised tetanus has kept the limb in an abnormal posture for a considerable period, and hysterical paralysis developing as the perpetuation of organic paralysis due to a nerve injury after regeneration has occurred, may be impossible to imitate. Lastly, it must be remembered that individuals vary considerably in the extent of movement they can produce at different joints. For example, a man developed a contracture of his hand with his fingers in extreme hyperextension as a result of a wound of the forearm ; at first sight this was thought to indicate that the condition was organic, but it was then found that the patient was capable of producing voluntarily an equal degree of extension in his normal hand.

Treatment

We have almost entirely given up hypnotism in the treatment of hysterical conditions, as our results were uncertain, and we have seen so many patients in whom prolonged treatment by hypnosis before admission had proved unavailing and had even given rise to new symptoms. Suggestion with the aid of electricity we rarely employ, except at the commencement of treatment in some cases of flaccid paralysis, in which the contractions produced in the paralysed muscles by faradism powerfully appeal to the patient's mind.

Our method now is to begin with a full explanation of the cause of the symptoms in language suited to the patient's intelligence and degree of education, followed by persuasion and re-education, combined in most cases with manipulation, which doubtless acts to some extent by suggestion. A very

important, but by no means essential, preliminary is the creation of a proper atmosphere of cure. Directly the patient is admitted, the sister encourages him to believe that he will be cured as soon as the doctor has time to see him, and she is often helped by the spontaneous efforts of other patients in the ward, who have been rapidly cured of similar symptoms and tell him of their cure. The medical officer sees him some hours later, and after examining him and coming to the conclusion that the condition is hysterical, he tells him as a matter of course that he will be cured the next day. By the following morning the patient is fully convinced that the hoped-for cure will take place ; as the medical officer is equally convinced that he will cure the patient, the two essentials for recovery are present. The nature of the actual treatment is really immaterial, but simple explanation, persuasion, and re-education have the great advantage of making the patient take an active part in his own cure, and remove any suspicion of charlatanism from the proceedings.

The patient is made to understand that any treatment he has already received has prepared the way, so that nothing now remains but a properly directed effort on his part, with our help, for complete recovery to take place. During the whole course of treatment he is engaged in conversation, and the meaning of each successive step is carefully explained. He is made to watch the contraction of the muscles and the play of the tendons of the normal limb, and to attempt to imitate them in the affected one.

In some cases it is not even necessary to touch the patient, mere explanation and persuasion being sufficient to cause him to relax any spasm which may be present, and then to perform the various movements of the part with quickly increasing strength and rapidity. In other cases the limb requires to be lightly supported at first, but here again no passive movements are employed. In cases of this kind the patient often expresses astonishment at the simplicity of the treatment, which succeeds in curing him in a few minutes, in spite of the fact that he has previously been given massage and electricity for months without any obvious result. The explanation is that now for the first time he is made to take an active part in the treatment—to use his

will power, instead of allowing himself to become a passive agent in the hands of the masseuse. A few masseuses and electrotherapeutists realise the importance of active effort; but I have frequently seen a patient reading a newspaper which he holds with one hand, whilst his other hand is being massaged or treated with electricity, exactly as if it did not belong to him. I have, indeed, very rarely seen a patient being encouraged throughout his massage or electrical treatment to take an active part in the proceedings. As a matter of fact, neither electricity nor massage is of any use in these cases, although the average massage and electrotherapeutic department is crowded with them; for recovery should take place very rapidly, and then nothing but the ordinary activity of everyday life is required to restore any residual weakness due to the muscular atrophy caused by prolonged disuse.

In many cases of severe contracture more active manipulation is required. In our earlier cases we often forcibly moved the limb in the direction opposed to the normal action of the contracted muscles, however much the patient might complain of pain, the movements being repeated until complete relaxation and the power to perform voluntary movements were restored. Now, however, we realise that the production of pain often produces a more or less subconscious resistance to the treatment in the patient's mind. We have found that in almost every case it is possible by explanation and persuasion to get him to relax his muscles, so that passive movements can be carried out with the production of little or no pain, however powerful the spasm may be. When little or no resistance to passive movements persists, they are combined with and finally replaced by active movements until the condition of the limb is normal.

When very great difficulty is experienced in getting the contracted muscles to relax, the limb should be placed in hot water and the manipulations carried out when the circulation has been artificially improved in this way. Some relaxation always occurs, because, as I have pointed out above, the rigidity is in part the direct result of the deficient blood-supply.

