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Part I.—Original Articles.

Morison Lectures.—Lecture IV.(1) By JOHN MACPHERSON, M.D., F.R.C.P.E.

Variation in Relation to the Origin of Insanity and the Allied Neuroses.

IN the two previous lectures (2) of this course the subject of "Variation in its Relation to the Origin of Physical Malformations, of Congenital Mental Defect, and of the Neuroses, such as Epilepsy, Hysteria, and Alcoholism," was considered. The correlation between congenital malformation and congenital mental defect was pointed out. The relation of the neuroses to one another, their heredity, and their distribution throughout mankind of all races, was insisted on. It was also shown that all these affections are genetic in origin and independent of so-called causes or influences due to the environment. For the environment is not, and cannot be, constant while the manifestations in question are, so far as we know, universal. It was further shown that congenital malformation and congenital mental defect are due to inherent processes, the nature of which is at present unknown, acting within the fertilised ovum. It is, moreover, certain that these processes must be independent of the environment of the elements contributed by either parent, of the immediate state of health of the parents or, with certain exceptions such as injuries or special disease, of the uterine environment. It is not asserted that diseases affecting the

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mother or even, on rare occasions, specific affections of the father may not deleteriously influence the growing embryo *in utero*. The fact remains, however, that in the majority of instances these defects are hereditary, that they may pass over several members of the same family, and in the case of animals over several members of the same litter—nay, even that they pass over one or more generations to re-appear in a succeeding one. In face of such facts, it is useless to speculate upon physical causes while the great innate cause remains obscure.

When dealing with mental defect, epilepsy, and hysteria, we had to do with comparatively simple variations. Insanity, on the other hand, is a complex of several different diseases which have only this in common—that they have, as their result or accompaniment, a more or less grave disturbance of the manifestation of normal mental processes. It requires very little consideration to understand that, in such a complicated congeries of functionating inter-dependent parts as the human body, the proper functionating of the nervous system must be liable to disturbance from a variety of causes outside itself. There are several great clinical groups into which, for the present purpose, insanity may be divided. The following table will set them forth at a glance:

TABLE I.

Clinical Forms of Insanity.

I. Mental defect.
II. Confusional (toxic) insanity:
  (1) The delirium of fevers.
  (2) Alcoholism, etc.
  (3) Puerperal insanities.
  (4) Dementia præcox.
  (5) General paralysis.
III. The recurrent insanities:
  (1) Mania-melancholia.
  (2) The neuroses.
  (3) Obsessions and impulses.
  (4) Paranoia.
IV. Dementia (organic and secondary).
V. Pre-senile and senile forms of insanity.

A clinical classification of insanity is, in the present state of our knowledge, the only possible one, for pathology is not yet

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sufficiently advanced to afford a basis of division; nor is there any hope that in the immediate future our knowledge of the minute anatomy of the nervous system will be so intimate as to form the basis of a classification. Etiological and symptomatological factors form a still less satisfactory means of division. It would be as reasonable to suggest a classification of diseases of the chest based upon the manner in which people catch cold, or upon the character of the cough, as a division of the forms of insanity based upon its causes or upon the variety or intensity of the mental symptoms. There remains the sound and practical method which has all along met with so much success in general medicine—the grouping of related facts in juxtaposition so as to render possible a comprehensive and co-ordinated conception of disease. By adopting this method we are enabled to grasp at once the family and personal history of the patient as well as the symptoms, and to apply to these all we know of the etiology, the pathology, the course, the duration, and the prognosis of the disease.

Confusional insanity.—The type of confusional insanity is the delirium of fevers. It is unnecessary to describe delirium at length, for it is known to all medical men and to the majority of the lay public. Briefly, delirium is characterised by illusions and hallucinations of the senses, by confusion and hurry of thought, by incoherent speech, by fragmentary delusions, and by physical restlessness. Whatever the cause of the delirium, at whatever age it occurs, or whatever its form, there is always present a combination of the symptoms mentioned. It is true that in some of the deliria secondary features or different combinations of the same features are present. It is by a familiarity with these altered combinations of the same features that we are able to distinguish one delirium from another according to their causation. Thus, we can tell without much difficulty acute alcoholism from the delirium of, say, enteric fever, and that of the latter from smallpox. But in all deliria, of whatever origin, the main features mentioned are always present. It should be emphasised that in delirium there is no constant emotional affection. If that fact were more rigorously kept in mind, embarrassing errors in diagnosis would be fewer, and the classification of insanity would be simpler than it is.

