

The Second Maudsley Lecture. Delivered by Sir FREDERICK MOTT, K.B.E., M.D., LL.D., F.R.S., at the Quarterly Meeting of the Medico-Psychological Association of Great Britain and Ireland, held at the Maudsley Hospital, Denmark Hill, S.E. 5, on Tuesday, June 7th, 1921.

MR. PRESIDENT AND MEMBERS OF THE MEDICO-PSYCHOLOGICAL SOCIETY,—Permit me to thank you for the great honour you have conferred upon me in asking me to give the second Maudsley Lecture; also for permitting me to deliver it in the Hospital which bears his illustrious name and which owes its existence to his generosity.

I propose to divide this address into two parts: the first will treat of the hospital, its inception and its aims and uses as conceived by the founder; the second part will deal with researches I have carried on concerning dementia præcox.

I.

THE MAUDSLEY HOSPITAL, PAST AND PRESENT.

It is now fourteen years since the late Dr. Henry Maudsley wrote me a letter saying he would give £30,000 to the London County Council if they would build a hospital in London for the study and investigation of mental disorders in their early stage, and the treatment of such with a view to preventing them being sent to the county asylums. The County Council acknowledged Dr. Maudsley's very generous offer, and the conditions upon which the gift would be made were drawn up by Dr. Maudsley and myself. They were that the hospital should be built within four miles of Charing Cross and be associated with the London University.

Dr. Maudsley recognised that the best and only method for providing means for the cure and prevention of insanity was by the encouragement of clinical and laboratory research, and he conceived the idea that a hospital with 100 beds and out-patient departments would enable a careful study to be made of cases of incipient mental disease, and if connected with the University it would become a centre for post-graduate teaching.

In 1907 I visited Kraepelin's clinic at Munich, and having long been acquainted with the remarkable clinical and anatomical research work which he and Alzheimer had carried on there, and knowing the influence this school had had upon psychiatry in the whole civilised world and Germany in particular, I was not surprised to find that this clinic attracted students and doctors interested in the study of mental

diseases from all countries. There was no such hospital and clinic in England, and in the preface of the third volume of the *Archives of Neurology* (1907) I expressed the following opinions:

“A fruitful field of study in psychiatry would be those early cases of uncertifiable mental affection termed neurasthenia, psychasthenia with obsessions, mild impulsive mania, melancholia, hysteria and hypochondria, which in many instances are really the prodromal stages of a pronounced and permanent mental disorder. The poorer patients suffering with these conditions first come into the hands of the practitioner, the dispensary or infirmary doctor, and the out-patient physician at the general or special hospitals. The better-class patients are sent by the practitioner to the neurologist; the generality of the poorer patients, and sometimes the better-class patients, are regarded by the medical man who has had no training in psychology as of little medical interest (for such patients do not, as a rule, benefit by drugs), and he finds it a wearisome task to listen to their story, to ascertain their inborn tendencies, and to find out the truth of what has happened to account for their strange conduct indicative of their not feeling, thinking and acting in accordance with the general usages of their social surroundings, and yet such patients may not be so antisocial as to be certifiable. Such cases are often in the hopeful and curable stage, and these, if studied carefully by trained medico-psychologists, could not fail to yield valuable results in regard to our knowledge of the causation, prevention and cure of insanity. Moreover, when the cases are followed up systematically they would throw much light on prognosis in similar cases. The majority of cases which are admitted to the asylum have long passed the hopeful stage; still, there are a certain number of early curable cases, and these, I maintain, would sometimes be much better if they had not been certified or sent to associate with chronic lunatics. Fortunate would be the community in which there was a fully-equipped and well-organised psychiatric clinic, under the control of a University, and dedicated to the solution of such problems. If suitable post-graduate training in medico-psychology and neuro-pathology were established, doubtless the Universities and licensing bodies might be induced to establish a diploma, very much on the lines of the Diploma of Public Health, which has largely contributed to raise the science of public health to the high position it now holds, thus conferring an inestimable benefit on the nation.”

Shortly after this was published Dr. Maudsley called upon me but I was out, and he wrote me a letter saying that he would give £30,000 to the London County Council if they would build a hospital in London for the study and treatment of acute mental disorders. I interviewed Sir John MacDougall, who advised me to represent to Dr. Maudsley

the desirability of making his gift subject to an association of the hospital with the London University.

In March, 1908, the Asylums' Committee reported as follows: "We desire to express for our own part the appreciation of the generous spirit in which Dr. Maudsley's offer has been made, and our conviction that its acceptance will confer a great and lasting benefit upon a class of sufferers, the effectual assistance of whom has hitherto been amongst the most difficult of social problems."

The offer was accepted by the Council, but for some years both Dr. Maudsley and I were almost in despair as to whether the Council would ever find a suitable site. At last, in 1912, the present site was purchased for £10,000, and plans were drawn up by Mr. Clifford Smith, the asylums' architect and engineer, in which I co-operated. A building strike occurred, and owing to the delay the cost of the building was increased by 25 per cent.

The hospital was only partially completed when the war broke out. King's College Hospital and the adjacent schools formed the 4th London General Territorial Hospital, upon the staff of which I served in the rank at first of Major, afterwards as Brevet Lieut.-Colonel, as neurological specialist. To this hospital was sent a large proportion of neurological cases; consequently I suggested to the War Office authorities that if the Maudsley Hospital was completed it would form a very useful addition, and be particularly valuable for the treatment of the more serious cases of war psychoneuroses and psychoses.