Passive movements are most effective if carried out by the

medical officer himself, as the patient is engaged in conversation the whole time and made to take an active part in the movements from a very early stage in the first sitting. For this reason we never employ the mechanical appliances for performing passive movements, which have been boomed to such an extent during the last few years. Even when complete relaxation of spasm has been attained and the normal movements have been restored to a hand, the patient is very apt to forget this, and to continue to make the other hand do the work of both. After the condition has persisted for many months or even three or four years, it is only natural that this should be the case at first, if he does not think about it, as he has become so unaccustomed to having two useful hands. It is, therefore, of the greatest importance to give the patient some occupation, such as basket-making or toy-making, which will necessitate his using both hands from the very day on which recovery occurs. At Seale Hayne Hospital we have found that the men enjoyed working at a pottery we instituted better than anything else, and this has had the desired effect of rapidly training them to use the hand which had previously been paralysed. At the same time the patient is instructed to be careful to use both hands for all ordinary purposes, such as dressing and feeding himself, and in the case of the right hand he should at once begin to write with it again. A musician should be encouraged to play his instrument.

Finally, the patient should be taught to keep the limb in the proper position by an effort of will, in order to restore the normal postural tone and postural length of the muscles. When the leg has been affected, it is necessary to give some re-education in walking for a few minutes in order to overcome any tendency to limp, due to the persistence of the abnormal postural length of the muscles involved in the contracture and of those which acted abnormally in order to compensate for the partial disability. Here again we have never found any apparatus, such as Zander's, necessary for the re-education of normal movements and restoration of full capacity, the ordinary activity of everyday life being quite sufficient, if the patient is made to understand that he must now use his limb exactly as if he had never been injured.

The following case is a single example out of a very large number, showing how rapidly complete recovery occurs even in very long-standing cases, in which all hope of cure had been given up.

Hysterical paralysis of the left deltoid of twenty months' duration, and hysterical contracture of the right biceps and triceps of nine months' duration, cured in a few minutes.—Pte. C., age twenty-eight, was wounded superficially over the left shoulder in August, 1916. He was in hospital for six weeks, and was then sent to his depôt. He was kept off duty, with the exception of walking exercises and attending lectures, on account of his inability to use his arm properly. He was then transferred to a labour company, and went to France in February, 1917. He received a slight wound of the right elbow in August, 1917. He was sent to England, and was in five different hospitals. He was transferred to Seale Hayne Hospital on May 14th, 1918, with a diagnosis of "spasm of the right biceps." On examination, it was found that his right elbow was rigid and flexed at slightly more than a right angle. He was unable to abduct his left arm, the deltoid being quite flaccid. The latter condition had evidentally been given up as hopeless, as no mention of the paralysed left shoulder was made on his medical case-sheet. He had twice had his right arm forcibly straightened under an anæsthetic in other hospitals, but on each occasion the spasm had returned. With explanation, manipulation and persuasion, the resistance of the muscles of the right arm was overcome in a few minutes. The left deltoid was stimulated with a faradic current in order to show the patient that the muscle could contract, and in ten minutes with vigorous persuasion he was able to move his left arm in any direction. He was immediately put on farm work and physical drill, and both arms soon became quite strong. He was discharged to duty on July 10th, 1918. (Captain S. H. Wilkinson.)