There are two kinds of delirium—febrile and sub-febrile. The febrile is that which accompanies various acute infectious

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diseases such as the exanthemata and such visceral affections as pneumonia. The sub-febrile occurs as a sequela to many fevers, as a result of various intoxications, after trauma and shocks, and as a consequence of exhaustion.

Confusional insanity is divided symptomatically into three kinds: (1) delirium, (2) confusion, and (3) stupor.

(1) Delirium, as we have already seen, is a result of acute toxic infection accompanied by pyrexia or fever. It occurs during the course of the exanthemata, in certain forms of puerperal fevers, and also, but less frequently, in various toxic infections of the system in which fever and profound toxæmia are present. The mental symptoms in all such cases are identical with the delirium of fevers in general, but vary somewhat according to the nature of the infection. It seems almost unnecessary to add that the symptoms vary in each individual, some persons scarcely manifesting any mental aberration no matter (within limits) how much the system is poisoned, while others become delirious on apparently trivial occasions. It is interesting in this connection to note the extreme liability of children to delirium. That fact, along with the fact that the liability varies so greatly among adults, teaches us the lesson of the inherent variation which exists among individuals. For if children differ from adults in this respect, one legitimate deduction must be that their cerebral organisation is less resistive and less stable. The few words which have already been said serve as a description of what I mean by delirium—the first division of confusional insanity.

(2) Confusion is the second form of this group of insanities. It is a sub-febrile delirium. The peculiar type of insanity which follows as a late symptom after the subsidence of the acute symptoms of typhoid fever must be familiar to most medical men who have had many cases of that troublesome disease to treat. The symptoms resemble in every particular those of delirium save that they are less acute and that they are much more prolonged; they might be described as a chronic manifestation of delirium. There are illusions and hallucinations of the senses, marked confusion of thought, incoherence of speech, but no constant emotional state. There may be mental exaltation of a kind; often there is mental depression, more often still a mixture of both. Besides typhoid fever other diseases may be followed by mental confusion. Thus

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we find it succeeding influenza, erysipelas, phthisis, and acute rheumatism. It also frequently occurs in susceptible subjects, as a result of prolonged exhaustion, after shock, especially surgical shock, after accidents of a severe kind, and, finally, after prolonged strain, physical or mental. But we must never lose sight of the great fact that it only succeeds such causative factors as have been mentioned in highly predisposed and neuropathic subjects. Alcohol is one of the prolific causes of a large group of confusional insanities. There are three recognised forms due to alcohol, *viz.* (1) acute alcoholism (delirium tremens); (2) a more chronic confusional insanity, often attended with stupor and similar to the mental affection which follows fevers; (3) alcoholic dementia, with or without systematised delusions of a distinctive type, and with or without paresis. In all forms of alcoholic insanity there is confusion, or, in other words, chronic delirium. These are the only forms of insanity in which alcohol exercises a distinct influence and in which it modifies the clinical symptoms. It is therefore highly important that there should be no dubiety in their diagnosis.

The insanities connected with pregnancy and child-bearing are wholly confusional. The term "puerperal mania" is a misnomer. It may be that a pure mania may coincide with any stage of the puerperium, but in that event the term "puerperal" is better avoided if clearness of description is to be preserved.

