

DEMENTIA PRAECOX.

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Some observations and a hypothesis.

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In treating cases of mental disorder one is constantly faced with the fact that we are almost entirely ignorant of the causation of the majority of cases. Some few mental conditions, particularly General Paralysis of the Insane, have been shown to possess a definite anatomical basis and a definite cause which at least indicates the direction in which we must look in the search for effective treatment, medicinal or otherwise. With regard to Dementia Praecox, however, we are entirely at a loss for a definite and constant aetiological factor, and consequently have no definite treatment and can hardly tell what manner of treatment should be tried. There has been much diversity of opinion with regard to the value of the classification devised by Kraepelin for a large group of cases previously

designated Hebephrenia, Katatonia, Adolescent Insanity etc., but there can be no doubt that all the cases which we are becoming accustomed to place under this heading possess certain features in common. So many gradations are found that it is at times impossible to decide into which of the many sub-divisions of *Dementia Praecox* we should place the case. In the course of a single case, one phase may supervene upon another, presenting very different symptoms both mental and physical at different stages of the disease. In spite of the diversity of mental symptoms which may be shown, there is a fairly general consensus of opinion as to all these symptoms being attributable to some common cause. A very considerable difficulty with regard to the diagnosis is introduced by some observers who maintain that it is not possible for a case of *Dementia Praecox* to recover. Such a contention only confuses the issue, and in discussing the disease I assume, as did

Kraepelin, Tanzi and many other high authorities, that in certain instances the disease is entirely recovered from, and in other cases there is partial recovery with some degree of mental impairment. Whilst admitting that it may be very difficult to distinguish certain recent cases of Confusional Insanity, Mania in early life, etc., from Dementia Praecox, I am satisfied that in the great majority of instances the diagnosis of Dementia Praecox can confidently be made by a psychiatrist of reasonable experience.

Dementia Praecox is not susceptible of any definite laboratory tests or absolute physical findings such as can be obtained in the majority of bodily diseases; consequently at the present time we have a vast number of Hypotheses and suggestions put forward to explain the mental changes observed during life and the physical changes which have been found after death. I know of no explanation which co-ordinates these various findings in such a manner

as will explain the pathogenesis and development of the disease and at the same time give an indication of the lines of treatment. For many years the age incidence has led psychiatrists to associate the condition with mental and physical "stress" during the period of adolescence, and it is easy to understand this tendency.

Very elaborate statistics have been prepared, particularly recently by Mott ( 1 ), which demonstrate conclusively a hereditary element. Some, such as Maudsley, have construed the findings with regard to heredity as indicating an attempt on the part of Nature to eliminate an unsound stock. There are those who believe that the mental and bodily changes are indicative of atavistic reversion, and quite recently White ( 2 ) and others have described the condition as a recessive disease in both its bodily and mental aspects. Against this view it can well be urged that Dementia Praecox is not an adapt-

ation to any conceivable set of circumstances, either in the previous life of the individual or of his ancestors: that it is in fact, as pointed out by Tanzi, the negation of all adaptation.

Kraepelin has ventured the suggestion that the disease may be due to an endogenous toxin from the reproductive glands, and this view seems to receive some support from the observations carried out by various observers who have examined the blood by Abderhalden's method and find indications of the presence in the blood of "defensive ferments" with specific action on the brain cortex and the testes(3) Mott ( 4) has studied the reproductive glands of a very large number of cases and found "primary regressive atrophy" in the gonads, both male and female, as well as changes in the cerebral cortex. From these pathological findings he concludes that "there is considerable pathological evidence forthcoming to show that Dementia Praecox is the result of an inborn germinal deficiency of reproductive energy of the reproductive

organs associated with progressive deterioration of psycho-physical energy". Such an interpretation is unsatisfactory, as it would be impossible on such a basis alone to explain the remissions, which are frequent, and the recoveries, which are occasional. Mott himself realises this difficulty, and suggests that possibly the cases which recover were not Dementia Praecox, but Confusional Insanity.

Subsequent observers have confirmed the findings of Alzheimer and others (5), who find in the deeper layers of the cerebral cortex definite degeneration with atrophy of the cells and neuroglia proliferation. Lugaro has endeavoured in a most suggestive way to co-ordinate the progressive systematic changes in the brain with disturbance of mental function as found in Dementia Praecox. This work is certainly of value, but in itself gives little indication of the starting point of the disease.

During recent years innumerable attempts have been made to associate this disease with changes in the organs of internal secretion. The subject has been approached from the anatomical viewpoint and also by means of empirical therapy. The results have been very discordant and do not seem to be susceptible of explanation. The chief difficulty in connection with the post mortem study of these glands lies in the fact that the acute intercurrent diseases which cause death themselves produce a great variety of changes, as has been clearly shown by Elliott ( 6 ), especially in connection with the adrenal glands.

Those who follow the modern psychological trend declare that as they can find evidences of early psychological disturbance in the cases investigated, the cause of the disease must be psychological and whatever anatomical and physiological changes may be observed are secondary to the original mental disturbance. It is very difficult to explain such an

assertion, more especially as the propounders of the theory have not, so far as I am aware, demonstrated in any way the mechanism by which the anatomical changes are brought about.

There has been much argument as to whether Dementia Praecox is a degeneration, a congenital defect, or a disease. The question has been fully discussed by many writers, and to me it appears incontrovertible that a diseased state offers the most satisfactory explanation of the many symptoms and structural changes. To assume that we are dealing with a disease process does not preclude heredity as an important factor. It may be pointed out that Tuberculosis and Dementia Praecox present very similar statistics with regard to inheritance: in fact the two are frequently associated in the same family history. If we were ignorant of the existence of the tubercle bacillus we might be tempted to say that tuberculosis was simply due to inborn weakness of the body cells. Lugaro made some pointed remarks

with regard to those who attributed to heredity any condition of which they did not know the cause. In passing, it seems almost worth while to refer to the age-long belief that tuberculosis and pronounced sexuality are closely connected. As to causal association there has been diversity of opinion. It may be that they share features in common: for instance, one thinks of the close relation of calcium metabolism with the reproductive glands and with the resistance of the individual towards tuberculosis. The occurrence of remissions in Dementia Praecox; of occasional, though infrequent, recoveries; the marked influence of acute intercurrent bodily diseases, are only explicable on the assumption that a definite active morbid process is taking place.

