

*The Physical Basis of Mental Disease.*<sup>(1)</sup> By IVY  
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IN bringing forward some evidence which would point to the biological course followed by some forms of nervous disease to be considered, I would first of all accept as a working hypothesis two generalisations which apply to all forms of disease. The first of these generalisations is that there is essentially no difference in kind between a physiological and a pathological process. The distinction is an arbitrary one; the course of disease is distinguished from that of health only in so far as it tends to compromise the continuation of a more or less perfect adaptation between the organism and its surroundings. There is no tendency in Nature either to kill or to cure; she is absolutely impartial as to the result of a conflict between organisms and a host; and it is a matter of complete indifference to her as to whether toxins are eliminated or not. In the same way diseases of the mind are the manifestation of a perfectly natural relation of the organism, such as it is, to the environment. If the mental processes are abnormal, it goes without saying that the brain must be acting abnormally whether the stimuli to abnormal action originate in the brain itself or in some other part of the body. For example, if a child with pneumonia be suffering from delirium and hallucinations, as is not infrequently the case, this must be considered a perfectly natural outcome of the relation of the brain to its environmental stimuli outside and inside the organism. The actual stimuli may originate in the intestine from masses of undigested food and the stimuli may play on the brain rendered hypersensitive by the toxins from the lungs; the process and its manifestations, as well as the final outcome, are matters in which nature plays an impartial part. It cannot be admitted that there is any form of nervous disease which does not come under this generalisation. It has been argued by some authorities that because insidious forms of insanity are marked only by the slightest variation from the normal course of mental life, and that because the mental abnormalities are only modifications, and often easily explainable modifications, of normal mental processes, that the so-called insanity originates in these processes, and not in the material substratum of the organism.

The fallacy of such an interpretation is obvious; it is tantamount to saying that slight albuminuria is the cause underlying early disease of the kidneys, or that a slight œdema may have something to do with the origin of circulatory disease. It is only natural that in the milder forms of mental disease the abnormal manifestations of brain activity should resemble normal mental processes; and even in the most advanced forms of mental disease there must be a close resemblance between abnormal ideation and conduct and perfectly normal ideation and behaviour. Even in advanced cases of Bright's disease the urinary elimination is more normal than abnormal; the abnormal constituents do not differ so much in kind as in degree from those of urine from healthy kidneys. It is not to be expected that in kidney disease bile or some other substance foreign to the organ would be the chief constituent of the eliminated fluid. The signs of insanity in any given case are the natural products of normal brain action mingled with the products of abnormal action. This does not, of course, preclude the possibility that under certain circumstances these abnormal products, such as delusions, hallucinations and perverted conduct, may not themselves be the direct stimuli to further abnormalities. The suicidal character of pathological processes is well seen in other organs of the body. A diseased heart, for example, is its own worst enemy; it not only fails to supply sufficient nutrition to the rest of the organism, but it starves itself by its inability to contract and expand properly, thereby increasing its own weakness. In the same way, certain phenomena of abnormal brain processes are in all probability due to the recoil on the brain of its own abnormal products in the matter of ideation and conduct.

The second generalisation which I would put forward as a working hypothesis is that in mental disease, as in all other forms of disease, diathesis is a factor which is of no practical importance from the point of view of eliciting ætiology. What does diathesis really mean? A patient with a "bad family history" comes under observation, and with a feeling of satisfaction as regards the cause of the disease it is concluded that here is a case of the nervous diathesis. But when asked what the diathesis means, the only answer to be obtained is that it is a habit of body, a constitutional tendency, something that is hereditary. Further than that no progress is made, and it