Dementia præcox affects young persons of a neurotic disposition almost without exception. This is Clouston's adolescent insanity. According to Kraepelin heredity has been ascertained to be present in 70 *per cent.* of all the cases. Over 60 *per cent.* of the cases are under twenty-five years of age; the great majority are under twenty years. Many of the subjects are intellectually bright, some of them even exceptionally brilliant; others, about 7 *per cent.* of the whole, are undoubtedly weak-minded. This is not to be wondered at, for the neurotic disposition is not limited to any intellectual grade, but is found in association with every variation in intelligence. Dementia præcox, which is a slow progressive disease, is a chronic confusional insanity produced by two factors, *viz.* a predisposing cerebral weakness and a physical intoxication. About 10 *per cent.* of the cases occur immediately after acute infection such as the exanthemata. The physical auto-intoxication of the majority of the cases is indicated by the type of

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the insanity, which is confusion, and by the destruction of the brain-cells in the cerebral cortex. It is this pathological effect of the poison which renders the prognosis so grave. Only about 8 *per cent.* of the cases make a good recovery.

Dementia præcox manifests its symptoms under three forms, *viz.* (*a*) hebephrenia, (*b*) katatonia, and (*c*) dementia paranoides.

(*a*) The word "hebephrenia" means "the mind of puberty." The term implies a confusional insanity, misnamed dementia, with elements of depression and exaltation, the latter being ill defined.

(*b*) Katatonia, or rigidity of the muscles, is characterised by confusion, with depression and exaltation, the latter being the better defined, and by various motor phenomena, such as catalepsy, convulsive states, automatism, and stupor.

(*c*) Dementia paranoides means the presence of chronic systematised delusion. The paranoiac form of dementia præcox is characterised by confusion, owing to which the delusions are necessarily indistinct, often extravagant and changeable. They bear, therefore, no true analogy to the delusions in chronic systematised insanity, which will be referred to later on. Stupor occurs with frequency in all forms of dementia præcox. The elements of confusion and stupor and the pathological changes in the cortex leave no doubt as to the relationship of dementia præcox to the great group of the confusional insanities.

(3) The third form which is included in the group of confusional insanity is stupor. Every case of this insanity is liable to lapse into stupor, which is a common phase of the malady. There is no stupor in the sense in which I am now using the word which is not connected with mental confusion. The term "melancholic" stupor is misleading because it is founded upon a misconception of the relationship of melancholia. Stupor follows the confusion of alcoholism, of post-febrile states, of shock and exhaustion, but more especially of that very grave mental affection of puberty and early adolescence which, whether we like the name or not, we must henceforth know as dementia præcox. After infection, poisoning, profound exhaustion, or some other debilitating cause a patient begins to show symptoms of mental depression or hebetude. This stage may last for days or for weeks. The depression may alternate with exaltation followed by mental confusion, hallucinations, excitement, and loss of the sense of orientation.

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Gradually mental obtusion sets in, which soon becomes so profound that the patient lies motionless, oblivious to his surroundings and to everything else besides.

From what has been said we see that delirium, confusion, and stupor are intimately connected with one another; that they merge into one another; that they are parts of one great clinical group which we know as confusional insanity; and, finally, that this group is a distinct group characterised by the mental symptoms which have been cursorily mentioned and caused by definite, generally well-known, factors, *viz.*, poisoning of the nervous system and exhaustion of various kinds.

It is necessary before passing from this group of diseases that I should say a few words on that important disease "general paralysis." However important it may be from a medical or social point of view, it is only important here in so far as it illustrates my subject. I shall therefore content myself by saying that general paralysis is only accidentally an insanity. As a rule organic diseases of the nervous system are not attended by mental disturbances. But this disease is an exception in so far as it attacks the cerebral cortex, which is the seat of the manifestation of conscious mind. It differs from ordinary forms of confusional insanity, which we have been considering in respect that its localisation of attack is limited and defined to certain parts of the brain cortex and in the degree and severity of its virulence. The delicate nerve-cells of the cortex are rapidly and extensively destroyed. The poison is so virulent that it profoundly and visibly affects almost every tissue in the body. Such a disease must necessarily have distinctive symptoms, and must differ in its clinical symptoms from other forms of toxic insanity. Its great cause is now believed to be syphilis, but it is not a syphilitic disease. It is theoretically held that the devitalising effects of the syphilitic poison upon the immunity of the body tissues result in a lowering of the vitality of these tissues, so that they are rendered incapable of resisting the invasion of bacteria or toxins which, in ordinary health, are innocuous, but which in disease take on a pathogenic *rôle*. General paralysis is a confusional insanity. Its toxic origin and pathological anatomy leave no doubt as to that, while the majority of the mental symptoms are of the confusional type.

