Alcoholic Insanity (Korsakow's Polyneuritic Psychosis): Its Symptomatology and Pathology.

By JOHN TURNER, M.B., Senior Assistant Medical Officer, Essex County Asylum.

INTRODUCTION.

(1) *Definition of Alcoholic Insanity.*

THERE are certain persons who, having taken alcohol to excess, develop a form of insanity characterised by distinctive features, clinical and pathological. [This is the form which I mean by "alcoholic insanity."]

There is a far larger number of persons in whom various forms of insanity are associated with drinking habits; but these forms present no characteristic features either clinically or histologically, and unless the fact of indulgence in alcohol can be established by inquiries into the personal history of the patient, it would be impossible from a study of the case alone, in my opinion, to adduce alcohol as the causative factor.

It is this larger class which I am unable to look upon as of alcoholic origin in the sense that alcohol was the causative factor.

What are the distinctive symptoms in a case of alcoholic insanity?

In my opinion it is only when a case presents the symptoms described by Korsakow as polyneuritic psychosis that we are justified in asserting that we are dealing with a case of alcoholic insanity. I know that it is generally asserted that Korsakow's disease is only one of the forms by which alcohol displays its deleterious action on the nervous system, and further that Korsakow's disease is not necessarily the result of alcohol.

As regards the first of these points, if it be allowed that alcohol is capable of producing a definite form of insanity, a form which can be diagnosed without a reference to past habits, and which can be recognised after death by characteristic appearances, then in default of these criteria the burden of proving that alcohol may also cause various forms of insanity, which we frequently meet with in persons in whom one can

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with certainty exclude this factor, rests with those that make the assertion.

As regards the second, my experience fully bears out Ascherson's (1) statements that "hard drinking has a share in the ætiology of Korsakow's disease in an overwhelming majority of the cases," and "a more careful investigation of the histories of the non-alcoholic cases would only serve to swell the number of the alcoholic at their expense. In typical cases alcohol can never be excluded."

I can recall one case of polyneuritic psychosis in a young woman suffering from pulmonary tuberculosis, apparently, from her own account, a model of propriety and sobriety, and with none of the physiognomical stigmata of alcohol, and unless I had been fortunate enough to obtain from a trustworthy source the true state of affairs, which was a life of drunkenness and immorality, this would have been included under the head of polyneuritic psychosis of non-alcoholic origin, and probably as due to tubercle.

(2) *The Relationship of Alcohol to Insanity.*

This appears to be of a three-fold nature:

(1) *Coincidental.*—That such a relationship should occur in many cases appears to be unavoidable when we consider the very large number of people who consume alcoholic drinks in some one or another form.

(2) *Sequential.*—The drinking of alcohol in most people produces a momentary pleasurable sensation, followed by a more remote feeling of well-being. So that it can easily be perceived why those in whom the highest inhibitory powers are deficient will be especially prone to over-indulgence. Under this heading come the Jane Cakebreads, who spend their time between the gin-shop and the prison, weak-minded persons or moral imbeciles unable to resist the attractions of alcohol, under the action of which they become a nuisance to the community. With such the alcohol is not the cause of the insanity, but the insanity is the cause of the drinking habits.

(3) *Causal.*—Here the drinking habits produce in certain predisposed cases a series of characteristic symptoms and a specific lesion of the nervous system, and from my point of view unless these symptoms or histological appearances can be

shown one is not justified in labelling every case where over-indulgence in alcohol can be proved as alcoholic insanity.

Numbers 1 and 2 make up by far the larger bulk of the cases in which alcohol is related to insanity, and account for the large percentage of cases of insanity which are wrongfully attributed to alcohol. As a matter of fact, as a causal factor in insanity it plays a comparatively insignificant *rôle*, 3 to 4 *per cent.* in women, and probably about the same proportion or rather less in men I find in the Essex County Asylum, whilst Dawson (2) puts the percentage of mental disease really attributable to alcohol at about 10 *per cent.*

As regards the various forms which authors describe as alcoholic psychoses, acute hallucinosis, chronic hallucinosis, alcoholic paranoia, and pseudo-paresis, etc., there seems to be very little accord among them as to what constitute diagnostic symptoms. And those which some of them give as such appear to me singularly inadequate.

Chotzen (3) emphasises the difficulty of differentiating the alcoholic psychoses from others of non-alcoholic origin. According to him the diagnostic features in acute hallucinosis are the dominance of aural hallucinations, the absence of hypochondriacal symptoms, and the tendency to recovery. But it is probably within the experience of many who have had a large acquaintance with lunatics that such a combination of characteristics may often arise without alcohol being a direct ætiological factor.

Stoddart (4) describes a chronic hallucinosis, which according to Chotzen is denied by some, at all events, as a sequel of acute hallucinosis. This author also gives as the chief distinction between alcoholic and true paranoia the absence of systematised delusions in the former. None of these varieties, except perhaps some cases of so-called pseudo-paresis, which more probably are cases of polyneuritic psychosis with gross brain lesions the result of arterio-sclerosis, show any characteristic pathological changes, and none, I contend, are capable of being diagnosed as alcoholic in default of a previous knowledge of alcoholic indulgence in the patient. No doubt in all these forms alcohol *may* be the exciting cause, in the sense that it has served to overturn an already tottering nervous system, but what I contend is that it is not a specific but an accidental stress, insomuch as such cases if subjected to other equally

powerful stresses would develop similar mental disturbances, and therefore there is nothing in the nature of the symptoms or in the pathological anatomy to point specially to alcohol as the exciting cause; whereas in true alcoholic insanity both the symptoms and the pathological anatomy present characteristic features.

In spite of the desire of ardent teetotallers to prove the injurious effect of alcohol on the nervous system, the balance of evidence is in favour of the view that it only in a very small proportion of cases can produce permanent and demonstrable effects on the nervous tissues, although, as is self-evident, it can in anyone induce a temporary interference with the conduction of nervous impulses.

In the majority of drinkers alcohol appears to exert grave toxic effects on other viscera whilst sparing the nervous system. The point of least resistance in most alcoholics is not the brain but the kidneys, the liver, or the blood-vessels.

(3) *Alcohol unable to Initiate Insanity except in Certain Predisposed Subjects.*

This is shown by the fact that although drinking to excess is very common in the community, the percentage of cases which develop insanity under the influence of this stress is very small. Probably not one person in a thousand who drinks to excess develops alcoholic insanity, but if alcohol was by itself an effective toxic agent in this direction then all who indulge in it to excess would suffer. Hence it is obvious that among the cases which succumb to alcohol in the direction of insanity we must seek for another—a predisposing factor.

We may postulate this other factor to be an initial or inborn instability of the nervous system, or in other words a congenital structural defect of this tissue.

When treating of the pathological appearances met with in the brain in cases of alcoholic insanity, I shall point out that in more than half the cases we can demonstrate a form of nerve-cell which with great probability represents immaturity of structure.

The deleterious effects of alcohol are far more liable as previously mentioned to affect other viscera than the brain. To take one instance, whilst outside asylums a certain form of

cirrhotic liver is looked upon as almost pathognomonic(*) of alcoholic excess, this lesion, as F. W. Mott (5) has pointed out, is very rarely met with in insane alcoholics, so that Mott has asserted that it is only persons with an inherently stable nervous system who can drink long enough to acquire advanced alcoholic cirrhotic liver.

(4) *The Relationship of Delirium Tremens to Alcohol Poisoning.*

It is well recognised that delirium tremens is apt to develop in heavy drinkers after the sudden deprivation of alcohol, and also that it may appear in a case of alcoholic insanity weeks or even months after residence in an asylum. Ascherson (1) refers to the likelihood of symptoms of delirium tremens appearing in a case of Korsakow's disease during the night at any time during the course of the case. Therefore it seems impossible that the toxic effects of alcohol can account for this phenomenon.