ultimately appears that to apply the term "diathesis" in the elucidation of a case is simply to use this technical term to say that the patient is suffering from the particular disease because it is assumed that apart from the diathesis the disease would not have occurred. A hundred people drink milk from a typhoid-infected source, and presumably from pooled milk; a half or a third of these contract fever. It is no explanation, although it is a fact, that these people have contracted the fever in virtue of a peculiar constitutional proclivity termed "diathesis." Those who have escaped have done so also in virtue of a peculiar tissue tendency called immunity. Some of the evidences of immunity called anti-bodies can be recognised, but no evidence of diathesis has so far been forthcoming. Is there in mental disease any evidence that diathesis throws the faintest light on the ætiology of any one type of insanity? Except in so far as tissue proclivity is not infrequently inherited, this question must be answered in the negative. That certain individuals are predisposed by their natural constitution to gout, rheumatism, and other forms of disease is a well-known fact, and that this predisposition is inherited is also generally accepted, but in addition to the predisposition there must always be a determining factor arising *de novo* in every case. The same thing applies to the part played by heredity in nervous diseases. The disease itself is practically never inherited. There is no evidence that mental disease is inherited more frequently than polydactylism. What is inherited is the diathesis, which by itself can never produce nervous disease; it always requires the addition of some new environmental factor. Thus diathesis could only be an important factor in determining the ætiological forces in the production of a pathological state if it could be shown that certain forms of the same disease could occur in which diathesis does not play a part. When, for example, it is said that diathesis is a factor in the incidence of general paralysis, it is at the same time meant that every case of general paralysis has the diathesis, or if not, how can the one class be distinguished from the other? And it must be admitted that if a case cannot occur without the diathesis, then diathesis is a negligible factor in estimating the ætiological forces in the disease so long as it remains only a term representing no physical or chemical entity in the form of a reaction.

The emphasis laid on heredity in nervous diseases has arisen from a comparison between heredity and congenital or develop-

mental abnormalities. Congenital nervous disease is common ; it is due to malformation in the morphological conformation of the brain or to intra-uterine disease. The most frequent cause of such conditions is syphilis, although it is probable that a variety of material conditions may lead to the acquisition on the part of the embryo of a nervous taint or disturbance. In any case it is necessary to bear in mind that whereas congenital disease of the brain is not infrequent, hereditary disease is a rarity.

Having cleared the ground of these considerations let us examine the phenomena in two types of insanity to see what relationship exists between brain degeneration and mental disease, and what guidance such a relationship affords in the interpretation of the processes underlying the diseases. The diseases to be considered are dementia præcox and general paralysis.

The first difficulty which presents itself in any such investigation arises from the fact that psychology, on which the science of psychiatry is largely founded, dates back to the times of the Greek philosophers, whereas our knowledge of the functions of the brain is of comparatively recent origin. The analysis and correlation of mental phenomena and brain phenomena have not developed *pari passu*, the result being that in mental science we employ terms and standards which possess little or no significance when we come to investigate the functions of brain, normal or abnormal, from the point of view of anatomy and physiology. It is true that, anatomically, the sensory spheres have been more or less sharply demarcated, and that experimental and clinical observation have gone far in this direction to procure an anatomical basis for certain mental phenomena. But the mental phenomena with which the alienist deals are for the most part on a different plane. They have reference to social conditions, they involve the complex participations of different portions of the brain correlated by association fibres. There is no centre, one may well suppose, for attention, sense of obligation and duty, or most of the attributes of responsible conduct ; yet conduct and its manifestations form the data on which the alienist bases his practical conclusions. These higher manifestations of the mental life have their anatomical basis in the development and education of association strands or paths linking up a great variety of brain centres, differing in quality and in number in

different individuals. The existence of such correlating and interconnecting fibres has been definitely determined by researches in embryology and comparative anatomy, although their exact relationship to mental phenomena is still for the most part highly conjectural. It is, however, most probable that a considerable proportion of mental cases owe their origin to an actual interference with, or destruction of, these association fibres, which appear late both ontogenetically and phyllogenetically. The complicated movements of walking or dancing depend on a perfect correlation of structures in man and animals, structures which extend from the soles of the feet to the Rolandic area of the brain, and include the indispensable accessory assistance of the organs of sight and hearing. The adaptation of locomotion is thus seen to be extremely complicated, involving the development and education in the history of the species and individual of the most diverse parts of the animal body. The adaptation of mind to its surroundings as expressed in the ratiocination and conduct of experience is likewise a process involved and complicated in the highest degree. It derives its subtle attributes (1) from the history and experience of countless ages, in different varieties of animals, (2) from the normal growth and development of the individual, and (3) from the presence of advantageous social surroundings affording the nutrition and educational influences necessary to its normal activity.