For some years I have endeavoured to satisfy myself as to the nature of this morbid process. One after another of the various aetiological factors as set forth by the Board of Control seem to apply to

Individual cases, but without any constancy except in the case of irregularities connected with the functions of reproduction. It is a time-honoured belief that such irregularities are a cause of mental derangement. This belief obtained for long amongst psychiatrists and was strongly advanced by Clouston, who based his conclusions upon extensive and acute clinical observations. During recent years there has been a growing tendency to depreciate this factor or to discard it entirely. Kraepelin, for instance, attaches no aetiological importance to auto-erotic practices, for which he advances two main arguments (1) that these practices are so common that there would be more cases of Dementia Praecox than is actually the case; (2) That the depletion of the nervous system by the loss of nucleo-proteids, which was at one time advanced as an explanation, does not apply in the case of the female sex, amongst whom the incidence of the disease is as great as amongst males. Both these arguments are superficial and ignore the

question of predisposition as well as the possibility of subtler changes in the metabolism of the individual which may account for morbid results.

The psycho-analytical school have studied the various forms of sex activity, but only from the psychological viewpoint, apparently ignoring entirely physiological concomitants and sequelae. Incomplete sex relationships and sexual desires which by reason of abnormality cannot decently be gratified have been credited with numberless effects on the Psyche, with the production of manifold neuroses. Scant consideration has been given to their action on the physiology of the nervous system and endocrine glands.

For some years it has seemed to me that the cases met with in the ordinary course of one's work could be regarded from the standpoint of physiology without losing sight of the fact that disturbances of mind, particularly as regards the emotions and instincts, can react upon the bodily state. I have endeavoured to provide for myself a working hypothesis

on which to base treatment. That hypothesis, put briefly, is - That excessive and abnormal sex excitement produces bodily changes which result in (1) functional derangement, and (2) organic changes in the central nervous system, more particularly in the cerebral cortex; and that these bodily changes are responsible to a large extent for the disease which we know as Dementia Praecox. This hypothesis is based primarily upon the history and clinical manifestations of a large number of cases which have come under my care.

The disease commonly occurs in adolescence. The subjects of the disease give clear evidence, either in their statements or conduct, of strong sexual feeling. This may arise spontaneously or be habitually evoked. When the patient does not come under treatment until adult life there is practically invariably a definite history obtainable of sex irregularities and neuroses of one sort or another, dating from the years of adolescence, as though the condition had been slow in development.

The data with regard to the sexual life and habits of patients depend entirely on the attitude of mind of the **observer**. Many, from instinctive sensibility, avoid the subject **entirely** and are satisfied to feel that the unnatural behaviour of the patients is simply one of the distressing manifestations of disease. Like an eminent physician who referred to the teachings of Freud, they are glad that it does not fall to them "to seek for pearls in that sty". When, however, a causal importance is attached to sexuality it becomes the duty of the physician to help and advise. Then it is that a history is obtained. By way of analogy there can be recalled the statistics which used to be compiled with regard to General Paralysis showing the proportion of cases in which there was a history or evidence of antecedent syphilis. The percentage would be very different now that the essential cause is known.

Therapeutic measures directed towards the

combating of erotism - supervision, cold baths, diet, bromides, and advice - frequently produce markedly beneficial results and occasionally cure. In the great majority of instances relapses are preceded by a state of emotional disturbance, and at such times the patient will commonly admit intensely erotic feelings and self-gratification. By the adoption of suitable treatment the relapse may be arrested.

In the early stages of the disease the practice of abnormal habits almost at once produces dilated pupils and exaggerated reflexes, which symptoms are followed by a state of mania. It is hardly necessary to repeat the observations which have so frequently been made with regard to the bodily effects of prolonged and unsatisfied sex desire in certain individuals. There are definite physical stigmata and alterations of manner which at once attract the attention of any experienced physician. These results are fully discussed in gynecological works

and elsewhere. That sex excitement can produce a profound influence upon the nervous system appears definite from two cases reported later - "E.C." and "G.C." (page 49). In the case of "E.C.", in spite of all efforts to prevent this, self-gratification is indulged in from time to time and is almost invariably followed by an epileptic attack. The patient herself admits that she has been addicted to the habit since early childhood and cannot remember a fit which was not preceded in this way. In case "G.C." abnormal sex habits were practised from early adolescence until the present time. Two years prior to admission she was operated on for exophthalmic goitre, most of the gland with the exception of the isthmus being removed. After the operation such habits resulted in apparently typical epileptic attacks. At about the same time she presented symptoms of tetany, for which she was treated in hospital. She herself realises the cause of her fits, manages to fight her habits

for fairly long periods, eventually gives way and has a succession of major fits. Neither of these cases is in any sense a typical Dementia Praecox, but both are able to give a perfectly lucid and reliable history.

The fits are not of a hysterical type and have at times seemed actually to threaten the lives of the patients. Especially in the latter case it appears reasonable to assume that altered metabolism due to excitement is responsible for the convulsive state.

It has often been remarked that exacerbations of mental symptoms occur in the menstrual periods. Not infrequently there is obtainable from the patient a history of ereticism, erotic dreams and hallucinations at such times. Two cases "M.E.T." and "R.K."- are illustrative (pp.50 & 51).

Here, as in the former cases, the patients are lucid in the intervals. They have very fair insight into their states and desire ardently to be cured. So far, "M.E.T." has shown little tendency to dementia but this may be due to complete physiological read-

justment during the three weeks which intervene between the acute phases. "R.K.", on the other hand, has shorter periods of lucidity, is definitely, though only slightly demented, and will undoubtedly proceed to profound mental dissolution if the acute attacks continue to recur.

The tendency to remission and relapse has frequently been remarked, and in my experience the relapse has invariably been preceded by sex excitement. Out of many examples I have selected two as having had particularly good remissions, when they were able to give a clear and reasonable account of themselves. As will be noted, in one case the patient recovered sufficiently to be discharged on three occasions - "P.H." and "G.M." (pp.51&52).

It may be objected that <sup>in</sup> the former of these cases the disease was not Dementia Praecox, but simple Mania. The symptoms were such, however, as mark the onset of many typical cases of the more serious

condition. At any time he may relapse and dement.

In text-books numerous examples of Dementia Praecox are quoted with a history of antecedent transitory affective psychoses. Surely it may reasonably be assumed that the same disease process was at work in the former illness. Many years ago Clouston noted the close association between brief maniacal attacks in early life and chronic adolescent insanity. G.M. is at present, and has been for many months in a quite typical katatonic state, regardless of her person and her surroundings, degraded in habits and wholly inaccessible. It is only possible to hope that some acute fever may intervene and again restore lucidity.