Bonhöffer (6), Kraepelin (7) and S. Cole (8) believe that delirium tremens and Korsakow's disease are but different forms of the same affection. There is a good deal to be said for this idea, but as delirium tremens is, as its name implies, an acute delirious condition, whilst alcoholic insanity is not necessarily so and in very many cases runs a chronic course without any acutely delirious episodes, I am disposed to believe (in common with these authors) that delirium tremens is set up by the accumulation of some toxin or toxins not directly alcoholic, but produced and liberated under certain conditions by the injurious effects of alcohol on the general bodily metabolism, forming a common but not inevitable accompaniment of alcoholic insanity in much the same way as the congestive seizures in general paralysis.

Wassermeyer (9) does not favour the view that it is of this nature, but looks upon it rather as an exacerbation of chronic *alcoholic* poisoning.

It should be noted that delirium tremens is liable to occur in cases which do not show any symptoms of insanity. These are cases which lack, I believe, the inherent mental instability necessary for the production of alcoholic insanity.

(*) From time to time doubts have been expressed as to the causal relation of hob-nailed liver and alcohol. See a letter in *Brit. Med. Journ.*, November 2nd, 1907, by Dr. H. B. Donkin.

The occurrence of high temperature in delirium tremens with no discoverable extra-cerebral cause was described by Magnan and later by Alzheimer (10). I have met with two cases myself. Unless these cases can be looked upon as fulminating forms of polyneuritic psychosis, their existence tends to show that delirium tremens of itself may be a fatal disorder and that it is not necessarily associated with polyneuritic psychosis.

(5) *The Diagnostic Sign of Alcoholic Insanity—Neuritis.*

The dominating features in the cases which I describe as true alcoholic insanity are symptoms referable to an interference with the passage of nerve impulses along the nerve-fibres, either peripheral or central.

To these symptoms I would apply the term "neuritic." Adolf Meyer (11) has already pleaded for an extension of the use of the term to all degenerated conditions with decay of myelin sheaths of any nerve-unit. And for the sake of convenience I have termed all symptoms neuritic which point to an interference in the passage of nerve currents, whether this interference is only temporary and not accompanied by histological changes in the nerve-fibres, or permanent and histologically demonstrable; and also whether it affects the peripheral nerve-tracts (sensory or motor) or the central in the spinal cord and cerebrum up to the highest associational tracts.

From this point of view I maintain that all cases of alcoholic insanity are accompanied by—nay I would add, are the result of—neuritic changes, and from a comparison of the symptoms in alcoholic insanity with those observed transiently in every attack of drunkenness the similarity between the two is easily appreciated, and some further evidence is derived in support of the contention that alcohol is responsible for these symptoms in both cases.

Similarity between the Symptoms of Drunkenness and the Symptoms of Alcoholic Insanity.

In the temporary alterations produced in the nervous system during every attack of drunkenness are foreshadowed the more permanent changes which occur in alcoholic insanity. These are, on the physical side:

(1) *Thickness of speech.*—The affected individual's mental sphere may be unclouded and he may be capable of making strong but unavailing efforts to enunciate clearly. This condition indicates that the central apparatus, the nerve-cells probably or the nerve-cell region, is in a condition to function, but that the nerve-cell branches—the nerves—fail to convey the cell impulses. I think we are justified in seeking for an explanation in interference with neural action and not muscular, as we have no data to show that muscle actions under *acute* alcoholic excess are in default, and we see that the involuntary muscles still perform their duty naturally.

(2) *Inco-ordination of gait.*—Here also the symptoms may be well marked at a stage when the mental sphere is relatively unclouded. The subject may be able to correctly appreciate his condition, and to make strong efforts to overcome the failure, but ineffectually. The striking parellelism between this inco-ordination of gait and that which follows as a result of polyneuritis would appear to warrant our regarding both as essentially similar in nature, only in one the interference in the conduction of peripheral impulses is temporary and leaves on its disappearance no discoverable histological alterations; in the other the interference is more or less persistent, and has a definite and demonstrable histological basis.

(3) *General blunting of sensation.*—A later phenomenon which co-exists with or follows the well-known psychical effects of alcohol referred to by some French writers (Chapin, etc.) as psycho-sensory anæsthesia. This phenomenon, including a deadening of sense of fatigue as well as of pain, finds its parallel in the frequency with which anæsthesia or analgesia is found in alcoholic insanity and degenerative changes in the posterior columns of the cord.

(3*a*) *Muscular hyperæsthesia.*—Hill Buchan (12) notes the frequency with which in the acute stage of an alcoholic attack there is a degree of sensitiveness to pressure in the calves which often passes off in a few days.

(4) On the psychical side the analogy is continued in the silly jocularity of one stage of drunkenness, the irascibility of another, the excessively emotional condition of a third; and the paramnesic troubles of alcoholic insanity find their counterpart in the almost instantaneous forgetfulness which so many drunkards display at some period of their debauch.

This similarity in the symptoms between intoxication and certain forms of insanity in which there is a history of alcoholic excess, is in favour of the idea that alcohol is capable of producing a special form of insanity presenting the symptoms met with in every attack of drunkenness. And further, in the absence of these symptoms, we are entitled to doubt the validity of the claim of alcohol as the causative factor in an attack of insanity merely because the subject can be shown to be addicted to alcoholic excess. We do not recognise special forms of insanity of adverse circumstances, tobacco or puerperal insanity, etc., on the sole ground that these stresses occur in association with insanity affecting a numerous class.

In the same way I desire to eliminate from true alcoholic insanity those cases in which alcohol as the exciting cause has acted merely as a general stress and to include only those cases in which it has been a specific stress, giving rise to characteristic symptoms and characteristic changes in the nervous system.

SYMPTOMATOLOGY.

The mode of onset is frequently sudden, that is, after perhaps years given to excessive alcoholic indulgence. Ascherson (1) found this to be the mode in 36 *per cent.* of the cases of Korsakow's disease which he investigated, and he found that in the cases showing multiple neuritis the onset was more frequently gradual, and that the mental symptoms may either precede or follow the neuritis. According to his figures the mental symptoms succeeded the neuritis in 28, developed with it in 21, and preceded it in only 7. In several of my cases signs of *peripheral* neuritis were absent or, at all events, not detected on admission to the asylum, but developed later on, sometimes several months after the total deprivation of all alcoholic drinks. Not infrequently (16·6 *per cent.* according to Ascherson) the symptoms follow directly after an attack of delirium tremens.

Epileptic or epileptiform attacks may precede the mental symptoms or develop during the course of the disease. In 114 cases of mine they were noted in 11 instances (9·6 *per cent.*)—5 times preceding an attack and 6 times during an attack.

Ascherson found the onset was of an epileptic nature in 15 *per cent.* of the 126 cases he collected, and that in 20 *per cent.* an epileptiform attack occurred during the course of the malady.

A. *Physical.*

Physiognomy.—As a rule there is a characteristic alcoholic countenance, but although this is familiar to both lay and professional observer, it is very difficult to place the finger on this or that feature which forms or helps to form this type. Apart from expression, the coarse capillary injection of the cheeks and of the nose especially and a somewhat dusky livid hue of the lips are very characteristic of the drinker. The general expression in a great many is one of silly self-satisfaction with a fatuous smile, which may be blended with a look of astonishment. A few, and generally the less typical cases, display an expression of fear or apprehensiveness. I think, perhaps, the most characteristic marks are centred around the mouth muscles; there is a curious looseness and indecision of the lips, and in instantaneous ($\frac{1}{16}$ sec.) photographs the lower lip, whilst talking, appears blurred owing to a fine tremor, which may often be unappreciable to the unaided eye. Sometimes there is a slight symmetrical ptosis giving a drowsy expression. Asymmetrical conditions in the working of the muscles of expression, especially in the *upper* zone of the face, are common.