The correlation of a normal mental life may be disturbed in a variety of ways, just as the process of locomotion may become abnormal from an infinite variety of causes interfering at one or more parts of the complicated mechanism. Disease of the posterior columns of the cord, disease of the internal ear, tumour of the brain, peripheral neuritis, are but a few of the processes which will manifest themselves in a disturbance of locomotion. Experimental research associated with clinical and pathological investigation has been successful in elucidating the nature of the processes which produce those disturbances. Is there any evidence to suggest the possibility of a similar solution of the problems which present themselves in psychiatry?

There is perhaps no type of mental disease which has excited more interest in recent years than that now known as dementia præcox. It presents itself in the majority of cases as a dementia of adolescence; there is, however, no denying its

appearance at a much later date. Affecting as it does the most highly and most recently developed aspects of the mental life, it is supposed by many to have its origin in the mental processes themselves. The lack of anatomical data bearing on the subject has tended to give a free hand to those who see in this disease a perversion of mental processes pure and simple. There is, however, considerable evidence for the view that these phenomena of the highly developed psychical centres are a manifestation of disturbances in the nervous substratum of the brain.

The disease begins sometimes gradually and sometimes suddenly. When it begins suddenly it may be in the form of a mania, resembling the delirium of typhoid or cerebro-spinal fever. There may be temperature, leucocytosis, and obvious disturbance of body functions. The acute condition may last months or years, but it spends itself in time, and the patient settles into an ordinary dement. The ordinary dement is a patient who has recovered from his brain disease so far as is possible. The destructive process has ceased and he is now adapted to his surroundings in a manner determined by the amount and quality of healthy brain-tissue at his disposal. He is the locomotor ataxic who, having lost the sensory reflexes from his feet, adapts himself, more or less, by the co-ordinating reflexes from his eyes; he is the man who, having lost the power of his right arm, adapts himself to his wants more or less imperfectly with his left; he is the man with the mitral disease who, though unable to meet the demands of a strenuous life, is still able to adapt himself to the simple claims of existence. True it is that these cases of dementia præcox are subject to subsequent attacks of mania or excitement and depression. These are, however, no part or recurrence of the original disease as a rule; they correspond to the excitement or depression which very often comes on a brain of unstable equilibrium, and, of course, the equilibrium of the brain in dementia præcox has been rendered unstable by the cutting out of the affected areas.

That these recurrent attacks of excitement and depression are not associated with a progressive destruction of the brain is evidenced by the fact that similar cyclic disturbances are frequently observed in long-standing cases of hemiplegia due to embolism or syphilitic endarteritis. The depression or

excitement may be, and undoubtedly often are, manifestations of the same cause, namely, an influence which causes exhaustion or depression even in the normal individual. Indigestion, nervous strain, worry and physical exhaustion may produce a mild degree of depression and excitement in ordinary individuals who are highly strung. The same causes operating on the brain of a dement will produce similar phenomena, only in greater degree owing to the lack of adaptation on the part of the partially destroyed nervous system.

It is not claimed that dementia præcox is a well-demarcated nosological entity like enteric fever or pneumonia. It is a clinical classification including the subjects of mental disease, in the early stages progressive from either an insidious or a sudden onset, but terminating definitely in most cases in a certain stage from which recovery is impossible. In a few cases genuine relapses may be observed, but in most cases when progress of the disease has ceased, they settle down to adapt themselves to their surroundings with the aid of such nervous structures as remain at their disposal.