There have been under my care three sisters and two sisters and a brother. In each family there was a definite insane heredity. In each family there were members apparently normal and efficient. It would be easy to attribute the mental breakdown in all the cases to failure in development, but in each case there

was also a history of sexual malpractices dating from comparatively early life, resulting in dementia praecox or conditions allied to dementia praecox at very varying ages. The main features of these related cases are given on pages 55 - 57.

These cases further serve to indicate the different types which tend to be produced when the disease manifests itself during adult life after the mind and body have seemingly attained their full development. None of these cases showed any indication of congenital mental deficiency. They had, in fact, been rather above the average in intelligence: useful and self-supporting citizens. In those with delusions it was found that these delusions, and hallucinations when present, all showed to a pronounced extent that "sexual tincture" emphasised by Clouston. Although some authorities regard such delusions as referable to youthful psychic experiences, I am satisfied that they depend upon and take

their character from bodily sensations which in turn depend upon metabolic processes. The delusions of interference so often complained of serve as an irrational explanation of actual physiological changes, whilst the patient who bemoans an irreparable diseased state of the reproductive system, so commonly attributed to the occult acts of other persons, is usually found to base the hypochondriacal delusions on persistent failure to achieve sexual satisfaction.

There have come under my notice several cases of what I can only describe as acute Dementia Praecox, in which the classic symptoms of the disease occur, where restlessness and excitement persisted, the patient steadily emaciated in spite of all treatment and generous diet. No bodily disease could be found by clinical examination, and an autopsy revealed comparatively little to account for death. Case "C.M."

(p. 53) illustrates clearly the type to which I refer.

Cases such as this are not common, but must have occurred in the experience of most practising

psychiatrists. With a full knowledge of the patient's history it is almost possible to prognosticate the post mortem findings. Death appears to have been the outcome of disordered metabolism, and in the absence of knowledge to the contrary one might feel inclined to conclude that diabetes had been the cause. Though it might be suggested that starvation produced the fatal result as in, say, anorexia nervosa, I personally ascertained daily that fully adequate nourishment was being taken. It may seem a rather unwarranted statement, but I am inclined to think that in certain cases dementia praecox per se can produce a fatal result.

Cases such as that quoted led me to direct particular attention to the state of the suprarenal capsules at post mortem examinations, as well as to any possible clinical manifestations and functional derangements of this. Thereafter it was unavoidable to pay attention to those physical conditions which have in recent years been referred to disturbances of

the adrenal function. The excitability, increased manifestations of emotion, large pupils, brisk reflexes, so often recorded as occurring in the early stages of the illness, assumed significance as signs consistent with hyper-function of the adrenal medulla and the thyroid gland which seems to be intimately associated with it. The torpor, retardation and vaso-motor disturbances of the later stages, the diminution or loss of sexual inclination, the increase in weight, the general stagnation, seem compatible with hypofunction of the same glands. Tanzi has described very clearly some of the features of the two phases

"Dementia Praecox, especially the hebephrenic variety, is often preceded by almost incredible degrees of onanism, to which the patients give way without limit or sense of shame. According to common opinion, indeed, such abuses are the determining causes of the disease. It is, however, more probable that the excitement of the genetic sensibility is in itself a symptom of the disease. The practices accompany the early stages of this long involutive process, and sometimes cause great emaciation, but it is not uncommonly the case that they afterwards cease suddenly and completely. It would appear that in the progressive involution of hebephrenia even genetic sensibility is involved. When every erotic stimulus ceases the patients begin to put on flesh, and after a few months they attain to a grossness and ugliness which, being displayed chiefly in the face renders them unrecognizable. At this stage of dementia praecox all the symptoms of the disease subside permanently: the negativism disappears, the

"systematized delusions melt away, the patient no longer abuses himself - he is an extinct volcano."

For such a hypothesis as is advanced, to be tenable it is necessary to show (1) that it is explicable in terms of known physiological facts; (2) that it can explain the physical and mental manifestations of the disease; (3) that it is consistent with the pathological findings. Added weight may be assumed to attach to the hypothesis if it is capable of co-ordinating the conclusions and theories which have been put forward by previous observers.

(1) Various morbid and incomplete forms of gratification of the reproductive instinct differ in essential features from the normal. Nature provided this function and gave to it its importance in the economy of the individual for the purpose of propagating the species. Under normal conditions, sex excitement tends to be present only when there is opportunity for reproduction, although spontaneous

arousal occurs to a varying extent during the adolescent period. The consummation of the act has been regarded for many years as possessing a sedative influence, with suspension for the time being of sex desire. Thus there are two phases to consider; firstly the preliminary excitement, and secondly the culmination of the function. Though I am not aware that there has been any experimental work carried out with regard to the relation of adrenalin to sex excitement, there can be no doubt that the phenomena evinced are in keeping with that excessive stimulation of the sympathetic system which is generally accepted as being the result of the outpouring of the secretion of the adrenal medulla. The culmination of the act is exactly comparable to what might be expected from excess of adrenalin in the circulation, causing a generalised discharge along the sympathetic innervation of the viscera. This accomplished, the excitement normally subsides. It is accepted that physical as

well as bodily influences may produce through the nervous system such a discharge of adrenalin. In abnormal gratification this period of excitement is unnaturally frequent or prolonged, and amongst the insane at least it will be found on inquiry that consummation is unsatisfactory; so that the sexual nisus continues until in some cases there appears to be established a "focus of irritation" which it is difficult or even impossible to overcome. In early cases of dementia praecox many observers have noted dilated pupils, heightened reflexes, emotional instability and other signs apparently consistent with hyper-adrenalin states. Many of the early cases of dementia praecox correspond very closely to the description generally given of sympathetico-tonic individuals. In the later stages of the disease the general sluggishness, low blood pressure, cyanosis of the extremities, tendency to chilblains, etc., are much more suggestive of the vago-tonic state. It is

generally accepted that it is possible for secreting glands such as the thyroid and adrenal medulla to be exhausted and the patient's condition certainly suggests that such a process of exhausted glands has taken place.