The facies of the female subject of alcoholic insanity is much more characteristic than that of the male.

Gait is only affected in subjects with peripheral neuritis of the lower limbs, and with these it is unsteady and waddling, with feet widely separated from the middle line, and a great tendency to fall or stumble, especially in the act of turning. With these conditions Rhombergism is almost always present although the knee-jerks may not be absent.

Deep reflexes.—Very valuable information is obtained as to the nature of the disease from the state of the tendon reflexes, especially the knee-jerks, and at the outset it may be stated that a case of insanity where the knee-jerks are absent or very slight, without the association of persistent Argyll-Robertson pupils, should always raise a suspicion of alcoholic causation in the mind of the examiner. In 68 of my cases the knee-jerks were present, normally or to an exaggerated degree, in only 21. In the remainder (70 *per cent.*) they were either very slightly marked or absent (in 39, or 57·3 *per cent.*).

In most cases there is a parallelism between absence of knee-jerks and inco-ordination of gait, generally with the accompani-

ment of alteration in the sensation of the lower limbs, but this is a rule to which there are many exceptions. Thus in 13 instances where the knee-jerks were very slight or absent, the gait and sensation were apparently unimpaired. On the other hand, in 21 instances where the knee-jerks were present, in 8 the gait was unaffected, in 10 it was affected, and in 3 there is no note as to its state.

In 9 cases the knee-jerks, absent on admission, gradually returned to a normal condition after admission to the asylum, and therefore after deprivation of alcohol, but in 3 cases a reverse condition occurred. This tends to show that the absence in all cases cannot be directly imputed to the alcohol; probably it may be a secondary result of vascular nature (endarteritis of small arteries?).

In 8 cases the knee-jerks remained after a more or less lengthy residence in the asylum, as on admission, absent, but the gait, which had been affected, became normal. It is not uncommon to meet with temporary alterations, *e.g.*, they may be absent, re-appear, and again disappear.

Ankle-jerks.—Dr. R. T. Williamson (13) states that loss of the ankle-jerks is one of the first signs of the injurious action of alcohol on the peripheral nervous system, often disappearing long before the knee-jerks. Since I saw this statement I have from time to time tested all my cases for this symptom, but so far I have notes only concerning 13. In 3 it was absent along with absence of knee-jerks. In 3 it was absent when the knee-jerks were present. In 2 it was present when the knee-jerks were absent. In 4 it was present when the knee-jerks were present, and in 1 case it was present in one foot only when both knee-jerks were slight. These numbers are small, but so far as they go they do not seem to any great extent to coincide with Dr. Williamson's results. Dr. A. Hill Buchan (12), in alcoholic cases associated with neuritis, found the ankle-jerks increased in 4 and absent in 19.

Pupils.—My experience quite coincides with Ascherson's (1) results. He found the most common condition was a sluggish reaction to light, and remarks that the special feature of the pupillary disturbance is that it is "transitory and varies much in intensity from day to day; a constant Argyll-Robertson pupil is, in my opinion, never found, and should always lead to a suspicion of tabes dorsalis or general paralysis."

The condition of the pupils in 68 of my cases was as follows:

(1) They were unequal in 26·4 *per cent.*; sometimes the right, sometimes the left was the larger, and sometimes the inequality shifted on different days from side to side.

(2) They reacted either very slightly and sluggishly to light or were rigid in 34·2 *per cent.*, but this condition was in most cases only temporary. Thus in 8 cases where they appeared at one time quite rigid to light the condition was temporary in 6; in 1 it developed after admission, and as the patient was shortly removed to another asylum the further state could not be recorded, and in the last case it was noted on admission, but no further note as to the condition is made in the later reports.

Sensation.—Testing for sensation among the insane is always a somewhat difficult and unsatisfactory proceeding, as owing either to mental dulness, defective intelligence, inability to fix the attention, or excitement, there is always uncertainty as to the accuracy of the replies, and this difficulty is most felt, perhaps, in alcoholic cases, associated as they are with amnesic troubles, great emotionality, and a great tendency to untruthfulness. For these reasons the results obtained can only be regarded as approximations to the truth.

The cases were tested for the temperature sense by hot and cold tubes, for light contact by cotton-wool, for ordinary tactile sense by the finger touch, for pain by pricking, and the accuracy with which they could localise impressions was also noted, as also the presence of anomalous subjective sensations. Nothing abnormal was noted in 18 out of 48 cases; in the remaining 30 (60 *per cent.*) some defect was encountered.

(*a*) The most commonly observed defect was some degree of anæsthesia or analgesia, which was noted in 18 cases.

(*b*) Hyperæsthesia was noted in 10.

In a few cases where anæsthesia was found at one period, hyperæsthesia was found later on, or *vice versâ*.

(*c*) Subjective sensations such as numbness, formication, pins and needles, or tenderness in the calves were present in 9 cases, and in 2 besides a feeling of pins and needles was met with in the hands only.

(*d*) The temperature sense was found to be unaffected in all but one of the 21 cases tested, and in this case at one period the cold tube was called hot but the hot tube was

correctly appreciated, but at a later period no anomaly was detected.

(*e*) The kinæsthetic sense was tested for in only 4 cases and was normal in all of them.

Quinquaud described a sign observed by him in chronic alcoholics in 1893. It is elicited by the patient placing the extended ring and middle fingers so that their tips rest with gentle pressure against the observer's extended palm. During the first few seconds nothing is noticed, but then one feels slight taps as if the bones were striking against one another and the observer's palm.

Fürbringer (14) and Hoffman (15), who investigated the subject among large numbers of people, arrived at fairly concordant results, *viz.*:

(1) That people in whom it is absent are in all probabilities not drinkers in the ordinary acceptation of the term.

(2) In a slight degree the presence of the sign does not justify the assumption of alcoholic abuse.

(3) A strong degree of phalangeal crepitation points with great probability to a drinker (in the proportion of 3 to 1 in the opinion of Hoffmann).

(4) The sign is of more value diagnostically than either tremor of the hands or tenderness of the calf muscles.

(5) It is less marked in women than in men.

Whilst Fürbringer believed that the sounds were produced in the finger-joints, Herz (16) believes that they are occasioned by very slight separations of the digital flexors from their sheaths, the tendons at the same time being in a state of tension.

From my own limited experience of this test among women I am not inclined to attach much importance to it alone, but taken in conjunction with other suspicious signs it may help to form a correct diagnosis in some doubtful cases. Whilst its presence is suggestive of alcoholic abuse, its absence by no means excludes this factor.

In 19 cases of alcoholic insanity I tested for it, usually at different times during the progress of each case; it was absent in 8, well marked in 5, and slightly marked in 6. Sometimes I could obtain it only in one hand, and sometimes on different occasions of testing it would be the right and then the left or *vice versâ*. As some of the cases were not tested

till after a more or less lengthy residence in the asylum, varying from a few months to three years, and therefore during all this period without alcohol, the large proportion of cases in whom I failed to get it may not be surprising, but it was well marked in some of those who had been longest here, and on the other hand in a case of delirium tremens it was absent on admission and when tested for twice later on. In some it seemed to vary very capriciously, *e.g.*, it was only slightly marked seven months after admission and absent the following month in one woman who was shortly after discharged. During her absence she drank heavily and was brought back having severely cut her throat; on re-admission the sign was not obtainable, but four months later it was present in both hands, and again four months later it was absent.