To sum up—the confusional insanities are due to the action

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of poison on the nervous system, especially the brain. Their type is delirium, no matter whether the delirium is acute and of short duration, or chronic and prolonged. They all result in an injury to the delicate structure of the brain cortex. That injury is more or less severe according to the nature of the poison, and according to the resistance which the brain-cells offer to the action of the toxine.

If it is asked "How do we know that there is a poison present in the blood of patients suffering from confusional insanity?" I reply that had we no other proof than the symptoms, the pathological results, and the course of the disease, there could scarcely remain a doubt as to its existence. We are indebted to Dr. Lewis Bruce of the Murthly Asylum for direct proof of the presence of a toxine which in all probability is the direct cause of the symptoms of this group of affections. There are two main diagnostic symptoms of infection of the system by toxines, *viz.*, pyrexia of fever and leucocytosis. In some intoxications both are present, in others, *e.g.*, phthisis and typhoid fever, there is pyrexia but no leucocytosis. In others there is leucocytosis, but no marked pyrexia. To this latter group belong the confusional insanities which I have named sub-febrile. Dr. Bruce's description is so important that I have asked and received his permission to quote some extracts from his published writings. It should be explained that in normal persons the number of leucocytes per c.mm. of blood is from 6000 to 10,000—they should not exceed 12,000. "Early in the disease and coinciding with the hyperleucocytosis (which was found on admission to be from 15,000 to 17,000), the percentage of polymorphonuclear cells was frequently above 70. [Let me explain that an increase in the number of polymorphonuclear cells is considered a certain sign of toxæmia.] Later in the disease, during relapses, it is quite common to get a hyperleucocytosis of 20,000 or 30,000 with a polymorphonuclear percentage of 80 or even higher. A relapse generally is preceded by a fall of the leucocytosis of 10,000 or 13,000 with a low polymorphonuclear percentage. As the excitement increases the leucocytes gradually rise, and the percentage of polymorphonuclear cells also rises until the attack reaches its height. When such a case recovers, the leucocytosis remains high." . . . "A notable feature of all these diseases is the fact that upon recovery taking place a hyperleucocytosis is

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present for months and even years after leaving the asylum. In cases which do not recover but become chronic the leucocytosis falls, and the percentage of polymorphonuclear cells is often below 50." (3) This is a startling fact, the importance of which is far-reaching. The object of a hyperleucocytosis is of course protective. The leucocytes increase in the blood for the purpose of protecting the system from the encroachments of the poison. Their *rôle* is always protective. The intoxication of the system does not cease when a patient has recovered from the mental disturbances manifested by the continued leucocytosis. When, however, the poison has done its worst, down come the leucocytes. The struggle is over; victory remains with the forces of destruction.

Similar changes in the leucocytes and other blood-constituents indicating indubitably a greater or less intoxication have been shown by Dr. Bruce to exist in general paralysis, hebephrenia, and even in alcoholism. This confirms Klippel's contention(4), who long ago held that the toxine in alcoholism was a secondary one, and that alcohol only predisposed the system to invasion by other poisons from the alimentary canal.

[Lantern slides of brain cortex indicating the destructive nature of these toxines upon the nerve-cells and the brain-structure in confusional insanity were shown.]