It is very difficult to apply physiological findings with regard to the endocrine glands in the study of disease, so great is the diversity of opinion amongst physiologists themselves. It may be accepted that there is no such thing as a simple uncomplicated result of an internal secretion, since a process of action and reaction appears to be going on continually between these glands. However, there are certain main points which appear to be generally accepted. For many years an association has been observed to exist between the supra-renal capsules and reproduction. There is no doubt as to the development of the organs of reproduction and of the adrenal cortex being comparable in point of origin and stages of maximum

growth. Overgrowth of the cortex apparently induces premature sexual development. Gaskell ( 7 ) regarded the thyroid gland, the adrenal cortex and the glandular part of the pituitary body as belonging to an old segmental series of glands which were once related to the genital and excretory apparatus and still retain the function of modifying growth and development. Whether sexual activity in its turn reacts upon the activity of the adrenal cortex is not clear. As remarked above, a phase of sexual excitement is comparable with the results of stimulation of the adrenal medulla, and it is very tempting to believe that the close conjunction of the two parts of the gland has some functional significance. Sajous ( 8 ) believes that the adrenal cortex is under the control of the autonomic system, and support seems lent to this view by the presence of choline bodies in the cortical cells, choline having an action on the autonomic system antagonistic to that of adrenalin. That excessive function of the thyroid gland may be followed

by hypo-function and myxoedema seems to be a fact. We know that the adrenal medulla can be exhausted of its supply of adrenalin by emotion and fevers. For the purpose of hypothesis there seems good ground for the assumption that persistent depletion of the adrenal cortex with signs of hyper-function may be followed by a state of functional inactivity. From clinical findings this appears to me to be the case. Excessive discharge of adrenalin apparently leads to increased metabolic changes. It has been suggested that adrenalin enters into the formation of an oxidase. On the other hand, insufficient adrenalin might be expected to produce diminished oxidation. The findings of numerous observers are in favour of such an interpretation; thus Pighini ( 9 ) as the result of extensive observations on the urine came to the conclusion that in the early stages of dementia praecox increased oxidation was taking place, while in the later stages the reverse was the case. These observations led him to support Kraepelin's suggestion that dementia praecox is not a degeneration, but a

metabolic disorder. As has been previously mentioned, some cases of the disease of long duration show degeneration or complete destruction of the adrenal medulla. From the appearance it seems that such destruction has been of very long standing. Whilst this certainly tends to show that the medulla is not essential to life, such a condition would undoubtedly explain some of the physical changes met with in advanced cases. The low blood pressure and vasomotor disturbance so frequently encountered are explicable as the result of adrenal deficiency. In the diagnosis of vago-tonia, considerable stress has been laid upon the condition of eosinophilia. In spite of some diversity of opinion there seems no doubt that there is at least in many cases an increase in the number of eosinophile cells in the blood. Lewis Bruce (10) stated that a transient eosinophilia at least occurred in every case, whilst Dide and Chenais (11) reported some increase in a large percentage of the cases they examined.

All the pathological findings in the brain and the reproductive system appear to be susceptible of explanation as the results of deficient oxidation.

When we consider that adrenalin is credited with an oxidizing function and that the oxidase granules of the cells of the cerebral cortex are of a lipoid character we at least have some indication as to the manner in which disturbance of function of both parts of the adrenal glands may cause imperfect function and later, atrophy of those cortical cells which are most involved in the disease. There is an increasing tendency to accept the view put forward by Elliott (12) that the adrenal cortex manufactures those lipoids which are essential for the development and maintenance of the nervous system. In spite of the obscurity which surrounds the functions of the adrenal cortex, it seems probable that the discharge of its secretory products is under the control of the nervous

system, and therefore any failure to supply the body with lipoids may be due, not to disease of the cortical portion itself, but to a disturbance of its innervation.

Since Eppinger and Hess ( 13) introduced their conception of vago-tonia and sympathetico-tonia there has been much criticism directed towards it. They believed that excessive function of either of the main divisions of the vegetative nervous system resulted in increased function of its antagonist. Although this view has been contested by Langley ( 14) there seems no reason why we should not encounter preponderance of autonomic action after failure or destruction of the adrenal cortex. Langley's observation ( 14 ) that the sympathetic system is developmentally of later origin than the autonomic would lead us to look for failure of the former system more readily than of the latter.

(2). The hypothesis which is being put forward has been applied in the study of a very considerable number of cases during the past three years. It has appeared to fit in with all the observed facts, both mental and physical. The excitement, restlessness, and other symptoms of the early stages, accompanied by loss of weight, increased reflexes and pupillary dilation always appear explicable as the result of bodily changes. When exhaustion proceeds to a certain point and the patient's life appears to be in danger, improvement not infrequently begins comparatively suddenly. When the physical exhaustion is produced by acute bodily illnesses, a similar improvement, both bodily and mental is observed for a time at least. The relapses which unfortunately are so common are preceded by eroticism in a vast majority of cases. Various observers have endeavoured to attribute the improvement which follows physical illness to purely

psychical causes. They explain that in a bodily illness accompanied by delirium there may occur amnesia for antecedent conflicts, etc. To me it seems much more reasonable to believe that during the constitutional disease there is a readjustment of physiological processes and metabolism. In the course of the disease there seems to come a time when no factor produces an appreciable improvement, although it must be admitted that recovery, or improvement with dementia so slight as to be negligible, does occur when it could hardly have been hoped for. In spite of Lugaro's ingenious association of mental and physiological changes, it is impossible for us to predict the nature of the mental disturbance which may arise through deficiency in function of the brain elements. The many varieties of General Paralysis, the changes in the mental state of a single individual in the course of this disease, give some idea of the almost unlimited possibilities in the mental sphere

of inflammatory and toxic influences. It is worth while to remark in passing that in general paralysis, which is undoubtedly an organic disease, the occurrence of a high fever is not infrequently responsible, apparently, for a markedly beneficial result upon the mental features of the case. In dementia praecox it seems as though pyrexia produced its beneficial results by exhaustion of a previously over active adrenal medulla. That such exhaustion does take place in fevers has been definitely shown.

Both bodily and mental changes might be expected to vary according to the age at which there began functional disturbance of the nutrition of the nervous system. Cases occurring in early life which have been called by Kraepelin and others "Dementia Praecocissima" are frequently difficult to distinguish from states of imbecility: in fact they cannot always be so distinguished. A retention of childish bodily and mental attributes seems susceptible of

explanation along the lines suggested, and the history is generally confirmatory. In the early stages of the disease, as has been mentioned, the patient is commonly excited and "sympathetico-tonic". During this stage it is the rule for menstruation to be suspended, as also occurs in states of hyper-thyroidism. Remissions in this stage are comparatively frequent. As the disease progresses, dilated pupils become a less conspicuous factor. The reflexes cease to be definitely exaggerated; the tendency to oedema, cyanosis, etc., becomes pronounced, and thereafter recovery is very rare.