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INDEX

Achalasia, 110
anal, 123
of the cardia, age of onset, 115
diagnosis of, 117
pathology of, 110
prognosis of, 119
symptoms of, 115
treatment of, 119
pelvi-rectal, 123
Achlorhydria, 22, 42, 65
after gastro-enterostomy, 27
and appendicitis, 49, 183.
and gall-stones, 194
associated with appendicitis, cholecystitis, dysentery and pancreatic disease, 48
chronic gastritis and atrophy of mucous membrane in connection with, 44, 79
constitutional, 73
familial, 77
following gastrectomy and gastro-enterostomy, 80
in Addison's anæmia, 65, 70
in subacute combined degeneration of spinal cord, 88
of cancer of stomach, 81
relative frequency in various conditions, 89
rheumatoid arthritis and, 51
treatment of, 101
Achlorhydric gastric diathesis, 42
Achylia gastrica. *Vide* Achlorhydria.
Addison's anæmia, 44
achlorhydria in, 65, 70
alcoholic cirrhosis of liver associated with, 79
blood destruction in, 64
blood in, 55
chronic gastritis and achlorhydria in connection with, 79
degeneration of spinal cord in, 85
familial occurrence of, 73
glossitis in, 90, 93
history and nomenclature of, 53
intestinal infection in, 93
method of recording size of blood corpuscles in, 57
mortality statistics, 78
nervous symptoms, 85
oral sepsis in, 90, 96
prophylaxis of, 100
remissions of, 96
Addison's anæmia—*continued.*
splenectomy in, 104
subacute combined degeneration associated with, 85
treatment, 101
Adrenalin in treatment of asthma, 228, 233
Aerophagy, 8
Air-swallowing, 8
Albargin in treatment, 165
Alcohol, effect on hypersthenic stomach, 24, 33, 40
Alcoholic gastritis, the achlorhydria of, 45, 79
Alcoholics, morning sickness of, 120
Alkaline treatment of ulcer, 36
Anæmia, "pernicious." *Vide* Addison's anæmia.
septic, 70
Anal achalasia, 123
Anaphylaxis and asthma, 218
Animal emanations and asthma, 221
Anisocytosis, 62, 72
Anti-dysenteric serum, treatment with, 160, 162
Appendicitis, 31
association of achlorhydria with, 48, 49, 183
chronic, 169
Bastedo's sign, 179
focal infection, 182
gastric symptoms, 170, 177
indirect evidence, 177
pain in, 180
symptoms of, 170
treatment of, 182
x-rays in diagnosis, 172
Appendicostomy, 167
Appendix, foreign bodies in, 176
tenderness of, 176
x-ray examination of, 172
Aspirin, hyper-sensitiveness to, 224
Asthma, adrenalin in treatment, 228, 233
anaphylaxis and, 218
animal emanations and, 221
bacterial toxins and, 223
cutaneous reactions in, 219
definition of, 217
emotional, 225
food and, 220
hay fever and, 221
hysterical, 225

Asthma—*continued.*
inheritance of, 229
internal secretions and, 226
pollen and, 221
reflex causes, 224
suprarenal glands and, 226
toxic idiopathies of, 219, 230
toxins and, 224
treatment, 230
Auto-intoxication, 11

Bacillary dysentery, 160
Bacillus coli and gall-stones, 193
infection of gall-bladder, 193
dysenteriæ, 150, 157, 160
Bacterial toxins and asthma, 223
Barium meal, 13
Bastedo's sign in chronic appendicitis, 179
Belladonna in treatment of gall-stones, 212
of ulcer, 38, 39
Bicarbonate of soda, neutralising power of, 36
Biermer's anæmia, an unjustified term, 55
Bile, examination of, 204
salts, 188
stasis of, 211
Biliary antiseptics, 208
colic, abortive attacks of, 197
acute, 198
gastralgia, 197
infection and gall-stones, 195
stasis, 195
prevention of, 211
Bilirubin, excess of, in blood, 64
in the urine, 199
Bismuth carbonate, neutralising power of, 37
Blindness, hysterical, following organic, 258
Blood, bilirubin in, excess of, 64
examination of, in achlorhydria, 62
in degeneration of the cord, 62
in Addison's anæmia, 55
Price-Jones method of recording size of corpuscles, 57
transfusion of, in Addison's anæmia, 105
Bone marrow, changes in, in Addison's anæmia, 98, 106
Bronchial centre, irritable, in asthma, 218, 220, 230

Cæcal stasis, 178
Cæcum, movable, 175
Calculi, biliary, 186, 193, 195
radiographic signs, 203
Cancer, gastric, achlorhydria of, 81, 85
Cardia, achalasia of, 110
Cardiospasm, 110, 113
Chalk, neutralising power, 37
Charcoal in treatment, 103, 167
Cholecystectomy, 214
Cholecystitis, 31, 184, 186
association of achlorhydria with, 49
biliary antiseptics in, 208
Cholelithiasis. *Vide* Gall-stones.
Cholesterol in food, 190
in the blood, 188
stones, 195, 203
Colectomy, 147
Colic, biliary, abortive attacks of, 197
acute, 198
muco-membranous, 16, 141
Colitis, ulcerative, 142, 143
ætiology of, 151
complications of, 156
diagnosis of, 157
historical notes, 150
intestinal lavage in, 144
morbid anatomy of, 152
prognosis of, 158
symptoms of, 152
treatment of, 159
with anti-dysenteric serum, 160, 162
use and abuse of purgatives in, 143
use of term, 140, 142
Colon, atony of, 14
congenital idiopathic dilatation of, 123
follicular ulceration of, 157
inflammation of, 140, 142, 151
lavage of, 144
motor functions of, 136
radiology of, 139
sigmoidoscopic examination of, 142, 151, 154
surgery of, 147
Congenital idiopathic dilatation of colon, 123
Constipation, causes of, 11, 14
in Hirschsprung's disease, 127
treatment of, 139
Constitutional achylia gastrica, 73
Contractures. *See* Hysterical contractures.
Corpuscles, red, changes in anæmia, 56