Recurrent insanity.—A sharp clinical line separates the confusional group of insanities from the group which for purposes of distinction I have termed "recurrent insanities." The recurrent insanities are degenerative in origin; that is to say, they occur in persons in whom the presence of an inherited neuropathic constitution has been variously estimated by competent observers at from 70 to 90 *per cent.* The hereditary tendency of the subjects is therefore very high—higher than in any other group of mental affections that we know of. Like the general neuroses (epilepsy, hysteria, etc.), their origin is obscure, and they occur without any apparent external cause. They manifest the inexplicable and uncontrollable periodicity of the functional neuroses. They occur in the great majority of cases for the first time in early adult life. Once they occur they have a tendency to recur, in some cases with unfailing regularity, in others with less apparent regularity, but in all cases there is the inherent liability to relapse. In marked contradistinction to the toxic insanities emotional disturbance is the dominant mental symptom.

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We owe to the recent writings of Kraepelin a deep debt of gratitude for having pointed out to us the astonishingly simple fact that mania, melancholia, and circular insanity are not separate entities but different manifestations in the periodic recurrence of one syndrome, which he names "manisch-depressive irresein." We have, unfortunately, no corresponding simple English synonym. We must be content for the present to speak of the entity as "mania-melancholia." Mania and melancholia present the same prodromal symptoms; they run a course of gradual increase, maximum intensity, and final subsidence, and they both tend in the individual attacks towards recovery. Their dominant features are the profound emotional disturbance, the recurrence of the attacks, and the alternate presence of the opposite phases of mental exaltation and mental depression in the same individual. Finally, in this group there is no confusion, no obscuration of intellect, and no tendency to stupor. Until quite recently we were in complete ignorance as to the pathology of the recurrent insanities and of the neuroses. We are again indebted to Dr. Bruce for throwing a ray of suggestive light upon the whole subject. His statements are so important that I find it necessary to quote him in his own words: "All the cases of folie circulaire which we have so far been able to examine exhibited depression or excitement of the simple melancholia or simple mania type. During the depressed stage we invariably found a high leucocytosis, with a polymorphonuclear percentage between 60 and 70. If a period of apparent sanity followed the depression, the leucocytosis still remained high, but the polymorphonuclear fell to about 60. When excitement set in it first fell to 10,000, 11,000, or 12,000, and the percentage of polymorphonuclear cells was also low, generally about 50. As the excitement increased, the leucocytosis gradually rose, culminating at the height of the excitement, and then gradually fell to normal. . . . These observations strongly point to the fact that the depression and excitement of folie circulaire (mania-melancholia) are quite different from ordinary attacks of mania and melancholia" (confusional insanity, dementia præcox).([5])

Further, he says: "Every case of epilepsy has shown hyperleucocytosis during the periods not only when the patients were suffering from epileptic seizures, but even in the intervals when the patients were quite free from attacks. The most marked

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period of hyperleucocytosis follows a fit or occurs during the period when the patient suffers from a series of seizures."

Does this hold good of all the recurrent insanities and the neuroses? That question cannot at present be answered, but there is a strong presumption in favour of its doing so. There is then a toxine in the blood in the periodic group of insanities which rises and falls with the occurrence of the attacks; which seems to disappear, exactly as the malarial toxine does, in the interval between the attacks; and which exercises a less deleterious influence upon nervous tissue than the toxines of the confusional insanities do. In the meantime all that we can say is that neither mania, melancholia, nor paranoia ever result from external infections, intoxications, or visceral diseases. Dr. Dercum says, "To speak of a delirium as a mania because it happens to be attended by excitement is certainly a gross misuse of terms and cannot be too strongly condemned. To designate a confusional insanity as a melancholia merely because the delusions are distressing or painful is equally unscientific and reprehensible. To say that a melancholia is caused by typhoid fever or that acute mania is caused by the abuse of alcohol is to utter nonsense."(6)