On such a basis of physiological functional disturbance it is possible to interpret the observation of Clouston:-

"The period of adolescence is very liable to psychological cataclysms in weak brains, attacks of mania which have special relationship to functions of reproduction. Especially it seems to me that the periodicity and remission of the *nisus generativus* in both sexes, and the menstrual periodicity which accompanies it in woman, are reflected in a corresponding periodicity and tendency to remission in the insanity that occurs during adolescence."

(3). Pathological observations on cases of Dementia Praecox have been directed primarily to the nervous system, and during recent years to the reproductive system and the endocrine glands. In the brain, Alzheimer and numerous subsequent observers have described the degrees of change from evidence of functional disturbance to actual death of cells ( 5 ).

Recent improved pathological technique has disclosed indications of diminished cell activity without gross injury to the cellular elements. In the interpretation of these changes there has been considerable diversity of opinion, and whilst some think they are indications of toxic influences, others, such as Mott and Shaw Bolton, regard the changes as the outcome of congenital weakness leading to premature senility.

It is generally conceded that the degree of change discovered bears a direct relationship to the duration of the illness and the acuteness of the symptoms.

I am not in a position to interpret such changes

myself, but I have noticed that very similar changes are recorded by a number of observers in the nervous system of patients who have suffered from Myxoedema (Mott, 15 ) and in the nervous system of animals after thyro-parathyroidectomy (Edmunds, 16 ).

Myxoedema has many features in common with advanced cases of Dementia Praecox, in which latter disease one observer finds definite stigmata of thyroid deficiency (Bernstein 17 ). In early cases of the disease there are no manifest changes in the nervous system. The late cases in which changes have been described are probably therefore those in which there has been such a failure of thyroid secretion, as is frequently indicated by the clinical appearance of the patient. It is known that the thyroid and supra-renal capsules are functionally related, and deficiency of either might be expected to produce excessive or diminished oxidation to such an extent as would provoke functional changes and eventually atrophy of

the nervous structures.

Although there is intimate relationship between the reproductive organs, the supra-renals and the thyroid, it is not well understood just how they interact. However, the suggestion has been put forward that one function of the adrenal cortex is to manufacture lipoids for the formation and growth of the nervous system and the reproductive elements.

As the adrenal medulla and cortex appear to have a common innervation and blood supply, it may be assumed that any disturbance of either cortex or medulla is capable of producing injurious effects upon the gonads. On such a basis the diminution or cessation of spermatogenesis and atrophic changes in the Graafian follicles, which have been described, seem capable of interpretation. That this may not appear a quite unwarrantable assumption, I would mention that according to Biedl ( 18 ), experimental hyperadrenalism appears to produce hypertrophy of the

adrenal cortex, whilst, as mentioned above, the prolonged feeding of white rats with cortical substance after preliminary hypertrophy, caused degenerative changes of which cessation of spermatogenesis was a marked feature (Hewer 19 ).

There has been no constancy in reports regarding the condition of the supra-renal glands in this disease.. (20) Kojima/conducted extensive observations, studying particularly the weight of the glands and their histological appearance. He found no evidence of constant change, and such differences as were observed, e.g., in the lipid content of the cortex, were attributable to the intercurrent diseases which cause death. My own experience has been that in cases dying without high fever the cortex is increased in depth whilst the medulla is apparently narrower than normal. This occurs in the findings of Eaignel-Lavastine (21 ). In a number of cases of long stand- where there had been considerable dementia for many years, I have

found complete destruction of the medullary substance, a well developed cortex, forming, as it were, a flat cyst in which, in place of medulla, there was a small amount of brown fluid. This last condition might be associated with the diminished metabolic processes and torpor found in those cases in which vago-tonic clinical manifestations prevail.

In the light of what has been said, a different interpretation may be placed upon the conclusions arrived at by various authorities. The view of Kraepelin, that dementia praecox is due to endogenous toxins produced by the reproductive glands is compatible with disturbances of function of the supra-renal capsules; whilst the view of Tschisch, (22) that "suppression or defective development of sexual activity is to be regarded as the cause of dementia praecox" is closely analogous with the hypothesis now

put forward. Pighini concluded as the result of his investigations that this disease is a metabolic disorder, but was not so specific in his explanation of the various features of the condition. The view that a developmental failure is responsible has been advanced by Mott and Shaw Bolton. Their findings are explicable as the result of deficient oxidation processes. The former observer is of opinion that the appearances of the cells, the staining of the lipoids, etc., are evidences of defective metabolism. The cell, for the efficient performance of its function, requires not only an inborn vitality but a regular supply of necessary materials, amongst others, the secretions of the various internal secretory organs. It is noteworthy that the degenerative changes are particularly observed in those structures into the formation of which there enter the special lipoids which are considered by some to be manufactured in the adrenal cortex. So far as the psycho-

genetic origin of dementia praecox is concerned, it may be conceded that a mental phenomenon which is capable of producing a change in the organs of the body can by disturbance of function, if long continued, lead to structural changes. In this way it is possible for a vicious circle to be established, and an analogy would seem to be presented by the part which is credited to emotion in the causation of diabetes mellitus. Jelliffe ( 23 ) in a consideration of the disturbances of the vegetative nervous system in dementia praecox concludes that "the desire in the heart of man" contains the chief answers to the problem. "The vegetative nerve disorders are the results of its mal-adaptations rather than its causes". The mal-adaptations, I believe, are due to the use of the generative functions contrary to the designs of Nature.

The importance of finding, if possible, a physiological basis of dementia praecox lies in the

fact that when the majority of cases come under my care there is already so much mental impairment that is is hopeless to attempt to apply psychological methods, at least with a view to cure. The patients are inaccessible and unimpressionable. It may be possible one day so to modify their bodily functions as to restore them to a state where mental therapy may be applicable.

It is in the hope of finding some deviation from the normal which might give an index to disturbed bodily function that I have examined the blood of a number of cases by quantitative chemical methods. The extensive work in this direction carried out in recent years by Folin, Myers and others has thrown much light on the diagnosis of nephritis, diabetes and other conditions. In view of the significance of sugar tolerance curves in hyper- and hypo-endocrine

diseases, glucose estimations in dementia praecox seemed likely to be of value. Creatinine was tested for at the same time, as being the nitrogenous constituent of the blood least subject to variation in consequence of extrinsic conditions such as food.