Sir Alfred Keogh, D.G., inspected and approved of the hospital, which was completed at the end of 1915, and opened for patients early in 1916 as a part of the 4th London General Hospital.

The Pathological Laboratory at Claybury was dismantled and the equipment transferred to the more convenient and spacious laboratory at the Maudsley Hospital.

I had frequent opportunities of talking over the progress of the building operations, and, when completed and open for the reception of neurological cases, of discussing with Dr. Maudsley the clinical and pathological work that was being carried on there, in all of which he took a great interest.

The Maudsley Hospital now had become widely known, and successive groups of American officers were sent here for training before proceeding abroad. Several distinguished foreigners who were driven from their country were enabled by grants from the Medical Research Council to work in the laboratory. Thus Dr. Sano, formerly the superintendent of the Acute Mental Hospital, Antwerp, and now the Superintendent at Gheel Colony, pursued valuable researches on "The Convolutional Pattern of the Brain in Identical Twins," published in the *Philosophical Transactions of the Royal Society*; "The Convolutional

Pattern of the Brain in Fifteen Pairs of near Relatives," published in the seventh volume of the *Archives of Neurology and Psychiatry*, and "The Description of the Brain of the Idiot Savant of Earlswood," published in the *Journal of Mental Science*. Prof. Marinesco, the distinguished neurologist of Bucharest, investigated "The Histology of Lethargic Encephalitis," "The Oxidase Reaction of the Central Nervous System," and "The Histology of Painful Neuromata in Amputation Stumps," which was published in the *Philosophical Transactions of the Royal Society*.

From the early part of 1915 and onwards I made researches on the brains of cases sent to me from France in connection with the effects of high explosives and gas poisoning, which formed the subject of the Lettsomian Lectures of 1916 and subsequent publications in vol. vii, *Archives of Neurology and Psychiatry*.

The clinical and pathological work which was being carried on here was much appreciated by Dr. Maudsley, and this was shown by a letter which I received from him in July, 1916, in which he says: "I have had two or three casual reports of all that the hospital is doing from visitors, who were very pleased. In getting the hospital on to right lines you are doing good pioneering work which cannot fail to have its reward, and it will depend, as you know I think, on you to make it what it should be; 'therefore be not weary in well doing.'"

Impressed by the lack of knowledge of neurology and psychology by medical officers, and especially in the diagnosis and treatment of the war psycho-neuroses, I started classes of instruction, which were first largely attended, especially by officers from the Dominions and United States; but later, owing to the blighting hand of officialdom, these classes died of inanition. I am glad, however, that I did start these classes of instruction, for it gave me the idea that many qualified medical men were anxious to acquire a knowledge of nervous and mental diseases if suitable courses of instruction were offered to them. I must tell you that the Pathological Laboratory continued to do the routine work for the London asylums during the whole time of the war as well as the pathological work for the hospital. Moreover, a part of the laboratory was utilised for the investigation of malaria by Sergt.-Major Nierenstein, Captain Thomson, and subsequently Capt. Mann. The original work of Sergt.-Major Prof. Nierenstein, of Bristol University, was of very considerable value, and formed the subject of a report on "The Presence of Hæmo-Quinic Acid in the Urine of Cases of 'Blackwater.'"

In September, 1919, the hospital was transferred to the Ministry of Pensions, and in April, 1920, with the approval and under the auspices of the L.C.C., I started classes of lectures and practical instruction for graduates of medicine, especially medical officers of asylums, to enable

them to sit for the Diploma of Psychological Medicine for the University of Cambridge, which had been established just before the war. The syllabus was submitted to Sir Clifford Allbutt and Prof. Sherrington, who was one of the examiners, and received their approval ; it did not quite correspond with that of the Cambridge University. An announcement was made in the journals that this course would be given with a view to preparation for qualified medical men who were desirous of taking the D.P.M. of the University of Cambridge. This caught the attention of the Registrar of the University of London, who wrote asking me if there was not a University of London. My reply was "Yes, but there is no diploma." The Royal Colleges also woke up at this eleventh hour. I may say that thirteen years ago I approached the President of the Royal College of Physicians urging him to support the establishment of a diploma in psychological medicine, but without effect. Possibly the lack of knowledge of neurology and psychological medicine of medical men serving in the Army and on the Pensions' Board and the very serious results which occurred in consequence, both during and after the war, opened the eyes of many of the distinguished heads of the profession who had served in the Army.

Now at last, after thirteen years, I have seen my wishes fulfilled by the establishment of a D.P.M. in more than one University and by the Royal Colleges. I agree with the Medical Correspondent in the *Times*, that attendance at lectures and practical instruction in neurology and psychology for the first part of the Examination for the Diploma, and attendance at the lectures and practical instruction in nervous and mental diseases for the second part of the Examination, is the best corrective to the growth of a superficial and spurious form of psychology which appeals to a certain class of people, whose minds are open to any suggestive influence, and who are ever ready to run after any new craze, good or bad. To such people psycho-analysis appeals. If only this mode of treatment remained in the hands of properly trained medical men well qualified by their personality, their study, knowledge and experience of the character and conduct of their fellow human beings, enabling them to handle the problems of the sexual instinct and its latent manifestations with delicacy and care, it would not matter ; but unfortunately it is getting into the hands of undesirable and unqualified persons.

