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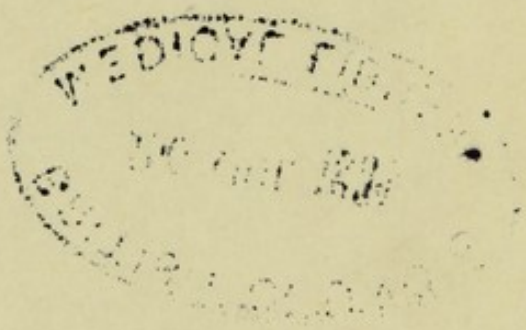

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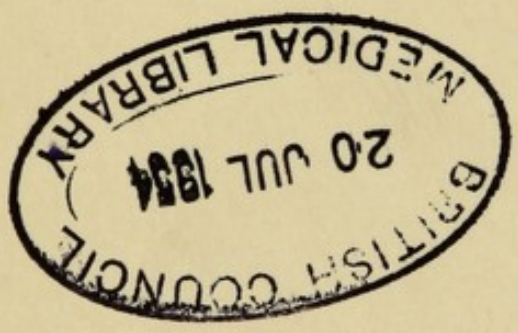

THE BIOLOGY OF MENTAL DEFECT

The Biology of MENTAL DEFECT

BY

LIONEL S. PENROSE, M.D., F.R.S.

WITH A PREFACE BY

PROFESSOR J. B. S. HALDANE, D.Sc., F.R.S.

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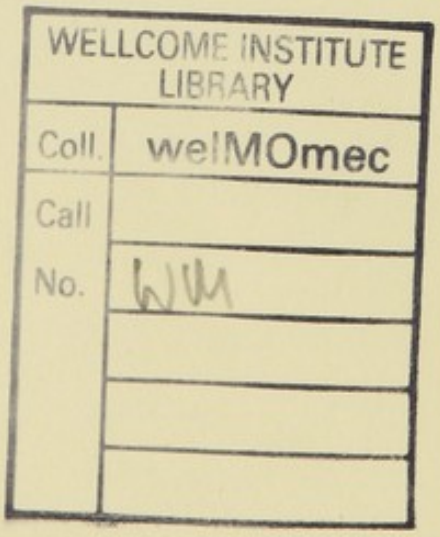

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PREFACE TO THE FIRST EDITION

I AM greatly honoured by Professor Penrose's request that I should write a preface to his book. Human abnormality, whether of a desirable or undesirable type, tends to generate violent emotions which are unfavourable to clear thought. As much nonsense has probably been written about genius as about idiocy, and as many men and women have perhaps been killed because they were too good or too intelligent as because they were too bad or too stupid.

The demonstration that some cases of mental abnormality were largely genetically determined led to exaggerated hopes of eugenical improvement. The demonstration that others could be improved by hormones, psychotherapy, or special teaching methods led to equally exaggerated hopes of another kind. Both schools of thought underestimated the immense complexity of the problem. This was first concretely shown in Penrose's now classical report (Colchester Survey) to the Medical Research Council in 1938, in which he demonstrated that mental defect could be due to a vast variety of different causes. There is nothing surprising in this. Everyone knows that visual defect is due to many causes, and that some kinds can be improved by spectacles, others by surgery, while yet others are at present incurable, though the incurable fraction is slowly decreasing. The brain is a vastly more complex organ than the eye, and can go wrong in many more ways.

A casual reader might well be discouraged by the final chapter of the book. We cannot do so much about mental defect as had been hoped in the recent past. Nor could we do as much about flying four hundred years ago as Leonardo da Vinci had hoped. But there is no reason to suppose that one problem is any more insoluble than the other. The solution of the problem of flight required the accumulation of a vast amount of data on very diverse topics during four centuries.

We do not know what data will be required. But among them

is certainly a knowledge of a great deal of normal human genetics. It must be emphasized that it is entirely normal to be the carrier of a recessive gene for some grave physical, chemical, or mental abnormality. Even where this is not so, the range of human variation is such that I believe very few normal married couples, if they could have a hundred children, would not have at least one seriously defective in one way or another.

At present we can neither stop such children from being born nor, save in a few cases, cure their abnormality. This is because we do not know how to do so. Even if we did, we might prefer to spend the necessary effort on the construction of greyhound tracks, jet-propelled bombers, or nylon hosiery. But no amount of good will, or of bad will (for some programmes have been motivated by a hatred of abnormality similar to that which led to the burning of choreics for witchcraft), would greatly reduce the number of such children born at present, nor make them normal, though many of them could be socialized to some extent.

We do not know what kind of knowledge we need. It is entirely possible, for example, that a suitable hormonal treatment of elderly mothers could halve the frequency of mongolism, or that a common gene exists so closely linked with that for Huntington's chorea that a simple test would often enable us to state which children of a choreic carried the gene responsible for the condition and which could safely marry. Neither of these possibilities is very likely at present, but neither can be dismissed. They would equally be a part of eugenics.

Apart from its practical aspect, I believe that the study of mental defect is of considerable philosophical importance. The question of why people are different or what determines their individuality is of the greatest interest, and to my mind is one of the questions which shows up the weakness of idealistic philosophies. It can be answered in a few cases. And the answers may be very surprising. "John Smith is a complete fool because he cannot oxidize phenylalanine" discloses a relation between mind and matter as surprising as transubstantiation, and a good deal better established. On the ethical side it raises the problem of human rights in a rather sharp form. Has a hopelesss idiot the right to life and care, though he or she is not a rational being nor likely to become one? If so, has a chimpanzee with

considerably greater intelligence similar rights; and if not, why not? If not, where are we to draw the line? Hitler gave one answer; Penrose gives a very different one.

I hope, therefore, that this book will not only be read by physicians, but by social workers and even by one or two of the Members of Parliament and Peers who have to frame the law as to mental defect and criticize its present administration. I think that it may claim to be as much a contribution to general culture as a book on primitive human societies or on other forms of incomplete human achievement.

I do not agree with every statement in the book. I do not suppose that Professor Penrose will do so ten years hence, for our knowledge of the subject is growing very rapidly. However, he has weighed the arguments in each case very carefully, and I know of no one better qualified to form a considered judgment.

I hope, therefore, that his book will not merely be used as a text-book by specialists, but will be recognized as a contribution both to thought and to humanism.

J. B. S. HALDANE

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FOREWORD

IN MY book on Mental Defect, published in 1933, an attempt was made to present the subject as one which provided great opportunities for scientific research. Methods suitable for application in this field were described and the social, medical and genetical aspects were distinguished. During the last fifteen years important discoveries have been made in medical genetics, many of which relate to mental defect, and new information has been brought to light concerning the social significance of low intellectual capacity. Consequently a need has arisen for reorientation of teaching, so that the problems of mental deficiency can be properly related to the rest of sociology and medicine.

The present book discusses mental deficiency from the point of view of human biology. The relevant subject-matter is so varied and extensive that it would be presumptuous for any single writer to try to deal with every aspect in detail. Indeed, to do so adequately would be equivalent to writing large sections of text-books on psychology, medicine, sociology and human genetics. To limit the task here, medical and psychopathological conditions encountered in mental deficiency practice are discussed chiefly within the framework of genetics. Full clinical descriptions of important pathological types of defect are given but some of the rarer peculiarities are only mentioned briefly. Since my approach to mental defect here is primarily biological, the practical administrative aspect of the subject is only sketched. Enough of the historical and legal background is explained, I hope, to enable the student properly to appreciate the vicissitudes of the concept of mental deficiency.

Since the compilation of a complete bibliography was not practicable, I have adopted the principle of providing references, most of which fall under one of two headings. Works of historical or basic interest are cited and also some which are typical of recent researches. The reader's indulgence is requested

if references to my own work are too frequently encountered. Many examples for demonstration purposes are taken from the Colchester Survey, carried out between 1931 and 1937 under the auspices of the Medical Research Council and the Darwin Trust, because these data were easily available to me. I wish to take this opportunity of thanking all those who have assisted in the task of preparing the manuscript of this book for the press, and, in particular, Miss Helen Lang Brown. Some of the photographs were kindly supplied by Mr H. Goodfellow and others by Dr E. D. Taylar. I am much indebted to Professor J. B. S. Haldane and to Dr E. O. Lewis for their helpful suggestions.

L. S. P.

Galton Laboratory,
University College,
London.
September, 1948.

During the course of five years there have been advances in the subject which have increased the understanding of both causation and treatment. A commentary on recent literature has, therefore, been provided together with additional references. At the same time the opportunity has been taken of making some corrections in the original text.

L. S. P.

September, 1953.

CHAPTER I

HISTORICAL BACKGROUND

Introduction—Early History—Extension of the Concept of Defect—The Advent of Mental Measurements—Comparative Nomenclature—Mental Defect as Social Incompetence—Defect and Instability—The Biological Viewpoint.

INTRODUCTION

MEN and women are not all alike in physical stature. Most of them vary within the limits which define a group popularly described as normal or average. A few are noticeably tall or noticeably short. In extreme cases the difference from the normal is so great that the man or woman qualifies to be called a giant or a dwarf. The same is true of intellectual stature. The bulk of the population is said to have normal intelligence but, undoubtedly, as with stature, a great deal of variation exists. Outstandingly clever people and very dull people are to be found in the general population. There are also giants and dwarfs of intellect. The one extreme has been exemplified by men of genius like Newton, Mozart and Darwin. The other extreme is represented by idiots who, in the most profound cases, cannot be credited with any mental processes at all.

Variation between individuals who are members of the same animal species is a biological rule to which the human race shows no exception. Different degrees of mental capacity are more noticeable and probably have a wider range in man than in animals. Domestic animals, such as dogs, are found to vary in mental ability, but the differences are difficult to measure. In man, unfortunately, very low degrees of intelligence are much more frequently encountered than the very high degrees at the other end of the scale, according to our ordinary, rather arbitrary, units of measurement. A great proportion of intellectual dwarfs do not survive to maturity; indeed, many of them do not even survive earliest infancy. In spite of this, the actual numbers

remain very large in this group and, biologically, it may be more interesting than the group formed by the intellectually brilliant.

EARLY HISTORY

A study of the history and growth of knowledge is helpful in the acquiring of a balanced outlook on the problem of intellectual defect. A useful source of historical information is the text-book by Barr (1904). In early times it seems probable that only the grossest examples of mental defect were considered remarkable. Even at the present day we find that, if relatively little attention is paid to mental health in any community, only the severest cases, idiots and imbeciles, are recognized. It is natural that provision for the care of the severest cases should be the first step when institutional accommodation is very limited.

The term "idiot", which now signifies only the most extreme cases of mental defect, formerly applied to the whole class of defectives. It is derived from a Greek word for a person who did not take part in public life. The same root is found in "idiom" and "idiosyncrasy". Originally the term applied also to untrained, ignorant or lay people, and it was used in this sense as late as the seventeenth century. "Imbecile", derived from the Latin *bacillus*, a stick, has always implied weakness, originally in a predominantly physical sense.

The ancients appear usually to have regarded idiots with aversion. In Sparta, under the laws of Lycurgus, the mentally defective probably shared the fate of other weakly infants, who were allowed to perish from exposure or were thrown into the river Eurotas. Among primitive peoples of the present day similar practices have sometimes been reported. The modern equivalent, politely called euthanasia, was carried out under the recent Nazi régime in Germany. There were ancient Roman laws, which provided for the killing of malformed or weakly children, though defectives were tolerated in Rome if they had value for amusement or diversion. In mediaeval times superstitions connected with witchcraft often determined harsh treatment for defectives. Some imbeciles were believed to be changelings without human souls. The rise of Protestantism did not at first tend to improve their status. Apparently Luther subscribed to the contemporary belief that the Devil was the father of idiots. It is recorded that on one occasion he recommended

that a twelve-year-old defective be drowned. His associates, however, appear not to have shared his opinions on this point. Possession by a demon or by an evil spirit was a theory easy to apply and difficult to disprove.

The early history of the subject is obscured by lack of discrimination between congenital physical deformity, such as produces cripples or dwarfs, and mental incapacity. Moreover, epileptics, psychotics and deaf-mutes have been frequently confused with the intellectually defective. The fact that these various conditions can coexist in the same individual often makes clinical analysis difficult even at the present day.

While some people interpreted the mutterings of idiots as conversation with the Devil, others believed them to be evidence of divine inspiration. In many communities defectives were regarded as especially innocent and holy. This attitude seems to have been more characteristic of Eastern than of Western cultures in early times. Both Confucius and Zoroaster in their writings instructed their followers to care for the weak-minded, to clothe them and to treat them kindly. The advent of Christian humanitarianism tended to improve the status of defectives in Europe. Under the rule of Constantine, the Bishop of Myra (the original Santa Claus) is said to have advocated protection of idiots. The term *crétin*, which is still used in France to cover many kinds of idiocy, is merely a corruption of *chrétien*, meaning Christian. The expression *les enfants du bon Dieu*, commonly applied to defectives, represented the same point of view. In England the early approach to the subject was more objective and, in the reigns of Edward I and Edward II, legislation was enacted to provide for the elementary management of an idiot or "born fool" (*fatuus naturalis*) and of his estate. A defective, moreover, was at that time distinguished from an insane person, whose mental capacity could fluctuate (*non compos mentis sicut quidam sunt per lucida intervalla*).

The medical and scientific study of defect began with the acceptance of defectives as belonging to the rest of humanity. Idiots are, in fact, members of the human race and, to a large extent, inevitable variants of the human species. Hippocrates described anencephaly and some other kinds of cranial deformity associated with severe defect. The inability of medicine to supply any plausible explanation or suggest any remedy for such

conditions, however, left the door open to superstitious speculation for many centuries. Even the earliest psychologists had little more than platitudes to offer. "The Defect in *Naturals*," wrote Locke (1689), "seems to proceed from Want of Quickness, Activity, and Motion in the intellectual faculties, whereby they are deprived of Reason." However, Locke did distinguish between defect and insanity. "In short, herein seems to lie the Difference between Idiots and Madmen, that Madmen put wrong *Ideas* together, and so make wrong Propositions, but argue and reason right from them; but Idiots make very few or no Propositions, and reason scarce at all." Early clinicians were not always so clear. "Ideotism", defined by Pinel (1806) as "total or partial obliteration of the intellectual powers and affections", was applied to cretins and other defectives and also to insane catatonic or stuporose patients.

Soon after the French Revolution, Itard's (1798) treatise on the wild boy of Aveyron initiated the practical scientific study of the psychology of defect. An unsuccessful attempt was made to educate a youth who had been found wandering in the forest. *Juvenis Averionensis* was the appellation supplied by the local professor of natural history, to agree with descriptions advocated by Linné, such as *juvenis lupinus Hessiensis*, 1544 (a young man found in Hesse among wolves) or *juvenis ovinus Hibernus* (a young man found among wild sheep in Ireland). Using methods established for training deaf-mutes by Périère, Itard was unable to educate his savage. However, he was able to give the first clear account of the psychology of a mentally defective person. The effect was to stimulate others to study the problem of educating the weak-minded, to find the potentialities of these unfortunates so that the best use could be made of their meagre mental resources. Séguin, a pupil of Itard, founded in 1837 a school for idiots in Paris. He was able to satisfy Pinel and Esquirol that it was worth while to pay more attention to defectives than had hitherto been thought necessary, and he was invited to apply his principles of training at the Bicêtre hospital. Thus, in keeping with the reforms which had been introduced into treatment of the insane by humanitarian psychiatrists, the status of the mentally defective was also raised. Esquirol referred to Séguin's mission as the removal of the mark of the beast from the forehead of the idiot.

Soon afterwards the need for providing special institutions for those persons who were obviously idiots was recognized in England. The training and care of these individuals was considered an eminently suitable object for charity. The philanthropist Andrew Reed expressed, in 1840, the hope that he might be allowed to do something for fellow creatures who were separate and alone but with "the Divine image stamped upon all". Largely owing to his efforts, the first asylum for idiots in England was founded at Park House, Highgate. It was a charitable institution under the patronage of Queen Victoria and the Prince Consort. "The principle which rules," said Reed, "is charity—Divine Charity." The success of the institution was so great that expansion was soon found necessary, and in 1849 Essex Hall, Colchester, was started as an annex for nearly a hundred patients with a view to teaching them simple mechanical employments. The remaining patients at Park House were all transferred to a newly built "model asylum" at Earlswood, Surrey, in 1855.

At about the same time Guggenbühl, whose sympathies had been specially aroused by the needs of the cretins and other dwarfs, common then in Switzerland, founded a training school for all types of idiots near the summit of a mountain close to Interlaken. It was thought that the pure atmosphere and the glorious panorama of nature's wonders at this site would help to awaken the dormant minds of the patients. As it turned out, Guggenbühl had promised too much. Ultimately his institution had to be closed and he himself was officially condemned as a charlatan. In spite of this, the impact of his philanthropic and experimental enthusiasm was felt in many countries. A more sober influence was that of Saegert in Berlin, who had formerly trained only deaf-mutes. He transferred his attention to the education of idiots, and in 1846 published a monograph on the cure of imbecility by intellectual means. In Saxony the persuasive powers of Ettmüller in 1844 led to the foundation of the first German state institution for the training of idiots; somewhat characteristically, attendance was made compulsory by law. Nevertheless, nearly all the institutions which sprang into being in Europe at this period were private organizations. They were usually charitable foundations, like the Alsterdorfer home near Hamburg, started by a minister of religion, Sengelmann, and administered by an unsalaried director.

In the United States a Commission was appointed in Massachusetts to enquire into the condition of idiots, under the chairmanship of Dr Samuel G. Howe, famous for his education of the blind deaf-mute Laura Bridgman. A similar commission was appointed in New York, with the result that, shortly afterwards, in both states, schools were opened in 1848. The teaching of defectives was modelled upon the European methods and Séguin was invited to assist in its development. In Pennsylvania, soon afterwards, the Elwyn Training School was opened, and again the directors received advice from Séguin, thus ensuring that the traditions of the earliest pioneers were maintained. In Ontario, Canada, an institution with similar objectives was started at Orillia in 1859.

Judging from the early reports of cases and the descriptions of training plans, most of the educational work was carried out on subjects who now would be considered to fall into the categories of idiots and imbeciles. That is to say, they were mostly quite ineducable in the ordinary scholastic sense, though many were able to be taught to converse, to be clean in habits and to enjoy simple games and occupations.

EXTENSION OF THE CONCEPT OF DEFECT

During the latter half of the nineteenth century the scope of training programmes was gradually extended to include the large number of cases whose mental capacities lay between the level of the imbecile and the normal range. The first investigator accurately to distinguish this group from the more severely handicapped cases appears to have been Duncan (1860), who wrote as follows in a report to their benefactors:

> "For all practical purposes, the objects of your Charity may be divided into three classes—simpletons, imbeciles and idiots. The first are those feeble-minded who have not been able to receive instruction in the ordinary manner, who do not possess the experience in life peculiar to those of their age in the social position and who are said to be 'dolts,' 'stupids,' and 'fools,' by the uncharitable. They have nearly all the faculties to a certain degree, but indicate their alliance to the true idiot by their physiological deficiencies and general inertia of mind. They are to be distinguished from the back-

ward and ill taught and unfortunately cannot always be said to be quite sane."

Since these cases were all to some extent educable, their inclusion widened the scope of the treatment of mental deficiency. The education of defectives began to merge with the ordinary scholastic problem of how to give the best training to backward children. The new problem was of quite a different nature from that involved in institutions in caring for children who could never be expected to take part in normal community activities. A great many of the simpletons might be expected, when trained, to be able to carry on as ordinary citizens. To achieve this end, special day schools for the education of the defective were founded in many countries. In England, the Idiots Act of 1886, which provided for the care of idiots and imbeciles, for example, was followed by the establishment of special schools by law in 1896. Mentally defective children between the ages of 7 and 16 were further provided for under the Elementary Education Act of 1899. In Italy, where provision for idiots had been tardy, day schools for training defectives, on principles advocated by the enthusiastic pupils of Montessori, were set up in several urban centres about the year 1899.

A British Royal Commission was appointed in 1904 "to consider the existing methods of dealing with imbeciles, feeble-minded or defective persons not certified under the Lunacy Laws". After four years the Commission (1908) reported that there existed in the community large numbers of mentally defective persons whose training was neglected and over whom insufficient control was exercised. Many were committed to prisons for repeated offences; many who did not require careful hospital treatment were to be found crowding the lunatic asylums; and also many were at large, both adults and children, who, in one way or another, were incapable of self-control and therefore exposed to constant moral danger. The Commission recommended the creation of a system whereby these mentally defective persons could at an early age be brought into touch with some friendly authority, trained as far as need be, supervised during their lives in co-operation with their relatives, or detained and in some measure treated as wards of the State. The Mental Deficiency Act, passed in 1913, embodied the main recommendations of the Commission.

THE ADVENT OF MENTAL MEASUREMENTS

It was not until after the invention of standardized intelligence tests that the true nature and extent of the problem of training the simpletons became apparent. Galton (1869) was among the first to suggest distributing intelligence, like other human characters, on a linear metrical scale ranging from idiocy to genius. He did not distinguish between potential capacity and actual academic or social success and he considered reputation to be an accurate measure of ability. His method is demonstrated in the following example, where he (Galton, 1889) distributed 1000 medical students, according to academic records supplied to him, in five classes. He rated 28 men distinguished, 80 considerable, 616 moderate, 151 with very limited success and 125 as failures. He made these comments: ". . . of the successful men, within fifteen years of taking their degrees, stood three Professors of Anatomy. . . . towards the bottom of the failures lay two men who committed suicide under circumstances of great disgrace, and the lowest of all . . . was hanged."

Intelligence as measured by Binet and Simon (1907), and by the more recent revisers of this test, was by intention closely related to scholastic success. The test provides a rapid method of ascertaining how many children in the population can be expected to need special education. It was primarily designed as an aid to teachers in the allocation of pupils to their correct grades or classes in schools. It was therefore scored in years and months of mental age. Children who would be likely ultimately to be economic and social failures in a competitive society could thus be distinguished at an early age, since success later on in life is closely related to educational aptitude. It soon became apparent that the numbers involved in this class were very large. In the United States, where psychologists and sociologists expended great energy on the problem, the group of mentally sub-normal people grew to prodigious proportions. Eventually the name "moron" was coined by Goddard to denote roughly the class described as simpletons by Duncan and subsequently called feeble-minded in England because the term "simpleton" was thought to be too derogatory.

COMPARATIVE NOMENCLATURE

It is convenient here to digress from the presentation of his-

torical facts and to draw attention to the nomenclatures which have developed in different countries to describe the different grades of defect. Confusion is apt to arise with the terms "high grade" and "low grade", which are widely used to connote relatively mild and severe cases respectively: i.e. a high-grade case is a mild one. Sometimes these terms are used to qualify cases within larger groups. For example, high-, medium- and low-grade imbeciles are occasionally differentiated for descriptive convenience. An important point to note is that, in the United States, the term "feeble-minded" now applies to the whole class of defectives whereas, in England, its use is restricted to the relatively high-grade cases. Scandinavian and German usage has favoured the expression "oligophrenia" to describe all types of mental defect. Several authorities in England and America also have recommended the general adoption of this cumbersome word. Other terms that have been used to mean the same thing are "amentia", "anergasia", "psychasthenia" and "phrenasthenia".

The roughly equivalent designations used in different countries are shown in Table I, together with the corresponding

TABLE I

NOMENCLATURE

Degree of Mental Defect	British	American	French	German	Approximate Binet Intelligence Level	
					I.Q. (children)	Mental Age in years (adults)
Mild (high-grade)	Feeble-minded	Moron	*Débile*	*Debile*	50–69	7–10
Severe (medium- or low-grade)	Imbecile	Imbecile	*Imbécile*	Imbecile, *Schwachsinnig*	20–49	3– 6
Severe (low-grade)	Idiot	Idiot	*Idiot*	Idiot, *Blödsinnig*	0–19	0– 2
All grades	Mentally defective, Amentia	Feeble-minded	*Arrièré*, *Oligophrénie*	*Geistesschwäche*, Oligophrenia	0–70	0–10

ranges of Binet intelligence-test level. Since children of different ages have to be compared, the Binet test score is usually expressed in the form of the intelligence quotient, an index which is almost independent of age between about 5 and 13 years. The intelligence quotient, or I.Q., is simply the measured mental age expressed as a percentage of the chronological age at the time of testing. For adults the intelligence quotient is not a valid concept. A fictitious base of about 14½ years of chronological age has to be used when the I.Q. of an adult is estimated. Some authorities prefer a base of 16 years and others use 14 years. Binet test scores for adults are therefore best expressed as mental age only.

There are special difficulties which arise in referring to the cases which are thought to be almost but not quite defective. Such terms as "mentally subnormal but not defective", "borderline" (*grenzformen*), or "mentally dull", "mentally retarded" and "poorly gifted" (*schwach begabt*) have been frequently employed, but their connotations are rather indefinite. In the early days, when only the idiots and other clearly abnormal cases were recognized, these distinctions between the different classes of higher grades did not come into consideration. There is fair agreement that the upper limit of idiocy should be set at a mental age of 3 years, or an I.Q. of about 20. The distinction between the imbecile and the feeble-minded or moron is less certain. The I.Q. of 45 is often used in England, whereas that of 55 has been suggested in America. The absolute upper limit of deficiency is commonly set at about the I.Q. of 70, but this criterion is subject to wide variations of interpretation. Some German authorities do not recognize the distinction between imbeciles and feeble-minded and place the upper limit of idiocy at a somewhat higher level than the mental age of 3. For instance, Weygandt (1936) considered that defectives should simply be divided into imbeciles and idiots according to whether or not they were capable of doing useful work (*geschäftsfähig*). The distinction between the borderline case and the normal is the most shadowy of all, because in this region the recognition of defect is based entirely upon the subject's social capabilities and these are not easily expressible in terms of mental age.

MENTAL DEFECT AS SOCIAL INCOMPETENCE

A new attitude became prevalent at the beginning of the

twentieth century, engendered by the appreciation of the large numbers that comprised the "moron" class. The defective was no longer an innocent sufferer deserving only pity. He was gradually becoming recognized as a menace. The growth of this idea has been well outlined by Davies (1930). "Morons," wrote Goddard (1914), "are often normal looking, with few or no obvious stigmata of degeneration, frequently able to talk fluently; their conversation, while marked by poverty of thought or even silliness, nevertheless commonly passes as the result of ignorance . . . yet they are the persons who make for us social problems." He stressed the close relationship of mental defect to pauperism, crime, intemperance and disease. The frequency of morons in the general population was estimated to be about 2 per cent., but among the delinquents, the paupers and those socially incompetent in other ways, the corresponding frequency was alleged to be 50 per cent. It thus became plain that mental defect was closely related to social incompetence. This realization led to a view of the subject which is generally accepted at the present time, namely, that whatever may be the individual's basic capacities, he is not to be considered mentally defective so long as he is socially acceptable. Legislation and practice both support this attitude.

An authoritative statement on this point was made in the British Report of the Joint Committee of the Board of Education and the Board of Control (Wood Report) in 1929, where a mentally defective individual was defined as "one who by reason of incomplete mental development is incapable of independent social adaptation". The Committee who prepared the report made the concept of mental defect more elastic than previous authorities had done, and drew attention to a group of the population alleged to be socially incompetent, amounting to 10 per cent., from which they considered most defectives, especially the feeble-minded or morons, originated. This lowest social group of the population was stated to include, "as everyone who has extensive practical experience of social service would readily admit", a much larger proportion of insane persons, epileptics, paupers, criminals (especially recidivists), unemployables, habitual slum dwellers, prostitutes, inebriates and other social inefficients than would a group of families not containing mental defectives.

In corroboration of this outlook, Lidbetter (1933) published a

large amount of data, which he collected in the course of social work, indicating that family groups of low economic status existed in the community. He showed that pauperism and poor mental and physical health were associated in many branches of these families and left the inference to be drawn that all these things were biologically inherited. Part of the association of these disabilities, however, seems to be due to the non-biological social law of inheritance of wealth, which also implies the inheritance of poverty in the same sense. Poverty used to involve diminished opportunities both for scholastic education and social training and also inadequate medical care. This point was not overlooked by Isserlis (1923), who attributed the low intelligence which he found in children poorly fed and clothed at least in part to the unfavourable environment associated with low economic status. The idea that 10 per cent. of the population are economically deficient, that is living in poverty, has its background in the social studies of Rowntree (1906) and of Bowley and Hogg (1925). The assumption that this part of the population forms a "social problem group", as understood by Blacker and others (1934), in which inborn mental defect is the chief determining characteristic, was not made by the earlier investigators. If mental defect is to be defined in terms of social incompetence, those relatively incapable of maintaining themselves economically in a competitive society are, by definition, mentally defective. The inference that the same people would be incompetent in a different environment or according to different standards is unjustified.

According to current British practice, mental measurements and clinical examinations are only relevant in so far as they help to decide the probable social value of the patient. In America a similar view is also generally held, and Fernald's ten points are commonly used as a guide rather than any single measurement. Under Fernald's (1917) system the physician must ascertain the patient's standing with respect to: (i) physical examination; (ii) family history; (iii) developmental history; (iv) school progress; (v) examination in school work; (vi) practical knowledge; (vii) social reactions; (viii) industrial efficiency; (ix) moral reactions; and (x) psychological tests, before deciding whether he may rightly certify the subject as mentally defective. It is possible to devise measurements of social competence, and Doll (1935)

recommends the use of a rating scale which can be scored in terms of "social age". If social competence is held to be the decisive criterion, it is logical to attempt its measurement though the task is beset with serious difficulties.

To the sociologist it may be an advantage to have a social criterion for defining a group, but to the biologist or psychiatrist such a definition is extremely unsatisfactory. Social criteria are not only changeable; they are relative, not absolute. Thus in a rural community scholastic defect is much less of a handicap than in a city. The requirements for success in industrial or commercial employment are very different from those on a farm, a quarry or a ranch. A good fisherman, herdsman or lumberman need not have many scholastic attainments, and if such workers were selected on account of scholastic successes, the results would probably be disastrous. A person whose abilities are entirely confined to clerical work is likely to be a failure in a community where manual work is the only means of livelihood. Not improbably, the gradually increasing importance of industry and commerce and of clerical and other technical occupations during the last hundred years has been a decisive factor in bringing the problem of feeble-mindedness into the foreground. Idiocy and imbecility are defects sufficient to cause social failure in an agricultural community, but the scholastically incompetent person is especially likely to be a social problem in an urban community.

DEFECT AND INSTABILITY

There are other causes of social failure of quite a different nature. It is convenient, though not absolutely free from logical error, to distinguish between mental defect and mental disorder. The symptoms of mental disorder include neurotic manifestations, hysteria and obsessions, psychopathic personality, depression, mania, paranoia, schizophrenia, confusional states, organic dementia and epilepsy. Any of these conditions may occur as superimposed phenomena in cases of mental defect. In some instances they may be part of the same disease process which has also caused the defect, and, when this is so, clinical differentiation of the coexisting defect and disorder may be impossible. Mental disorder is undoubtedly a frequent cause of social failure. If it appears early in life, say before the age of 18 years, it

is liable to be classed with defect from the administrative point of view. Indeed, selection of cases for institutional treatment is strongly biased by the tendency to certify, and hence to remove from the community, just those cases of defect in which symptoms of disorder are present. Thus the criterion of social failure—so simple and practical from the sociological and administrative points of view—leads to unreasonable complications when the matter is considered from the aspect of medical or biological science. The danger of confusion is not great if the discussion is limited to idiots and imbeciles but, in the discussion of feeble-mindedness or of the "moron," the great variety of standards on which social failure may be judged must constantly be kept in mind.

THE BIOLOGICAL VIEWPOINT

From what has been said it is now easy to see that a question such as, "What is the cause of mental defect—is it inherited and, if so, to what extent?" cannot be answered directly. The person who asks such a question exposes his ignorance by his underrating the complexity of the biological subject-matter. Mental defect, we are told, is equivalent to social incompetence. To obtain a proper understanding of mental defect, the conditions, which are present in those cases of social failure classified as defectives, must be analysed. The biological, psychological and medical background of each factor must be examined separately. My aim in the present book has been to try to do this and at the same time to discuss the methods by which such analysis can be carried out. Since many of the conditions leading ultimately to social failure are found in the early life of the individual, sometimes before his birth, the study of genetics will play an important but by no means exclusive part in their description. Social scientists, whose preoccupation is with economics, law or political philosophy, are liable to forget that man is an animal and to neglect the biological problems which underlie the structure of human society. No apology is needed for making an attempt to redress the balance by emphasizing the importance of human biology in the elucidation of the phenomena of mental defect. Before beginning a detailed clinical and genetical survey of this problem, however, more must be said about the definition and extent of the field and about the social and psychological background of the modern concept of mental deficiency.

CHAPTER II

INCIDENCE, DEFINITION AND MEASUREMENT

Crude Incidence—The British Royal Commission of 1904*—Mental Deficiency Acts—The Survey of* 1929*—Comparison with other Surveys—Distribution of Intelligence Test Scores—Male and Female Distributions—Intelligence and its Measurement—Cultural Differences in Intelligence—Sense Deprivation—Physical Measurements—Head Size and Brain Weight—General Physique—Stigmata of Degeneration—Mental Defect and Socio-economic Status—Military Criterion of Defect.*

CRUDE INCIDENCE

STATISTICS are, or have been, available in many different countries showing the number of persons assigned to institutional care under the category of mental defect. Great discrepancies are noticeable when the returns of different countries are compared with one another, and they are due to social rather than to biological variations. In any locality the number of cases certified is limited by the provision of institutional beds. The extent of such provision, in its turn, depends upon the attitude of the civilization concerned towards defectives, the wealth of the citizens and their desire to use their means in this particular way. The number of beds provided never exceeds a small fraction of the number of persons who could reasonably be certified defective, if so desired. Hence the statistical return of certified cases must not be taken as a measure of the actual biological frequency of mental inferiority in a given population. The very reverse can be true, namely, that, unless the general level of intelligence is high, only a few of the most pronounced cases of defect are differentiated from the normal population.

A great deal depends upon the legal definition in force in the area concerned. Beyond this, the manner of interpretation of laws is subject to local practical needs. In many countries no specific differentiation is made between defective and psychotic patients, and even where such distinction is made, as in England,

many cases of defect drift into hospitals for the insane. Furthermore, other types of institutions, such as homes for paupers, for the infirm or for the destitute, as well as prisons and reformatories, undoubtedly contain their varying proportions of defective inmates. Sometimes charitable or private institutions do not supply figures for official returns. Table II shows samples

TABLE II

Name of Country	Approximate Population (in millions)	Inmates of Institutions for the Mentally Abnormal (about 1935)			
		Numbers (in thousands)		Incidence in Population (per thousand)	
	n	*i*	*d*	*i*/*n*	*d*/*n*
		Insane	Defective	Insane	Defective
England and Wales	40·00	150·3	38·8	3·75	0·97
Scotland	5·00	18·4	2·9	3·78	0·58
Denmark	3·70	9·2	5·4	2·47	1·46
Sweden	6·20	18·7	5·3	3·00	0·85
U.S.A.	127·50	409·6	80·4	3·21	0·63
Switzerland	4·15	13·4	2·1	3·21	0·51
Canada	11·00	30·6	7·7	2·80	0·70
Germany	66·40	130·5	28·9	1·96	0·44
France	41·80	86·3	10·4	2·06	0·25
Norway	2·80	5·4	0·3	1·93	0·11
Italy	42·20	75·1	8·3	1·77	0·20
Finland	3·67	6·0	0·0	1·62	0·01
Japan	97·70	15·6	0·7	0·16	0·01

of figures, collected by the present writer (1939*c*.) from the official reports referring to the year 1935 or, in some cases, a slightly earlier year. The incidence of certified defectives varies from zero to over 1 per thousand. It runs parallel, though somewhat irregularly so, to the incidence of patients certified insane. In countries where relatively few beds, i.e. less than 2 per thousand of the population, are provided for every type of mentally abnormal person, little attention is paid to mental defect as a separate entity. When this is so, there may be no separate hospitals for defectives. Even in countries which make considerable provision for defectives there remains the problem of how to deal with patients who are psychotic or epileptic and also defective. These patients are often classified primarily as insane or epileptic, as this is considered the major factor of

importance, but differences in administration lead to unavoidable ambiguities of interpretation of the figures.

The incidence of cases of mental defect in a general population can only be ascertained by a survey directed specifically to that end. The actual number of defectives ascertained will depend upon the criterion used for defining the group. It will also vary with the degree of thoroughness with which the work of the survey is carried out. Again, the number will depend upon the representativeness or otherwise of the population sampled. An important factor in the sample is the age composition of the population investigated. The standards applied to different age groups may be quite different, whether they concern intellectual or social achievement. The same standards, moreover, may not apply with equal force to the two sexes. Finally, the selective effect of the relatively high mortality rate of defectives must be considered.

THE BRITISH ROYAL COMMISSION OF 1904

The first large-scale attempt to count the total number of mentally defective persons in any community was undertaken under the auspices of the British Royal Commission in 1904. Instructions were given to medical men in selected districts to visit schools, hospitals and institutions of all kinds and, further, to make enquiries of clergy, local medical practitioners, charity organizations and the police, with a view to ascertainment of all cases of defect. The criteria of defect used in the survey were both educational and social. The incidence in the general population, inferred from this investigation by Tredgold (1908), was 4·6 per thousand. Since the patients were not compared with the numbers in the general population by age group, very little of biological interest can be gathered about the true frequency of defectives. From the administrative point of view this figure was valuable because it provided an estimate of the upper limit for the number of people likely to require special educational or institutional provision. All such cases can be said to be "potentially certifiable", but not "certifiable" in a strict sense because, according to some interpretations, no case can be actually certified unless the need for care and control is evident to the physicians and magistrate concerned. The relation between certifiability and insanity is similar. Referring to

the Lunacy Act of 1857 in his evidence to the Royal Commission, Clouston remarked, "The only definition of insanity in this country is that a case is certified by two doctors." Nothing could indicate more clearly the danger of accepting legal procedure as a criterion for use in the scientific study of mental abnormalities.

MENTAL DEFICIENCY ACTS

The British Mental Deficiency Act of 1913, which followed the report of the Royal Commission, was amended in 1927 and is still in force. Definitions of defectives have been laid down, and, though they may be administratively convenient, they are of no assistance to the biologist. First of all, for general purposes,

> "Mental defectiveness means a condition of arrested or incomplete development existing before the age of eighteen years, whether arising from inherent causes or induced by injury."

Four subdivisions of mental defectives were also specified, idiots, imbeciles, feeble-minded persons, and moral defectives.

In practice, the category of moral defect is rarely used and the differentiation of the other three types is more often made on grounds of intellectual level than upon agreement with the legal prescription. In the case of the feeble-minded, however, the interpretation of the Acts usually insisted upon is that no adult can be certified in this class unless the need for care, supervision and control is combined with insufficient protection for themselves or for others. The Local Education Authority is responsible for finding all children in its area who come within the definitions laid down in the Acts, and is obliged to make special provision for their education. Defectives of any age who are found neglected, abandoned or otherwise in need of help, as well as those found guilty of criminal offences, are dealt with by the Local Mental Deficiency Authority.

Less elaborate legal definitions are found to be efficient in the United States and Canada. The Mental Hospitals Act of Ontario (1937) defines "mental defective" and "mentally defective person" as "a person in whom there is a condition of arrested or incomplete development of mind, whether arising from inherent disease or injury, and who requires care, super-

vision and control for his own protection or for the protection of others."

The British Education Act, 1921, defined mentally defective children as those incapable of receiving proper benefit from instruction in the ordinary schools by reason of a defect of mind. Those in whom the defect does not amount to imbecility have to attend school up to the age of 16 years, and special schools or classes are provided for their reception and instruction. The criterion of defect here is, primarily, inability to achieve the necessary scholastic standard. A child who is more than two years retarded in school work is considered a candidate for the designation of mental defect and one who is three or more years retarded can almost certainly be so classified. Tests which measure scholastic ability are very valuable aids to diagnosis. Even so, a child's good or bad behaviour is a factor which tends to enter into the assessment. Hence special schools for defectives, instead of being training places for the intellectually backward, have tended to become dumping grounds for especially troublesome backward children, together with those who are so obviously ineducable that their parents cannot reasonably object to their being removed from the ordinary classes. Thus, the fact that social behaviour enters into the diagnosis of defect during the school age period tends to maintain the stigma attached to defect and seriously diminishes the usefulness of the special education provided by the Local Education Authorities. The following figures (Table III), derived from Lewis (1929), summarize the educational locations of ascertained cases of defective children. Some four-fifths of all the feeble-minded children and even one-quarter of the imbeciles and idiots were attending ordinary school classes.

TABLE III

ALL DEFECTIVE CHILDREN ASCERTAINED IN SPECIFIED AREAS (Lewis, 1929)

Feeble-minded	Imbecile or Idiot	Total	Location
1638	131	1769	Public elementary or private school.
124	58	182	Special school.
138	112	250	Institution.
191	212	403	At home.
2091	513	2604	All locations.

In 1944 a revised Education Act replaced that of 1921. The Local Education Authority now has the duty of ascertaining all children over the age of 2 years, who require special educational treatment, and the objectionable term "defective" has been dropped.

THE SURVEY OF 1929

A second survey of the incidence of mental defect in the general community in England and Wales was carried out by Lewis (1929) for the Departmental (Wood) Committee. The object again, as with the Royal Commission of 1904, was to ascertain the extent of the problem to be dealt with from the point of view of the administrators of the Mental Deficiency Acts and also of the Education Acts. Lewis had therefore to discover the frequency of all cases which were "potentially" certifiable or notifiable under either code. Imbeciles, idiots, feeble-minded and the educationally and morally defective, as defined by the Acts, were included. A very detailed and complete survey was made in six districts which were representative samples of the whole community. The results can be briefly summarized by stating that 8·57 persons per thousand in the general population were found to be mentally defective. The contributions of the categories idiot, imbecile and feeble-minded to this total were roughly in the ratio 5 : 20 : 75.

Some of the most significant points of the investigation remain concealed unless the age grouping of the ascertained cases is taken into account. Table IV has been constructed from the figures given in the Wood Report. Although the totals indicate that the general incidence is 8·6 per thousand, there are remarkable fluctuations shown when age groups are separated. The incidence represents a complex relationship between social and educational needs and the biological constitution of the population at each age. In early life defectives are difficult to recognize except in extremely severe cases and, up to the age of 4 years, the child is not called upon to perform any duties of significance to the community. Its mental condition is considered to be the concern of its parents. During the school period, however, intellectual deficit is brought sharply into the foreground. Between the ages of 10 and 14, moreover, accurately standardized tests can be applied to determine the degree of intel-

TABLE IV

INCIDENCE OF DEFECTIVES BY AGE GROUPS

(Figures derived from Tables 2 and 17 of the Wood Report, 1929.)

Age Group (years)	Population Sampled (in thousands)	Defectives Ascertained	Incidence (per thousand in population)
0– 4	57	69	1·2
5– 9	57	882	15·5
10–14	58	1486	25·6
15–19	57	617	10·8
20–29	102	860	8·4
30–39	91	515	5·7
40–49	82	441	5·4
50–59	60	294	4·9
60+	59	170	2·9
Total	623	5334	8·6

lectual capacity. In this range the ascertainment, if so desired, can be done solely by psychometric tests. After the end of the school period, the proportion of defectives suddenly drops because the rigid standards of scholastic environment no longer apply and there are more opportunities for adjustment by choosing suitable employment. Thereafter, as age advances, the continuous falling off of the incidence of ascertained defect may be due either to lack of standardized tests for adults or to selective mortality favouring the normals. The peak of incidence occurs at the age of 12 years; at this point it rises to 30 per thousand, or 3 per cent.

COMPARISON WITH OTHER SURVEYS

Investigations in countries other than England have been made to determine the frequency of defectives. As might be expected, the results are not very consistent. Binet and Simon (1907) quoted the findings of a ministerial commission in France which reported 1 per cent. of boys and 0·9 per cent. of girls to be defective. They also mentioned that other authorities had given much higher estimates: Vaney suggested 2–4 per cent. and Thamin and Abadie 5 per cent. for the proportion of defective children of school age.

American estimates, based on the testing of school-children, usually have varied between 2 and 3 per cent. Naturally much

depends upon definitions. As Yerkes (1921) pointed out, according to a current definition that anyone with a mental age of 12 years or less was defective, almost half the white males drafted into the American army in 1917 must have been defective. If, however, a mental age of 8 were taken as the limit, less than 2 per cent. would fall into the defective group. Of the children entering school for the first time in Massachusetts, 2·6 per cent. were considered to be defective and 11·2 per cent. retarded though not defective, by Dayton (1939). The figures are liable to differ widely in different States or localities. The Scottish Survey (1933) led to an opinion that more than 1·5 per cent., but not so many as 3 or 4 per cent., of school-children were to be found in the mentally defective category. Dahlberg (1937) estimated that 3 per cent. of boys and 1·7 per cent. of girls in Sweden required education in special classes for the mentally defective.

DISTRIBUTION OF INTELLIGENCE TEST SCORES

So long as social valuation enters into the criterion of estimation there is little hope of obtaining figures which can be of immediate scientific value. To a large extent, however, this objection is avoided by the use of standardized mental tests. The same test can be applied to different populations without prejudice. A limiting performance can be agreed upon below which scores can be said to indicate defect. Naturally, the result of defining the group of mentally subnormal children in this manner will differ from the results of classifications based upon general behaviour.

One of the earliest studies on the distribution of test scores was made by Jaederholm in Stockholm. The figures, analysed by Pearson (1914), brought out clearly the fundamental nature of the problem. A group of children, considered to be feeble-minded and on this account excluded from the ordinary public schools of the city, was examined with a modification of the Binet test. A sample of the total population of children was also available. Several important points became clear. First, it was shown that the distribution was absolutely continuous over the whole range of scores. There was no indication whatever of a natural boundary between the normal and abnormal distributions. Secondly, if the diagnosis of defect had been made solely

on the test scores, a somewhat different group would have been selected as abnormal from that which had actually been chosen. There was, indeed, a strong correlation between the criterion for defect and the test score, about +0·8. However, since the correspondence was not perfect, there was a large overlap between the test scores of the two classes. Finally, the distribu-

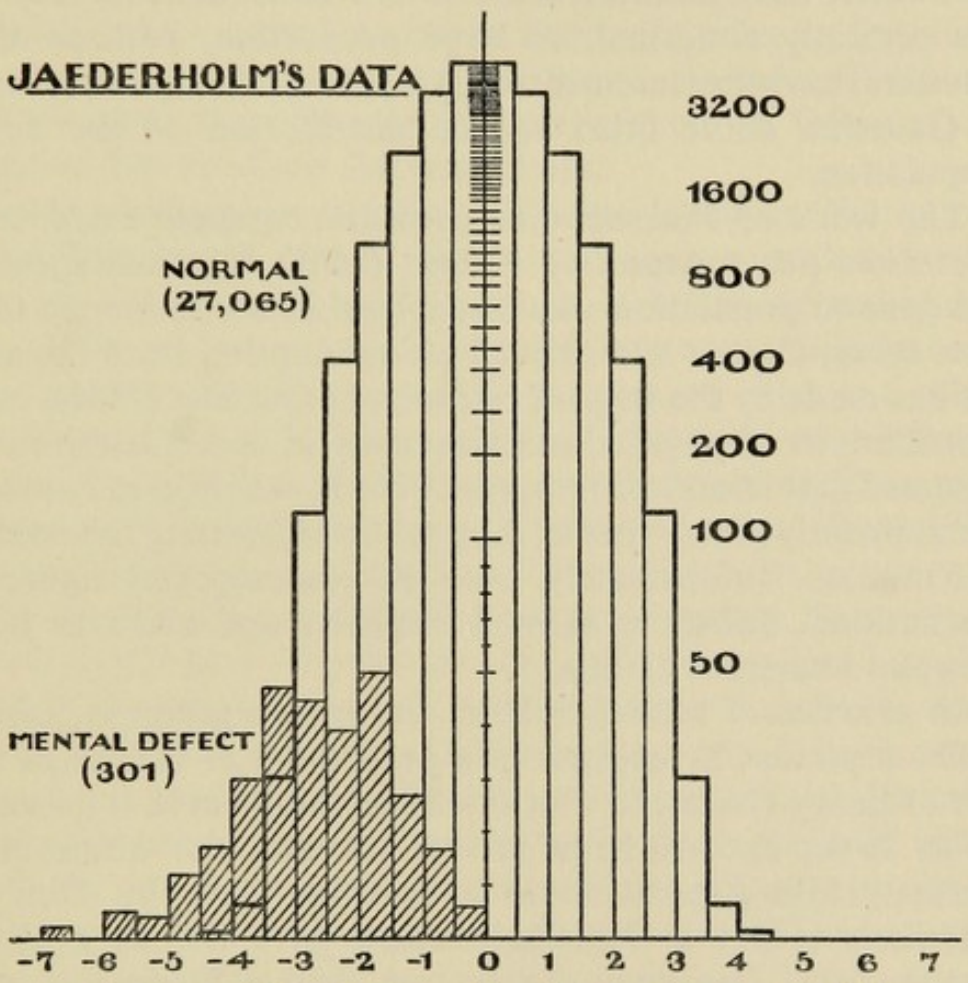


Figure 1.—Distribution of intelligence (Pearson, 1931)
Estimate based on Binet test of 301 defective and 261 normal children.
(Standard deviation = ±1.)

tion of intelligence scores in the general population approximates to the "normal" or Gaussian form. Thorndike (1925) made an extensive study on this point and on the whole he agreed with this conclusion. No very striking results follow from the observation, which merely indicates that the measurement of the character in question is determined by a multiplicity of small causes which can each act at random positively or negatively.

These findings are well illustrated by Pearson's diagram, Figure 1. The picture is very similar to that obtained for

measurements of stature in the general population. In both cases the main bulk of the population falls within the limits of twice the standard deviation. Mental dwarfs or, in the case of stature, physical dwarfs with measurements below these limits can be arbitrarily excluded from the normal population. Nevertheless, only a relatively small proportion of defectives, or dwarfs, have measurements so low as to indicate that they are certainly abnormal. A large proportion, perhaps three-quarters, have measurements which still can be contained under a Gaussian curve fitted to the distribution of the normal population.

The work of Pearson thus provided concrete evidence for the views put forward by Galton (1869) that intelligence in the general population was distributed in a continuous Gaussian curve. Galton had derived his assumption from the calculations made by the Belgian astronomer Quetelet (1846), on the distributions of physical measurements in men. Galton further assumed that idiots and imbeciles were about equal in number to the eminently gifted, that is, each group amounting to about 250 per million. Unfortunately, even the contemporary figures for institutional defectives showed imbeciles and idiots to be ten times as numerous as this.

In samples of school-children the lowest group is liable to suffer depletion by absence of a proportion of defectives from the ordinary classes, so that the distribution curve is inaccurate at its lower end. A large survey, covering the whole of the normal child population in a specified area, by Duff and Thomson (1923) in Northumberland gave rise to a slightly asymmetrical frequency distribution with a hump just above the mean value and a tail straggling into the minus scores. This skewness of distribution may have been due to some irregularity in the scoring of the tests rather than to any natural peculiarity in the population. A complete survey (Matthews *et al.*, 1937) of all the children of school age living in one small rural district gave rise to a similarly skewed distribution. In this district, 6 children out of 187, or 3·2 per cent., had scores deviating by more than twice the standard deviation below the normal value for the general population.

The distribution of Binet scores, expressed in terms of intelligence quotients, is usually found to be fairly symmetrical.

This was demonstrated by Terman (1916) and has been confirmed more recently by Roberts, Norman and Griffiths (1938). A sample of 192 subjects from a survey made in an urban centre, embracing the complete child population of certain age groups was analysed. Roberts considered that the distribution of I.Q. was Gaussian, with mean almost 100 and standard deviation 15 points. The Gaussian form of the distribution was thought to extend as far as about three and a half times the standard deviation below the mean. Quetelet (1846) had demonstrated that the distribution of stature followed the Gaussian law to about the same limits.

If we choose to assume the reality of a Gaussian distribution for intelligence, we can decide that any score outside twice the standard deviation from the mean is to be considered exceptional. This enables us to define exactly how many children come into this class, that is to say, 2·27 per cent. at either end of the scale. The standard deviation calculated for random samples of the child population by different observers varies from early estimates of 13 points (Terman, 1916) and 12 points (Burt, 1922) to larger estimates based on more comprehensive samples, such as the Scottish Survey (1933), of 16 to 17 points. Terman and Merrill (1947) gave 16 points as correct for the revised L and M forms of the test, but Terman (1925) assumed that for the Stanford Revision the value was 15 points. If we then take the mean I.Q. of the population to be 100 and the standard deviation exactly 15 points, we can conveniently place the I.Q. below which the scores are to be considered exceptionally or abnormally low at 70, or $100-(2\times15)$. Scores over 130 can be considered exceptionally high.

When tests are used which are not scored in terms of mental age, the I.Q. cannot be obtained directly. However, the scores of any test can be expressed in terms of the standard deviation calculated from a random sample. If so desired, the score of plus or minus one standard deviation can be arbitrarily defined as equivalent to 15 points of I.Q. above or below 100. In this way the I.Q., preferably referred to as "mental ratio", could be defined, like the nautical mile, as a convenient constant unit of measurement. It would be correct when applied to Stanford-Binet results and approximate for any other test of intelligence.

Two equivalent scales are shown in Figure 2. A curve giving the probable approximate distribution of Binet intelligence quotients in the general population, within the age group 10

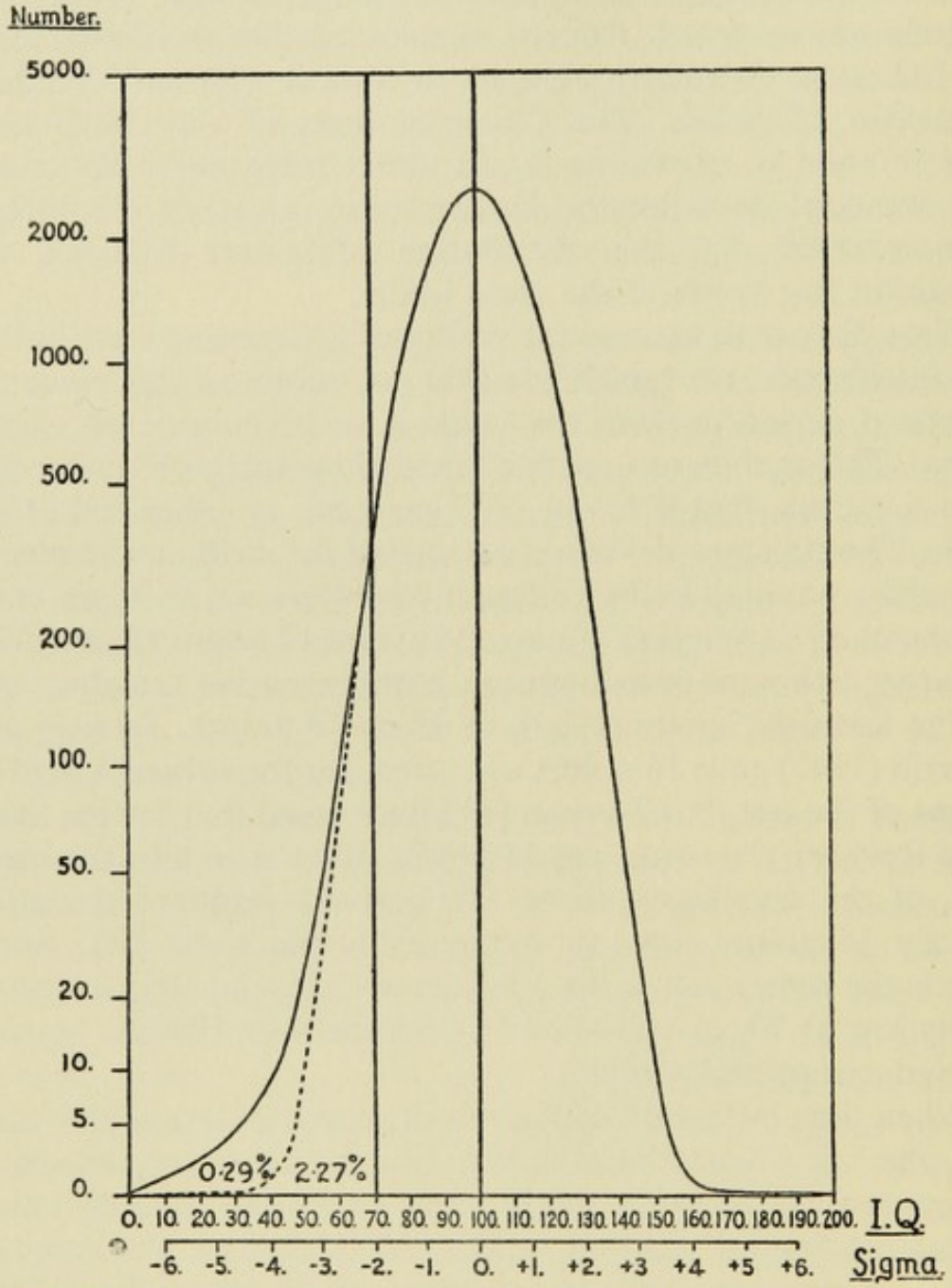


Figure 2.—Theoretical distribution of intelligence test scores for the age group 10 to 14 years in the total population

to 14 years, has been drawn. The ordinate, y, is expressed in a logarithmic scale of the type $\log (1+f)=y$, where f is the frequency of each I.Q. value. The whole distribution is slightly skewed. If we remove a segment of the population, who score

less than 70 or are beyond $-2\,\sigma$, we shall actually remove rather more than exactly the 2·27 per cent. whose measurements would be included under a Gaussian distribution. The tail of the actual distribution, based partly on estimates given by Lewis and partly upon I.Q. ratings for this age group, obtained by the Massachusetts Department of Health, extends to zero. A total population of 100,290 would include about 2560 cases below the 70 line. The Gaussian distribution in the table covers 99·7 per cent. of the total population, leaving 290 outside its confines. Also the Gaussian population includes 2270 of the group who are, on the basis of test measurements, mentally defective. The curve shown in the figure is, of course, only one theoretical explanation. A single skewed curve might be found to cover the whole distribution accurately (see also page 45).

MALE AND FEMALE DISTRIBUTIONS

There is general agreement among different observers that the distribution of intelligence test scores for males is more widely scattered than it is for females. Terman (1925) showed that, on the Binet test, there were more boys than girls in the highest scoring groups of children. There appear also to be more males who have very low scores. The effect can be expressed succinctly by saying that the standard deviation of intelligence scores is usually found to be greater for boys than for girls. In the Scottish Survey (1933) the difference was as 17 points to 16. Similar findings were reported by Duff and Thomson (1923), and Roberts (1945) stated that boys were 13 per cent. more variable than girls on intelligence tests. Thus, if males and females are to be judged on the same scale, we shall expect to find a preponderance of male defectives in the extreme, or low grade, groups. In fact, most large surveys do show such a peculiarity. Lewis (1929) reported a high incidence in males, especially in the low grades.

The excess of male idiots and imbeciles is liable to be counterbalanced by a converse excess of females of feeble-minded, or moron, grade, as in Pollock's (1926) data. It is difficult to be certain whether or not this effect represents a genuine biological difference between the sexes. The recognition of an excess of male institutional cases might be due to some form of social selection, e.g. if male cases are more difficult to look after at

home than females. This view is supported by Wildenskov (1942), who found that 60 per cent. of institutional cases in Denmark were males. The excess of females recognized to be feeble-minded could also be due to a relative lack of social tolerance for women in this grade as compared with men. Furthermore, since intelligence tests are devised mainly by males, their content may favour the success of males at the top end of the scale. In spite of these possible sources of error it seems best to accept the data on their face value for the present and to assume that males are really rather more variable than females with respect to mental capacity. In the analogous case of stature, males show slightly more variation than females. As pointed out by Pearson (1897), this difference disappears if the greater average stature of males is taken into consideration and the coefficient of variation used instead of the absolute standard deviation. The same property is found for head measurements of adults. If we confine ourselves to the absolute measurements in all these characters, as we do in the case of I.Q., the male is found to be the more variable sex.

INTELLIGENCE AND ITS MEASUREMENT

It is generally assumed that the tests devised and used by psychologists measure something closely allied to the criteria of social and scholastic efficiency by which we judge mental defect. Many psychologists prefer to be more definite and to assert that there is a quantity, "general intelligence", which can be estimated in every individual and that this quantity is the true index of mental defect, normality or mental superiority. That is a convenient assumption. Intelligence, as considered by Spearman (1927), is an abstraction like the idea of size. Intelligence tests measure Spearman's "g" in the same way as a measurement of length, breadth or girth might be used to estimate an abstract quality of an object, which we could call its size. The fact that we have a number of mental tests available, which are positively correlated with one another, only tells us that these tests have some property or properties in common. Any three tests by themselves define a "g" of some sort. With a larger number, the "g" cannot be precisely defined. The assumption that we are actually measuring one thing, general intelligence, agrees reasonably well with the known facts about

testing. As Thomson (1939) has repeatedly pointed out, it is the simplest assumption to make, but it is not the only explanation and probably not the correct one. The skill with which mental tasks are performed is due to a large number of small causes, some environmental and some hereditary. In discussing general intelligence we must remember that its existence is only a convenient hypothesis. The facts are the test scores. To be precise, we should only speak of ability of each subject on a given test and not of his intelligence level.

CULTURAL DIFFERENCES IN INTELLIGENCE

The concept of general intelligence tends to become strained when people with very different cultural backgrounds are compared. The traditional idea of separating mankind into constituent races each endowed with a particular set of mental qualities has received little support from the findings of modern genetical research. Qualities known to be determined genetically are distributed throughout all groups of mankind. The question of distinguishing races genetically has been resolved into the identification of the same genes in different populations. The populations are then distinguished by differences in gene frequencies. The A.B.O. series of inherited antigens shows marked gene frequency differences in populations all over the world, but the M.N. types are more evenly distributed. No qualities have been found to occur in every member of one racial group and in no member of another. The differences between races in respect of measurable qualities are often found to be much less than might be commonly supposed. Morant (1939), for example, showed that differences between means of physical measurements among the so-called European races were small and often statistically negligible.

Few people have attempted to justify Langdon Down's (1866) scheme for the ethnological classification of idiots. The clinical entity of "mongolism" was described, but it had nothing to do with racial Mongolians. Microcephalics were thought to be related to an Aztec race. A rather indefinite negroid type was included in the list, to which Davenport (1944) has recently drawn attention, and also a Malayan type.