I have included paranoia (progressive systematised insanity) among the recurrent insanities. It is not, however, a periodic but a continuous affection. There is, moreover, no hyperleucocytosis, and, so far as we as yet know, no toxæmia. If there is a toxine, it is of an essentially different nature from the toxines we have been discussing. In paranoia, however, there is a distinct periodicity in the course of the symptom, as evidenced by the marked remissions and exacerbations which are one of the chief clinical features of the disease. Again, paranoia is allied to mania-melancholia in that it is a degenerative, highly neuropathic condition arising without known cause and of the pathology of which we are in entire ignorance. The typical form of the disease begins with a phase of depression extending over many years, and accompanied by delusions of the same depressive type, especially delusions of persecution. After a long but indefinite period, generally many years, the phase of depression and the distressing delusions which accompany it give place to an opposite condition of mental exaltation, with delusions of a corresponding character, chiefly of grandeur. It is necessary to distinguish carefully between

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paranoia and the dementia paranoides of dementia præcox, which is a confusional manifestation of delusions with wholly different symptoms and course. It is impossible here to enter upon a detailed description of paranoia or to defend the position it occupies in the classifications of the leading alienists of Europe and America. There are many varieties of paranoia, many of them by no means typical, but they are all amenable, with slight apparent discrepancies, to the descriptive definition given above. It cannot be too strongly insisted on that mania-melancholia and paranoia are in many respects identical with the neuroses. They depend upon no external causes for their origin any more than epilepsy or hysteria do. It is interesting to observe the fact that many of the subjects of the mania-melancholia syndrome as well as many of the subjects of epilepsy have a weakness for alcohol, especially, as Kraepelin points out, after one or more attacks have been passed through. There can be no doubt that an intemperate indulgence in drink may precipitate an attack of mania or of epilepsy which might otherwise have been delayed in its occurrence. Hence has arisen, probably, the mistaken idea of the causal connection of alcohol to this group of diseases. In a previous lecture the connection between the different neuroses was illustrated by comparing the age of onset in each form. In the same way the relationship of the functional insanities to the neuroses may be shown. Thus, paranoia in the great majority of patients first comes under notice between the ages of 25 and 40 years. It has to be remembered, however, that the progress of this disease is slow and insidious, and that the age of actual commencement is probably very much earlier. Seventy-five *per cent.* of the cases of mania-melancholia begin before the age of 25; seventy-five *per cent.* of the cases of epilepsy begin before the twentieth year; eighty-six *per cent.* of the cases of hysteria before 25; and 77 *per cent.* of the cases of alcoholism under 30 years (sixty-two *per cent.* occur under 25).

The next class of the recurrent insanities is that of obsession and impulse. Of the hereditary and neuropathic origin of this group there can scarcely be a doubt, and I do not know that there is any difference of opinion among specialists. It is pretty generally assumed that they are manifestations of neurasthenia; but while not disputing the theory—nay, while concurring with it to a certain extent—it may be pointed out that such an ex-

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planation does not solve the problem of their origin: it only throws us back upon the other insoluble question, "What is neurasthenia?" The imperative ideas which form the basis of all obsessions, are as varied as there are thoughts in the human mind. The most common obsessions are those arising from acquired neurasthenia and are of the nature of weakness, fear, and indecision. Such obsessions, exaggerated to any considerable extent, constitute in themselves a very serious mental affection. But when anti-social obsessions take such a firm hold of the mind that they cannot be thrown off by the subject, the matter is more serious still, and a pathological mental state of grave import is present.

[Lantern slides showing the comparatively slight nature of the changes in cortical cells, even after prolonged subjection to various forms of recurrent insanity, were shown.]

I have already dealt with the neuroses, and they will only be incidentally referred to again as occasion requires. Dementia implies a weakening of the expression of ordinary mental processes. It varies from the most partial impairment up to a complete suspension of the common characteristics of human intelligence. Dementia may be congenital, or it may succeed gross disease of the brain attended by destruction of its tissues, or it may be consequent upon organic impairment of the cortical cells (or portions of them) due to the causes which we have seen to be the origin of the great group of confusional insanities. It is not, as we might expect, a frequent consequent of the recurrent insanities. When it does succeed the latter it is not because of a destructive toxic process, but because of a tendency to premature involution or senile brain degeneration on the part of the subject, which premature senility is one of the special marks or stigmata of the degenerate or neurotic as a class. Indeed, it is a fair question to ask how far a certain proportion of dementias, occurring in comparatively early life, are not of the nature of premature involutions. The larger proportion of demented patients in asylums are the products of the confusional insanities and more especially of dementia præcox.