Since the Laboratory has been under the Ministry of Pensions a number of men have been doing research work here, notably Dr. Golla who is giving the Croonian Lectures this year on "The Objective Study of Neurosis," the following Japanese gentlemen, Dr. Matsumoto, Dr. Morowoka, Dr. Hayao, Dr. Uno, Dr. Kominami, and their work will be published shortly ; also Mr. Kenneth Walker and Dr. Prado y Such. I mention all these names because it shows that

active research has been done, although the Hospital has had no patients since November 1st, 1920. Unfortunately there is no likelihood of the hospital being opened for the purpose for which Dr. Maudsley made his generous gift for some time to come; consequently a research which I had contemplated on metabolism in dementia præcox, and for which the Board of Control gave me a grant, cannot be carried on.

It will thus be seen that the hospital has fulfilled two out of the three wishes of Dr. Maudsley, namely—practical instruction and lectures in psychological medicine have been given for more than a year. The classes have been well attended by a number of men in the L.C.C. asylums' service and from various parts of Great Britain, and many of them have been enabled to pass the examination for the Diploma for the Universities of Cambridge, London, or that of the Conjoint Board. I have been extremely fortunate in being able to get a first-rate panel of lecturers, and I take this opportunity of thanking them for their services.

They were as follows:

Dr. Golla, who has given lectures on Physiology of the Nervous System and Practical Physiology in Part I of each of the three courses of lectures, as well as Clinical Demonstrations in Neurology in Part II of the First and Second Course.

Dr. Lowson, who gave Lectures on Psychology and Demonstrations in Practical Psychology in Part I of the First Course.

Dr. Hubert Bond, who gave lectures on the Diagnosis, Prognosis and Treatment of Mental Diseases and Demonstrations of Same and Legal Relationships of Insanity for Part II of the First and Second Course.

Sir Bryan Donkin, who gave lectures on Crime and Responsibility for Part II of the First Course.

Dr. F. C. Shruballs, who lectured and gave demonstrations of cases on the Practical Aspect of Mental Deficiency for Part II of the First and Second Course.

Dr. William MacDougall, who lectured on The Psychology of Conduct for Part II of the First Course.

Dr. Bernard Hart, who lectured on The Psychoneuroses for Part II of the First and Second Course.

Dr. W. C. Sullivan, who lectured on Crime and Insanity for Part II of the Second Course.

Dr. E. Mapother, who lectured on the Symptoms of Mental Disease for Part II of the Second Course.

Dr. Devine, who gave the lectures on Psychology and the Demonstrations on Practical Psychology for Part I of the Second and Third Courses.

I lectured and gave practical instruction and demonstrations on The

Anatomy of the Nervous System for Part I of the First, Second and Third Courses, and lectured on the Pathology of Mental Diseases, including Brain Syphilis, its Symptomatology and Treatment; also gave Clinical Demonstrations in Neurology for Part II of the First and Second Courses.

I should particularly like here and now to express my deep sense of obligation to the Board of Control and the Medical Research Council for the generous way in which they have supported me in grants for carrying on researches in the Laboratory, and by the aid thus afforded enabling me to publish the same with proper illustrations.

Maudsley on Body and Mind.

Before commencing the second part of my address I will quote some passages from Dr. Maudsley's Goulstonian Lectures on "Body and Mind" given fifty years ago, which show that he was fully aware then of the importance of the objective study of the mind and its disorders and the inter-relation of function of body and mind:

"Mental disorders are neither more nor less than nervous disease in which mental symptoms predominate, and their entire separation from other nervous diseases has been a sad hindrance to progress. No doubt it is right that mental derangements should have, as they often require, the special appliances of an asylum, but it is certainly not right that the separation which is necessary for treatment should reach to their pathology and to the method of its study. So long as this is the case we shall labour in vain to get exact scientific ideas concerning their causation, their pathology and their treatment.

"Clearing then the question as completely as possible from the haze which metaphysics has cast around it, let us ask—How comes idiocy or insanity? What is the scientific meaning of them?"

Yet at the present day we find many authorities attributing mental disorders to psychogenic causes instead of to pathogenic conditions. It has been my endeavour to show that mental processes are subordinate to physiological processes and that mental disorders and diseases are due to pathological physiogenic conditions, and I am sure that in doing so and in encouraging research on those lines I shall be clearly following out Maudsley's wishes. In these same lectures Maudsley emphasises the importance that the generative organs have upon the mind, and he asks the question whether each of the internal organs has not also a special effect, giving rise to particular feelings with their sympathetic ideas. But this was long before our knowledge of the endocrine system; still, he shows by his reference to the sexual organs what an important influence they have upon the mind in health and disease, as the following passages show:

"We have indeed to note and bear in mind how often sexual ideas

and feelings arise and display themselves in all sorts of insanity, and how they connect themselves with ideas which in a normal mental state have no known relation to them, so that it seems as inexplicable that a virtuous person should ever have learnt as it is distressing that she should manifest so much obscenity of thought and feeling!