Grigant ( 24 ) found that "the fat load of the cortical cells (of the supra-renal capsules) varies directly with the percentage of cholesterin bodies circulating in the blood". Also Pighini ( 25 ) stated that he could detect cholesterin in the cerebro-spinal fluid of 43 per cent. of the cases of dementia praecox examined, and that this substance could not be demonstrated in healthy persons. It seems then, that quantitative estimation of cholesterin in the blood might give an indication of the state of the supra-renal cortex during life.

The results of the examinations are shown in tabular form. Unfortunately the insane do not lend themselves readily to the necessary withdrawal of

blood specimens, especially when in the acute phases of their ailment, and it is just in those acute phases that one would expect to find any deviations from the normal which may occur. Consequently the number of observations recorded is too small to warrant any definite conclusions. Weston (26) in 1916 reported the results of quantitative sugar estimations in a long series of cases of insanity. He classified the cases of dementia praecox as "mild", "moderate" and "severe", and was unable to draw any inferences. The only justification for presenting the present series of figures is that they have been carried out on blood taken from patients whilst in definite phases of their disease. An accumulation of such figures may lead to a tangible result.

The methods used are those of Myers (27), which seem most useful in a laboratory equipped for clinical purposes. Considerable difficulty was experienced in obtaining satisfactory chemicals for the estima-

tions. One sample only of picric acid was used throughout as conforming to the test referred to by Folin and Doisy ( 28 ). The glucose used in the making of the standards was "analytically pure" and was rendered anhydrous in a hot-air oven before weighing. It was only possible to secure one sample of creatinine for comparative purposes. In the estimation of cholesterin the strictest anhydrous conditions - drying tubes, extraction thimbles, flasks and condensers in the hot-air oven - and the use of "analytical reagent" sulphuric acid and acetic anhydride failed to produce a colour which quite matched the only sample - a rather crude one - of Naphthol Green B. which was available. Consequently in all the results which are recorded a standard cholesterin solution in chloroform was treated simultaneously with the unknowns and used for comparisons. The readings were made with a Kober colorimeter, the various suggestions of Folin ( 29 ) being carried out.

Unfortunately I have not been able to carry out yet a series of observations on normal blood which would be necessary to give value to the figures. However, as will be noticed, the examinations relate to a considerable variety of cases, comprising various acute phases and also a stage in convalescence sufficient for a return to ordinary life, Though the results vary considerably they do not seem susceptible of any explanation so far. It is not easy to find amongst cases of dementia praecox willing or easy subjects for glucose tolerance tests. So far I have only been able to carry out three such tests which are submitted rather as negative findings than to support any conclusions.

The hypothesis is advanced as the outcome of clinical observations made on a large number of cases. It appears on both physiological and pathological grounds that irregularities of the reproductive

functions are capable of producing the disease which we know as dementia praecox. It is felt that observations conducted with this hypothesis in mind may lead to some treatment, whilst at the present time Medicine is apparently, to all intents and purposes, helpless in the treatment of such cases, and such recoveries as do occur are spontaneous.

Though the observations on the chemical constituents of the blood which are presented do not appear to be of positive value, it is hoped that further pursuit of the subject may at a later date yield profitable results.

Summary.

1. That frequency with which irregularities of the reproductive function are associated with Dementia Praecox, the nature of the manifestations of the disease, both bodily and mental, and the age of incidence justify the belief that there is a causal relationship.

2. The course of the disease indicates that the bodily changes are at first functional and liable to recovery. In the later stages there are organic changes and failure or suppression of function.

3. The changes observed clinically seem explicable as the result of disturbance of the vegetative nervous system and the endocrine glands, especially the supra-renal capsules.

4. The structural changes noted in the cerebrum and gonads appear to be due to failure of oxidation processes, and are similar to those associated with diseased states and experimentally produced conditions involving the endocrine organs.

5. Heredity is probably a predisposing factor in

the same sense that preponderance of function of either of the main divisions of the vegetative nervous system is a family characteristic.

6. Psychological causes seem to contribute towards the disease in so far as they are capable of modifying the functions and metabolism of the body, thus establishing a vicious circle.

7. As in tuberculosis, "a fool seldom recovers", so in dementia praecox we cannot expect to effect cure by advice on mental and bodily hygiene, for the very nature of the disease renders the patient incapable of appreciating such advice.

To render the patient amenable to psycho-therapy seems possible by no other means than those directed towards re-establishment of physiological equilibrium. The hypothesis which is put forward seems to offer at least an indication of the direction in which treatment may one day be found.

E.C., admitted July, 1920, aged 18. Of good physique; free from manifest bodily disease: no history of insanity or neuroses in the family. A history of epileptic fits since 8 years of age, accompanied by confusion, and hallucinations, auditory and visual, usually of a sexual character. As fits were always preceded by dilated pupils and mild excitement she was questioned with regard to sexuality. Admits auto-erotic habits since a small girl. Careful observation and inquiry showed that fits were preceded by self-gratification, which was often started by erotic dreams. In spite of her efforts to resist the inclination she gives way periodically, has a succession of fits, then gradual improvement. Though bright and fairly industrious in intervals between attacks, she is slowly deteriorating.

G.C., admitted June, 1919, aged 32. Average intelligence. No history of mental defect, but sister definitely childish. Patient earned her livelihood as a needlewoman until 2 years prior to admission when she had exophthalmic goitre, for which she was treated at four teaching hospitals in London. Finally much of the thyroid was removed. Two months later she had convulsive attacks of epileptic type, subsequently treated as tetany. On admission she had signs of tetany - spasm of



R.K., admitted January, 1918, Good physical condition and average intelligence. History informative. On admission was stuporose, negative, with grimaces and mannerisms. After course of cold baths she improved temporarily and gave a clear account of herself. Admitted self-abuse - acquired the habit at the age of 12. Could not refrain, especially at periods which recur every 21 days. During past four years has had recurrent attacks at menstrual periods. Appeared to be improving and attacks were less severe, but recently had dilated pupils, was actively hallucinated and had vague persecutory delusions. Admitted returning to her former habits but said she simply could not help herself. In lucid intervals is bright and pleasant, but shows a little mental deterioration.