A tendency sometimes has appeared in modern times to reverse the direction of Down's philosophy and to suggest that

some racial groups are altogether less intelligent than others. Porteus (1931), for example, found that Australian native adults were inferior to white or Asiatic children in test performances. Such field studies encounter great difficulties and require to be interpreted with caution. Marked discrepancies between scores on all kinds of tests have been found when white and coloured populations of the same country have been compared. The result, in the United States, is that proportionately far more coloured than white children could be classed as mentally defective. There is also more illiteracy among the coloured population and ability to do tests is strongly influenced by educational background. Analysis of the army intelligence tests (Yerkes, 1921), applied to large numbers of males in 1917, showed that some racial or cultural groups were much more capable than others. For example, at every camp, the mean scores of whites were superior to those of negroes but a striking feature of the results was the large amount of overlapping in the distributions. Negroes from northern states, such as New York and Ohio, however, were superior to whites from the southern states, Georgia, Arkansas, Kentucky and Mississippi (Garrett, 1945).

Even where culture is fairly homogeneous, as in Jamaica, Davenport and Steggerda (1930) found distinct differences between white, coloured and intermediate groups in the adult population. The selection of subjects was not random, so that their conclusions are open to criticism (Hogben, 1931*a*). The coloured group, however, was found to be definitely superior in mental arithmetic. The white group was superior in most verbal tests and in general knowledge. In tasks related to musical ability, coloured children and adults were at least equal to corresponding white subjects, though whites excelled at drawing. Interesting results have been obtained with American Indian children: the mean score of a group on Binet tests was much lower than that of Europeans of the same ages, but they did significantly better than European children on the Porteus maze test (Sparling, 1941).

The Porteus test is less closely correlated with educational capacity and more strongly correlated with industrial capacity than the Binet (Berry and Porteus, 1920). If some other test than the Binet, involving more "performance" and less scholastic knowledge, were used to pick out defectives, a group

would be selected whose personnel in the higher grades would be very different. The practical value of the scholastic type of test is mainly due to its use in estimating just those qualities which make adjustment in a highly industrialized civilization easy or difficult. Tests dependent upon special sense discrimination are not used for the diagnosis of defect, though it is possible to imagine a civilization in which the recognition of tunes or colours was as important as, say, arithmetic is to us. Some brilliant scholars are less capable of recognizing common tunes than are most imbeciles. No amount of intelligence can enable a colour-blind person to appreciate colours which he cannot physiologically perceive.

SENSE DEPRIVATION

Cases of sense deprivation are in some ways analogous to people with cultural habits foreign to the community. They must not be confounded with the intellectually defective. The ordinary intelligence tests do not work well with deaf or blind subjects and it is often very difficult to estimate correctly the true comparative I.Q. level. Such patients are sometimes more intelligent than they at first appear to be, and the same is true for some of those physically handicapped by paralysis from an early age. Performance tests can be used for children handicapped by deafness. With the blind, verbal reasoning and memory tests are applicable (Hayes, 1941).

The physically handicapped person needs, in general, to have a greater mental capacity than the physically normal to reach an equivalent level of social adaptation and usefulness. Pintner (1931) found that the average amount of scholastic retardation in congenitally deaf children was 2–3 years. Blindness also causes retardation, but in a lesser degree. The rare misfortune of blindness coupled with deafness necessitates a very high level of basic intelligence, both in the patient and the teacher, in order that successful relationship with the rest of civilization may be attained. This has been demonstrated, however, in the case of Helen Keller (1921) in the U.S.A. and again, more recently, in the U.S.S.R. in the case of Olga Skorokhodova (1947).

PHYSICAL MEASUREMENTS

If our civilization depended solely on the physique of its

population, it would be perfectly reasonable to pick out socially incapable persons by physical measurements rather than by mental tests. On the whole, psychophysical tests show rather poor correlations with scholastic capacity. For example, Bagley (1900) found that quickness of motor reaction had a negative relationship to class standing. Sensitivity to pain, however, showed a positive correlation with intelligence. This observation agrees with the finding that some idiots, though by no means all, take pleasure in hitting their heads or limbs against hard objects or even in having their teeth extracted. Strength of grip was found by Doll (1916) to be positively correlated with the intelligence level in defectives, to the extent of +0·62 to +0·81, and the mean readings for his patients were lower than those for normals.

Stature and weight are also correlated positively with intelligence, though the relationship is not constant enough to be of much predictive value. The very extensive survey made by Goddard (1912) demonstrated that morons, imbeciles and, especially, idiots were all inferior to normals both in mean stature and in mean weight between the ages of 5 and 25 years. In the group of morons, however, there was extensive overlapping with the normals, and it is in this range that discriminative measurements might have been of greatest practical value. Pearson (1914) pointed out, after scrutinizing Norsworthy's data on 150 defective children, that as far as height and weight were concerned, with the exception of one dwarf, all of the defectives might have been selected out of a group of normal children of adequate numbers.

Within the defective group, body weight is a rather poor index of mental grade. Doll (1916) found the correlation for these two characters to be of the order of +0·3, and Ashby and Stewart (1933) gave a value of +0·24. Whiting (1915) found correlations of +0·324 and +0·154, respectively, for mentality and weight and for mentality and height in criminals. Weight is a more comprehensive measurement of general body size than any linear measurement (Burt and Banks, 1947), such as stature or sitting height, and it is of special clinical interest. Weight shows greater variation in defectives than among normals because of endocrine and nutritional disturbances and intercurrent diseases, which are more frequent in defectives

than in normals. The weighing of patients is, in any case, a routine procedure and the wider statistical possibilities which arise out of it should not be neglected.

HEAD SIZE AND BRAIN WEIGHT

It would be interesting and useful if it could be shown that a close relationship existed between head size and intelligence. The relatively large size of the brain in man as compared with other animals is mostly due to the greater development of his cerebral cortex: it is probably to this accumulation of grey matter that he owes his superior intelligence. It is natural enough to inquire whether some relation may not hold between size of the head—which is largely determined by the size of the brain—and intelligence in members of the same species. In the case of man, males and females have to be classified separately otherwise we should start with the *a priori* fallacy that males, with their larger average size of head, were more intelligent than females. Similar reasoning has led some observers (Oliver, 1932) to suppose, unjustifiably, that if the brains of negroes can be shown to be smaller than those of Europeans, the negroes must necessarily be mentally inferior.

Among homogeneous groups of school-children, as well as university graduates, Pearson (1902) was able to demonstrate a weak but positive and significant relationship between head size and intelligence. The correlation coefficients varied between +0·097 and +0·139. A more recent study by Estabrooks (1928), on a group of school-children all aged 6, gave the result of correlating their scores in various intelligence tests with the cranial capacities, calculated from Lee's (1901) formula. Estabrooks separated out children of different racial origins but, as each group gave similar results, the final figures for the whole group can be taken as representative. Most of the correlations were significant. They varied between +0·08 and +0·31 and were, on the whole, higher than those found by Pearson.

Among institutional defectives surveys can easily be made comparing intelligence level with head size in suitable age groups. Appendix 1 gives the distributions of cranial capacity, estimated by Lee's formula, in 440 male and 332 female adult patients. The correlations with intelligence are low, but that

for the females is significant. A noticeable feature in both tables is the very wide variation of head size, especially in the lower ranges of I.Q. The average brain size falls off with diminishing mental grade, but the variability increases. This effect probably applies both to brain weight and to head size. Large heads, found in idiots, are not always due to hydrocephalus; they can also be associated with large, histologically normal but functionless brains, as in megalencephaly (Apley and Symons, 1947). Increased variability was also demonstrated in measurements of convolution width, made by Ashby and Stewart (1935) on brains of 54 defective subjects as compared with 8 normals.

Furthermore, Ashby and Stewart (1933, 1934) took measurements of brain weight, among other observations, on defectives. The correlation for brain weight and mental age was found to be +0·15. They pointed out that, since body weight was significantly correlated with mental age ($r = +0{\cdot}24$) and closely correlated with brain size, the association might be attributed to the basic fact that defectives were as a general rule smaller physically than normals. All mean measurements diminish slightly with I.Q. until the imbecile level is passed, below which there is a sharp fall.

Although the mean value of head size for all defectives together is undoubtedly subnormal, the degree of subnormality is insufficient for general purposes of diagnosis. In the series of male institutional cases shown in Appendix 1, for example, the mean cranial capacity was 1402 c.c. with a standard deviation of 134 c.c. The mean is below the average for a group of 100 normal adult males from the same general population, namely, 1423 c.c., but here the standard deviation was only 89 c.c. This normal value is considerably lower than estimates given by Berry and Porteus (1920) for Australian males, but for those the standard deviation found was smaller, 79 c.c. The greatly increased variation in defectives makes prediction of intelligence from measurements of head size of little practical value. The extreme cases, hydrocephalics and microcephalics, will be obvious enough without recourse to measurement in most cases. Sometimes, however, it may be convenient for the clinician to be able to establish whether or not the head measurements of a supposedly defective infant are normal since mental

tests at ages below 5 years are not always reliable. For this reason, the figures for mean length, breadth and height of head, given by Berry, are included in Appendix 2.

GENERAL PHYSIQUE

Taken all together, the mentally defective are physically inferior to the rest of the population. It has yet to be determined whether this finding represents a biological phenomenon or whether it is due to a variety of external causes, social, nutritional and clinical. There is little doubt of the presence of definite diseases, hereditary or acquired, in a large proportion of recognized cases of mental defect, and diminished vitality can be a direct consequence of such disease. Mongolian imbecility, for example, carries a mortality rate, as calculated by the present writer (1932*a*) from Brushfield's data, some nine times as high as that for the general population.

Analysis of routine physical examinations which had been carried out on 14,176 retarded school-children was published by Dayton (1930*b*), and significant associations were found between the number of physical defects observed and the amount of individual mental retardation, both for males and females. Skin disease, infestation and venereal disease were found with excessive frequency among mentally subnormal soldiers by Hodgson (1941). Physical disability of almost any kind also lowers economic efficiency in adult life and alters the threshold of certifiability. The tendency for pathological physical conditions or morbid behaviour reactions to be concentrated in the defective group may be partly due to this indirect social effect.

Instead of basing diagnosis of defect upon social incompetence, it is possible in some cases to use the criterion of physical diagnosis. Thus it is fairly safe to assume, without making any test of intelligence or of social adaptation, that a mongolian child, a microcephalic, a phenylketonuric or an untreated cretin will be a potentially certifiable defective. Diseases cause intellectual defect in so far as they attack the central nervous system. The amount of intellectual damage varies with the type of disease and with its severity. Williams (1926) listed 490 cases of neurological defects among children in schools for supposedly mentally normal cripples. The result, given in Table V, shows

TABLE V

CHILDREN IN SCHOOLS FOR CRIPPLES (490 CASES) (Williams, 1926)

Clinical Diagnosis	Percentage at Each Intelligence Level			
	Above Average	Average	Below Average	Nearly Defective
Infantile paralysis .	18·1	48·7	25·6	7·5
Infantile hemiplegia .	8·8	32·4	30·9	27·9
Cerebral diplegia .	0·0	15·1	24·2	60·6

that mild degrees of mental retardation are often found in such cases. A study of 167 feeble-minded patients and 333 imbeciles or idiots, by Gordon, Norman and Berry (1933), showed that neurological abnormalities were to be found in many of the high-grade cases and in most of the low-grade cases. In the survey by Dawson and Conn (1931), encephalitis lethargica was found to diminish I.Q. in children. Conversely, children with rheumatic chorea showed no loss of intelligence as compared with the control population.

Somatic diseases, which reduce general vitality, may affect the intellectual level, and so possibly may chronic malnutrition. The physical weakness associated with hookworm infestation has been shown by Smillie and Spencer (1926) to have a very definitely deleterious effect on mental functioning. Perhaps the same is true for other parasitic diseases that are endemic in native populations. The actual loss in terms of I.Q. occasioned by physical diseases may not always be very great, e.g. a drop of 10 points, but if there is poor initial capacity the change may be sufficient to make just the difference between normality and certifiable defect.

STIGMATA OF DEGENERATION

Historically physique has been of importance in the diagnosis of mental defect, particularly on account of the work of Lombroso (1887), who drew attention to the "stigmata of degeneration" present in certain cases. Malformations of the ears, hands and palate, as well as cranial deformities, were considered characteristic of degenerate mental types. No satisfactory evidence for this view has been brought forward. Degenerate ears, hands and palates are found among those in whom mental

defect does not come under consideration. The difference between normals and defectives in this respect can only be expressed in terms of a difference in statistical frequency between the two groups. This difference is not as great as was formerly supposed. Channing and Wissler (1905) could find no significant deviation from the normal in the palatal structure of higher-grade defectives and Burke (1931) found no distinction between idiots and imbeciles in respect of other stigmata.

There is a real concentration of physical peculiarities in some clinical types of cases, for example among mongols, microcephalics and subjects with endocrine disorder. In such conditions, where there has been a gross disturbance of development, many structures show a dysplasia which can be attributed to retardation of growth at an early, critical period (Ford and Frumkin, 1942). Retardation of development can also account for the diminished size of defectives as a group. Dentition and puberty have also been found to be delayed by Davenport and Minogue (1930). Here again, careful sorting out of cases with endocrine defects, such as cretins and pituitary dwarfs, might make the issue clearer. Jaensch (1930) showed that the capillary structure of the nail-bed is abnormal in defectives. These vessels are easily seen with a low-powered microscope if a drop of oil is applied to the skin surface. The malformation, however, is only found when there is a failure of endocrine secretion, probably of a pituitary hormone. Abnormalities of growth can also be occasioned by rickets and by congenital syphilis, which leave their marks on defectives as they would on normal children. Such signs are now recognized as stigmata of disease and not of degeneration.

MENTAL DEFECT AND SOCIO-ECONOMIC STATUS

Since the estimate of defectiveness is closely allied to judgments of social competence, we may expect to find that I.Q. and social or occupational class are correlated. The coefficient of +0·28 was given for this association by Duff and Thomson (1923), and that of +0·25 by Gray and Moshinsky (1938). Burt (1926) estimated the mean intelligence of adults in the different occupational categories. These are shown in Table VI. Since these estimates of I.Q. are for adults, they must be accepted with reserve.

TABLE VI

Occupational Category	Average Intelligence Quotient (Burt, 1926)
I. Higher professional : administrative	153·2
II. Lower professional: technical executive	132·4
III. Highly skilled: clerical	117·1
IV. Skilled	108·6
V. Semi-skilled	97·5
VI. Unskilled	86·8
VII. Casual	81·6
VIII. Institutional	57·3

A commonly adopted procedure is to test children and classify them by the occupations or incomes of their parents. For example, Preda and Mates (1939) found a mean I.Q. of 115 for children of parents with academic training, a mean of 105 for the children of parents in clerical occupations, 98 for the children of skilled workers, and 91 for those of unskilled workers. Such results are sometimes used as an indirect method of arriving at the intelligence measurements of the previous generation, on the assumption that intelligence level is in some way transmitted from parent to child. Material from different sources and obtained by the use of different tests tends to be very similar. An example is given in Table VII. Figures like these are easily obtained and are of intrinsic interest, but do not prove that the classes of parents listed necessarily have

TABLE VII

SCORES OBTAINED BY A RANDOM SAMPLE OF URBAN CHILDREN ON THE PROGRESSIVE MATRICES PERCEPTUAL TEST (PENROSE, 1939 *e*)

Paternal Occupation	Number of Children tested	Mean Chronological Age		Mean Score
		Years	Months	
I. Business owners	41	9	9	27·7
II. Professional	5	9	10	29·8
III. Highly skilled	29	10	2	28·0
IV. Clerical and commercial	72	9	10	27·1
V. Skilled manual workers	277	9	10	24·2
VI. Unskilled workers	217	9	11	21·6
— Unknown	19	9	4	21·0
Total	660	9	10	24·0 *

* The standard deviation of the score for the whole group was approximately 12·7.

mean intelligences distributed in the order shown for the children. All observers agree, however, that the children in the professional and clerical occupational groups are better at verbal and scholastic tests than the children in the less skilled occupational groups. As shown by the results in Table VII, the same seems to be true for tests of non-verbal reasoning.

An extension of this type of analysis into the range of mental defect brings to light another phenomenon. Table VIII gives the distribution of defectives at the Royal Eastern Counties' Institution, Colchester, according to mental grade and occupation of father. Clearly the patients drawn from various social groups differ from one another in mental grade. The technical occupations, I to IV, contribute more patients of imbecile and

TABLE VIII

PATIENTS IN THE ROYAL EASTERN COUNTIES' INSTITUTION (Penrose, 1938)

Occupation of Father	Borderline (*a*)	Feeble-minded (*b*)	Imbecile (*c*)	Idiot (*d*)	Ratio (*a*+*b*) : (*c*+*d*)
I. (Directive) . .	11	28	49	42	30 : 70
II. (Professional) . .	2	3	3	4	42 : 58
III. (Minor professional)	1	10	9	6	41 : 59
IV. (Clerical) . . .	6	15	32	20	29 : 71
V_1. (Skilled labour) .	50	108	126	60	46 : 54
V_2. (Unskilled labour) .	93	242	186	83	55 : 45
Unknown . . .	16	42	28	5	86 : 14
Total . . .	179	448	433	220	49 : 51

idiot grade than of borderline or feeble-minded grade. Unskilled labourers and men of unascertained occupation (which often meant that the father was unknown and the child illegitimate) contribute more children of high-grade defective types than imbeciles and idiots. Three processes—economic, medical and biological—probably combine to produce this pattern. First, in the homes of the higher income groups the borderline and high-grade cases can more easily be given the kind of training and education they need to prevent their becoming social problems, and they are not likely to require public assistance. The institutional training of idiots, on the other hand, is of great social advantage to the families in which they occur and is sought after more in the higher than in the lower

occupational classes. Formerly the poorer social groups had to rely on charity for the training of their low-grade cases, while the more comfortably situated could afford it almost as a luxury. Secondly, since medical and nursing care is likely, in the past, to have been satisfactory only when the income of the family was adequate, the idiots in the higher-income groups have had a better chance of survival as compared with those in the lower income groups. Thirdly, if the children of fathers in the more skilled occupations are, indeed, more intelligent than those of fathers in less skilled occupations, the proportions of all defectives, born in the two groups, will differ. An excess of feeble-minded among the children of unskilled workers could be expected.

A similar question arises in comparing urban and rural populations. Terman and Merrill (1947) found that the mean I.Q. of 1964 urban children was 105·7 and that for 940 rural children 99·2. More potentially certifiable cases were ascertained in rural than in urban areas, in proportion to the populations, by Lewis (1929). The ratio of the incidence, urban to rural, was 6·7 to 10·4 per thousand inhabitants. However, the same distinction between the two types of areas examined was maintained for all grades of defect, including idiots, and was shown for adults as well as for children. The effect was attributed by Lewis to the migration of the more mentally able part of the population from the country to industrial towns.

MILITARY CRITERION OF DEFECT

According to the results of testing the personnel of the American army in the First World War (Yerkes, 1921), a mental age of 8 years, corresponding to a Binet I.Q. of about 60, divides those who should be accepted for military duty from those who should be rejected. Men with mental test ages between 8 and 10 years were thought to be suitable for special labour battalions. However, the relationship of test score to military efficiency was never clearly determined. Correlations between officers' ratings of military value and intelligence as measured by tests were low, and varied from +0·5 to +0·23. Conscientious objectors to military service were found to be above the general level of intelligence (May, 1920).

During the Second World War there was a great deal of

testing of young adults in all English-speaking countries, but the results have not been made public to any large extent. It has been the general aim of those, who select personnel for military duties, to exclude defectives but very different standards have been used at various times, so that many of the results obtained were of more technical than scientific interest. There have been many differences of opinion about the military usefulness of defectives. Anderson (1940) pointed out that defectives sometimes make more satisfactory naval ratings than their more intelligent brethren, provided that no psychopathic traits are present. Hecker, Plesset and Grana (1942) state that, although the I.Q. of 60 or over is required to meet U.S. army induction standards, an I.Q. of 75, judged by the Binet or Kent test, should be the lower limit. Esher (1941) considered all cases below 7 years and 11 months mental age untrainable. In a specially studied sample of 100 cases, referred for examination by the British army on account of supposed mental defect, he found that 80 per cent. had relatively high mental ages, i.e. from 9 to 11 years. The drop in intelligence test scores that normally occurs with advancing age was commented upon, and Esher further recommended paying careful attention to school standards. Another side of the picture was demonstrated by Haskell and Strauss (1943), who examined the military service records of 100 ex-mentally-defective patients with a mean I.Q. of 70·7. After periods of service lasting some years, 31 had received promotion and only 12 had been discharged.

The brief Kent emergency test was used by Atwell, Bloomberg and Wells (1941) in the U.S. army, but later was replaced by batteries including non-verbal elements. These writers stated that the basic reason for acceptance or rejection should not concern mental age, still less the intelligence quotient, but should be the subject's capacity in relation to army demands. Myers (1942) believed that intelligence tests for screening purposes should be preferably non-verbal and supplemented by "job analysis". It is evident that, although the standards of intelligence required for success in armed services and success in civilian life are not exactly the same, the experience in the use of tests during the war might have important future bearings upon the concept of mental deficiency in civilian life. Finally, it must not be inferred that mentally defective persons cannot

adapt themselves to wartime strains. Benjacar (1940) reported that institutional cases co-operated well with air raid precaution work and useful constructional tasks. They showed no more liability to panic than normals and were very susceptible to efficient leadership; their reactions varied from blissful ignorance to moderately intelligent patriotic interest.

CHAPTER III

PRINCIPLES OF CLASSIFICATION

Traditional Dichotomies—Pathological and Subcultural Defect—Medical Grouping of Institutional Cases—Institutional Samples—Mental Defect and Biological Fitness—Fertility of Lower-grade Defectives—Fertility of Higher-grade Defectives—Family Data on the Two Groups—Parental Consanguinity and Grade of Patient—Summary of Dichotomies.

TRADITIONAL DICHOTOMIES

IT HAS been customary in almost every serious medical treatise on mental deficiency to attempt to divide the patients into two classes. One traditional method was based upon the usual medical system of separating "congenital" disease, with its origin before birth, from "acquired" disease, due to accidents which happen later. Shuttleworth (1895), for example, called defect due to cerebral abnormality, arising from formative or developmental defect, congenital. He referred to that which resulted from inflammatory or degenerative processes as non-congenital. Several uncertainties make this dichotomy unsatisfactory. First, it cannot be assumed that a disease or a degeneration, though it may have its onset in childhood or later life, has not its origin in prenatal events. Secondly, congenital does not imply hereditary, since the prenatal environment controlling development is not the same for all. Thirdly, injuries which occur during birth are difficult to ascribe to either class, though frequently they are classified as congenital.

A more ambitious and more usual classification separates cases in which the origin is in the germ plasm from those in which the origin is environmental. In other words, the classifier has to decide whether to blame nature or nurture. The terms "endogenous" and "exogenous" have had a very wide currency all over central Europe to indicate this opposition. Other descriptions have usually been employed, in English language text-books, to indicate the same things. Thus Ireland (1877) used

"genetous" to signify hereditary causation and defined acquired disease by specification, e.g. hydrocephalic, epileptic, paralytic. The words "primary" and "secondary" were introduced by Tredgold (1908) to signify the product of impaired germ cells on the one hand and environmentally arrested development of a potentially normal brain on the other hand. The substitution of new terminology did not remove fundamental errors, but rather tended to perpetuate them. The difficulty obscured here is that, in a large proportion of cases, as Wildenskov (1934) has pointed out, both hereditary and acquired factors combine to produce the end result of mental defect. For a biologist it is merely a platitude to state that the condition of a living organism at any time is the product of both its nature and its nurture. It is also obvious to a mechanic that the performance of an engine at any time, under given conditions, depends both upon how efficiently it has been constructed and how carefully it has been handled. Medical methodology, however, for reasons which are excellent in clinical practice, repudiates the simultaneous diagnosis of more than one disease. If mental defect is the disease in question, the physician has no option but to diagnose it either as belonging to some hereditary or some acquired type. The method is not very inaccurate when we are concerned only with severe cases, idiots or imbeciles. It fails badly in the analysis of milder cases, where social adjustment is decisive in determining whether or not the patient is to be classified as feeble-minded.

PATHOLOGICAL AND SUBCULTURAL DEFECT

A fresh approach to the problem of clinical classification was made by Lewis (1933), who suggested the division of defectives into "pathological" and "subcultural" types. The term "physiological" would be more natural than "subcultural", but it has been used in too limited a sense, for example by Juda (1936), to indicate only borderline cases. Among recognized cases of mental defect we find a certain number suffering from definite physical diseases or pathological conditions, which interfere with the functioning of the brain in one way or another. There is little doubt that a very large proportion of idiots and imbeciles are correctly described as "pathological" on the basis of clinical investigation. It is immaterial whether or not the diseases in question are due to environment or heredity. Lewis

himself, however, tentatively suggested that the majority of cases of pathological defect were environmental in origin.

There are statistical grounds for Lewis's classification if we assume that the distribution of ability on intelligence tests, in a normal human population, should be Gaussian. Far too many individuals exist, whose abilities are more than three or four times the standard deviation below the normal mean, to be fitted under a Gaussian curve. On that assumption, only about 1 idiot among 10,000 and 1 imbecile among 6 could belong to a normal population with a standard deviation of 15 I.Q. points (see Table IX). For the feeble-minded, the position is different and,

TABLE IX

LOWER LIMITS OF THE DISTRIBUTION OF INTELLIGENCE IN THE GENERAL POPULATION

(Age Group 10–14 years)

	Observed Defectives (percentage)	Normal Gaussian Distribution Prediction (percentage)
Feeble-minded . .	2·26	2·23
Imbecile . . .	0·24	0·04
Idiot . . .	0·06	0·00
Total . . .	2·56	2·27

on the basis of intelligence tests alone, the great majority of them might be regarded as members of the normal population. Diminished intellectual capacity of relatively mild degree can be interpreted as failure to meet the demands of local culture. Hence, the term "subcultural" can be applied to most of the feeble-minded, though few imbeciles or idiots can be reasonably included in this category.

MEDICAL GROUPING OF INSTITUTIONAL CASES

Lewis's dichotomy, though the best so far devised, is difficult to apply in clinical medical practice, particularly in so far as actual institutional cases are concerned. Those cases, in which a chronic neuropathological condition or a developmental deformity is observed, can be separated clinically from the rest, but sometimes no known disease can be identified. It is never certain that more detailed examination with more knowledge could not

have detected significant anomalies. A residue always remains of undiagnosed defectives who cannot be certainly distinguished from subcultural or physiological defectives. For example, in the Colchester Survey (1938) of 1280 patients, 308, or 24·0 per cent., showed no definite clinical abnormalities such as might be supposed to indicate pathological conditions underlying the defective mental state (see Table X). These 308 patients were relegated to a residual group which would contain nearly all the subcultural cases as defined by Lewis. In a somewhat similar survey Halperin (1945) found that 45 per cent. of the cases had no relevant clinical manifestations though, as in most American institutional samples of defectives, epileptics were excluded. In

TABLE X

EXAMPLE OF MEDICAL GROUPING OF INSTITUTIONAL CASES

Grade	Total Number of Cases	Clinical Group		Residual Group	
		Number	Percentage	Number	Percentage
Borderline . .	179	145	81·0	34	19·0
Feeble-minded. .	448	284	63·3	164	36·7
Imbecile . . .	433	340	78·5	93	21·5
Idiot . . .	220	203	92·3	17	7·7
Total. . .	1280	972	76·0	308	24·0

the classification of defectives recommended for use in the United States, there is a class of "undifferentiated" cases. This has not quite the same connotation as residual or aclinical, since instances of "familial" defect are excluded. However, the group is a large one, as shown by its comprising 2137 out of 5238 Massachusetts certified defectives in 1939, for example.

Among the idiots in the Colchester Survey, 7·7 per cent. had no clinical abnormality, though, of course, autopsy might have revealed unexpected pathological processes in the central nervous system. Among the imbeciles, 21·5 per cent. were left in the residual group and among the feeble-minded 36·7 per cent. Of the borderline patients, however, fewer were without clinical signs of abnormality, because most of them (98 out of 179) were definitely mentally disordered, i.e. epileptic or psychopathic; otherwise they would not have required care, supervision and control. The same consideration applied in a lesser degree to the feeble-minded.

It is not quite clear how far the term "pathological defect" was originally intended to cover psychosis, epilepsy, psychopathy, delinquency and so on, but something more than mere subcultural defect is needed to justify certification of high-grade cases. If "subcultural" and "pathological" are to be exclusive terms, most certified cases have pathological defect in the sense that, mentally or physically, they suffer from some chronic illness. It is for scientific medical enquiry to determine, if possible, whether the illness has caused loss of mental ability, whether it is a concomitant or associated phenomenon, or whether it has no relevance to mental grade. If a patient needs to be in a hospital or institution, there must be something wrong with him or with his environment and it is part of the duty of the physician to find out what is wrong. In the great majority of certified cases of mental defect the interplay of causal factors leading to the eventual admission to hospital is so complex that any exclusive classification into types will be only an approximation.

Many of the cases in the clinical group will be attributable to single causes. These may be rare harmful genes or environmental accidents. In such cases, it can be assumed that, in the absence of the clinical abnormality, the subject would have had average intelligence. Whether the level of ability would have been high or low is a matter of indifference in relation to diagnosis. This applies to most of the severe cases and particularly to idiots.

Among the feeble-minded and borderline cases it is otherwise. The potential mental level even in the absence of disease is the chief factor of importance. The majority of feeble-minded defectives are not far removed from the normal but they are liable to require care, supervision and control. Lack of training or disabling illness, coexisting with subcultural mentality, merely increases the likelihood of certification. In borderline cases, however, the intellectual defect is rarely, by itself, sufficient to necessitate institutional supervision. Additional factors, causing social incompetence, are usually present if care and control are necessary for such people. Thus, in high-grade cases, it is rarely possible to specify only one cause of social failure.

INSTITUTIONAL SAMPLES

The group of defectives who are cared for in institutions is

actually composed of two classes. One class contains the severely defective cases, idiots and low-grade imbeciles, with disabilities due, in most cases, to disease or malformation, whose mental capacities would be normal in the absence of disease. A considerable proportion—in England, probably more than one quarter—of all cases of severe defect in the community are to be found in institutions. The other class contains more mildly defective cases, high-grade imbeciles, feeble-minded and border-

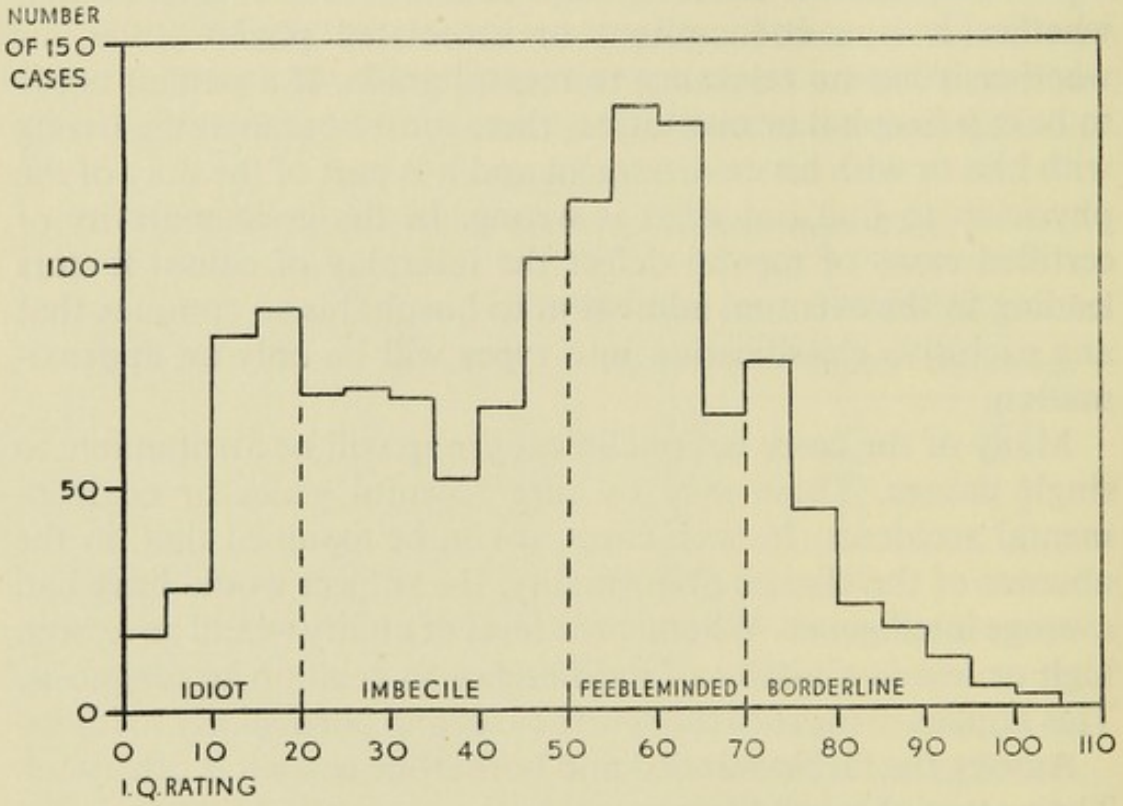


Figure 3.—Institutional sample of defectives (Colchester Survey, 1938)

line patients, with subcultural intellects. Usually their intellectual defect alone is not pronounced enough to have prevented some adaptation to society in the absence of extraneous factors. These additional factors can be physical or mental infirmities. Sometimes institutional training is needed mainly to counteract antisocial influences at home. Only a very small fraction of all persons with subcultural intellects are actually certified defective; this proportion can be estimated roughly as 3 per cent. in England.

The requirements of these two classes are so different that sometimes institutions are staffed to deal only with one or other

type. In the Colchester Survey the two types could be differentiated, irrespective of age grouping, by intelligence level as measured by the Binet I.Q. The distribution shown in Figure 3 has a natural dividing-line at about I.Q. 37, or for adults at a mental age of a little over 5 years. The severely affected cases, e.g. those with I.Q. of 0 to 39, moreover, were considerably younger than those with milder degrees of defect, I.Q. 40 and above. The most frequent age and I.Q. range for the low-grade group was 10 to 14 years with I.Q. 15 to 19, whereas the most frequent range for the high-grade group was 25 to 29 years of age with I.Q. 55 to 59. The sex incidence was also different in the

TABLE XI

CERTIFIED CASES OF MENTAL DEFECT IN ONE AREA SERVED BY A LARGE INSTITUTION (July, 1933)

Description of Case	Number under Statutory Supervision or Guardianship	Number in the Institution	Total
Feeble-minded	47	88	135
Imbecile	149	94	243
Idiot	30	31	61
Total	226	213	439
Males	90	124	214
Females	136	89	225

two groups, in that males predominated greatly among the low grades. The complete table, showing all age groups, is given in Appendix 3.

The statistics of institutional cases given in the reports compiled by Dayton (1939) show the same general trend (see Appendix 4), for there is a sudden "jump" in numbers between the I.Q. group 30 to 39 and 40 to 49. It is improbable that in the population as a whole there is any natural demarcation between the two institutional classes. As shown in Table XI, a disproportionately large number of certified cases of imbecile grade, in a sample area, were not in the institution, but were cared for under statutory supervision or guardianship. The large excess of males in the institutional group was also probably due to selection.

The cases requiring care and supervision in a hospital, which supplies nursing and training facilities, are those which have the most urgent claims for admission. The idiots need attention on account of their helplessness and the feeble-minded need supervision on account of their propensities for maladjustment in the community. Between these classes is a group, mainly composed of imbeciles, who are too low grade to be problems in the community and yet are capable of looking after themselves to some extent in the sheltered environments of their own homes, the homes of foster parents or guardians, public assistance institutions or general hospitals.

The elaborate and sometimes illogical legal methods by which patients reach training schools and institutions tend to prevent the inmates from forming a homogeneous group. A few cases are placed privately and, for some, training is provided under charities; most of these cases are severely affected. Those placed in residential special schools, under the Education Acts, are mild cases of intellectual defect, as are also those who come under supervision by reason of court proceedings under the Children Act or other Acts or in consequence of their infringement of criminal law. The most usual method of placing, however, i.e. through magistrate's order under the Mental Deficiency Acts, is used for all grades and types. From the point of view of practical administration these alternative methods of procedure are useful although, in a biological analysis of the phenomena of defect, they are disturbing factors which merely add to the natural difficulties of investigation.

MENTAL DEFECT AND BIOLOGICAL FITNESS

The type of social failure which determines mental defect is, as we have seen, closely allied to educational failure. The prevalence of associated disease in institutional patients indicates a third type of failure, namely, that from the point of view of health. Closely related to individual physical unfitness is another type of failure, which may be called biological, and we may ask how far defectives are biological failures. The ultimate test of biological fitness is ability to reproduce. Failure to reproduce may be due to disease, injury or accident. It may also be due to genetical constitution. Natural selection determines which genes are carried on to future generations and which are obliterated.

The perpetuation of a gene depends upon the effective fertility of its carrier. That is to say, it depends upon how many offspring reaching an age capable of reproduction are produced by each individual who carries the gene. If the gene confers fertility, in this particular sense, greater than the average level for the species, its carrier is biologically successful and the prevalence of the gene tends to increase. Conversely, if the gene's possessor has diminished fertility, this gene will tend to die out. Unless replaced by fresh mutations, a gene which effectively reduces fertility will tend to disappear from the population.

The effective fertility of an individual can be interfered with at various levels. The embryo may fail to develop or its internal harmony may be so disturbed that it fails to survive early life. Genes which cause such disturbances of development are termed "lethal" or "sublethal", and the individuals in whom their effects are manifest are necessarily infertile. Anencephaly is a lethal condition in man and so also is infantile amaurotic idiocy. No affected subjects can have children of their own. Less severe diseases can cause partial loss of fertility, which may be mainly socially conditioned, as, for example, in congenital paralysis, blindness or deaf mutism. In the case of such a disease as haemophilia, diminished fertility is due to relatively early death from haemorrhage. As far as mental defect is concerned, low-grade cases are mostly unable to reproduce at all. By this biological criterion they can be differentiated from high-grade cases.

FERTILITY OF LOWER-GRADE DEFECTIVES

Among idiots there is almost complete absence of effective fertility, for reasons which are usually both physical and social. With imbeciles, fecundity is possible but rare. For example, among the parents of defective patients of all types, only a very small number are of imbecile grade. In the Colchester Survey, only four imbeciles and no idiots were discovered among 2560 such parents. Also, no idiots in the sample of patients had children of their own and only 7 out of 138 female imbeciles over the age of 16 (with a mean age of about 29 years) had offspring. These 7 imbeciles had, on the average, two pregnancies each and about half of the offspring might have been expected to reach maturity. The actual fertility of imbeciles in the general population is probably lower than this sample would suggest, since

pregnancy in a defective is an important determining factor in selection of the case for institutional care.

Roughly, the lower limit of mental grade compatible with reproductive activity seems to correspond with the division between the two classes of institutional defectives already described, and rests at an I.Q. between 35 and 39 points. The decisive factors are physical development and general appearance, but ability on the Binet test is a rough guide. Menstruation occurs in female idiots unless the endocrine system is grossly disturbed. Hence fertility among them is a possibility. The fact that idiots are not fertile is probably due as much to psychological as to physiological circumstances, in that they do not attract mates. The male low-grade case is even more handicapped in this respect than the female. The same applies to males of imbecile grade for, in so far as can be judged from institutional cases, effective fertility in male imbeciles is much rarer than it is in female imbeciles. Danenhower (1948) found no appreciable abnormality in menarche, periodicity and menopause in defective females.

FERTILITY OF HIGHER-GRADE DEFECTIVES

The question of fertility among the feeble-minded has been the cause of much speculation and is still unsettled. In so far as the milder types of defectives can be considered members of the general population, it may be expected that they will share in the differential fertility which has been shown to be present when occupational groups are examined. The occupational groups with the highest birth-rate are among the least skilled. Members of the professional and highly skilled groups have many fewer children (Carr-Saunders and Jones, 1937). People with Binet I.Q. of 70 or thereabouts are only capable of unskilled labour or even casual labour and, therefore, should belong to a high fertility group.

In assessing the fertility of the feeble-minded, two points need consideration. First, the number of children of feeble-minded individuals may be large as compared with those born to parents of normal intelligence, but the total contribution to the next generation depends also upon the number who have no children. The effective contribution may not actually be as great as the finding of a few large families with feeble-minded parents would

suggest. Secondly, biological fertility is concerned with the number of children who reach full maturity. This cannot be measured unless families are followed up for the period of a whole generation. Thus, if the children of defectives should be physically weakly as compared with the rest of the population, the effective fertility of the parents can be subnormal even though their families are large. On these points it is difficult to obtain exact information but some facts are suggestive. In an important survey, made by the Departmental (Brock) Committee on Sterilization (1934), on the offspring of people notified as mentally defective, the proportion of children who died under the age of one year was about double that for the general population.

Since severe defect is associated with infertility, a break must come somewhere in the line of increasing average size of family with diminishing intelligence. Is the change sudden or gradual? There are some reasons for supposing it to be gradual. For example, Jones (1934) in his survey of the general population of the Merseyside found that fertility in the very lowest social grade, measured by the mean size of family, was less than that in the grade immediately above it. Studying the parents and grandparents of defectives in the Colchester sample and classifying them by mental grades led to the conclusion, demonstrated in Table XII, that the greatest fertility occurred when parents had a mean I.Q. of about 80 or 90 points. When parental mental capacity was below this, the families were smaller. To sum up, the measurement of effective fertility associated with any given intelligence level depends upon ascertaining the number of people who have no children at all, as well as upon the viability of the offspring.

A difference between the fertility of males and females has been observed in the milder cases of defect. In numerous surveys defective mothers have been ascertained more frequently than defective fathers. This phenomenon was observed and recorded by Rosanoff (1931), Halperin (1945) and in the Brock Report (1934) on very different types of material. It also appeared in the Colchester Survey, where three times as many mothers as fathers of patients (i.e. 12 per cent. against 4 per cent.) were considered to have a mental level equivalent to a defective category. These findings agree also with what is known of the biology of specific conditions causing severe defect, such as phenylketonuria; Jervis

TABLE XII

RELATIVES OF INSTITUTIONAL DEFECTIVES (1938)

Approximate I.Q. of each Grandparent	Number of Cases	Mean Number of Uncles and Aunts per Patient (Registered Births)*
122 and 100	6	5·17
100 and 100	1663	6·22
100 and 78	55	6·47
100 and 56 or 78 and 78	17	7·35
78 and 56	3	6·00
56 and 56	5	4·80

Approximate I.Q. of each Parent	Number of Cases	Mean Number of Sibs per Patient (Registered Births)*
122 and 100	9	2·89
100 and 100	797	4·72
100 and 78	196	5·45
100 and 56 or 78 and 78	113	4·52
100 and 34 or 78 and 56	54	3·82
78 and 34 or 56 and 56	24	3·58

* These means cannot be directly compared with means obtained for the general population because the families are all selected by the presence of at least one child and are therefore too large ; they can be rightly compared with one another.

(1939) reported three females who had offspring but no actually fertile males are on record. One partial explanation is that there are more female than male defectives within the fertile range. Another cause might be the impossibility of ascertaining defective fathers of illegitimate offspring. Furthermore, since care of the child depends more upon the mother than upon the father, a defective mother is more likely to be noticed by social workers than a defective father. While these factors may partly explain the difference, psychological and cultural circumstances must also be taken into account. The initiative in sexual approach, as well as in the economics of the family, belongs chiefly to the male. Hence, low mental capacity is a more serious biological handicap to a male than it is to a female.

FAMILY DATA ON THE TWO GROUPS

As already indicated in the previous chapter and demonstrated in Table VIII, family history investigation which starts with higher-grade cases leads to different results from that which

starts with lower-grade cases. An inverse relationship holds between occupational levels of father, home conditions as judged by cleanliness, size and comfort, and the mental levels of certified patients. If feeble-minded and borderline patients are separated from idiots and imbeciles, it is found that in the first group home conditions are, on the average, subnormal and, in the second or low-grade group, they are probably distributed as in the general population. Table XIII shows the results obtained

TABLE XIII

PERCENTAGE DISTRIBUTIONS OF RATINGS OF HOMES OF INSTITUTIONAL DEFECTIVES

Rating of Home Conditions	Feeble-minded or Borderline (482 cases)*	Imbecile or Idiot (531 cases)*	Fictitious General Population
A. Very good . .	0·6	4·9	5
B. Above average .	10·4	21·7	20
C. Average . .	44·2	49·7	50
D. Below average .	34·6	18·8	20
E. Very bad . .	10·2	4·9	5
Total . . .	100·0	100·0	100

* 145 feeble-minded patients and 122 imbeciles and idiots had no homes.

in the Colchester Survey after the homes of 1013 patients had been visited and rated by social workers.

Closely parallel to the occupational and social findings in the patients' families are the actual assessments of intelligence on relatives. In the Colchester Survey, again, 12·1 per cent. of the parents of 448 feeble-minded cases were considered to be themselves feeble-minded or imbecile, whereas only 6·5 per cent. of the parents of imbeciles and only 2·7 per cent. of the parents of idiots could be placed in the defective category (Appendix 10).

Comparison of mental grades of parents in two simplified classes of patients, high and low grades, is shown in Table XIV. Mental subnormality is more noticeable among parents of the high-grade patients. The same applies, in a lesser degree, to grandparents. With respect to sibs, the situation, as shown in the same table, is a little more complex. If defect occurs among the sibs of any patient, it tends to be of the same degree as that in the patient. However, the sibs not classified as defective or retarded are usually found to be brighter when the patient is a low-grade case than when the patient is a high-grade case. As shown

TABLE XIV

NUMBER OF PARENTS AND SIBS IN DIFFERENT GRADES
(Colchester Survey, 1938)

Patients' Grades	Grades of Parents					
	Superior	Average	Borderline or Feebleminded	Imbecile or Idiot	Unascertained	Total
Borderline or feebleminded (627 cases)	4	835	346	3	66	1254
Imbecile or idiot (653 cases) . . .	7	1073	196	1	29	1306
Total (1280 cases) .	11	1908	542	4	95	2560

Patients' Grades	Grades of Sibs					
	Superior	Average	Borderline or Feebleminded	Imbecile or Idiot	Unascertained	Total
Borderline or feebleminded (627 cases)	28	1677	453	58	105	2321
Imbecile or idiot (653 cases) . . .	40	1968	312	109	120	2549
Total (1280 cases) .	68	3645	765	167	225	4870

in Chapter VI, actual testing with the Stanford Binet confirms these results.

Similar considerations, in a more diluted form, apply to uncles, aunts, cousins and more distant relatives.

Attention has been repeatedly drawn to these differences in family history found for severe and mild cases by observers in many different countries, for example, by Lewis (1933), Wildenskov (1934), Halperin (1946) and by Roberts (1947). However, Brugger (1939) held that the decisive differentiating factor was not the grade of the patient but the clinical type of the case. Undoubtedly there is much overlapping of the concepts of low- and high-grade defect, of the subcultural and pathological concepts and the residual and clinical concepts; the dichotomies produced by them are not coextensive. The biological concept of fertility seems, however, capable of clearing away some of the confusion. If severe or low-grade cases were defined as those essentially

infertile, then it is obvious that no parents of patients could be severe cases, although sibs and collateral relatives of patients could be. The possible causation of severe defect is subject to the restriction that severe defect cannot be transmitted from parent to child and this restriction does not apply to the causation of high-grade defect.

PARENTAL CONSANGUINITY AND GRADE OF PATIENT

It has frequently been noticed that, among parents of institutional and other defectives, blood relationship is more common than in the general population. The results of some early surveys were analysed by George Darwin (1875). Estimates of the incidence of defective patients with first-cousin parents ranged from 2·9 per cent. to 3·8 per cent. Later, Shuttleworth (1886) calculated that 2·9 per cent. of the defectives at the Royal Albert Institution had first-cousin parents and that, altogether, 5 per cent. had parents who were in one degree or another consanguineous. The incidence of cousin marriages of all degrees in the general population has declined in the last fifty years and is now little more than 1 per cent. (Bell, 1940). Even when this decline is allowed for, these figures for parents of defectives were phenomenally high.

Cousin parents of all degrees are more commonly found for low-grade than for high-grade patients. Combining the figures from the Colchester Survey with those from a survey made by Duff and Dingee (1941) at Orillia, Canada, leads to the result shown in Table XV. The total consanguinity rate is abnormally

TABLE XV

PARENTAL CONSANGUINITY: INSTITUTIONAL CASES
(Penrose, 1938; Duff and Dingee, 1941)

Degree of Parental Relationship	Cases with Related Parents			
	Borderline and Feeble-minded		Imbecile and Idiot	
	Number	Percentage	Number	Percentage
Illegal unions, incest, etc. . .	10	0·9	6	0·3
Cousins of all types . . .	26	2·2	63	3·0
All types of consanguinity .	36	3·1	69	3·3
Total number of patients surveyed	1172	100·0	2190	100·0

high, more than twice that in the general populations from which the cases were drawn. Though the total rate is almost the same for the high-grade and low-grade patients, its detailed composition is quite different. Incest and other illegal unions are remarkably frequent among parents of institutional high-grade cases; this is partly due to the preferential selection, for institutional care, of cases whose parents are known to have committed incest. Such parents and, as well, their children often have subcultural mentality. With regard to the legitimate cousin marriages, the position is reversed. These are more numerous (3·0 per cent.) among the parents of low-grade cases (especially idiots) than among parents of high-grade defectives (2·2 per cent.). As will be explained later, the finding strongly suggests that, among the idiots, there are to be found rare conditions due to recessive genes. The recessive type of inheritance is quite characteristic of many kinds of low-grade defect, though it is not true, as Goddard (1914) originally suggested, that all or even a large number of defectives are caused by one special recessive gene.

SUMMARY OF DICHOTOMIES

The descriptions of the two classes into which defectives can be roughly divided are summarized in Table XVI. The two groups of cases can be termed "mild" and "severe", but, as previously pointed out, the qualities that are listed as characteristic of the two types of cases are not specific and there is a great deal of overlapping. Nor are the properties listed in this table intended to be exhaustive. It may, however, be useful to consider the problem of defect within this framework, because of the primary biological difference between the two groups expressed in terms of fertility. In consequence of this, the genetical causes in the two groups are necessarily different. As might be expected, several types of idiocy are determined by recessive genes which can be transmitted by normal parents. Among the mild, or fertile, group, no such restriction of genetical causes need be expected and dominant genes may be causal factors through more than one generation. The lack of any marked distinction between the cases of mild defect and members of the general population makes it reasonable to assume that the same genetical mechanisms which produce variations in intelligence in the

TABLE XVI

THE TWO MAIN GROUPS OF INSTITUTIONAL CASES OF MENTAL DEFECT

Group	I	II
Degree of defect	Mild	Severe
Incidence of group in general population	Common: 2 per cent.	Uncommon: ¼ per cent.
Proportion of group institutionalized	Few: 3 per cent.	Many: 25 per cent.
Sex incidence	Females predominate	Males predominate
Psychological classification	High grade, simpleton, moron, feeble-minded (modal I.Q. about 57)	Low grade, imbecile or idiot (modal I.Q. about 17)
Predominant medical classification	Physiological, aclinical, residual, associated with behaviour disorders	Pathological, clinical, associated with physical malformations
Mental capacity in absence of disease	Subcultural	Normal
Biological classification	Fertility normal or increased	Infertile
Traditional view on causation	Hereditary, primary, endogenous	Environmental, secondary, exogenous
Status of relatives	Parents, brothers and sisters rather frequently defective, but not sharply distinguished from normals	Parents rarely defective; brothers and sisters occasionally defective and sharply distinguished from normals
Typical hereditary causes	Common genes: multiple additive genes	Rare genes: specific recessive genes
Typical environmental causes	Deprivation; cerebral disease or injury in childhood; antisocial environment	Pre-natal maternal influences; cerebral disease or injury in very early life
Aims of treatment	Special education, socialization	Elementary training, nursing
Physical measurements	Means and variabilities within normal range	Means below normal, increased variabilities

general population will be determining factors in the production of mild defects. The genetical factors, as those which cause normal variations in stature, are certainly multiple and possibly additive in their effects. Perhaps the simplest way of looking at the matter is implied by the relative frequencies of cases in the two groups. The certifiable cases of defect in Group I are common and the responsible causes are ordinary common events, either environmental or genetical. Conversely, the cases in Group II are much rarer and the events which produce them tend to be relatively rare accidents, rare diseases or rare genetical processes.

The separation of cases into these two classes is natural also from the point of view of institutional objectives. The mild cases require social training and special education so that they may be, as far as possible, returned to the community better fitted to become useful citizens than formerly. They may require medical treatment, an essential part of which is often psychiatric. The severe cases present a different problem; they cannot be expected to take any actively useful part in community life, except under constant supervision. Moreover, the lowest grades are permanent invalids requiring continual nursing care and the usual aim is little more than to make them as happy and as comfortable as possible.

CHAPTER IV

PROBLEMS OF CAUSATION

Nature and Nurture—Gene Mutation—Germ Plasm Injury—Anticipation —Mutation and Selection—Rare Dominant Genes—Irregularity of Manifestation—Rare Recessive Genes—Additive Genes—Sex-linked Genes—Rarer Types of Inheritance—Maternal Genetical Influences—Maternal Environment—Intranatal Environment—Postnatal Environment—Methods of Distinguishing between Nature and Nurture—Intelligence of Twin Pairs —Evidence from Children in Foster Homes.

NATURE AND NURTURE

As every living organism is the product both of hereditary and environmental influences, the problem of finding a cause for any given peculiarity resolves itself into an examination of both types of agency. An influence which acts equally upon all individuals in a species or an agency which is common though not universal cannot be blamed for a rare deviation. We may suppose, however, that an unusual concatenation of common agencies can cause rare peculiarities. In human genetics the principle of looking for rare agencies as the causal agents responsible for rare diseases is quite important. Of necessity, most common genes are not very harmful. Genes responsible for hereditary diseases are also, of necessity, relatively rare. If this were not so the species would be very unstable. Thus in speaking of specific causes of mental defects we shall, in the main, be thinking of rare events.

The distinction between causes, which are said to be hereditary or part of the individual's nature and those which are environmental or pertaining to nurture, must be based upon temporal sequence. Consider, for example, a machine such as a watch. Certain metallic alloys and other substances are prepared and out of them the wheels, spindles and framework are fashioned. They are then assembled and finishing touches are applied before the watch is ready for use. After this, the watch is expected to go for a long time provided that it is wound up

regularly and not dropped on the floor or allowed to get damp or full of dust. Eventually the bearings get worn down or a part breaks. If it should fail to work, say on account of a broken spindle, the cause may be attributed to faulty materials, faulty machining or construction or to misuse, by specifying the chief unusual circumstance which is connected with the accident. We might speak of everything that happened to the watch before it left the factory as constituting its heredity, and everything that happened to it after that as its environment. The division might also be made at a point before the parts were assembled.

The analogy with human abnormalities is obvious. We usually accept the results of injuries and unfavourable agencies that affect the organism after fertilization as environmental, and all relevant previous circumstances as part of its hereditary nature. The time sequence of the previous events, however, is of great interest. Instead of attempting to ascribe our causes to either nature or nurture, we can simplify the objective and merely ask which of two events was the earlier. In practice it is convenient to divide the developmental time-scale into various epochs, as is shown in Table XVII. Causes which act in the pre-conceptual period, before the formation of the individual zygote, are usually

TABLE XVII

TIMING OF POSSIBLE CAUSES OF MENTAL DEFECT

Usual Terminology	Epoch	Agency
A. Genetical, hereditary, endogenous, due to nature	(i) Remote	Spontaneous gene mutation in ancestral germ cells.
	(ii) Recent	Spontaneous or induced gene mutation or other changes in parental germ cells.
B. Environmental, exogenous, due to nurture	(i) Early prenatal	Retarded early stages of growth; abnormal embedding of fertilized ovum, maternal disease.
	(ii) Late prenatal	Intrauterine disease; malnutrition, infection, incompatibility.
	(iii) Intranatal	Abnormal birth.
	(iv) Postnatal	Diseases or accidents in infancy or childhood; unfavourable social environments.

classed as hereditary, but it might be more accurate to speak of causal agencies acting in this epoch as genetical.

The practical value of a temporal scheme lies in its relation to the problem of treatment. Palliative or curative measures can indeed be attempted with any disease irrespective of the time of its origin. Cataract, whether inherited or acquired, can be treated by the ophthalmic surgeon and it is almost immaterial to the physician prescribing insulin whether diabetes is due to inborn metabolic infirmity or intercurrent disease. Preventive or radical measures, however, are directed so that the disease is attacked at its source. The more recent the occurrence of a disturbance which is responsible for existing cases of defect, the more easily will it be controlled and eliminated as a cause of new cases in the future. This crucial point makes the antithesis between nature and nurture so important practically.

GENE MUTATION

A gene which produces disharmony in development must have arisen by mutation at a definite point in time; such a time may have been remote or recent. Experimental geneticists have found that mutant genes responsible for all kinds of abnormalities are constantly arising afresh, but the rate of mutation at any one locus is usually very slow as compared with the life-history of the animal concerned. Genes have to be copied at every cell division and the process of copying occasionally goes wrong (Haldane, 1932*a*). In the fly *drosophila melanogaster* the upper limit of spontaneous mutation frequency for a single gene is about once in 10,000 life-cycles. The usual rate is probably less than one in a million life-cycles. Some genes are more liable to mutation than others.

Muller and Settles (1927) showed that the mutation rate could be increased artificially by exposing flies to X-rays or to β-rays from radium. Previously known spontaneous mutation rates were thus speeded up 150 times. Heat, according to Goldschmidt (1929), can have a somewhat similar effect and, recently, Auerbach and Robson (1947) found that mustard gas could cause an increase in mutation rate. More recently still, other poisons, like phenol and certain carcinogenetic substances (Demerec, 1947), have been proved to have comparable effects, though none of these agents is as powerful as radiation. In all such cases we are

concerned, for practical purposes, with an environmental effect. Yet mutation of a gene which occurred in response to an overdose of X-rays in the germ cells of one person would affect, not him, but his immediate or remote offspring. Here is an environmental agency which affects the germ plasm, that is, one which changes nature.

Sometimes the mutation is not a change in a single gene but a deletion, a breakage or a rearrangement in one or more chromosomes. There are also rare possibilities: some genes are known which cause other genes to mutate faster than usual. Such genes might produce somatic mutations, that is, could cause changes to take place in the nuclei of those cells of the body which form the organism itself but which do not contribute to the next generation. Some possible human cases of somatic mutation of unknown origin have been reported (Zlotnikoff, 1945).

GERM PLASM INJURY

In the nineteenth century it was generally believed that spontaneous changes in the germ plasm were of rather frequent occurrence. Darwin accepted this view because he saw that spontaneous hereditary variation was a necessity in the mechanism of evolution. The causes of mutation were unknown; popular, as well as medical, doctrine held that external poisons could injure the germ cells. In spite of the teachings of Weismann (1893), who propounded the principle of the unchangeable nature of the germ plasm, medical authorities clung to the older viewpoint. It was not unusual for alcohol, lead poisoning or toxins produced in organic diseases, such as syphilis and tuberculosis, to be credited with the power of altering the parental germ plasm is such a manner as to produce monstrosities in the offspring. Plumbism in the father has been considered responsible for stillbirths by Paul (1860) and responsible for epileptic defect by Thomson (1923). Savage and Goodall (1907) believed that phthisis in a parent increased the tendency to nervous disorder in the offspring, and Langdon Down (1866) believed that it could cause mongolism. The effect of poisons on the germ substances was termed, by Forel, "blastophthoria", from the Greek βλαστός, a bud or germ, and φθόρος, destruction. The concept has no clear scientific meaning but tends to appear from time to time in medical literature. It was asserted to be a very

important element in the causation of mental diseases and defects by Myerson (1923). Tredgold (1937) subscribed to the doctrine that many different environmental factors could effect changes in the germ cells and thus cause mental defect.

In view of the recent discoveries that chemical as well as physical agents can increase mutation rate, the subject cannot be lightly dismissed. However, we must ascertain that the concentration of a noxious substance in contact with the germ cells is high enough to have a reasonable probability of being effective. In the case of alcoholism, for example, this likelihood seems remote. Experimental work on animals has sometimes appeared to support the theory of alcoholic blastophthoria, in particular the work of Stockard (1923). The parental generations of guinea-pigs were subjected to alcohol fumes and it was claimed that the offspring were frequently malformed in consequence of germ plasm impairment. Subsequent workers, Durham and Woods (1932), were not able to obtain the same results. Bourneville and Leflaive (1884) attributed human hydrocephaly and numerous malformations leading to idiocy to spirit drinking by the parents. Moreover, Bertholet (1909) maintained that alcoholism in a male could cause histologically demonstrable pathological changes in the testes. Later researches have not tended to substantiate such claims. It was demonstrated by Elderton and Pearson (1910) that the children of alcoholic parents were not inferior but, if anything, superior physically and mentally to those of abstinent parents, though these opinions were disputed (Keynes, 1910). In the Colchester Survey, the children of alcoholic parents were found no less numerous and no more often defective than the children of non-alcoholic parents of similar mental grades. It used to be thought that alcoholic intoxication of parents at the time of intercourse could affect the offspring adversely, but it is difficult to understand how a concentration of alcohol sufficient to injure the spermatozoa or ovum could be achieved. The possibility that spermaticidal chemical substances, such as lysol, deliberately used in douches with a view to contraception, might harm some spermatozoa and cause mutation in them, but fail to kill them, has to be considered. At present there does not seem to be any tangible proof of the existence of this factor as a cause of congenital defect. De Réyni and Murphy (1932) concluded, from experimental work on animals, that, with

regard to the ovum, the first effect of irradiation was to destroy its power of becoming fertilized. The same "all or none" quality may characterize the action of poisons on the spermatozoa.

ANTICIPATION

It has been further claimed that when germ plasm is vitiated there is often a tendency for it to continue to degenerate for a long period. If so, the second generation of animals is more severely affected, more grossly malformed than the first generation of abnormal offspring. The process is said to lead to "anticipation" in the sense that the onset of the disease in affected individuals is earlier in every succeeding generation. Mott (1910) strongly upheld this hypothesis, maintaining that, by virtue of anticipation in hereditary diseases, "rotten twigs were continually broken off the tree of life." The additional assumption of the existence of protean influence, known as the "neuropathic diathesis", which was the cause of all mental and nervous diseases, was proposed by Tredgold (1929) to account for the presence, in the same pedigree, of various types of insanity and defect. Once injured, the germ plasm was capable of a wide range of manifestation, beginning with mental illness of comparatively late onset, or psychopathic temperament, in one generation and culminating in idiocy in the remote offspring.