“Considering, too, what an important agent in the evolution of mind the sexual feeling is, how much of thought, feeling and energy it remotely inspires, there is less cause for wonder at the naked intervention of its simple impulses, in the phenomena of mania, when co-ordination of function is abolished in its supreme centres and the mind resolved as it were into its primitive animal elements. The reciprocal influence of mind on organ and organ on mind is well illustrated in the sex organs.

“The morbid self-feeling that has its root in the sexual system is not unapt to take a religious guise.”

II.

FURTHER RESEARCHES ON DEMENTIA PRÆCOX.

Throughout Maudsley's writings, which extend over fifty years, one finds that he views mind and its disorders from a broad biological aspect, and one of his sayings is: “Nature is unmindful of the individual, mindful only of the species.”

Natural selection and the survival of the fittest is still going on whereby weak types are eliminated, and should the social conditions be such as to prevent this natural selection and survival of the fittest, racial decay must inevitably set in.

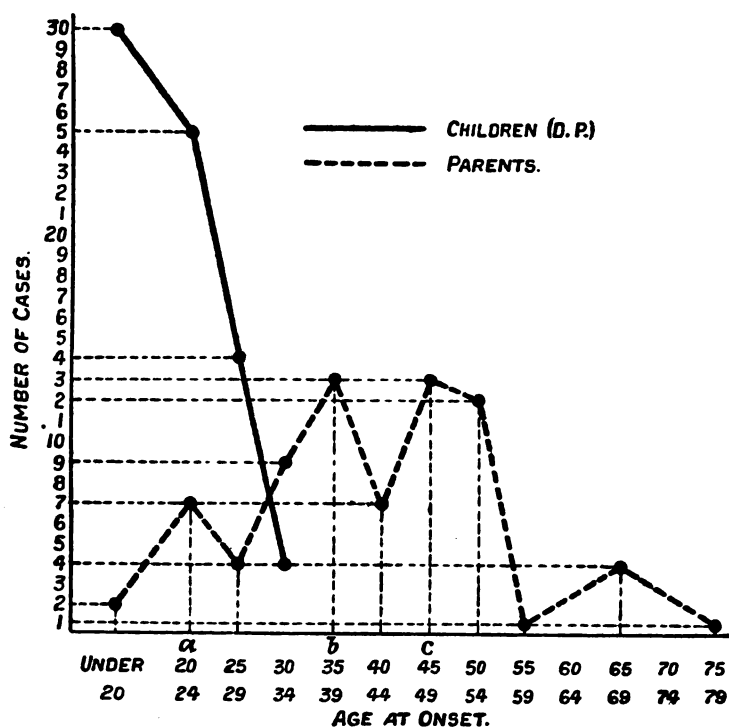
Impressed by the teaching of Morel, who in 1859 pointed out that the progressive uninterrupted transmission of a neuropathic type leads finally to special degenerative forms, to imbecility and idiocy, and with the diminished capability of production of the latter kind the stock gradually becomes extinct, Maudsley says that Nature always tends to end or mend a degenerated stock. This dictum received proof from my investigations on anticipation.

Anticipation and Survival of the Fittest.

In 1911 I published statistical data relating to the age of onset of insane offspring and of insane parents. This was based upon a card system relating to 3,118 relatives who had been admitted to the London County asylums and made up from 14,050 families. This analysis showed a singular tendency to the occurrence of insanity at an earlier age in the offspring than in the parents.

In 1917 I made a further analysis of the relative cards since 1911—a

period of six years. This analysis was limited to insane parents of offspring of which a diagnosis of dementia præcox was made. The graph is similar in its characteristics with regard to the graphs of the age of onset of the parents, but in respect to the age of onset of the offspring, instead of 47.9 per cent., as in the first analysis, being under twenty-five upon admission, 75 per cent. of the cases suffering with dementia præcox were under the age of twenty-five on admission.



The curve of the parents resembles very much the general curve of the asylum cases with three periods of greater intensity: adolescence (a); G. P. period (b); involutional period (c).

No cases of dementia præcox were among the parents, and this agrees with Rudin's investigations. Seeing that a great many cases were either insane before certification or by their conduct had given prodromal evidence of oncoming insanity, it is probable that all the cases commenced before the termination of the adolescent period of life. This fact supports Maudsley's contention that there is a tendency to end or mend a degenerated stock. Now, how could Nature otherwise act, in ending or mending a degenerated neuropathic stock, except

by bringing disease on at an early age, by which the organ of external relation, the brain, becomes diseased, and thus renders an individual so affected unable to compete with his fellows in the struggle for existence? Clearly such a condition of a disordered mind would operate by natural selection in the struggle for existence and survival of the fittest among primitive people; but among civilised people, where the struggle for existence and survival of the fittest does not eliminate poor types but rather tends to preserve them, other than natural methods must be adopted, *viz.*, segregation. Fortunately, cases of dementia præcox sooner or later become anti-social and are sent to asylums, where they are usually detained for the rest of their lives.

But my investigations on the reproductive organs of both sexes in this disease show that Nature has adopted an even more certain method of eliminating this form of degeneracy in a stock, *viz.*, by progressive regressive atrophy of the testis and ovary. In the cases of females this regressive atrophy not infrequently occurs after the first pregnancy, and all the evidence goes to show a lack of the psycho-physical energy connected with the sex instinct—an instinct which energises and dominates all the cells of the body for the purpose of the preservation of the species. This lack of psychophysical energy is one of the striking features of this disease, and it shows it both in disordered mental and bodily functions.