P.H., admitted April, 1913. Private R.M.L.I. Emaciated, but without organic disease. Maternal aunt and paternal uncle insane. In a state of acute excitement; somewhat confused, mischievous, destructive. An inveterate masturbator. Treatment directed towards this last symptom: bromide, cold baths, employment when possible. Excitement slowly subsided, became utterly casual. Delusions of a sexual character. Gradual subsidence of symptoms, Discharged December, 1914. Re-admitted in February, 1915. Was then depressed, seclusive, would not go out, had delusions of reference; contemplated suicide. Improved rapidly and was discharged in September, 1915.



He joined the Army, served in France, and when last heard of was doing well

G.M., admitted January, 1921. Was twice previously under treatment. Physically well developed. Of average intelligence. Father alcoholic prior to birth of patient. Mother had fits as a child but these ceased at the age of 14, and she appears to be a normal and intelligent woman, though rather nervous. Patient had "hysterical fits" at night from 10 to 12. Menses at 14. Shortly after, she had chorea. Admitted in 1915. An inveterate masturbator; retarded, negative, resistive; grimaces and mannerisms; dirty in habits. Gradually improved and was discharged recovered. Readmitted after a year. Typical katatonic, with hallucinations and impulsive violence. After 15 months she apparently recovered and was discharged. Re-admitted after 14 months. When asked about her known habits, she replied "Three months ago. I couldn't help it". In December, 1921, had a severe attacks of influenza and became approximately normal. About a month later, after attending the patients' ball, her pupils dilated, she admitted return to abnormal habits. Has deteriorated steadily since and will become a chronic dement.

C.M., admitted 1915.

Fair physique, but thin and haggard. History very incomplete, but she had apparently been of more than average intelligence. Confused, restless and hallucinated. Passed into a state of very acute mania, followed by stupor and resistiveness. Habits very degraded. Gradually improved and in January, 1917, was sent on trial with view to discharge. Soon relapsed and on return admitted recurrence of morbid sexual practices. In spite of treatment and advice this continued. She went to incredible lengths in an endeavour to obtain sexual satisfaction and deteriorated rapidly, both mentally and physically. Dieting and other treatment failed to arrest emaciation, and she died with no clinical signs of any bodily disease; diabetes, phthisis and blood conditions having been suspected.

Post Mortem examination. The heart was very small and had a translucent appearance. There was slight hypostatic congestion of the lungs with a minute focus of suppuration at the left base. Stomach, intestines and other viscera normal, except for slight congestion in areas of the bowel. The supra-renals were very large, especially the cortex, which was yellow and apparently loaded with lipoid, in several places projecting like lentils, a condition which has been described as tendency to adenoma formation. There was no apparent cause for the emaciation which had occurred.

E.L., admitted May, 1914, aged 20. Father alcoholic.  
First Cousin insane. Patient's mental symptoms followed a confinement three weeks prior to admission. In a state of acute excitement, which subsided, leaving her in a typical katatonic condition - stuporose, dull and anergic. Acute periods occurred occasionally with hallucinations and violent impulses. Intensely erotic, degraded in habits. For six years she was a seemingly hopeless case of dementia praecox. In July 1920, she had a cough and slight pyrexia. Could not be examined satisfactorily on account of stupor and negativism. Treated as possible tuberculosis. Temperature continued raised for two months. Mental condition steadily improved. She gained weight; became apparently normal. A little childish, but probably has always been so. Discharged recovered after three months trial, and a year later apparently still well and earning her living at a factory.

Father had several mental breakdowns. Collateral relatives neurotic..

married

R.B. / Admitted April, 1915, aged 29. Very depressed, dull, introspective. Ideas of unworthiness. Attempted suicide by cutting throat. Resistive; difficult with food. Very slow, but progressive improvement. Recovered sufficiently to be discharged on an undertaking, March, 1917. Re-admitted in February, 1918; again depressed and suicidal. Pregnant. Remained depressed until 6 months after delivery. Passed into a state of katatonic excitement: grimaces, gesticulations, degraded in habits. Excitement and depression recurred until early in 1921. Became very thin and feeble. Gradually improved mentally and physically. Again discharged on undertaking, October, 1921. A history of abnormal sex practices since the age of 15: admitted to have preceded each emotional disturbance. When convalescent, fear of giving way to her habits caused numerous requests for bromides or other sedatives.

E.E.G. Single. Admitted February, 1918, aged 51. Melancholic; delusions of changes in viscera; mannerisms and impulses. Gradually improved. Discharged on an undertaking, June, 1920. Had been under certificate for 2 years when 21. Admitted addiction to masturbation for some years previous to that, which habit was resumed at 40, about which time she became religious and seclusive. For a number of years had been assistant curator at a botanical

museum. She was an expert botanist and apparently had been very intelligent.

R.E.G., single, aged 49, admitted April, 1922. Depressed, hypochondriacal, delusions, suicidal impulses. Believed people shunned her because they knew of her unnatural sexual practices, which dated from adolescence. Described by relatives as "always sensitive and inclined to morbidness". Had a nervous breakdown at 31. She has visual hallucinations of an unpleasant sexual character. Believes her body is permanently ruined because her sexual feelings have altered. She is rapidly dementing: is negative slovenly and impulsive. A typical paranoid dement.

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Family "W".

E.M.W., single, aged 37, admitted March, 1919. Father insane. Several relatives suffered from neuroses and tuberculosis. Of family of nine, patient, two brothers and two sisters have been under certificate. She was previously admitted at the age of 33 in July, 1915, prior to which she had "nervous breakdowns" for three months each year for five years. Had been engaged in business. Was well educated and intelligent. On first attack was maniacal, mischievous and entirely irresponsible. On the second attack in a state of paranoid dementia with hypochondriacal

Family "W" (continued).

delusions and ideas of unworthiness. History of sexual irregularities from early life. On each occasion she improved sufficiently whilst under treatment to be discharged on an undertaking.

S.A.W. Male. Single, aged 35. Admitted March, 1915. Mental symptoms noted by family for three years prior to admission. Very dull and anergic. Numerous irrational beliefs about bodily state and food: required tube feeding. Took no interest whatever in his surroundings. Addicted to masturbation. Cyanosis of extremities. Mental condition was rapidly deteriorating when he contracted acute tuberculosis. He died, March, 1916.