Blood-pressure.—According to my experience, which is at variance with Ascherson's on this point, the tendency is for the blood-pressure to be raised, often to a very marked degree; in some it remains within normal limits and in a small minority it is persistently low. There seems to be no definite relation between the mood and the height of pressure, and the cases in which the mood is continuously euphoric may be associated, and generally are, with extremely high tensions.

This condition of the pressure is only what might be anticipated considering the frequency of granular kidneys, cirrhotic conditions of the liver and thickening of the walls of the blood-vessels, which are so often found at the autopsy in these cases. I have records of the systolic pressure from 26 cases taken daily for a week or fortnight and at different periods in the disease. Twenty-one of these cases were between the ages of thirty and fifty-nine, and in 12 (or 57 *per cent.*) the average pressure was high (above 130 mm. Hg. up to 200 or more). The mood was markedly euphoric in 9 out of these 12; in only one was it depressed. In 7 (33 *per cent.*) the average pressure was within normal limits (110 to 130), and the mood was euphoric in 6 of these. In only 2 was the average pressure low (below 110).

In 5 cases sixty or more years of age the average pressure was extremely high in 3 (191, 218, 284) and the mood was euphoric in 2 and depressed in the third. In the remaining 2, considering their age, the average pressure was within the normal limits.

Blood.—A differential count of the leucocytes was made in nine typical cases, in each case for fourteen consecutive days. The only difference from the normal standard appeared to be a slight diminution in the number of polymorphs and increase in the number of lymphocytes. But when these results were compared with the differential count in six control cases, taken from apparently healthy and sane women whom I had no reason to suppose were addicted to alcoholic habits, there was found also in these latter a high lymphocyte count, although not quite so high as occurred among the cases of alcoholic insanity. In one only of the nine was the polymorph count increased, varying between 10,000 and 12,000 per c.mm., rising on one day to 20,000. This woman was somewhat anæmic and had been several years in the asylum.

Of the two whose lymphocyte count ranged highest, one had been in the asylum for some years, the other had recently been admitted.

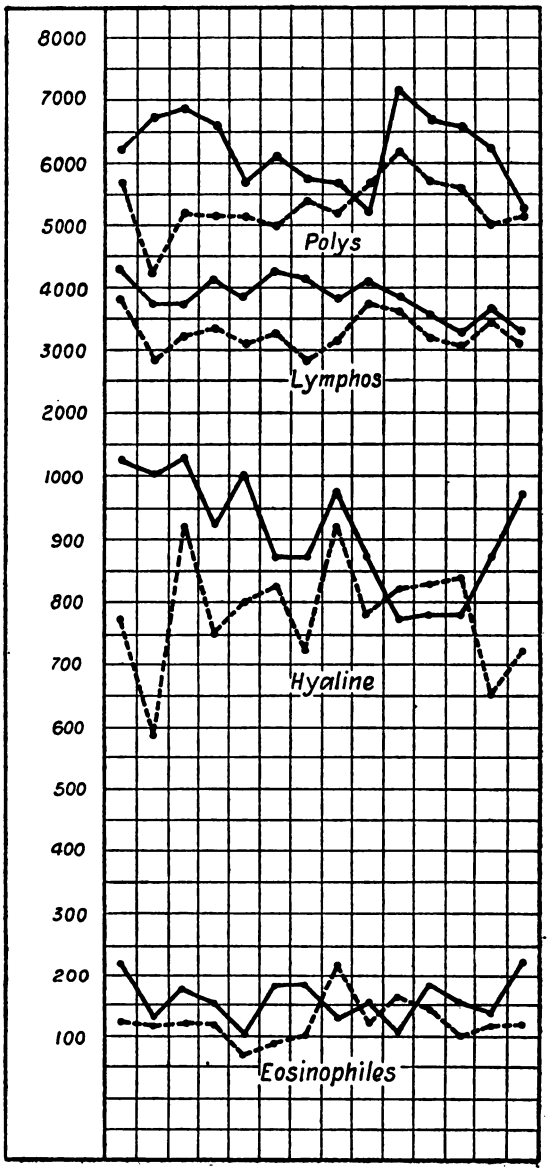
In the annexed chart is shown the average curves in the nine patients (continuous line) and those for the six controls (dotted lines).

The result of these examinations adds no fresh testimony to the view that confusional insanity of alcoholic origin is of an auto-toxic nature ; only one case showed a polymorphonuclear leucocytosis, and that not of a very marked character. The lymphocytosis also when compared with the control cases is too slight to have much significance, even if one were justified in regarding lymphocytosis as evidence of chronic toxic conditions.

Coagulation-rate.—In the same nine cases in which a blood-count was made, the coagulation-rate was tested by Wright and Paramore's method ; and taking (at blood-heat) below 130 seconds as a quickened rate and between 130 and 150 as normal, I found that it was slightly quickened in three and normal in six. Lawson (17), who tested the blood in all classes of alcoholic cases, found that in the great majority there was no delay, but in a few cases with wet brain and meningeal symptoms it was retarded.

Urine.—So far as my observations go the urine presents nothing specially characteristic in alcoholic insanity ; it is generally pale and with low specific gravity and contains a trace of albumen in 57 *per cent.*, but this percentage, although

CHART 1.



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it looks high, is not more than has been noted among the insane generally. Ascherson found a trace of albumen in only 12 *per cent.* of his cases. The peculiar orange colour described by Leopold Levi, and which this observer ascribes to an excess of urobilin, Ascherson only found twice. French writers appear to lay great stress on this character. I do not find any mention of it in my notes, and, as I have just said, in the great majority of cases the colour is pale.

The *cerebro-spinal fluid* does not appear to show any characteristic changes, but, so far as I know, too few cases have been examined on this point to speak dogmatically. Wassermeyer records two cases where negative results were obtained, the fluid being very clear and without lymphocytes. In two cases of delirium tremens he found a slight opalescence but no lymphocytosis. In two cases of mine, also, the fluid was quite clear, devoid of cells, and, in fact, showed no departure from the normal.

B. *Mental.*

The three cardinal symptoms are:

(1) Loss of memory.

(2) Disorientation to place, time and persons.

(3) Confabulation or pseudo-reminiscence,

and if these, or at all events the first two, are not present at one time or another in the course of a case, one should be very chary of diagnosing alcoholic insanity. Of very great diagnostic significance also are the peculiarities of mood displayed by subjects of this form of insanity.

I shall examine briefly these four symptoms in the order named.

Loss of memory.—This is chiefly for recent events, and according to Ascherson and others the defect usually coincides with the duration of the patient's illness; it is antero-grade as it is called, and it is active, *i.e.*, facts continue to be forgotten so fast almost as they are acquired, and a very characteristic sign of alcoholic insanity is shown by the inability of patients to remember the date, which they have just been told and made to repeat. If they do not instantaneously forget, it is only necessary to divert their attention momentarily by plying them with some other question. They cannot tell a few hours after

what they have had for dinner, or what their occupation was the previous day, or earlier in the present. They cannot find their way about the building, or their own beds, months or even years after residence in the asylum, and if asked to perform some duty, probably forget all about it on their way to carrying it out.

Wehrung calls attention to the fact that in Korsakow's disease (and he is speaking of the disease following alcohol), *total* amnesia never occurs and isolated remnants of normal memory are found.

In a very large number of cases the defect ultimately, after a period varying from a few months to years, improves, or may even apparently altogether disappear; and also it should be noticed that the defect may vary from day to day, so that on some days it is difficult to detect, whilst on others it is very pronounced. These peculiarities, besides serving to differentiate it from the quite similar defect often noted in aged people, senile amnesia, also point to the affection being at first a functional one, although the small proportion of cases which completely recover shows that it eventually takes on an organic character, the length of time required for this change varying in very wide limits in different cases. As Ascherson points out, this condition of affairs coincides with the morbid anatomy of the disease.