The main difficulty in accepting the hypothesis of anticipation is its total lack of support from observations in the field of animal genetics. The effects of mutation do not get progressively worse. They remain the same, but their manifestations may vary considerably according to the rest of the genetical constitution of the individual and in response to the environment. In the study of human families, the apparent occurrence of anticipation is very frequently observed, especially in respect of conditions whose range of onset age is wide, as in mental illness (Rüdin, 1916). The phenomenon is not confined to deleterious qualities. Galton (1869) stated that "the sons of gifted men are decidedly more precocious than their parents. . . . I do not care to quote cases, because it is a normal fact, analogous to what is observed in diseases and in growths of all kinds, as has been clearly laid down by Mr Darwin." However, there are good reasons for supposing that the cause of the phenomenon lies in the special selection of data, which is inevitable in collecting human

material, rather than any natural peculiarity of the germ plasm itself.

The span of life and the generation time in man are very lengthy as compared with the period during which any family is kept under close observation. Very commonly, familial instances of hereditary or supposedly hereditary disease are only discovered because a parent and a child are both found to become affected at about the same time. When this is so, the parent, who will be on the average some 25 to 30 years older than the child, must have developed the disease 25 to 30 years later in life than the child. For example, if a father and son both appear on the books of a mental hospital within the space of a few years, the onset of acute mental illness will be found, almost invariably, to be at a later age in the father than in the son. The parent suffers from, say, an involutional condition with onset at the age of 55 and the son from a psychotic episode at about the age of 30. If three generations are represented simultaneously in a mental hospital, the effect is accentuated and we may find a grandparent suffering from senile insanity coincident with a very early psychosis or mental defect in the grandchild. These are the familial types which appear in human data. The complementary types, where disease in the parent has an early onset, say at 30 years, and the equivalent condition does not develop until the age of 55 in a child, born when the parent is 25, will rarely be observed. A period of 50 years must elapse between the onset of the disease in the parent and the onset in the child. Unless families are observed for very long periods, such cases will undoubtedly be missed. The exclusion of cases that show the converse of anticipation is assisted by the comparative infertility of individuals who suffer from chronic mental or physical diseases beginning early in life, who consequently tend to be infertile. Cases in which the parent had idiocy and the child senile psychosis never occur because of the infertility of idiots and not because the underlying hereditary influence undergoes a progressive change for the worse.

MUTATION AND SELECTION

Whenever a gene has among its possible manifestations the effect of making its possessor totally infertile, one particular specimen of the gene will be lost to the race. In ordinarily stable

conditions, that is, when a population is genetically constant, this loss is balanced by new mutation. If this were not so, all the genes producing hereditary defects associated even with relative infertility would have been eliminated in past ages by natural selection. In the absence of new mutation, dominant defects are rapidly eliminated from the population but, for recessive defects, the process is exceedingly slow. There are, however, exceptional cases because a gene which, in one setting, reduces fertility can in another setting cause increased fertility and these two effects might equalize. The conditions of equilibrium and the rate of natural selection under different conditions have been intensively investigated by Fisher (1930), Haldane (1932*a*) and Wright (1931).

The mutation rates of human genes, which cause lethal defects, can be estimated on the assumption that the population is in equilibrium and that gene loss through infertility is made good by mutation. However, at present such estimates are very provisional because of possible counterbalancing influences; the most important influence concerns hybrid vigour, or heterosis, as discussed in Chapter VI. The typical pedigree where new mutation can be postulated is one in which a condition known to be regularly dominant appears sporadically, that is, without affected parents.

RARE DOMINANT GENES

In human genetics, it is customary to speak of genes, which produce marked effects in single or heterozygous form, as dominant. The diseases inherited in this way are loosely termed dominant conditions. It would be more accurate to refer only to heterozygous genes and heterozygous defects because the term "dominance" has other meanings in genetics. However, when dealing with rare human dominants, no confusion is likely to arise from the use of the traditional terminology.

Defects due to rare dominant genes in man have characteristic pedigrees. In the standard case, where the presence of the gene is manifested in every heterozygote, three criteria are to be satisfied.

(i) There is sharp distinction between affected and unaffected persons in the same family.

(ii) Every affected person has an affected parent.

(iii) Approximately one half of the children will be affected in every sibship when there is an affected parent.

Very few inherited diseases agree precisely with these specifications. There are, however, many which conform closely enough for a single rare dominant gene to be considered the main causal factor. Among such conditions in man are Huntington's chorea and brachydactyly. Only the serological characters, such as the A, B and O, the M and N and the Rh series, conform perfectly. This is probably because the number of physical or chemical steps between a gene and its corresponding serological antigen is very small. In most diseases and malformations, as emphasized by Grüneberg (1947), the number of steps between the gene and the result observed clinically is very large, so that opportunities for modification of the final picture are extensive. When there are many steps, the final manifestation of the gene may be modified by actions of the other genes present in the individual, by environmental causes or even by quite unpredictable circumstances, which some investigators prefer to call the effects of chance. The results of modification appear in pedigrees as irregular modes of transmission; these are highly characteristic of human genetics.

IRREGULARITY OF MANIFESTATION

The repetition of exactly the same condition in generation after generation is such an unusual phenomenon in human pedigrees that it is worth while to examine in some detail the types of modification which are likely to occur. The time-honoured method of presenting pedigrees with black spots to signify affected cases is misleading and conceals the complexity of the material. This is especially true of dominant diseases associated with mental defect, where transmission is always irregular.

Even in such a typically dominant condition as Huntington's chorea, there is much irregularity in manifestation of symptoms and of the age of onset. In many hereditary diseases age of onset is closely allied to severity, for if the age of onset is very late, this is biologically equivalent to a mild case with average time of onset. Skeletal deformities, which show very strong dominance in some families, like ectrodactyly (absence of digits), in other families are quite irregular.

The path of transmission of the heterozygous gene may be

evident from the pedigree (Hanhart, 1945), in spite of many skipped generations. This skipping proves the presence of "normal overlaps", that is, persons who carry the dominant gene but who are, nevertheless, unaffected. Accordingly, if a condition known to be due to a dominant gene arises in a pedigree without any known ancestor having had the defect, it is not always safe to assume that there has been a recent mutation, though this is often an attractive hypothesis. When there is much modification, it is a matter of considerable difficulty to determine whether or not the main cause should be ascribed to a single dominant gene. There are, however, certain sources of variation in pedigrees which can be explained on genetical grounds, and some of them can be distinguished from one another by careful observation.

Modification of the effects of a gene in different members of the same family may be caused by the other autosomal genes in each individual. When this is so, we may expect to find a moderately significant degree of likeness in type of disease, with respect to severity, age of onset and symptoms, in different members of the same family. There will also be a tendency for such modification to produce a number of types which merge into one another, as, for instance, in Huntington's chorea.

When different clinical types are only found in separate pedigrees, as in some of the different forms of hereditary ataxia or the myopathies, more than one basic gene usually has to be postulated. When two or more distinct conditions are known which are very similar clinically and differ only in age of onset, the hypothesis that they are due to two or more allelic genes may be entertained. Alleles are genes which are situated at the same locus on the chromosomes of any individual. In the standard case there are only two alleles which can occupy any locus, one dominant and one recessive gene, for example, but there may be any number of them. Allelic genes are found to affect the same organic system of the body in slightly different ways, that is, like those for the A, B and O antigens, they have parallel effects. Several diseases of the same type, differing slightly in severity or in symptoms, may be due to genes at the same locus.

A further complication may arise on account of the interaction of allelic genes. Sometimes one or other of the series of possible allelic partners may alter the dominance of the main pathological gene and produce irregularities of a peculiar type in

pedigrees. This may be the case in dystrophia myotonica, where there is very little relationship between the severity of the disease in the parent and that in the children (Goldschmidt, 1938).

If there is a continuous series of clinical types but little or no resemblance between affected members of the same family, the variation may be interpreted as due to environmental or even to chance effects. Conversely, some similarities of symptoms within families may be attributed to environmental similarities.

A condition due to a single dominant gene may be differently manifested in the two sexes (sex influence) or confined to one sex (sex limitation). An example is early baldness, which is almost confined to men (Harris, 1948). Care is needed to distinguish sex-limited genes from genuinely sex-linked genes in pedigrees. Modification of a dominant defect by a sex-linked gene is another possibility, difficult to distinguish from sex influence except by accurate analysis.

The student of human pedigrees should also be warned that sometimes conditions that appear clinically identical or only very slightly different may be due to entirely different genes leading to approximately the same end results by diverse processes.

RARE RECESSIVE GENES

Completely recessive genes are those which do not manifest themselves in the heterozygote but only produce effects in homozygotes. That is to say, an individual with a recessively determined defect possesses the same pathological gene in duplicate. These two similar genes must have been inherited, one from each parent. The rules for the recognition of a disease due to a rare recessive gene follow from these facts. They apply to diseases with an incidence not greater than about 1 in 1000. Detection of common recessive traits is less straightforward.

(i) Affected and unaffected persons in the same family can be sharply distinguished.

(ii) Parents and all immediate ancestors are unaffected.

(iii) Father and mother are found to be blood relatives more frequently than expected from the consideration of the general population rate of consanguineous unions.

(iv) More than one offspring is likely to be affected. The proportion of affected in a series of small families will usually exceed the Mendelian expectation of one-quarter but it will

approach one-quarter in large sibships. This is a statistical consequence of the mode of selection of sibships in human data by the presence of at least one affected offspring.

(v) Occasionally cases occur in collateral branches of the same family group.

Since recessively determined diseases can, and usually do, arise in families where parents are perfectly normal, the effect of natural selection upon the genes responsible for them is very weak. Types of mental defect known to be due to recessive genes, like amaurotic idiocy and phenylketonuria, appear quite unexpectedly in families, and undoubtedly have been doing so for thousands of years in spite of the fact that the sufferers are themselves almost always completely infertile. The genes are carried on in the general population unobtrusively and their presence only comes to light when two carrier parents have a child, and then only in one-fourth of their children.

Although two abnormal mutant genes are eliminated each time an infertile recessive type is produced, it is not wise to infer that this loss has to be made good by new mutation in a stable population. The incidence of a rare recessive disease fluctuates rapidly if the degree of inbreeding alters. Moreover, if the carriers of the gene should be even very slightly more fertile than the rest of the population, this could counterbalance the rare loss of genes in the infertile recessives.

The visible effects of recessive genes are subject to modification both by environment and extraneous individual constitution. The range of variation of recessive diseases, however, is found to be more restricted than that of dominant diseases. Fisher (1930) pointed out that perfectly regular dominance of an abnormal gene is a very unusual phenomenon. He supposed that modification of the effects of harmful dominant mutants gradually progressed in a favourable direction under the influence of natural selection. He attributed the partial suppression of the harmful genes to the accumulation of genetical modifiers. A dominant mutant gene tends, thus, to acquire more and more the properties of a recessive trait. Natural selection cannot easily proceed further than this. Its action upon recessive genes is very slow. Hence, further favourable modification of abnormal recessive traits by the same method is not to be expected. Theoretical objections have been raised against Fisher's theory by

Haldane (1930), but it is a stimulating idea and may help considerably in the interpretation of the genetics of human defects.

ADDITIVE GENES

Some genes have characteristics which have been termed intermediate between dominant and recessive qualities. The colour of the Andalusian fowl is normally black, but a dominant mutant gene makes it bluish grey (Bateson, 1913). When two such genes are present, the bird is white with only small splashes of dark pigment. Thus the dominant, i.e. the heterozygous, type is intermediate between the normal type and the recessive or homozygous type. The pair of genes together are additive and have about double the effect of a single gene of the same sort. In man, this type of inheritance undoubtedly occurs. It has been described, for example, in Cooley's anaemia or thalassaemia (Valentine and Neel, 1944). Here, in the heterozygous form, the gene behaves as an ordinary dominant character, producing mild chronic anaemia. If two heterozygotes mate, one-quarter of the offspring are severely anaemic and suffer from a variety of symptoms, such as jaundice and enlarged spleen, in early life. As usual in human pedigrees, the manifestation of the gene is especially variable in its heterozygous form. If the heterozygous condition is exactly intermediate between those of the two corresponding homozygotes, there is sometimes said to be "absence of dominance", which means, in fact, absence of recessiveness. This use of the term "dominance" is confusing in human genetics and it is more convenient to classify such genes as perfectly additive.

Certain types of mental defect may be due to genes with additive tendency, and some pedigrees can be so interpreted. The family shown in Figure 4 contained defectives of all grades, but none was of any known specific type. Since the parents of the large sibship with three cases of severe defect were cousins, the hypothesis of recessive inheritance for these cases of imbecility and idiocy can be reasonably entertained. However, both parents and several other members of the family showed signs of mental inferiority, not amounting to severe defect but varying from mild defect to apparently normal mentality. This relatively mild subnormality shows an irregularly dominant type of

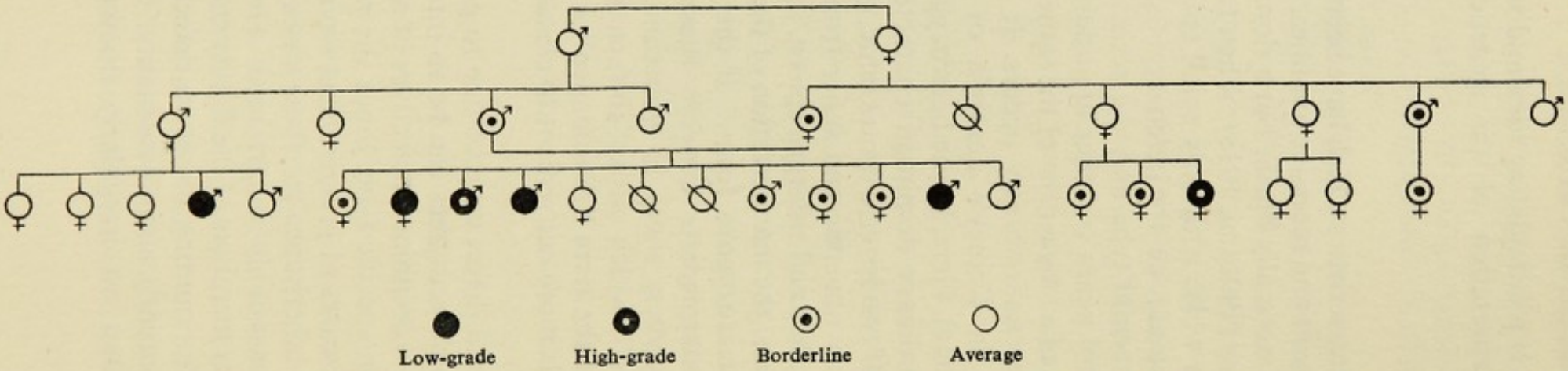


Figure 4.—Pedigree showing mental defect of no specific clinical type

The low-grade cases here are apparently due to an incompletely recessive gene, i.e. one with additive effects (Colchester Survey, 1938, Case No. 46)

inheritance which could be attributed to the same gene that caused the severe defect in homozygotes.

Human genes which cause rare recessive diseases do not usually give rise to noticeable effects in the heterozygous carriers. Genes responsible for characters which cause common variations, however, may more often be additive in their effects. In fact, from the genetical analysis of normal variations in stature or intelligence, it has usually been inferred that these are due to the combined effects of a large number of additive genes at different loci.

SEX-LINKED GENES

In man, sex-linked inheritance, or transmission of genes in the X chromosomes, presents very noticeable peculiarities. So far the only genes which have been assigned with certainty to the X chromosome are recessive or almost completely recessive abnormalities. The rules for the recognition of rare sex-linked recessives can be summed up as follows.

(i) Males are almost exclusively affected and are distinct from normal males.

(ii) Approximately one-half the males in an affected sibship show the condition and half the females are carriers. Female carriers are unaffected when the gene is completely recessive.

(iii) Both parents are nearly always normal, but maternal uncles are often affected. The sons of the sisters of an affected male, or of his maternal aunts, can be similarly affected. An affected father cannot transmit to his son.

(iv) In the extremely rare case of an affected female, her father and all her sons must also show the condition.

A few rare diseases associated with mental defect are transmitted in this manner. In general, the genes on the X chromosome do not play any greater part in the causation of mental defect than might be supposed from the fact that there are twenty-three autosomes to one sex chromosome in man. It is not easy to detect any phenomena which could be ascribed to sex-linked genes even in quite large quantities of pooled data. In sex-linked inheritance, fathers tend to resemble their daughters and not their sons; mothers resemble their sons more than their daughters. Hence, if defective fathers had more defective daughters than sons, and *vice versa*, genes on the X chromosome

could be blamed. The Colchester Survey brought to light 240 patients whose fathers were judged to be of higher mental grade than their mothers and 93 patients whose fathers were definitely of lower mental grade than their mothers. In Table XVIII the male children in the families where the mother was inferior and the female children in the families where the father was inferior are grouped together. If sex-linked factors were significant causes of variation in mental grade, these classes should contain more defectives than the two remaining possible groups of offspring. In this sample no appreciable difference in mental grade between the two groups of offspring is noticeable. The conclusion may perhaps be reasonably drawn that, although rare kinds of mental defect due to recessive sex-linked genes are known, there is no outstanding tendency for sex-linked genes to influence the genetics of mental deficiency (see also page 163).

TABLE XVIII

A Test for Sex-linked Genes as Causes of Mental Inferiority

Comparative Mental Grades of Parents and Sexes of Offspring	Grades of Offspring (patients and their sibs)						
	Superior	Average	Borderline	Feeble-minded	Imbecile	Idiot	Total
(i) Father superior to mother Sons . .	4	223	91	96	46	19	479
(ii) Father inferior to mother Daughters .	0	151	64	66	30	7	318
Total . . .	4	374	155	162	76	26	797
Percent. in each grade . . .	0·5	46·9	19·4	20·3	9·5	3·3	100·0
(iii) Father superior to mother Daughters .	4	196	95	97	38	15	445
(iv) Father inferior to mother Sons . .	1	156	56	62	23	13	311
Total . . .	5	352	151	159	61	28	756
Percent. in each grade . . .	0·7	46·6	20·0	21·0	8·1	3·7	100·0

If common sex-linked genes are significant factors in determining mental grade, the offspring in classes (i) and (ii) should be inferior to those in classes (iii) and (iv). This is, however, not so.

RARER TYPES OF INHERITANCE

Another type of inheritance could occur if the responsible gene were located on that portion of the sex chromosomes where crossing-over can take place between the X and Y chromosomes (Haldane, 1936). The criterion for supposing a gene responsible for a defect to be so located is that it is transmitted from a father to his sons if he has received it from his father, and that it is transmitted from a father to his daughters if he has received it from his mother. There is no evidence that such genes play any large part in the causation of mental defect, but they may cause occasional rare cases. (See Table XXXVII, page 172.)

Another peculiar kind of inheritance which would show characteristic features in a pedigree is that caused by genes located on the part of the Y chromosomes which does not cross over with the X chromosome. A trait so determined would be transmitted from fathers to all their sons and would never appear in any female.

More important in the present context, as pointed out by Haldane (1938*a*), is the genetics of abnormalities due to chromosome aberrations. Snell and others (1934, 1935), who induced changes of chromosome structure (translocations) in mice by X-rays, found that rather less than half of the offspring of irradiated mice had unbalanced chromosomes. Such offspring hardly ever developed normally and usually had hydrocephalus, anencephalus or other gross developmental defects involving the anterior part of the neural tube. If such conditions arose in man, the pedigrees would resemble those of irregularly dominant abnormalities associated with sterility. Transmitting parents would be always normal. A certain number of the offspring in each generation—not any exact Mendelian proportion—might be abnormal. Unbalanced chromosome sets may contain too much or too little genic material. In mice the abnormalities resulting from too much or too little chromatin were not distinct from one another. The ability of some unbalanced embryos occasionally to develop normally has been attributed to special, as yet unknown, environmental circumstances.

MATERNAL GENETICAL INFLUENCES

Besides the genes situated on the chromosomes in the cell nucleus, the cytoplasm of the cell contains substances, called

"plasmons" by von Wettstein in about 1920, which influence the development of the individual. They have been named "plasmagenes" (Darlington, 1944). Since the sperm cell contains very little cytoplasm, plasmic substances must be inherited almost entirely by way of the ovum. Up to the present time few instances of such inheritance have been established in experimental genetics. It is a possibility not to be overlooked in human pedigrees, if a disease affecting both sexes equally is always transmitted through the mother. Leber's hereditary optic atrophy, which sometimes occurs in association with mental defect, might be inherited in this way (Imai and Moriwaki, 1936), but great care must be exercised to distinguish cytoplasmic inheritance from that which is sex-linked or sex-limited.

The action of some genes is delayed, in that they affect the next generation and not the individual who carries them. For instance, the liability to twinning in cattle has been attributed to a recessively determined trait in the mother. Similarly, Bonnevie and Sverdrup (1926) have suggested that a recessive factor in the human mother makes her liable to give birth to twins. Hammond and Walton (1934) found that in rabbits a particular maternal constitution, inherited recessively, was responsible for producing a high proportion of atrophic foetuses. To investigate the possibilities of such conditions in man, the occurrence of abnormalities in the children of sisters would be sought. When dealing with a rare condition, the pedigrees would also be examined for any tendency of the mother's parents to be consanguineous.

Another method of gene action which has recently become a focus of medical study arises when there is a genetical difference of a specific kind between mother and foetus. Such disparity is known to be significant with respect to the Rh series of genes. Typically, the mother lacks an antigen, because she is homozygous for a gene which fails to produce this antigen, but the foetus inherits the antigenic gene from its father. The familial picture will be, to some extent, similar to that found when a maternal recessive factor is directly responsible for disease in the offspring. However, when there is antigenic incompatibility, the paternal side of the family may show affected individuals. The father himself might be affected though the mother could not be. The possible importance in the field of mental defect of antigenic differences between mother and foetus has been investigated by

actual search for antigens rather than by pedigree studies. Yannet and Lieberman (1944) and Snyder and others (1945) have made studies which suggest that cases of defect, unspecified clinically, show an abnormally high frequency of Rh positive types with an abnormally high frequency of Rh negative mothers. This implies that the presence of the D antigen in the foetus and its absence in the mother is a cause of mental defect. Later work, however, has not borne out the original contentions. The appearances of antigenic incompatibility in pedigrees have been described in detail by the present writer (1947). In rare cases, it may be a cause of defect associated with neurological signs. Other antigens may play their part also, because, as Waterhouse and Hogben (1947) have demonstrated, incompatibility between mother and foetus with respect to the A, B, O series of antigens is a cause of diminished viability in the offspring though the clinical details as yet are obscure.

MATERNAL ENVIRONMENT

The influences, correctly described as environmental, which act adversely upon the growing embryo from the time of fertilization of the ovum until birth are very numerous; for convenience they can be grouped under separate headings: (i) physical agents; (ii) nutritional effects; (iii) infections; (iv) maternal sensitization; effects connected with (v) maternal age and (vi) maternal parity. Further details are given in Chapter X.

(i) The development of the ovum in its very early stages can be interfered with by the action of X-rays. Cases have been reported in which very large therapeutic doses of X-rays have been given in the second month of pregnancy with the object of producing abortion (Goldstein and Wexlar, 1931). There was a direct effect on the foetus and miscarriage invariably resulted. Examination of the embryo showed, in some cases, colobomatous clefts of the retina associated with neuroepithelial tumours. Murphy (1929) found evidence that therapeutic maternal irradiation during pregnancy might not produce abortion but could still affect the growing embryo. In a series of 74 recorded cases there were only 36 normal children born, 23 imbeciles with heads of abnormal size and 15 offspring otherwise malformed or diseased. The effect, however, must be a rare one, for no instance of therapeutic maternal irradiation was found among

546 pregnancies terminating with malformed offspring investigated later by Murphy (1947). The exposure required to produce malformation is probably large, much more than that used for ordinary X-ray photography.

(ii) It is usually believed that a drug taken to produce abortion is either successful or has no effect on the growing embryo, but precise evidence is difficult to obtain. Experiments reported by Warkany (1947) have suggested that maternal nutrition in the early stages of foetal growth is a decisive factor in producing certain abnormalities. Some of these abnormalities are mimics of genetically determined features, and when this is so they are termed "phenocopies". Exactly how such experimental malnutrition produces its effects is not clear. The damage might be directly due to lack of certain vitamins or proteins, or it might indirectly be due to some complex toxic disturbance occasioned by the malnutrition of the mother. Murphy's (1947) survey showed that the frequency of severe foetal defects was no greater in the offspring of mothers with renal hypertension and albuminuria than in a random sample of pregnant women. He did find that diets deficient in calcium, phosphorus and vitamins B, C and D were common among pregnancies leading to foetal malformations, thus supporting the hypothesis that maternal nutritional deficiency may be a contributory cause.

(iii) With regard to toxins caused by infectious diseases, we are upon surer ground. Congenital syphilis is the classical example. The *treponema pallidum* can actually enter the embryonic substance; if this happens early, miscarriage is produced and, if later on in pregnancy, the child is born with signs of congenital syphilis. When the foetal resistance is higher or the infection milder, the effects of the disease may not be shown until later, as in congenital general paresis. Among other organisms known to penetrate to the foetal tissues are malaria parasites, though it is doubtful whether these can be responsible for mental deficiency. *Toxoplasma* is a protozoal parasite rarely found in man, but cases are definitely known where it has infected the foetal nervous system and caused progressive destruction, leading to idiocy. Bacterial diseases can be transmitted from mother to foetus, but no certain instance is known of such transmission having caused mental defect. Virus infections, however, are sometimes transmitted and may do great damage to the

foetus. Smallpox has long been known to be capable of transmission in this way, though it is not known to cause mental sequelae in the child. It has also been demonstrated recently that rubella, or German measles, can infect the foetus (Gregg, 1941). If the mother suffers from rubella during the early months of pregnancy, then there is danger that the foetus may develop cataract and deafness, with mental defect. Another known virus disease which can cause idiocy by infecting the human foetus is equine encephalomyelitis, but this is fortunately a very rare occurrence.

Experimental evidence of infection with virus diseases has been reported by Hamburger and Habel (1947). Microcephaly and impairment of growth of the entire embryo were produced, by injecting 48-hour chick eggs with *influenza A*, with great consistency. When injection was made at 4 days, the embryo died but was not malformed. Mumps virus did not produce specific malformations, but raised the incidence of types produced in uninfected eggs and was lethal in its effects.

(iv) As already mentioned, if genetically determined differences in constitution exist between mother and foetus, the mother may become sensitized and form antibodies inimical to foetal development, though this does not actually occur in every instance where it could occur. In all the cases so far established the effect of such sensitization acts by causing anaemia at a relatively late stage in foetal life. There may be disturbances also at earlier stages of development. These maternal influences though ultimately due to genes are, from the point of view of the foetus, part of the intrauterine environment.

(v) Although the means by which the foetus is influenced is obscure, there is little doubt that the age of the mother is very significant in the aetiology of malformations. In mongolism the effects of maternal age are particularly noticeable, since half the known cases are born at the maternal age of 38 years or later. In many other malformations, e.g. congenital hydrocephaly, a similar relationship has been observed, though the association of the incidence with maternal age is not always so striking. The incidence of binovular twinning also increases with maternal age. The prevalence of multiple births in the later maternal age groups can perhaps be regarded as a slight biological compensation for the higher infant mortality in this range, due to all types of foetal abnormality.

(vi) A disease dependent upon maternal age is difficult to separate aetiologically from one dependent upon the number of previous pregnancies (parity), because the two effects are so closely correlated. There is evidence that order of birth can have independent effect and that the first born, as well as those children born at the end of a long series of pregnancies, are less viable than those born in between, irrespective of the maternal age. Foetal malformations appear to be slightly commoner in the children of mothers having their first pregnancies (primiparae) than for the second and third. Ideas as to the possible reasons for these peculiarities are as yet in the speculative stage. Opinions are divided in implicating mechanical causes conditioned by uterine size, the maternal vascular condition and hormonal influences. It is to be remembered also that disturbances due to sensitization become more marked in later pregnancies.

INTRANATAL ENVIRONMENT

The importance of abnormal birth conditions in the causation of lesions of the central nervous system and the implied significance in causing mental defect was emphasized by Little (1861). Since that time some investigators, notably Doll, Phelps and Melcher (1932), have attributed practically all cases of cerebral diplegia to birth injuries. Most clinicians, however, recognize that the contribution of these accidents to mental deficiency as a whole is relatively small and that diplegias usually have other origins. According to Ehrenfest (1931), a large proportion of children are very slightly injured, when birth is quite normal, and new-born infants often show signs of cerebral injury such as nystagmus. Prematurity, in the sense of the infant's being exposed to the birth situation before it is quite fully developed, is held to be a factor predisposing to more serious cerebral injury because of fragility of the foetal blood vessels. Rydberg (1932) has made an extensive study of the problem and concluded that the most serious signs of cerebral injury in the newly born infant are twitchings, spasms, rigidity, disturbances in breathing, cyanosis and drowsiness. Many infants who show these signs die, and others recover. Among the recoveries there are undoubtedly some who show marked mental retardation, usually, but not always, accompanied by persistent neurological signs.

POSTNATAL ENVIRONMENT

According to legal definition, any accidents, which cause a deterioration in intelligence sufficient to imply social failure and which take place before the age of 18, may be considered causes of mental defect in a particular subject. If the suspected cause is to be considered the actual one, the subject must have had average mental capacity before the cause became active. In the case of accidents or diseases which cause cerebral injury in childhood, the history of normal ability before the event should be obtainable. The effect of hereditary disease which becomes manifest at a special point in the life of the individual must be differentiated. Most of these hereditary conditions, however, are progressive, like cerebromacular degeneration or some of the ataxias, whereas the effects of cerebral injury are usually stationary. Difficulty arises when the predominant symptoms are those of behaviour disorder. A behaviour disorder, developing in a person of fundamentally low intelligence, may give rise to a need for certification as, for example, in a case of encephalitis lethargica. The disentangling of cause and effect leading to the diagnosis of mental deficiency can be very complex in such instances (Penrose, 1932*b*). Another difficult type of case to classify can arise after cranial injury in childhood, in which behaviour disorder is marked although neurological signs are minimal and loss of intellectual powers only slight.

Finally, the training of a child and its emotional environment have to be considered. Antisocial training can produce a need for care and control in a person of low intelligence, where powers of independent judgment may be weak. It is still a matter for investigation to determine how far a psychopathic, antisocial personality can be brought into being by unfavourable surroundings during infancy and childhood. Many authorities believe that this is possible and of frequent occurrence. Similar theories apply to the origins of some psychoses; mental illnesses, which develop early, may prevent a normal intellectual level from being attained.

METHODS OF DISTINGUISHING BETWEEN NATURE AND NURTURE

The problem of allocating the cause or causes of mental defects either to inborn or acquired characteristics with scientific

accuracy has been shown to be much more complex than formerly supposed. When Galton (1875) first drew attention to the study of twins from this point of view, little was known about hereditary mechanisms. The principle, however, remains a good one. Since each member of a pair of monovular twins has exactly the same genetical equipment, it can be supposed that any dissimilarity between them which is manifest must be due to different environmental agencies. This statement requires two reservations. First, some developmental processes are asymmetrical. Just as the two sides of the body are unlike though they carry the same genes, so one monovular twin can differ naturally from the other in spite of having the same constitution. Secondly the environments for monovular twins, even for those separated at birth and subsequently reared apart, are similar during gestation. The maternal age, parity and state of health are the same for both, so that to some extent such twins are congenitally similar as well as genetically similar. In so far as this is so, the study of twins differentiates between happenings before and after birth rather than between happenings before and after conception. It is a remarkable fact that conjoined twins tend to be much less similar to one another than monovular twins who develop separately. In extreme cases, one of the pair can develop normally, or almost so, while the other may remain a collection of rudimentary parts. Whether these marked differences found in conjoined pairs can properly be attributed to peculiarities of environment is doubtful. Dahlberg (1945) has made the suggestion that, when there are no genetical or environmental causes evident, we are justified in ascribing twin differences to chance.

The comparison of monovular twins with binovular, on the assumption that for binovular pairs the environment is just as constant as for the monovular, is also misleading. Binovular pairs are genetically just as much alike as ordinary sib pairs, that is brothers and sisters. Maternal factors are constant for both types, but postnatal environment is usually more dissimilar for binovular than for monovular pairs. Hence the importance is evident of not drawing inferences about the maximum effect of environment from the study of monovular twins reared apart.

One other point needs attention, namely the method of deciding whether or not a pair of twins is actually monovular.

The probability of monovularity is increased by every similar trait found in the two. Some traits are more valuable indices than others. Sex, of course, must agree in monovular pairs and serology is extremely useful as a method of excluding cases who differ in any antigen. Physical measurements are convenient, but not always conclusive. Eye colour is a good character because it has so many genetical determinants; even this character fails in rare instances of heterochromia. Evidence from dermatoglyphs, including finger ridge counts, has proved a valuable instrument for twin diagnosis.

Another method of attempting to assess the significance of postnatal factors on the development of the individual's intelligence and behaviour is to compare adopted children taken to new homes with their sibs who remain in the original home surroundings. Unfortunately for purposes of research, many adopted children are those whose parents are unknown; often they have no full sibs. In spite of this, such experiments give extremely useful information and they avoid some of the difficulties inherent in comparison of twins.

Yet another method of comparing nature and nurture is based upon the assumption that environmental factors which cause variations in any character we desire to study are evenly distributed over the whole population. The expected degree of likeness between relatives, on the assumption that all variations are genetically determined, is then calculated and this degree is compared with the observed likeness. If the observed value agrees with the expected value, the only significant source of variation can be held to be heredity. For example, the expected likeness between sibs on the basis of certain assumptions about the mode of inheritance of stature would be equivalent to a correlation of +0·5. Since the observed likeness of stature in sibs has been found to be of the same order by many different observers, it can be argued that environment plays little part in determining stature. The argument, however, cannot be quite sound, since the stature of children is undoubtedly affected by nutritional factors.

The basic assumption that environment is evenly distributed is of doubtful validity. Environment can be similar for members of the same family group, and so a family likeness is produced. The effect is strengthened because families in different social and

occupational groups may be exposed to quite different environments. As pointed out by Hogben (1933*a*), even if the basic assumption of chance distribution of external circumstances were correct, it would not follow that a cause is unimportant simply because it is too infrequent to disturb materially the average likeness between relatives. The types of environmental agencies which can alter intelligence for better or for worse are elusive but are probably just as real as those, like malnutrition, which can affect physical size.

INTELLIGENCE OF TWIN PAIRS

The intellectual similarities of monovular twin pairs were noted by Galton, but the first psychometrical study in this field was made by Thorndike (1905). The resemblance of twins in mental traits was found to be twice as great as that for ordinary sibs. Merriman (1924) made a much more extensive study, testing 200 twin pairs with the Stanford-Binet, and he separated the two types, monovular and binovular, from one another. He showed that twinning itself was not associated with any mental handicap, and he also concluded that environment was insignificant as a cause of twin resemblance. Tallman (1929) used the same method, which consisted of finding the mean difference in score for pairs of children in a given relationship. Since the difference can be positive or negative, a better index would have been the mean square difference, which is equal to twice the "variance" or square of the standard deviation within the group of pairs used. However, 63 monovular twin pairs differed, on the average, by 5·1 points, whereas 39 binovular pairs differed by 7·4 points. From the assumption that the standard deviation of Binet I.Q. in the general population is 15 points, we can infer that the average difference to be expected between two children of the same age, tested at random, would be about 17 points.* Tallman's group of non-twin sibs had an average difference in I.Q. of 12 points. Thus, not only were sib pairs more like one another than pairs of children chosen at random, but binovular twins were again more alike than ordinary sibs. Twins of like sex

* Mean difference of pairs $= \sqrt{2/\pi} \times \sqrt{2} \times (\text{S.D.})$

$$= \frac{2 \times 15}{\sqrt{\pi}} = 16{\cdot}9$$

because mean deviation equals $\sqrt{2/\pi} \times (\text{S.D.})$

and sibs of like sex were more similar than comparable pairs of unlike sex.

The ratio of the variance of twin pairs, or sib pairs, to the variance of all pairs in the same sample taken at random can be used as an index of their likeness in terms of correlation. Thus if V_p is the variance of the twin pairs, i.e. half the mean of the squares of the differences between their measurements, and V is the variance of the whole set of measurements calculated in the ordinary way, irrespective of pairing, then $V_p/V=1-r_p$ or $r_p=(V-V_p)/V$. This value, r_p, is equivalent to the intraclass correlation coefficient of Fisher (1938). It is convenient to use this coefficient to express the likeness of twin or sib pairs. If monovular twin pairs were exactly alike in their intelligence measurements, their mean difference would be zero, their variance within the group of pairs zero, and their intraclass correlation unity. In practice, differences between monovular pairs are found, and it is usually conceded that they represent, in the main, the effects of environment, though they may also be caused by inaccuracy of measurement. Presumably at least as much of the variance of binovular pairs is due to the same causes. On the other hand, similarities of environment, occasioned by the fact of their being twins, will tend to make binovular measurements more alike than corresponding measurements for ordinary sib pairs. Holzinger (1929) has suggested allowing for this by making the discrepancy between the variances of monovular and binovular twins (in terms of the binovular variance) the decisive measurement of hereditary influence. That is, if V_m is the variance between monovular twins and V_b that between binovular twins, Holzinger's index, h^2, which is intended to measure the proportion of variation due to heredity in the trait concerned, is obtained thus:

$$h^2=\frac{V_b-V_m}{V_b}=\frac{r_m-r_b}{1-r_b}.$$

If the index has the value of unity, all variations in the trait are due to heredity; if it has the value zero, they are all due to environment.

The results reached by use of this formula must not be too rigidly interpreted, but are of intrinsic interest. Wingfield (1928) found, for example, $r_m=0{\cdot}90$ for I.Q. in 42 monovular pairs and

r_b=0·70 in 57 binovular pairs. The Holzinger index, h^2, is therefore 0·67 and can be interpreted as meaning that nature is twice as powerful as nurture. Newman (1942) gave values of the same index, 0·68 for Binet I.Q. and 0·80 for Otis I.Q.; for ability in science, the index was only 0·34 and for arithmetic tests only 0·12. For physical characters, like stature and weight, the indices were higher, 0·81 and 0·78 respectively. Herrmann and Hogben (1933) considered that hereditary influences accounted for about half the total variation in the intelligence measurements of children. Judged by twin data alone, hereditary influence would be somewhat stronger. Thus, r_m, for intelligence measured by the Otis test, was 0·84 and r_b, 0·48; hence the Holzinger index would be 0·69. Holzinger (Newman *et al.*, 1937) himself, using the Binet I.Q., found r_m=0·88, r_b=0·63 and h^2=0·68.

Data of more immediate interest in relation to mental defect have been published by various investigators, who collected sets of twins one or both of whom were defective mentally. Rosanoff (1931) found 33 monovular both affected and 2 cases with one normal and one affected. Among the binovular twins, he found 32 both affected and 28 cases with one of the pair normal. Similar results were obtained by Smith (1929), who found the discrepancy between the two types of twins, with respect to mental defect, even greater. Surveys of this kind, however, must be interpreted cautiously. In the case of mongolism, for instance, except for two instances of affected twins who may have been binovular (McKaye, 1936; Jervis, 1943), all reported cases in twins are of two kinds, monovular and both affected or binovular and only one affected. Hence, by all methods of twin analysis, it would appear that environment plays no appreciable part in the causation of mongolism. This conclusion, however, is certainly false since factors related to maternal age are undoubtedly very important in the aetiology, p. 186.

The fact that monovular twins usually have very similar early environments makes it difficult for any method of twin analysis to give information about prenatal phenomena. Occasionally, however, cases of monovular twins are noticed who differ very much in mental capacity at birth. In the pair described by Hobbs (1941), one child had a Binet I.Q. of 109 and the monovular twin sister had a Binet I.Q. of 57; the discrepancy could have been due to injury of one twin at birth. Other cases, such as that of

Lewis (1936), which shows that endocrine dystrophy can occur in only one of monovular twins, and those of Dennie (1924) and Penrose (1937), which show congenital syphilis in only one of such a pair, are also of clinical interest because they indicate the extremes of differential environmental effects which can occur even in the prenatal period.

Twin study can further be used to indicate the possible effects of environment in the formation of character traits. Newman (1942) found that between monovular twins marked differences in temperament often developed and increased with age, even when the twins were reared together. It is not impossible for psychosis to develop in only one of a pair of monovular twins, but this, according to Smith (1929) and Rosanoff, Handy and Plesset (1935) is rare; Hobbs (1941), however, quotes several such cases. Since the diagnosis of defect, especially in the higher-grade groups, depends upon social adjustment, these studies cannot be ignored in the search for causes of mental defect in the environment of early childhood. The investigation of cases of monovular twins reared apart enabled Newman to affirm that such pairs showed greater differences, both in mental ability and personality, than pairs reared in the same environments.

EVIDENCE FROM CHILDREN IN FOSTER HOMES

The effects of environment upon the intelligence levels and personalities of children not brought up in their own homes have been studied by Freeman, Holzinger and Mitchell (1928). A large number of children were examined; they were given intelligence tests before placement in foster homes and at various intervals subsequently. The new environment, from the point of view of educational opportunity as well as social training, was on the average an improvement upon the original home environment, though the foster parents varied in intellectual and social level. The foster children showed a significant tendency to develop resemblance to the foster parents, both in mental level and in behaviour. The longer the period of adoption, the more marked was the change. The investigators concluded that improvement in environment increased the intelligence. In the whole group of 401 children, a correlation of +0·48 was obtained between intelligence and foster-home rating. Pairs of unrelated children reared in the same foster home developed

significant positive intercorrelations for intelligence. Also, the correlation between children and their foster parents on the Otis test scores was found to be +0·37. These results are of particular interest in the study of mental defect because many of the actual parents of the children placed in foster homes were rated as feeble-minded and even more were considered to be morally defective. In spite of this background, few cases of serious misbehaviour occurred in the foster homes. The significance of these findings would be very much diminished if there were reasons for supposing that more intelligent foster parents selected more intelligent foster children. The investigators admitted that this might have occurred, but not, they believed, to a sufficient extent to invalidate their conclusions.

Burks (1928) made a somewhat similar analysis of children in foster homes in California and again found significant correlations between foster child and foster parent (especially the mother) with respect to intelligence. Her conclusions were guarded but, after making a number of corrections, she asserted that 17 per cent. of the variance of I.Q. was contributed by home environment and that an exceptionally good environment could raise the I.Q. rating of intelligence more than 20 points. A substantial reduction in mental defect in a community would be achieved if the general level of intelligence were even raised 5 or 10 points. Comprehensive claims for the beneficial effects on I.Q. of good home environment and education, especially at the infant school level, were made by Wellman (1945), but these have not been accepted as valid by critical authorities (Thomson, 1947).

The converse analysis, of children adopted or fostered in similar environments, has also been made to find out whether, despite improvement of opportunities, differences in mental level remain, presumably because they are due to genetical causes. Lawrence (1932) tested illegitimate children in orphanages and found significant relationship between intelligence of the child and occupational status of the father, even though most of the subjects had never had home environments of their own since the age of one year. In the extensive study of 800 children in orphanages, carried out by Carr-Saunders and Jones (1927), a differentiation with respect to intelligence, corresponding to occupational class, was reported, but this differentiation tended to become obscured as length of time of residence increased.

Investigation of the problems of nature and nurture in children educated away from the usual family surroundings provides samples, which can be much larger and more homogeneous than are possible with twin studies. The method is less spectacular than twin analysis, but deserves to be used more widely. Both methods, however, have given results which show that the postnatal environment can contain decisive psychological factors tending to cause or prevent the development of mental defect.

CHAPTER V

METHODS OF ANALYSIS IN HUMAN GENETICS

General Principles—Association and Dissociation of Characters in the Same Person—Linkage—Gene Frequency—Deviations from Random Mating in Man—Parental Consanguinity Formula—Multifactorial Genetics in Man—Correlation Coefficients between Relatives of Different Degrees and Types—Assortative Mating—Mendelian Ratios—Birth Rank and Maternal Age.

GENERAL PRINCIPLES

THE understanding of the biological background of mental defect implies a knowledge of the formal principles of human genetics. In man, genetics is not an experimental science carried out with laboratory animals. The data are provided by circumstances outside the control of the investigator and their study forms a descriptive and inductive science with some resemblance to astronomy as opposed to experimental physics. Some acquaintance with elementary biology and animal genetics is necessary but is not sufficient for the analysis of human genetical data. Special difficulties have to be met by special techniques not usually dealt with in biological text-books. A descriptive outline of methods, which have proved useful in genetical analysis of mental defect, is therefore given in the present chapter.

In earlier chapters it has been emphasized that mental deficiency is not an inherited character in the ordinary sense. To obtain a true picture, the various influences, recent and remote, which combine to produce the end result have to be separated from one another. The analysis can proceed to the recognition of the effects of particulate genes in certain well defined instances. In such cases the arithmetic of gene frequency can be applied with advantage. Quite commonly, although a disease can be attributed to a single gene, the gene is only a part cause of mental defect. In some patients the presence of a known hereditary condition may be incidental and unconnected with the mental changes.

The reasons for the association of physical and mental defects, so frequently found in institutional cases, are not always strictly genetical. A disability like blindness can be distributed evenly over the population, in so far as mental capacity is concerned, and yet, owing to the extra difficulties encountered by a disabled person in social and educational adjustment, the risk of such a person's being diagnosed defective is accentuated.

Another extraneous cause of such a combination was emphasized by Pearson (1931). Both mental and physical disabilities and chronic diseases depress the social status of the individual, who is subject to them, and of his family. Owing to the tendency for mating to be confined within one social stratum, hereditary defects of quite different kinds, especially those which are dominant, can become concentrated in the same individual or in different members of the same closely related group. This type of familial concentration is similar in principle to the concentration of genes in different localities, climates and societies, known as racial grouping. However, the assumption is too often made that these processes lead to the formation of special "social problem" groups, reservoirs of defect and degeneracy in populations. Such theories cannot be justified in the absence of careful application of statistical genetical methods. To assume that such groups of genetical origin exist before these principles are applied is prejudicial to scientific enquiry.

ASSOCIATION AND DISSOCIATION OF CHARACTERS IN THE SAME PERSON

In human genetics it is important to distinguish clearly between association of characters and genetical linkage. Since the concurrence of (or positive correlation between) two symptoms or traits can arise in a number of different ways, it is useful to examine methods of distinguishing the causes of such concurrence.

The first idea to examine is that two associated traits are manifestations of the same gene. This is called "pleiotropism" and is a well known phenomenon in experimental genetics. There are many steps between the chemical process initiated by a gene and the final morphological or clinical result. Sometimes

the interrelationship between pleiotropic effects can be ascertained by careful pathological enquiry on experimental animals (Grüneberg, 1947). More often, no connection can be found other than the fact that the two symptoms, such as polydactyly and retinal degeneration, tend to arise in the same individual. It is simpler to assume the existence of one gene rather than of two and the explanation of pleiotropism should always be first considered. For example, an abnormality, such as hereditary cataract which occurs in a case of mental defect, may be ultimately conditioned by the same gene as that which causes the defect. Manifestations of pleiotropism can be variable, in that the association of hereditary disease and mental symptoms may occur in one case but not in another, as for example, in the hereditary ataxias.

Effects due to environment, superficially resembling pleiotropism, can also give rise to positive correlations between characters. Thus, malnutrition can diminish body weight and also interfere with development of the teeth. Two such effects would be positively correlated in the general population and also within sibships.

Instead of assuming only one gene to explain two associated traits, we can assume two genes to be acting. This does not imply that the two genes are genetically linked in the sense of being located together on one chromosome, as has been too frequently assumed in the literature of human genetics. Several other types of association are possible and indeed usually much more probable. The social concentration of genes for various defects in a population, after the manner suggested by Pearson, is statistically similar to geographical concentration of genes. Thus, van Herwerden and Boele-Nyland (1930) noted a positive correlation between dark hair and blood antigen B in the general population of Holland and attributed this to uneven geographical grouping. The test for this kind of hypothesis is to examine sibships. If racial concentration, or its equivalent, is solely responsible for the association in a sample of unrelated individuals, this correlation will disappear within the sibship because there the parental types are fixed. This simple test appears to have been neglected by race theorists.

Less attention has been paid to the dissociation of characters than to their association. Two characters can, however, tend

to be negatively correlated. This may happen if they are physiologically compensatory, like length and breadth of the head among people of equal cranial capacity. More interesting, genetically, is the behaviour of two dominant allelic genes. The presence of one precludes the presence of the other on the same chromosome. Thus, there is a slight negative correlation between their effects if they are separately dominant, like the A and B blood antigens. The fact that blood group AB is found to be much less frequent than it should be in the general population, on the assumption that both A and B are quite independently assorted, is, in itself, strong evidence in favour of their being due to allelic genes. Table XIX summarizes these points concerning association and dissociation.

TABLE XIX

Cause of Relationship between Two Genetical Characters	Direction of Association	
	In General Population	Within the Sibship
Same gene (pleiotropy) . .	+	+
Geographical grouping . .	+	0
Allelic genes	−	−
Linked genes	0	+ or −

LINKAGE

Genetical linkage of two genes does not cause any correlation of the characters which they determine in a general population of unrelated individuals. Within a sibship or within a group of collateral relatives, it produces either an association or a dissociation according to whether the two genes concerned are in the phase of coupling or of repulsion. Both phases are equally frequent in ordinary circumstances with random mating. If two rare recessive traits were closely linked, however, the coupling phase would cause their association in sibships with consanguineous parents (Haldane, 1950)* but the repulsion phase would not be noticeable.

The mistake is often made of supposing that two characters appearing simultaneously in certain members of a sibship are necessarily linked. This can be avoided by realizing the necessity

* *Ann. Eugen., Lond.*, **15**, 15.

of demonstrating the complementary picture of the same two characters in repulsion in another sibship. If blue eyes and fair hair were assumed to be genetically linked, then we should be able to collect sibships where the traits were associated; there would also be sibships where those sibs who had blue eyes had dark hair and those who had brown eyes had fair hair. The analysis of genetical linkage involves difficult mathematical problems. One certain linkage is known in man, namely, that between the genes for colour blindness and haemophilia. The search for other linked characters is likely eventually to prove a fruitful inquiry, because knowledge of the dispositions of genes upon the human chromosomes will greatly help in classifying pedigrees of hereditary diseases. At present we are always dogged by the suspicion that two pedigrees of apparently the same disease may be really due to different genes. A map of the human chromosomes, like that of *drosophila* prepared by Morgan (1919) and his associates, will eventually tend to allay such doubts. Knowledge of linkage will also be valuable in assisting eugenic prognosis, see pages 220 and 273.

The peculiar condition of very close linkage of genes with similar effects, believed by Fisher to account for the behaviour of the Rh complex (Race, 1944), may be commoner in genetics than was formerly supposed. However, crossing over in such systems is so rare that close linkage of this type cannot be distinguished from one gene with multiple effects in ordinary work on human pedigrees.

GENE FREQUENCY

The concept of gene frequency is of fundamental importance in the genetics of wild populations, which human populations resemble much more closely than selected breeds of laboratory animals. The idea is essential to the mathematical study of evolution because many of the processes of natural selection can be expressed in terms of progressive increase or decrease in gene frequencies. In the shorter-term problems of human populations, the concept is also indispensable. The elementary theoretical results were discovered independently by Hardy, Pearson and Weinberg.

Let us suppose that the frequency of a given gene, A, in the general population is represented by p. Further, let the

frequency of the allelic partner gene, a, be $1-p$. Every chromosome is represented twice in each person, so that three types of individual are possible. These are (i) AA, those homozygous for A; (ii) Aa, those heterozygous for both A and a; and (iii) aa, those homozygous for a. The frequencies of these three classes in a system of random mating will be p^2, $2p(1-p)$ and $(1-p)^2$, respectively. If the gene a is infrequent as compared with gene A, class (ii) will be much more numerous than class (iii). Thus, if $p=\frac{9}{10}$, the relative numbers in the three classes are as 81 : 18 : 1.

It can be easily appreciated that in the case of a rare recessive defect, whose genotype is represented as aa, the heterozygous carriers of type Aa will be much more prevalent than the people actually showing the disease. If, as Goddard (1914) suggested, all mental defect were due to a single recessive gene a, the type aa must have a frequency in the community of about 2·56 per cent. The frequency of gene a would thus be $\sqrt{0{\cdot}0256}$ $=0{\cdot}16$. Hence, the relative numbers of the three types AA (normal), Aa (normal but carrier of defect) and aa (defective), if mating in the general population were at random, would be

$$70{\cdot}56 : 26{\cdot}88 : 2{\cdot}56.$$

More than a quarter of the population would be carriers, a much greater proportion than the 10 per cent. supposed to constitute the social problem group.

An important consequence of random mating is that, under its influence, the ratios of the various genotypes to one another remain constant. This can be easily verified in the full table of all the possible parents and children of each genotype with suitable frequencies assigned, as shown in Table XX. Here the simplest case is considered: there are supposed to be two alleles, A and a, neither of them recessive. Their initial frequencies are p and q (where $q=1-p$). The frequencies of each possible type of mating are found by multiplying together the initial frequencies of the two parental types. It is further assumed that each type of mating produces the same total number of offspring, that is, fertility is constant. Thus, if each $AA\times AA$ mating produces two AA children, each $AA\times Aa$ mating will produce one AA child and one Aa child. The total numbers of children of each genotype are seen to be distributed

TABLE XX

RANDOM MATING OF PARENTS (GENERAL CASE)

Possible Matings				Offspring		
Parental Genotypes			Frequency	Frequency of each Genotype		
Father		Mother		*AA*	*Aa*	*aa*
AA	×	*AA*	p^4	p^4	—	—
AA	×	*Aa*	$2p^3q$	p^3q	p^3q	—
AA	×	*aa*	p^2q^2	—	p^2q^2	—
Aa	×	*AA*	$2p^3q$	p^3q	p^3q	—
Aa	×	*Aa*	$4p^2q^2$	p^2q^2	$2p^2q^2$	p^2q^2
Aa	×	*aa*	$2pq^3$	—	pq^3	pq^3
aa	×	*AA*	p^2q^2	—	p^2q^2	—
aa	×	*Aa*	$2pq^3$	—	pq^3	pq^3
aa	×	*aa*	q^4	—	—	q^4
All types			1	p^2	$2pq$	q^2

in the same proportions, p^2, $2pq$ and q^2, as were assumed for the parental generation.

From such a table the proportions of genotypes which can be derived from each type of parental mating can be calculated for any gene frequency. In the case of a dominant and recessive allelic pair, where *AA* and *Aa*, for example, are indistinguishable, the table can be simplified and would appear as in Table XXI. By substituting the value of 0·16 for q and 0·84 for p in Table XXI, on the hypothesis that a single recessive gene with frequency 0·16 is the cause of all mental defect, Table XXII is obtained. It is clear that the great majority of defectives

TABLE XXI

RANDOM MATING OF PARENTS (RECESSIVE GENES)

Possible Matings		Offspring		
Parental Genotypes		Frequency	Frequency of each Genotype	
Father	Mother		Dominant Type *AA* or *Aa*	Recessive Type *aa*
AA or *Aa*	*AA* or *Aa*	$p^2(1+q)^2$	p^2+2p^2q	p^2q^2
AA or *Aa*	*aa*	$pq^2(1+q)$	pq^2	pq^3
aa	*AA* or *Aa*	$pq^2(1+q)$	pq^2	pq^3
aa	*aa*	q^4	—	q^4
All types		1	p^2+2pq	q^2

TABLE XXII

RANDOM MATING OF PARENTS (RECESSIVE GENE WITH FREQUENCY 16 PER CENT.)

Parental Matings*	Frequency	Offspring: Percentages of each kind*	
		N	*D*
N × *N*	94·95	93·14	1·81
N × *D*	2·49	2·15	0·34
D × *N*	2·49	2·15	0·34
D × *D*	0·07	0·00	0·07
All types	100·00	97·44	2·56

* *AA*, or *Aa*, classified as normal, *N*; *aa*, as defective, *D*.

would, in such a system, be derived from normal parents Both parents would be normal for 1·81/2·56, or 71 per cent. of defectives, and one normal for 0·68/2·56, or 27 per cent. of them. All in all, 84 per cent. of such parents would be normal and 16 per cent. defective. This is not far from the proportions actually found in some estimates, but the theory is nevertheless certainly fallacious. No single recessive gene could be responsible for all the different clinical varieties of mental defect, and the distribution of intelligence is continuous. An important principle, however, is demonstrated here, namely, that the rarer a recessive condition, the fewer instances will there be of affected parents. Indeed, the proportion of cases with affected parents is the same as the gene frequency (q). Hence in extremely rare recessively determined diseases the random mating table can still be almost correct even if all affected individuals are infertile.

DEVIATIONS FROM RANDOM MATING IN MAN

If the mating system in the population studied is not random, gene frequency calculations may require considerable adjustment. In human populations there are two common kinds of departure from random mating, due respectively to (i) inbreeding, and (ii) assortation. Both processes tend to increase the frequency of homozygotes in the population. The first has special significance in relation to recessive inheritance and will be discussed immediately. The second, assortative mating, will be considered later.

Inbreeding in man is limited by laws and customs, and commonly the closest type of union is that between first cousins. In some primitive communities incest occurs, while in others even first-cousin marriages are considered abnormally consanguineous. All European communities which have been subject to genetical observation contain first-cousin marriages in excess of random expectation and thus show a definite tendency towards inbreeding.

It has been known for a long time, and commented upon by Darwin (1868), that parental inbreeding probably favours the appearance of certain congenital defects in the offspring. Garrod (1902), however, was the first to explain the mechanism. Alkaptonuria, an extremely rare abnormality, was found to arise from consanguineous unions in more than half the known cases. Garrod pointed out that a very rare gene could only easily occur in both parents if they had a common ancestor. In this way the observations, that defects such as the deaf-mutism observed by Boudin (1862) were associated with inbreeding, could be given a clear biological interpretation. On analysis of the gene frequencies involved, it becomes plain that only in rare recessive diseases—the rarer the better from this point of view—is consanguinity of significance. The necessary formulae relating gene frequency to parental consanguinity were explicitly given by Lenz (1919).

PARENTAL CONSANGUINITY FORMULA

The following argument only applies to recessively determined diseases whose frequency in the general population is less than 1 in 1000 and preferably less than 1 in 10,000 and which occur in populations where close inbreeding is uncommon. Call the frequency of first-cousin unions, in the general population, α; this quantity will vary in most communities under consideration between $\frac{1}{2}$ and 2 per cent.

Let the three genotypes be represented thus:

Genotype	Phenotype	Frequency
BB	Normal homozygote	p^2
Bb	Normal heterozygote	$2pq$
bb	Affected homozygote	q^2

where $p+q=1$ and q is, say, 1/100.

Now, in the limiting case where the frequency q approaches

zero, every relevant family showing affected homozygous offspring, *bb*, is derived from a pair of normal heterozygous parents, *Bb*. Consider, therefore, the case of a given heterozygous individual, *M*. The chance that he will mate with a first cousin is α, and the chance that he will *not* mate with a first cousin is $1-\alpha$, or, for practical purposes, unity.

The chance that *M's* first cousin will be heterozygous for the rare gene *b* is $\frac{1}{8}$ (see Table XXIII); so that the chance that *M* mates with a heterozygous first cousin is $\alpha \times \frac{1}{8}$. Now, if *M* mates with an unrelated person, the chance that his mate will be heterozygous is $2pq$, or, for practical purposes, $2q$, since p is very nearly equal to unity.

The total chance of mating with a heterozygote is, therefore, $\frac{\alpha}{8}+2pq(1-\alpha)$, that is nearly $\frac{\alpha}{8}+2q$. Hence, the frequency, *F*, of first-cousin unions among all matings which can give rise to defective homozygous offspring must be $F=\left(\frac{\alpha}{8}\right)/\left(\frac{\alpha}{8}+2q\right)$ $=\frac{\alpha}{\alpha+16q}$ (see Appendix 5). In making an expected estimate of *F* from an observed frequency (q^2) of known cases of a recessive condition, cases known to have consanguineous parents should, as far as possible, be excluded.

It does not follow from these considerations that any union of first cousins will necessarily produce recessively affected offspring. In the general population the proportion of unrelated matings liable to give rise to affected offspring of the particular kind is $4q^2$. According to the previous argument, cousin matings exposed to the same risk will constitute a proportion, $4q^2 \times \frac{\alpha}{16q}=\frac{\alpha q}{4}$. That, however, is only a very small proportion of all first-cousin marriages, i.e. only $\frac{\alpha q}{4} : \alpha$ or $\frac{q}{4} : 1$. Thus, while first-cousin marriages are more likely to lead to recessively affected offspring than are random unions, the chance that any given child of a consanguineous union, taken at random, will be affected with a given recessive abnormality is still quite remote, i.e. of the order of 1/400 if $q=1/100$.

The biological effect of inbreeding is most marked when recessive traits are rare. Furthermore, an increase in the amount of inbreeding effectively increases the incidence of a rare recessive defect, but causes little change in the incidence of a common recessive character. Consequently, the incidence of rare disease of recessive origin fluctuates from time to time and from place to place according to the amount of inbreeding in the community concerned. Haldane and Moshinsky (1939) have pointed out that a reduction in the number of cases of rare recessive defects is likely to be taking place at the present time in European communities because inbreeding is becoming less frequent. The gene frequencies corresponding to each condition, however, are not appreciably changed.

MULTIFACTORIAL GENETICS IN MAN

Much attention is paid in all books dealing with human genetics to dominant, recessive and sex-linked types of inheritance. These can be strikingly demonstrated in pedigree studies. Actually the type of inheritance most commonly observed in human genetical material is due to the combined actions of more than one gene. Indeed, the number of genes involved can be very large. The genetical basis of characters, whether physical, like stature, head size and cephalic index, or mental, like intelligence level, specific ability or temperament, is mainly multifactorial. So is the basis of the inheritance of qualities like susceptibility to common disease. If the physical or mental types which are considered, by Sheldon and others (1940, 1942) and Draper and others (1944), to be related to these susceptibilities are genetically determined, they are also multifactorial. Any character which does not clearly segregate but which gives rise to a continuous distribution cannot be determined solely by one gene. Usually, numerous environmental influences also contribute. It seems therefore worth while to devote some space to the discussion of the theory of this important branch of human genetics, which, indeed, involves one of the earliest established techniques of genetical analysis.