In my Morison Lectures and in *Studies of the Pathology of Dementia Præcox*, I have pointed out the intimate correlation of the sex organs and the endocrine system. Naturally the mental symptoms develop progressively, and show themselves first by a disintegration of the psychic unity affecting the highest of the psycho-physiological levels. It might be argued that the degeneration of the sexual organs was secondary to the mental deterioration, and that the mental deterioration was of psychogenic origin, but I have given reasons which I shall develop a little more fully later why this is not the cause.

COMPARISON OF AN ACQUIRED DISEASE (GENERAL PARALYSIS) WITH DEMENTIA PRÆCOX, AN INBORN GERMINAL DISEASE.

A comparison of the mental and bodily conditions of an acquired disease—general paralysis of the insane—with the mental and bodily conditions found in dementia præcox, will be the argument which I should advance to show that dementia præcox is a vital defect of the reproductive organs and of the brain, in particular, and probably of the whole body.

The Testes and Spermatogenesis in General Paralysis and Dementia Præcox.

If we compare the reproductive organs in general paralysis with those of dementia præcox, we shall observe that in the most advanced cases of dementia paralytica portions of the testes, sometimes the whole testes, show signs of active spermatogenesis, and this applies to general paralysis, due to congenital as well as acquired syphilis. Indeed I have found in a case of tabo-paralysis, due to congenital syphilis, live spermatozoa in the vesiculæ eight hours after death. If we compare the average weight of the testes in eighteen cases of general paralysis after removal of the tunica vaginalis and epididymis, with the average weight of the testes from a similar number of cases of dementia præcox, we shall find that in the former the average weight of the organ was 18 grm. and in the latter 12. Moreover, this is in spite of the fact that in cases of general paralysis there was evidence of chronic inflammation with adhesion of the tunica vaginalis, so that sometimes one organ was considerably atrophied. In no case did we fail to find spermatozoa in the vesicular fluid or in an emulsion of the testes in general paralysis; whereas in dementia præcox in considerably more than half the cases no evidence of spermatozoa could be found. On section of the organs in dementia præcox the spermatic tubules may appear white, owing to the lipoid contained in them, but this does not always show that the organs on microscopic examination will present normal histological appearances, for reasons which I will state later. Generally speaking, however, especially in more advanced cases and those testes weighing 12 grm. or less, the tubules to the naked eye, or when examined with a hand lens, appear attenuated and of a greyish or greyish-white colour, instead of milky white, and there is obviously in these cases an increase of interstitial tissue.

Whereas on the one hand in general paralysis, especially in organs where a number of tubules have been atrophied, owing to local specific gonorrhœal or syphilitic inflammatory reaction causing obstruction to the vasa efferentia, the hormone interstitial cells of Leydig are clearly seen upon microscopic examination; on the other hand, in dementia præcox these hormone cells are difficult to observe and sometimes impossible to find. There can be no shadow of doubt about the existence of a progressive regressive atrophy of the testes in the majority of the cases of dementia præcox. Generally the atrophy is proportional to the number of years or the early age at which the disease first became manifest; but there were a few cases in which the testes appeared to be of average weight, and in which active spermatogenesis could be found on microscopic examination and in which spermatozoa were found in the vesiculæ. I shall deal with these

in the demonstrations which I shall give at the end of the lecture when I refer more particularly to the recent researches which I have been making with Dr. Prado y Such by a special technique.

The Ovaries in General Paralysis and Dementia Præcox.

Now when we come to compare the ovaries of the cases of general paralysis with those of cases of dementia præcox the subject becomes more difficult in one way and easier in another. It becomes more difficult to estimate the respective average weights, because in most of the paralytic women who have died the process of involution of the reproductive organs has commenced.

There have been, however, a few cases of congenital syphilis causing the juvenile form, and these present a striking difference to those of cases of dementia præcox as regards the appearance of the ovaries upon section. In the former one observes maturing Graafian follicles, whereas in the latter these are not observed. In a general paralytic woman from acquired syphilis there are usually large numbers of *corpora lutea vera* whereas in dementia præcox there are relatively few, even when the disease has affected married women. On microscopic examination one seldom sees in cases of dementia præcox any evidence of primordial follicles showing any tendency to develop a zona granulosa, and still more rarely to form even the early stages of a Graafian follicle, whereas normal follicles in all stages of development may be found in cases of paralytic dementia, whether due to acquired or congenital syphilis, and in spite of long mental disease and bodily intercurrent disease of the same nature, as proved fatal in the cases of dementia præcox. As a general rule if the patient suffering with general paralysis has died before the involutorial period, one finds on microscopic examination abundant evidence of maturation of the primordial follicles with the formation of atretic follicles and corpora atretica. These maturing follicles do not go on to a complete ripe Graafian follicle because of the mental and bodily disease from which the patients are suffering, and in this respect differing from the male paralytic, in which, as I have said, active living spermatozoa exist. Now this seems to prove that the acquired disease—general paralysis—has not affected the specific vital energy of the ovum, and this fact may be correlated with the fact that in the testes, even in advanced general paralysis which has lasted many years, we still find evidence of productive energy by the existence of active spermatogenesis.