Disorientation in time and place or mental confusion.—The patients have no idea where they are or whence they came; they cannot say how long they have been in the asylum, and although they may only have come the preceding day, will tell you that they have been there three or four months. Ofttimes they cannot specify even approximately the time of day, and will be talking of going to bed shortly after they have arisen, or clamouring for their mid-day dinner late in the evening. The disorientation as to place varies very much in different cases: some imagine they are in a hospital or parish infirmary, but in cases where the symptom is more marked they imagine themselves to be still in the place from which they have just come, or think they are still in their own home and speak of having to get their husband's dinner ready. Ascherson likens this disorientation to a state of stupor or pathological sleep, or rather to a very prolonged state of awakening from sleep.

Paramnesia-confabulation or pseudo-reminiscence.—I have

notes of it in 42 out of 70 cases (60 *per cent.*), but it was probably present in a larger proportion, for it is a symptom very liable to be overlooked unless specially inquired for, and I find that in my earlier cases which were not so strictly tested for this point it is much less frequently noted than in the later cases. Ascherson regards it as an essential feature of the malady, and although he only records it in 70 *per cent.* of the 126 cases he collected, says that he has rarely seen an instance of the disease in which it was absent.

Judging from my notes it most frequently takes the form of erroneous accounts of recent visits to various places, or long detailed accounts of shopping the day before, or allusions to visits paid to public-houses, when the patient is very likely in bed and unable to walk. References to having performed the household duties that morning or the preceding day, getting meals ready and attending to the children are very common.

Wehrung limits the term "pseudo-reminiscence" to the recalling of imaginary events arising in conversation, when there occurs to the patient some picture which he proceeds to identify as an actual past experience—confabulation to the fabrication which a patient uses to bridge over awkward gaps in his memory.

It is very difficult to draw a sharp line of demarcation between pure confabulation and ordinary delusions or hallucinations. I can recall one case who, lying in bed and able to enter into a connected conversation, would occasionally rap on the wall, call out in a loud voice, "Shop!" and then ask for "half a quartern of whiskey, please." This difficulty is further exemplified by the morbid ideas relating to sexual or maternal instincts. No less than eleven women out of seventy (nearly 16 *per cent.*) had erroneous ideas that they had babies or children in bed with them, or that their husbands had been in bed with them during the night and had just got up. All such instances seem to me to partake largely of the nature of confabulation, although they are generally classified under delusions.

Several hypotheses have been put forth to explain the disordered nervous mechanism underlying paramnesia. Korsakow suggested that owing to enfeeblement of mental power, external impressions received and stored up in the memory cannot be fully retained, but that traces of them remain; the association formed from these traces of memory, themselves imperfectly

made, when again brought before consciousness in an act of recollection constitute a false reminiscence.

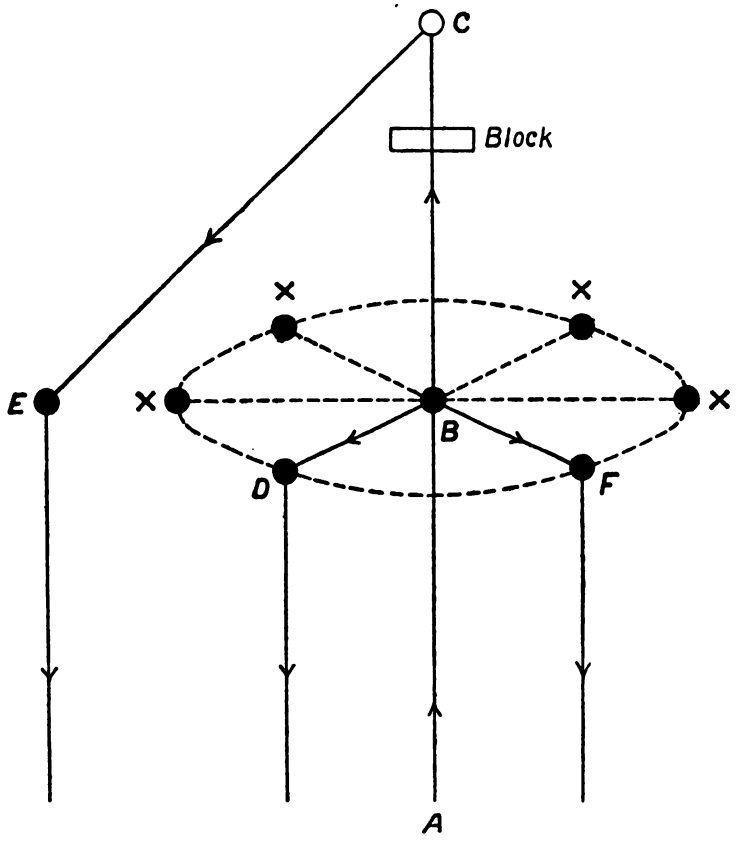
Ascherson's explanation is as follows: "The stimulus afforded by an impression from without alters the constitution of those neurons which subserve the processes of ideation in such a way that a free communication is opened up for the passage of impulses from one of them to another; thus an association of ideas takes place and a concept is made. If the original stimulus be sufficiently strong, it at the same time incites into action certain higher neurones, whose function is to control and inhibit ideation, and through the control so exercised communications are established only between a certain fixed number of the lower neurons, and a limit is placed upon the kind of association formed; but if the original stimulus is not strong enough to rouse the function of these higher neurons, there is nothing to guide the impulses along any definite paths, and either too few or too many communications between the lower neurons are opened up. The associations formed are therefore too scanty or too numerous and the ideation faulty. These communications made at the time between the lower neurons constitute paths of least resistance for future mental operations; therefore when a recollection subsequently takes place it is a false one. The fundamental fault is a failure of power, in this instance of power to control or to inhibit the association of ideas."

In accordance with my belief that the essential nature of the lesion in alcoholic insanity is a blocking or impediment in the passage of impulses along nerve-fibres, I venture to put forth an explanation based on this assumption and on McDougall's (19) theory of inhibition by drainage. If we postulate that there is an obstruction in the channels of communication between the lower and higher neurons which Ascherson refers to (or possibly between the higher neurons themselves), it will result that an impulse arriving at the lower neurons finds its further course upwards impeded by the obstruction before mentioned, and it will tend consequently to spread along other paths than those along which it normally does, and thus fresh association paths are opened up and new and false concepts ensue.

This explanation differs from both the preceding insomuch as the fault is assumed not to lie in want of power in the initial

impulse, but to an impediment in its course towards the higher neurons. The following diagram will perhaps serve better than long descriptions to make my meaning clearer. The dark circles *D*, *E*, *F*, *B*, *X*, etc., represent a series of neurons on a

CHART 2.



lower level, and the clear circle *C* one on a higher level. The impression from without sets free an impulse which normally spreads to *D* and up to *C*. Although there are paths of communication with all the other neurons, yet because these paths represent channels of greater resistance the impulse has originally taken the path mentioned leading to *D*, and each repetition of the impulse renders the resistance less and less along this tract, and the path becomes more and more organised. The

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higher neuron *C*, which for the sake of clearness is represented alone and which has communications on all sides like the lower, sends an impulse to the lower neuron *E*, because, as will be explained further on, this happens to be the one which offers least resistance, and the ultimate result of the impression is to set up impulses along the efferent channels *E* and *D*, which subserve the production of a normal concept. But supposing there is a block in the channel between the upper and lower neurons, then the impulse, instead of spreading upwards, flows along the path of next least resistance to the neuron *F*, which it discharges, and the final results of the impression in this case are impulses flowing along the efferent channels *D* and *F*, which subserve the production of an abnormal or false concept.