Galton (1889) published the results of his observations on family likeness and individual variation in respect of stature in man. He observed that if sets of paired measurements of

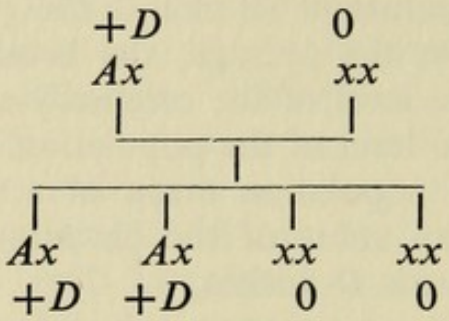
related persons were plotted against one another, the degree of familial likeness could be estimated. The method was to take a group of men of the same stature and to find, for example, the mean stature of their brothers. Thus, the mean stature of brothers of men 72·2 inches tall was found to be 70·3 inches; whereas the mean stature of all men in the general population was 68·2 inches. On the average, the brothers stood about halfway between the level of the originally specified group of men and the normal level of the population. In general, if the deviation from the population mean of a given man is D_1 inches and the mean value of the deviation, from the same origin, of his brothers is D_2 inches,

$$\frac{D_2}{D_1}=r', \text{ or the regression coefficient.}$$

In such a case as this, where the distribution is symmetrical because it is immaterial which brother is taken first, r' is equal to the correlation coefficient. Substituting, $D_2=70{\cdot}3-68{\cdot}2=2{\cdot}1$ and $D_1=72{\cdot}2-68{\cdot}2=4{\cdot}0$, the value, $r'=2{\cdot}1/4{\cdot}0=0{\cdot}5$, is obtained. In actual practice the series of mean values of brothers' statures will not lie perfectly upon a straight line on a scatter diagram and the regression coefficient has to be calculated by finding the covariance and variance. When the table is symmetrical, as with brother–brother pairs, the correlation coefficient—the product moment coefficient of Pearson and Bravais—is identical with the regression coefficient because the variances of the two compared groups are equal. In the more general case, where, say, parents and children are studied, there are two regression coefficients differing from one another by virtue of the different variances of the two classes compared; the correlation coefficient is then the geometric mean between the two regression coefficients.

The genetical background of the regression or correlation value of $\frac{1}{2}$, which was so frequently found by Pearson in comparisons of measurements of pairs of sibs or of parents and children, is extremely simple. Let the gene A be responsible for a quantitative alteration in a metrical character by the amount $+D$. Should a parent have such a gene, his stature will be $+D$ above the normal, assuming that the allelic gene x he carries is neutral in this respect. Suppose the other parent

has average stature, neutral genes and zero deviation. The parent whose genotype is Ax will transmit the gene A to half the offspring. Hence the average deviation from the normal in the stature of his offspring will be $+D/2$, as can be seen in the chart:



Similarly, half the brothers or sisters of a propositus of type Ax with deviation $+D$ will have deviations $+D$; thus, the mean stature deviations of the sibs will be $+D/2$. The regression coefficient in either case is $(+D/2) \div (+D) = \frac{1}{2}$.

The fraction, $\frac{1}{2}$, which measures the correlations of many metrical characters in parent–child and sib pairs, is a direct consequence of the fact that a parent transmits to each offspring half of his genic material. This is only strictly true of autosomal genes. In the case of sex-linked genes, when sex of parent and child is specified, the situation is different.

It is easy go see that this argument can be extended to any degree of relationship. If a grandparent has a gene causing the deviation $+D$, one-quarter of his grandchildren will have it. Their mean measurement will be $+D/4$ and the regression coefficient, or measure of likeness, is $\frac{1}{4}$. In general terms, the degree of hereditary likeness between the two relatives depends, as shown in Table XXIII, upon the number of steps in the relationship.

The actual degree of likeness is the same as the probability of having the same gene as the propositus only if each gene has its full effect independently of other genes that are present. In reality the effects of genes can be hidden on account of their recessivity, through modification by other genes or by environmental influences. These factors usually diminish familial likeness of related persons; but in the case of environment, which modifies members of family groups all in the same sense, likeness is increased.

TABLE XXIII

Type of Relationship to Propositus	Number of Steps in Relationship	Degree of Hereditary Likeness, i.e. probability that the relative carries the same gene
Sib, parent, child . . .	1	$\frac{1}{2}$
Half-sib, uncle, aunt, nephew, niece, grandparent, grandchild	2	$\frac{1}{4}$
First cousin, great uncle, great nephew, great-grandparent, great-grandchild . .	3	$\frac{1}{8}$
First cousin once removed .	4	$\frac{1}{16}$
Second cousin . . .	5	$\frac{1}{32}$
General case	n	$1/2^n$

CORRELATION COEFFICIENTS BETWEEN RELATIVES OF DIFFERENT DEGREES AND TYPES

The theoretical correlation coefficients between relatives for hereditary characters can be derived from distributions of parents and offspring as in Table XX. In the standard case we assume that each gene asserts its effects independently and that such effects are precisely additive (Fisher, 1918). Thus, the gene *A*, present in homozygous form *AA*, will be supposed to exert just twice as much effect as when it is present in heterozygous form *Aa*. This is equivalent to saying that the gene *A* is perfectly additive. On this assumption the correlation between parent and child can be shown to be exactly $\frac{1}{2}$, irrespective of the gene frequency. The same result follows for pairs of sibs and the distributions for these two cases are given in Appendix 6. The argument can be extended to cover any degree of relationship and the correlation coefficients, worked out by this method, are the same as the degrees of hereditary likeness given in Table XXIII. Sometimes the average measurement of the two parents (Galton's mid-parental measurement) is correlated with the measurement in the child. In this case the expected coefficient is $1/\sqrt{2}$, or 0·71, when perfectly additive hereditary factors are the sole causes of variation.

If, instead of dealing with one pair of genes, we considered a set of three or more additive allelic genes, the resulting correlations would be unaltered. They would also be unaltered if we took a series of several gene pairs at different loci, *A* and *a*,

B and *b*, *C* and *c*, etc., provided that all combinations were perfectly additive.

The result is altered, however, when genes are not perfectly additive. The standard exception occurs when one gene is completely recessive to another, e.g. the types *AA* and *Aa* are equivalent, but both differ quantitatively from the type *aa*. In the case of dominant or recessive genes, the correlations are all reduced and the amount of reduction depends upon the gene frequency. The parent–child correlation becomes $\frac{q}{1+q}$ and that for sibs $\frac{1+3q}{4(1+q)}$. For a rare dominant character ($q \to 1$), the reduction is very slight. With a rare recessive character ($q \to 0$), however, the parent–child correlation coefficient approaches zero and the sib–sib correlation approaches $\frac{1}{4}$. For common genes, e.g. when $p=q=\frac{1}{2}$, the parent–child coefficient becomes $\frac{1}{3}$ and the sib–sib coefficient $\frac{5}{12}$.

The theory of correlation as a measurement of hereditary likeness was extended by Hogben (1932) to include the effects of sex-linked characters. In the female there are three types, which can be assumed in the general case to be the results of perfectly additive genes ; tables can be worked out for every kind of relationship. The overall correlations for parent–child and for sib–sib pairs are still $\frac{1}{2}$, as with autosomal additive characters, but they differ when sexes are specified. Thus, with sex-linked additive genes the father–son correlation is zero, those for father–daughter and for mother–son $1/\sqrt{2}$, or 0·71, and that for mother-daughter $\frac{1}{2}$. Brother and brother are correlated in the degree $\frac{1}{2}$, brother and sister, $1/2\sqrt{2}$ or 0·35, and sister and sister, $\frac{3}{4}$. The coefficients, which apply to pairs one or both of whose members are females, are reduced if the sex-linked character under consideration is recessive. Examination of correlations between relatives for traces of this pattern may be used as a test for the presence or absence of the effects of sex-linked genes in metrical family data.

ASSORTATIVE MATING

As previously mentioned, there are processes other than inbreeding that cause departures from random mating. In human populations tendencies have been observed for people to

choose partners resembling themselves in one or more characteristics. This can be termed phenotypical assortation. Thus in North America people with light-coloured skins tend to mate with one another and the same holds good for people with dark skins. Less noticeable, but significant, is the tendency for the fair and dark complexioned in European communities to mate with one another. Degree of assortation can be measured conveniently by a correlation coefficient estimating the likeness of husband and wife with respect to the trait in question. Pope and Pearson (1908) estimated the likeness of husband and wife pairs in respect of physical traits, such as eye colour, stature and general physique, in this way and found positive correlation values of the order of 0·2 and 0·25 for most of them. Davenport's (1917) extensive data on stature correspond with an interparental coefficient of 0·33. Mental traits have also been studied and positive values have been found indicating tendencies for persons of like temperaments to mate. The likeness between husband and wife with respect to intelligence level has been shown to be very strong; it seems to be represented by a coefficient of the order of 0·5.

If physical or mental measurements are assumed to represent the effects of perfectly additive genes, assortative mating in the parents gives rise to precisely predictable alterations in the likeness between parents and children, sibs and other related pairs. In general, positive assortation in parents increases all measurements of hereditary likeness. Moreover, if the same degree of assortation continues for many generations, a state of equilibrium is approached in which the new values of the degrees of hereditary likeness are dependent in a simple manner upon the degree of parental assortation. Then, if the inter-parental likeness is measured by the correlation coefficient, m, the parent–child and sib–sib coefficients become $\frac{1+m}{2}$. The mid-parent and child coefficient is raised to $\sqrt{\frac{1+m}{2}}$. Thus, if $m=\frac{1}{2}$, as is the case with inter-parental intellectual stature, the expected parent–child and sib correlation coefficients are both raised to $\frac{3}{4}$ and the mid-parent and child coefficient is raised to $\sqrt{\frac{3}{4}}$, or 0·87. We can learn from consideration of various factors—(*a*) those which tend to diminish likeness between

relatives, such as dominance and recessivity, and (*b*) those which raise the likeness, such as assortative mating—that the observed values of correlation coefficients intended to measure the influence of hereditary factors must be interpreted with considerable caution.

MENDELIAN RATIOS

Although the ultimate confirmation of any hypothesis of a single dominant or recessive gene as the cause of a defect depends upon finding a Mendelian ratio among the offspring in relevant families, conditions suitable for crucial tests are not found often in human data. In the case of a rare dominant abnormality, where there is always full manifestation, the normals and abnormals will be represented in the ratio of 1 : 1 among the pooled offspring of affected individuals. With recessive conditions the position is less favourable owing to the fact that, unless at least one child in a sibship is affected, the sibship will not be recorded. Thus in small sibships the expected Mendelian ratio of normal to abnormal is 3 : 1, but in the sibships actually recorded there will be too few normals. Actually, when the number of sibs is S, the ratio, expected normal to expected abnormal, is $3[1-(\frac{3}{4})^{S-1}] : 1$. Thus, if the size of the sibship is 4, the ratio of normal to abnormal will be nearly 2 : 1; and this is about the value commonly found in human data on recessively determined rare conditions.

For precise estimation the modified expected number of affected children can be calculated in each sibship containing a recessively determined defect. Expected and observed numbers can be added up over a series of sibships and compared. This method has been specially advocated by Hogben (1931*b*), who has provided tables of expectations and their standard sampling variances for sibships of each size. An example is given in Table XXIV, where the agreement between observation and expectation, on the hypothesis of a true 3 : 1 ratio, is satisfactory. A more refined method of wider application has been devised by Haldane (1932*b*), by means of which the most probably true ratio of affected to normal can be estimated. The choice of method should depend upon the manner in which data are collected (Haldane, 1938*b*). In data from medical literature the precise influence of sampling is often very difficult

TABLE XXIV

FACTORIAL METHOD OF TESTING RECESSIVE HYPOTHESIS ON SIBSHIPS CONTAINING CASES OF PHENYLKETONURIA (Munro, 1947)

Size of Sibship, S	No. of Sibships of size S, N_S	Total No. of Sibs, $S.N_S$	Number of Sibs Phenylketonuric		Variance of Expected Number,* $N_S.K_S$
			Observed	Expected, $S.N_S/4[1-(\frac{3}{4})^S]$	
1	6	6	6	6·00	0·00
2	7	14	8	8·00	0·86
3	6	18	10	7·78	1·58
4	5	20	8	7·31	2·10
5	7	35	13	11·47	4·14
6	5	30	12	9·12	3·88
7	2	14	4	4·04	1·94
8	3	24	8	6·67	3·52
9	1	9	2	2·43	1·38
10	2	20	5	5·30	3·18
11	1	11	2	2·87	1·81
12	1	12	3	3·10	2·02
13	1	13	4	3·33	2·23
Total .	47	226	85	77·42	28·64

Out of 226 sibs, altogether 85 were affected against 77·42, the expected number on the recessive hypothesis. The difference between the observed and expected values here is 7·58, which is slightly but not significantly greater than the standard error, $\sqrt{28·64}$, or 5·35.

* See Appendix 7.

to determine, because families containing a large number of affected members are likely to be published. Innumerable cases with "negative family history" may remain unrecorded.

BIRTH RANK AND MATERNAL AGE

In sibships which contain affected members, tests can be made for environmental agencies, and in particular, for the effects of maternal environment. Abnormal offspring may be found to occur unduly frequently in the first-born children or in children whose births are preceded by exceptionally large numbers of pregnancies. Also the age of the mother or of the father can be aetiologically important. By far the simplest method of testing such hypotheses is the comparison of data on the cases of the abnormality in question with the statistics on the general population. There are two difficulties, however, first, that the effects of birth order and parental age are closely

related and may be awkward to disentangle, though we can ascertain which effect is the more significant. Secondly, adequate general population statistics are not always available. When they are not satisfactory, a control group has to be built up from the internal evidence of the data on the families containing abnormals. Thus, in a sibship of size S containing d defectives and no sibs of unascertained status, the random chance that the first birth (or any other specified birth) results in a defective is d/S. When a series of sibships is available, the expectations

TABLE XXV

OBSERVED AND EXPECTED NUMBERS IN EACH BIRTH RANK AND MATERNAL AGE-GROUP IN SIBSHIPS CONTAINING 121 CASES OF ANENCEPHALY, HYDROCEPHALY OR SPINA BIFIDA. (Penrose, 1946)

Birth Rank	Maternal Age							Total
	15–19	20–24	25–29	30–34	35–39	40–44	45–49	
1	**1** 0·93	**11** 14·22	**13** 9·21	**5** 3·00	**1** 0·83	—	—	**31** 28·19
2	— 0·08	**5** 7·75	**6** 10·96	**3** 9·16	**1** 1·83	—	—	**15** 29·78
3	—	**2** 2·49	**6** 6·71	**6** 7·03	**4** 2·80	— 0·33	—	**18** 19·36
4	—	**1** 0·44	**2** 4·78	**3** 3·73	**5** 2·67	**1** 0·50	—	**12** 12·12
5	—	**1** 0·12	**2** 2·77	**2** 2·56	**8** 5·17	**2** 0·73	—	**15** 11·35
6	—	—	— 1·06	**1** 2·23	**2** 1·79	**1** 0·40	—	**4** 5·48
7	—	—	— 0·42	**1** 1·92	**2** 1·33	**2** 1·17	—	**5** 4·84
8	—	—	—	**3** 1·31	**5** 1·57	**1** 1·09	**2** 0·54	**11** 4·51
9	—	—	—	**1** 0·51	**1** 1·03	**2** 0·86	—	**4** 2·40
10	—	—	—	— 0·40	**1** 0·47	**2** 0·38	**1** 0·09	**4** 1·34
11	—	—	—	—	**1** 0·27	— 0·30	—	**1** 0·57
12	—	—	—	—	— 0·09	**1** 0·25	—	**1** 0·34
13	—	—	—	—	—	— 0·35	—	— 0·35
14	—	—	—	—	—	— 0·20	— 0·08	— 0·28
15	—	—	—	—	—	—	— 0·09	— 0·09
Total	**1** 1·01	**20** 25·02	**29** 35·91	**25** 31·85	**31** 19·85	**12** 6·56	**3** 0·80	**121** 121·00

TABLE XXV—*continued.*

Number of Cases	Mean Birth Rank		Mean Maternal Age in Years	
	Observed	Expected ±S.D.	Observed	Expected ±S.D.
121	**4·00**	3·38±2·44	**31·69**	29·77±5·94

Difference between Observed and Expected Mean Values		Standard Error
Birth rank	+0·62	$\pm\sqrt{\frac{2\cdot44}{120}}$, i.e. ±0·22 (ranks)
Maternal age	+1·92	$\pm\sqrt{\frac{5\cdot94}{120}}$, i.e. ±0·54 (years)

in each birth rank, for all sibships, are summed and the distribution of the expectation totals compared with the observed totals. Sibships in which all the known members are affected give no information.

The method can easily be used for comparing expected and observed numbers of cases of different maternal or paternal age groups. Table XXV shows an example of such a calculation, based upon 111 sibships each containing one case of foetal deformity of specified type and 10 sibships each containing two such cases. Every sibship's contribution, in the table, included at least one sib known not to have any of the deformities in question. If two sibs fell within the same age group, their expectations were added together. The expected and observed values in such tables can sometimes be conveniently compared by the χ^2 test. In this instance, the means and standard deviations of the distributions of the expectation totals were calculated and used for a comparison with observed values. For both measurements, birth rank and maternal age, the means for the abnormals are significantly greater than would be expected. The discrepancy between mean observed and mean expected maternal age, which represents a tendency for older mothers to have malformed offspring, is small but significant. The difference, +1·92 years, is 3·56 times its standard sampling error. For birth order, the corresponding difference, +0·62

ranks, is only 2·78 times its standard error. Inspection, however, shows that this difference might have been more marked but for a tendency for first-born children to be malformed. The strong correspondence which exists between birth rank and maternal age makes it difficult to ascertain the full independent effects of the two variables unless further refinements of statistical technique are introduced.

CHAPTER VI

THE GENETICS OF INTELLIGENCE

Inheritance of Intelligence—Inheritance of Social Ability—Intelligence Levels of Parents and Sibs of Defective Patients—Correlations between Relatives—Regressions—Threat of Decline in Intelligence Level—Equilibrium of Intelligence and Fertility.

INHERITANCE OF INTELLIGENCE

IT HAS already been shown that the commonest feature of people recognized to be mentally defective is poor intellectual capacity. This is the chief predisposing cause of social failure in early life. Intelligence, measured by any known test, is a graded character and it resembles other quantitative measurements, such as stature. From the point of view of genetics it is not a simple character. It does not usually segregate, and probably represents the combined effects of a great number of genes and environmental influences.

Each different mental test measures a different aspect of intelligence, just as measurements of stature, span or girth measure different aspects of body size. All scholastic intelligence tests are closely related to one another and they are also related, less intimately but significantly, to non-verbal and performance tests. Thus, success or failure by one standard predicts, to some extent, success or failure on another test.

The results of tests in general use agree quite well with estimates of intelligence, which could be inferred from qualitative examinations of people and expressed perhaps in terms of rating scales. Some tests are more accurately constructed or are inherently more reliable than others, but the most reliable are not necessarily the best measurements of the fictitious quantity, which represents what is commonly implied by the term intelligence. It might be a good plan to study separately the genetics of each type of test performance, e.g. verbal and non-verbal, if accurate scientific results were desired. Tryon (1929), for

example, was able to give a convincing demonstration, with rats, of the genetical principles of ability to traverse mazes. The inheritance of this particular ability was evidently multifactorial.

INHERITANCE OF SOCIAL ABILITY

In view of the acknowledged definition of mental defect as social failure, the most logical method of studying its inheritance is to examine the genetics of social failure directly. This has been attempted by Doll (1937). A scale was devised for measuring social ability—expressed, quite unnecessarily, in the form of a "social quotient"—by rating accomplishments pertaining to social maturity. Doll examined a number of families and estimated the degree of social maturity of each member. He concluded that the social quotient level might be largely an inherited character. The mid-parent and child correlation coefficient was 0·75. A very high degree of assortative mating, with respect to social maturity, was evident in these families. The expected value of the mid-parent-child coefficient, on the assumption of additive gene inheritance, would thus be exceptionally high (above 0·9). The observed value is too low to agree with an additive gene hypothesis.

Measurements of the social quotient correlate closely with Binet scores, but the home and cultural environment probably has even more effect on the social rating than upon Binet test results. Social maturity can only be crudely estimated. It has many dimensions and is not a character that naturally lends itself to genetical analysis.

INTELLIGENCE LEVELS OF PARENTS AND SIBS OF DEFECTIVE PATIENTS

Data available for the study of the inheritance of intelligence can be obtained from examination of the sibs and parents of known cases of defect. The simplest plan is to exclude the patient, that is the propositus, from the sibship. If the patient is young, it may be possible to test sibs and obtain measurements of their mental abilities, but in very few cases will it be possible to do this with parents. Mental tests are not, as a rule, accurately standardized for application to people at all ages, though Wechsler's scale for adults may ultimately meet this need. In the parent-child relationship, comparison of adult and child test

achievement is of questionable validity and rating scales often have to be relied upon for assessment of mental capacity. The figures given in Table XXVI were obtained in the Colchester Survey (1938) from the families of 1148 patients, whose parents were known well enough to be rated with confidence for mental ability. The tendency for the general average level of the sibs to

TABLE XXVI

MENTAL GRADES OF PARENTS AND SIBS OF 1148 PATIENTS

Grades of Parents	Patients and Sibs: Number in each Grade						
		S	N	D	F	Imbecile	Idiot
		Superior	Normal or Average	Dull or Borderline	Feeble-minded		
S×S	Patients	—	—	—	—	1	—
	Sibs	—	—	—	—	—	—
S×N	Patients	—	—	1	3	2	3
	Sibs	8	15	—	—	—	—
N×N	Patients	—	—	100	216	303	178
	Sibs	59	2753	174	56	47	23
N×D	Patients	—	—	40	86	51	19
	Sibs	1	552	173	79	28	12
N×F or D×D	Patients	—	—	11	62	26	14
	Sibs	—	196	97	65	17	9
N×Imbecile or D×F	Patients	—	—	6	32	13	3
	Sibs	—	60	33	39	13	5
D×Imbecile or F×F	Patients	—	—	2	9	12	1
	Sibs	—	17	11	28	9	1

follow the average grade of the parents is clearly shown. Comparison with test results indicated that the difference between any two of the adjacent ratings was approximately equivalent to 22 points of Stanford-Binet intelligence quotient. On this basis, equating *S* with 122, *N* with 100, etc., the mean levels of parent and child intelligence can be directly compared, giving the results shown in Table XXVII.

The mean level of the sibs drops regularly as the mean intelligence level of the parents descends, though, perhaps because of errors in classifying parents, the sib level drops more slowly. If

TABLE XXVII

ESTIMATED MEAN MENTAL RATIOS OF PARENTS, SIBS AND PATIENTS

Type of Mating	Parents	Sibs of Patients	Patients
S×S . .	122	—	34·0
S×N . .	111	107·6	38·9
N×N . .	100	96·7	37·4
N×D . .	89	88·0	50·5
N×F or D×D . .	78	82·0	49·4
N×Imbecile or D×F . .	67	75·1	50·7
D×Imbecile or F×F . .	56	67·3	45·0

S=122 F= 56
N=100 Imbecile= 34
D= 78 Idiot= 12

perfectly additive genes were wholly responsible for grades of intelligence, the means for parents and children should always agree. The fact that the means for the sibs of patients are somewhat higher than the means for the parents, when the parents are in the defective range, suggests that some of the genetic factors producing defect of this magnitude are heterozygous. A similar explanation might be put forward to account for two children with intelligence close to the normal level who were derived from a mating of brother and sister, both with low-grade mentality (Penrose, 1934*a*). On the other hand, a large proportion of the offspring of unions of parents who are both in the defective class are lost sight of through death in early infancy. Among the sibs of the patients, in the lowest row of Table XXVI, were 25 (not rated) who died in early infancy as against 66 of known mental grade. For the whole sample of 1280 patients in the same survey, the deaths in infancy numbered 906 against 4645 sibs of classified mental grade; this would correspond to 12·9 for a sample of 66 classified sibs. Possibly the increased infantile mortality rate among the offspring of very dull or defective parents is due to the occurrence of cases of low-grade defect who, if they had not died and thus escaped

classification, would have lowered the mean level of the sibs in a marked manner (as in Figure 4).

An important feature of the material summarized in Tables XXVI and XXVII is the noticeable tendency for the grade of patient to have an inverse correspondence with the grade of the parent. When the parents have normal mental capacity, there is clear segregation between the patients and their relatives. In the families where parental abilities are subnormal, the distinction is lessened; the patients are higher and the sibs lower. This is merely a further illustration of the circumstances discussed in Chapter III, namely that the patients fall mainly into two biological groups, the low-grade infertile cases, and the high-grade fertile types who are capable of transmitting genes tending to cause low scholastic capacity to their children.

CORRELATIONS BETWEEN RELATIVES

The most usual approach to the problem of inheritance of intelligence utilizes the correlation technique. To obtain reliable results, the families selected should be a random sample of the general population. Unfortunately few surveys with accurate testing and careful sampling have ever been made. Some of the most interesting results of measurements of likeness in mental ability are summarized in Table XXVIII. Information about the parent and child relationship is particularly scanty. The important estimates of Willoughby (1928) and Jones (1928) differ considerably, though both were made on random samples. The true

TABLE XXVIII

CORRELATION COEFFICIENTS FOR INTELLIGENCE

Source	Type of Related Pairs		
	Parent–Child	Sib–Sib	Parent–Parent
Burt *et al.* (1911)	0·34	0·48	—
Thorndike (1928)	—	0·60	—
Willoughby (1928)	0·35	0·42	0·44
Jones (1928)	0·53	0·49	0·60
Herrmann *et al.* (1933)	—	0·32	—
Matthews *et al.* (1937)	—	0·30	—
Penrose (1938)	—	—	0·39
Cattell *et al.* (1938)	0·84	0·77	0·81
Roberts (1940)	—	0·54	—
Halperin (1945, 1946)	0·37	—	0·65

value of this correlation coefficient is not necessarily as high as 0·5, though it is often assumed that the likeness for intelligence must be the same as that found for stature of parents and children by Pearson and Lee (1903).

Estimates for sib pairs can be obtained from data on schoolchildren. Numerous surveys have been undertaken with variable results, according to the tests used and the methods of sampling. The careful survey of Roberts (1940) gave a value of 0·54 for the sib–sib coefficient. Thorndike's measurement was higher than this, but most other surveys have given lower values. Again, it cannot be assumed that the sib–sib likeness for intelligence is necessarily correctly expressed by the correlation coefficient of 0·5. Even if repeated surveys should give values centring round this figure, the interpretation is difficult. A certain amount of the likeness of sibs must be attributed to similar surroundings, in the family and in the home. The real coefficients—which measure purely genetical effects—are possibly all somewhat lower than those observed. Conversely, dominance and recessivity of the component genetical factors may lower the expected values, as already pointed out (pages 106 to 108).

A most important factor to consider is the inter-parental correlation because, for intelligence, this is probably very large; it is evidently of the order of 0·5. The effect of this is to raise by 50 per cent. whatever expected correlations we may assume to be reasonable on genetical grounds with random mating. If perfectly additive factors were responsible for intelligence level, the coefficients for parent–child and sib pairs should be 0·75, and such values have only been obtained in selected samples, like that of Cattell *et al.* (1938). It seems safe to conclude from the study of these coefficients, as does Willoughby, that only about half the variance of intelligence is due to genetical causes.

REGRESSIONS

Data which are unsuitable for correlation calculations can sometimes be used for determining regressions. For example, Burt (1943) has published figures comparing the mean mental ratios of fathers in different occupational groups with the mean ratios of their children. He showed that the children's mean levels were always situated between those of the fathers and the mean I.Q. for the general population, 100. For example, fathers

in the highly skilled clerical occupations had a mean I.Q. of 117·1 and the children of fathers in this class had a mean I.Q. of 109·1. Conversely, unskilled labourers were shown to have a mean I.Q. of 86·8 and their children's mean I.Q. was 92·0. If the means for children (or sibs) of sets of propositi regress exactly halfway towards the general population mean, this would imply correlation coefficients of 0·5.

In the case of mothers, less information is available than for fathers. Occupational grouping has not been much used for estimating adult female intelligence in the normal range. However, the children of mentally defective parents have been studied on many occasions and, as previously mentioned, most defective parents are female. The enquiry, initiated by the Departmental Committee on Sterilization (1934), on defective parents produced figures showing that 16·9 per cent. of the children were defective and 23·5 per cent. were retarded. In four-fifths of the cases the mother was defective, but test results were not published. Visser (1936) investigated the offspring of parents, who had attended special schools, and came to the conclusion that only very few of the new generation could be rated defective. The position is more easily understood when actual test results are given, as in the small but careful survey of Ainsworth, Wagner and Strauss (1945). The mean I.Q. of the defective mothers was 66·1 and that of the children 91·1 in 15 cases. This, like the results of similar enquiries, indicates that the children of defective parents regress further towards the normal than would be expected if mental defect were due to additive genes alone.

Regressions for estimating the mental likenesses of sibs, half-sibs, cousins, etc., can be obtained by testing relatives of defective propositi. If the investigation is confined to the fertile group, that is, to those patients with mental ratios above 50, fairly good approximation to the halfway regression points are obtained for sibs. For half-sibs or nephews and nieces, with additive gene inheritance of intelligence, we should expect regressions three-quarters of the way towards the normal average, and for first cousins, seven-eighths. The observed and expected means, in a sample of tested propositi and relatives taken from my own data (1939*a*), are shown in Table XXIX. The patients in the fertile range, with I.Q. 50 or above, have sibs whose mean I.Q. is situated not far from the mid-point between their own

TABLE XXIX

MEAN STANFORD-BINET I.Q. FOR DEFECTIVE PATIENTS AND THEIR RELATIVES

	Type of Relationship to Patient	Number of Pairs	Patients' Mean I.Q.	Relatives' Mean I.Q.	
				Observed	Expected on Additive Gene Hypothesis
(i) Patients with I.Q. 50 or above	Sib	101	65·8	84·9	82·9
	Half-sib, nephew or niece	143	63·2	89·5	91·8
(ii) Patients with I.Q. below 50	Sib	120	24·2	87·4	61·1
	Half-sib, nephew or niece	90	33·3	95·1	83·3

mean level and 100. Half-sibs, nephews and nieces of a similar set of patients were found to have a mean I.Q. situated not far from the point three-quarters of the way between the mean level of these propositi and 100. The results are in fair agreement with the hypothesis that intelligence level is due to additive genetical factors. On the other hand, for propositi with I.Q. below 50, the relatives of the same types are of considerably higher level than would have been expected on the same additive gene hypothesis. The mean I.Q. for these relatives of low-grade cases is still definitely subnormal, but genetical factors responsible for such low-grade defect cannot all be perfectly additive. In some cases the causal genes are completely or incompletely recessive. In others, new mutations or environmental accidents are responsible.

THREAT OF DECLINE IN INTELLIGENCE LEVEL

The hypothesis that intelligence level is largely due to additive genes, combined with the observation that fertility is greatest when intelligence is subnormal, leads to a widely held view that genes causing low intelligence are continually becoming more prevalent. The complementary genes, producing high levels of intelligence and associated with small sibships, are assumed to be dying out. A gradual lowering of intellectual level in countries where differential fertility of this type has been found is considered to be almost inevitable. A summary of this argument has

been given by Thomson (1947). If intelligence were purely the result of environment or of chance variation, it would be immaterial whether the stock were bred from the lowest or the highest levels. However, the likenesses between sibs, twins, parents and offspring, and between other types of related pairs, are of an order which suggests that genes do play an important part, though not an exclusive one, in determining intelligence level. Thus the problem of the threatened decline in intelligence is a real one.

The correspondence between size of sibship and intelligence level has usually been measured by finding the mean numbers of sibs in samples of school-children classified according to mental test results. Correlation coefficients varying between −0·11 and −0·30 have been repeatedly found by different observers for intelligence of a child and the number of its sibs. Put in another way, it appears that, over a wide range, a fall of 15 points in I.Q. level is approximately equivalent to an increase of 25 per cent. in sib number. On the assumption that intelligence is entirely determined by additive genes, the amount of the expected drop in the mean level of the population can be calculated. Current estimates of this expected decline are of the order of nearly two points of I.Q. per generation (Burt, 1946). It can easily be appreciated that a decline in general level must be accompanied by a great increase in the number of defectives, particularly those in the high-grade and borderline classes, and a decrease in the number of children of scholarship standard.

So far, no satisfactory direct evidence of declining intelligence in any modern community has been presented, and there are several reasons for doubting the full implications of the arguments by which its prediction is supported. Inasmuch as intelligence level is not determined by additive genes, the argument is weakened. For example, very high intelligence might be recessively determined and the largest reservoir of carriers of high intelligence might be in the general population; the relatively low fertility of the highly gifted would then be less important than it appeared to be. The prediction of decline, however, is more seriously invalidated if environment plays any considerable part in determining the intelligence level. A slight change in the direction of more favourable environment during one generation could easily swamp any effect due to changes in gene

frequency caused by differential fertility. The increase in stature and weight of children that has been observed in a great many countries during the last half century has been attributed to improved nutrition. Yet a differential fertility with respect to such measurements as stature and weight is likely to be a widespread phenomenon, that is to say, the smaller the children the larger is the number of their sibs. From data given by Boas (1910) on children in Toronto, the correlation coefficient for stature of a child and the number of its sibs can be shown to be $-0{\cdot}09 \pm 0{\cdot}01$. On this evidence, coupled with the assumption that stature is determined by additive genes, a decline in stature could confidently have been predicted. Actual measurements, however, given in official reports indicate that the mean stature of Toronto children continues to increase year by year.

Exactly the same kind of phenomenon can be found if we examine longevity instead of intelligence or stature. Beeton and Pearson (1901) showed that longevity could be interpreted as a character determined by heredity. Expectation of life, moreover, is more favourable in the higher income groups (where fertility is low) than in the lower income groups (where fertility is high). It follows that the genes responsible for long life are gradually being eliminated. Nevertheless, the expectation of life in modern times has been gradually lengthening.

These paradoxes indicate that predictions about declining intelligence level based upon similar logic are likely to be unreliable, because intelligence, stature and health are all positively intercorrelated in the general population. It can, however, be argued that, even though the physique of children is improving under modern conditions of nutrition and hygiene, the underlying genetical framework of the population is being weakened by differential fertility, and that consequently we are living in a fool's paradise. The point is rather academic because we cannot accurately predict the needs of future environments. Moreover, the paradox might prove to be capable of explanation on non-genetical assumptions. For example, if birth order and intelligence or physique were negatively correlated, i.e. the first child, on the average, more intelligent or healthy than the second, the second than the third, and so on, a negative correlation between size of sibship and intelligence or health would certainly follow. The general level of these characters in the community could

therefore be an inverse consequence of the mean size of the family irrespective of genic background. A reduction in birth rate would automatically cause a rise in mean intelligence and physique. These points may not be very significant in human populations, but they indicate avenues for further research.

EQUILIBRIUM OF INTELLIGENCE AND FERTILITY

Differential birth rate with respect to intelligence level is probably not an entirely new phenomenon. It may have prevailed for a very long time. Galton (1869) drew attention to the remarkable infertility of men of genius, as shown by historical records. If intelligence had been declining for many centuries or even for one century, a decrease in the proportion of intelligent people in many countries would surely have been quite noticeable by now. The possibility that such differential fertility is a natural biological process, consistent with genetical equilibrium (Gorer, 1947), has rarely been considered. Could not the apparently greater fecundity in groups with relatively lower intellectual capacity be part of a biological compensatory mechanism?

It has been pointed out already that lethal recessive genes are lost when the homozygous type occurs in the offspring of carriers. The population can be in equilibrium if there are continual new mutations or if the gene, in heterozygous form, confers a slightly increased fertility on the carrier. Exceptional vigour in heterozygotes is a phenomenon well known in plant genetics and is called "heterosis". In a somewhat analogous manner, the almost normal carriers of irregularly dominant genes that occasionally cause severe defects (e.g. achondroplasia) can be rather more fertile than the average. The increased fertility of mild cases can compensate for loss of genes in the relatively infertile severe cases. Eugenists are accustomed to draw attention to populations in which defects of all kinds are concentrated, which interbreed only among themselves and which are alarmingly fertile. This increased fertility, however, may represent a natural consequence of the prevalence in the parents of heterozygous genes for lethal or sublethal defects.

Consider, for example, a purely hypothetical population divided into three groups. There will be a large group with slightly superior intelligence, say I.Q. 103, comprising some 90

per cent. of the fertile population, and a small group with greatly inferior intelligence, say I.Q. 73, comprising 10 per cent., a "submerged tenth" or social problem group. Let us suppose that there is also a small infertile group of mental or physical weaklings. We will assume that intelligence is due to a single perfectly additive pair of allelic genes, *A* and *a*, that those in the upper group are all *AA*, that those in the small inferior group are all *Aa*, and that the weaklings are *aa*. Further, let us assume, for the sake of simplicity, that mating takes place within the groups but never between them. There will be two types of mating only. In the slightly superior group, $AA \times AA$ will produce nothing but slightly superior offspring, *AA*. In the inferior group, the matings $Aa \times Aa$ will give rise to $\frac{1}{4}$ *AA* (superior), $\frac{1}{2}$ *Aa* (inferior) and $\frac{1}{4}$ *aa* (sublethal weaklings or imbeciles), who, we will suppose, do not survive or at least are not able to be parents. The perfectly additive nature of the gene will imply that these sublethal weaklings have an I.Q. of 43. When there is a tendency towards recessivity, the I.Q. of weaklings will be still lower. Now, this total population can be in perfect equilibrium with respect to the character, intelligence, if the birth rate in the inferior group is more than twice that in the superior group, i.e. 4·0 children as compared with 1·9 (see Table XXX). This is necessary because in the inferior group only half the offspring will replace the parental type. One-quarter will contribute to the superior group and one-quarter will be infertile.

Unless they possessed a greatly increased birth rate, the inferior group would gradually die out. In Table XXX there is

TABLE XXX

IMAGINARY POPULATION WITH COMPLETELY ASSORTATIVE MATING: INTELLIGENCE LEVEL DETERMINED BY A PERFECTLY ADDITIVE GENE PAIR

Types of Mating	Frequency of Mating Pair	Relative Birth Rate per Family	Offspring		
			AA(I.Q. 103), Superior	*Aa*(I.Q. 73), Inferior	*aa*(I.Q. 43), Sublethal Weaklings
$AA \times AA$	90	1·89	170	—	—
$Aa \times Aa$	10	4·00	10	20	10
All types	100	2·10	180	20	10
Parental pairs in next generation			90	10	—

exact replacement every generation. Note that the mean I.Q. of the offspring is the same as that of the parents. It is also interesting to consider the fact that the birth rate of the inferior group would not need to be so high if mating were not so assortative, that is if the groups intermarried more at random.

It seems not unreasonable to suppose that both tendencies with respect to intelligence, assortative mating and differential birth rate, may be natural phenomena of great antiquity and part of a biological equilibrium, which has been established in past ages by natural selection. The model population demonstrated in Table XXX is crude and represents an extreme case, but it has a fair degree of resemblance to the conditions believed by many observers to exist in human communities. Burt (1946) states that the children from the poorest social classes are greatly below the average in mental ability and have nearly double the average birth rate. Though poor economically and scholastically retarded, members of such groups may be biologically as fit as their apparently more favoured neighbours. The groups more lavishly equipped with genes for intellectual qualities not only depend upon the less scholastically inclined for manual labour but for replenishment of genic material. For replacement of intelligence genes lost on account of the relatively low fertility of the highly intelligent, the large birth rate of the supposedly inferior group is a necessity. This equilibrium is stable and it also is not interfered with by the occurrence in the population of extra cases of low-grade defect, evenly distributed among the offspring of superior and inferior groups, caused by rare recessive genes or environmental accidents.

CHAPTER VII

RARE DOMINANT DEFECTS

General Principles—Huntington's Chorea—Epiloia—Dystrophia Myotonica —Neurofibromatosis—Acrocephaly—Arachnodactyly—Miscellaneous Abnormalities—Naevoid Amentia.

GENERAL PRINCIPLES

In human genetics a dominant defect is an abnormality which depends upon the presence of a gene in heterozygous form. Dominance is recognized in pedigrees mainly by continued transmission from parent to child. It follows that such a phenomenon can be observed only if an affected person is fertile. Thus, any easily recognizable dominant defect must be mild enough not to interfere seriously with reproduction. This comparative innocence of dominant defects can be exemplified by constant manifestation of mild symptoms, as in night blindness, or by an onset postponed until after the reproductive period has been reached, as in glaucoma. Alternatively, the condition may have a variety of manifestations, so that some affected individuals are fertile whereas others are not. The variability may be expressed in terms of severity of symptoms or in time of onset.

Any dominant disease serious enough to cause marked mental defect will be liable also to produce infertility, and hence the gene must be variable in manifestation if its dominance is to be recognized. Large degrees of variation in symptomatology and age of onset are, in fact, quite typical of the dominant diseases which are associated with mental defect. The result is that it is often difficult to establish the mode of inheritance, and exact Mendelian ratios are rarely exhibited.

When a dominant gene causes idiocy, the parent certainly cannot be similarly affected. Either he will show comparatively mild indications of the same trait or the disease may be completely suppressed and he will be in the class of "normal overlaps". A third possibility is that the disease arises by new mutation in a

parental germ cell and it first appears in an offspring who will not transmit it. The occurrence of a defect, otherwise known to be dominant, in a single offspring of normal parents, with unaffected sibs, ancestors and collaterals, suggests this possibility.

HUNTINGTON'S CHOREA

The most typical of rare dominant conditions associated with pronounced mental changes is the hereditary chorea first described by the American physicians Waters, Lyon and Huntington, between the years 1841 and 1872. The disease was probably derived from English immigrants, and in earlier times their affected ancestors and collaterals suffered penalties for supposed witchcraft (Critchley, 1934).

Usually the disease begins in middle life with the gradual development of disorderly involuntary movements. As the choreic symptoms progress there is, commonly but by no means always, a change in the mental state, first producing a confusional type of psychosis and later a complete dementia. In the early stages of the disease there is marked increase of muscular tone, and in the later stages there can be wasting and rigidity. According to Bell (1934), about one-third of the cases remain free from mental symptoms. The age of onset varies from 5 to 70 years and is slightly earlier in females than in males. The mean, given by Bell for 460 cases of both sexes, is 35·5 years, with a standard deviation of 12·4 years. In some cases of early onset, mental defect is present. Indeed, if dementia occurs before the age of 18 years, it can legally be called deficiency and such cases are occasionally admitted to institutions, certified as defectives. Usually, at least on admission, these cases would belong to the high-grade group.

The cerebral pathology is a chronic degeneration not only of the nerve elements in the cortex but also of those in the thalamus and corpus striatum. The progressive nature of the lesions should make fairly easy the differentiation of these patients from those with other types of disease, affecting the corpus striatum, causing choreic involuntary movements. Also, the history of similar disease in one or other parent is very often obtainable.

Biologically there are several points of interest. The illness arises relatively late in life, so that it does not seriously interfere with the fertility of most of those whom it affects. There is,

moreover, a significant relationship between the ages of onset in affected members of the same family. According to Bell (1942), the correlation of onset age in parent and child is 0·59 and between sibs it is 0·46. Among the published pedigrees there appears to be no instance known for certain in which the disease appeared in a family where previous generations were unaffected. In such a case the disease might be supposed to have arisen by new mutation in a germ cell of the normal parent. However, the variable age of onset makes such presumptions hazardous. No doubt cases have arisen by new mutation, from time to time, to balance those cases in which early onset has diminished fertility. Otherwise selection, acting over a very long period, should have reduced the incidence to insignificance, unless, indeed, possession of the gene, in the stages before chorea develops, confers an enhanced reproductive capacity. On the other hand, since the family history, that is the finding of an affected parent, forms one of the criteria of diagnosis, sporadic cases would tend not to be diagnosed as Huntington's chorea except by the boldest of clinicians.

EPILOIA

The syndrome of tuberose sclerosis, sebaceous adenoma and epilepsy constitutes a highly characteristic problem in the genetics of mental defect. The condition was first recognized by Bourneville (1880) and the name epiloia was suggested by Sherlock (1911) to indicate the whole variable pathological complex. Most noticeable is the "butterfly" rash on the cheeks, nose, chin and forehead, actually formed from skin tumours but sometimes mistaken for an inflammatory eruption such as acne rosacea. The rash is due to tumours, fibrous in consistency and considered to be sebaceous adenomata, which begin in early childhood and develop slowly. Those on the face, reddish and vascular, were first fully described by Pringle (1890). Similar tumours, or plateaux of hard skin, occur on other parts of the body, notably on the scalp and the back, and these are usually brownish or white in colour. The nail-beds are sometimes involved. The distributions of skin lesions tend to be roughly, though not precisely, symmetrical. Pigmented naevi and soft neurofibromata have occasionally been described in these cases also. The condition is illustrated in Plate I.

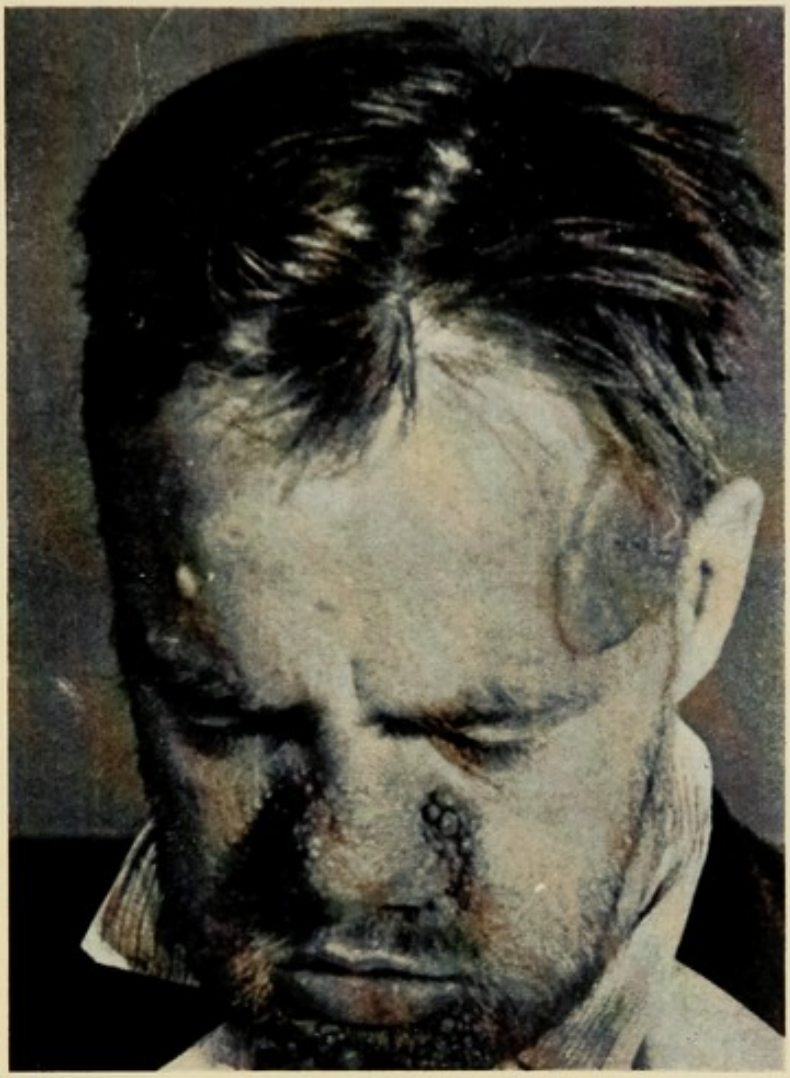


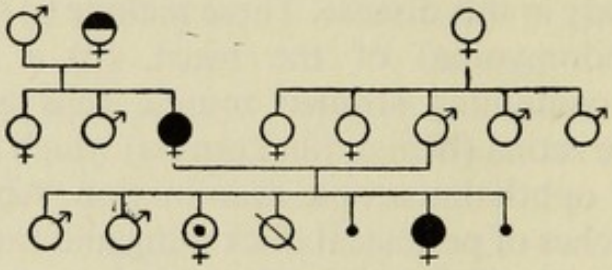
Plate I—Epiloia in a male epileptic imbecile, aged 28
Note the typical sebaceous adenomata around nose and mouth and the raised plaque on forehead.

Associated with the skin lesions is a condition known as tuberose sclerosis of the brain. Multiple nodules are found in the cortex and other parts of the brain substance. They may occur in the ependyma of the lateral ventricles and in the cerebellum. The consistence of these tumours has been likened to cartilage, rubber or potato (hence the name tuberose), and in the ventricles they have the appearance of candle gutterings. Histologically they are shown to be mainly gliomata containing large multinucleated cells and undifferentiated nerve elements (Bielschowsky and Gallus, 1913). Paralysis with signs of pyramidal lesions does not occur as commonly as the gross cerebral pathology might suggest. Other rare types of tumour are found in different parts of the body in this disease. These include (i) striated muscle tumour (rhabdomyoma) of the heart, (ii) a mixed kidney tumour also containing striated muscle cells and (iii) nerve tumours of the retina (benign phakomata) which appear as grey plaques under ophthalmoscopic examination. Abnormalities of the bones, patches of periosteal thickening and rarefication have been described (Gottlieb and Lavine, 1935).

The mental symptoms of the condition vary from profound idiocy to psychosis. Epilepsy is almost always present in severe cases and sometimes the fits are of extremely frequent occurrence. On the other hand, sebaceous adenoma can occur without being associated with any obvious mental disturbance at all. Also, epilepsy may be the only symptom in the absence of mental defect or visible skin tumours. The disease shows a perplexing variety of manifestations in different patients, and cases with almost every combination of signs have been found. This is shown by Farber's (1931) autopsy records of 27 cases of rhabdomyoma of the heart, in which he found tuberose sclerosis associated in 18 cases, kidney tumours in 14 cases and sebaceous adenoma in at least 4. The presence of two or more of these rare conditions in the same individual can hardly be attributed to chance. It is probable that the whole group of lesions and the mental disturbances are pleiotropic effects of a single gene which is irregularly dominant. In consequence of great variability of manifestation, precise Mendelian ratios are not likely to be found in many families.

The interpretation of family histories in cases of epiloia is made especially difficult because, even in the same family, the

affected persons may show quite different signs. Fuhs (1925) traced the condition through five generations. This, however, is exceptional. In most published pedigrees only two or, at most, three generations have affected members. Figure 5 shows a pedigree where the disease occurred in grandmother, mother and in at least one of her daughters. In about half the severe cases associated with mental defect, and perhaps in more, it is impossible to trace any indication of familial incidence. Cockayne (1933) pointed out that, though there was clearly a tendency to dominance in certain families, in others new mutation may be held responsible. In some families, though the parent



● Epiloia
◒ Sebaceous adenoma
⊙ Congenital heart lesion
⊘ Died in infancy
• Miscarriage

Figure 5.—Pedigree of Epiloia (Gunther and Penrose, 1935, Case No 8)

may not show the disease, he may yet be a normal overlap and carry the gene.

Genetics of human diseases can scarcely ever be fully accounted for, and one or two families have been reported in which recessive inheritance would naturally be postulated because parents were both normal and consanguineous. Consanguinity can occur occasionally in the parents of dominant abnormalities, as in the general population. However, the possibility that a recessive type exists cannot be excluded. Neglecting this consideration, the frequency of epiloia due to a dominant gene in the general population in England can be estimated at 1 in 30,000. If one in every four cases were the

result of new mutation, an estimation of the mutation rate can be made. This would amount to about 1 in 120,000 per individual per generation (Penrose and Haldane, 1935). From this it would appear that, taking the generation time as a unit, man may be somewhat more mutable than *drosophila*.

Analysis of known family histories shows that there is a tendency for the severity of the disease to be greater in some families than in others. Sometimes only sebaceous adenoma is found in several members as the main symptom (Shelmire, 1918); in others a more complete syndrome may be repeated. Berg (1913), for example, observed a father and daughter both with sebaceous adenoma, tuberose sclerosis and kidney tumours, though the father's father had a kidney tumour without other features. More usually, affected members in the same family show great variety in the signs and symptoms they possess. The cause of these variations can, at the present time, be most credibly attributed to genetical modifying factors. Environment has not been shown to play any significant part in the aetiology. Order of birth and maternal age are without demonstrable influence. The sexes are equally affected.

The grade of defect in institutional cases of epiloia may be very low (see Appendix 8) and a certain amount of slow deterioration occurs. The variable manifestation of the gene probably, together with a relatively high mutation rate, makes possible the rare phenomenon of a dominant gene which is responsible for a very severe type of defect.

DYSTROPHIA MYOTONICA

There appear to be three distinct diseases which have sometimes been classed under the generic name of myotonia (Bell, 1947). The earliest to be recognized was a clearly dominant condition, myotonia congenita, or Thomsen's disease, in which the chief symptom is inability to relax muscles of the limbs immediately after their contraction. Mental deterioration does not accompany the disease, but psychosis may develop in later life. A more common disease also inherited as a dominant trait is dystrophia myotonica. Here the clinical picture is variable, but the syndrome is nevertheless quite characteristic. In the most severe cases, mental defect is associated with myotonic symptoms, muscular wasting, frontal baldness and cataract. Subjects

are usually normal at birth and the disease is slowly progressive. Myotonia, shown by stiffness of movements of the hands and feet, commonly appears in early adult life with wasting of the affected muscles, especially in the forearms and the sternomastoids; tendon reflexes are diminished. The cataract is of a peculiar type, beginning at about the age of 30 with small peripheral opacities detectable only with a slit lamp. The third disease in the group, known as paramyotonia, is a rare intermittent type of Thomsen's disease in which the symptoms are precipitated at any age by exposure to cold.

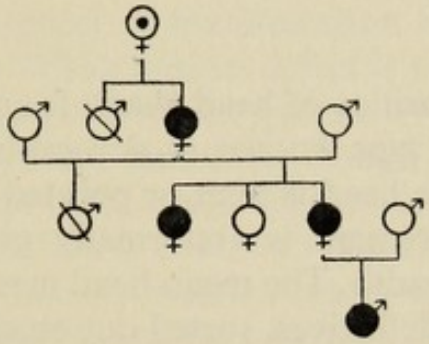
The age of onset of dystrophia myotonica is variable; the mean is 24 years, with a standard deviation of 13 years, and the pathological changes which take place are related to the time of onset. Mental defect is an accompanying symptom when the onset is early. If mental deterioration takes place in later life, i.e. after the 18th year, the case cannot be considered to belong in the category of amentia and dementia would be the correct designation. Thus few cases of dystrophia myotonica are found in hospitals or colonies for the mentally defective. Those certified defective are likely to be in the feeble-minded or imbecile class, though some published pedigrees contain cases of low-grade defect present from birth.

All the myotonias appear to be inherited as dominant conditions and all known cases are probably heterozygous for the abnormal genes in question. Dystrophia myotonica, however, shows variability of manifestation. This disease is remarkable in that affected sibs have similar symptoms and onset ages, whereas affected parents and their affected children have very different ages of onset. Transmission can take place through individuals who are apparently quite normal. In consequence of the lack of correlation between onset age in parent and child, the phenomenon of antedating is often very noticeable. As Goldschmidt (1938) originally suggested, the effect may be due to modification by allelic genes. Some authorities hold the view that when a mild form of the disease (e.g. cataract only) occurs in the parent and a severer form (e.g. dystrophy and mental defect) occurs in the offspring, this antedating indicates a real process of worsening in succeeding generations. However, as previously pointed out, until the effect of selection of families by severe disease in the offspring has been fully examined, the inherently improbable

hypothesis of progressive worsening cannot be entertained (Penrose, 1948). Part of the antedating is undoubtedly due to the biological fact that, when the disease is of early onset, fertility is so much reduced that severe cases are unlikely to be observed as parents (pages 66, 67.)

NEUROFIBROMATOSIS

Multiple nerve tumours of the type described first by von Recklinghausen (1882) are sometimes found associated with mental deficiency. The tumours are mostly small and subcutaneous. They enlarge progressively and sometimes occur in



● Neurofibromatosis with feeble-mindedness
⊙ Neurofibromatosis only
⊘ Died in infancy

Figure 6.—Pedigree of neurofibromatosis (Colchester Survey, 1938, Case No. 255)

enormous numbers, covering the whole body: patches of pigmented skin are usually present. Hashimoto (1890) counted 4503 tumours on the skin of a middle-aged Japanese man suffering from the disease.

Neurofibromatosis is sometimes associated with a mild degree of subthyroidism. Affected persons are usually short of stature. Preiser and Davenport (1918) found that nearly 10 per cent. of the cases are definitely mentally defective. Numerous family histories have been collected (Cockayne, 1933) and they are, on the whole, consistent with the hypothesis that an irregularly dominant gene is responsible. This cannot be regarded as having been proved. The general appearance of the findings in pedigree studies (see Figure 6) is not unlike that shown by epiloia. Some cases appear to be due to new mutation. In both diseases latent

forms may occur, which are not always recognized in family investigations. In neurofibromatosis, mildly affected persons may show pigmented skin patches only. Some writers hold that the two diseases are the same, or at any rate closely related to one another, because there are some common factors in the cerebral histopathology, for example the occurrence of giant cells.

There seems to be no obvious relationship between the severity of neurofibromatosis and the degree of mental impairment. In this respect the disease differs from epiloia. Furthermore, defectives with neurofibromatosis are seldom found among the low-grade cases (see Appendix 8).

ACROCEPHALY

Among the curiosities of head shape found among the mentally defective is a type known as acrocephaly or oxycephaly. This means that the head is high or pointed; in metrical terms, the vertical measurement is abnormally great in comparison with length and breadth. The mean head measurements of adult male acrocephalic defectives, sorted out on clinical grounds, are given in Table XXXI. The vertical measurement in acrocephaly is seen to be greater and the whole cranium wider and shorter than the average in a control group of adult male patients. As with many conditions encountered among defectives, it is doubtful whether there is a single type of acrocephaly or a number of different closely related types. In the classical syndrome, originally described in 1912 by Crouzon (1929), cranofacial dysostosis,

TABLE XXXI

MEAN HEAD MEASUREMENTS IN GROUPS OF ADULT MALES (mm.)

	Breadth (i)	Length (ii)	Height (iii)	Cephalic index (i)/(ii)
5 Acrocephalic defectives . .	153·4	180·8	136·6	0·85
10 Microcephalic defectives . .	131·6	180·0	115·5	0·73
11 Mongoloid defectives . . .	142·5	174·6	125·7	0·82
All types of defectives of comparable grades	146·9	188·3	131·2	0·78
General hospital population (Goring, 1913)	149·3	190·4	132·9	0·78
Normal Australians (Berry and Porteus, 1920)	152·5	193·7	134·6	0·78
Standard Deviation	4·7	5·8	5·2	0·03

the skull deformity is associated with exophthalmos; atrophy of the optic nerves may result from bony pressure upon them. The skull itself tends to be thin, especially at the vertex, and X-ray examination reveals irregularities of texture known as "digital" markings. These markings are due to local rarefication of the bone and they do not correspond with the underlying convolutions.

The Crouzon type of acrocephaly has been repeatedly traced in more than one generation of a pedigree. The inheritance appears to be dominant and the sexes are equally affected. The gene, like those responsible for other dominant defects, tends to have a variety of degrees of manifestation and there is much normal overlapping. When mental defect is present, the patient tends to belong among the milder grades. Probably cases arise from time to time by fresh mutation, though no estimate of the frequency of such sporadic cases appears to have been made. The mutation explanation is credible when severe cases arise in a family where no similar condition can be traced after careful search. Ferriman (1941) found that the majority of acrocephalic cases were, in this way, sporadic, but uncertainty as to new mutation always remains when, as here, irregular dominance is known to occur.

Acrocephalosyndactyly was originally described by Apert (1906) as a crippling deformity in which the hands and feet are seriously malformed by a welding together of the ends of the digits. Associated skull peculiarities are even more marked than in the Crouzon type. Mental defect, though again usually not of a severe degree, is a common accompaniment. Nearly all the cases are sporadic and most of them can be assumed to be due to fresh mutations. Occasionally other members of the pedigree show acrocephaly without syndactyly. In the family recorded by Mohr (1939), however, a father and five of his nine children were affected with the full syndrome of acrocephalosyndactyly.

A condition related to acrocephaly, though the head is too wide laterally rather than too high vertically, is known as hypertelorism and is characterized by abnormally increased distance between the eyes. Mental defect is usually associated when the deformity is severe. A fundamental anomaly in this, as in the acrocephalic types, is premature synostosis of the components of the cranial base. In hypertelorism the sphenoid bone in

particular is abnormally shaped and the sella turcica may be deformed to the detriment of development of the pituitary gland. The osseous peculiarities were described by Greig (1924). Affected individuals may show signs of obesity and hypothyroidism, which perhaps is secondary to dyspituitrism. It has been claimed that hypertelorism appears in families as a dominant character; in such cases it may be a variant of craniofacial dysostosis and not necessarily connected with mental changes (Abernethy, 1927). When coupled with severe defect, it sometimes gives the impression of recessive inheritance.

As with many other congenital peculiarities, the greater proportion of cases of hypertelorism are not obviously familial; those where familial incidence is obvious tend to be selected for special mention in medical literature. In the absence of standardized measurements and distributions, by virtue of which mild degrees of hypertelorism can be separated from normal variations in cranial structure, the genetics of the condition is necessarily obscure. Draper and others (1944) believe that children with wide interocular distances are especially susceptible to poliomyelitis. The relationships between interpupillary distance, mental grade and general health should be fully investigated biometrically as a preliminary to genetical studies in this field.

ARACHNODACTYLY

Long spidery fingers and toes, combined with long limbs, are found together with coloboma and dislocation of the lens of the eye and congenital heart defect in a syndrome named after Marfan (1896), who first drew attention to it. Sometimes there is also a narrow thorax with marked kyphosis and a long, narrow head. According to Olcott (1940), the condition is clinically almost the exact reverse of achondroplasia, though its manner of inheritance may be similar. There are many pedigrees on record which indicate transmission of a single main gene from parent to child, but they are probably not fully representative.