E.W.W. Female, single, admitted May, 1918, aged 43. She had been depressed for years. Latterly had delusions about her bodily state and food. Sat brooding continually: required to be washed and dressed. Difficult with food. Negative in every way. Poor peripheral circulation; oedema of feet. Believed that people attracted attention to her because her appearance had been altered in some strange way by masturbation, which had been practised since childhood. She was becoming progressively worse when she was transferred to another hospital, in December, 1918

Sex.	Creatinine. mg. to 100 c.c.	Sugar. per cent.	Cholesterolin. per cent.	Remarks.
1. E.S.* F.	4.386	.143	.144	For many years subject to alternating phases of stupor and excitement. Negative and resistive. At time of examination in state of resistive stupor, with sudden impulses, katatonic type.
2. G.G. F.	4.46	.115	.207	A hebephrenic of long standing. Very dull and listless. Emaciated in spite of dieting.
3. M.C. F.	2.12	.101	.182	Has been in a profound stupor for several years. Entirely mute and dependent. Slightly resistive. Formerly impulsive.
4. V.S. F.	2.26	.115	.179	A recent case. Paranoid and excited.
5. E.M. F.	2.31	.115	.221	Recent mania with hallucinations and confusion. Likely to develop into a typical case of dementia praecox.
6. P.P. F.	2.64	.197	.26	Recent stupor. "Stupor attonita".
7. E.S. F.	2.84	.114	.163	Recent mania. Developing paranoid delusions.

\* This case, about 6 weeks after the blood was examined, abruptly passed into a uraemic state and died after convulsions lasting 12 hours. At the post mortem examination there was found definite chronic parenchymatous nephritis, unsuspected until the uraemic symptoms developed.

<u>Sex.</u>	<u>Creatinine.</u> <u>mg. to 100 c.c.</u>	<u>Sugar.</u> <u>per cent.</u>	<u>Cholesterin.</u> <u>per cent.</u>	<u>Remarks.</u>
8. S.J. F.	2.85	.115	.203	Recent paranoid case with outbursts of excitement
9. M.A. F.	3.12	.141	.212	Convalescent from stupor at time of examination. Apparently making a good recovery.
10. M.M. F.	2.99	.113	.16	Convalescent after depressed and partially stuporose condition.
11. M.H. F.	2.75	.125	.167	A very degraded and demented katatonic. Stuporose At times impulsive.
12. G.R. F.	2.29	.105	.163	Katatonic stupor. Emaciating for no ascertainable reason. Mental deterioration has been rapid.
13. E.M. F.	1.941	.117		Katatonic stupor: unaltered for three years. Quite dependent.
14. J.A. F.	2.156	.113		Katatonic. Impulsive. Mischievous, but usually stuporose.
15. W.I. Male.	2.43	.098		Katatonic excitement. Restless day and night.
16. D.W. M.	2.14	.11		Katatonic stupor. Makes no movement spontaneously and is mildly resistive.

Remarks.

Cholesterin.  
per cent.

Sugar.  
per cent.

Creatinine.  
mg. to 100 c.c.

Sex.

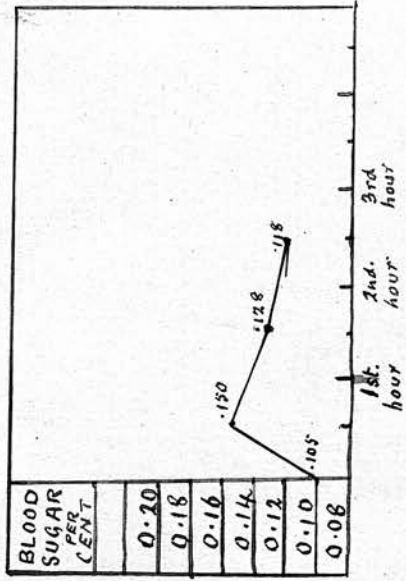
17. G.M.	F.	.131	At present in a state of pronounced katononia. Subject to outbursts of excitement.
18. J.S.	F.	.105	Just emerging from a maniacal phase of which she has had many. In intervals shows the irrationality and apathy of a hebephrenic.
19. J.S.	F.	.118	Has been for several years a demented hebephrenic. Automatic and dull.

To ensure uniformity of results as far as possible, the blood examined in each case was taken in the morning before breakfast and at least ten hours after the previous meal.

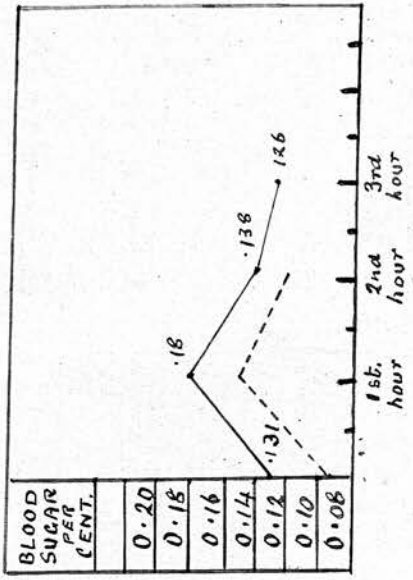
Though the figures given are in the absence of a series of normal figures of value for comparative purposes only in respect of the different phases of dementia praecox, I append the figures which Myers

using the same methods, accepts as a normal average:

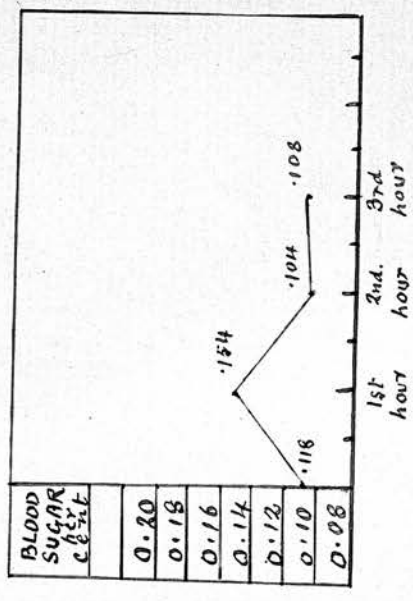
Creatinine	1 - 2	0.09 - 0.12
Sugar		0.14 - 0.17
Cholesterin		



Case 1. Katatonia - mania.



Case 2. Katatonia - stupor.



Case 3. Hebephrenia with long-standing dementia.

Glucose tolerance tests. These were carried out in the manner advocated by Killian (quoted by Myers). It will be noted that all three curves approximate to that which Killian gives as an example of the normal. This is shown in a broken line in Fig. 2.

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