The theory of inhibition by drainage allows us to form a conception why the initial impulse from *B* takes the path to *D* rather than the other paths open to it. We must suppose that *D* has recently been discharged, and during this process it drains energy from all its branches towards the outgoing impulse along its axon, but this necessitates the lowering of the resistance in (amongst others) the channel between *B* and *D*. So that when *B* is discharged the impulse tends to spread along the channel to *D* rather than along the other channels open to it. And the same line of reasoning shows why a certain amount of its energy is directed towards the higher neuron *C*, and why from *C* a certain amount is sent to *E*.

The theory of inhibition by drainage supplies the only physiological explanation which can at present be given to the process of association, and it reduces all associations to examples of association by contiguity.

Conduct and peculiarities of mood.—One half of my cases presented euphoria, those in whom it was well marked displaying by their beaming expression and tendency to laugh at everything their condition of entire self-satisfaction. Jocularity, if one may use the word as a convenient one to express a frame of mind which is continually, in season or out, pouring. out silly and vulgar jokes and primed with all the popular catch-words and phrases of the moment, is common, combined with extreme garrulity. These cases are at the same time highly emotional and easily moved to tears. Many are very irascible, and apt on slight provocation to become rude, impudent and abusive. It should be mentioned that occasion-

ally the euphoric mood is a late development, and may not appear till some weeks or months after admission to the asylum. Such cases may at the onset be acutely melancholic or in a dull, heavy, lethargic condition. Finally there are some who, although of a morose and sullen aspect, will often surprise one by displaying a cynical humour of no mean quality. It is true that the great majority of cases do not give any special trouble in the asylum; they can generally attend to their personal wants. They are neat and show considerable aptitude for work; but nevertheless I cannot agree with Ascherson that there is nothing in their conduct to justify their being certified as insane. I am strongly of opinion that asylum and prolonged treatment (in default of adequate special inebriate homes) is the very best thing for them, as it certainly is for their unfortunate relatives or offspring, and that they are in every sense of the word certifiable lunatics. I would define a lunatic, or at all events a certifiable lunatic, as anyone who is more or less persistently and perniciously out of harmony with his environment. And by the latter term I include all those whose general conduct is prejudicial to themselves or to the community.

All cases of alcoholic insanity come within the scope of this definition. No one disputes the validity of a certificate which consigns a person to an asylum solely because such a one is actively suicidal. Much more, then, should there be no cavilling at certificates which consign to an asylum persons suffering from a form of mental disorder, not only harmful to themselves and to their property, but demoralising to all those with whom they have to live; and a disorder which, unless so treated, will almost inevitably go from bad to worse, resulting in untold misery to children or other relatives, and not improbably injury or death to the subject. Ascherson refers to the depressing and demoralising effect of asylum treatment. I cannot speak on these points, because, notwithstanding a fairly large experience of these cases, I have seen neither. And although he considers that suicide is not likely to be apprehended, one of the most determined suicidal patients I have known was the subject of alcoholic insanity.

Although, as Ascherson remarks, in many cases there appears to be a speedy restoration to sanity, at all events as regards their behaviour, yet persons who are quickly discharged are

almost sure to relapse when again exposed to temptation. The histories which are often forthcoming in these cases show how pernicious such people become when not properly looked after, and the demoralising influence they must exert on young children especially, in my opinion, would over-ride any suppositious demoralising influence which asylum surroundings could exert on the subjects of this disease.

Psychiatric hospitals which Ascherson advocates for the treatment of this complaint do not at present exist in England, and if they did I do not believe they would lend themselves for the favourable treatment of alcoholic insanity. The only chance in my opinion to get lasting good results, and it is at best a very slender one, is prolonged detention in an asylum or inebriate home.

Before concluding this section on the symptomatology of the disease I may add that Serbsky (20) has pointed out an important characteristic which, according to him, serves to differentiate Korsakow's disease from other illnesses with like symptoms, and this is the retention of the patient's character and personality.

Morbid Anatomy and Pathology.

One of the earliest, at all events among English authorities, to deal exhaustively with the pathological anatomy of alcoholic insanity was Bevan Lewis. It is evident, however, from his clinical description of the disease that his conclusions are largely based on cases which do not accord with the definition given in the first part of this paper, and therefore, as is to be expected, they do not to a large extent tally with the results that others have obtained in Korsakow's psychosis nor with my own observations.

Dr. Bevan Lewis (21) lays great stress on glial proliferation (scavenger cells) in the first and lower layers of the cortex. The brunt of the affection according to him falls on the nerve-cells of the lower pyramidal and polymorphic layers, and takes the form of fatty degeneration, especially of the apices and dendrites. He records an increase of nuclear elements around the cells and vessels; atheroma and fatty changes in the intima, small aneurysmal dilatations and plugging of the lumen with emboli, and believes that the initial lesion is a vascular

one—"an extensive endarteritis of a most chronic and insidious character."

In the spinal cord it is in the region of the posterior columns that changes are most manifest; these are increased vascularity, thickening of vessel walls and collections of amyloid bodies. The sclerosic change takes the form of a circular investment "originating in its investing membranes and creeping inwards along the vascular tracts, and especially along the posterior median *raphé*."

He regards the fatty changes in the nerve-cells as a more acute process, and the sclerosic as the result of a much slower and more gradual poisoning of the tissues.

Cole (8) has made a most careful and complete examination of the nervous system, muscles, heart, etc., in three cases of Korsakow's disease. My results are practically in accord with his, so that it will be unnecessary to quote from his description, except on points in which his more thorough examination included parts which I omitted to study.

I have examined the nervous system, liver and kidney in twelve cases of the disease, and although my observations in individual cases are much less complete than Cole's, they cover a wider range of cases, and if on this account alone possess a value which observations, however thoroughly made on a very limited number of cases, lack.

The naked-eye inspection of the brain shows, as a rule, nothing of special interest. In eight cases there was more or less marked atrophy, generally along the vertex and sometimes implicating the parietal and frontal lobes in their entirety. The membranes appeared natural to the naked eye in seven; in the other five there was slight opacity over the sulci, but in no case was there adhesion to the cortex. The membranes of one of the cases which appeared natural to the unaided eye showed under the microscope endarteritis of its vessels.

The basal vessels were healthy in nine, atheromatous in two, and calcified in one.

The routine microscopical examination of the cortex was made from sections taken from the topmost part of the ascending frontal, including the paracentral lobule. The tissues were fixed in absolute alcohol, embedded in paraffin and stained (in the earlier cases) by toluidine blue or Unna's polychrome blue. But in many cases sections from other parts of the

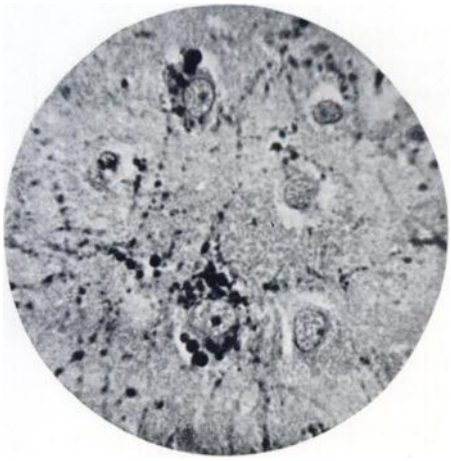

FIG. 1.