Mental defect is not considered to be an essential feature, but numerous instances of its concurrence with arachnodactyly are known. Usually they appear in families as isolated cases and the signs and mental grades vary greatly from one patient to another (Dax, 1941). It is by no means certain that arachnodactyly itself can be considered a unit. It has been reported to

occur in association with retinitis pigmentosa, with blue sclerotics and brittle bones, and even with sickle-celled anaemia. Elongation of the digits can accompany disorders of pituitary function. Care is needed also in distinguishing mild manifestations from commoner types of long fingers and limbs connected with what are presumably normal variations in stature.

MISCELLANEOUS ABNORMALITIES

Some dominant skeletal defects are encountered, from time to time, among the mentally defective just because, by random assortment, two anomalies will occasionally coincide in the same person. It has sometimes been assumed, if such a condition as the lobster-claw deformity or other type of ectrodactyly occurs in a mentally defective subject, that the two are causally connected (Weygandt, 1936). The lobster-claw deformity and cleidocranial dysostosis are two dominant conditions with variable manifestation in some pedigrees, but in neither of these malformations is mental defect a characteristic feature.

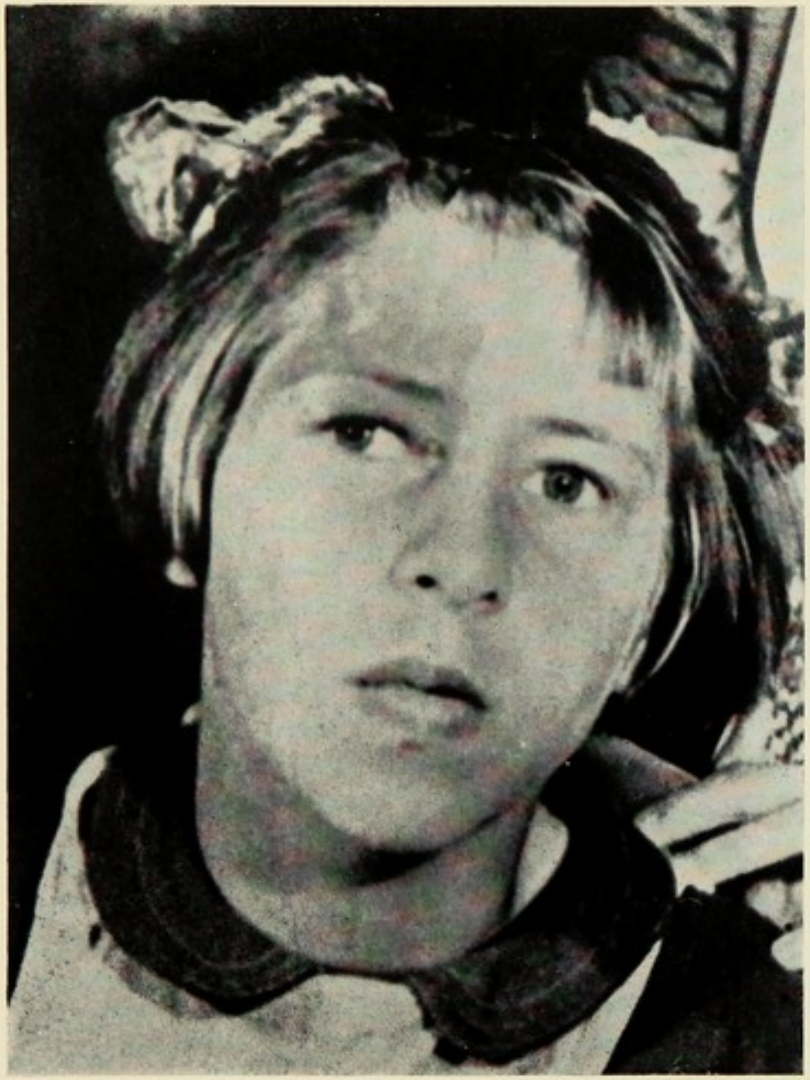
The position of achondroplasia, now usually called dyschondroplasia or chondrodystrophy, is similar. This is a very well known condition first properly distinguished by Parrot (1878). A disturbance of the growth of all cartilaginous bones leads to gross shortening of the limbs. The deformity appears to be due to a dominant gene with somewhat irregular manifestation, and it can be an incidental factor complicating rather than causing mental defect. Mørch (1942) has studied a large series of cases from the genetical point of view. Transmission of the fully developed condition from parent to child is a rarity, and the majority of cases are thought to be due to fresh mutation. The incidence rises significantly with increasing parental age.

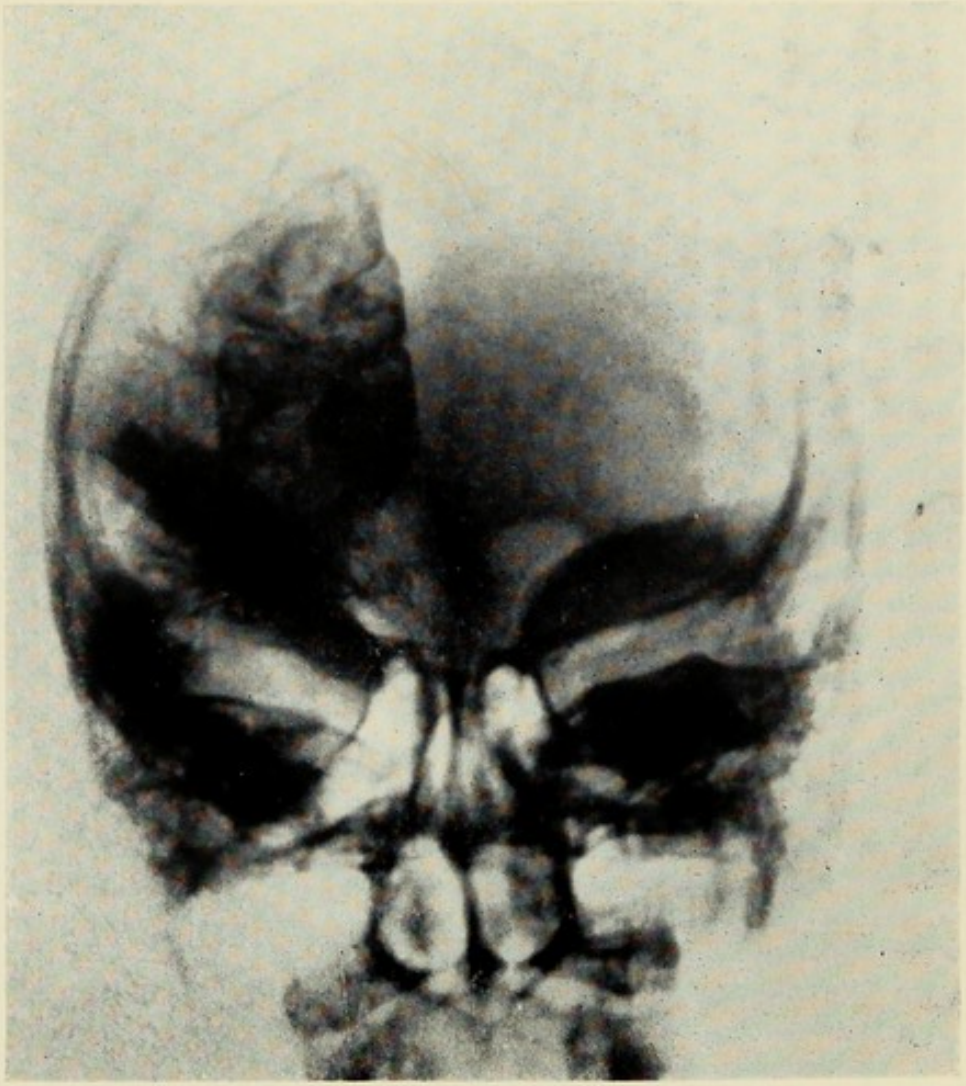
Another interesting, rare condition, hyperostosis frontalis interna, probably transmitted as an irregular dominant (Knies and le Fever, 1941), is sometimes associated with mental defect. The disease is characterized by progressive thickening of the frontal region of the skull together with atrophy of the cerebrum. It occurs most noticeably in females and may be accompanied by endocrine disorders, such as obesity, attributable to disturbance of pituitary function or to disordered metabolism. As the onset of the condition is usually in adult life, the loss of mental power which follows is usually diagnosed insanity rather

than defect. The brain atrophy may be an essential part of the disease and not just a secondary effect of the bone changes, but Stewart (1941) has shown that the cerebral atrophy is not the cause of new bone formation, as some had thought.

An extremely rare developmental abnormality of the brain, characterized chiefly by absence of the olfactory nerve tracts and known as arhinencephaly, has been observed in idiots (Stewart, 1939). There are associated defects of the nose, maxilla and palate in the mid line as well as hypoplasia of the cerebral hemispheres. The condition has been observed by Grebe (1944) in several members of the same family. Two affected brothers had two paternal uncles and one other paternal relative similarly affected. Surviving cases were feeble-minded and each showed median cleft palate, hypoplasia of nasal septum and absence of olfactory sense. Other relatives may have been very slightly affected. A heterozygous gene with irregular manifestation is possibly the basic cause of arhinencephaly.

Aniridia (congenital absence of the iris) has been reported in many families as a fairly regular dominant character. Sporadic cases also occur which may be due to new mutation. Møllenbach (1947) considers that the malformation is significantly associated with diminished intellectual capacity. He has estimated that the mutation frequency is about 1 in 100,000 per individual per life cycle. Not all the cases, however, are necessarily of the same genetical type. Schachter and Ourgaud (1948) made observations of the association of aniridia and mental defect in two pedigrees. Among other developmental eye defects, sometimes showing dominant inheritance though often quite irregularly, are colobomata of the iris and chorioid. Here, there has been imperfect closure of the embryonic optic cup in a manner somewhat analogous to the failures which occur in cases of harelip and cleft palate. Although such colobomata are found in defectives, it is uncertain how often mental subnormality can be considered to be a pleiotropic effect connected with the malformation. A similar problem occurs in cases of harelip and cleft palate—a condition which also is liable to show irregular dominance in pedigrees. Malformations of the eyes or mouth tend to produce blindness or speech disabilities and interfere considerably with social competence even though the intellect itself may be unimpaired. They are also biological handicaps





Plates IIa and IIb—Naevoid amentia: Sturge-Weber-Kalischer syndrome

This female epileptic imbecile, aged 12, has both parietal naevus and calcified cerebral vessels, seen in the X-ray. There is hemiplegia on the left side of the body.

and reduce the fertility of their victims. Such malformations could not persist in the community if they were not sometimes caused by fresh mutation. They only can occur in pedigrees covering many generations when dominance is irregular.

NAEVOID AMENTIA

There are some developmental abnormalities encountered among defectives of which strictly familial cases have never been reported. One such condition, the syndrome of naevoid amentia, better known as Sturge–Weber or, more correctly, Sturge–Kalischer disease, as Weber (1947) himself modestly points out, implies a combination of meningeal and facial angioma. The naevus of the skin is predominantly unilateral and calcification of intracranial vessels on the affected side can be shown by X-ray. Hemiplegia is often an accompaniment and epilepsy an almost invariable symptom. Mental impairment is usually of mild degree and is not closely related to the extent of the lesion. The main features of the condition are shown in Plates IIa and IIb. Although familial incidence of this syndrome does not seem to have been recorded, the occurrence of multiple naevi, Osler–Rendu disease, is known to be a dominant trait in some families. When the naevus also affects the retinal or cerebral vessels there is some analogy to the naevoid types of amentia. Cystic naevus of the cerebellum, the retina and other organs, known as the syndrome of von Hippel and Lindau, has been described in more than one generation. It may be due to a heterozygous gene, though most cases are of sporadic occurrence, as shown by Craig, Wagner and Kernohan (1941).

Careful family investigation might reveal abortive forms of Sturge–Weber disease in relatives. At present the origin is an open question. Possibilities are irregular dominance, fresh mutation of a gene presumably dominant and intrauterine environmental accident at a very early stage in development. Somatic mutation of an unstable gene is a further possibility suggested by the tendency for unilateral lesions. Infective disease of the foetus is a possible cause (Landtman, 1948).

CHAPTER VIII

RARE RECESSIVE DEFECTS

General Principles—Phenylketonuria—Microcephaly—Cerebral Diplegia—Choreoathetosis—Friedreich's Ataxia—Tay-Sachs Disease—Juvenile Amaurotic Idiocy—Gargoylism and Related Diseases—Retinitis Pigmentosa—Miscellaneous Conditions.

GENERAL PRINCIPLES

RECESSIVE defects depend upon the presence of two similar genes, one derived from each parent. In rare diseases with this type of causation, the homozygous recessive defective has normal parents, who are both heterozygous for the gene in question. Defects due to recessive genes are more easily identified than those due to dominant genes. Rare recessively determined defects are usually more severe and their manifestations vary less from patient to patient than dominant abnormalities. Also, family histories are highly characteristic. Sharp segregation between affected and unaffected sibs is the rule and parental consanguinity is a most useful pointer. Evidence of inbreeding carries more weight in the diagnosis of a recessive defect than the estimation of Mendelian ratios, especially in diseases which are associated with mortality early in life.

Natural selection acts against recessive defects very slowly because, although the homozygote may be quite infertile or even non-viable, the heterozygous carrier need not be abnormal in any way. In some diseases, however, the carriers may show mild or abortive signs of the recessive trait; mild signs of this type are inherited as irregular dominant characters. A summary of known instances of such tendencies towards intermediate inheritance has been made by Neel (1947). If heterozygous carriers are endowed with even a minute advantage in fertility as compared with the rest of the population, genetical equilibrium can be maintained in spite of the elimination of occasional infertile homozygotes. This fact makes the mutation

rate of genes causing recessive defects very difficult to estimate even in a population where the degree of inbreeding is constant.

Recessive genes are responsible for a great variety of abnormalities in man and not a few of these involve serious interference with mental function. In contrast to those due to dominant genes, recessive mental defects are to be found mainly among the low-grade cases, idiots and imbeciles. Such diseases are rare in the general population and have gene frequencies of the order of 1/200. Biologically, their importance lies partly in the fact that they are of so many different types. A large proportion of the people in the general population are carriers of at least one recessive gene capable of producing severe abnormality in the offspring, if mating occurred between two people carrying similar complementary genes. The presence of such genes may be totally unsuspected until inbreeding takes place. By experimental inbreeding in cattle, Mead, Gregory and Regan (1946) discovered six or seven recessive abnormalities among the progeny of six dairy bulls of supposedly good stock. In human populations, the comparable method is to examine the progeny of consanguineous parents and compare them with those of unrelated parents, on the assumption that the offspring of cousin parents will contain examples of rare recessive abnormalities. The method can usefully supplement the more usual procedure of finding consanguinity rates in parents for special groups of diseases.

The survey by Bell (1940) demonstrated the existence of a higher incidence of parental consanguinity among patients in hospitals for neurological diseases than for hospital patients generally. A similar phenomenon has been demonstrated in surveys of defectives. In the Colchester Survey, 128 cases showed signs of disease in the nervous system, which would be treated in general medicine as neurological conditions. Of these 128 cases, 8, or 6·2 per cent., had consanguineous parents. Among the remaining patients the corresponding consanguinity rate was 37 out of 1152, or 3·1 per cent. A similar result was reported by Duff and Dingee (1941). Hence, rare recessive genes probably play an important part in the aetiology of those neurological diseases which are found among the mentally defective.

If we examine the problem from the opposite point of view

and collect together all sibships of defectives where the parents are known to be related, additional evidence of recessive inheritance can be obtained. The familial incidence of defect, especially low-grade defect, is found to be significantly greater in sibships for which parental consanguinity is present than in those for which it is absent. As can be seen in Table XXXII, the incidence of stillbirths and that of deaths in early infancy is also increased slightly in the consanguinity group. Mental

TABLE XXXII

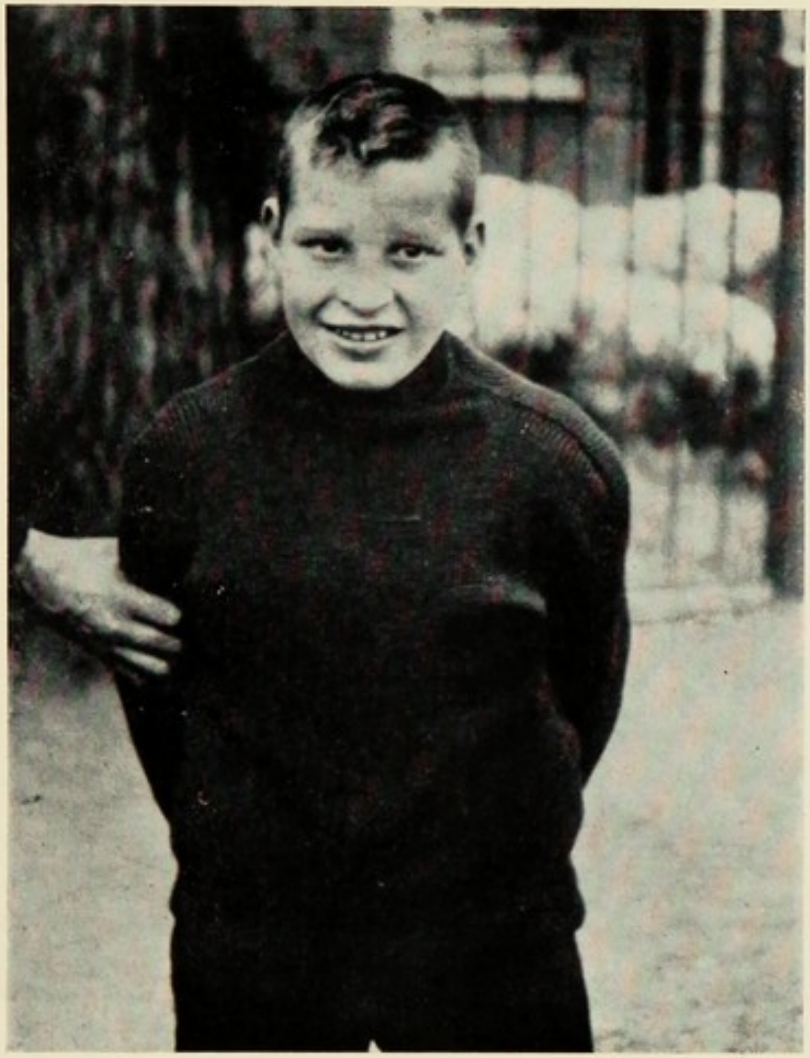
MENTAL DEFECTS IN SIBS OF PATIENTS WITH AND WITHOUT RELATED PARENTS : COLCHESTER SURVEY, 1938

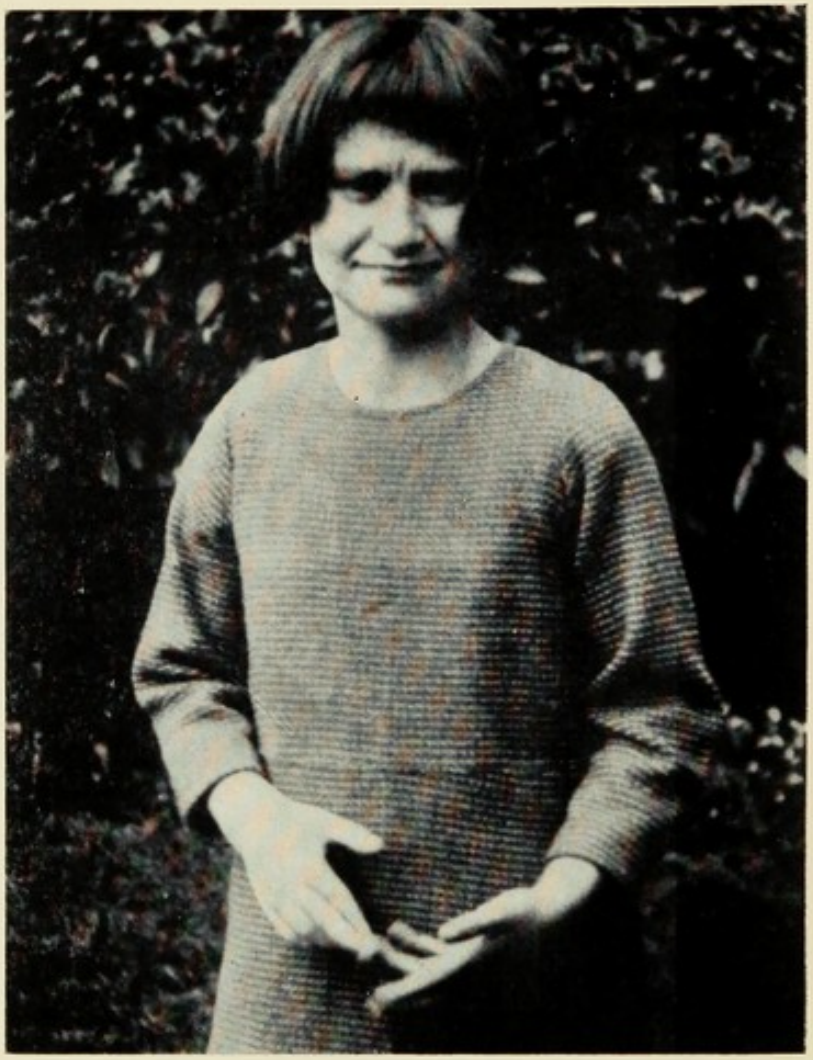
	Parental Consanguinity			
	Present		Absent	
Number of patients	45		1235	
Number of sibs	254		6375	
Percentages of sibs:				
Normal intelligence: Superior	0·8		1·0	
Average	47·2		55·3	
Dull	9·1	60·2	7·4	67·1
Unascertained	3·1		3·4	
Mentally defective: Feeble-minded	4·3		4·1	
Imbecile	2·8	10·2	1·7	6·5
Idiot	3·1		0·7	
Miscarriage or stillbirth	15·4	29·6	13·6	26·4
Died in early infancy	14·2		12·8	
Total	100·0		100·0	

defect is a graded character and so analysis of such sibships, in the hope of finding agreement or disagreement with the Mendelian ratio of one-quarter, is not always justified. In sibships where a particular disease divides the members clearly into affected and unaffected groups, convincing demonstrations of the recessive type of inheritance can be given (page 109).

PHENYLKETONURIA

A Norwegian biochemist, Fölling (1934), first described an abnormality, of which an essential feature is the urinary excretion of about 1 g. daily of phenylpyruvic acid, a ketonic acid with the formula, $C_6H_5.CH_2.CO.COOH$. The excretion is usually continuous throughout life and has been observed in infancy. Occasional cases showing intermittent excretion have





Plates IIIa and IIIb—Phenylketonuric idiots, brother, aged 16, and sister, aged 20 (Munro, 1947, Family No. 3). The hair in these patients was darker than is usual in phenylketonuria. Note the manneristic position of the sister's hands.

been recorded. Every case so far examined has shown intellectual defect. This is commonly of a severe degree, amounting to imbecility or idiocy.

The name "phenylketonuria" (Penrose and Quastel, 1937) seems preferable to the original, more cumbersome designation "imbecillitas phenylpyruvica" and also to "phenylpyruvic oligophrenia", favoured by American workers. The shorter name emphasizes the biochemical nature of the abnormality and brings the nomenclature into line with that of other comparable abnormalities, such as alkaptonuria, cystinuria and pentosuria.

The test for phenylpyruvic acid in the urine is so simple and striking that the failure of clinicians to observe the reaction until so recently is puzzling, even allowing for the difficulty of obtaining specimens from subjects of low mental grade. When the acid is present, a deep bluish green, which fades within a few minutes, is obtained on the addition of a few drops of 5 per cent. ferric chloride solution. If desired, alkaline urines can first be neutralized by the addition of dilute sulphuric acid. The urine has also a detectable aromatic odour. Naturally, Fölling's discovery stimulated other people to look for cases and success in this respect was reported first in Great Britain and then in France, the United States, Switzerland and Canada.

The clinical picture is peculiar in many ways. To the casual glance these patients appear to be just ordinary imbeciles, but the skilled observer may occasionally diagnose a case correctly before the urine has been tested. Some 60 per cent. of the cases are of the idiot grade and 30 per cent. imbecile. There is a slight tendency for the same grade to be repeated in affected members of the same sibship. Most patients are good-tempered and those with sense enough to learn to talk are co-operative and friendly. Hyperkinesis, which takes the form of digital mannerisms, is often conspicuous in low-grade cases. Some of the patients have epileptiform seizures in infancy and childhood. Phenylketonuria has been ascertained more frequently in females than in males, but this difference may arise simply because females are healthier and live longer than the males. Two cases are shown in Plates IIIa and IIIb.

Among the distinctive physical features in severe cases are dwarfing of stature and reduced head measurements as compared with the normal average. The incisor teeth tend to be

widely spaced and the skin, which may show pigmented patches, is unduly subject to dermatitis. There is sometimes a tendency to excessive sweating. Kyphosis is very common. On the neurological side, the constant feature is accentuation of all reflexes, both superficial and deep, in a manner reminiscent of the brisk responses obtained in hyperthyroidism. Abnormal quantities of creatine are excreted in the urine (Pugh, 1940). Ordinarily there is no paralysis and no increase in muscular tone, though Jervis (1937) has asserted that spasticity is a typical finding. Fair hair and blue eyes are very common characteristics. In some Norwegian patients the hair was colourless, as in the albino. Comparison of hair colours of the imbeciles with those of their normal brothers and sisters indicates that dilution of hair pigment is part of the syndrome, though, as with normals, the shade may darken with maturity.

On the whole, the physical health of these patients is surprisingly good and few autopsies have been carried out on institutional cases. In one of these instances, multiple nerve tumours were found (Penrose, 1939*b*), but the association may have been fortuitous. No very constant and characteristic pathological findings have so far been recorded. Degenerative changes in the cortex, basal ganglia and in the liver have been described and have led Delay, Pichot *et al.* (1947) to suggest that the condition is related to Wilson's disease, hepatolenticular degeneration. The ferric chloride test for phenylpyruvic acid made on all tissues gives negative results.

The pathological chemistry of phenylketonuria centres round two main questions: (i) Where does the phenylpyruvic acid come from? (ii) How is the anomaly which allows this abnormal metabolite to be excreted related to the associated mental peculiarities? The quantity of the acid excreted depends on the diet. It can be increased by feeding either laevo- or dextrophenylalanine and temporarily abolished by a protein-free diet. After a few days of protein-free diet, however, a patient starts again to excrete the acid, which must then be derived from endogenous metabolism. Feeding with excess of amino-acids other than phenylalanine, such as tyrosine and alanine, does not increase the quantity of phenylpyruvic acid in the urine. Thus it is very probable that phenylalanine, although a common and necessary constituent of ordinary diet, is the source of the

abnormal excretions. Phenylalanine itself occurs in the urine and also phenyllactic and phenylacetylglutamic acids. The finding of yet another substance by Dobriner *et al.* (1943) has not been confirmed.

After feeding normal subjects on phenylalanine in sufficient quantities, phenylpyruvic acid can be detected in the urine. A dose of about 15 g. of the natural or laevo variety is needed to produce this result, but 0·5 g. of dextro-phenylalanine is sufficient. This may indicate that excessive laevo-phenylalanine is changed into dextro in the body and that the dextro substance is then deaminized in the kidneys and liver by the enzyme discovered by Krebs (1935). Only traces of the acid are found in the blood and cerebrospinal fluid of affected imbeciles, but high concentrations of laevo-phenylalanine are demonstrable. Evidently, in the abnormals some enzyme capable of utilizing laevo-phenylalanine is absent. The disturbance of reflexes, resembling thyrotoxicosis, suggests active poisoning by excess of abnormal metabolites, but the failure of pigmentation and of abnormal physical growth suggest a kind of internal nutritional deficiency. By studying the cerebral blood-supply in phenylketonurics, Himwich and Fazekas (1940) found that their low level of mental activity might be attributed to diminished rate of oxidation.

Pedigrees of phenylketonuria can be interpreted without much hesitation as demonstrations of the mode of inheritance of a rare recessive Mendelian trait. The main features include significant familial incidence, which is practically always confined to brothers and sisters. Environmental agencies, such as those connected with maternal age and order of birth, do not appear to be of significance. There is sharp segregation between normal and abnormal members of the family. Cousin parents are relatively frequent. The recessive hypothesis has been further strengthened by calculating the probable magnitude of the familial ratio of affected to normal members in sibships. After making due adjustment for mode of ascertainment, the ratio is very close to 1 in 4. Except in two families in the United States, cited by Jervis (1937), where the mother was phenylketonuric, parents have been reported to be of about average mental capacity. In the great majority of instances they have been examined and proved not to be excretors of phenylpyruvic

acid. In 47 families, analysed in Table XXIV, all the parents were unaffected and five pairs (10 per cent.) of them were first cousins. Jervis found that 5 per cent. of the parents of the phenylketonurics in the United States Institutions were first cousins. Of the parents of Norwegian patients, 14 per cent. were first cousins (Fölling *et al.*, 1945). All these percentages are significantly higher than the frequencies of first-cousin marriages in the general populations concerned, which are probably below 1 per cent. and may be as low as 0·6 per cent. (Table XXXIII.)

TABLE XXXIII

Source	Initial Cases	Brothers and Sisters		Parents		
	Phenyl-ketonuric	Phenyl-ketonuric	Normal	Phenyl-ketonuric	Normal	First Cousins
Munro (1947) .	47	38	141	0	94	10
Jervis (1939) . .	125	72	270	2	248	14
Fölling *et al.* (1945)	22	18	86	0	44	6
Total .	194	128	497	2	386	30

The frequency of phenylketonuria in the general population was estimated by Munro (1939) to be about 1 in 50,000 in the United Kingdom and by Jervis (1937) to be about 1 in 25,000 in the United States. In Norway the incidence may be a little greater. These incidence frequencies are likely to be approximately correct and they agree fairly well with the observed proportions of first-cousin parents when the Lenz formula (Appendix 5) is applied. The high incidence in Norway may, however, be illusory because the distribution was found to be uneven; there was a tendency for some of the cases to be concentrated in isolated districts where inbreeding was unavoidable. In one small region, Hvaler, a single ancestor possessing the gene might have been responsible for the four cases found there. Judged by institutional surveys, the incidence is high in France (Rhein and Stoeber, 1936) and low in Switzerland (Brugger, 1942).

The gene frequency, calculated in Table XXXIV from the square root of the incidence, amounts to 1 in 173 in the United States and 1 in 245 in the United Kingdom.

TABLE XXXIV

GENE FREQUENCY OF PHENYLKETONURIA

Survey	Case Frequency * (q^2)	Gene Frequency (q)	Carrier Frequency ($2q(1-q)$)
United States	1/30,000	1/173	1/86
United Kingdom	1/60,000	1/245	1/122

* Excluding cases known to have consanguineous parents.

The frequency of carriers of the gene, which is almost double the gene frequency, is of the order of 1 in 100.

Up to the present time no phenylketonuric of Jewish origin has been discovered. Cases of German, Irish, Italian, Slavonic and Dutch origin were found in the United States, but there were no cases found among American negroes. In his survey of cases in the United Kingdom, Munro (1939) found a rather higher incidence in the west of England than in the east, particularly in the north-west. The distribution of the blood antigens A and B in phenylketonurics and their sibs (Table XXXV) showed a higher incidence of B than did the English population from which these cases were drawn, though the incidence of A was not raised. That is to say, these families tended to resemble groups of peripheral Europeans (Boyd, 1939) in respect of their blood group frequencies expressed as percentages.

TABLE XXXV

PERCENTAGE DISTRIBUTIONS OF BLOOD GROUPS

Population and Number Tested	O	A	B	AB
Phenylketonuria sibships (179)	45	39	13	3
England (9000)	47	42	8	3
Northern Ireland (784)	56	30	12	2
Southern Italy (1460)	49	29	19	3

Out of more than 500 reported cases, only three females are known to have had any offspring (Jervis, 1939). Affected persons are therefore extremely infertile. On the other hand, the families in which cases occur are no smaller than the average size in the community. Heterozygous carriers are normally fertile. As they are so much more numerous than homozygotes, the proportional loss of genes at each generation through the infertility of phenylketonurics is very slight.

It is of interest to enquire whether any traces of the effect of the abnormal gene can be observed in heterozygous carriers. Depressions associated with persecutory ideas are perhaps more frequent in close relatives of phenylketonurics than in the general population. The mean age of onset of the mental disturbances, observed in 20 members of such families, was about 50 years. Fölling, Mohr and Ruud (1945), in their Norwegian studies, doubt the significance of the findings. Fölling (1934) thought that parents were liable to spontaneous excretion of phenylalanine, but this observation has not been confirmed. Detection of carriers by means of closely linked marker genes remains an interesting possibility which requires much further investigation.

MICROCEPHALY

Few descriptive terms in medicine have more vagueness than the diagnosis of microcephaly. Any cranium noticeably below the average size, appropriate to the age of the subject, can be called microcephalic. One clinical tradition, without specifying age, confines the description to heads measuring less than 13 inches in circumference. This measurement, according to Gall, represents a minimum below which idiocy is inevitable. Many types of cases with small heads occur. Some have been described as due to X-ray treatment of the mother during pregnancy. Others belong to dwarfs, whose heads are diminished in size in proportion to the rest of the body. In mongolian dwarfs the head is disproportionately small. Some institutional samples show an excess of microcephalic males as compared with females (Appendix 8): the mental grade is almost always low.

Abnormally small heads can be separated from the normal by actual measurement, if suitable norms are provided, but the shape of the head is also important. A class of cases can be clinically distinguished from the rest of defectives by the fact that the head is diminished greatly in the vertical measurement and in width but is less abnormal in length. An example is shown in Plate IV. These cases with low cephalic index can be fairly well distinguished from the rest and, by limiting the term "microcephaly" to this class, mongols, acrocephalics and other defectives who may have small heads of quite different shapes can be excluded (see Table XXXI). The group of relatively long-headed

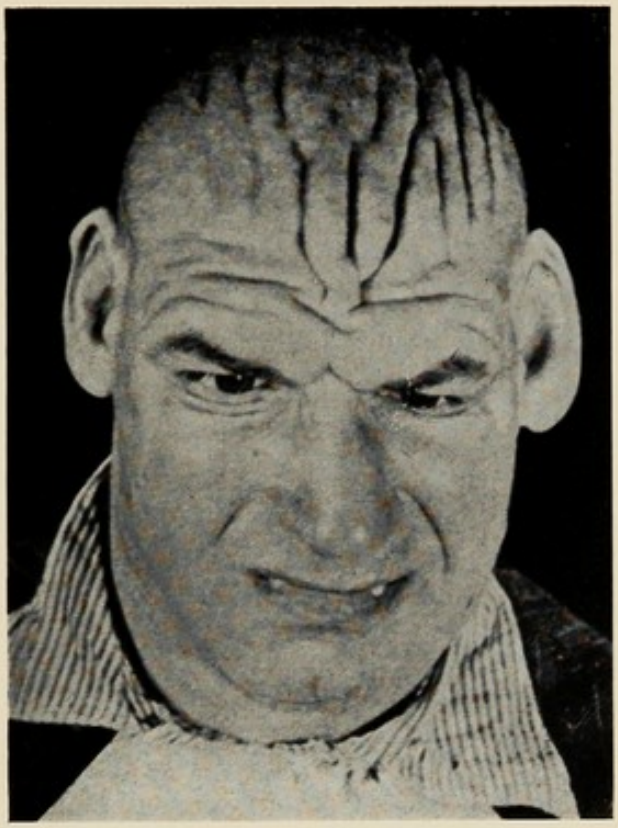


Plate IV—Microcephaly in a male idiot, aged 29. He is very friendly and is fond of music.

Head measurements: breadth 120 mm, length 176 mm, height 105 mm, cephalic index 0·68.

The scalp shows deep longitudinal furrows which are a feature of some of these cases.

microcephalics includes a type which is due to a single recessive gene and which has been termed "true microcephaly".

Recessive true microcephaly is a highly characteristic condition. Patients are invariably below the average stature. They are usually active and physically fairly healthy. The rest of the body, though dwarfed, is often well developed; it contrasts with the head size by its relatively normal musculature and sexual organs. Some of these patients make quick, furtive movements, which, together with their stooping posture, are reminiscent of some of the lower animals, and they were called "bird men" by Lombroso. The face is not so much reduced in size as the head, so that a relatively normal nose, chin and large ears may contrast with the receding forehead and low vertex in a manner reminiscent of the popular idea of a criminal type. These peculiarities were alleged by Langdon Down to constitute an Aztec type of defect. Psychologically, true microcephalics found in institutions are usually of the low imbecile grade. Though reputed to be querulous and bad-tempered, if well treated they are among the happiest and most harmless of patients. A case is illustrated in Plates Va and Vb.

Familial cases of true microcephaly were reported by Barr (1904) and cousin parents were noted by Shuttleworth (1875). A pedigree given by Hanhart (1943) shows 10 interrelated cases with parental consanguinity in two sibships. Halperin (1944) described three instances of affected sibs with normal parents. Altogether, the familial incidence seems to be a little lower than would be expected if all cases were due to recessive genes and there may be other causes for conditions which are clinically very similar. Most of the parents of microcephalics are apparently quite normal, but mental diseases and defects are found in some. Whitney (1930) reported a sibship which contained six cases of microcephalic imbecility; one sib and both parents were not microcephalic, but were mentally defective. Psychosis appeared in one parent of microcephalics in both pedigrees given in Figure 7. As in phenylketonuria, there is a possibility that the gene may predispose the heterozygous carriers to mental abnormality. The gene frequency of true microcephaly has not been estimated in any population; probably it is of the same order as the frequency of the gene for phenylketonuria.

The brain in recessive true microcephaly is extremely small and may weigh less than 1000 g., but it need not show pathological lesions. The cortical convolution pattern is much

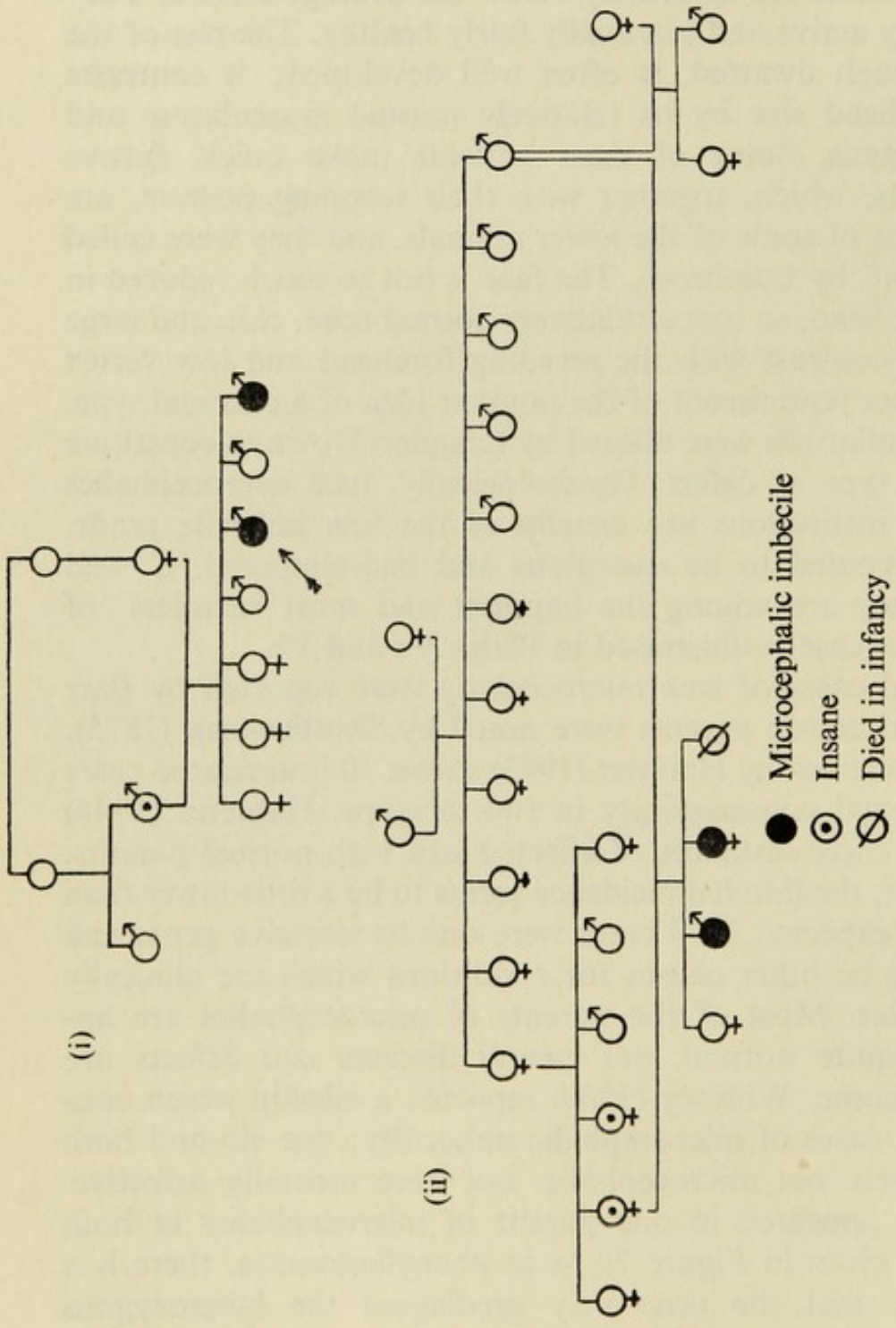
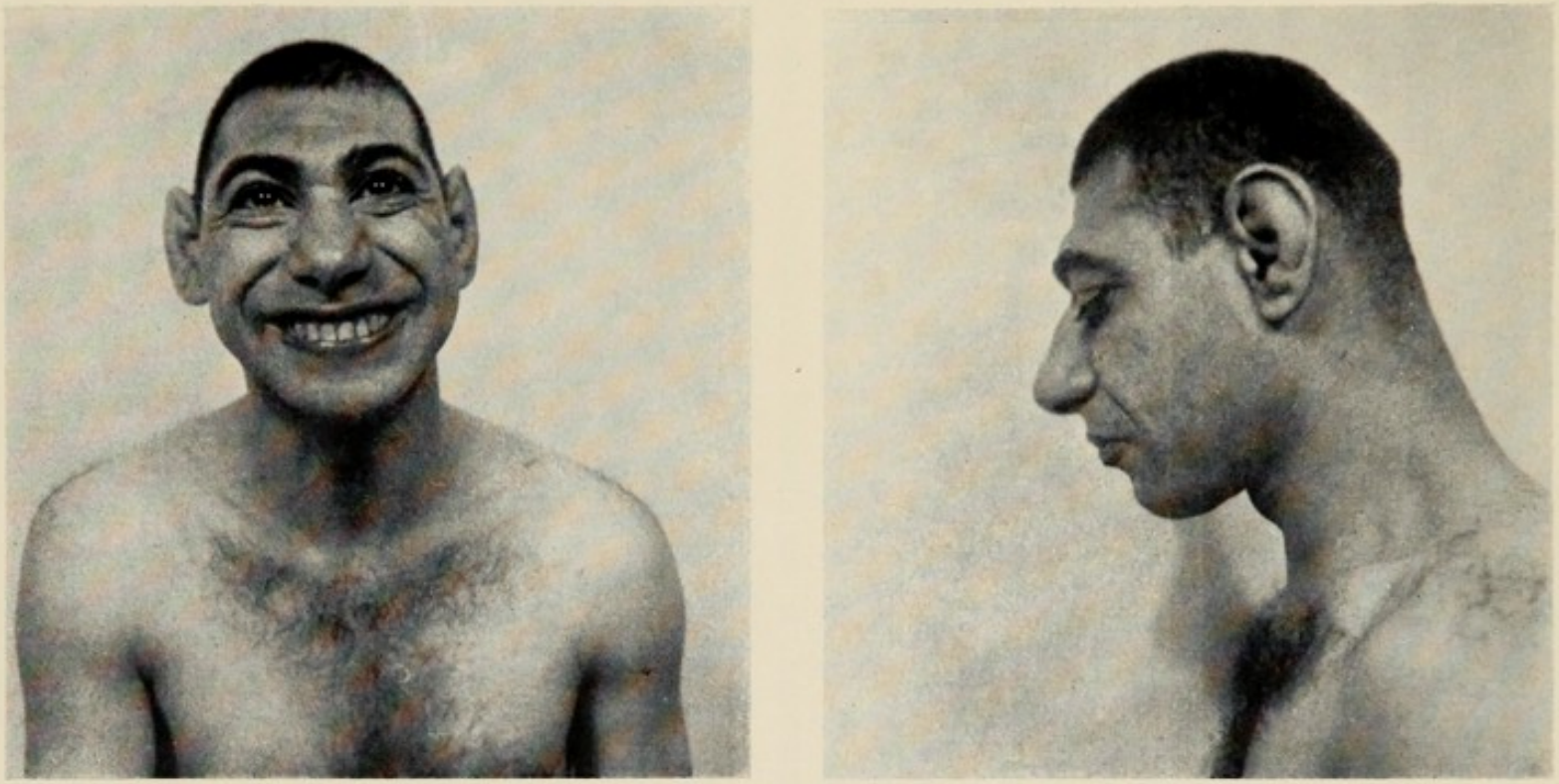


Figure 7.—Two pedigrees of recessive microcephaly
(i) The father of the two microcephalics suffered from a paranoid psychosis at the age of 41. The arrow indicates the patient shown in Plates Va and Vb.
(ii) The family is from the Colchester Survey, 1938 (Case No. 942). The mother and aunt of the microcephalics suffered from manic depressive psychosis.

simplified. In consequence of the small cerebrum, the cranial vault shows premature synostosis and considerable thickening as compared with the normal. As pointed out by Shuttleworth (1875), the skull peculiarities are not the cause of the brain



Plates Va and Vb—Recessive Microcephaly in a male idiot, aged 32

Note the small cranium with dysplastic ears and the well-developed shoulders. Head measurements: breadth 117 mm, length 154 mm, height 106 mm, cephalic index 0·76. The pedigree is shown in Figure 7 (i).

defect, as originally supposed by Virchow, but a secondary effect of the small brain. If an anthropologist should find a skeleton of a microcephalic, he might well conclude that it had belonged to a different species from *homo sapiens* though closely related. It is remarkable that a single gene can produce such a gross change, compatible with life if not with fertility.

CEREBRAL DIPLEGIA

Symmetrical spastic paralysis, chiefly affecting the lower limbs, is an important and not very infrequent symptom found in conjunction with mental defect. It can occur in a large variety of diseases and has many different causes. In the cases originally described by Little (1843), paralysis of cerebral origin, bilateral and fairly symmetrical in distribution, was the predominating or perhaps the only symptom. It is present at birth and is usually first noticed at about the age of 6 months or later. Neurologically the condition is almost stationary, though it may appear to worsen with age in consequence of muscular contractures. Sometimes it becomes accentuated after specific fevers (Dawidenkow, 1926).

The legs are most severely affected, but other parts of the body also suffer. When all four limbs are seriously involved, the term quadriplegia is applicable. Commonly there is some involvement of the facial muscles, which tend to overact when speech is attempted. The legs tend to assume a stiff scissor-like posture and the feet assume a flexed position, so that the subject who learns to walk has to do so on his toes. When paralysis affects the arms, the hands are held with flexed wrists and the fingers can be hyperextended. In typical cerebral diplegia, all tendon reflexes are brisk, particularly in the legs. There is increased tone in the muscles of affected limbs and the plantar responses are extensor. The abdominal reflexes are usually present.

Mental defect is not an invariable accompaniment, but there is a positive correlation between the severity of the neurological symptoms and the degree of intellectual impairment. On careful examination, however, patients physically handicapped by cerebral diplegia are found to be more intelligent than at first expected. After testing all cases in a sample of over 100 diplegic and hemiplegic children, McIntyre (1938) reported that only 18 were defective and 21 others were of dull or borderline

intelligence. (See also Table V, page 36.) Emotionally they have a tendency to be cheerful and even euphoric. Institutional cases may be of any grade, but imbeciles predominate. The sexes are affected with equal frequency.

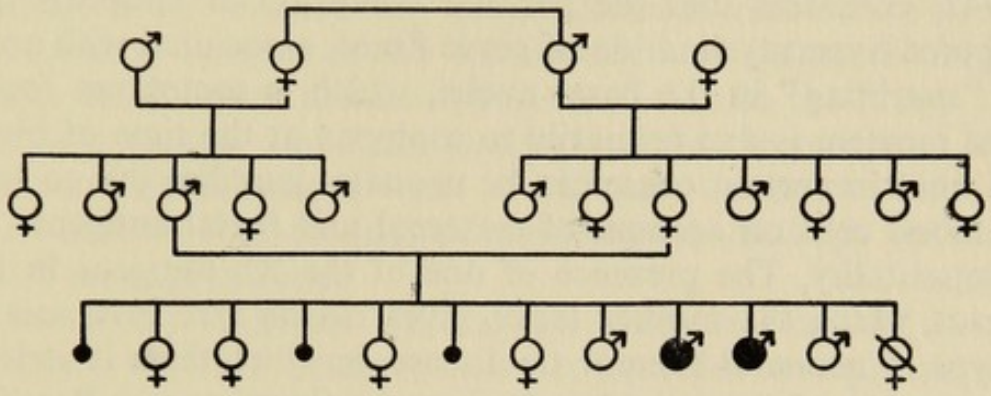
The pathological lesion in the majority of cases must be primarily related to the pyramidal system, but it may be very difficult to demonstrate any characteristic changes in the cerebral cortex, either macroscopically or microscopically. In some cases there may be lesions in the basal ganglia, particularly in the caudate nucleus, the putamen and the globus pallidus. The average size of the head is not diminished as compared with that of other individuals of the same mental grade. As the condition is not by its nature progressive, one explanation is developmental abnormality associated with absence rather than degeneration of certain nerve tracts. Furthermore, cerebral diplegia is sometimes accompanied by congenital malformation, such as club foot or dislocation of the hip (Wollenberg, 1909).

The original hypothesis of Little, that congenital cerebral diplegia was due to injury or to asphyxia at birth, has not received much support from neurologists in the past, partly because paralysis due to cerebral trauma or infection would be unlikely to affect both sides of the body equally. Nutritional deficiency at an early period of intrauterine development is credited by Stewart (1942) as the cause of some cases. Anoxia during the process of birth is now believed to be an important cause of symmetrical cerebral lesions. This view has been upheld in particular cases on clinical grounds by Evans (1948). The wholesale ascription of all types of infantile cerebral palsy to birth trauma, as implied in the work of Doll, Phelps and Melcher (1932), cannot be accepted as valid. There are many instances where the condition has all the characteristics of recessive gene determination (see Figure 8). Parental consanguinity and affected sibs have been frequently reported. Hanhart (1936) found seven cases in four related sibships, in which all the eight parents had a common ancestor, born in the seventeenth century.

CHOREOATHETOSIS

Though in the majority of diplegias the predominant clinical

signs indicate defect of the pyramidal tracts, many cases show signs also of involvement of the extrapyramidal system. A few cases, moreover, have mainly or exclusively signs of extrapyramidal lesions. These extrapyramidal symptoms are peculiar squirming movements and contortions which are evident as soon as voluntary action is attempted. Slight athetotic signs are often found associated with diplegia, especially in the



● Cerebral diplegia
○ Unaffected
⊘ Died in infancy
• Miscarriage or stillbirth

Figure 8.—Pedigree of two brothers with spastic diplegia. The elder had very slight signs and was normally intelligent. The younger was typically diplegic with a Binet I.Q.72 (Colchester Survey, 1938, Case No. 333). The type of parental consanguinity does not suggest partial sex linkage.

face, but the extreme picture of choreoathetosis is so characteristic that it warrants being considered as a separate condition. Moreover, in severe cases of choreoathetosis, signs of pyramidal disease, such as permanently increased muscular tone and extensor plantar responses, may be absent. Deafness is sometimes an additional complication. The mental grades of cases with extrapyramidal rather than pyramidal signs, though distributed widely over the whole range from normal capacity to idiocy, are somewhat higher than the average for all diplegics (see Appendix 8). Male and female cases are found in about equal numbers.

As with specifically pyramidal diplegias, the neurological signs in athetotic cases do not show a tendency to progression, though disabilities secondary to abnormal muscular action may increase with age. Pathological changes in the basal ganglia are to be more confidently expected when athetosis is present than when it is absent.

The causes of choreoathetosis, again, are multiple; foetal malnutrition and anoxia are not ruled out. Indeed, Norman (1947) considers that the peculiar condition of unevenly distributed hypermyelination of nerve fibres, associated with areas of "marbling" in the basal nuclei, which is sometimes found post mortem is due primarily to asphyxia at the time of birth. Another important cause can be neonatal jaundice due to lysis of blood cells on account of maternal and foetal antigenic incompatibility. The presence of one of the Rh antigens in the foetus, which the mother lacks, gives rise in rare instances to a type of neonatal haemolytic disease, in which there is serious destruction of the basal cerebral nuclei (kernicterus). Possibly there may be other types of antigens which can have the same effect occasionally. In surviving cases mental retardation results, with symptoms of choreoathetosis. However, there are also cases of diplegia, with predominantly extrapyramidal symptoms, which are examples of recessively determined defect. It is not clear, in such cases, whether the condition should be regarded as a variant of the commoner type of recessive diplegia or as due to a different recessive gene.

FRIEDREICH'S ATAXIA

Allied to the cases of congenital diplegia are those which come under the heading of paraplegia, in which the lower limbs only are affected. The group of paraplegias, however, of which Friedreich's ataxia, first described in 1863, forms an important example, are progressive diseases. The onset is delayed until physical and mental development are completed in the majority of cases and, thus, if associated mental deterioration takes place, the condition is usually described as dementia rather than as amentia. Friedreich's disease and the recessive types of spastic paraplegia, according to Bell and Carmichael (1939), begin, on the average, at the ages of 12 years and 15 years respectively. Though the degenerative lesions are primarily

in the spinal cord, occasionally mental defect is an accompaniment and, for this reason, these conditions can sometimes be found among inmates of institutions for defectives.

The dominant types of spastic paraplegia, to which the ataxia of Marie belongs (Sjögren, 1943), often cause degenerative mental changes. These diseases tend to arise later in life and are strictly irrelevant to the present study. The age of onset is subject to great variability. Though the mean age of onset is 34 years, it can occasionally occur in childhood, and in such cases mental symptoms can be classified as defect. A large number of different disease types are found in the group of hereditary ataxias and there is considerable disagreement between the classifications used in different countries. This is partly due to very inconstant pathological findings in the central nervous system.

The cardinal signs of Friedreich's ataxia are loss of deep reflexes in the legs, extensor plantar responses and pes cavus deformity, associated with ataxia and nystagmus. Sense of position and vibration are lost in the legs and sometimes also in the arms (Saunders, 1914). Mental defect must be classed among the associated anomalies, which include scoliosis, spina bifida, digital malformation and degeneration of the optic nerve. Retinal degeneration is a rare accompaniment, but its occurrence in sibships closely related to those containing cases of Friedreich's ataxia led Francheschetti and Klein (1947) to postulate a common genetical background for the two conditions.

The recessive nature of the majority of cases of Friedreich's ataxia is established by the fact that all parents are unaffected and that there is sharp segregation of the affected and unaffected children. Moreover, about 10 per cent. of the recorded cases have first-cousin parents. The same holds true for the allied disease, recessive spastic paraplegia, in which the clinical signs are quite similar, with the exception that deep reflexes are present and may be exaggerated. In both diseases males are slightly more frequently affected than females. A notable feature of the sex incidence is a tendency for males to be mainly affected in some sibships and females in others. Haldane (1941) has suggested that this may be evidence for the hypothesis that the genes responsible for both conditions are partially sex-linked recessives.

TAY-SACHS DISEASE

An example of a recessively determined condition, traditionally referred to in medical literature as familial rather than hereditary, is known as infantile amaurotic idiocy. This extremely rare disease, which is liable to occur in more than one child of normal parents, was first described clinically among an inbred Jewish population in London by Tay (1881) and the pathology was examined by Sachs (1887). The majority of cases have been found in Jewish families, though Hanhart (1943) has reported several instances in the population of Switzerland. Slome's (1933) analysis of published sibships clearly indicates that the condition is due to a single recessive gene in spite of a slight excess of female cases. The proportion of cases with first-cousin parents ranges from 11 to 40 per cent. in different populations.

The clinical features of the disease first appear at the age of a few months in a previously healthy infant. These are nystagmus and absence of voluntary movement. The ophthalmoscope reveals the presence of a brownish red spot in the macular region of the fundus. In the course of a year or so the condition advances to a state of profound idiocy, with paralysis, complete optic nerve atrophy and blindness (amaurosis); death occurs before the age of 2 years. The cerebral pathology consists in a degeneration first of the nerve cells of the pyramidal system and later of all the other nerve elements. This appears to be due to a biochemical deficiency which prevents the body from utilizing certain lipoid, that is, fatty, constituents of the brain cells. Under the microscope, the cells are seen to be swollen and filled with fatty substances.

The peculiar lipoid degeneration of nerve cells which occurs in this disease is closely paralleled in some other conditions of genetical origin. Among these are the juvenile type of amaurotic idiocy and gargoylism, which are recessive. Niemann-Pick disease is an allied condition in which visceral deposition of lipoids is characteristic: one type has its onset in adult life, is dominant and causes mental deterioration, but is not specially associated with mental defect. Pfändler (1946) described a family in which an increase in all lipoid constituents of the blood was inherited as a dominant character. The affected males had jaundice with enlargement of liver and spleen, but

not the females. At the present time it appears that a great variety of different conditions may fall into the category of lipoidoses. The proper allocation of these cases will only be made possible when more is known about the chemistry of the lipoid substance, sphingomyelin, which is present in abnormal quantities in various tissues in all these diseases.

JUVENILE AMAUROTIC IDIOCY

The genetics of the juvenile type of amaurotic idiocy were described in a classical monograph by Sjögren (1931); it is somewhat similar to Tay-Sachs disease, but arises at about the age of 6 years with extremes of 2 to 11 years. The early signs are progressive blindness, absence of facial expression and loss of power in movement. There is also an early disturbance of balance and co-ordination, which causes a peculiar gait: the subject leans forward with bent knees. Together with pyramidal nerve tracts, the extrapyramidal and cerebellar systems are affected at an early stage. The eye sign to appear first is a dark red patch on the macula. This is followed by retinal degeneration, both central and peripheral, which gives rise to a pigmented retinochorioiditis accompanied by optic atrophy.

The course of the disease may run for a period of from 5 to 10 years. During this time the intellect falls from a normal level to profound idiocy. A characteristic feature is the prevalence of epileptic attacks in the intermediate stages. The concurrent gradual loss of all motor functions is associated with paralysis, which is partly flaccid and partly spastic in character. In the final stages there is emaciation and complete helplessness. Microscopically, the nerve cells of the brain can be seen to be packed with globules of fatty substance.

Genetically, this disease, which can be referred to as a cerebromacular degeneration, is clearly the result of a rare recessive factor. Sjögren found that, among 145 sibships containing affected children, 23 parental pairs, or 15 per cent., were first cousins and 26 parental pairs were consanguineous in other ways. The parents of every case were unaffected and the familial incidence among sibs could be estimated at not less than one-quarter. In the Swedish population, the frequency of the gene which is responsible is of the order of one in two hundred.

GARGOYLISM AND RELATED DISEASES

A dystrophic condition, considered now to be a disorder of lipoid metabolism, was first described by Hunter (1917) and has been named gargoylism by Ellis and others (1936). A strange appearance is produced in an affected child. The skull shows a tendency to hypertelorism and hydrocephaly; radiological examination of the base shows an enlarged sella turcica. The stature is dwarfed and the spine bent forwards owing to defective vertebral bodies in the lumbar region. Enlargement of the liver and spleen, due to the accumulation of unidentified substances, causes the abdomen to protrude and, in some cases, there are milky corneal opacities in the eyes. The disease is noticeable at a very early age and is connected with severe mental defect in nearly every case. Superficially, the cases resemble cretins. Gargoylism is not a rapidly progressive disease, though most subjects succumb before reaching adolescence.

In the literature, summarized by Halperin and Curtis (1942), 33 male and 25 female cases had been recorded. The inheritance would appear to be recessive in the majority of families, though sex-linked transmission is not ruled out in others. First-cousin parents were found for 2 of the 40 recorded sibships.

A transitional type of gargoylism has been described by Jervis (1942); affected members of a sibship showed lipoid changes in the brain, typical of those characterizing amaurotic idiocy. Another dystrophic condition, in which osseous deformities predominate and which gives rise to a facial appearance reminiscent of gargoylism, was originally described by Morquio (1929). Not all cases are defectives. The main features of the disease are abnormalities of the bones, cartilages and joints, described as osteochondrodystrophy, which may be mistaken for rickets. The chest is grossly deformed. Some of the small bones of the wrist may be missing altogether. The joint surfaces are irregular and enlarged, the stature is dwarfed, there is kyphosis and enlargement of the cranium. Like gargoylism, the condition is usually recessive, but it does not seem to be a very clear clinical entity. A mild condition, similar to Morquio's disease, has been reported to be inherited as a heterozygous irregularly dominant disease (Shafar, 1941).

There is a large group of diseases, extending from osteochondrodystrophies to macular degenerations, and a number of

others not relevant to the study of mental defect, all of which are due to disorders of lipoid metabolism. This does not prove that they are genetically related to one another, though, of course, it is possible that they could represent the effects of a series of allelic genes. It is, however, convenient to group them together for purposes of systematic pathological classification, just as we can group together phenylketonuria and alkaptonuria. Different genes can, nevertheless, produce the same type of end result by quite different mechanisms, because the metabolism of a given essential substance in the body can be disturbed in a variety of ways. In amaurotic idiocy the lipoids are deposited in the brain cells. In gargoylism, also, there are intracellular cerebral deposits of similar lipoid substances found in the nerve cells and free deposits of other kinds of lipoid are found in the interstitial tissues of the basal ganglia (Ashby, Stewart, and Watkin, 1937). In both diseases fatty substances may be found in the reticuloendothelial cells of the spleen and liver. Another condition, known as Gaucher's disease, is characterized especially by visceral lipoid deposits and, in the Schüller-Christian syndrome, dwarfism and pituitary obesity can be combined with deposits in the bone marrow. The osseous deformities of gargoylism and Morquio's disease probably also have their origin in similar dystrophic processes. Excess of blood lipoid is found in xanthomatosis of the skin, another rare member of the same disease group, not typically associated with mental defect; the genetics are obscure.