Sexual Organs and Psychophysical Energy.

The question then arises: What is the cause of this failure of vital energy, and what influence has it on the body as a whole

and on the production of the mental symptoms? There is evidence to show that the organs of reproduction play an important part in regulating and controlling the functions of the endocrine system.

I have not time to develop this part of the subject, but there are many facts which support this statement; but it may be asked: What relation has this regressive atrophy of the reproductive organs which are dominant in the life of internal relation upon the central nervous system which controls all sensori-motor activities? From a broad biological standpoint it may be assumed that after puberty the psychophysical energy of the whole body is expended in response to the three primal instincts—self-preservation, propagation and the herd instinct, which last has arisen out of the first two. If sexual desire is lost one great source of psychophysical energy dries up and this must lead to an increasing development of the self-regarding sentiment, because nearly all the passions and altruistic sentiments have their roots in the instinct of propagation and the tender emotions connected with the care and nutrition of the offspring. But it may be argued that the mental symptoms precede the loss of function of the sexual glands, and therefore, while one will not admit that the pathological physiogenic conditions are secondary to the psychogenic, one cannot avoid an explanation of why the mental symptoms precede the loss of the sexual activity. The explanation, to my mind, is that in this disease there is a failure of vital energy of the cells of the whole body, manifested especially in the two most important to show symptoms, namely the closely inter-related sexual organs and the brain, and particularly in that part of the brain which constitutes the highest psycho-physiological level; the level which has been the last to come phylogenetically and ontogenetically and is the first to go. For this reason I am doubtful whether cases of dementia præcox can benefit from psycho-analysis.

Comparison of the Pathological Changes in the Nervous System in Relation to Symptoms in General Paralysis and Dementia Præcox.

It may be argued by those who are in favour of the psychogenic origin of dementia præcox that the pathological changes found in the nervous system are insufficient to account for the mental symptoms which occur in this disease. I believe that there is sufficient to account for the symptoms if we regard the disease from a physiological point of view. It is quite obvious that the gross changes which are met with in dementia paralytica, changes involving the destruction of the neural elements proportional to, and accountable for, the degree of paresis and dementia which are met with, do not exist in dementia præcox. In this disease the naked-eye appearances are those of a normal brain. There are no inflammatory changes in the vessels;

no thickening of the membranes; no wasting of the brain substance with corresponding increase of cerebro-spinal fluid such as is found in paralytica dementia. Whatever the physiogenic cause, then, it can only be found by microscopic examination.

Neural Activity Dependent upon Physiological Processes and Evidence of their Failure in Dementia Præcox.

Now, it has been known for a long time that there are microscopic changes affecting particularly the nucleus with diminution of the Nissl substance, distortion and shrinking of the cells of the brain, associated with a lipid degeneration of the cytoplasm affecting especially the higher levels, but not limited to any part of the brain in dementia præcox (*vide* Plate X). How can we then, it may be asked, associate these anatomical findings with a disorder and loss of function of the neuron systems to account for the symptoms? It is difficult, but there seems to me to be evidence in the decay of the nucleus of a failure in the specific vital energy of the neurons. Now what part does the nucleus play in the function of the neuron, and how is it related to the Nissl substance? The Nissl substance, as MacCallum has shown, is a nucleo-proteid containing phosphorus and iron. The Nissl granules do not exist in the living cell, but there must be this nucleo-proteid present in another form; the larger the cell the more abundant it is. This is evidence to show that this basophile staining nucleo-proteid has a specific biochemical function. We know that experiments involving fatigue cause a disappearance of the Nissl substance, which indicates that functional neuron activity is dependent upon it. Now Marinesco has shown that upon all the processes of the dendrons and the cell body there are oxidase granules, but none on the axon. These granules consist of a lipoid substance containing an unsaturated fatty acid substance on the surface, which takes up molecular oxygen (O_2) from the blood. The iron and probably the phosphorus contained in the basophile (Nissl) substance of the cell which is also found in the dendrites, and not on the axon, would therefore act as a catalase on this molecular oxygen and convert it into free atomic oxygen ($O-O$). When the stimulus comes to the neuron it may not cause a response, but as a result of a succession of stimuli—that is, summation—the resistance in the grey matter at the synaptic junctions is overcome and the stimulus is perceived. This may be explained by the fact that an insufficiency of catalase has been formed by the first wave of stimulus to bring about changes in the synaptic junctions to enable it to pass through to the receptor centres.