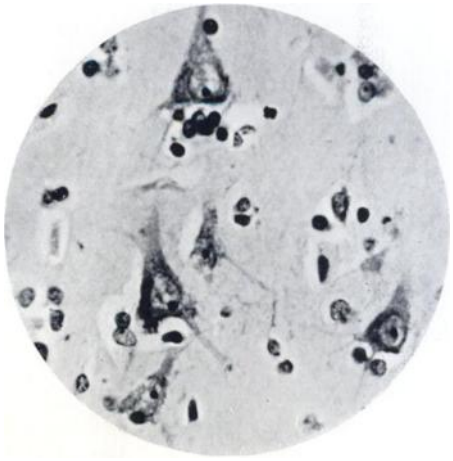

FIG. 2.

FIG. 3.

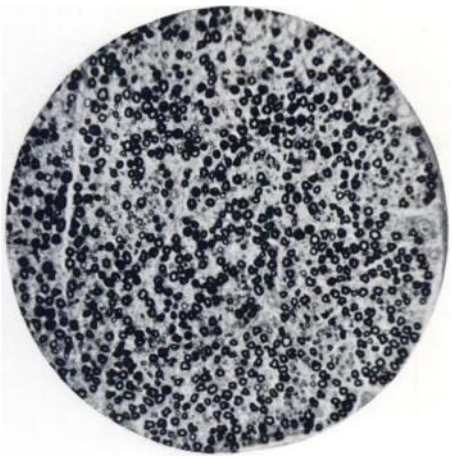

FIG. 4.

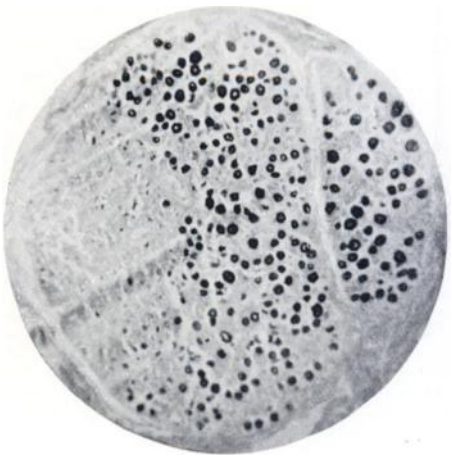

FIG. 5.

To illustrate Mr. JOHN TURNER'S paper.

Adlard & Son, Impr.

cortex and from the cerebellum were also examined, and in five cases the cortex was treated by a modified Marchi method for changes in the tangential and other cortical and medullary fibres, and for showing the presence of fatty degeneration in the nerve-cells.

The ordinary Nissl preparations of the cortex show nothing characteristic, not even the condition of the Betz cells or the proliferation of nuclei around the nerve-cells and vessels. To discover the lesions especially associated with alcohol we must, I believe, examine sections treated by methods which reveal changes in the myelin sheaths, and we must carry out our observations over a large area of the brain to get constant positive results, because sometimes one area and sometimes another is affected.

Meynert's striæ are not interfered with. The first or outer layer in seven cases showed a small spider-cell proliferation, but not to anything like the extent either as regards numbers or size of cells to that which is commonly seen in general paralysis or cases of terminal dementia. In the sections stained by osmic acid the body of these small cells was usually found to be filled with small black stained (fatty) globules, and there was either a marked diminution or total absence of the myelinated tangential fibres. The second layer in five cases appeared natural, the cells well formed and in good numbers, but in one of these five some sections stained by osmic acid showed that these apparently healthy cells were in a state of well-marked fatty degeneration (Fig. 1). This is not, however, a general peculiarity in alcoholic cases, as other cases similarly treated failed to show any such degeneration, and it is commonly found in non-alcoholic toxic cases, *e.g.*, acute delirious mania. In the remaining seven cases changes were visible in the toluidin blue or polychrome sections, which took the form of shrinking and uniform dark staining with paucity in number. Such changes, however, if one may judge from a single case stained by osmic acid, were not associated with fatty degeneration. The pyramidal cells (third layer) do not show any marked structural changes, except where prolonged pyrexial conditions or probable secondary toxæmic infection complicates the cases. They are, however, often (six out of eleven of my cases) beset with numerous little cells in their pericellular spaces (see fig. 2). These little elements, the free nuclei, satellites or neuronophages

of different authors, differ in size and general appearance; many appear to be free nuclei, round or oval, densely stained and 5 or 4 μ in diameter; many have a small quantity of cytoplasm of a square or oblong shape attached to one side of the nucleus, which stains with polychrome of a faint pinkish tint (best seen by artificial light). The nuclei of these latter cells are often somewhat larger and paler than the free nuclei, and may show definite chromatin dots arranged around the periphery or scattered irregularly throughout the nucleus. These in all probability represent lymphocytes, and perhaps immature forms of plasma-cells. A third variety is characterised by a much larger (7 to 9 μ) and clearer nucleus with a distinct nucleolar dot and well-defined rim of cytoplasm. These I am inclined to regard as endothelial nuclei, although, perhaps, some of them represent the mesoglia cells of Ford Robertson.

The Betz cells.—Changes corresponding in appearance to a state of axonal reaction were found in 7 of my 12 cases, and in 2 out of 4 cases of delirium tremens. S. Cole found similar changes in all 3 of his cases, and they have been observed by Gilbert Ballet, Faure, Babinski, Chancellay, and others. Their absence has been noted by H. W. Miller (22) in a case in which a similiar change was present in the anterior horn cells. Cole believes the change is brought about by the selective action of secondary toxins. I (23) previously supposed that it was a genuine axonal reaction secondary to neuritic changes in the pyramidal tracts.

My further observations, however, on large numbers of all forms of insanity lead me now to believe that both these assumptions are incorrect. I find (over 300 cases) that a similar form occurs in 42 *per cent.*; 70 *per cent.* in epileptics, 60 *per cent.* in imbeciles (not epileptic), a similar proportion in cases with marked melancholic symptoms, and only 20 *per cent.* in general paralytics, and I have elsewhere stated my reasons for regarding this form of cell as one indicating a condition of defective development—an immature cell.

In my 12 cases of alcoholic insanity it was found in 7, or 58 *per cent.*, a proportion therefore lower than it is met with among epileptics, imbeciles, and melancholic cases, but higher than the general average.

This form of change was also found in the anterior fore-horn cells in 2 of the 9 cords examined, and in both of these

it was only noted in the region of the lumbar enlargement. The lower proportion here is quite in accord with my findings concerning this form of cell in insanity in general, namely, that it is much less commonly found in the fore-horn cells than in the Betz cells.

The first 5 of my cases in which the cord was examined for tract degeneration gave results which seemed in favour of the view that the change was an early condition of axonal reaction, for in the 3 cases where degeneration was found in the pyramidal tracts the Betz cells showed this change, and in the 2 where no degeneration was found in the pyramidal tracts the Betz cells did not show the change. In the 4 following cases, however, although pyramidal tract degeneration was absent in all, 2 of the brains showed the change in the Betz cells and 2 did not.

The strongest point against this being a true axonal reaction is the comparatively early stage of what would constitute an axonal change that they show in cases where it is known that the pathological conditions are of old standing. When we get a severance of the axon, as by hæmorrhage into the centrum ovale, in the course of fourteen or fifteen days the Betz cells have passed into an advanced stage of alteration and are shrunken, very pale, with no chromatoplasm, and a very small shrivelled nucleus. So that it seems reasonable to expect that an equivalent picture of advanced cell alteration would be met with if a similar pathological condition (*viz.*, destruction of the axons) was at work in these alcoholic cases; although the probability must be borne in mind that an interference in the continuity of the axon or its destruction remote from the cell, as by pyramidal tract degeneration, may be followed by slower and perhaps slighter changes than by a lesion of the axon close to the cell. The experimental work on the production of axonal reaction has been chiefly done by plucking out or cutting through the axons of the hypoglossal nerve quite close to its cells of origin, and in hæmorrhage into the centrum ovale the lesion also would be quite close to the origin of the axons of the Betz cells. I know that years after amputation of a limb this change has been shown in the half of the cortex corresponding to the limb movements, but the intrepretation which has been put on this coincidence may need qualification when it is seen how commonly a similar change is found in the absence of amputation.