RETINITIS PIGMENTOSA

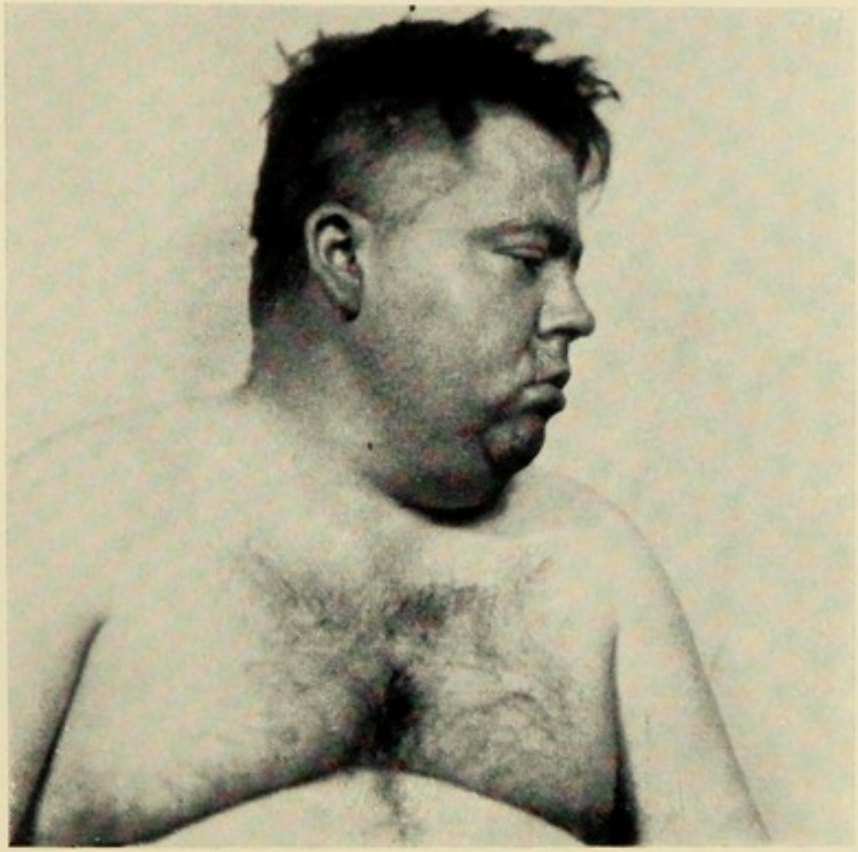
Progressive degeneration of the retina, starting peripherally and giving rise first to reduced night vision and later on to optic atrophy and total blindness, is sometimes an uncomplicated condition. The dark pigmentation of the deep layers of the retina, which are exposed by the degeneration of the superficial structure, can be clearly seen under the ophthalmoscope. Possibly there is also a real enlargement of the pigment cells and Dax (1938) repeatedly demonstrated the presence of a melanophorotropic substance in the urines of affected subjects. In an extensive survey of published cases, Bell (1922) found that severe disorder of the central nervous system, causing epilepsy, idiocy and other defects, was present in 37 out of 919 cases,

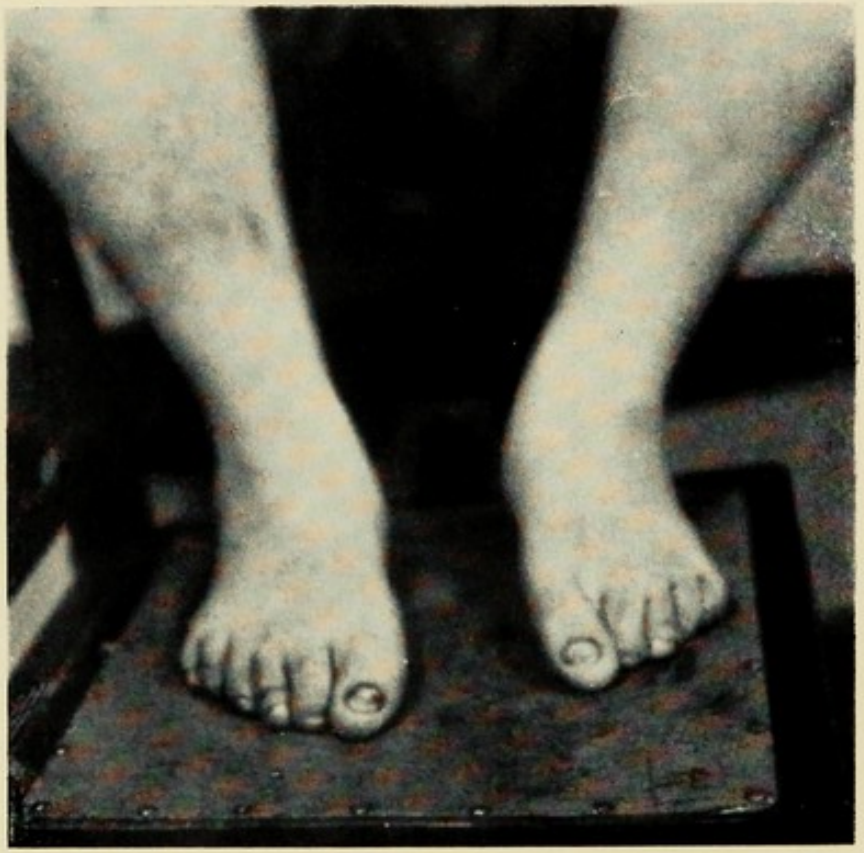
or in 4 per cent. Wortis and Shaskan (1940) examined 41 new cases and reported mental defect in 2 of them.

The significance of the condition, from the point of view of mental deficiency, mainly depends upon its association with other abnormalities. One of the commonest associated peculiarities is deaf-mutism, another is polydactyly and a third is pituitary dystrophy. The retinal degeneration which occurs in some cases of spastic ataxia and also that which occurs in cerebromacular degeneration may sometimes be difficult to distinguish clearly from typical retinitis pigmentosa. It is not surprising that many different types of pedigrees of retinitis pigmentosa have been found. In some the condition appears to be dominant and in others recessive. In some families partial sex linkage is a reasonable explanation, and in others sex limitation. Not infrequently the disease seems to occur in an isolated case with no affected near relative. Evidently there are a number of different genes, or combinations of genes, which can produce similar effects.

The most important type of retinitis pigmentosa found in relation to mental defect is associated with both polydactyly and pituitary dystrophy. It was originally noticed by Laurence and Moon (1866), but Bardet (1920) and Biedl (1922) supplemented their description and the disease has become known as the Laurence-Moon-Biedl-Bardet syndrome. A comprehensive review of the subject has been made by Cockayne, Krestin and Sorsby (1935). These authors, in agreement with some others (Jenkins and Poncher, 1935), attribute the coincidence of so many peculiarities in the same patient to close linkage of two or more genes, concerned in producing the main constituents of the pathology. The theory is difficult to disprove: it cannot, however, be regarded as probable unless sibships can be presented in which the separate genes are seen to be in repulsion. For example, we need to demonstrate that sibships exist in which some members are affected with retinitis alone and others, without retinitis have obesity and polydactyly. The supposition that it is impossible for a single gene to give rise to changes both in the ectodermal and mesodermal structures,which underlies the linkage theory, need not be taken as a basic biological principle.

The Laurence-Moon syndrome does not often cause very severe defect, though mental impairment seems always to be





Plates VIa and VIb—Laurence-Moon syndrome in a feeble-minded male aged 30. He has retinitis pigmentosa, obesity and polydactyly on the right foot. The parents were first cousins once removed. Three sisters were normal and one sib, who died in infancy, had six toes on one foot.

present. The usual mental age is from 5 to 7 years. There is considerable variability both in the degree of defect and in the physical signs, even among different affected members in the same sibship. Furthermore, although there is little doubt that the inheritance is recessive, the gene is not completely recessive. Close relatives, who may be heterozygous carriers, occasionally show some slight sign, such as polydactyly or obesity. For example, in the family recorded by Griffiths (1931), there were at least two children affected and three normal. The mother was obese and her brother was polydactylous. The patients of Ellis and Law (1941) only had infantilism and retinal dystrophy, but again a maternal uncle had polydactyly. A typical example of the syndrome is shown in Plates VIa and VIb.

MISCELLANEOUS CONDITIONS

Among the types of low-grade defect there are undoubtedly a large number of rare recessively determined diseases. Some of these have only been infrequently described and others still remain undetected. For example, Kallman, Barrera and Metzger (1940) recorded a sibship containing four microphthalmic children of whom three were imbeciles and the parents were cousins. Sjögren (1935) described 40 defectives suffering from congenital bilateral cataract in 30 sibships. The combination of cataract and mental defect was obviously not fortuitous, and two sibships had first-cousin parents. Two sibships with defectives suffering from keratosis of the hands and feet were recorded by Hanhart (1947); one of the patients had corneal dystrophy also. In both families the parents were consanguineous.

In an extensive survey of a peasant population in Sweden, Sjögren (1932) was able to discover a large number of imbeciles in related families. The tendency for more than one sib to be affected, together with the demonstration of common ancestry in many instances, convinced him that the cases were due to a recessive gene, although no specific pathology could be found. There were considerably more male than female imbeciles in the group, i.e. 34 against 18, a disparity for which no satisfying explanation was advanced. Sharp segregation was found between the normal and abnormal sibs with respect to mental grade and 6 per cent. of the sibships had consanguineous parents. Though it is quite possible that a single recessive gene,

causing a hitherto undetected metabolic disturbance, might be the cause of all these cases, it is also conceivable that more than one type of disease was included in the sample. The estimated true ratio of affected to total sibs was significantly less than one-quarter. Moreover, in isolated communities the interpretation of a high parental consanguinity rate as evidence for recessive determination presents difficulties. For example, in the general population of one north-Swedish district, investigated by Böök (1948), the proportion of first-cousin marriages was nearly 7 per cent.

In earlier times, cretinism was found frequently in isolated mountainous districts and was attributed to inbreeding. Cretins, and other subjects with varying degrees of thyroid deficiency or dysplasia, are frequent in the Allgau district of Germany. Lang (1929) found that these defects were associated with deaf-mutism and were concentrated in families. A clan of about 10,000 people, living in this same district, was investigated by Stidl (1935), who reported 32 cretins among them, 5 of whom were idiots, 17 were imbeciles and 10, simpletons. There were numerous examples of sibships containing more than one case. The general impression obtained from pedigrees containing cretins is that a gene, in homozygous form, may be responsible for a disposition to the disease, but that it is not always manifested. A combination of environmental influences, such as lack of iodine in the diet or peculiarities in the water supply, with genetical predisposition, would seem a probable mechanism of causation. Dysthyroidism of a comparatively mild degree, producing goitre in near relatives or parents of cretins, might be taken as evidence for a slightly abnormal heterozygous disposition. Some authorities, however, deny that heredity has any influence on the development of cretinism.

With respect to deaf-mutism, the situation is reversed. Here there is little doubt that, in perhaps the majority of cases, recessive genes are the cause but, only occasionally, are affected subjects mentally defective. According to Lindenov (1945), feeble-mindedness is a complication only when retinitis pigmentosa also is present. The association of deaf-mutism with parental inbreeding observed by Boudin (1862) has been amply confirmed by Hanhart (1943), who has convincingly demonstrated that recessive genes could be the sole determining factors in a large number of pedigrees.

CHAPTER IX

RARE SEX-LINKED DEFECTS AND THE PROBLEM OF SEX LIMITATION

General Principles—Myopathy—Anidrotic Ectodermal Dysplasia—Microphthalmia—Miscellaneous Pedigrees—Endocrine Dystrophies—Partial Sex-linkage—The Biology of Sex Limitation in Hereditary Disease.

GENERAL PRINCIPLES

IT has been previously emphasized that, with respect to the natural history of intelligence, there are many inequalities between the two sexes. Analysis of existing data with a view to the detection of the action of sex-linked genes, i.e. those located upon the X-chromosome, has not indicated that they play any noticeable part in the genetics of mental defect as a whole. The possible effects of sex-linked genes in determining the variations of mental ability in the general population can be studied by correlating intelligence level in special types of related pairs. The available material for such tests is limited and few observers have taken the trouble to correlate intelligence separately in pairs of fathers and sons, fathers and daughters, brothers and sisters, etc. However, no very marked differences would be expected between the values of such coefficients in practice, for two reasons. First, only about 1 gene in 24 contributing to the total effect will be sex-linked, and, secondly, as shown by Stanton (1946), assortative mating tends to level out the expected differences due to sex-linkage. To demonstrate that two correlation coefficients have significantly different values needs very large quantities of data. The results obtained by Herrmann and Hogben (1933), showing higher coefficients for brother and brother, sister and sister, than for brother and sister pairs, require confirmation on larger numbers. Moreover, unless parents are also tested, sib pair coefficients are susceptible to many different explanations. Willoughby (1928) calculated parent-child coefficients of each sex type and

was unable to demonstrate any tendency which could be interpreted as due to sex-linked genes affecting intellectual level.

Some pedigrees of rare defects show a pattern traditionally interpreted as the result of a rare gene carried on the X-chromosome. All males who possess the gene are affected, but the heterozygous female carriers, who transmit it, are unaffected. The inheritance is always through the mother and the disease is usually confined to males. The theory of the inheritance of rare sex-linked mutants in man is best understood in terms of gene frequency. Suppose that a rare gene *h*, carried on the X-chromosome, has frequency *q*, and its normal allele, *H*, has frequency *p* in the general population; then males will be of two types, *H*Y and *h*Y, because they have one X- and one Y-chromosome each. Affected males, *h*Y, will thus have an incidence *q*, say, 1 per ten thousand. Females, however, because they have two X-chromosomes, will be of three types, *HH*, normal, *Hh*, carriers, and *hh*, affected. Hence, the frequency of affected females will be q^2, or 1 per hundred million. The heterozygous carrier females, on the other hand, will have an incidence of $2pq$, approximately double the incidence of affected males. The only practical possibility of producing an affected female arises if an affected male mates with a maternal cousin, for such a female will be much more likely to be a carrier than one chosen from the general population. However, should the disability caused by the gene diminish an affected male's fertility, affected females will be of extremely uncommon occurrence even in closely inbred populations.

As with abnormalities due to genes situated on the autosomes, all those due to sex-linked genes must have originally arisen by mutation. If a sex-linked gene causes lowered fertility in affected males, it will tend to be eliminated from the population, at a rate which is intermediate between that for a dominant and that for a recessive defect but nevertheless quite rapid. Provided that the heterozygous female carriers are no more fertile than females in the general population, the mutation rate can be estimated, from a knowledge of the frequency and fertility of diseased males, in the manner described by Haldane (1939). For haemophilia, the rate is about one in 50,000 per X-chromosome per generation. Additional information may be obtained concerning the relative mutation rates in males and females, if a

representative sample of pedigrees of a given sex-linked disease can be collected. The mutation rate for the haemophilia gene is probably higher in females than in males.

A disease due to a sex-linked gene may be severe enough to prevent the affected males from having any offspring at all. When this is so, it is impossible to discover, from pedigrees, whether the causal gene is really sex-linked or whether it is a rare dominant autosomal gene whose effects are entirely limited to members of the male sex. In either case, inheritance must always be through the mother, who must be an unaffected carrier. Half the sons will be affected and half the daughters will be transmitters on either hypothesis (Table XXXVI). The

TABLE XXXVI

IDENTITY OF PEDIGREE TYPES FOR SEX-LINKED AND MALE SEX-LIMITED LETHAL GENES

	Sex-linked Lethal Gene, *h*		Male sex-limited Gene, *a*	
	Male Genotypes	Female Genotypes	Male Genotypes	Female Genotypes
Parents: All Unaffected	*HY*	*Hh*	*AA*	*Aa*
Offspring: Unaffected	*HY*	*HH* or *Hh*	*AA*	*AA* or *Aa*
Affected	*hY*	—	*Aa*	—

distinction between the two types of inheritance only can be made when affected males are fertile. In the case of sex-linkage, fathers cannot transmit the disease to their sons, for genetical reasons, whereas in the case of autosomal inheritance they can. With regard to the two fully accepted cases of sex-linkage, colour-blindness and haemophilia, the knowledge that the causal genes are fairly closely linked (Haldane and Smith, 1947) helps to establish their location on the X-chromosome. Eventually, the supposed location on the X-chromosome of some genes, which are responsible for rare cases of mental defect, may also be established or disproved by testing for linkage.

MYOPATHY

The typical picture, interpreted on traditional lines as evidence for sex-linkage, was shown in a pedigree published by Allen,

Herndon and Dudley (1944). Imbecility associated with muscular dystrophy (myopathy) was confined to males and transmitted through females for five generations (Figure 9). In Bell's (1943) survey of the inheritance of myopathy, three types of pedigrees were observed. These types corresponded to: (i) a dominant disease with onset at about 18 years; (ii) a recessive disease with earlier onset (at 11 years); and (iii) a sex-linked type with even earlier onset (at 5 years). Commonly, myopathy is not associated with mental changes, but cases of the sex-linked type are occasionally found in institutions for the mentally retarded, with an intelligence of the feeble-minded level. In these patients there is early onset and rapid progression of physical symptoms. Initially the affected muscles are enlarged and fibrous; the enlargement (pseudohypertrophy) is followed by wasting. An interesting biochemical accompaniment is the excretion of large quantities of creatine in the urine.

In the family recorded by Allen and his colleagues the association with mental retardation appears to have been unusually marked. Some of the affected males had neurological as well as muscular and mental symptoms. Since the hereditary myopathies are mainly degenerations of muscular tissue, localized at first to groups or even to single muscles, involvement of the central nervous system is a late development regarded by most authorities as quite secondary.

ANIDROTIC ECTODERMAL DYSPLASIA

A curious rare condition, almost confined to males and usually inherited through the female line, is characterized by absence of sweat glands (anidrosis) and peculiarities of the skin and other ectodermal tissues. The skin is smooth, hair growth is scanty, dentition is faulty and teeth may be absent altogether. Patients suffer severely in hot weather. Among the pleiotropic effects of the gene concerned, diminution of intellectual capacity to the level of feeble-mindedness has been recorded. Halperin and Curtis (1942) collected and analysed a group of published cases. In these sibships, if allowance was made for selection by at least one affected male member, one-half of the males were affected and no females, as would be expected on the hypothesis of sex-linked inheritance.

Similar conditions, not necessarily related in any way to

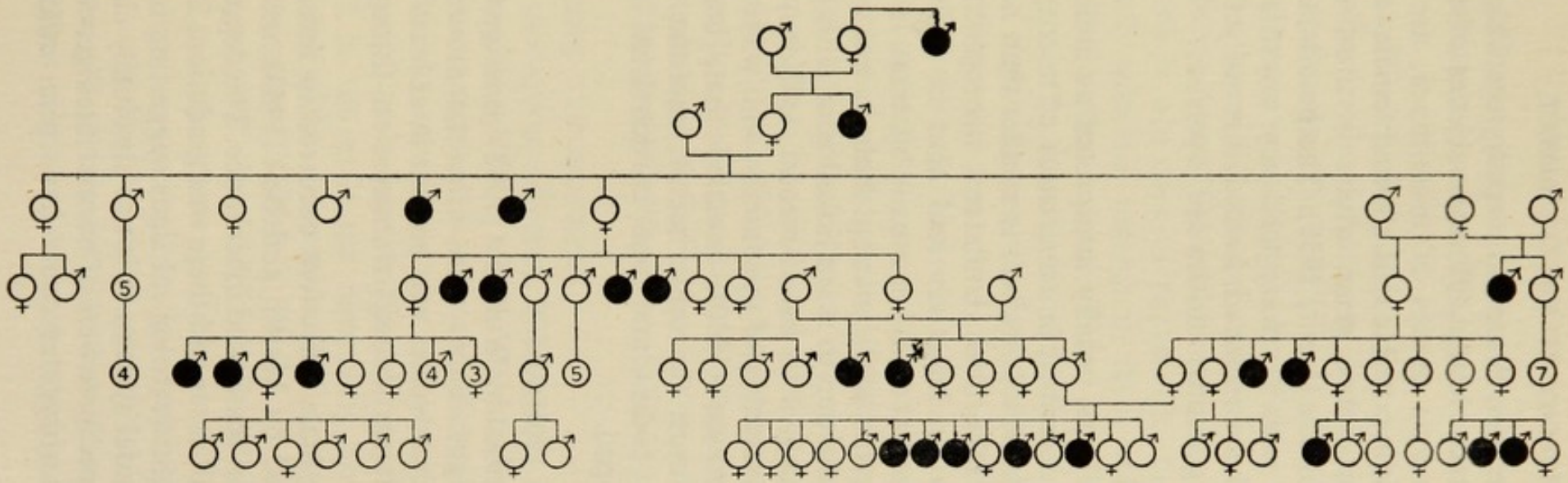


Figure 9.—Pedigree of myopathy with imbecility showing supposedly sex-linked type of inheritance (Allen *et al.*, 1944)

mental defect, have been described in pedigrees which indicate autosomal dominance. Many different varieties of ectodermal dysplasia, with various modes of inheritance, are listed by Cockayne (1933). It is possible that affected females are heterozygotes for the sex-linked gene, which is, thus, irregularly dominant in the female (Levit, 1935). The possibility of autosomal inheritance with a strong tendency towards male sex limitation has not been excluded. Indeed, it is not yet clear how many clinical and genetical entities are involved.

MICROPHTHALMIA

The type of pedigree, usually interpreted as indicating sex-linkage, has been described in some cases of microphthalmia. In this condition the whole eyeball is smaller than normal and may be grossly malformed. Unilateral microphthalmia can occur sporadically in defectives and also in individuals of average ability. Familial cases are usually bilateral. In a pedigree described by Roberts (1937), microphthalmia was confined to males and apparently due to a sex-linked gene with pleiotropic effects, one of which is to cause mental deficiency. Autopsy carried out on one member of this family, who was an idiot, by Whitnall and Norman (1940), revealed that, besides malformation of the eyes, the optic nerves, chiasma tracts and lateral geniculate bodies and one corticovisual area were imperfectly developed.

MISCELLANEOUS PEDIGREES

A pedigree described by Wolfslast (1943) contained five males with spastic diplegia. There were athetotic movements and nystagmus; low-grade defect was present in at least two of the cases. The inheritance showed transmission through normal females.

A family where male defectives occurred in several generations was described by Martin and Bell (1943) and explained on the hypothesis of sex-linked inheritance. The degree of defect was not equal in all cases and there was gradation. Some of the defectives had slight neurological signs suggesting involvement of the extrapyramidal system. It is not absolutely clear that all the females in the pedigree were of normal intelligence, and some of the female heterozygotes could have been mildly affected

without exciting comment. The distinction between sex-linkage and sex limitation in such a pedigree cannot be made with certainty.

Pelizaeus-Merzbacher disease is a progressive demyelinization of white matter producing spastic paralysis and idiocy in the first decade of life. It is an extremely rare disease and males are much more frequently affected than females. Since males who have the disease never transmit it, the assumption made by Gates (1946) and others that it is due to a sex-linked gene is not easy to prove. The fact that females are occasionally affected, though in most instances less severely than males, is assumed to be due to the gene's incomplete recessivity in the female, but this could be true also of an autosomal dominant gene, fully manifested only in the male.

The position with respect to Leber's hereditary optic atrophy is even more obscure. Here the disease consists in a degeneration of the optic nerve, transmitted both by affected and unaffected females to both sons and daughters, but only very rarely transmitted by affected males. Cytoplasmic inheritance has been blamed (Imai and Moriwaki, 1936), as well as sex-limited and sex-linked genes. Fortunately, although mental changes may occur in connection with the disease, their onset usually occurs late in life and the student of mental deficiency need not feel called upon to decide the most likely mode of inheritance.

ENDOCRINE DYSTROPHIES

The endocrine equilibrium is normally different in the two sexes. If a gene produces effects which are related to endocrine equilibrium in any way, it will not be surprising if its manifestation in the two sexes is uneven. For example, almost exclusive prevalence of premature baldness in males can be credibly attributed to the male sex hormones, since eunuchs do not suffer from baldness; nevertheless, a single autosomal gene could be responsible (Harris, 1946).

Disturbances of thyroid gland function in the direction of excessive activity (toxic goitre) or of diminished activity (colloid goitre) are commoner in females than in males. In an extensive study of goitre in Maryland, Davenport (1932) found 222 affected females against 75 affected males. The inheritance of either type of goitre, toxic or colloid, suggests a dominant

female sex-limited condition. Hyperthyroidism may predispose to disorders of behaviour and thus prove an occasional part cause of certification in high-grade female defectives. Insufficiency of thyroid function, in the form of juvenile myxoedema or cretinism, is an important cause of defect and is also more prevalent in females than in males. In cretinism, the head is of normal size and the brain well developed. In consequence of lack of thyroid hormone, postnatal growth is stunted and the brain may fail to function above the imbecile level in untreated and sometimes also in treated cases. This failure of mental functioning even after administering thyroid extracts in large amounts suggests that there are associated defects, either metabolic or endocrine, in many cretins.

Among institutional defectives, some are found who show signs both of thyroid and pituitary disorder and others whose conditions can best be described as polyglandular dystrophies. These diseases can be found in both sexes. Pituitary disorders, however, are more noticeable in male defectives than in females. The adipose type with genital infantilism (Fröhlich's syndrome), due to failure of secretion of the anterior part of the pituitary gland, can be associated with low-grade defect and tends to be male sex-limited. Hypogenitalism is more easily recognized in males than in females, but the condition of pseudo-hermaphroditism can only occur in males. Pedigrees, showing mentally defective males with hypogenitalism and some degree of physical feminization with a suggestion of pituitary disorder, have been described by Kallman and others (1944). The genetics of these conditions are at present obscure and many complicated explanations have been offered, involving the sex chromosomes. In view of the fact that hypogenitalism and obesity occur sometimes in females and, indeed, in female close relatives of affected males, unequal manifestation of the same genetical cause in the two sexes seems to be the most logical explanation.

PARTIAL SEX-LINKAGE

Pedigrees of recessive spastic paraplegia (page 155) show certain peculiarities which suggest that the gene concerned is located on part of the X-chromosome which can cross over with the Y-chromosome. There are two tests for this hypothesis

in recessive diseases. The first test is that males are chiefly affected in some sibships and females in others. The second test is that, when parents are first cousins, relationship through the father's father is associated with affected sons and relationship through the father's mother with affected daughters.

The first test, by itself, is not quite convincing, because there might be forms of sex-limitation which made males more vulnerable in some families and females in others. That males are mostly affected in some families and females in other families is a common phenomenon in human genetics (Harris, 1948). It may be termed "familial sex-limitation" and it has been repeatedly observed in medical genetics since the subject was first discussed by Sedgwick (1861). The simplest explanation of this process is that it is due to modifying genes, which alter the resistance of one or other sex to the pathological action of the main gene concerned. It seems, *prima facie*, unlikely that partial sex-linkage could be a phenomenon widely enough spread to account for all observed instances of familial sex-limitation.

In evaluating the meaning of the second test, that concerning types of cousin parents, we are on firmer ground, even though the quantity of relevant data will always be rather small. With respect to recessive spastic paraplegia, for example, the evidence obtained from types of consanguinity is fairly good. The same test is also very favourable to the hypothesis that a partially sex-linked gene causes xeroderma pigmentosum, a rare skin disease occasionally associated with mental defect. In this disease the skin becomes inflamed and pigmented when exposed to sunlight and remains scarred and freckled thereafter.

As previously mentioned, some kinds of retinitis pigmentosa may be due to partially sex-linked genes and mental defect is an accompaniment in a few cases. Again, Snyder and Palmer (1943) have reported a family with a condition similar to Pelizaeus-Merzbacher disease, appearing as a recessive character with a suggestion of partial sex-linkage.

There might be hitherto unrecognized causes of defect with the partially sex-linked mode of inheritance. In the Colchester Survey, analysis of the sibships with different types of first-cousin parents gave a slight indication that this might be so. In addition, it was possible to arrange sibships according to whether the father's father or the father's mother had the

higher intelligence level. Thus, a test for the possible effects of dominant or additive partially sex-linked genes, which altered intelligence level, could be made on a plan similar to that described earlier (Table XVIII) for testing the influence of fully sex-linked factors. If intelligence level were influenced by partially sex-linked genes, the grandchildren grouped in the upper

TABLE XXXVII

A Test for Partial Sex-Linkage of Genes influencing Mental Level

Comparative Mental Grades of Paternal Grandparents and Sexes of Grandchildren	Grades of Grandchildren (patients and their sibs)					
	Average	Borderline	Feebleminded	Imbecile	Idiot	Total
(i) Grandfather superior to grandmother. Grandsons .	19	5	2	3	1	30
(ii) Grandfather inferior to grandmother. Granddaughters	19	5	11	—	—	35
Total . . .	38	10	13	3	1	65
(iii) Grandfather superior to grandmother. Granddaughters	13	3	6	4	1	27
(iv) Grandfather inferior to grandmother. Grandsons .	14	6	8	2	1	31
Total . . .	27	9	14	6	2	58

Classes (i) and (iii) comprise 15 sibships, (ii) and (iv), 13 sibships.

half of Table XXXVII should be more intelligent than those grouped in the lower half. There are, in fact, fewer defectives of all grades and more normals in the upper half of the table; but the numbers are too small for the inequality to be statistically valid.

THE BIOLOGY OF SEX LIMITATION IN HEREDITARY DISEASE

There are many conditions, the causes of which are fairly well established but which nevertheless occur more frequently or

more severely in one sex rather than in the other. In many recessively determined abnormalities, males predominate. This occurs, for instance, in albinism, alkaptonuria, diplegia, paraplegia, retinitis pigmentosa and juvenile amaurotic idiocy. There were also more males with Sjögren's recessive type of imbecility; and the predominance of male cases applies to low-grade defectives generally. Two exceptions are phenylketonuria and anencephaly, though even here it is not certain that the excess of female cases does not result from greater severity of the diseases in males and consequent liability of affected males to elude observation.

Conversely, many diseases which have onset in late or middle life are commoner in females or have earlier onset in females. Bell (1934) showed that this was so in Huntington's chorea and Malzberg (1935) showed that mentally ill choreic males entered hospitals, on the average, more than five years later than corresponding females. Manic depressive psychosis has a marked tendency to occur in more than one member of the same family, and some dominant genes are probably involved in the predisposition. Here, again, the mean age of breakdown is significantly earlier in females than in males (Malzberg, 1935; Dayton, 1940); also the incidence is definitely higher in females.

Levit (1935) pointed out that the delay in onset of dominant diseases until after the end of the reproductive period should not necessarily be attributed to involutional changes. Natural selection tends to eliminate stocks in which dominant defects occur early enough in life to interfere with fertility. We can thus expect selective processes gradually to modify dominant diseases and to postpone their times of onset. This tendency cannot act efficiently after the end of the reproductive period. Since the reproductive period lasts longer in males than in females, we might expect that natural selection would postpone the onset of dominant diseases in males later than in females.

It is more difficult on biological grounds to explain why males should be more severely affected than females in recessively determined conditions. Early onset, severity and diminished fertility are characteristic of the defects which come into this group. Possibly the solution is to be sought in the greater degree of fertility of females than males among defectives of

equally low grade. Slight modification for the better in the female seems to be of more biological value than it would be in the male. The argument applies to all types of low-grade defect, irrespective of the mode of inheritance. The prevalence in human data of inherited diseases, severe in the male and mild enough in the female to allow fertility, thus may be the result of natural selection.

It is unwise in the present state of knowledge to attempt to specify the nature of the genetical processes by which the manifestation of diseases in the two sexes is caused to differ. The theory has often been advanced that sex-linked genes are the modifying factors which produce more male than female cases of severe defect. This idea has had support from Sjögren (1932, 1935) and from Rosanoff (1931), but it has been strongly disputed by Csik and Mather (1938) on statistical grounds. There seem to be no objections to the simpler view that the genes concerned are differently manifested because the sexes are constitutionally different. It appears likely also that the variations in reaction, within the sexes, to different abnormal genes, depend chiefly upon the autosomal constitution.

CHAPTER X

DEFECTS OF OBSCURE ORIGIN AND ENVIRONMENTALLY DETERMINED DISABILITIES

Incidence of Foetal Malformations—Anencephaly, Hydrocephaly and Spina Bifida—Clinical Picture of Mongolism—Aetiology of Mongolism—Foetal Infections—Congenital Syphilis—Prenatal Cerebral Injury—Birth Trauma —Postnatal Injury and Disease.

INCIDENCE OF FOETAL MALFORMATIONS

A BIOLOGICALLY important group of conditions of obscure origin is considered under foetal malformations. Too little is known to enable them all to be classified accurately under more specific headings. Their importance here lies partly in the surprisingly high proportion of such malformations that cause mental defect, often of an extremely severe degree. In a survey of 13,964 births at the Liverpool Maternity Hospital, Malpas (1937) found that 1 per cent. had gross malformations of the central nervous system. Yet another 1 per cent. showed miscellaneous defects. Some deformities, like anencephaly and mongolism, are invariably associated with mental defect and others, like club foot, spina bifida and harelip, occasionally. Murphy (1947) examined the deaths and stillbirths in Philadelphia, over the period of a year, and traced all individuals whose death certificates recorded the existence of congenital malformation. On this basis he estimated that approximately 0·5 per cent. of live-born and 3 per cent. of stillborn individuals were malformed. The incidence in the white as compared with the coloured population was as 9 to 5, and for parents of British origin, judging by the United States Government statistics on infant mortality, the incidence was higher than for any other group.

Nomenclature of these conditions is troublesome because several types of deformity often coexist in the same individual. Thus, spina bifida occurs with or without hydrocephaly and either of these conditions can occur with talipes (club foot).

Furthermore, congenital cardiac disease frequently accompanies mongolism. The most extreme deformity present usually determines the diagnosis. Table XXXVIII shows the frequencies of the important types. Hydrocephaly is the most common deformity shown in this table and it was also the most common condition in Murphy's material.

It is interesting to note that, if intelligence could be measured at birth in every child, the incidence of mental defect might be found to be much higher than that observed at school age.

TABLE XXXVIII

FOETAL MALFORMATIONS IN A SERIES OF 13,964 BIRTHS, AFTER MALPAS (1937)

Abnormality	Number of Cases	Percentage Incidence
Nervous System		
Anencephaly and related conditions	52	0·37
Spina bifida	39	0·28
Hydrocephaly	58	0·42
Mongolism	18	0·13
Total	167	1·20
Miscellaneous		
Talipes	23	0·17
Malformed hands	16	0·11
Absence of radius	2	0·01
Harelip and cleft palate	17	0·12
Hypospadias	16	0·11
Congenital cardiac disease	10	0·07
Gastroschisis	5	0·04
Other	38	0·27
Total	127	0·91

About 1 per cent. would be idiots. On the other hand, the normal variability would be much greater than is observed in later life, because prematurity, postmaturity and different individual rates of development would complicate the picture. This serves to emphasize that when the incidence of mental defect in a given population is stated, the age group must also be specified. By the age of 10 years the incidence of idiocy has dropped to 0·06 per cent. because of the high mortality rate of low-grade defectives, and thereafter it doubtless continues to fall.

The study of the causation of these foetal malformations presents one of the most baffling problems in medicine. The one

certainty is that the defects must originate at an early stage in the embryonic development. On the whole, the grosser malformations are initiated earlier than the slighter ones. The most significant period of development, from the point of view of these malformations, precedes the 12th week of pregnancy. Any environmental cause to be sought must act before that time and the crucial period may be as early as six to eight weeks.

An additional difficulty in establishing causes arises from the likelihood that the origin of such a condition as anencephaly, for example, is not the same in all cases. At certain critical stages in development several widely different types of disturbance may lead to similar results, in the same way that, in later life, there may be many different causes for the same reactive symptom like a fever or a convulsion. Snell and Picken (1935) found that anencephaly in mice might follow from the presence of too much chromatin or too little. There are other genetical causes for similar conditions in animals. One kind of hydrocephaly in the mouse is due to a single recessive gene (Grüneberg, 1943); another kind is due to a different gene, also recessive. Again, Kaven (1938) irradiated pregnant female mice in the early critical stages of gestation and found that many sorts of malformations were produced in the offspring. Some of the treated embryos developed anencephaly. Evidence has been brought forward by Warkany (1944) to show that maternal malnutrition and maternal poisoning, at critical stages, can also cause foetal malformations in experimental animals. In all of these processes the point of time in embryonic development at which the disturbance is produced seems to be more important, in determining the resulting type of malformation, than the exact nature of the agent. Gillman and others (1948) have produced hydrocephalus and spina bifida in rats by saturating the maternal tissues with trypan blue.

A monstrosity found in some stocks of guinea-pigs, characterized by defect of the lower jaw in mild instances and complete absence of the head in the most severe instances, is known as otocephaly. Wright (1934) has shown that it is partly determined by genes, because some stocks are more prone to it than others. Nevertheless, even in highly susceptible inbred strains many offspring develop normally. Some unknown factors, possibly connected with the maternal environment, contribute to the

causation. This condition exemplifies the way in which the circumstances existing before conception combine with those existing during individual development to cause foetal abnormality in a mammal.

Developmental peculiarities caused by specific environments but which resemble established genetical traits are termed phenocopies (page 80). The proportion of human malformations that are phenocopies is far from being known at the present time. In some cases genetical causes, in others environmental causes are to be suspected. In yet others, a combination of causes is to be blamed. Consequently, human data on foetal malformation must be surveyed simultaneously from the points of view both of genetics and of the study of maternal environment.

ANENCEPHALY, HYDROCEPHALY AND SPINA BIFIDA

It is convenient to group together all the malformations of the nervous system, partly because they have certain common features in their natural history and partly because such malformations are often associated with one another in the same individual. All these defects must originate very early in embryonic life, probably within the first 8 weeks, and their causation therefore is limited to events occurring not later than the very early prenatal period.

Spina bifida is not necessarily associated with mental defect. Very mild cases of spina bifida occulta are compatible with quite normal development and are believed by some authorities to be common in the normal population. Anencephaly, on the other hand, is not compatible with mental functioning or even with independent life for more than a day or two. The brain is replaced by amorphous vascular tissue and the vault of the skull is absent. Hydrocephalics occupy an intermediate position, though most congenital cases show marked mental defect. In some of these, the child may live many years although the head may continue to enlarge, occasionally to a prodigious extent, and consequently the skull can become so extremely thin that membranous lacunae appear or multiple Wormian bones develop in the sutures. The ventricles are enormously dilated and the cortex is stretched and deformed out of all recognition. As with some other types of neurological defect, in spite of great

disability due to blindness or paralysis, the subject's intelligence may be greater than the casual observer would be led to suppose.

Familial investigation of nervous system malformations usually leads to a negative result in the sense that second cases of the same kind are comparatively rarely discovered in near relatives. Sometimes, however, the same abnormality is repeated in more than one sib. Familial anencephaly was reported by Schade (1939), for example. The familial cases, though unusual, are not rare enough to excite sufficient interest to make their recording in medical journals popular. Murphy (1936), moreover, drew attention to the fact that, though the same abnormality is sometimes repeated in a sibship, at least as frequently different abnormalities occur in two or more sibs.

Familial incidence is no certain proof of genetical causation. Even so, the first task of the investigator is to establish that the familial occurrence is not due to chance coincidence. With common conditions, that is, conditions with an incidence of the order of 1 per cent. or more, this is not always easy, and careful study of unselected samples is required. The available evidence suggests that familial incidence in these malformations is slight but significant. If one child with anencephaly or spina bifida is born, the chance that the same pair of parents will have another child with severe neurological malformation lies between 3 and 10 per cent.

Reservations have to be made in forming an estimate in any given sibship because, as has been shown in Table XXV, pages 110 and 111, there is a marked tendency for the risk of malformed offspring to increase in the later maternal age groups. The same applies to statistics of stillbirths generally (see Table XXXIX), and this is not surprising, for foetal malformation is an important cause of stillbirth and also of neonatal mortality (Holland and Lane-Claypon, 1926). Birth rank by itself has apparently much less effect than maternal age, though there seems to be an increased risk of malformation for the first born (Penrose, 1946). Possibly there is, also, increased risk for very young mothers as well as for those nearing the end of the childbearing period.

At the present time, with the limited knowledge available, it is impossible to decide between the relative claims of different hypotheses concerning causation. Theories which are in the running for explaining all of the cases partly, or some of them

TABLE XXXIX

INCIDENCE OF STILLBIRTHS ACCORDING TO MATERNAL AGE

Maternal Age	Maternities	Stillbirths	Incidence of Stillbirths
15–19	25,849	558	0·022
20–24	177,191	3,774	0·021
25–29	184,352	4,279	0·023
30–34	165,819	4,776	0·029
35–39	103,426	4,030	0·039
40–44	31,974	1,745	0·055
45–49	2,323	171	0·074
All Ages	690,934	19,333	0·028

From *Statistical Review of England and Wales for the Year* 1945 (New Annual Series, No. 25), Tables—Part II, Civil, p. 113.

completely, are single genes with low manifestation rates; chromosome abnormalities; antigenic incompatibility; and adverse maternal influences, which might be, in their turn, partly due to the hereditary constitution of the mother. The antigenic theory has received some support from Wiener (1946), who reported several cases of spina bifida in infants born to mothers, who were Rh negative and who had Rh antibodies in their blood sera. If the data on familial cases, particularly cousins, were obtained in sufficient quantity and children of like-sexed sibs were found more often malformed than children of unlike-sexed sibs, this would suggest antigenic incompatibility as a part cause even in the absence of serological data.

Another explanation, which needs careful study, is that mentioned by Kemp (1944), namely, that fresh mutations account for many cases. It is undeniable that foetal deformities of the nervous system tend to be lethal and that every time such a child is born and dies, genes which are causal will be lost. It can be argued that, to conserve equilibrium, the genes for anencephaly, etc., must be continually replaced by new mutation. If so, the new mutation rate in man must be astonishingly high. However, if anencephaly is not a single entity, several kinds of rare gene mutations, or chromosome changes, might be responsible.

Inferences about mutation rate in diseases whose incidence is related to increased maternal age or parity need to be very guarded. A great number of cases occur, in sibships which are

larger than the average, because of the associations of foetal malformation with advanced maternal age and high parity. That is to say, some cases would not have occurred unless the mother had been exceptionally fertile, and these are, as it were, extra births not taking part in the genetical equilibrium of the general population.

CLINICAL PICTURE OF MONGOLISM

A central position in the study of mental deficiency is occupied by the problem of mongolism. Some 5 per cent. of institutional cases belong to this class. In early times these people were probably confused with cretins and were thought to be caused by parental tuberculosis. Langdon Down (1866) gave the first clear description and termed them mongolian or mongoloid imbeciles because of a superficial resemblance to normal oriental peoples and particularly to the Kalmucks. The hypothesis, added later by Crookshank (1931), that these cases were derived from Mongolian ancestors and, further, that they represented an atavistic return towards the orang-utang, has no scientific validity. Actually the malformation has been reported in almost all parts of the world, even among the children of negroes and Chinese. It is much more frequent, however, in populations of European origin than among American negroes (Thompson, 1939).

The malformation affects, in some degree, almost every part of the body. Many of the characters by which mongolism is recognized are also found individually in other types of detectives and even in normal subjects. Of the external peculiarities, the most noticeable are dwarfed stature, small round head and dysplastic features. The retardation of growth has been studied by Benda (1947), who considers that the mongolian infant is of normal length at birth, that it deviates progressively from the normal as it grows older and ultimately reaches, on the average, a stature equivalent to that of a normal child of 10 years. Body weight is correspondingly reduced. The head is notable for its small dimensions. The anteroposterior diameter is greatly diminished and the cephalic index is high (see Table XXXI). The hair is usually straight and sparse; the skin is dry. The face, which suggests an oriental configuration only in some cases, is notable for its flatness and hypoplastic nature, with a short and squat nose, small rounded ears and oblique palpebral fissures.

Cataract, myopia, strabismus and speckled iris are characteristic of the eyes themselves; blepharitis and conjunctivitis often develop round them. The mouth shows a protruding lower lip, thickened buccal mucosa and a fissured tongue with enlarged papillae. Development of teeth is retarded and irregular. Unusual susceptibility of mucous membranes to infection is indicated by the prevalence of nasal and respiratory catarrh. The mortality rate at all ages is very high and the expectation of life at birth is about 9 years. One female living to the age of 83 has been reported (Simons and Speijer, 1937).

The limbs, like the trunk, are stumpy. Joint ligaments are lax and mongoloid children sit comfortably in the tailor-wise position. The hands and feet are broad and clumsy, and webbing (zygodactyly) of fingers and toes is not uncommon. The little finger tends to be very short and to curve inward. Of particular interest is the configuration of the creases and the finer dermal ridges on the palms and soles. A single transverse crease often runs across the palm of the hand, the two creases on the little finger may be replaced by one only; a marked cleft occurs between first and second toes. The dermal ridges, first studied by Cummins (1936), indicate a strong tendency towards a more transverse arrangement than is usual in normal hands. This is shown especially in the position of the main line from *a* and the axial triradius *t* as demonstrated in Figure 10. A large, rather L-shaped ulnar loop is the most characteristic type of fingerprint pattern (Turpin and Caspar-Fonmarty, 1945).

Other abnormalities include umbilical hernia and small genital organs. On the neurological side, the absence of signs of organic disease is remarkable. Epilepsy is no more common than among members of the general population.

The mental grade varies from idiocy to an upper limit at about the 7-year level, as judged by the Binet tests. Institutional cases have a mean I.Q. between 20 and 25 points, but those living at home may be of slightly higher grade, and if so can be useful in domestic occupations under supervision. Typical mongoloids have cheerful and friendly personalities. Their capacities for imitation and their memories for music and complex situations may be found to range far beyond their other abilities.

The underlying pathology of the condition is still obscure in spite of much intensive investigation. The brain shows no

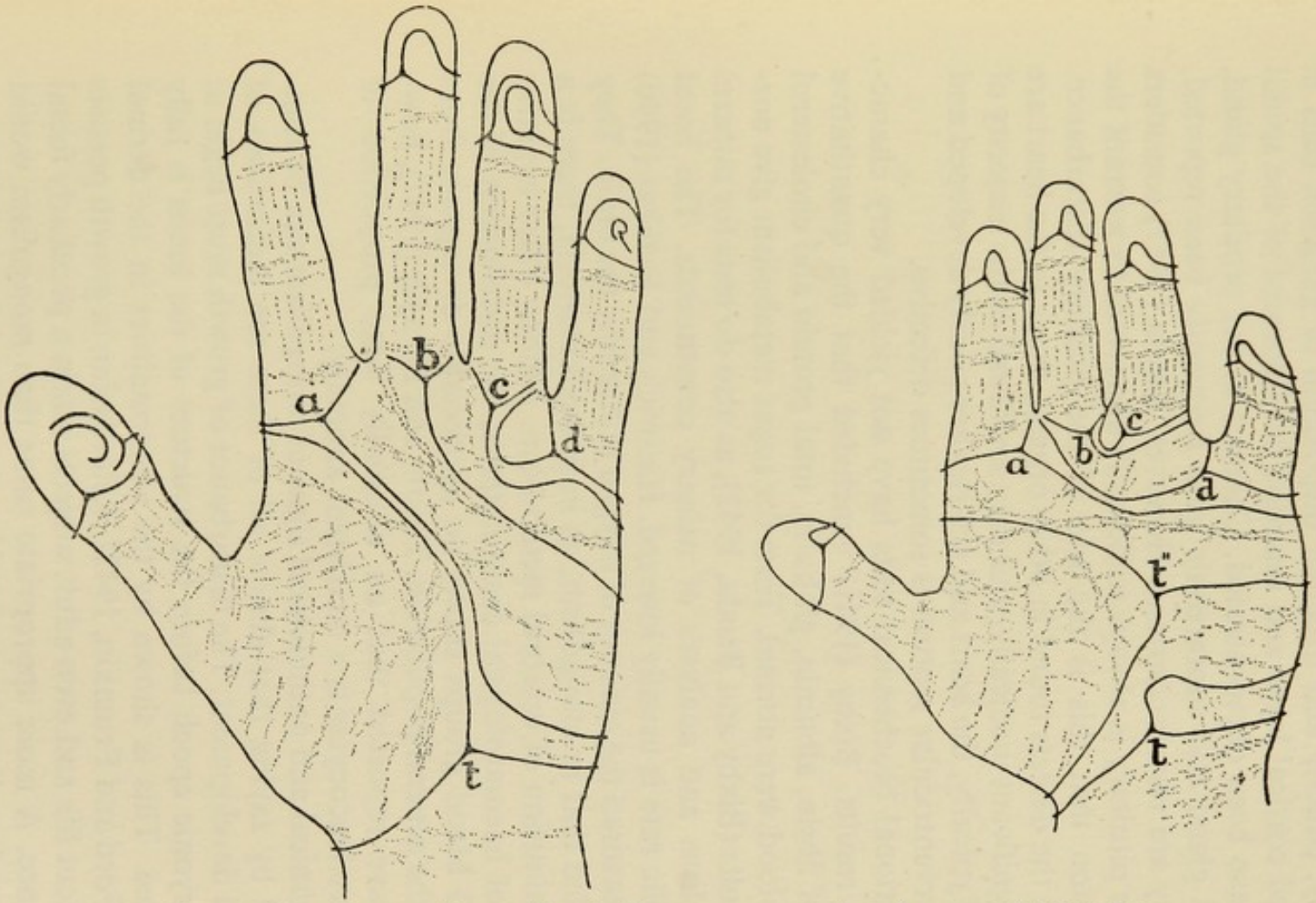


Figure 10.—Comparison of main lines on normal and mongoloid palms

Prints of the right hands of two adult males are represented. The interdigital triradii, *a*, *b*, *c*, and *d*, are the sources of the main lines of the dermal ridges.

Note the transversality of the mongoloid hand, the proximity of *b* and *c* and the reduplication of the axial triradius, *t*. The finger tip patterns are all loops on the mongoloid hand; there is also a continuous transverse palmar crease and one crease, instead of two, on the fifth digit.

constant morphological peculiarities other than a tendency towards embryonic convolutional patterns and a disproportionately small cerebellum and brain stem (Davidoff, 1928). Histologically, paucity and irregular disposition of ganglion cells in the third cortical layer and retarded development of the spinal cord have been demonstrated. Changes in the pituitary gland, thyroid gland and suprarenals have frequently been reported, but they are very inconstant. However, Benda (1947) considers that the pituitary is always sufficiently abnormal to warrant the conclusion that this is the site of the primary disturbance. Among the defects found in other organs, those in the heart are most significant medically, and they are found in the majority of cases. Typically, the heart and arteries are poorly developed and the interventricular septum is sometimes defective.

Functional biochemical tests have not yielded very characteristic results. Bixby (1941) concluded that the quantitative levels of fibrin, albumin, globulin, total protein and cholesterol in the blood were normal. Tests for sugar metabolism give normal results (Bixby and Benda, 1942), as also do tests for mineral metabolism and analyses of urinary constituents. The basal metabolic rate is usually lowered. Himwich and Fazekas (1940) have measured the amount of oxygen utilized by the brain. They concluded that in mongolism, as in phenylketonuria, there is a real diminution of cerebral metabolism. Among other negative results of haematological examinations, the distribution of the A, B, O blood groups shows no appreciable divergence from that in the general population. Turpin and Bernyer (1947), however, have reported that an unusually large proportion of immature leucocytes is a consistent anomaly.

The clinical and pathological signs of mongolism can be summarized by saying that almost all of them are indications of retarded development. The disturbance of growth must begin at an embryonic epoch before the structure of the limbs is fully completed. This is shown by the abnormalities in the dermal ridges (Ford and Frumkin, 1942). Retardation in growth persists throughout life and even adult subjects retain a peculiarly foetal appearance. A more appropriate name than mongolism would have been foetalism or, preferably, generalized foetal dysplasia. Since the individual signs are not specific to the condition but may occur, though less frequently, in other types of cases and

Plate VII—Mongolism in two imbecile brothers aged 10 (Colchester Survey, 1938, Case No. 750) and 5 years, with a normal child aged 2½ years.

As compared with the normal child, the younger mongoloid is seen to have a small head, decreased stature and dysplastic features. The characteristic fold of skin covering the inner canthus of each eye (epicanthic fold) was clearly marked in this case.

even in normal subjects, the diagnosis of mongolism is made by deliberately or unwittingly adding up the points in its favour. Taking only seven items—namely, (i) Binet I.Q. from 15 points to 29; (ii) cephalic index, 0·83 or higher; (iii) epicanthic fold over either eye; (iv) fissured tongue; (v) presence of blepharitis; (vi) transverse fold on either palm; (vii) single crease on either little finger—we can say that any patient with four or more of these characters is almost certainly a mongolian type of imbecile. The introduction into the list of more items and the application to them of individual weightings could be used for the construction of a diagnostic instrument of any desired degree of accuracy (see Plate VII).

AETIOLOGY OF MONGOLISM

In consequence of the high mortality rate of mongoloids at all ages—possibly as high as nine times the average—the incidence of the condition in the population diminishes in each successive age group. At birth, surveys have indicated that the incidence in populations of European origin is of the order of 1 in 700. Malpas (1937), as shown in Table XXXVIII, found 18 cases among 13,964 births, or 1 in 776, while Jenkins (1933) recorded 6 cases out of 3818 births in a Chicago maternity hospital, or 1 in 636. These estimates contrast with the survey made by Doxiades and Portius (1938), who ascertained 58 mongoloid defectives in a total general population of all ages of 415,431 in Germany, implying an incidence of 1 in 7000.

The incidence also varies with maternal age in a remarkable manner, as can be seen from the statistics given in Table XL and Figure 11. The numbers of cases in each maternal age group are taken from Beall and Stanton (1945). The control population is calculated on the basis of the distribution of births in census returns of the years corresponding to the birth dates of the mongoloid cases. The method thus makes allowance for the changing distribution of maternal ages in the general population in a way which was not possible in similar surveys of Jenkins (1933) and Bleyer (1938). Nevertheless, the results of all such analyses are substantially the same. The mean age of the mother at the birth of a mongol child averages about 37 years, compared with a mean age of 29 years for all births. The absolute incidence remains low, at a rate less than 1 per thousand births, until the

maternal age group 30 to 34 years is reached. After this, it begins to rise rapidly, attaining a figure between 2 and 3 per cent. in the quinquennium 45 to 49. Furthermore, Benda (1947) asserts that

TABLE XL

DISTRIBUTION OF MONGOLOID IMBECILES WITH RESPECT TO MATERNAL AGES AT THEIR BIRTHS

Maternal Age Group	Male Cases	Female Cases	Observed Total Number	Expected Total Number	Ratio of Observed to Expected	Absolute Incidence per 1000 Births
15–19	1	2	3	7·75	0·39	0·6
20–24	5	4	9	29·62	0·30	0·5
25–29	12	7	19	34·06	0·56	0·8
30–34	7	7	14	25·79	0·54	0·8
35–39	19	12	31	16·74	1·85	2·8
40–44	15	17	32	6·30	5·08	7·6
45–49	6	7	13	0·71	18·31	27·5
All Ages	65	56	121	120·97	1·00	1·5

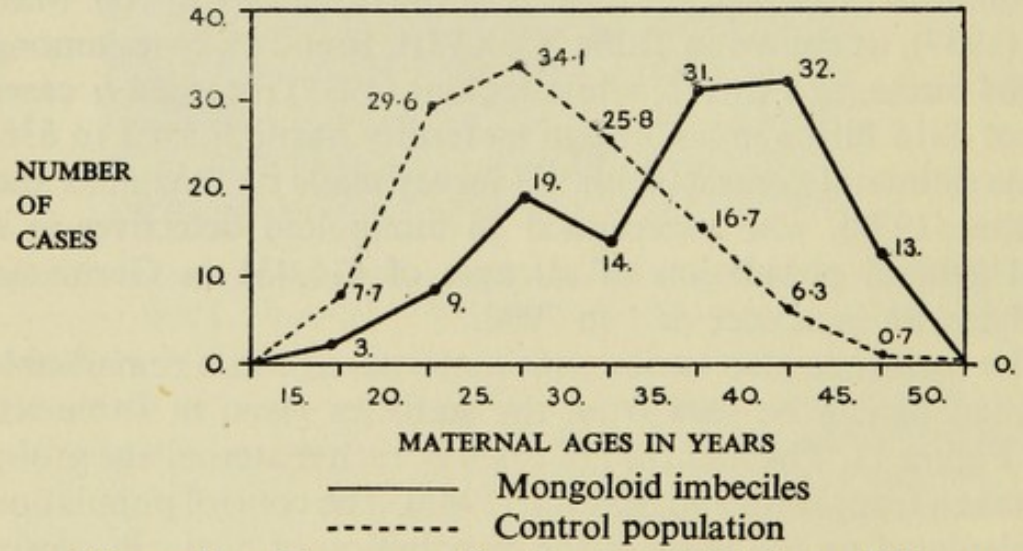


Figure 11.—Frequency distribution of births at different maternal ages

the maximum level of 10 per cent. may ultimately be reached at extremely advanced maternal ages.

Other variables associated with maternal age, like age of the father and order of birth, when taken by themselves also appear to be significantly related to the incidence of mongolism. However, the associations are not strong enough to exclude the possibility that they are only reflections of the maternal age effect.

With respect to the paternal age, the position can be cleared up by partial correlation. Thus, in 150 sibships containing at least one mongol each (Penrose, 1933), the correlation for maternal age and incidence of mongolism among the children, (r_{mi}) was +0·36, that for paternal age and mongolism (r_{fi}) was +0·29. Since the correlation between maternal and paternal ages (r_{mf}) was +0·83, the partial correlation between paternal age and mongolism for constant maternal age ($r_{fi.m}$) was $-0{\cdot}01 \pm 0{\cdot}04$, that is, as near to zero as could be wished. Hence it may be concluded that paternal age has no real effect.

The problem of the effect of birth order is more complicated, but it can be shown that, when the influence of maternal age is eliminated, any residual effect due to order of birth by itself is too small to be significant except in very extensive material (Penrose, 1934*b*).

The interval between the birth of the preceding child and that of the mongol has often been noticed to be longer than usual for sibs. Murphy (1947) considered that the births of malformed infants of all kinds, including mongols, tended to be preceded by a period of diminished fecundity, expressed either by a long non-pregnant interval or by a series of miscarriages. Conversely, Fantham (1925) attributed mongolism to too frequent pregnancies. Yerushalmy (1945), however, considers that, after allowing for the effect of maternal age, an increased stillbirth rate is associated with both relatively long and short intervals between pregnancies and possibly the same may be true for mongolism. Closely related to this question are the facts about fertility of the mothers of mongoloids. Jenkins (1933) believed that sibships containing mongol children had fewer members than average sibships. In the Colchester Survey, however, sibships, selected by the presence of at least one mongol, were larger than those selected by the presence of at least one defective of other type. There were also somewhat more deaths in early infancy in the mongol sibships though slightly fewer miscarriages were recorded, as shown in Table XLI. The incidence of defectives in the mongol sibships was very low, only 8 in 366 sibs and 4 of these were probably also mongols.

Maternal health during pregnancy has been carefully studied by many observers with a view to elucidating the cause of mongolism, without leading to any definite results. Premature

TABLE XLI

SIBS OF PATIENTS IN COLCHESTER SURVEY (1938)

Diagnosis	Mongolism		Other Types of Defect	
Number of patients	63		1,217	
Number of sibs of patients	366*		6,263†	
Number of sibs per patient:				
Normal intelligence:				
Superior	0·05	4·20	0·05	3·42
Average	4·02		2·79	
Dull	0·11		0·40	
Unascertained	0·02		0·18	
Mentally defective:				
Feeble-minded	0·03	0·12	0·22	0·35
Imbecile	0·06		0·09	
Idiot	0·03		0·04	
Miscarriages or stillbirths	0·54	1·49	0·72	1·37
Died in early infancy	0·95		0·65	
Total	5·81		5·14	

* Among these were 4 cases of mongolism.
† Among these were 7 cases of mongolism.

delivery or threatened abortion might be the effect, but could not be the cause, of a malformed foetus. Maternal endocrine disturbance in the early months has been often suspected, but the evidence is not convincing; Myers (1938), however, showed that the incidence of dysthyroidism was high in mothers of mongols. No consistent maternal abnormality has been found and it would have to be assumed that many different kinds of ill health were significant. The mechanism by which the mother's age changes her predisposition to have a malformed offspring is still quite obscure. Apart from the possibility of some peculiarity directly determined by ageing of the maternal tissues, in particular the endometrium, nutritional or endocrine disturbances have been blamed. Antigenic incompatibility might be significant, because immunity develops better in mature than in immature animals and the elderly mother might be prone to develop transient immune reactions against the embryo in its early developmental stages. On the whole, there seems to be no definite evidence of any maternal illness or disability characteristic of pregnancies terminating in the birth of a mongolian child.

Familial cases have been described in medical literature, and

indeed they are not so uncommon as some observers (Goddard, 1914) have supposed. Sibships containing four cases have been reported by Babonneix and Villette (1916) and by Péhu and Gaté (1937), and instances of three cases in one sibship have been reported by Fantham (1925), van der Scheer (1919) and Benda (1947). Pairs of affected sibs occur about once for every hundred single cases collected at random and some of them receive mention in the medical journals from time to time. Examples of uncle and niece, aunt and nephew, as well as first-cousin pairs can be found when large enough surveys are attempted, as well as pairs of cases interrelated in other ways (Doxiades and Portius, 1938; Lahdensuu, 1937 and Hanhart, 1944). With such a common condition it is difficult to produce convincing evidence that the familial cases are due to familial concentration and not to chance sampling. Moreover, in some of the familial instances the diagnoses are open to doubt (Fantham, Babonneix and Villette). Furthermore, the occurrence of more than one case in a sibship might not be genetical but due to a consistent peculiarity of maternal environment.

There does not appear to be any anomaly in the sex distribution that would suggest the action of fully or partially sex-linked genes. Parental consanguinity is rarely found and has never been reported in a family with two or more affected sibs; this fact argues against recessive inheritance. A recessive gene might act differently and cause an unaffected mother to have abnormal offspring (see page 78). A dominant gene whose manifestation was determined by intrauterine environment is a plausible explanation. An unbalanced chromosome configuration could also give rise to a similar effect in pedigrees. In either case, the very low observed familial incidence remains to be accounted for. About half the normal sibs of mongols, though normal, might be assumed to be susceptible and could have been affected if suitable pathogenic factors, such as those connected with maternal age, had been present. Otherwise a great number of embryos must fail to develop. The noticeable miscarriage rate in sibships containing mongoloid imbeciles is not abnormally high, so that the sibs which failed to develop fully must be assumed to die at a very early stage.