Experiments and observations show that neural function depends upon the circulating blood carrying oxygen to the tissues. Thus Mosso

found that a patient who had been trephined, and in whom the pulsation of the brain could be felt, lost consciousness six seconds after the pulsation had been made to cease in consequence of compression of the carotid arteries. The blood supply of the grey matter is six times as great as that of the white matter, and there is reason to believe that all the active oxidation processes take place in the grey matter. Moreover, delay in passage of an impulse is in the grey matter. Whereas neuronic fatigue occurs from over-stimulation in the cell and its dendrons, where the oxidase granules are situated and where the oxygen is essential for functional activity; experiments show that the axon, the conducting agent of a nerve-fibre, is incapable of being fatigued by stimulation even when contained in an atmosphere of nitrogen. The stimulus conducted along the axon is therefore biophysical, but in the cell and dendrons, under the influence of a stimulus, it may be assumed nuclear catalase is liberated and acts upon the oxidase granules in the grey matter, converting molecular O_2 into $O-O$, whereby a vital bio-chemical process is set up in which $O-O$ is used up and CO_2 produced. This vital process engendered by the impulse is necessary for its transmission through the synapse to the next neuron. The precise nature of this vital process we do not know; it may be of an amoeboid nature, or an alteration of the surface tension at the synaptic junction. In a neuronic system there are two sets of neurons in the chain—neurons of the first type of Golgi, in which the axon leaves the grey matter and is covered with myelin, and neurons of the second type in which the axon does not leave the grey matter, so that the intercalary neurons of the second type always enter into the synapse. As these consist largely of nucleus, it follows that there is abundance of catalase available at the synapse to convert the molecular oxygen into free atomic oxygen. In the cortex of the brain these intercalary neurons form definite layers of granules, and act as receptors for afferent projection systems and association systems of neurons, well exemplified by the double layer of granules in the half vision centres. Marinesco found abundant oxidase granules in this layer of granules (plexiform cells of Cajal).

If, then, we can assume that neural activity depends upon the physiological processes in the grey matter, which I have indicated, then it is a rational hypothesis to put forward that the failure of function in dementia præcox may be correlated with a failure of oxidation processes in the grey matter, owing to a deficiency of the vital energy of the nucleus, as shown by morphological and bio-chemical changes in the nucleus and a failure in the production of the substance which is the antecedent of the Nissl granules.

The lipid granules which are found in the cytoplasm in dementia præcox and senilis are an expression of a deficient metabolism of the

neuron (*vide* Plate XI). Similar appearances are found in the neurons of old people and old animals; and we may regard the change as it occurs in dementia præcox as a wide-spread loss of vitality and premature decay affecting the cells of the highest physiological levels first, but occurring at all levels. Although the neurons when so affected cannot function normally and dissociation of systems of the highest evolutionary levels occurs, the neurons are not necessarily dead, there is a suspension of function of some and suppression of function of others according to the degree of intensity of the nuclear decay. I have dealt at fuller length in the Morison Lectures upon this theory of failure of neuron activity.

Recent Observations on the Histology of the Testes and Ovaries in Dementia Præcox.

At the last meeting of this Society I gave a demonstration of the "Histological Changes in the Reproductive Organs in Health and Disease," and I pointed out that there were three or four cases of dementia præcox in which I had found active spermatogenesis and several in which the macroscopic appearances might have passed for normal. A very pertinent question was put by a member regarding these cases. Why should the testes appear normal and active spermatogenesis be found in some cases of dementia præcox if this disease is associated with a germinal deficiency causing a regressive atrophy? I replied that every case that is diagnosed clinically as dementia præcox is not necessarily a case of that disease, especially if it be a case of relatively short duration as regards mental symptoms, as these cases were. But the case in which I had the greatest difficulty to show any regressive atrophic change was one that had been diagnosed dementia præcox by a very skilled and competent authority, so that it was necessary to find another explanation, and this is the one I will offer. Every pathological process which is of a primary progressive nature must have a beginning, and the technique which I at first employed may not have been sufficiently refined to show the earliest changes. Dr. Prado y Such (a pupil of Ramon y Cajal), a worker in this laboratory, has co-operated with me in a further research to demonstrate the finer histological changes by a special silver method of staining of frozen sections of tissues impregnated with gelatine, so as to hold all the delicate structures together *in situ*. We have been able by adopting this technique to show changes in these earliest cases where there is no loss of weight of the organs and normal naked-eye appearance and further upon microscopic examination showed active spermatogenesis. Sections of the testis of a young man who died of infective endocarditis were prepared and stained by the same method for comparison.

The Various Stages of Regressive Atrophy of the Testes.

I will throw on the screen lantern-slides showing on one side the normal, on the other the three stages met with in dementia præcox (*vide* Plates II–VII). It will be observed that even in the earliest first stage a commencing regressive atrophy can be seen, for some of the tubules are beginning to shrink; there is a crinkling of the membrana propria; the tubules are not so closely approximated as in the normal and there is a corresponding increase of connective tissue; there is a greater abundance of lipid granules in the Sertoli cells; the spermatogenesis is not so active and the spermatozoa are not so numerous. Under an oil-immersion many of the spermatids and spermatozoa seem to be ill-formed and tend to be stained with the acid rather than the basic dye (*vide* Plate I).

In the second stage there is a complete or almost complete arrest of spermatogenesis, but many of the tubules still contain spermatogonia and spermatocytes and even spermatids; the cells of Sertoli contain abundant lipid granules; the basement membrane is greatly thickened and there is excess of interstitial tissue.

In the third stage the tubules are very small; there is a complete or almost complete disappearance of the spermatogenic cells, the only cells remaining being the Sertoli cells, which may or may not contain coarse lipid granules and droplets. The interstitial tissue is often dense and always increased; it contains a variable amount of lipid.