It is not the case that these symptoms appear first in adolescence. They may appear well on in middle life; and it is almost certain that a considerable proportion of so-called defective children are in reality the subjects of that disease, which, if it first appeared in adolescence, would be termed "dementia præcox."

A child who has been perfectly healthy, bodily and mentally, begins to show evidence of backwardness or waywardness at the age of eight. There is nothing to account for the condition. What is the explanation offered? He or she is put down as a higher grade imbecile; there are those who refer to all cases of dementia præcox in adolescence as high-grade imbeciles; that means no more on the evidence than that they are dements, but it implies without the slightest evidence that they are the subjects of congenital or hereditary disease. It may be that some of them are the victims of a brain deformity, which does not manifest itself till late in life; but there is no other organ in the body which shows a similar proclivity to this form of pathological affection if this be the case. Cases of congenital cardiac kidney or liver disease do occur, but they are comparatively rare, and manifest themselves early in life. There is no reason to believe that imbecility should so frequently first manifest

itself in adolescence, whereas congenital diseases in other organs should show signs immediately after birth. It is far more likely that these cases of so-called imbecility or weak-mindedness which appear in early life, in adolescence, and in late life, and which go a certain length and become stationary, are really cases of cerebritis, giving rise to all grades of brain disturbance and brain destruction, and which, when they pass off, leave the brain with a varying amount of healthy tissue at its disposal. There can be no doubt that there are cases of dementia præcox from which recovery may be practically complete. But even when the damage is extensive, it never progresses in a chronic course to a fatal issue in the same manner as a progressive disease like general paralysis; in fact most of these cases live to an extremely old age.

I have recently had the opportunity of examining the brains of two cases which I put under the category of dementia præcox. One was that of a woman, æt. 65, who for many years had been in a stationary condition of dementia. Her illness had commenced when she was about twenty-five years of age, and at that time she had to be put under restraint on account of what was regarded at the time as mania. For at least the last twenty years of her life the mental condition was not disturbed by any marked storms of emotion or periods of depression, although occasionally she might be slightly excited or depressed. In this patient's brain there were well-marked atrophic changes in the frontal and prefrontal areas.

The second case was that of a young man, æt. 25, who died as the result of an acute appendicitis. His history and whole condition was typical of dementia præcox. In the frontal lobes in this case also there were atrophic changes.

It is not suggested that the primary brain lesion in such cases is to be found in the frontal areas. The atrophic changes may be secondary, and a much more exhaustive examination of the brain is necessary to establish the relation of structure to function in these cases.

#### *Adaptation in Mental Disease.*

Whether convolutions, fibres or layers of neurons are primarily affected is not known. The important thing is that in dementia præcox the disease as such stops early, and the patient



goes on afterwards leading a perfectly healthy and normal life so far as his brain admits. He may break down later as a result of over-strain, especially if he has not been confined to an asylum. What is the significance of this? In dementia præcox, as in other diseases, there is an infinite variety in the degree and extent of the damage done. In very slight cases asylum treatment may not be necessary. These patients recover to the extent of the trouble not being recognisable—a very common thing in heart and kidney disease. They participate in an exacting and strenuous life, and there is a breakdown, or possibly a recurrence of the disease. If a breakdown, then the prospect of recovery without dementia is good; if, however, a recurrence of the disease, new areas may be involved, leading to a dementia. Such considerations indicate the necessity of making accurate investigation into the antecedent history of all mental cases. It is only by a careful noting of the clinical course and character of the disease that a later examination of the brain can be of use. It is extremely improbable that these cases go on to gradual deterioration of the brain. The brain in most cases is affected early in life, and as an organ, undergoes little change compared with normal brains after the primary attack has passed off.