The analogy with otocephaly in guinea pigs might be considered for another type of explanation. There is some evidence,

though not of a very conclusive nature, that certain peculiarities, like transverse palmar line, fissured tongue or immature leucocytes, occur more frequently among near relatives than in the general population (Turpin, Bernyer and Teissier, 1947). Possessors of such traits might be abortive cases of mongolism.

The fact that in all but two instances (MacKaye, 1936; Jervis, 1943) twins, selected by one of them being a mongoloid imbecile have always been found to be either monovular and both affected or fraternal and only one affected, is held to be additional evidence of hereditary influence in the condition. Nevertheless, at the present time the mode of action of the hereditary background is obscure and is much less important, from the point of view of preventive treatment, than the environmental factors dependent upon maternal conditions.

FOETAL INFECTIONS

The passage of pathogenic organisms from the mother to the foetus, though fortunately not of common occurrence, has been recognized as an established fact for more than two centuries. Düttel (1702) was able to gather together the evidence for transmission of smallpox (variola) to the foetus because of the striking effects produced by the eruption on the foetal skin. Sometimes the mother is immune and shows no sign of the disease and yet she is able to transmit it. A considerable list can be compiled of other infectious diseases, which have been known for a long time to be transmissible to the foetus. Ballantyne (1902) reported instances in which varicella, scarlet fever, measles, erysipelas and typhoid fever behaved in this way. Foetal anthrax and tuberculosis are also known. Most important in the study of mental deficiency are the diseases which specifically cause cerebral infection. Epidemic cerebrospinal meningitis and equine encephalomyelitis (Medovy, 1943) have been diagnosed in exceptional cases. In some instances, as for example that described by Roback and Kahler (1941), the foetus is found to have suffered from encephalitis though the causative organism cannot be ascertained with certainty. Though in most cases of cerebral infection the foetus dies *in utero*, a few may survive, and, if so, idiocy will be a probable result.

Protozoal parasites can also pass through the placental barrier. Prenatal malarial infection is known and also maternal

transmission of toxoplasmosis. The toxoplasma organism thrives on young growing tissues and an infected infant may harbour the parasite for some years. During this time, widespread destruction of the nervous system, including the retina, takes place with the formation of cysts and scars, which become calcified; profound idiocy follows. Fortunately, this condition is extremely rare; a case has been reported in England by Jacoby and Sagorin (1948). The disease is of great theoretical interest as it demonstrates incontestably that an infection transmitted through the mother to the foetus can cause idiocy.

In recent years attention has been drawn to the harmful effects of maternal rubella in the early months of pregnancy. In an Australian epidemic described by Gregg (1941), several mothers were affected and those who caught the disease during the first few months of pregnancy gave birth to defective infants. The children showed a variety of abnormalities, including deafness, blindness due to cataract or retinitis, heart malformation and mental retardation. Since that time physicians have been on the alert to discover similar cases and a great many have been reported. An appreciable proportion of deaf-mutes have mothers who give histories of rubella during pregnancy. By no means every case of maternal rubella produces foetal malformation. The harmful result depends upon the severity of the disease and the period of pregnancy in which the infection occurs, as well as upon unknown factors. In an extensive Swedish survey of over 20,000 pregnancies, by Grönvall and Selander (1948), maternal rubella was reported in 28 cases, 2 of which ended in abortion, 25 resulted in healthy infants and only 1 child was malformed. Nevertheless, taking all acute virus diseases together, these were found to have occurred ten times as frequently among mothers of malformed infants as in the whole sample. Maternal mumps had the worst record, with 5 malformed infants and 1 abortion out of 34 cases, and poliomyelitis came next. Evidently there are many problems yet to be solved in this field. Possibly most infants are naturally resistant to these diseases but others are susceptible. Addair and Snyder (1942) have brought forward some evidence which suggests that a recessive gene may cause increased susceptibility to poliomyelitis in children. Some of the differences in foetal resistance to infections may similarly be of genetical origin.

CONGENITAL SYPHILIS

The best known and the commonest type of intrauterine infectious disease associated with mental defect is congenital syphilis. The frequency of syphilitic defectives has long been a disputed point. The uncertainty is partly due to the diagnostic unreliability of serological reactions, like the Wassermann and Kahn tests, in congenital syphilis, except in cases with very pronounced lesions. Also the variety in the characteristic clinical signs is large and some of them, like interstitial keratitis, are late in appearance. Surveys of institutional defectives to ascertain the incidence of congenital syphilis, based only upon serological tests, have given extremely varied results. Among the larger groups reported, Thomsen (1911) obtained only 31 positive reactions among 2051 unselected defectives, i.e. 1·5 per cent., and Weiss and Izgur (1924) found 41 positive in a group of 1633 cases, i.e. 2·5 per cent., whereas G. F. Cobb (1931)* obtained 129 positives among 1275 cases, or 10·1 per cent. Some of the tests in general use occasionally give falsely positive results and genuine cases, in which congenital syphilis has been present but has become arrested, can be serologically negative. In the Colchester Survey (1938), congenital syphilis was diagnosed in 51 out of the 1280 cases and 41 of them had consistently positive blood Wassermann reactions. In the remaining 10 cases, some physical signs, highly characteristic for diagnosis, were present. Benda (1940) diagnosed congenital syphilis in 80 out of 2000 patients at Wrentham State School, Massachusetts, and 54 of 76 tested cases had positive serology. The rest were diagnosed on clinical signs and history. The signs in the eyes, on which stress has been laid, are interstitial keratitis, chorioiditis, scleritis and pupil anomalies. Nerve lesions are exemplified by eighth-nerve deafness, paralysis and hyperactive reflexes. Other physical peculiarities include notched teeth, bossed skull, scars on the lips or nose and poor general physique with anaemia and wasting. In Stewart's (1930) survey of 190 defectives with congenital syphilis, 84 per cent. had positive blood Wassermann reactions. These were all cases of "late" congenital syphilis, as opposed to the early or acute fatal type of the disease, and the clinical signs were very numerous and variable.

* Personal communication.

The question as to how far syphilis can be counted a true cause of mental defect affords much opportunity for discussion. Most authorities agree with the view, expressed by Benda (1940), that, in certain cases, severe mental defect is caused by gross cerebral lesions. The syphilitic origin of the mental degeneration in juvenile paresis is scarcely open to doubt. But if a mongol has congenital syphilis, as was the case in one of the Colchester patients, the infection must be considered as incidental.

The responsibility of syphilis is difficult to estimate in cases where the mental defect is of a mild type and stationary. Congenital syphilitic infection can sometimes be considered a part cause of certifiability. In the Colchester Survey, 50 patients with congenital syphilis (excluding the mongol) had an average intelligence quotient of $42{\cdot}7 \pm 19{\cdot}8$, not significantly different from the general average for all patients, 40·4. The parents and sibs of the syphilitic cases were no less intelligent than the average for the whole sample of institutional cases. Syphilitic disease, however, can lower I.Q. by several points; for example, from 50 to 20 in an affected monovular twin (Penrose, 1937). Nevertheless, blindness, deafness or other disabilities in these subjects were contributory causes favouring their certification and also, sometimes, supposed or actual immorality.

PRENATAL CEREBRAL INJURY

Mechanical injury to the foetus, before birth, has been postulated by some writers as a cause of malformation or cerebral haemorrhage but, in the absence of more evidence, such views must be treated with scepticism. Jansen (1932) attributed deformities, which had their origins in the very early months of pregnancy, to pressure due to abnormal smallness of the sac containing the amniotic fluid. Increased pressure could cause stagnation of the blood in the developing bones and lead to all kinds of osseous malformations. Van der Scheer (1927) transferred the same explanation to mongolism. The traditional theory that skeletal and other deformities can be caused by amniotic bands is subject to the same uncertainties as that of Jansen. Even if amniotic peculiarities are considered to be specific causes, we are no nearer to an understanding of the nature of the pathological process until it is known why the structure of the amniotic sac should be anomalous.

Another kind of intrauterine injury has been postulated, by Schreiber (1939), in which the pathological effects on the foetus are thought to be due to chronic anoxia. Continuous anoxia, in cases of maternal mitral stenosis or frequent maternal convulsions, is credited with causing degenerative changes in the foetal nervous system in the late months of pregnancy. The type of lesion supposed to be produced in this way is a diplegia. Somewhat similar views have been put forward from time to time as to the possible dangers to the child of prolonged labour, during which the supply of oxygen to the brain may be reduced to a low level by compression of the cord or by other mechanical processes. These dangers are particularly great in cases of premature delivery. Premature infants, according to MacGregor (1943), are particularly liable to asphyxia, which may lead to subarachnoid and interventricular cerebral haemorrhage.

A type of cerebral injury, the existence of which has been well established for many years, is that due to severe haemolytic disease in the foetus. The products of the destruction of red blood cells are extremely toxic to the foetus (Hampson, 1929) and are apparently absorbed strongly by nerve cells in the basal cerebral ganglia, causing these cells to degenerate. Although the disease starts during the later months of pregnancy and the affected child may be born jaundiced, it is unusual for the most marked effects to be noticeable until a few days after birth. Some cases of severe neonatal jaundice (icterus gravis neonatorum) recover and many die. A few partially recover and carry residual signs, but complete recovery also occurs. Among the possible permanent effects are spastic paralysis of the limbs with athetosis and mental retardation. The degree of mental defect varies from very slight retardation to imbecility. Wiener and Peters (1940) showed that in many cases severe neonatal jaundice was due to maternal sensitization by foetal red cells, which contained an incompatible Rh antigen inherited from the father. Other antigens of the Rh series can, on occasion, cause haemolytic disease, and, very rarely, antigens of other kinds, such as those at the A, B, O locus. Fortunately, however, only about 1 child in 20 which is constitutionally incompatible with its mother in respect of the most dangerous antigen, the D of the Rh group, suffers from haemolytic disease (Race, 1946). Again, only a very small proportion of affected children develop mental symptoms in consequence.

The discovery of the significance of maternal-foetal incompatibility is of great biological interest. As shown by Haldane (1942), natural selection acts in these cases against heterozygous individuals in a peculiar manner. The equilibrium of many such antigenic genes can be unstable and circumstances can arise in which elimination of the relatively unfit heterozygotes actually causes an increase in the prevalence of the genes which produce the dangerous antigen. This is a most paradoxical result from the point of view of traditional ideas about evolution.

BIRTH TRAUMA

During birth itself there are, indeed, many opportunities for cerebral injury of a very definite nature. However, in order to prove conclusively that a child has become mentally defective in consequence of injury at its birth, we should need evidence of its mental normality before birth, and this cannot be obtained. Jenkins and Glickman (1934) found that the I.Q. of one identical twin, whom they supposed to be birth-injured, was only 15 points lower than that of the uninjured sib. There is, nevertheless, a good deal of indirect evidence that birth trauma is the decisive factor in a limited number of mentally defective cases; they probably do not exceed 1 per cent. of patients of all types. The points in favour of this diagnosis are asymmetrical neurological signs, which can be interpreted as due to cerebral injury, coupled with a history of abnormal or protracted birth. Asymmetrical spastic lesions can also be due to other causes, but symmetrical lesions are rarely due to mechanical injury. See also pages 88 and 152.

Delivery as a breech, or in the persistent occipito-posterior position, is a likely situation to cause intracranial haemorrhage by over-stretching and consequent tearing of cerebral vessels. A typical injury is tearing of the tentorium of the cerebellum, which leads to subdural haemorrhage. This is more liable to happen with infants born at full term than with premature infants and it is likely to occur in difficult forceps deliveries. Prematurity is an important predisposing cause for other types of vascular injury because, in a premature infant, structures are more fragile than in a mature infant and more easily damaged, either by congestion or by direct pressure. Brander (1938) found

that premature infants were, on the whole, less intelligent than the average. In a survey of 376 school-children in Finland, whose records showed that they had been prematurely born, 11·2 per cent. were rated defective on the basis of I.Q. 70 or less. Within the group there was a correspondence between birth weight and intelligence. Thus some of the mental inferiority of premature children can reasonably be attributed to the special dangers they encounter at birth.

A history of difficult labour needs to be very carefully weighed because the difficulties are rightly emphasized, in obstetrical practice, from the maternal rather than from the foetal point of view. Ehrenfest (1931) pointed out that most children, even after normal birth, show slight signs of intracranial injury. If there has been serious injury, nystagmus, retinal haemorrhage, pallor, inability to make sucking movements and feeble cry may be noticed immediately. Respiratory disturbance and a tense fontanelle are definite signs of intracranial haemorrhage (Munro, 1930). In normal circumstances the slight signs rapidly disappear. When they persist and the child survives, paralysis may soon be evident. There is no constant relationship between the severity of the residual physical disability and the amount of mental retardation. In the Colchester Survey, the cases with neurological signs of birth injury were scattered over all the intelligence levels. Dayton (1930) found no correlation between mental grade and abnormal labour among defectives.

Birth injury is more likely to occur at a mother's first delivery than in later deliveries. Munro (1930) found that 63 out of 117 cases (54 per cent.) of intracranial birth injury were the results of first pregnancies. McGovern and Yannet (1947) reported 12 cases of asymmetrical spastic cerebral palsy in infants with histories of birth trauma, and of these 9 were first births. Six out of 11 cases, in the Colchester Survey, whose mental defect was attributed to birth injury were first births. In urban societies, however, where families are usually small, proportions of first born above 50 per cent. are not always significantly high. The effect of primogeniture is more striking in a sibship where the birth-injured first child is followed by a succession of normal infants delivered normally. Normal intelligence in the parents and in all other sibs are also points in favour of the diagnosis of the traumatic origin of mental defect in a patient.

POSTNATAL INJURY AND DISEASE

A great variety of accidents are capable of diminishing intelligence in early postnatal life but they are all of very infrequent occurrence. Direct injury to the brain, caused by falls or other accident to an infant, is a very rare cause of mental defect—an even rarer cause than birth trauma—but nevertheless a real one. In some patients the neurological signs are slight and behaviour disorder can be the most noticeable sequel. The history of the case, coupled with the most careful neurological examination, must be the source of information on which diagnosis is based. Hemiplegia is a likely finding (Holden and le Marquand, 1929). The mental level is not usually grossly diminished in postnatal traumatic cases.

More serious, and somewhat more numerous, are cases due to infectious disease in infancy. Acute meningoencephalitis has been known to follow vaccination (Coyle and Hurst, 1929) as an extremely unusual complication. More often encephalitis occurs quite sporadically and it can lead to mental defect, though most affected children who recover do not suffer noticeable retardation (Brain, Hunter and Turnbull, 1929). Cerebrospinal meningitis, encephalitis lethargica and encephalitis complicating acute infectious diseases, such as measles and scarlet fever, have been known to produce mental deterioration as after-effects. By the time patients are brought to the notice of the mental deficiency expert, the acute illness has long been over, usually many years ago. It is then extremely difficult to trace the exact history of the mental deterioration and to relate it precisely to the disease to which it has been attributed. Until records are obtainable of routine mental tests taken before and at intervals after such illnesses, the precise effects on intellect will remain doubtful. Here again, as in the case of injury, the neurological signs are the most significant points for diagnostic purposes. Irregular lesions of the basal ganglia rather than defects of the pyramidal tracts are likely to follow cerebral infections in childhood.

CHAPTER XI

MENTAL DISORDERS

General Principles—Epilepsy—Symptomatic Epilepsy—Electroencephalography—Idiopathic Epilepsy—Psychoneurosis—Psychopathic Personality—Moral Deficiency—Mental Defect and Crime—Administrative Relationship between Crime and Defect—Affective Psychosis—Schizophrenia—Organic Psychosis: Juvenile General Paresis—Organic Psychosis: Encephalitis Lethargica.

GENERAL PRINCIPLES

It is convenient to distinguish between mental disorder or illness and mental defect. Failure to make this distinction has caused much confusion in the past. In order to make the maximal use of the distinction, disorder and defect must be considered as two dimensions of variation. Thus, theoretically, a person of any level of intellectual capacity can suffer from any degree of mental illness. The susceptibility to disorder may indeed be correlated with intelligence level, in that certain kinds of defect may predispose to epilepsy or psychosis. In epiloia, for instance, mental disorder is part of the symptom complex. Conversely, mental illness, as the primary condition, may contribute to a lowering of intellectual capacity; for example, Dawson and Conn (1931) found that the mean I.Q. of 49 epileptic children, attending the Royal Hospital for Sick Children in Glasgow, was only 80·6. In order to be logical, we should always attempt to assess what the intellectual level would have been in the absence of the disorder.

It may be doubted if mental illness, whether in the form of epilepsy, neurosis or psychosis, should be regarded as a true cause of intellectual defect, but it is quite certain that mental illness is a very important contributory factor in the selection of cases for certification or for institutional treatment. As shown in Chapter III, the high-grade cases seen in institutions are only a very small sample of all those of comparable ability in the general population. They require care and control because

they are out of harmony with their social environments, and often this is due to a mentally disordered state. Hence, to infer that poor intellectual capacity naturally leads to mental disorder, on the basis of institutional observations, would be manifestly incorrect. In the interests of exact inquiry into causation, the polymorphic theory that all kinds of mental abnormalities are evidence of a basic neuropathic diathesis must be rejected.

EPILEPSY

The mental disorder most characteristic of defectives is some form of epileptic seizure. There is a wide range of symptoms that come under this heading, and infantile convulsions are included as well as major and minor fits and other variants. Convulsions in early infancy can occur in a great variety of conditions, some of them are intercurrent, like tetany due to nutritional deficiency, and they are not necessarily indications of abnormal cerebral development. A history of convulsions, however, is frequently obtained for children who, later on, show definite signs of epilepsy or develop into cases of mental defect. Convulsions repeated over a period of weeks or months in early life and petit mal attacks in the first two years are more likely to be followed by chronic disorder than isolated attacks (Thom, 1942).

SYMPTOMATIC EPILEPSY

There are two ways of regarding spontaneous epileptic attacks. They can be looked upon as symptoms of underlying cerebral malformation and disease or even of temporary physical and chemical disturbances which interfere with the normal nervous rhythms. This view was supported by Wilson (1929), who protested against the tendency of neurologists to ascribe a sinister prognosis to every case of epilepsy on the grounds that it was in itself an incurable disease.

The symptomatic kind of epileptic attack is seen in such a condition as epiloia, where brain tumours are part of the syndrome. Fits also occur in amaurotic idiocy and other progressive degenerative diseases. In comparatively stationary conditions, like phenylketonuria and cerebral diplegia, epileptic attacks may occur in infancy or early life, but tend to become

much less frequent as age advances. Almost any gross disturbance of cerebral functioning can be accompanied by epileptic manifestations, and, consequently, an association between the severity of mental defect and incidence of fits can be demonstrated.

In the United States and in Canada, where there are separate hospitals for epileptics, defectives who have prominent epileptic symptoms can, for administrative convenience, be treated primarily as epileptics rather than as defectives. In England this procedure is not adopted, and it was possible in the Colchester Survey to compare in the same institution the proportion of

TABLE XLII

INCIDENCE OF EPILEPSY AMONG PATIENTS OF SPECIFIED CLINICAL TYPES

Type	Number of Cases	Number Epileptic			Percentage Epileptic
		Certain	Doubtful	Total	
Mongolism	63	0	1	1	1·6
Endocrine disorder	88	3	10	13	14·8
Congenital syphilis	50	3	11	14	28·0
Neurological lesion	128	36	23	59	46·1
Skeletal malformation	142	20	14	34	23·9
Miscellaneous abnormalities	87	12	10	22	25·3
Others: Idiopathic epilepsy	210	119	91	210	29·1
Others: Non-epileptic mental disorder	204	—	—	—	29·1
Others: Residual group	308	—	—	—	29·1
All patients	1280	193	160	353	27·6

epileptic cases in given categories with one another. Those cases which had quite definite symptoms were classified under the heading of certain epilepsy and those who had merely a history of convulsions or who had seizures of obscure types, such as vasovagal attacks, were classified as doubtful. The results are shown in Table XLII, in which the incidence of epilepsy in cases of different pathological types is set out. Nearly half the cases with neurological lesions had fits of some kind, as did nearly one-quarter of those with abnormalities of the skeleton, including the cranial malformations, microcephaly, hydrocephaly and acrocephaly. With respect to mental grade, most surveys have shown, as might be expected, that epilepsy is a

more frequent symptom among low-grade defectives than among the higher grades. Waggoner and Sheps (1944), however, found no relationship to intelligence level among defectives.

ELECTROENCEPHALOGRAPHY

The new technique of electroencephalography has developed out of Berger's (1929) discovery that the quiescent brain normally produces rhythmical electrical discharges which can be measured. The use of this technique has enabled Gibbs and Lennox (1938) to demonstrate that, in cases subject to petit mal, or minor attacks, which do not lead to generalized convulsions, the normal cerebral rhythm is disturbed. A combination of a slow wave and a "spike" recurring about three times per second is the characteristic feature. Forced breathing, which artificially lowers the threshold for epileptic attacks, may induce dysrhythmia more readily in epileptic than in non-epileptic subjects. However, in patients subject to major seizures only, it is often very difficult to detect any dysrhythmia by such methods.

Kreezer (1939) made investigations of cerebral rhythms in several types of defectives and observed abnormally slow occipital "alpha" rhythms in some low-grade cases. No very characteristic pictures were obtained in mongols and phenylketonurics, for example; the abnormal alpha rhythms were found among low-grade cases and they were attributed to immature cerebral organization. It is very difficult to obtain satisfactory results with this technique unless the patient is fully co-operative. This means that mentally defective cases available for encephalographic study are limited in number. The chief importance of such investigations probably lies in detecting potential epileptics among the higher-grade cases. Some psychopathic patients certified on account of behaviour disorders may prove on examination to be subject to subclinical petit mal attacks.

IDIOPATHIC EPILEPSY

Epilepsy in the majority of subjects, whether they are of normal or subnormal intelligence, is not classified as symptomatic. The term "idiopathic" has been used in medicine for these cases, in which the cause is largely unknown. There seems to be an inborn tendency to dysrhythmic cerebral activity

coupled with absence of any detectable structural abnormality. In a person, who is liable to convulsions of the major type or to the slighter minor epilepsy and who does not suffer from any known physical disease, the epilepsy itself has to be regarded as a primary condition. Idiopathic epilepsy is found in about 1 to 2 per thousand among the general population of school-children (Henderson, 1948). Some estimates are higher than this and there is difficulty in deciding exactly what constitutes the diagnosis. Lennox, Gibbs and Gibbs (1940) found that a very large proportion, e.g. some 10 per cent., of normal subjects showed occasional abnormalities on electroencephalographic examination. They also found that an even greater proportion, about 60 per cent., of the relatives of known epileptics had abnormal rhythms. That the cerebral dysrhythmia is in some way inborn, or part of the somatic constitution, is hardly to be doubted, but its relationship to actual epilepsy is far from clear.

The psychology of epileptics, apart from the fits, is an important study. Stoddart (1926) considered that idiopathic epilepsy is best regarded as a symptom of a special kind of mental disorder which sometimes amounts to psychosis. The main peculiarities are to be found in the personality and in behaviour reactions. For example, Freeman (1935) reported a pair of monovular female twins only one of whom had epileptic attacks though both had unusually egocentric dispositions. The epileptic subject is liable to be unusually emotional, but also shallow and sentimental. Ideas are stereotyped; narrowness of outlook, self-pity and childish desire for affection and attention are coupled with irritability and liability to outbursts of anger and violence. In the intervals between attacks, epileptics can behave very sensibly. It is sometimes hard to believe that a patient who seems so well at one time may quite suddenly, before, after or in substitution of an epileptic attack, become so disturbed as to be dangerous to others.

Should an epileptic subject have the additional misfortune of being scholastically retarded, the double handicap can be sufficient to lower social efficiency to the level of certifiable mental defect. Thus there is a large class of cases of idiopathic epileptics who require care and control, either as defectives or epileptics, according to the prevailing type of administration.

In Table XLIII the grades of 210 patients of this kind are shown and compared with the grades in an institutional population of 1280; the incidence was 16·4 per cent. Males were rather more frequently represented than females. Idiopathic epileptics were distributed over all grades fairly evenly and their mean I.Q. was 41·2±22·4 (Appendix 8).

The influence of epilepsy on intellectual level is not clearly understood. Although many subjects are subnormal, the disability is not inconsistent with normal or even exceptional ability. Famous epileptics, like Dostoievsky and van Gogh,

TABLE XLIII

DISTRIBUTION OF CASES WHOSE MAIN SYMPTOMS WERE THOSE OF MENTAL DISORDER, (Colchester Survey, 1938)

Diagnosis of Mental Disorder	Mental Grade				Total
	Dull	Feeble-minded	Imbecile	Idiot	
Idiopathic epilepsy . . .	30	57	81	42	210
Psychoneurosis and perversion	56	53	20	3	132
Affective psychosis . . .	4	17	3	0	24
Schizophrenia	8	11	16	13	48
Total mentally disordered .	98	138	120	58	414
Total population of patients examined	179	448	433	220	1280

have made splendid contributions to human culture. It is sometimes believed that intellectual deterioration is a common consequence of epileptic attacks, but there is little direct evidence of this. There remains the danger that drugs, such as bromides and barbiturates, administered in order to control the fits may themselves stultify the intellectual processes. A recent remedy, sodium dilantin, though it has disagreeable effects, like thickening of the gums, appears to be less inhibiting than the barbiturates to the intellectual functions. A few epileptics do show gradual loss of intelligence, but these are cases in which there is either a progressive organic disease or a marked degree of psychosis. In a survey of 85 institutional epileptic defectives over a period of 10 years, Falk and others (1945) were unable to demonstrate any consistent fall in I.Q., except in the case of three patients who were psychotic as well as defective.

The conditions grouped under the heading of idiopathic epilepsy are not homogeneous. In the first place, there are widely different degrees of severity and frequency of attacks in different subjects. This fact puts genetical investigations on very uncertain ground. A recessive condition has been described by Lundborg (1903), known as myoclonus epilepsy because of muscular twitchings which occur even in the absence of fits. The disease is not characteristically associated with mental debility. Many investigations have been carried out with a view to establishing the existence of some degree of familial concentration in respect to epilepsy. Among the most extensive studies are that of Conrad (1935) and those of Rosanoff and others (1934) on twins. In the Colchester Survey, 6 patients among the 210 idiopathic epileptics had first-cousin parents, a proportion high enough for suspicion of recessive determination to be reasonably entertained. When idiopathic epileptics are taken together as a group, their relatives do not show a high incidence of the same condition. For example, the incidence of epilepsy in relatives of the same group of 210 was one-and-a-half times as high as the incidence in relatives of patients otherwise classified. The excess was statistically significant, in view of the large numbers involved, but not very striking in practice.

We might assume that there are genes which lower the threshold to stimuli normally insufficient to cause seizures. The genes might act by making slight structural or chemical changes in the nervous system which predisposed to dysrhythmia. To some extent the whole question is a matter of degree because strong enough stimuli, such as electric currents passed through the cerebrum, will produce a convulsion in anyone. There are well established examples of inherited predispositions to spontaneous or induced fits in rodents. One of the best instances is the spontaneous convulsions which occur in Viennese white rabbits. The peculiarity has been shown by Nachtsheim (1939) to be due to a single recessive gene.

PSYCHONEUROSIS

The relatively mild, though often very chronic types of mental disorder, such as obsessional neurosis, anxiety states and hysteria, probably occur just as frequently in defectives as in the population at large. The psychoneuroses differ from the

psychoses in that they respond well to psychological treatment, whereas the psychoses do not. Psychoneurotic disabilities add to the complications of institutional supervision of defective patients of all grades and types, and, from time to time, they are part causes of these patients' certification. Neurosis can hardly be credited with being a cause of intellectual defect and, in contrast to epilepsy, it is not a natural consequence of disease of the central nervous system. Its importance in the present connection lies in the likelihood that a neurotic child may not do himself justice in a test of intelligence and may thereby be wrongly rated. A competent psychometrician will be on the alert to detect an anxiety state which interferes with test performance. Part of his work is to allay such anxiety and to obtain the patient's confidence before making a report on the intelligence level.

The relationship of psychoneurosis to the more serious forms of behaviour disorder, which lead to social incompetence, is not a simple one. Some cases, where theft, violence or arson may be due to underlying obsessions or phobias, are susceptible to psychotherapy. When children, whose intellects are subnormal, commit neurotic misdemeanours they are more likely to be found out than children of greater ability. They are easily led by more skilful malefactors and are sometimes suggestible enough to be made to perform the parts of scapegoats.

Thus neurotic states are among the factors which contribute to the certification of cases of antisocial behaviour disorder, who swell the numbers of high-grade defectives in institutions and account for at least 10 per cent. of all admissions. The distribution, with respect to mental grade, of all cases in the Colchester Survey whose main symptoms were of mental disorder is shown in Table XLIII. In the absence of mental disorder, these cases would all have been diagnosed aclinical or residual. The concentration of neurotics among the higher-grade cases is noteworthy and, in these patients, neurosis was the main reason for certification.

Closely allied to the psychoneuroses are the sexual perversions, which include aberrations ranging from indecent exposure to homosexuality. These occur with considerable frequency among defectives, as indeed they do also in every section of the population. Their apparent prevalence among defectives may

be due simply to failure of concealment. Bestiality is a charge which sometimes precedes certification for mental defect, but little is known about its prevalence generally. The fact that sexual irregularity, like promiscuity and incest, occurs not very uncommonly in the families of defectives may indicate that the patients concerned are drawn from social strata in which the canons of behaviour are less restrictive than in the general population. From the biological point of view, this relative lack of sexual inhibition may be connected with the high fertility believed to be possessed by the subnormally intelligent. If so, it should be looked upon perhaps as part of the normal biological equilibrium rather than as evidence of moral depravity.

The genetics of the psychoneuroses have been but little studied, partly on account of the elusive nature of the facts and partly because marked changes in psychological reactions can be produced by environment. Brown (1942) analysed records of relatives of neurotic patients and Slater (1943) compared family histories of men referred for psychological symptoms in the army with a control group. Pollock, Malzberg and Fuller (1939) made an extensive study of the familial incidence of all kinds of mental disorders, including the psychoneuroses. The outcome of all these enquiries has been to demonstrate some degree of familial concentration of neurotic traits, but the significance of this concentration is not necessarily genetical. Moreover, there is no indication of any pleiotropic genetical association between neurosis and intellectual defect. The view held by Lang (1940) that homosexual perversion is due to genetical sex-reversal, i.e. that there exists a gene which turns females into males, is interesting but as yet supported by insufficient evidence; Darke's (1948) study of 100 male homosexuals gave no encouragement to this theory.

PSYCHOPATHIC PERSONALITY

There are certain types of mental disorder characterized by antisocial behaviour, not amounting to insanity as generally understood, which do not respond readily to psychotherapy. These are often classed under the broad heading of psychopathic personality, a diagnosis which has been interpreted in a variety of different ways (Curran and Mallinson, 1944). The name implies that the antisocial patient is recognized to be

mentally ill and should be treated as a medical problem rather than a case for retributive punishment. People with psychopathic personalities are by no means always intellectually retarded. Excellent descriptive case-histories have been given by Burt (1925). Repeated antisocial acts can sometimes be interpreted as evidence of profound mental disorder of a schizophrenic variety, as part of an epileptic psychosis or of organic disease, such as encephalitis lethargica.

Psychiatrists are often in doubt as to the correct description of a given disorder and there is a natural tendency to make an inclusive category for the residual clinical material. Patients diagnosed as having psychopathic personality undoubtedly form a heterogeneous group. They include pathological liars, thieves, sex perverts, drug addicts, and so on. The common factor which they share with one another, of relative immunity to social influence and refusal to learn by experience, points to the conclusion that these patients are more closely allied to psychotics than to neurotics. In an institution their training is a long and arduous process with prospects of repeated disappointments for those under whose care they are placed. It is however, well to note that punishment has no beneficial effect and is likely to be harmful. As Alexander and Staub (1929) have shown, antisocial acts can arise from a deep unresolved feeling of guilt, which punishment may actually tend to fortify.

MORAL DEFICIENCY

It was largely with a view to the control of cases of psychopathic personality, combined with mild intellectual defect, that the British Mental Deficiency Acts included the category of "moral deficiency". Such persons were defined, in 1927, as those "in whose case there exists mental defectiveness coupled with strongly vicious or criminal propensities, and who require care, supervision and control for the protection of others". At the present time this category is generally admitted to be of administrative use only and, even for this, its value is slight.

The historical origin of the concept of moral defect was the belief, widely held in the latter part of the nineteenth century, that criminals represented a variant of humanity degenerate morally, intellectually and physically. The protagonists of this theory, whose work under the name of "criminal anthropology"

has been summarized by Havelock Ellis (1890), exerted an influence, even in 1913, upon the experts who drafted the Mental Deficiency Acts. Anatomists such as Broca and early students of human heredity like Prosper Lucas and Morel laid the foundation of criminal anthropology and initiated an enormous amount of measuring of prisoners. In 1869 a paper read at the British Association by Wilson proved that habitual criminals must be morally defective by showing that their heads were abnormally small. All manner of physical peculiarities were taken into account, in a similar fashion, by observers in France and other European countries, until the apex was reached in the work of Lombroso (1887) of Turin. Some weaknesses in the theory were revealed by Galton, who suggested that composite photography of criminals should reveal the features common to all members of the class. Actual experiment showed that composites of criminal faces, particularly of those who were defective and insane, gave rise to pictures rather pleasing and noble, both in feature and expression, which could pass for rather blurred but not uncomplimentary portraits of ministers of religion. The fundamental factor common to all kinds of criminals is that they are all human. Finally, Goring (1913) published a very complete survey of convicts in Parkhurst Prison and expounded the view that, though the criminal was, on the average, physically and intellectually inferior to the man who arrested him, a criminal type did not exist. Controversy persists, however, at the present day, but claims that there are physical stigmata for criminal behaviour are becoming less ambitious than formerly (Hooton, 1938) and they are strongly disputed. Hrdlicka (1939) states definitely that there are no physical signs by which a prospective criminal can be recognized.

If there is no criminal type, it follows, almost as a formal corollary, that there is no morally defective type. The search for specific inheritance of criminality or moral defect is therefore senseless. Goring (1913) demonstrated that close relatives of convicts, that is to say, their brothers and parents, were more likely to be convicted of crime than were members of the general population. Also the proportion of sibs convicted was increased if one or both parents had been convicted. Furthermore, there was evidence of assortative mating of criminals. Surveys of twin

sets of convicts, carried out by Lange (1929) and by the Rosanoffs (1931), indicate that hereditary constitution is of considerable importance in the chain of events leading to conviction. Nothing more definite than this can be reliably concluded. It is impossible here satisfactorily to disentangle the genetical factors from the influences of social environment. Undoubtedly low socio-economic status produces conditions in a population more favourable to the growth of delinquency than comfortable surroundings (Jenkins and Brown, 1935). Many valuable statistical facts are presented in the report by East, Stocks and Young (1942) which plainly reveal the complexity of the problem. In so far as mental illness or defect predisposes to crime and in so far as these disabilities are inherited, so also could criminality or delinquency be inherited, but this is a very remote connection with the direct effects of genes.

MENTAL DEFECT AND CRIME

The overlap between mental deficiency and criminality can be studied by finding out how frequently criminals can be considered defective. Goring (1913) showed that men convicted of theft, arson, wilful damage to property and sexual offences were less intelligent than violent criminals and considerably less intelligent than embezzlers, bigamists and other perpetrators of fraud (see Table XLIV). In a survey of 309 adolescent delinquents, Stefanescu-Goanga (1939) found 99, or 32 per cent., mentally defective; among those convicted of homicide or theft, the proportion of defectives was even higher. Though

TABLE XLIV

RELATION OF TYPE OF CRIME TO MENTAL GRADE (after Goring, 1913)

Crime	Number of Cases	Number Defective	Percentage Defective
Violence to property (theft, burglary, arson, wilful damage)	402	58	14·4
Sexual offences (rape, perversion)	101	13	12·9
Violence to person (murder, manslaughter, robbery with violence, etc.)	219	17	7·8
Fraud (forgery, embezzlement, bigamy)	226	7	3·1
Total	948	95	10·0

Frankel (1939) estimated that only 15 per cent. of 1000 murderers were actually defective, the mean mental age of 722 tested members of the group was only 11 years, so that many must have been intellectually dull.

Taking criminals of all types together, Pailthorpe (1932) estimated that 15 per cent. were defective, whereas East (1944) gave a corresponding figure of only 0·5 per cent. Goddard's (1914) early estimate for the same percentage in the United States was 55, but Thompson (1940) reported that only 2·4 per cent. of sentenced offenders in New York were mentally defective, though he also stated that 6·9 per cent. had psychopathic personalities. The proportions rated defective depend upon the current definitions of mental defect and also upon the ages of the subjects. Burt (1925) pointed out that among juvenile delinquents 7·6 per cent. could be accurately rated defective, but that 25 per cent. were dull and an even greater proportion were educationally backward. East, Stocks and Young (1942) found a total frequency of mental retardation of 14·7 per cent. among 4000 delinquent boys.

In all known data, male criminals predominate numerically over females, especially where crimes of violence are concerned. This is a point to be remembered when we observe the greater numbers of females certified defective in the borderline groups. To some extent the provision of accommodation in prisons is complementary to provision of beds in mental hospitals of all kinds. For example, a young, adult, mentally retarded male may commit a crime of violence and be sent to prison, whereas a female of the same age and grade perhaps becomes sexually promiscuous and is certified mentally defective.

ADMINISTRATIVE RELATIONSHIP BETWEEN CRIME AND DEFECT

The standards of defect in different communities react in a remarkable way upon the proportions of cases admitted to hospitals for defectives as compared with those sent to prisons or reformatory institutions. On the whole, if trouble is taken to recognize and to treat the defectives, the number of prisoners is reduced. Thus in the states of New York and Utah, where the annual admission rates to hospitals for defective and epileptic patients were over 20 per 100,000 inhabitants in 1935, about

23 persons per 100,000 were received from courts into state prisons. In states admitting fewer defectives, more prisoners were received, and in Arkansas, Arizona and Nevada, where no defectives were reported, the average number of persons received, per annum, into state prisons was about 66 per 100,000 (Penrose, 1943). This effect is partly attributable to administrative differences in relation to white and coloured populations. More attention is paid to the problem of mental defect among the white than among coloured delinquents.

The same relationship is observed when all types of mental abnormalities are grouped together. In the Union of South Africa, for example, administrative differences are very noticeable when the European and non-European populations are compared, as in Table XLV. The total proportions of cases

TABLE XLV

INSTITUTIONAL POPULATION OF UNION OF SOUTH AFRICA IN THE YEAR 1935 (Penrose, 1943)

Population	Number of Inmates of Mental Hospitals per thousand of the population	Number of Prisoners per thousand of the population	Total
European .	3·27	0·45	3·72
Non-European	0·82	2·56	3·38

requiring care and control are not very different in the two groups, but among Europeans the diagnosis of mental illness or defect predominates whereas, among the coloured populations, behaviour disorders are most frequently classed in the category of crime. In European countries there is marked variation in the provision of beds for mentally ill and defective people. The gradient shown in Table II (page 16) is correlated with an inverse gradient representing the number of convictions for serious crimes or of prisoners. That is to say, there is an inverse relationship between the number of beds provided for the mentally ill or defective and the number of people in prison (Penrose, 1939*c*). This appears to be true for each age group. On the average, the provision of two mental hospital beds will make one prison cell unnecessary. Per inmate, prisons are about twice as expensive to run as mental hospitals, so that

even on financial grounds there is no loss in treating delinquency as a medical rather than as an ethical problem.

In administrative practice there is considerable difficulty in deciding how best to provide for delinquents, who are not enough retarded for them to be certified mentally defective on intellectual grounds alone. The legal solution of providing a category of moral deficiency has not proved to be very useful. In the first place, the implication that there is a type of individual with inborn absence or weakness of morals is not in accordance with modern scientific observations. Secondly, the legal confusion of delinquency with intellectual incapacity has led to the saturation of institutions for defectives with high-grade patients, selected on account of antisocial behaviour. The juxtaposition of these psychopathic cases with the well behaved patients, who are definitely inferior mentally, is unfavourable for the efficient training of both groups. The solution suggested by many investigators is that high-grade defective delinquents require separate institutions (Dybwad, 1941). Humphreys (1940) recommends that special institutional supervision should be made for psychopathic defectives because this is needed in any case for a small proportion of defectives. The care of these cases could be combined with the care of psychopaths, who are merely dull or scholastically retarded, more easily than with the amenable defective patients. Such procedures would be more favourable to the scientific investigation and treatment of delinquency than methods which are based upon a confusion between intellectual defect and disordered personality.

AFFECTIVE PSYCHOSIS

Among institutional cases of mental defect, a few patients are found who suffer from manic and depressive states. Only very rarely are these patients sufficiently ill to warrant their transfer to hospitals for mental disorder. It is difficult to distinguish a mild manic attack in a person of low intellect from a manifestation of hysterical neurosis. Indeed, it is characteristic of manic and depressive states in defectives that they are rather milder than in people of average mental ability. Myerson and Boyle (1941) and others have expressed the view that the true manic depressive states occur only in people of average or superior ability. This may be reasonably doubted, but it seems

to be true that the symptomatology of affective disorders alters with the intellectual level. In the concepts of Freud (1925), the ego, and consequently the super-ego, of the defective is weak. Thus the conscious and unconscious feelings of guilt and unworthiness, characteristic of the affective disorders, engendered by hypertrophic super-ego, are lessened. True manic depressive psychosis in an idiot is practically unknown. When manic states occur in defectives, they may be accompanied by visual hallucinations, which are rare phenomena in average subjects. Mild chronic mania is not uncommon. It should be remembered that most defectives are young at the time of ascertainment and that affective psychoses are usually diseases of late or middle life and are unlikely to be contributory causes of certification for defect.

As already mentioned (Chapter IX, p. 173), manic depressive disease tends to be transmitted from parent to child in some families in a manner suggesting that a single heterozygous gene is the main cause. In view of the great variety of different types of affective psychoses which occur, it seems very improbable that one gene only is responsible for them all. Moreover, acute attacks of mania or depression are often traceable to disturbances in the psychological environment of a subject, so that only the predisposition need be accounted for genetically. The mean age of onset, which is earlier in females than in males, is in middle life and does not seriously overlap the reproductive period. In a very mild form the manic temperament is not incompatible with social and biological success and may even help the individual. The fact that the onset of illness is later in the male than in the female may be interpreted as due to selective modification by nature, because the male reproductive period continues longer than that of the female.

SCHIZOPHRENIA

The type of psychosis most intimately associated with mental defect in actual clinical practice is some form of schizophrenia; there are certain important similarities in the two conditions. In the pure form, originally described by Kraepelin as dementia simplex, a subject gradually develops a mental condition which cannot be distinguished, by clinical tests, from a state of profound defect. If a schizophrenic psychosis arises in early

adolescence, normal mental potentialities may actually remain, but it is impossible, by means at present at our disposal, to revive them. The personal history is the essential test by which these cases are differentiated from other idiots with no gross physical abnormalities.

Schizophrenia characterized by very early onset, originally called dementia praecocissima by de Sanctis and named dementia infantilis by Heller, is an important though infrequent cause of mental defect. Bradley (1941) has made an extensive study of the disease. Cases have been described both in boys and girls. Deterioration of emotional and intellectual faculties takes a rapid course, can begin as early as 4 or 5 years of age and, in rare cases, 2 years, according to Grebelskaja-Albatz (1934). If delusions or hallucinations are present, they are only noticeable in the early stages. Encephalitis and organic degenerative diseases are excluded as possible diagnoses by the absence of neurological signs. The fact that the child was intellectually normal at an earlier age needs to be very carefully established.

The common types of dementia praecox, in which the disease starts in adolescence or in early adult life, do not, or should not, come into the province of mental defect. It is, of course, not very unusual to find that defectives, certified under the Mental Deficiency Acts on account of behaviour disorders, subsequently develop characteristic schizophrenic psychoses (Rohan, 1946). If necessary such cases can be transferred to hospitals for the mentally ill.

Sometimes isolated symptoms that form part of the characteristic picture of schizophrenia are found in mongols, phenylketonurics and other classes of patients. Catatonia with waxy flexibility, stuporous states, outbursts of violence, stereotypy, negativism and mannerisms occur in low-grade defectives, and their psychiatric significance is difficult to determine. Earl (1934) inclines to the view that they are really signs of psychosis. Alternatively, they can be regarded as modes of reaction of an infantile nature, which imply that instinctual and emotional development has been retarded along with the intellectual development.

Schizophrenia of all types is commoner and of earlier onset in males than in females (Malzberg, 1935). It is also associated

with greatly lowered fertility (Kallman, 1938), and for this reason tends to show a recessive rather than a dominant type of inheritance. There is, however, little uniformity among the patients diagnosed schizophrenic and no single gene can be held responsible for all cases. Some family histories may suggest a single autosomal recessive gene as a likely cause, others a single sex-linked recessive gene. The genetical aspect of dementia praecocissima has received very little attention. Evidently a regularly dominant gene cannot be the main cause. Familial incidence in sibships has not been emphasized in the literature, but there remains a possibility of recessive inheritance. Most psychiatrists who have studied these very early cases have been on the alert for the effects of environmental crises in the causation, but convincing evidence for this has not yet been brought to light. In view of the possible importance of degeneration of the gonads as the primary seat of the trouble in schizophrenic adults (Mott, 1919; Hemphill, 1944), signs pointing in this direction might be especially worthy of note in cases of dementia praecocissima also.

ORGANIC PSYCHOSIS: JUVENILE GENERAL PARESIS

The peculiar form of neurosyphilis which causes insanity in adults is paralleled by a type of congenital syphilis which causes progressive mental defect in children or young adults and which is known as juvenile general paresis. A full clinical description was given by Stewart (1933). The usual history is of a gradual mental and physical deterioration, which begins during school age and in some cases is initiated by convulsions. Occasionally the deficiency is observed in infancy, but usually the intelligence is at first quite normal. The child becomes increasingly stupid, neurotic, indifferent to its surroundings, dirty in its habits and eventually bedridden, with contracted limbs, marked emaciation and, in fact, all the features which distinguish the third stage of the adult type. Sometimes, in the early stages, euphoria and mildly grandiose ideas can be observed. Neurological signs characteristic of general paralysis are invariably present. Slurred speech is an important sign and persistent grinding of the teeth is held to be a symptom of some diagnostic value. As in other forms of syphilitic amentia, the external signs of congenital syphilis may be entirely absent. With regard to the

microscopical appearances, treponemata are usually abundant in the cerebral cortex; otherwise the morbid histology resembles that of the adult form. The diagnosis in typical cases is not difficult, as the Wassermann test in the cerebrospinal fluid is strongly positive. The disease can be arrested completely by fever treatment and other antisyphilitic measures. Some degree of intellectual impairment remains, although, if treatment is started early enough, the residual effect may be mild.

Familial cases of juvenile paresis are not common, but the coincidence of the adult form in a parent with the juvenile form in the child has been reported in the medical literature. Kanner (1935) gives an interesting summary of these reports (see Table XLVI). Among the adult cases especially, but also among

TABLE XLVI

PARESIS IN PARENT AND CHILD (Kanner, 1935)

	Father	Mother
Son	8	2
Daughter . . .	1	4

In addition to these cases, 75 were reported as having neither parent known to be affected.

juvenile cases, there are more males than females. There seems also to be a relative excess of father-son and mother-daughter pairs. It has always been difficult to understand why syphilis should attack one part of the body in one subject and a different part in another. Either the treponema which causes general paresis is a specially neurotropic variant or some people are constitutionally predisposed to react to syphilitic invasion in this peculiar manner. The sex limitation, tending to confine the disease to males, is of genetical interest because there may be families in which females are more likely than males to be affected. The figures shown in Table XLVI agree with other observations and suggest that here again is a disease exhibiting the puzzling phenomenon of familial sex limitation.

ORGANIC PSYCHOSIS: ENCEPHALITIS LETHARGICA

An important type of organic psychosis connected with intellectual defect is sometimes the aftermath of encephalitis

lethargica. Hall (1923) analysed reports on residual mental symptoms of the post-encephalitic state in patients, who contracted the disease in the epidemics from 1919 to 1922, and found that severe mental disorder was not a frequent complication. However, changes in moral behaviour were prevalent. In juvenile cases it was common for an affected child, previously normal, to become intellectually stunted and emotionally irritable. Cases of thieving, suicidal and homicidal tendencies have been reported. Many such adolescents, of both sexes, become problem children and they may eventually require institutional care after passing through the police courts. The amount of intellectual loss is not great; the mental age on tests tends to remain at the level reached before the illness. Dawson and Conn (1926) compared the mean I.Q. for children, who had suffered from encephalitis lethargica, with that for their normal sibs and found that there was a fall of 16 points attributable to the disease.

Clinically it is sometimes difficult to be sure of the diagnosis, because severe late results can follow an acute illness which, at the time, was not recognized as encephalitis lethargica. Other forms of encephalitis also may mimic the disease. The development of a psychopathic personality in a previously normal subject may be almost the only evidence of previous cerebral illness. Usually, however, neurological residual signs can be detected. The appearance of the Parkinsonian syndrome, with mask-like face and rigidity of the limbs, should make the diagnosis easier. Oculogyric crises, i.e. recurrent spasms of the ocular muscles, and permanent difficulty in convergence are characteristic signs. In children, nocturnal excitement occurs together with inversion of the sleep rhythm.

Owing to their lack of self-control and the suddenness of onset of their passions, combined often with an attractive personality, post-encephalitic defectives are among the most tragic cases found in institutions. They may be dangerous to themselves or to others and, since the mental impairment is usually mild, they present difficult problems; they cannot be blamed and are quite irresponsive to correction. So far as is known, there is no hereditary predisposition.

CHAPTER XII

TREATMENT

General Principles—Case Histories—Technical Aids to Physical Diagnosis —Comparisons with Normal Infant Behaviour—Psychological Tests— Specific Medical Treatments—Psychological Training—Eugenic Prognosis —Preventive Treatment—Positive Eugenics.

GENERAL PRINCIPLES

THERE are three possible objects of medical treatment, cure, alleviation and prevention. All these aims have their places in the treatment of mental defect. The emphasis on one or another depends upon limitations imposed by the nature of the particular case under treatment. In the interests of efficiency, as accurate a diagnosis as possible has first to be made. In mental deficiency practice, diagnostic investigations have to be made in two separate fields, the physical and the psychological, and the results combined.

CASE HISTORIES

Much depends upon an accurate case history. This must include a record of maternal health and the elements of a pedigree investigation in every case. Often it is desirable, though not always practicable, to make careful clinical examinations of other members of the patient's family.

The most important facts to obtain in routine family history work are ages, preferably the dates of birth, with mental status and general health reports on the parents and all sibs of the patient. The occupational and educational status of each of these relatives, as well as any interesting physical peculiarities, can be usefully noted down. Miscarriages and stillbirths must also be carefully recorded. Consanguinity of any type in the parental and grandparental generations always has to be enquired about and an exact record made of any interrelationship discovered. It is much more important to obtain accurate data

on every patient's sibship and other close relatives than it is to make elaborate pedigree studies in a few selected cases.

Details of maternal health are relevant to the patient's own life history during the embryonic and foetal stages. The circumstances of the patient's birth, neonatal condition and infantile development are particularly important, though they are often difficult to ascertain with accuracy. In all cases of mental defect it is of primary interest to know whether the defect has developed in a subject who was previously apparently normal. Moreover, the condition may be stationary, it may have improved or it may have been progressing unfavourably. Parents have to be most carefully questioned on these points and hospital records must be consulted whenever possible.

TECHNICAL AIDS TO PHYSICAL DIAGNOSIS

In earlier days it was often considered sufficient to wait until a patient died before making a careful pathological investigation. With modern methods of care, even low-grade patients live for a long time and it is desirable to obtain the maximal amount of information about each case as it comes under observation. Apart from routine procedures, like chest X-ray for excluding tuberculosis, and ordinary medical examination, there are numerous special techniques particularly adapted for studying defectives.

A defective child is more difficult to examine clinically than a normal child because it may be impossible to obtain the patient's co-operation. In low-grade cases neurological tests are almost confined to measurement of muscle tone and eliciting of reflexes. Ophthalmoscopic examination is also troublesome, but its findings are objective and extremely important. Unsuspected optic atrophy, coloboma of the chorioid, retinal degeneration or tumours may be found on examination of the fundi. The condition of the cornea may be the chief clue to diagnosis, as, for example, in congenital syphilis. Cataracts of unusual type may be revealed.

Many conditions can best be appreciated in X-ray plates. This is true of generalized osseous dystrophies, such as Morquio's syndrome and dyschondroplasia. The skull can be very usefully studied in lateral X-ray views; in these, the bony peculiarities characteristic of acrocephaly, microcephaly and hydrocephaly

are easily detected and the shape of the sella turcica examined. Recently, the technique of pneumoencephalography has come into prominence as a diagnostic instrument in cases of severe defect. After displacing the cerebrospinal fluid with air by lumbar puncture, the outlines of the cerebral cortex and of the lateral ventricles can be seen by use of X-rays. The process is claimed not to be dangerous if competently carried out, with surgical precautions, preferably under anaesthesia (Levinson, 1947). When cortical atrophy is present, its degree and location can be estimated. The method is useful for detecting hydrocephaly, arachnoiditis, subdural haematoma and cerebral abscess as well as tumours. Characteristic pictures are shown in several specific types of defect (Delay, Desclaux and Pichot, 1947; Mäurer, 1939).

Examination of the urine for abnormal constituents has special interest since the discovery of phenylketonuria. There may be other, somewhat similar, diseases as yet undetected, and the systematic investigation of specimens with reagents such as Millon's, as suggested by Pugh (1940), or by chromatographic methods (Williams, 1946) should lead to new discoveries. Tests for the excretion of hormones may help to suggest the possibility of endocrine therapy as well as to define clinical types. The investigations on blood chemistry by Bixby (1940), on mongols, and by Kondritzer (1940), on phenylketonurics, used methods which could be applied more extensively.

The techniques of serology, which have advanced very rapidly in recent years, have much to contribute in the future to the field of mental defect. No longer is the Wassermann or Kahn test for diagnosis of syphilis the only use which a pathologist can make of a blood specimen from a defective. The search for maternal and foetal incompatibility necessitates taking samples of blood both from the patient and from his mother. Typing of the sera of patients, of their sibs and of their parents may eventually help to locate upon particular chromosomes the genes responsible for defects. When fairly close linkages are eventually found, these will be used to help in the diagnosis of abortive or mild cases of known hereditary diseases. At the present time it is difficult to explain to parents or to doctors the value of typing sibs of defectives for linkage purposes. Typing a single family may involve a lot of trouble and give very little information.

Only when very large amounts of data have been collected and put on record will useful linkages be established (Appendix 9).

COMPARISONS WITH NORMAL INFANT BEHAVIOUR

Since the diagnosis of mental defect is primarily a question of behaviour, the psychological examination of the patient is critical. There are many modern technical devices which can be employed in the diagnosis of mild or high-grade cases, where determination of the level of intelligence as exactly as possible is a matter of great practical importance. Among severe or low-grade cases, the ascertainment is useful for planning care and training and has significance also from the biological and genetical points of view.

If a subject's ability does not reach beyond the mental age of 2 years, few standardized tests can be effectively employed, not even the methods for infants recommended by Merrill and Palmer. Reliance has to be placed upon observations of behaviour to determine the mental level of an idiot as compared with the normal. Thus, the defective who cannot talk, walk or feed himself must be rated at less than 1 year. Those between 1 and 2 years in mental age can make an attempt at walking and feeding and respond to habit training. More accurate estimates of mental age can be made for idiots by reference to Gesell's (1928) norms or to those given by Tredgold (1947). Due allowance must, however, be made for physical disability, especially when paralysis or blindness is a complication.

Before birth there are some signs which may suggest normality or deficiency in the foetus. Spontaneous foetal movements (quickenings) are normally felt by the mother towards the end of the 5th month of pregnancy. Absence of strong normal movements, or presence of foetal convulsions, may indicate maldevelopment of the nervous system. Anencephaly, hydrocephaly and some other osseous malformations can be demonstrated by X-rays.

The condition of the child immediately after its birth can be studied in order to exclude the diagnosis of idiocy or of imbecility, but not of mild mental defect. Signs of normality, such as crying, yawning, sneezing and stretching, can be observed in the first day of life. Discrimination of sweet taste and appreciation of cold temperatures are evidenced during the first 2 weeks.

The subsequent development of motor co-ordination can be summarized as follows. At the age of 1 month*, the infant should attempt to lift its head when held on the shoulder, at 2 months, it can hold its head erect for a few moments, and, at 4 months, hold it steady when being carried. At 1 month, crawling movements are made when the child is laid prone on a flat surface, but, at 2 months in this position it can also lift the chest slightly. At 4 months, it attempts to sit up and stays sitting when supported. At 6 months, it can sit momentarily without support. At this age, too, it can roll from dorsal to prone position and can grasp, pick up and hold an object in either hand. At 9 months, it can sit without support and, a little later, can pull itself up into a standing position.

At 1 year, the infant can lower itself from standing to sitting position and can walk with help. Standing and walking without help are established at 15 months and climbing stairs, or getting into a chair, is possible at 18 months. At this age also, a pencil is used spontaneously for scribbling and a tower of three blocks can be constructed. Ability to walk backwards is achieved at 21 months.

At 2 years the child should be able to run and to build a pile of six blocks; six months later, it can go downstairs alone and pile up seven or eight blocks. Tests with form boards become practicable at this stage and thereafter standardized performances can be measured or timed.

The development of language is of particular interest in the pattern of normal intellectual growth. An infant aged 1 month gives heed to sounds and in its cry is said to differentiate between expressions of pain and hunger. At 2 months, it attends to a speaking voice and may smile. Laughter is attained at 4 months and also elementary vocal response can be elicited. At 6 months, well marked vowels or syllables ("aroo" or "agoo") are produced spontaneously and familiar voices are recognized. Sounds like "da-da" or "pa-pa" are used to express pleasure at 9 months.

The child of 1 year should be able to say about two "words", that is, sounds which are attached to real situations or objects, and it also reacts to very simple commands. Four words should be enunciated at 15 months and about six words at 18 months.

* I.e. during its second month.

At this period the child can learn to point, on request, to its eyes, nose or hair.

At 2 years, the child can name objects or pictures of objects and, after 2½, has sufficient linguistic development to make possible the application of the Binet type of test.

In the first 2 years, and particularly in the first months, there are great variations in normal children. Variations in general health, nutrition and maturity at birth are significant causes of differences in rates of development. The defective child is generally supposed to develop in the same way as the normal but at a slower rate. This may not be always true. Irregularities in rate of development, as well as in the order of appearance of different achievements, are quite characteristic of infants both normal and defective. Consequently the diagnosis of mild intellectual defect is extremely difficult and unreliable in the first 2 years of life. Gross departures from the normal, such as occur in imbecility or idiocy, are usually unmistakable.

PSYCHOLOGICAL TESTS

After the age of about 2½ years, the standardization of achievement in normal infants becomes progressively more reliable. The co-operation of the child can be obtained and mental growth from that time onwards proceeds steadily. Techniques of many kinds for measuring mental abilities are available, though most of them do not deal very accurately with the pre-school level.

From the scholastic point of view educational level is predicted with fair accuracy by the various revisions of the Binet test. Many intelligence tests, which include pictorial, geometrical, numerical and verbal items, either in mixed order or in sets of similar items of increasing difficulty, can be employed for similar purposes. The Otis tests and the Kuhlman-Anderson scales are useful with high-grade or borderline cases. When dealing with defectives, whose abilities are insufficient for them to be able to profit by ordinary school classes, manual dexterity and appreciation of shapes are tested by form boards and other devices, usually made of wooden blocks. According to Pichot (1948), these methods originated in France and were developed by Séguin at Bicêtre. The manual performance tests most commonly used have been collected and standardized by Arthur

(1943). The use of words is not required in the solution of such tests, and so for deaf children gestures can be substituted for verbal instructions. It is often remarkable how much better is the performance of institutional cases of all grades on manual tests than on verbal or numerical tests. This may be partly due to the selection of cases for certification that are scholastically retarded. Careful psychometric examination can sometimes reveal hidden abilities in apparently quite low-grade cases and in patients who suffer from deprivation of special senses. Performance tests suitable for deaf children have been standardized by Drever and Collins (1944) and accurate information concerning the abilities of the visually handicapped has been obtained by Hayes (1941) with a modified Binet test.

If the scores of a subject on different tests, verbal, performance, etc., are all measured in general population standard deviation units, they can be expressed as a profile. Irregularities of ability, which should be of much interest to teachers, can thus be clearly shown. Uneven scoring on tests of various types, in different parts of the same test or sub-tests of a battery, is also a phenomenon of clinical importance. Babcock (1930) demonstrated that a relatively high score on tests involving routine memory, such as vocabulary tests, combined with a relatively poor score on tests involving adjustment to new situations, such as those requiring appreciation of absurdities, was characteristic of some mentally disordered states. Myers and Gifford (1943) have made use of this knowledge to set up a differential method of scoring the Binet Revision (Form L). Search for uneven performance of this type may be valuable in diagnosing psychopathic defectives. Caution is needed in the interpretation of psychological profiles because there are normal differences between males and females. More striking than this is the effect of age on the relationship between different abilities. Vocabulary tends to increase with experience, but ability to reason accurately in new situations decreases gradually in adult life. In addition to these points, attention must be paid to the literacy and educational opportunities of the subject when a psychological profile is being studied.

As further aids to the diagnosis of psychopathy in defectives, use may be made of association techniques. Heuyer and Courthial (1936) found that a considered judgment, based upon the

results of questionnaires and association tests, agreed well with psychiatric diagnoses made by ordinary methods in 87 out of 114 children attending a psychiatric clinic, some of whom were defective. The Rorschach Test or the Thematic Apperception Test can be valuable, but standardized responses, based upon those given by people of average intelligence, are not very helpful for defectives whose imaginations are less active than normal. Lack of response or stereotypy does not imply a disordered mind if the intelligence is limited. Again, inventories and questionnaires are also not very suitable for use with defectives, because these tests fail to take into account the effects of varying intelligence level upon the answers. The chief value of all these techniques with defective subjects, and possibly also with others, is that they provide material which can conveniently be used at an interview to stimulate phantasy and thereby to produce information for the psychologist to interpret in the light of other knowledge.