The most interesting stage is the first, and Dr. Such and I are continuing our researches in order to see if it is possible to determine the earliest phase of this progressive decay of the germ-cells in the formation of the spermatozoa in the spermatids. So far as I am aware no account exists of the normal process in the human subject. We shall look for changes in the centrosome, in the mitochondria and in the archiplasm that forms the head of the spermatozoon. But the difficulties, as you may imagine, are great to detect pathological changes in bodies lying in the spermatids, which themselves are no larger than a red blood-corpuscle; moreover, the spermatids exist in unlimited numbers. Yet in respect to the testis this is a fundamental proposition which requires answering in order to prove how it comes to pass that there is a primary failure in the specific energy of the nuclear substance of the male germ-cell. The fact that the Sertoli syncytial or nurse-cells contain abundance of lipid in testes where there is a failure of spermatogenesis indicates that this failure is not due to a lack of the raw material, but that the spermatogenic cells are unable to utilise this phosphorised lipid ester by exhibiting evidence of a formative capacity to build up fresh nuclear substance.

The Pathological Changes in the Ovaries in Dementia Præcox.

In the ovary, where the primitive follicles are in limited numbers, the condition of the germinal vesicle and germinal spot (nucleus and

nucleolus) in respect to the chromosomes and chromatin network can be studied comparatively in the normal and in dementia præcox much more easily than in the testes.

Our preliminary investigations show that in dementia præcox the nucleus of the ovum in the primordial follicles is deficient in the chromatin network ; the nucleus is swollen, often irregular in outline, and the intranuclear network thin and sometimes ruptured, giving the nucleus the appearance of being vacuolated. Not infrequently the nucleolus takes the acid dye more than the basic. The changes are like those seen in the nucleus of the cortical neuron. Not infrequently frozen sections stained with Scharlach and the silver method show fatty degeneration changes of the germinal vesicle. The fatty degeneration of the nucleus of the primordial follicles can be seen even under a low-power magnification. Occasionally a follicle can be seen with its single layer of granule-cells separated from the theca interna, indicative of degeneration of the ovum. When these follicles are examined with an oil-immersion lens it is seen that the ovum is dead or dying, for it does not show the intra-nuclear network ; only the nucleolus is visible, and the remainder of the nucleus consists for the most part of intra-nuclear, coarse and fine lipoid granules. I have placed under the microscope sections to illustrate this degenerative change, which is striking when a comparison is made with the appearances presented by the ova contained in the ovary of a young woman who committed suicide (*vide* Plate VIII, fig. 1).

Another interesting fact revealed by this method of staining is, that in the normal ovary around the primitive follicles are abundant fine lipoid granules similar to those seen in the Sertoli cells. These same granules can be observed in similarly stained sections of the pituitary gland and between the cubical cells lining the colloid vesicles of the thyroid ; they are probably oxidase granules. In several cases of dementia præcox frozen sections of the ovaries stained in a similar manner we have not found these granules, or, at any rate, far less abundant in the stroma around the primordial follicles. Therefore these preliminary investigations tend to show in the ovary (*vide* Plates VIII and IX) :

(1) A failure of the primordial follicles to mature, even to the extent of a single layer of cells, except rarely, and then not to go beyond a single layer of cells to form a zona granulosa, which is generally separated from the theca interna.

(2) A degeneration of the nucleus.

(3) Replacement by ingrowth of stroma.

There is, I think, then, considerable pathological evidence forthcoming to show that dementia præcox is the result of an inborn germinal deficiency of productive energy of the reproductive organs

associated with a progressive deterioration of psycho-physical energy, the morbid manifestations of which show themselves in the whole body, but especially in the brain, particularly and firstly in its highest evolution level.

CONCLUDING REMARKS.

In conclusion I wish that I had the philosophic understanding and the command of language to express my thoughts as eloquently and lucidly as Dr. Maudsley possessed.

During fifty years his great mind was reflected in numerous classical works, now too little read and appreciated. His essays on Hamlet, Swedenborg and Vital Energy are remarkable efforts of his earliest philosophic literary attainments. I am showing here to-day the MS. of some of his works, and it will be observed how very few are the corrections in his recent great book on *Organic to Human*—a remarkable proof of the logical sequence of thought he possessed, combined with a remarkably full and accurate memory. His classical work *The Physiology and Pathology of Mind* was subsequently published in separate parts as *The Physiology of Mind* and *The Pathology of Mind*. An eminent American psychiatrist, now dead, told me that Prof. James of Harvard recommended his students to read these two books, and I can assure members of this Association who are not familiar with these works, they will derive, as I have done, much profit from reading and studying them.

I had the privilege of knowing Dr. Maudsley personally for the last ten years of his life. I had many opportunities of conversing with him on most subjects. I was always struck by his remarkable insight into the characters and conditions of men; he did not suffer fools gladly, not even clever fools, and he had an especial contempt for all that was shallow and superficial. His thoughts, like his writings, were tinged with pessimism and the vanity of things human. Hid beneath a hypercritical and often cynical exterior was a very kind and affectionate nature, which was readily touched by the real suffering of others.

Maudsley received no titular honour. Nevertheless it was recognised by those who knew, and it is that which matters, that he belonged to an "order of merit" that will not perish and be forgotten. His contributions to medical science and philosophy and the foundation of this hospital will, aided by this lectureship, keep his memory ever green. It can be truly said of Henry Maudsley—

"Exegi monumenta aere perennius."

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