The insanities of old age commence to make their appearance earlier in life than is generally supposed. Thus we find in late middle life a particular form of melancholia which is known as "climacteric" melancholia begin to appear. It is a prolonged, very emotional, and somewhat unfavourable form.

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This is the true melancholia. There is no melancholia of early life and no mania of late life. That is to say that, with the exception of the melancholia of the climacteric and senile periods, mania and melancholia, as isolated and uncomplicated entities, only occur as phases of the great mania-melancholia syndrome which as a rule makes its appearance for the first time in early adult life. No doubt such a statement as I have just made sounds dogmatic and altogether too sweeping; nevertheless for the present it must remain until refuted upon uncontrovertible clinical testimony. At a later age than the climacteric the forms of insanity become of the senile type; in other words, they are dementias of involution. The symptoms are again confusional, complicated with the loss of memory, with emotional disturbances, with illusions and hallucinations of the senses, or with vague systematised delusions.

Such, then, is a brief and altogether too short *résumé* of the principal features of the elements of the classification which I have placed before you. In order to determine the relative frequency of the various diseases I have prepared the following table:

TABLE II.

Percentage of different Forms of Insanity admitted into Asylums in Germany and America.

	Cases.	*Per cent.*
I. Congenital defect	1314	4·1
II. Confusional insanities:		
Puerperal insanities	618	1·9
General paralysis	2850	8·9
Alcoholism	5881	18·5
Dementia præcox	4757	15·0 (44 *per cent.*)
III. Recurrent insanities:		
Mania-melancholia	5013	15·8
Paranoia	1027	3·2
Epilepsy and hysteria	2607	8·3 (27 *per cent.*)
IV. Senile insanity	5149	16·2
V. Dementia	2500	7·8
Total	31,716	99·7

(Compiled from figures kindly supplied by Dr. Dercum of Philadelphia and Professor Myer of Königsberg.)

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The two prominent features of this table are the diversity of the clinical forms which constitute the group of affections which we loosely term "insanity" and the various proportions which the separate entities bear relatively to the whole group. It is manifest that their pathogeny or causes must be as varied as their clinical manifestations are diverse; for a glance at this table will suffice to show that insanity is not a simple affection, but a group of wholly distinct affections with only the artificial connecting-link that they all result in a disturbance of mental processes. Congenital mental defect must depend upon maldevelopment of the brain. In the large majority of cases this, as we have seen, is a germinal variation, correlated to well-defined physical malformations which are known as physical stigmata of degeneration.

We have good grounds for believing that the confusional group of insanities are always associated with the presence of a toxine which acts injuriously upon the nervous system. In the subjects of alcoholism that poison is, in the first place, alcohol followed by a secondary intoxication. In general paralysis it is believed, in a majority of instances, to be a secondary intoxication rendered possible by a previous syphilitic infection. In puerperal mania the infection is not constant, but is due to the invasion of the system by more than one micro-organism.

With regard to dementia præcox, we have seen that *70 per cent.* of the subjects are hereditarily predisposed; that some of them are congenitally weak-minded; and that many of them owe their malady to the effect, in the first instance, of such infections as those of typhoid fever, scarlet fever, and perhaps phthisis and other similar diseases. After reading Jeandelize's interesting treatise on "thyroid insufficiency" and Dr. Lewis Bruce's articles in the *Journal of Mental Science* (1895) on the treatment of certain forms of insanity with thyroid extract, I cannot help thinking that in insufficiency of thyroid excretion, particularly of the secretion of those small but highly important glands known as the parathyroids, we have an exact parallel to the clinical picture presented in certain phases of dementia præcox. We know how important the function of the thyroid gland is in the causation of cretinism and of myxœdematous insanity, but we know nothing of the effects of partial suspension of its secreting function or of the influence of the para-