Defæcation, inefficient, 12, 179
Dental infection and Addison's anæmia, 94
and gastric ulcer, 32
Desensitisation in asthma, 230
Diagnosis of nervous disorders of stomach and intestines, 1, 3, 11
Diaphragm, spasm of, 9
Diarrhœa, hysterical, 16
in ulcerative colitis, 153, 158, 162
nervous, 14
Diathesis, achlorhydric gastric, 42
hypersthenic gastric, 19, 171

Diet in gall-bladder disease, 208
Dietetic treatment in duodenal ulcer, 35, 39
Digestion, nervous disorders of, 13
physiology of, 46
Douche, intestinal, method of administration, 146
Ductless glands and asthma, 226
Duodenal bulb, 25
contents, examination of, 204
diathesis, 19
Duodenum, streptococci in, 94
ulcer of, 19, 26, 35
diagnosis of, 204
Dyschezia, 12, 179
Dysenteric anti-serum in ulcerative colitis, 160, 162
Dysentery, amœbic, 157
association of achlorhydria with, 50
bacillary, treatment with anti-dysenteric serum, 160
diagnosis of, 157
epidemic, 150
Dyspepsia, acid and atonic, use of terms, 4, 5
appendicular, 169
flatulent, 8
gall-stone, 190, 196
intestinal, following gastro-enterostomy, 48
nervous, 2, 3
neurasthenic, 4
reflex, 34

Eggs, cholesterol in, 190
Emotional asthma, 225
Emotions, depressing, symptoms due to, 11
Enemata, 13, 144, 146
Entamœba histolytica, 157, 176
Enterospasm in chronic appendicitis, 179
Eructation, repeated, 9

Fæces, character of, in colitis, 153, 165
Familial achlorhydria, 73
Addison's anæmia, 73, 77, 100
gastric and duodenal ulcer, 29
Fatigue a cause of asthma, 226
Fistula, gall-stones passing through, 200
Flatulent dyspepsia, 8
Flavine in treatment, 166
Flexner's bacillus, 150, 160
Food, asthma and, 220
cholesterol in, 190
in treatment of duodenal ulcer, 36, 39
irritating properties of, 33, 40
retention in stomach, time of, 24
Friedreich's ataxy, hysterical ataxic paraplegia associated with, 241, 242
Functional disorders of nervous origin, 1

Gall-bladder, infections of, 206
Gall-stones, biliary antiseptics in, 208
bio-chemical investigations, 204
bio-chemistry of formation, 187
diagnosis of, 204
dietetic treatment, 208
incidence of, 189
infection in pathogenesis of, 190
medical treatment, 207
pain and tenderness in, 200
passage of stones, 199
prophylaxis, 207
surgery of, 214
symptoms of, 196
typhoid fever as factor in, 193
x-ray signs, 203
Gas in the stomach, 8, 10
Gastralgia, biliary, 197
Gastrectomy, achlorhydria following, 80
Gastric diatheses, 19, 25
hypersthenic, 22
juice, 24, 35, 45
symptoms of chronic appendicitis, 170
psychasthenic, 10
Gastritis after gassing, 5
alcoholic, achlorhydria of, 79
chronic, complicating primary achylia gastrica, 44
in connection with achlorhydria and Addison's anæmia, 79
Gastro-colic reflex, 14, 16
Gastro-enterostomy, achlorhydria after, 27, 80
intestinal dyspepsia following, 48
sequelæ of, 41
Glossitis in Addison's anæmia, 90, 93