An important evidence of the acute character of the onset of some of these cases is to be found in the examination of the cerebro-spinal fluid. Two cases of acute katatonia, with temperature, abdominal distension and foul-smelling diarrhoea came under observation almost simultaneously. In the cerebro-spinal fluid of each there were considerable amounts of globulin, albumen and albumose. There was also in each case a large number of mononuclear cells in the fluid. Syphilis and tubercle were excluded in each case. One patient died, and the other recovered. It was impossible to get a *post-mortem* examination on the case which died, and the other case, which recovered from the acute attack, is now a chronic dement in a stationary condition; the stationary condition has lasted two years. His general bodily health is excellent, but his mental activity has gone.

#### *Adaptation in General Paralysis.*

The relation to syphilis is constant. The nature of that relation is obscure. Five, ten or fifteen years elapse after the

infection before symptoms appear, and in infantile general paralysis the patient is five, ten or fifteen years before the symptoms appear. There would at first sight appear to be a long intercurrent period of well-being. Leaving aside all problems of predisposition as regards seed and soil, what is likely to be the natural history of general paralysis? General paralysis would appear to be a chronic encephalitis of insidious origin and extremely slow progress. It begins in all probability while the syphilitic disease is still active, and does not manifest itself symptomatically for a considerable time—it may be five, ten or fifteen years. As in the case of gouty kidneys or cirrhosis of the liver, the disease may be present, giving only occasionally a hint of something abnormal, but not revealing itself in its true colours until the physiological reserve has been exhausted. In general paralysis, careful examination of the history may reveal the existence of transient periods of depression or excitement years before admission to the asylum; there may be the history of an epileptiform convulsion, or a transient paresis, but it is only when compensation has broken down, when normal adaptation has become impossible, that the patient, as a rule, comes under observation. Removal from the abnormal stress of circumstances induced by mental excitement, the rest and quiet of institution treatment with the improved nutrition and administration of drugs may induce a remission. Compensation, so to speak, may be restored, but of course on a different basis from that of normal health, because the damage to the brain is irreparable.

In general paralysis a positive reaction is almost invariably obtained with the blood and cerebro-spinal fluid in the later stages of the disease. It would be a matter of great importance to determine in what proportion of cases of secondary syphilis the cerebro-spinal fluid would be found to be abnormal, because there is every probability that in these cases the blood and fluid would be found to be abnormal during the whole course between the earlier period following the infection and the time when the symptoms of general paralysis become manifest.

As to the immediate factors in the pathogenesis of the disease nothing can be definitely said. It has not yet been proved that spirochætes are actually present in the cerebro-spinal tissues, although the analogy from sleeping-sickness would suggest this

possibility. It is not impossible that the anatomical changes are induced by a more or less permanent effect produced by the spirochætes on the blood-serum of the patient, whereby abnormal products in the serum possessing an affection for cerebro-spinal tissues, and more especially the neurons in definite areas, produce from time to time, depending on other conditions, an irritation of the elements in the brain which are ultimately destroyed. Amyloid kidneys occur in syphilis apart from suppurating cavities or other focal lesions from which noxious substances could be absorbed. The blood in these cases almost invariably gives a positive Wassermann reaction, and it may be suggested that substances in the serum, due to the initial infection, produce a distinctive effect on the small arterioles in amyloid kidneys. These changes may be due to a permanent twist which the metabolism of the body has received from the syphilitic infection, and may possibly continue after the syphilitic organisms have ceased to be active. On the other hand the peculiar latency of syphilis, its temporary abeyance for perhaps ten or twenty years, with subsequent activity, must be borne in mind.

In any case the result of these observations is to indicate that there is a definite structural basis for the symptoms of dementia præcox and of general paralysis; that in dementia præcox the active stage of the disease is short and often acute, and that the chronic dements in asylums are for the most part cases of dementia præcox who have been cured so far as the somatic ailment is concerned, and in whom the dementia is the natural expression of accommodation between such brain as is left and the environment. General paralysis is, on the other hand, a chronic disease; it is gradually progressive; there may be periods of remission lasting for months and even years, but it does not tend to come to a standstill in the same manner as dementia præcox. A general paralytic almost invariably dies as a result of his disease, a case of dementia præcox almost never.

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