SPECIFIC MEDICAL TREATMENTS

In so far as mental defect is not a disease but merely the expression of normal variation in the intellectual capacities of members of the human species, to speak of cure is absurd. The problem—which indeed arises acutely also in making adequate provision for individuals of unusually high intelligence—is how best to make use of their qualities for the benefit both of the individual concerned and of the rest of the community. The idea of cure as a medical aim is closely associated with the removal of a pathological condition. If a patient is institutionalized on account of low scholastic capacity alone, it is the relationship of this individual to society that is pathological. Treatment in such cases aims at providing special educational and training facilities that will enable the patient to return to the community well enough equipped to be able to maintain himself satisfactorily thereafter. That this is not always possible may be the fault of society rather than of the individual. The rest of humanity may need to be cured in order to be able to tolerate the individuals concerned.

When low mental capacity is coupled with a mental or a physical disease, as is so frequently the case in institutional defectives, the radical cure of such a disease, on the assumption

that in its absence the mental level would be sufficiently normal, is the primary aim of medical treatment. However, attempts have also been made to find some general treatment which may be expected to raise the intelligence level itself, almost regardless of the nature of the defect. For example, administration of stimulant drugs, such as caffeine and benzedrine, may temporarily improve test performance. Their continued administration, however, does not raise the intelligence level. Cutler, Little and Strauss (1940) and Moskowitz (1941) have reported experiments which indicate that benzedrine may have a little value as an aid to education in some cases. Efforts to increase mental capacity by feeding with thiamine or other vitamins, such as riboflavin (Stevenson and Strauss, 1943), have also been fruitless, though it remains possible that occasionally vitamin deficiency may be found to be a part cause of scholastic retardation. In the particular case of phenylketonuria, thiamine deficiency is evidently not part of the pathology (Bates, 1939). On the other hand, administration of large doses of alpha tocopherol (vitamin E) is beneficial in some cases of myopathy. It improves the physical condition and retards the degenerative process.

More convincing therapeutically is the use of thyroid extract in cases of cretinism, and particularly in juvenile subthyroidism with myxoedema. The good results of the treatment depend upon the lack of complications of thyroid deficiency. A child who is born a cretin may respond well physically to thyroid replacement therapy, but is unlikely to reach the average level of intelligence. If, however, the first signs of cretinism develop later, as in juvenile myxoedema, complete cure should be expected if continuous thyroid administration can be begun at once. Improvements have been noted in cases of pituitary dystrophy and even in mongolism after feeding the subjects on thyroid extract. However, this treatment is only effective in so far as thyroid deficiency is part of the clinical picture. Much physical harm can be done by the indiscriminate use of thyroid extract. Treatment of pituitary disorders by attempting to replace the missing hormones artificially has not been successfully applied to cases of mental defect. The possibility of improving low-grade cases suffering from undeveloped gonads by supplying them with sex hormone substitutes, such as

testosterone or stilboestrol, has not yet been fully explored. Overaction of the adrenal cortex in children is associated with abnormal sexual precocity and is occasionally accompanied by high intelligence; hence the effect on intelligence of injections of corticotrophic hormone seems worthy of investigation. Hemphill (1944) has summarized the possibilities of endocrine therapy in the psychoses; its application to cases of mental deficiency is to be awaited with interest.

An important field for therapy concerns plegic defectives. The potentialities of plegics, which are often much higher than at first supposed, can be developed by continuous movement training, massage and encouragement (Doll, Phelps and Melcher, 1932). A training plan to improve muscular co-ordination, described by Longwell (1935), is said to enable some cases to make considerable intellectual and social advances.

Recently attention has been drawn to the therapeutic possibilities of feeding epileptic defectives on massive quantities of glutamic acid (Albert, Hoch and Waelsch, 1946). Doses amounting to 12 g. or more, in three doses daily over a period of months, appears to control fits, to regularize cerebral rhythm and to increase intelligence significantly. Zimmerman and others (1948) have reported that the average gain of 6 to 8 points in Binet I.Q. is achieved in 6 months and that thereafter no further improvement is obtained. The enhanced mental functioning might be attributed partly to the amelioration of minor epileptic disturbances. If the interruptions caused by petit mal can be eliminated, an increase in the span of concentrated attention necessary for learning can be expected. Glutamic acid appears to have a position of special importance in cerebral metabolism and an adequate supply is essential for normal functioning. There are difficulties in its proper administration for therapeutic purposes and large quantities are not readily obtainable. Food saturated with this substance is unpleasant to take and can produce dyspeptic symptoms.

There are other forms of treatment, physical and psychological, for which claims have been made as to their efficacy in raising the intelligence level. Cerebral ionization has been extensively applied by French physicians in the manner advocated by Bourgignon (1929). The treatment, as described by Chouraqui (1941), is periodically to pass an ionizing current

through the cerebrum for some hours, after feeding the subject on calcium salts. Improvement in mental capacity, though not, of course, cure, has been reported in cases of diplegia, hemiplegia, mongolism and in other types of severe defect. The mental improvement was objectively demonstrated by an increase in the sensitivity of the vestibular nerve, measured by its chronaxie.

Violent methods also have not been neglected. Craniotomy, to allow the microcephalic brain to enlarge, was tried half a century ago without effect. Coma and convulsion therapy (Humphreys *et al.*, 1943) and even leucotomy have been recently used on patients of all grades who have psychotic symptoms, with little if any permanent benefit in the majority of cases. These violent treatments are not, however, expected to improve the intellectual capacity, but only to alter behaviour. They are presumably justified if they succeed in aiding socialization (Mackay, 1948; Engler, 1948).

PSYCHOLOGICAL TRAINING

Claims are made from time to time for new educational methods, which result in raising the intelligence as measured by standardized tests. It is not surprising that some methods of teaching should prove more beneficial than others. Apart from this, the familiarity of a child with test situations is likely to facilitate performance on the tests themselves. By kindness and indulgence, the measured I.Q. can be increased in timid or illiterate subjects. Caution is required in accepting claims that I.Q. has been increased by education because test scores also improve naturally with practice. Repetitions of the same test, even at intervals up to a year, can induce improvement and re-testing at short intervals has a much greater effect. An increase of 2 to 4 points is obtained in the second administration of a Binet test within a few days (Terman and Merrill, 1947) and the Binet score is less subject to change in this manner than are the scores of most tests. Patterson (1946) has investigated the effects of re-testing defectives with the performance tests which are included in the Arthur battery.

The most important work carried out in the field of training defectives is unspectacular. It is not highly technical but requires unlimited patience, good will and common sense. The reward is

to be expected not so much in scholastic improvement of the patient as in his personal adjustment to social life. Occupations are found for patients of all grades so that they can take part as fully and usefully as possible in human affairs. This process, which has been termed socialization, contributes greatly to the happiness not only of the patients themselves but also to those who are responsible for their care.

Socialization programmes differ according to the grade of the patients concerned. Among idiots and imbeciles, besides ordinary habit training, a great deal can be done to encourage occupational interests. With children, teaching still tends to follow lines laid down by Montessori and Séguin. A great deal of training at home is possible but, in many urban districts centres for occupational classes at the pre-school level are provided to relieve mothers of the care of defective children for a large part of the day. In an institution much depends upon numerical strength and enthusiasm of the staff. When buildings and equipment are good, remarkable results can be obtained in creating a social life for low-grade children. Adult imbeciles can also be provided with occupations and they will continue to carry out elementary tasks, which may appear intolerably dull, with the utmost diligence. Percussion bands and large-sized toys have been successfully used for the amusement of adult idiots (Fitzgerald, 1938).

The socialization of the feeble-minded involves two quite distinct problems which arise on account of two distinct reasons for certification, namely scholastic inefficiency and social ineptitude. As far as possible, the institution or special school must act as a tutor, devoting special attention to the scholastic difficulties of feeble-minded children. As much reading, writing and arithmetic as the pupils can absorb is slowly presented in classes where competition with normal children is excluded. Melcher (1939) and Patterson (1947) recommend that scholastic learning should be regarded as incidental, not essential, for defectives. Manual skills can be more easily developed when tension, due to this obligation, is relieved.

Speech disabilities are much commoner in feeble-minded than in normal children; they occur in about half of all feeble-minded children and are universal among low-grade cases. As shown by Svikin and Lyons (1941), there is considerable scope for special

treatment of these defects in higher grade cases with a view to increasing self confidence as well as economic fitness. Occasionally high-grade females have ability in linguistic matters, and when this is so, elementary teaching of foreign languages may give them useful exercise (Angiolillo, 1942). Acting in plays, singing and reciting all have their value in speech training. Feeble-minded subjects of both sexes often have artistic talents and these should be given every opportunity for development.

The importance of games and sports, as well as that of organized clubs, such as Boy Scouts and Girl Guides, have been rightly emphasized. In early times religious teaching was considered to be particularly valuable. A great variety of occupations, which tend to foster in the patients a sense of social usefulness and responsibility, have been successfully incorporated into training schemes. Defectives are not naturally antisocial. They are naturally very friendly and are particularly susceptible to influence during the formative years. There are good prospects for scholastically retarded children whose special education is taken in hand early in the school period and who are not exposed to social environments conducive to the development of behaviour difficulties.

In consequence of the neglect of communities to provide the most favourable educational facilities for feeble-minded and borderline children, the majority of high-grade defectives admitted to institutions have already developed antisocial tendencies. Thus a problem, quite separate from the primary educational one, confronts those who have care of them, namely, the re-education and rehabilitation of neurotics and psychopaths. The occupational programmes already planned for the training of defectives, who are not mentally disordered, are also valuable for psychopathic subjects, but are insufficient. They are often on too juvenile a level for the relatively sophisticated high-grade patients to appreciate; many of these may resent detention with those who are intellectually their inferiors. Some of these cases of behaviour disorder require the employment of the highest degree of psychiatric skill and attention, which the duties of medical staffs in charge of defectives often leave little opportunity to exercise. The correct treatment of defectives who have become neurotic, psychopathic or delinquent is still largely an unsolved medical problem.

EUGENIC PROGNOSIS

Not infrequently relatives of a patient ask what are the chances that their future children will suffer from the patient's condition. The relative who enquires is commonly a parent or a sib of the patient. In the light of present knowledge on human genetics, fairly accurate estimates can be given in particular cases, though these instances are likely to be rare. For a condition known to be due to a rare dominant gene with full manifestation, the task of making a prognosis for a future generation would be simple. The offspring of an affected person each have half a chance of being likewise affected; an unaffected person cannot transmit.

There are two main difficulties with a rare dominant gene, like that for epiloia, which usually present themselves in practice. These are due to irregular manifestation and to mutation. If manifestation were an all-or-none process, it would be feasible to multiply the probability of a child's carrying the gene by the manifestation rate to obtain a more accurate estimate. Such treatment is unreliable because, if manifestation is altered by genetic modifiers, it will vary in different families. When modification is expressed by differences in age of onset, the difficulty can be easily appreciated. The sib of a Huntington's chorea patient, for example, cannot usually be known with certainty to be affected or unaffected until middle life is reached. The prognosis for his children becomes more favourable with every year that passes and finds him without signs of the disease. Attempts are still being made to detect very early signs of the disease, and if these prove successful the accuracy of prognosis will be greatly increased (Minski *et al.*, 1938; Patterson *et al.*, 1948).

It is easy to allow for the effect of new mutation on the prognosis for near relatives in a disease due to a fully manifesting dominant gene. Assuming that dyschondroplasia is a disease of this sort, Mørch (1942) points out that if both parents of a case were unaffected, the prognosis for their subsequent children, for the children of their normal sons and daughters and for their nephews and nieces would be equal to the incidence of the disease in the general population. In irregularly manifesting dominant conditions, the convenient assumption that a sporadic case is due to new mutation cannot safely be made.

The prognosis for relatives of patients with recessively determined defects can often be given with considerable accuracy.

Degrees of manifestation are seldom of importance and the frequency of carriers in the population can be estimated. Parents who have already had one phenylketonuric child can be informed that the chance of another similar child is 1 in 4. The unaffected sib of a phenylketonuric has two chances in three of being a heterozygous carrier and, provided he does not marry a cousin, his chance of mating with a carrier is only about 1 in 100. The unlucky chance of both parents being carriers is thus only $\frac{2}{3} \times \frac{1}{100}$. Since, even then, only 1 child in 4 will be affected, the chance that any unaffected sib of a phenylketonuric patient will have a phenylketonuric child is $\frac{1}{4} \times \frac{2}{3} \times \frac{1}{100}$, or $\frac{1}{600}$. This is not a very serious risk and, for more distant relatives, the corresponding risk is negligible.

The special case of sex-linked inheritance leads to the specific prognosis, in the usual example of an affected son of normal parents, that half the subsequently born sons will be affected. Half the daughters, like their mothers, are carriers. The same prognosis can be given for totally sex-limited diseases causing severe defects. In most instances, where sex differences are important in determining manifestation, no general rules can be usefully laid down.

A common type of prognostic problem is presented by parents, both of normal intelligence, who have had one child of idiot or imbecile grade but with unspecified diagnosis. The risk of low-grade defect for the children subsequently born to these parents can be calculated roughly on the basis of known sibships (Penrose, 1939*d*). Table XLVII (A) shows the classification of 1897 sibs of 487 low-grade propositi whose parents were normally intelligent. Thus, some 2·8 per cent. of sibs of low-grade cases are likely to be of the same low mental grade. As compared with the incidence in the general population, this is almost a tenfold increase (see Table IX, page 45).

If parents are normal and consanguineous, the likelihood, that a low-grade defective child of undetermined type is the result of recessive inheritance, affects considerably the risk of repetition of low-grade defect in the sibs. According to the small group of sibships pooled in Table XLVII (B), the risk is 14·3 per cent. In the case where two idiots or imbeciles have been born to normal unrelated parents the risk is of the same order. The danger that a cousin marriage between normal parents will produce imbecile

offspring, in the case where no near relative is so affected, though slightly greater than the risk for unrelated parents, is not great. The discussion of gene frequencies, in Chapter VI, has shown that this risk is not so serious as might be surmised from the value of parental consanguinity as a diagnostic instrument.

When one or both of the parents are of subnormal mentality, i.e. with mental ratio less than 85, and one low-grade defective has been born, the chance that another child will be of equivalent grade is about 10 per cent. As shown in Table XLVII (C), the risk of mild defect in such a sibship is also considerable.

TABLE XLVII

MENTAL GRADES OF SIBS OF IMBECILE AND IDIOT PROPOSITI
(Parents of Known Mental Grade)

Mental Grades of Sibs		Normal	Dull	Feeble-minded	Imbecile or Idiot	Total
Mental Ratios of Sibs		85 and above	70–84	50–69	Below 50	
(A) Parents of normal intelligence (487 propositi)	Number	1715	99	31	52	1897
	Percent.	90·4	5·2	1·6	2·8	100·0
(B) Consanguineous parents of normal intelligence (14 propositi)	Number	39	1	2	7	49
	Percent.	79·6	2·0	4·1	14·3	100·0
(C) One or both parents of subnormal intelligence (138 propositi)	Number	280	101	78	54	513
	Percent.	54·6	19·7	15·2	10·5	100·0

Eugenic prognosis, where degrees of mental ability within the range of mild defect and normality are concerned, can be estimated roughly on the basis of the additive gene hypothesis. The mean intelligence of the children will approximate to the average level of the two parents, i.e. the mid-parental value. The expected range of variation in the children is difficult to specify accurately. It is increased by parental consanguinity (Hogben, 1933*b*).

In so far as mental disorders are part of the complex of mental defect, the prognosis in respect of children of mentally disordered adults is relevant. With respect to manic depressive psychosis, the estimated proportion of affected children, from parents one of whom is affected, is said to be of the order of one

in three (Rüdin, 1933). For schizophrenia, the corresponding proportion is one in ten. These estimates take little or no account of variations due to sex and onset age. With epilepsy, the corresponding proportion is still lower, though here, as in other problems of mental disorder, the relation of genes to the manifest disease involves a large number of unknown steps.

PREVENTIVE TREATMENT

It is often held that feeble-minded parents make such unsatisfactory parents that, for this reason, they should not be allowed to have children of their own, irrespective of genetical considerations. To a limited extent the truth of this is undeniable, but feeble-minded parents are not naturally unkind to their children. They tend to be indulgent, and their faults in looking after their children's health and well being are due to ignorance, not malice. In consequence of neglect or parental desertion, children of feeble-minded people are liable to become charges upon the general community, and this is in itself considered objectionable.

The actual proportion of the children of defectives who are of the same mental level as their parents, or lower, is a matter of dispute which cannot be settled so long as definitions of defect vary. The nature of assortative mating, with respect to mental defect, must also be first understood. If the figure of nearly one-third defective, given in the Brock Report (1934), be accepted, the burden of defective children on an industrialized community could be lightened by preventing defectives from procreating. Owing to the fact that the great majority of defectives of all grades are born to parents who cannot be classed as defective themselves (see Appendix 10), the reduction of defect in the community by preventing all known cases from having children would not be spectacular.

There is no precise genetics of social inefficiency, so that the idea that it can be prevented on the basis of genetical theory is essentially invalid. Furthermore, the most severe cases of mental defect, those most easily recognized, are infertile in any event. Rational measures can be suggested for the control of special conditions whose manner of inheritance is known, but the general principles of preventive treatment of mental defect usually advocated are, for the most part, based upon considerations of social convenience.

On the assumption that it is undesirable for people who are certifiably mentally defective to have children, there are several methods available to bring about this end. Among the methods advocated, or used, are segregation, prevention of marriage, sterilization, contraception, abortion and, finally, euthanasia.

Segregation of defectives during the major part of the reproductive period is the commonest device in general use. If the patients concerned are unable to maintain themselves in the community and need care and control, for this reason, over a long period, institutional segregation or supervision of some kind is a necessity. The troublesome feature, from the administrative point of view, is that patients from time to time must be tried out on leave of absence; they sometimes go away on their own account or are discharged and illegitimate offspring may result.

Somewhat similar difficulties would arise if people, once certified defective, were forbidden by law to marry. The suggestion has been made that, if defectives were always prevented by law from marrying one another, this would encourage illegitimate unions. Discouragement of matings between defective partners, however, would be an efficient means of reducing the incidence of deficiency in communities where assortative mating tendencies were very strong.

Voluntary or compulsory sterilization holds a very prominent place in the popular mind as a means of controlling mental defect. Laws permitting the sterilization of defectives, usually by vasectomy in males and salpingectomy in females, have been in force in many areas of the United States since 1907, and up to the end of the year 1947 more than 15,000 male cases and 8000 female cases had been dealt with in this way. The early history of the legislation has been well summarized by Landman (1932). Since it is not known how many children would have been born nor how many of these children would have been socially incompetent if the sterilizations had not been performed, the net social and biological achievement is hard to estimate. In Germany, where a very large number of sterilizing operations were carried out in a brief space of time after 1933, the majority of defectives so treated were inmates of institutions and unlikely to have had offspring. An account of the working of the Danish sterilization laws has been given by Kemp (1946). Sometimes sterilization, or

even castration, has been used as a punitive measure. From the scientific point of view this is to be strongly deplored, as, indeed, is also the possibility of political bias entering into the selection of cases for this operation.

The recommendations of the Brock Report (1934) were greatly influenced by the view that sterilization should be a therapeutic attempt to aid those who had good grounds for believing that they might have defective children. A voluntary measure of this kind, however, might become essentially compulsory in cases of defect, where sterilization was an alternative to institutional confinement. Against this, it has also been frequently asserted that sterilization helps defectives in their social adaptation because it limits their responsibilities. For example, according to Mickelson (1947), sterilization of feeble-minded parents is beneficial to the children previously born to them. Other authorities believe that sterilization encourages immorality. From the biological point of view, the effects of limited use of voluntary sterilization are likely to be negligible, though considerable medical and social advantages might be obtained by its use in carefully picked individual cases.

It is difficult to justify compulsory sterilization of defectives on genetical grounds. However, if it were granted that all individuals with I.Q. below 70 should not be parents, there would still be great problems set. No tests of intelligence are accurate to 1 per cent. and there is no natural boundary at I.Q. 70. It is absurd and unfair to apply an all-or-none measure to a continuous distribution, like that of intelligence. The difficulties involved in certification are great enough, but certification, unlike sterilization, is not an irreversible process. Quite apart from practical administrative problems, the moral issue of who has the right to decide whether or not someone else is or is not fit to have children is far from being settled.

The most feasible methods of preventing offspring likely to be mentally defective are contraception and abortion. Since the majority of parents of known recessively determined defects are normally intelligent, there should be no difficulty in instructing them how to avoid further offspring, after the birth of a child affected in this way, if they so desire. The same could apply to a mentally normal parent with sebaceous adenoma, for example. The peculiar maternal age distribution of many severe foetal

abnormalities, including mongolism, shows that a great reduction of their incidence could be brought about if pregnancies at the extremes of maternal age were avoided. Prospective healthy mothers should be encouraged to have their offspring between the ages of 22 and 30 in order to minimize the risks of foetal malformation. This age range is also the most favourable from the point of view of maternal health. Actually, the tendency to limit families, which has affected both Europe and North America during the last few decades, has reduced the births in the later more than in the earlier maternal age groups. If this process were to continue, a reduction in the proportion of births resulting in mongoloid imbeciles, hydrocephalics, etc., could confidently be predicted (Beall and Stanton, 1945).

The objection is sometimes raised against contraception as a eugenic instrument that it is only used by conscientious and, therefore, by comparatively eugenically desirable parents. A better understanding of the risks involved in specific cases, which are often not so much greater than those to which every pair of prospective parents are exposed, may help to remove this danger.

The use of abortion for eugenic purposes has attained legal status in Denmark and is permitted when a feeble-minded female is pregnant. There are occasions when this may be an obviously humane proceeding. Furthermore, with the routine use of X-rays in pregnancy, anencephaly and some other types of gross cranial abnormality could be detected in the later months and premature labour might be induced, though it is standard obstetrical practice to allow such pregnancies to continue until full term. Since the majority of grossly abnormal foetuses die soon after birth, the medical question is usually limited to how best to treat the mother.

Infant mortality is high among idiots and imbeciles, but many of them continue far into adult life. The object of medical science in civilized communities is to keep people alive. This principle has no exceptions and it applies also to low-grade defectives of all kinds. Nevertheless, it has not infrequently been argued that, on humanitarian grounds, a return to the methods of the Spartans is desirable, though of course modern society insists upon the term "euthanasia". The case for painless destruction of low-grade defectives has been ably set out by

Kennedy (1942), who claimed that it was justified by aesthetics, medicine, morals, convenience and common sense. In reply, the idiots' right to live was brilliantly pleaded by Kanner (1942). Not only are these low-grade defectives harmless, they are not responsible for their own condition; they can be happy and they can stimulate human feelings and parental love. By all canons of civilized society, they have a right to demand care and comfort even if they are unable to give adequate returns. The ability of a community to make satisfactory provision for its defectives is an index of its own health and progressive development; the desire for their euthanasia is a sign of involution and decay of human standards.

POSITIVE EUGENICS

As I have tried to demonstrate throughout this book, the broad problems of eugenics cannot be solved until the mode of action of natural selection on the human race is much more fully understood than it is at the present time. It may be relatively easy to point to genes which appear altogether bad; for example, those which make their possessors victims of epiloia or of Huntington's chorea. Even these may not be unfavourable in all circumstances. Carriers of "bad" genes may sometimes have compensating advantages.

The position is quite different when we try to identify "good" genes. The human types which are accepted by eugenists as desirable can be specified to some extent. Good general health, high resistance to disease, handsome physique and high fertility, coupled with such qualities as great intellectual ability, courage, honesty, compassion and steadfastness are all desired in the same individual. Nothing is known, however, about the actual genes which might form the basis for such qualities. All that is certain is that some of these qualities are to some extent inherited. Assuming that excellence in each quality is not incompatible with excellence in any other, it should be theoretically possible, as Galton (1869) believed, "to produce a highly gifted race of men by judicious marriages during several consecutive generations."

That evolution in civilized man was subject to a great variety of social agencies, which did not apply to animals and plants, was clearly understood by Galton. Subsequently, Pearson

(1909) after examining the same problems, asserted that civilization, by allowing the unfit to survive, was suspending the process of natural selection. It can be argued that the function of eugenics is to compensate for the biological errors of social life. This aim seems to underestimate the potentialities of biological adaptation. The human species is very variable and variation within the species is favourable for long-term survival; Fisher (1930) called this variance the "energy" of the species. Given sufficient energy, the human race should be able, even without the aid of eugenics, to adapt itself biologically to civilized life without risking extinction.

Practical positive eugenics depends first upon finding out the manner of inheritance of desirable qualities. If it should be discovered that they are mostly due to genes in homozygous form, then the traditional methods of establishing pure lines by inbreeding, used by animal fanciers, could be encouraged. A race of men might eventually be produced in which almost every individual had all the best qualities. Apart from the danger that such a group might be relatively infertile, its possibilities of further evolution would be greatly limited. Its facilities for adaptation to new environments would be weakened because the collectively desirable quality of variation would have been deliberately reduced.

If, on the other hand, desirable qualities should prove to be due to genes in heterozygous form, quite different methods of breeding would be favourable to their increasing prevalence. Maize is commonly grown from seed which is obtained from crossing two different pure lines, because the heterozygous plant grows more vigorously and produces more yield than either homozygous type. Whatever the system of mating, there is an upper limit to the total proportion of heterozygotes that can be formed at each generation among the offspring of a complete population. For a single pair of alleles, the maximal proportion of heterozygous offspring is two-thirds but, with more alleles, there can be more heterozygous types. In human genetics there are some indications of heterozygous vigour in the increased fertility of people with slightly less than the average amount of scholastic ability.

It is abundantly clear that, in the present state of knowledge concerning human genetics, the prospects of positive eugenics,

in the sense hoped for by Galton, are extremely narrow. Advances are continually being made in genetical science and in the problems of the relationship of genetical constitution to environmental stresses. Notwithstanding, even when the scientific knowledge of human heredity eventually becomes as complete as that of experimental animals and plants, the utmost caution will be required in its application. The central problem, of what types of human beings are required, involves an insight into the future which at present we do not possess. The ultimate aim will have to be to compromise between the maximal vigour of the phenotypic population and its maximal potentialities for the future.

Against this background, the study of mental defect will continue to hold an extremely important place in the fields of medicine, psychology and genetics. The idiot, in earlier times alternately despised as an outcast or venerated, now is seen as an integral part of the human race in its struggle for evolution and survival, unwittingly yielding information of the greatest value in the progressive understanding of the biological structure of the whole group. High-grade and borderline mental defect are phenomena which have come into prominence only since human life has become urbanized and industrialized. Civilized communities must learn to tolerate, to absorb and to employ the scholastically retarded and to pay more attention to their welfare. Subcultural mentality must inevitably result from normal genetical variation and the genes carried by the fertile scholastically retarded may be just as valuable to the human race, in the long run, as those carried by people of high intellectual capacity.

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APPENDICES

APPENDIX 1

Cranial Capacity and Intelligence Level in Adult Defectives—Males

Cranial Capacity	Intelligence Quotient										Total
	(0)	(10)	(20)	(30)	(40)	(50)	(60)	(70)	(80)	(90)	
2000 to 2099	—	—	—	—	—	1	—	—	—	—	1
1900 to 1999	—	—	—	—	—	—	—	—	—	—	—
1800 to 1899	—	1	—	—	—	—	—	—	—	—	1
1700 to 1799	—	1	3	1	1	—	—	—	—	—	6
1600 to 1699	2	2	1	1	5	4	2	—	2	1	20
1500 to 1599	—	9	9	7	8	10	9	8	1	2	63
1400 to 1499	2	11	16	14	14	25	21	17	3	2	125
1300 to 1399	2	16	12	18	16	26	27	10	6	—	133
1200 to 1299	3	8	8	3	10	16	5	6	3	—	62
1100 to 1199	1	7	4	3	5	5	1	—	—	—	26
1000 to 1099	—	—	—	—	1	—	—	—	1	—	2
900 to 999	—	—	—	—	—	—	—	—	—	—	—
800 to 899	—	1	—	—	—	—	—	—	—	—	1
Total	10	56	53	47	60	87	65	41	16	5	440

Cranial Capacity and Intelligence Level in Adult Defectives—Females

Cranial Capacity	Intelligence Quotient											Total
	(0)	(10)	(20)	(30)	(40)	(50)	(60)	(70)	(80)	(90)	(100)	
2000 to 2099	—	—	—	—	1	—	—	—	—	—	—	1
1900 to 1999	—	—	—	—	—	—	—	—	—	—	—	—
1800 to 1899	—	—	—	—	—	—	—	—	—	—	—	—
1700 to 1799	—	—	—	—	—	—	—	—	—	—	—	—
1600 to 1699	—	—	—	1	—	—	—	—	—	—	—	1
1500 to 1599	—	1	—	—	1	1	—	1	—	—	—	4
1400 to 1499	1	2	2	3	3	5	5	1	—	1	—	23
1300 to 1399	—	4	7	5	10	16	8	16	3	1	1	71
1200 to 1299	1	6	6	5	16	25	21	13	7	3	1	104
1100 to 1199	—	11	7	5	6	22	10	7	2	3	1	74
1000 to 1099	3	10	7	3	10	5	5	3	—	—	—	46
900 to 999	1	—	—	2	2	2	—	—	—	—	—	7
800 to 899	1	—	—	—	—	—	—	—	—	—	—	1
Total	7	34	29	24	49	76	49	41	12	8	3	332

(0) signifies the range 0 to 9, (10) signifies 10 to 19, etc. Correlation of male cranial capacity and intelligence quotient, $r = +0{\cdot}088 \pm 0{\cdot}047$.

Correlation of female cranial capacity and intelligence quotient, $r = +0{\cdot}176 \pm 0{\cdot}054$.

Cranial capacity is calculated from measurements, in millimetres, of length, l, breadth, b, and height, h, by the following formulae:

Cranial capacity for males $= (l-11)(b-11)(h-11) \times 0{\cdot}000337 + 406{\cdot}01$.

Cranial capacity for females $= (l-11)(b-11)(h-11) \times 0{\cdot}000400 + 206{\cdot}60$.

APPENDIX 2

APPROXIMATE MEAN HEAD MEASUREMENTS OF NORMAL SUBJECTS (Berry and Porteus, 1920)

	Year of life	Length	Breadth	Height
Boys . .	At birth	120	96	98
	1st	151	126	112
	2nd	166	130	116
	3rd	172	136	120
	4th	174	137	122
	5th	176	139	123
	10th	183±4	145±5	126±4
	15th	188±6	149±5	129±5
Girls . .	At birth	120	96	98
	1st	155	123	111
	2nd	164	129	115
	3rd	167	132	120
	4th	169	134	122
	5th	170	135	123
	10th	178±5	140±4	126±4
	15th	183±6	144±4	130±5

Measurements are in millimetres and standard deviations range from 4 to 6 mm.

APPENDIX 3

INTELLIGENCE QUOTIENTS OF SAMPLE OF INSTITUTIONAL DEFECTIVES (Colchester Survey, 1938)

Age in Years	Intelligence Quotient																					Total	Males	Females
	(0)	(5)	(10)	(15)	(20)	(25)	(30)	(35)	(40)	(45)	(50)	(55)	(60)	(65)	(70)	(75)	(80)	(85)	(90)	(95)	(100)			
(0)	—	1	1	1	—	—	—	—	1	1	—	—	1	—	—	—	—	—	—	—	—	6	5	1
(5)	3	5	2	5	7	7	7	5	4	3	1	1	2	2	3	—	1	—	1	—	—	59	36	23
(10)	5	5	17	25	17	10	6	9	8	10	18	14	18	9	6	4	3	—	1	—	—	185	112	73
(15)	6	6	21	13	17	5	19	8	7	21	17	26	27	15	20	10	1	2	2	—	—	243	125	118
(20)	—	4	13	14	10	6	14	5	10	18	15	21	25	12	19	10	8	9	4	—	—	217	126	91
(25)	1	3	9	9	5	14	10	10	9	26	24	34	30	14	11	8	6	4	1	4	2	234	119	115
(30)	1	1	3	8	3	10	2	6	10	12	17	19	14	8	7	5	2	3	2	1	1	135	73	62
(35)	—	1	4	5	1	9	5	5	9	4	7	8	6	1	7	4	1	—	—	—	—	77	42	35
(40)	1	—	4	2	4	2	1	2	3	4	5	5	6	3	2	—	—	—	—	—	—	44	23	21
(45)	—	—	4	4	2	2	3	—	1	1	1	4	2	1	2	2	1	—	—	—	—	30	18	12
(50)	—	1	2	2	1	5	—	2	3	1	5	1	—	1	1	—	—	—	—	—	—	25	15	10
(55)	—	—	2	1	2	1	2	—	2	—	1	1	—	—	—	1	—	—	—	—	—	13	8	5
(60)	—	—	2	—	—	1	—	—	—	—	1	1	—	—	—	—	—	—	—	—	—	5	3	2
(65)	—	—	—	—	1	—	1	—	1	—	1	—	—	—	—	—	—	—	—	—	—	4	3	1
(70)	—	—	—	—	1	—	—	—	—	—	1	—	—	—	—	—	—	—	—	—	—	2	2	—
(75)	—	—	—	1	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	1	—	1
Total	17	27	84	90	71	72	70	52	68	101	114	135	131	66	78	44	23	18	11	5	3	1280	710	570
Males	10	15	54	60	46	42	45	32	33	49	61	73	69	32	42	19	11	9	6	2	—	710	—	—
Females	7	12	30	30	25	30	25	20	35	52	53	62	62	34	36	25	12	9	5	3	3	570	—	—

(0) signifies the range 0 to 4, (5) signifies 5 to 9, etc.

APPENDIX 4

NUMBER OF PATIENTS RESIDENT IN MASSACHUSETTS STATE SCHOOLS FOR THE MENTALLY DEFECTIVE, compiled by Dayton (1939)

I.Q.	Males	Females	Total
0– 9	174	164	338
10–19	301	222	523
20–29	317	300	617
30–39	341	315	656
40–49	512	508	1020
50–59	461	549	1010
60–69	316	445	761
70–79	103	164	267
80–89	14	24	38
90+	2	6	8
Total . .	2541	2697	5238

APPENDIX 5

TABLE SHOWING PERCENTAGE OF FIRST-COUSIN PARENTAGE (F) * FOR CASES WITH RARE RECESSIVE DEFECTS

Case Frequency	Gene Frequency	Frequency of First-cousin Matings in the General Population (α)		
		0·5 per cent.	1·0 per cent.	2·0 per cent.
q^2	q	(F)	(F)	(F)
1/1,000	1/32	1·0	2·0	3·8
1/10,000	1/100	3·0	5·9	11·1
1/100,000	1/316	9·0	16·5	28·3
1/1,000,000	1/1,000	23·8	38·4	55·6

$$*(F) = \frac{100\alpha}{\alpha + 16q}$$

N.B. If the defect did not decrease chances of parenthood, the correct formula would be

$$(F) = \frac{100\alpha}{\alpha + 16q\,(1-\alpha)/(1+15q)}$$

APPENDIX 6

Correlation Tables for a Metrical Character due to a Single Autosomal Gene Pair

(i) Parent and Child

Genotype	*aa*	*Aa*	*AA*	Total
AA	—	p^2q	p^3	p^2
Aa	p^2q	pq	p^2q	$2pq$
aa	q^3	pq^2	—	q^2
Total . .	q^2	$2pq$	p^2	1

(ii) Sib and Sib

Genotype	*aa*	*Aa*	*AA*	Total
AA	$\frac{1}{4}p^2q^2$	$p^2q-\frac{1}{2}p^2q^2$	$p^3+\frac{1}{4}p^2q^2$	p^2
Aa	$pq^2-\frac{1}{2}p^2q^2$	$pq+p^2q^2$	$p^2q-\frac{1}{2}p^2q^2$	$2pq$
aa	$q^3+\frac{1}{4}p^2q^2$	$pq^2-\frac{1}{2}p^2q^2$	$\frac{1}{4}p^2q^2$	q^2
Total .	q^2	$2pq$	p^2	1

Measurements, corresponding to the genotypes *AA*, *Aa* and *aa*, can be denoted by x, y and z, respectively. If the heterozygote *Aa* is perfectly intermediate, we put $x=1$, $y=\frac{1}{2}$ and $z=0$ and calculate the product moment correlation; for both tables, (i) and (ii), the result is exactly 0·5. If *A* is completely dominant and *a* completely recessive, $x=y=1$ and $z=0$; the correlation in table (i) becomes $\frac{q}{1+q}$ and that in table (ii) is $\frac{1+3q}{4(1+q)}$.

APPENDIX 7

Table of Numbers required in Factorial Test for Sibships containing Recessive Abnormalities

S=number of children in a sibship, including an affected member.

$S/4[1-(\frac{3}{4})^S]$=expected apparent number affected in a sibship of size S, on the supposition that one-quarter of all children in such families are affected. Note that, in large sibships, the expected number closely approaches one-quarter.

K_S=variance of expected number of affected sibs in sibships of size S.

S	$S/4[1-(\frac{3}{4})^S]$	K_S
1	1·000	0·000
2	1·143	0·122
3	1·297	0·263
4	1·463	0·420
5	1·639	0·592
6	1·825	0·776
7	2·020	0·970
8	2·222	1·172
9	2·433	1·380
10	2·649	1·592
11	2·871	1·805
12	3·098	2·020
13	3·329	2·335
14	3·564	2·446
15	3·801	2·658
16	4·041	2·867
17	4·282	3·074
18	4·526	3·279
19	4·770	3·481
20	5·016	3·682

APPENDIX 8

Intelligence Quotients in Special Types of Institutional Defectives

Associated Disease	Number of Cases			Mean I.Q.	Standard Deviation of I.Q.
	Males	Females	Total		
Neurofibromatosis	4	2	6	67·8	9·5
Psychoneurosis	69	63	132	63·8	19·1
Craniofacial dysostosis	2	1	3	54·0	25·7
Post-encephalitic	10	11	21	53·9	26·6
Psychosis	43	29	72	48·2	24·0
Post-traumatic	19	4	23	45·0	24·5
Congenital syphilis	23	27	50	42·7	19·8
Epilepsy	69	50	119	41·2	22·4
Congenital hemiplegia	8	3	11	36·4	14·4
Choreoathetosis	6	5	11	35·5	14·9
Hydrocephaly	5	1	6	32·0	19·8
Hypertelorism	2	5	7	31·7	18·2
Spastic diplegia	30	25	55	29·1	21·0
Acrocephaly	11	6	17	28·6	19·9
Microcephaly	18	5	23	24·6	14·8
Mongolism	41	22	63	22·8	7·9
Phenylketonuria	21	26	47	19·9	12·6
Epiloia	2	3	5	11·8	10·7
Sample containing all types of patient (Appendix 3)	710	570	1280	40·4	25·6

APPENDIX 9

Test for Linkage of the Genes responsible for Two Uncorrelated Segregating Characters, $\overline{P}$ and $\overline{T}$

All known sib pairs are grouped into four classes according to presence or absence of $\overline{P}$ and $\overline{T}$; $\bar{p}$ indicates absence of $\overline{P}$ and $\bar{t}$ indicates absence of $\overline{T}$.

Class	Description	Type of Sib Pair	Number of Pairs
(i)	Like in $\overline{P}$ and like in $\overline{T}$	$\overline{P}.\overline{T}$ with $\overline{P}.\overline{T}$ $\overline{P}.\bar{t}$,, $\overline{P}.\bar{t}$ $\bar{p}.\overline{T}$,, $\bar{p}.\overline{T}$ $\bar{p}.\bar{t}$,, $\bar{p}.\bar{t}$	a
(ii)	Like in $\overline{P}$ and unlike in $\overline{T}$	$\overline{P}.\overline{T}$ with $\overline{P}.\bar{t}$ $\bar{p}.\overline{T}$,, $\bar{p}.\bar{t}$	b
(iii)	Unlike in $\overline{P}$ and like in $\overline{T}$	$\overline{P}.\overline{T}$ with $\bar{p}.\overline{T}$ $\bar{P}.\bar{t}$,, $\bar{p}.\bar{t}$	c
(iv)	Unlike in $\overline{P}$ and unlike in $\overline{T}$	$\overline{P}.\overline{T}$,, $\bar{p}.\bar{t}$ $\bar{P}.\bar{t}$,, $\bar{p}.\overline{T}$	d

The recombination value, x, is given by the formula,

$$\frac{1-4x}{K}=\frac{ad-bc}{(b+d)(c+d)}\pm\sqrt{\frac{(a+b)(a+c)}{(b+d)(c+d)(a+b+c+d)}}$$

The crossing-over value is $\frac{1-\sqrt{(1-4x)}}{2}$

When one of the characters is due to a rare recessive gene, e.g. phenylketonuria, $K=3$.

APPENDIX 10

Mental Status of Parents of 1280 Patients (Colchester Survey, 1938)

Classification	Description	Number of Patients	Sexes of Parents	Number of Parents in each Mental Grade						Percentage of Parents known to be Defective
				S	N	D	F	Imb.	Unascertained	
By sex of patient	Male	710	Male	6	580	69	22	0	33	3·1
			Female	2	521	103	65	2	17	9·5
	Female	570	Male	3	427	80	26	1	33	4·7
			Female	0	380	99	78	1	12	13·9
By mental grade of patient	Borderline	179	Both	1	255	63	18	0	21	5·0
	Feeble-minded	448	,,	3	580	159	106	3	45	12·1
	Imbecile	433	,,	4	687	92	55	1	27	6·5
	Idiot	220	,,	3	386	37	12	0	2	2·7
By clinical type of patient	Mongolism	63	Both	0	119	5	2	0	0	1·6
	Endocrine disorder	88	,,	2	135	24	9	0	6	5·1
	Congenital syphilis	50	,,	0	75	9	6	0	10	6·0
	Neurological lesion	128	,,	3	230	13	8	0	2	3·1
	Skeletal malformation	142	,,	1	227	35	12	1	8	4·6
	Miscellaneous abnormalities	87	,,	1	141	20	9	0	3	5·2
	Idiopathic epilepsy	210	,,	2	321	52	29	0	16	6·9
	Non-epileptic mental disorder	204	,,	1	293	69	26	0	19	6·4
	Residual group	308	,,	1	367	124	90	3	31	15·1
Total of each classification	All patients	1280	Both	11	1908	351	191	4	95	7·6

S=Superior; N=Normal or average; D=Dull or borderline; F=Feeble-minded; Imb.=Imbecile

APPENDIX 11

COMMENTARY ON RECENT LITERATURE

GENERAL PROBLEMS

The relativity of our judgments about mental capacity and their dependence upon social valuation have been again stressed by Lewis (1951). Nevertheless, for studying the basic problems of causation of defects, mental measurement is essential. A survey of the sibs of defectives, reported by Roberts (1952), tends to confirm the view that, among the feeble-minded, the genetical factors influencing intelligence level are multifactorial and additive, whereas, among the low-grade cases, other causes are most prominent. It was thought possible to distinguish between the two groups fairly clearly on the basis of family history, though not in terms of mental grade of the patient. The question as to what tests give the best indication of mental qualities desirable in a civilized community is still unsolved. Tizard, O'Connor and Crawford (1950) have analysed the different factors which are detected by intelligence tests in high-grade patients and have shown the great variety of pattern found in different individuals. The use of any one test is bound to lead to biased diagnosis. An important commentary on this problem comes from the work of Tryon (1942) on the abilities of rats. Although it is possible, by selective breeding, to produce strains of animals which are specially gifted for one particular task, such hereditary abilities are markedly specific. Inherited ability to traverse one type of maze may not correlate at all with that for another type.

Among general surveys of mental and physical traits that of Dewan (1948) is of particular interest. The proportions of well-adjusted and psychopathic subjects were ascertained at different levels of performance on the Canadian Army M intelligence test. There was a definite association between high test level and emotional stability except, perhaps, among the very highest scorers. A part cause of the main effect may be that serious mental disturbances greatly reduce efficiency on tests. Richards (1951) has shown that cases of schizophrenic psychosis of early onset, occurring on a basis of normal intelligence, can become indistinguishable, on casual observation, from imbeciles and idiots, and are often so certified.

A contribution to the ascertainment of the relation between birth weight and intelligence has been made by Roberts and Asher (1949), who showed that birth weight was, on the average, not lower but was more variable in backward children than in the general population. Fang (1949) has brought forward evidence that the hands of undifferentiated defectives, on the average, differ from normals in respect of certain specified dermal ridge counts. An attempt to apply the Kretschmer system of typology has been made by Duis (1952) who explained that a large number of "endogenous" cases were of the "dysplastic" type.

Efforts have been made to answer by direct measurement the question as to what will happen to intelligence level in a community where children with low I.Q. have more brothers and sisters than children with high I.Q. Along with other evidence of negative association between fertility and intelligence, this idea has motivated several enquiries comparing mean I.Q. of children at the present time with that of other children, tested in the same place in former years. A most substantial investigation was carried out by the Scottish Council for Research in Education (1949), the results of which can be summarized thus. In 1932, 87,498 children were given an intelligence test and their mean score was 34·5 points with a standard deviation of 15·5 points; in 1947, children of the same age groups as before, numbering 70,805, had a mean score of 36·7 with a standard deviation of 16·1. Over 1000 children, sampled at random, were given the Binet test in the two surveys and here there was no appreciable change in the mean. Family size had a correlation with intelligence measurement of −0·28, and, consequently, it is generally believed that the observed constancy of mental level, or even improvement, is a temporary effect due to environmental factors. Behind this façade, a decline is said to be in progress. Cattell (1950) and Emmett (1950) carried out surveys of comparable nature in other areas and were also unable to detect any deterioration.

The possibility that the observed stability may be due to genetical equilibrium (Penrose, 1950) might be further explored. Although there is evidence that moderately low intellectual level is associated with increased fertility, the same is not true for mental illness. As for mental defect, there is marked assortative mating for mental disturbance (Penrose, 1944), but it is doubtful whether any type of psychosis is associated with increased fertility. Undoubtedly schizophrenia reduces family size (Essen-Möller, 1935). The principle, that equilibrium can be easily reached in a population if the heterozygote is slightly more fertile than either homozygote, is an important one (Gowen, 1952). Experimental evidence shows that the carriers of a lethal recessive trait can often be fitter than the rest of the normal population. Thus the search for signs of increased fertility in carriers

of recessive traits, or among bearers of dominant abnormalities, is worthy of attention in the mental as well as the physical sphere.

SEROLOGY

Although a great deal more has been learnt in recent years about the nature of various types of blood antigens (Race and Sanger, 1950) and their distribution in populations (Mourant, 1951), the relationship of these factors to mental deficiency still requires to be further clarified. The early suggestion, that antigenic incompatibility of the foetus with its mother may be a cause of non-specific mental defect in the offspring, has received little support from critical surveys. Pantin (1951) found no evidence of excess of cases of Rh incompatibility in a large series of defectives studied in England; the result is in agreement with the findings of Böök, Grubb, Engleson and Larson (1949) based upon a Swedish population of defectives. An enquiry made by Gilmour (1950) led to the same conclusion; he found incompatibility between mother and foetus even less common among defectives than in the general population. He pointed out that there was, nevertheless, good evidence for the assumption that a small number of cases following kernicterus are due to Rh incompatibility. This is to be expected as a corollary to the work of Levine, Katzin and Burnham (1941) locating the origin of haemolytic disease of the newborn in maternal immunization. It is not yet certain in what proportion of institutional cases the defect is due to this cause. Böök and others found only three cases of Rh-encephalopathy among 977 examined. But by no means all suspicious cases, i.e. those with athetosis and a history of neonatal jaundice, show evidence of Rh incompatibility on blood typing. Other antigenic systems may be involved and recent surveys of haemolytic disease of the newborn have confirmed the importance of the ABO system in this connection (Shamir and Gurevitch, 1953).

The systematic blood typing of patients with specific diagnoses can be undertaken with more than one aim in view. Family data on a series of over 100 mongol imbeciles were collected by Lang-Brown, Lawler and Penrose (1953). These results were useful for twin studies as well as for exclusion of association between the disease and any known antigen. Incompatibility was found to be rather less evident than in the general population, a phenomenon shown also by other surveys of mongolism and possibly connected with the relatively late maternal ages and birth ranks of these cases. Further data on the possibility of linkage between the ABO locus, the MN locus and phenylketonuria (Penrose, 1951*a*) leaves the matter still undecided. The investigation of hereditary ataxia by Schut (1951),

from a similar point of view, was also unrewarding. A linkage study of Huntington's chorea (Leese, Pond and Shields, 1952) gave negative results; and, at the moment, the prospects of using encephalography, for detecting as yet unaffected carriers of the gene, seem better than those of using genetically linked traits. However, it is encouraging that, in fields unconnected with mental defect, two examples of linked autosomal genes have recently been discovered. The loci for the Lutheran and Lewis antigens have been shown to be close together by Mohr (1951) and those for elliptocytosis and the Rh complex by Lawler (1953).

SINGLE GENE EFFECTS

A thorough examination, in Denmark, of families selected by the presence of cases of epiloia (Borberg, 1951) supports the view that many of them arise by fresh mutation; the disease is considered to be an essentially different entity from neurofibromatosis though the genetics may be similar.

Karabanow (1950) recorded a family in which oxycephaly, without mental defect but connected with furrowed scalp in the frontal region, appeared as an irregularly dominant character; and in which a pair of monozygotic twins were both affected. Evidence that achondroplasia is not infrequently found associated with feeblemindedness has been collected by Morris and MacGillivray (1953). A pedigree of a case of naevoid amentia recorded by Kirman (1950) suggests that some examples of congenital plegia in relatives might have been abortive forms of the same condition.

The fact that the occurrence of recessive traits is facilitated by parental consanguinity has led Sutter and Tabah (1952) to evaluate variations in the stillbirth rate in different districts of France in genetical terms. A correlation between stillbirth rate and consanguinity was found and this possibly indicates that many of the infant deaths were due to lethal recessive genes.

Of special interest in the study of known recessive traits is the recent work on phenylketonuria. Clinical studies have included measurement of the degree of hair colour dilution (Cowie and Penrose, 1950) and a great many biochemical investigations. Jervis (1947) showed fairly convincingly that the main error is inability to produce tyrosine from phenylalanine. Since then, by testing liver substance obtained at autopsy, Jervis (1953) has demonstrated that an enzyme, normally present and capable of performing this change, is absent in phenylketonuria. Thus the fundamental defect is absence of a critical enzyme. This produces direct effects, like raised phenylalanine level in the blood and excretion of phenylpyruvic acid in the urine and in the sweat, and less direct effects, such as impaired

cerebral function, reduced growth of the head and dilution of hair colour (Penrose, 1951*b*).

Other recessive traits reported upon recently include mental defect of high-grade type with cataract and cerebellar ataxia (Garland and Moorhouse, 1953) in the offspring of first cousins and spastic diplegia associated with any grade of defect (Böök, 1949). It is clear that the recessive types of spastic diplegia must be carefully separated from those due to other causes. Those in which the main feature is athetosis seem to be usually attributed to birth injury. Richards (1950) attributes cases of athetosis with deaf mutism to trauma or to antigenic action.

The analysis of the biochemical effects of a gene is a most promising field for research (Harris, 1953) for here is a meeting place between genetics and medicine. Congenital methaemoglobinaemia is likely to be due to a recessive gene; it is familial and has been shown to result from absence of a critical enzyme (Gibson, 1948). In some cases cure has been achieved by feeding on ascorbic acid (Deeny, Mundrik and Rogan, 1943); but when the disease is associated with mental deficiency, as is sometimes the case, no intellectual improvement has been thus obtained. A very difficult branch of this subject concerns the lipoidoses (Thannhauser, 1950). Some types of gargoylism can probably be counted among these even though it is not always possible to demonstrate the presence of abnormal lipoids, as in the case described by Millman and Whittick (1952). Five male cases occurred in one family, showing sex-linked or sex-limited inheritance. The clinical appearance was quite typical of gargoylism in each case but there were no corneal opacities.

A study by Sjögren and Larsson (1949) on microphthalmos and anophthalmos showed that the sex-linked (or limited) type can only occur very rarely. Usually the sexes are equally affected and a very irregular dominance often occurs. In rather more than one-third of the cases there is mental retardation. Sex-linked (or limited) congenital hydrocephalus has been described by Bickers and Adams (1949).

ENVIRONMENTAL CAUSES

The effects of irradiation on the germ cells, and the production of abnormalities in the offspring by new mutations thus induced, have recently been studied from several points of view. Haldane (1947) calculated the total number of deaths from recessive mutations which might result from an atomic explosion. These would be spread over very many generations and it appears that they would form only a small fraction of the number of immediate deaths. The load of mutations (Muller, 1950) is in danger of being increased by the

common use of X-rays in medicine and by occupational hazards in specific industries (Haddow, 1952). An increased mutation rate would not, however, necessarily lead to deterioration of the human stock: it might merely lead to more rapid evolution.

Information on the aetiology of congenital malformations has been obtained by Record and McKeown (1949) who found an incidence rather lower than that given by Malpas and agreeing roughly with Murphy's. An increased risk for anencephaly and spina bifida in first births was noted and late maternal ages were in excess for hydrocephaly. Harelip and cleft palate also showed association with late maternal age (MacMahon and McKeown, 1953). In the case of anencephaly a seasonal variation was observed; cases were born most frequently in December and least frequently in June (McKeown and Record, 1951). In spite of the evidence of environmental influence and the low familial incidence, Böök and Rayner (1950) believe that a general predisposition to anencephaly exists. The genetical position is somewhat similar to that of twinning where there is evidence of maternal effects related to age (Duncan, 1866; Dahlberg, 1926) on the one hand and evidence of very low familial incidence on the other (McArthur, 1951). It seems that the genetical dispositions involved are very common but rarely manifested.

Experimental production of abnormalities in laboratory animals is becoming an accepted method of enquiry in this field. Giroud and his colleagues have shown that vitamin lack is an important factor and have measured the threshold of concentration required in the mother. Malformations occurred in rats, for example, when maternal vitamin B_2 sank to one-third of its normal level (Giroud, Lévy, Lefebvres-Boisselot and Ettori, 1951). Severe degrees of maternal anoxia have been shown by Ingalls (1950) to produce foetal abnormalities.

Injury at birth is an important cause of mental defect in a few cases (Penrose, 1949*a*); they are difficult to diagnose with certainty because the history is rarely sufficiently detailed. Malzberg (1950) has shown that there is an overwhelming predominance of first-born children in cases where birth trauma is alleged to be a significant cause. Postnatal injuries are also undoubtedly important in special cases (Boldt, 1948) but they probably are less often causal than infections. Whooping-cough is blamed by Levy and Perry (1948). Fortunately toxoplasmosis is only a very rare cause though Burkinshaw, Kirman and Sorsby (1953) have shown that defectives, like the general population, develop immunity to the parasite as they grow older. A family study by Herndon and Jennings (1951) indicates that the susceptibility to poliomyelitis is partly genetically deter-

mined: so also may be the liability to infections which lead to severe loss of mental powers.

MONGOLISM

The incidence of mongolism diagnosed at birth has been ascertained recently in England by Carter and MacCarthy (1951) who made a general estimate of one in 620. Owing to a very high infant death rate the number in the population at all ages drops to a figure of rather less than one in 3500 (Penrose, 1949*b*). There is some evidence that in familial cases the mean maternal age is lower than is usual for mongols, especially when the relationship between them is through the mother (Penrose, 1951*c*) as, for example, in affected maternal half-sibs. Many authorities doubt that there is any genetical background worthy of consideration and emphasize the importance of intrauterine environment and, particularly, the state of the mucosa (Engler, 1952). Øster (1953) found six new cases of mongolism among about 1750 sibs, born alive, of 513 propositi. He considered this (erroneously, as I think) to be an insignificant increase as compared with the general population incidence at birth. On the other hand, Lelong, Borniche, Kreisler and Baudy (1949) record a well-documented case of a mongol imbecile mother who gave birth, at the age of 30, to a male mongol imbecile child. Complementary to this case is that of Sawyer (1949), who described a female child aged 13, perfectly normal mentally and physically, whose mother is a mongol imbecile now in an institution. These are the only properly authenticated examples of offspring from affected mothers and the finding that one child out of two is affected is a very unlikely event on a random hypothesis, i.e. less than one chance in 300. It seems probable that mongolism has a genetic basis very common in the population. Some mothers can be more predisposed than others and some zygotes more likely to be affected than others. By analogy with the genetics of a type of tooth defect in mice (Grüneberg, 1951) mongolism may be a threshold effect produced by more than one gene. Perhaps a kind of all-or-none reaction retarding development might occur when the summation of genic and environmental effects in mother and foetus reaches a limiting concentration. Mittwoch (1952) has examined the chromosomes of a male case and found them to be normal in appearance, which does not support the suggestion that translocation is the cause (see p. 77).

The clinical aspect of the syndrome of mongolism continues to attract attention. A study by Lowe (1949) on the ocular peculiarities indicates that these are among the most characteristic features of the disease; practically every case shows defects of the iris with white fibrous nodes, sometimes known as Brushfield's spots. Confirmation

of previous descriptions of anomalous leucocytes has been provided by Shapiro (1949). The dermal ridge counts of the finger-tips have been studied by Holt (1950) and a remarkable lack of variation, as compared with normals, in the total count was observed. Fang (1950) found that third interdigital palm patterns were especially frequent in mongol subjects and that the close relatives seemed also to have a raised incidence of the trait. Similarly an increased incidence of distal axial triradius has been found in sibs and parents of mongols (Penrose, 1949*c*).

TREATMENT

The search for new methods of therapy and the revaluation of existing methods (Wallin, 1950) continue to increase in scale. Attention is being given to problems of training from the point of view of preparing the patient to be a useful citizen outside, rather than inside, the institution by using workshops as experimental preliminaries to subsequent gainful employment (Tizard, 1953; Rockower, 1953). The occupational adaptation of high-grade patients has been studied intensively by Tizard and O'Connor (1952). Very careful testing is recommended so that the subject's aptitudes as well as his latent abilities may be fully recognized. For this purpose the Wechsler-Bellevue test, which correlates highly with Binet I.Q. (McKenzie, 1951), has been much used. It is well suited for adult patients but, according to Alderdice and Butler (1952), although it tests more special factors than the Stanford-Binet, its diagnostic signs are unreliable. Tizard also has emphasized the importance of psychiatric treatment as an adjunct to manual or intellectual training and he recommends using group therapy. It is clear that the emotional state is an important factor in success or otherwise of educational efforts (Kanner, 1952), and that the atmosphere of a well-run institution can be conducive to significant improvements in mental ability as measured actually by standardized tests (MacMahon, 1952).

Though the initial enthusiasm for glutamic acid administration has subsided, several favourable reports have continued to appear (Quinn and Durling, 1950*a*, *b*; Foale, 1952) though it is not claimed that more than a slight improvement is to be expected. Weil-Malherbe (1949) attributed the stimulating effect to an adrenergic action which might be produced equally well by other aminoacids. However, Milliken and Standen (1951), on the basis of a well-controlled investigation, maintain that no effect at all is produced by glutamic acid treatment. Another interesting attempt at generalized cure has been unsuccessful, namely, the use of a preparation obtained from *celastrus paniculata*, used for many years

in India as a mental stimulant (Morris, MacGillivray and Mathieson, 1953). On the other hand, many treatments concerned solely with physical wellbeing have proved to be most valuable as, for example, the use of calcium fluoride for controlling dental caries in children (Chatham, 1949). Many dietetic experiments have been carried out on phenylketonuric patients, with the object of keeping the phenylalanine level in the body as low as possible, on the assumption that this substance is toxic in excessive quantities. Marked improvement in the mental state of a patient, aged 2, when fed on a phenylalanine-free diet, was reported by Bickel, Gerrard and Hickmans (1953).

In a very different field, Benda (1953) records the effects of treating mongol imbeciles by oral doses of pituitary hormone. The preparation used contains a large amount of growth hormone and seems undoubtedly to have had some effect in increasing the size of the patients to whom it was fed. A definite increase in mental powers was also noted though the prospects of anything resembling cure still seem remote.

Some remarkable results were recorded by Krynaw (1950) using a method of radical removal of the diseased cerebral hemisphere in cases of infantile hemiplegia. In twelve cases the operation initiated marked improvement in personality and a lessening of spasticity. Penfield (1952) pointed out that this treatment was an extension of earlier operations in which focal lesions causing epilepsy had been removed. He considers, moreover, that the radical methods of hemispherectomy are not usually necessary. Cases must be very carefully selected and when abnormal brain tissue can be removed considerable benefit can result. After successful hemispherectomy there follow (i) reduction of epileptic seizures, (ii) improved mental functioning and social behaviour, and (iii) freedom from spasticity. Experience with the treatment in defectives with hemiplegia shows that intelligence level is not altered but that behaviour becomes more cooperative. An entirely different experimental type of treatment is the attempt to restore function to damaged areas of the brain by increasing the arterial supply by surgical means (Beck, McKhann and Belnap, 1950); the results are alleged to have been favourable in certain cases.

The advocates of sterilization as the standard method of preventive treatment welcome the gradually increasing use of this measure in numerous areas of the United States of America (Butler, 1951). A carefully compiled evaluation of the results of applying such methods in North Carolina has been set down by Woodside (1950). Between 1929 and 1947, 349 males and 1477 females had been sterilized, 58 males castrated and 17 females ovariectomized. In spite

of numerous legal safeguards, the procedure leaves something to be desired. The measures are far more frequently applied to defectives than to any other class of case. Although allegedly voluntary, the patient who is faced with the alternatives of sterilization or institutional confinement can hardly be said to be a free agent. Moreover, since the number of mentally deficient people in North Carolina is alleged to be 71,000, the sterilization of 100 cases each year is unlikely to have any eugenic effect even if the crude assumption is true that like breeds like. The main value of these laws is to ease the burden of parenthood for those who find it too great.

A new approach to the whole problem of negative eugenics is being made by the experimental use of oral contraceptives. Among the possible methods of preventing fertilization examined by Pirie (1952) the most ingenious are those which act by inhibiting hyaluronidase, the enzyme which normally enables the sperm to get through to the ovum. Experiments on a volunteer population with a harmless substance, phosphorulated hesperidin, by Sieve (1952) have provided a promising start on this problem. The time may not be very distant when conception during any specified period can be prevented simply by a dose taken by mouth. Such a treatment could be used by people of low mental capacity much more easily than the methods which are recommended at birth-control clinics at the present time. They would be preferred greatly to sterilization both on the principles of humanity and of expediency.

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