Hæmatemesis in chronic appendicitis, 171
Hæmoglobin, estimation of, 56, 62
Hepatitis in cholecystitis, 188
Heredity and asthma, 229
Hirschsprung's disease, 123
symptoms of, 127
treatment of, 131
Hunger, habitual, 24
pain, 34
Hydrochloric acid, treatment by, 101, 213
Hyperæsthesia, gastric, 3, 4
Hyperbilirubinæmia, 64
Hyperchlorhydria, 3
constitutional, 22, 25
in duodenal ulcer, 26
Hypercholesterolæmia, 188
Hypersthenic gastric diathesis, 22

Hypertonic and hypotonic stomach, 20, 25
stomach in case of duodenal ulcer, 26
Hypnotic suggestion, curve of gastric acidity during, 10
Hypnotism in treatment of hysterical conditions, 294
Hypochlorhydria, 3
Hypochondriasis, intestinal, 14
Hysteria, 2
in chronic cases, 266
Hysterical anæsthesia, 283
and organic hemiplegia combined, 249, 251
asthma, 225
ataxic paraplegia, associated with Friedreich's ataxy, 241, 242
blindness, 258
contractures, changes secondary to deficient circulation, 279
common in civil life, 262
diagnosis of, 292
etiology of, 272
localised tetanus theory, 264
pathogenesis of, 268
postural length and tone, 288
reflex theory, 265
treatment of, 294
variety of postures, 274
diarrhœa, 16
dyschezia, 12
element in organic disease and injury of central nervous system, 235
exaggeration of progressive nervous disorders, 236
incontinence of urine, 257
paralysis associated with organic paralysis, 244, 246
differential diagnosis, 247
paraplegia, 237, 253, 256
pseudo-constipation, 11
symptoms in disseminated sclerosis, 236
vomiting, 5

Idiopathies, toxic, in asthma, 218, 230
Idiosyncrasies, 227
Ileal kink, 174
stasis, 13, 177
Injury, muscle contractures following, 264
Internal secretions and asthma, 226, 228
Intestinal dyspepsia following gastro-enterostomy, 48
hypochondriasis, 14
infection in Addison's anæmia, 93
treatment of, 101
Intestinal lavage, 144, 146
stasis, 12, 147
Intestines, nervous disorders of, 11
Iron, excess of, in viscera, 64

Jaundice, colour of skin in, 65
in gall-stones, 199
Jejunal ulcer after gastro-enterostomy for duodenal ulcer, 28, 41
Joints, hysterical disorders of, 285
stiffness of, 281

Kephir in treatment, 103
Kidney disease, associated with ulcer, 38

Liver, cirrhosis of, and alcoholic gastritis, 79

Magnesium sulphate, effect on gall-bladder, 212
Manipulative surgery, 262, 296
Mastication, efficient, necessity of, 45, 47
Megacolon from anal achalasia, 129
from pelvi-rectal achalasia, 128, 131
Megalocytosis, 57, 59, 72
Mercury tube in treatment of achalasia of the cardia, 118, 120
Milk feeds in treatment, 36
soured, in treatment, 103
Morning sickness of alcoholics, 120
Mortality statistics of Addison's anæmia, 78
Muco-membranous colic, 16
Muscle contractures following injury, 264
Muscle-sense, deficient, re-education of, 240
Muscle-tone, 291

Nasal irritation and asthma, 231
Nervous diarrhœa, 14
diseases, progressive, hysterical exaggeration of, 236
regressive, hysterical perpetuation of, 243
disorders of intestine, 11
of stomach, 1, 3
dyspepsia, 2, 3
origin, of functional disorders, 1, 3
system, central, hysterical element in organic disease and injury of, 235
symptoms and signs of organic disease, 247
Neurasthenia, an organic disorder, 2
Neuroses, classification of, 2, 3

Œsophagus, functional obstruction of, 111
idiopathic dilatation of, 110
obstruction of, diagnosis of, 117
malignant, 117, 118
treatment of, 119
peristaltic action and distension of, 113
Olive oil, in duodenal ulcer, 36, 40
in treatment of gall-stones, 212
Oral sepsis, 32, 48, 52
associated with appendicitis, 182
in Addison's anæmia, 90, 96
treatment of, 101