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thyroid gland on the mental functions, except what physiologists like Jeandelize tell us. It is suggestive that the causes which produce many of the forms of confusional insanity also produce organic or functional disease of the thyroid and parathyroid glands. These are syphilis, alcohol, tuberculosis, fevers, and various infections. The nervous results of removal of the thyroid, more especially of the parathyroid glands in animals, are briefly as follows: mental confusion, manifested by indifference to surroundings, apathy, and depression. At other times there is displayed great agitation, accompanied by delusions of terror, illusions and hallucinations of the senses. At other times there is delirium of the maniacal type. These symptoms are followed by somnolence, rigidity of the muscles, catalepsy, coma, and death. It is significant to observe in this connection that some authorities consider that one of the functions of the thyroid secretion is to keep the body free from noxious organisms and their toxines. The effects of extirpation are much more serious in young animals than in those which have reached full development. It is the same in the human species. The results of imperfect development or of disease of the glands before completed adolescence is to arrest absolutely the growth and the function of the nervous system at the stage of supervention of the gland affection. As a consequence of operations for the total or partial removal of the thyroid gland in man a host of nervous symptoms, the chief of which are tetanic convulsions, have been observed. On the mental side there have been noted "agitated" melancholia, stupor, delusions of persecution, accompanied by acute phases of excitement and depression. It is unnecessary to point out that these mental symptoms are those which we have already designated confusional. While the symptoms of cretinism and of myxœdema are known, we are at the stage of ignorance regarding the result of acquired thyroid insufficiency in adolescence and adult age. A few interesting observations of a clinical kind have, however, been made by Jeandelize, Bruce, Easterbrook,(7) and others. From these it would seem that the symptoms of myxœdema are not necessarily present in cases in which thyroid insufficiency may be judged to be the cause of nervous disturbance; that the mental symptoms may be intermittent; that maniacal agitation, illusions and hallucinations, delusions of persecution, and, finally, dementia result

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from this cause. The great number of bodily changes which are directly due to thyroid insufficiency—for instance, the changes which are indicative of premature old age, of various forms of rheumatism and gout, and of arterial sclerosis—leave no room for doubt as to the important *rôle* which the thyroid gland exercises in the economy of the body. Those who hold, therefore, that failure of its proper secretion is the cause of climacteric melancholia and of the pre-senile insanities are probably not in error. If the thyroid and parathyroid glands play such an important part in the production of abnormal nervous phenomena, we may be tolerably certain that an equally important part is exercised by the other ductless gland, by the bone marrow, and by the pituitary gland, etc. In the elucidation of the causes of insanity therefore we have to do, not with hereditary imperfection of the nervous system alone, but also with bodily changes which are equally important.

What we call the neuropathic constitution must imply three things: (*a*) a structural variation from the normal type of cerebral architecture, implying a gross difference in the size and arrangement of the nerve-cells, or both; (*b*) structural variation in the form and functions of various bodily organs; and (*c*) a diminished power of immunity on the part of the body tissues against invasion by toxines and the products of micro-organisms. Now, all these features must be correlated with the physical conformation, although we have scarcely begun to realise that supreme fact. When we do realise it ultimately our whole conceptions will have undergone such a radical revolution that the neuropathic constitution, so far from being an abstraction and an intangible entity such as I am trying to grope after, will have become a fact of the utmost importance in medical and social science.

(1) Delivered before the Royal College of Physicians, Edinburgh, January 30th, 1905.—(2) Delivered before the Royal College of Physicians, Edinburgh, February, 1904.—(3) *Journal of Mental Science.*—(4) *Archiv de Med.*, 1892, and *Annal. Med. Psychol.*, 1894, 1903-4.—(5) Dr. Bruce's classification is different from the one used by me.—(6) *Journal of Nervous and Mental Diseases*, vol. xxviii, New York, 1901.—(7) Jeandelize, *L'Insuffisance Thyroidienne*, Paris, 1903; Bruce, *Journal of Mental Science*, 1895; Easterbrook, *Brit. Med. Journ.*, 1900.

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