Pain in chronic appendicitis, 180
in gall-stones, 200
Pancreatic digestion, 47
disease, association of achlorhydria with, 50
Pelvi-rectal achalasia, 123
Peristalsis, deficient, 14
"mass," 15
reversed, 177
Persuasion. *See* Psychotherapy.
Plombières douches, 144, 146
Poikilocytosis, 56
Pollen, asthma and, 221
Postural length and postural tone, 289, 291
Postures, variety of, in hysterical contractures, 274, 288
Pregnancy, hypercholesterolæmia during, 189
vomiting of, 6
Price-Jones method of recording size of blood corpuscles, 57
Psychasthenic gastric symptoms, 10
Psychical causes of asthma, 233
Psychoneuroses, classification of, 2
Psychotherapy, 2
in asthma, 233
in treatment of combined organic and hysterical nervous disorders, 241, 243, 248, 250, 252, 257, 259
of hysterical contracture, 263, 267, 270, 273, 276, 278, 283, 286, 295, 298
Purgatives, some results of, 11
use and abuse of, 143
Pyloric obstruction, severe vomiting due to, 7
Pylorus, obstruction of, 38, 40
Pyorrhœa alveolaris, 32, 48, 94

Rectal stasis, 179
Rectum dilated, 12
Reflex causes of asthma, 224, 231
theory of contractures, 265, 269
Rheumatoid arthritis and achlorhydria, 51
functional element in, 260
Rovsing's sign in chronic appendicitis, 181
Ryle's tube, 22

Salicylates in biliary disease, 209
Salivation in achalasia of the cardia, 116, 122
profuse, in waterbrash, 121
Sclerosis, disseminated, combined organic and hysterical incapacity in, 236, 239
Serum, anti-dysenteric in ulcerative colitis, 160, 162
horse, 163
polyvalent, 161
Sigmoidoscopy, 142, 151, 152, 154
Silver nitrate in treatment, 165
"Sinking" sensation, 30
Sippy's method of treatment, 36
Skin, lemon colour in Addison's anæmia, 65
reactions in asthma, 219
Smoking, effect on hypersthenic stomach, 33, 40
Sodium citrate in milk feeds, 36
Spa treatment of gall-stones, 213
Spasm, hysterical, 264
Spinal concussion, 254, 256
cord, subacute combined degeneration of, 62
achlorhydria in, 88
anæmia associated with, 86
in Addison's anæmia, 85
intestinal infection in, 93
secondary to gastric cancer, 81, 85
Splenectomy in Addison's anæmia, 104
Sprue, anæmia associated with, 59
Stomach, atrophy of mucous membrane, 79
cancer of, achlorhydria of, 81, 85
dilatation of, atonic, 3
nervous disorders of, 1, 3
normal, 20
spasmodic hour-glass contraction, 177
time of retention of food in, 24
ulcer of, 20
x-ray examination of, 3
Stools, character of, in colitis, 153, 165
Streptococcus longus, duodenal, 95
Suggestion. *See* Psychotherapy.
Suprarenal glands and asthma, 226, 228

Tabes, hysterical incapacity in, 240
Tannic acid in colitis, 146, 165
Test-meal, fractional, 3, 21, 43, 72
Tetanus, localised, 262, 264, 269

Tobacco, effect on hypersthenic stomach, 33, 40
Tongue in Addison's anæmia, 90, 93
Tonsillar infection in production of ulcers, 31
Toxic idiopathies in asthma, 218, 230
Toxins and asthma, 223, 224, 230
Transfusion of blood, in Addison's anæmia, 105
Typhoid fever, 51
and gall-stones, 191

Ulcer diathesis, 171
duodenal, 19
acute, 32
diagnosis of, 33, 204
dietetic treatment in, 36, 39
essential exciting causes, 31
predisposing cause of, 25
family, 29
hyperchlorhydria in, 26
hypertonic stomach in, 26
prevention of recurrences, 39
secondary exciting causes, 32
treatment of, 35
Ulcer—*continued.*
gastric, 20
family, 29
jejunal, after gastro-enterostomy, 28, 41
Urotropine in biliary disease, 209

Vagotonia, 23
Van den Burgh's test, 64, 68
Vaso-motor disturbances, 227
Visceroptosis and gall-stones, 196
Vomiting, alcoholic, 120
in chronic appendicitis, 171
hysterical, 5
in pregnancy, 6
waterbrash, 120

Waterbrash, 120

X-ray examination of the colon, 139
of duodenum, 25
of stomach, 3
X-rays in diagnosis of chronic appendicitis, 172
of gall-stones, 203

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