The characters which constitute the immature form are large, globose or swollen cells, with a finely granular condition of the central chromatoplasm, whilst that in the dendrites, the apex, and around the periphery of the cell-body retains its usual character of large spindle-shaped bodies. The nucleus is almost invariably displaced, lying either quite high up near the apex or against one side of the cell, but it otherwise appears to be in a normal condition. When we meet with cells of this kind in which the structure of the nucleus is affected, so that it is either small or crenated, dense or with ruptured membrane, it is an indication that the immature cell has fallen a victim to a super-imposed pathological change, and equally so if the entire cell-body is small and of a pale ground-glass-like aspect and the dendrites attenuated and lacking their normal Nissl bodies, or if the whole cell-body and branches stain deeply.

Although I believe that in the great majority of alcoholic cases the axonal-like condition of the Betz or fore horn cells is really an immature condition, the possibility must be admitted that in those cases where morbid changes affecting the axons of these cells are present, they may represent a real axonal change. I am unwilling, however, to allow that degenerative changes in remote parts of the axon are always effective in producing axonal reaction in the particular cells whose axons are affected. A reference to the table on p. 56 shows that of the 9 cases where the cords and generally the posterior tibial nerves were examined, in no less than 4 cases (Nos. 2, 5, 6, and 7) there was no correspondence between the incidence of axonal-like cells in the cortex and cord, and changes in the pyramidal tracts or posterior tibial nerves. Cole also, it may be mentioned, refuses to allow that the change is secondary to an axis-cylinder affection.

In only 2 of my cases was the immature form uncomplicated by added morbid modifications ; in one other, whilst on one side the form was pure on the other it was not. And the most common change found superadded to the initial defect of structure was the darkly stained form which I described many years ago as common in cases of acute delirious mania. This was found in 6 cases. In 2 cases the cells were in the condition termed by Nissl "acute cell change" and by Marinesco "coagulation necrosis."

It has been asserted that the darkly stained cell referred to above is also in this condition, but there is no justification for such an assertion. In the experimental work on the production of coagulation necrosis by subjecting animals to a high temperature we in all likelihood get a pure form of this change, uncomplicated, that is, by additional pathological factors, and as Goldscheider and Flatau (24), two pioneers in this line of research, show in their coloured plates and description, the change is unaccompanied by any signs of dark staining. The chromatoplasm forms into finer and fewer grains and loses to a large extent its affinity for the stain, so that the cell appears paler than normal, and finally the entire cell-body and even the nucleus is stained a dull pale uniform blue or lilac (with polychrome). When as the result of pathological conditions generally, but not always, associated with high fever, we find coagulation necrosis in the human nerve-cells, a similar picture is presented to that described in animals, but if, as sometimes happens, they not only show an entire disappearance of visible chromatoplasm but also stain deeply, we have here in all likelihood evidence that the morbid conditions giving rise to this state of affairs are not simply those necessary to produce coagulation necrosis, but that in addition other and probably toxic factors are at work.

In the change, however, which I termed dark staining of the nerve-cells, and which occurs so often in these alcoholic cases, the whole character of the alteration is distinct from coagulation necrosis, and in cells which prior to the alteration possess normal Nissl bodies, these structures remain, so far as can be seen, intact; the dark staining affects the between substance, and may, and does, obscure the chromatoplasm, but there is no appearance at any stage suggesting a disintegration or solution of it. The nucleus of the cell is increased in density up to complete homogeneity with nearly black staining, and at the same time it is shrunken generally in proportion to its density. The cells in which prior to the dark staining change, there has been a deficiency of tigroid substance, as in immature forms, when they become affected will of course show no appearance of Nissl bodies in the darkly stained areas where it was originally deficient, but they will be found apparently intact, but obscured in the apex, dendrites, and periphery of the cell-body. This darkly stained condition of the Betz cells was

also found in one (perhaps two) of the four cases of delirium tremens.

Dehio has described a dark staining of the nerve-cells in experimental alcoholic poisoning (acute) in animals.

A large excess of pigment is often found, and in sections stained by polychrome it usually appears of a bright yellow colour, but in sections stained in osmic acid it generally colours nearly or quite black, and is then probably of a fatty nature.

The polymorphic cells show no constant or peculiar structural changes, but around them is an even greater collection of satellite cells than around the pyramidal cells.

Glia.—In none of the cases (excepting the very moderate proliferation noted in a few cases in the first layer) was there any increase in the glia. This corresponds with Cole's experience, but is markedly at variance with Bevan Lewis's findings—a discrepancy which I attribute to the inclusion among his cases of many in which alcohol was only a coincidental or sequential occurrence.

Vascular changes.—In 4 out of 11 there was a notable increase in the perivascular cells. In 5 out of 11 the cortical arteries were thickened and in 2 of these endarteritis was noted. In 3 there were small cortical hæmorrhages.

Before leaving the brain I may mention that two Italian observers (25) have recorded an alteration of the corpus callosum in alcoholic subjects; the morbid process seemed to be one characterised mainly by degeneration of the myelin sheaths, with formation of granular cells and proliferation of neuroglia, the axis cylinders being in greater part preserved.

Montesano (26) noticed plasma-cells in four cases in rabbits given up to 12 c.cm. of absolute alcohol diluted with water, but C. Reichlin (27), repeating these experiments, was not able to discover them, and as this absence of plasma-cells agrees with the findings of Nissl, Alzheimer, etc., he believes that an intercurrent affection must have caused the death of Montesano's animals. I have never seen typical plasma-cells in human brains from alcoholic cases, although one often comes across cells which may well be early stages in a condition toward plasma-cells, and which I believe to be lymphocytes.

The spinal cord was examined in nine cases. The condition of the fore-horn cells has already been alluded to, but it may

be further mentioned that in eight certainly, and probably in all nine, there was a marked accumulation of pigment which stained black with osmic acid and was probably of a fatty nature. In neither of the two cases of delirium tremens in which the cord was examined was any of this pigment observed. In five of the cases there were no signs of tract degeneration. In the other four there was both recent and old degeneration of the exogenous fibres of the posterior columns, most marked in the lumbar region in two, most marked in the cervical in one. The pyramidal tracts were degenerated in three.

The posterior roots were degenerated in two, in one of these in the intra-medullary region only, and the anterior roots were degenerated in the intra-medullary region in one. On this point of Marchi reaction in the roots Cole utters a warning against the appearance being due to *post-mortem* damage, which is very likely to occur in the intra-medullary part. It is interesting to note that in the two cases where the lumbar fore-horn cells showed an axonal or immature character, in one the tract degeneration of the posterior columns was most marked in the lumbar region and there was intra-medullary (? artefact) Marchi reaction in the anterior roots. In the other the tract degeneration in the posterior columns was least marked in the lumbar region. In both cases the pyramidal tracts were affected.

Nerves.—I examined the posterior tibial nerves in seven cases and in all but one there was evidence of disease, patches throughout the cross-section showing a marked disappearance or even entire absence of myelin fibres (Figs. 3 and 5). In one of the two cases where the popliteal nerves were also examined the change was found to be much more marked in the more peripherally situated posterior tibial than in the more centrally situated popliteal. In two cases where marked changes were found in the posterior tibials, the median was in one unaffected and in the other showed very slight changes. In a subacute case recorded by Cole, he similarly found marked fibrotic atrophy in the posterior and anterial tibials and much less change in the arm nerves. In an acute case he records intense acute degeneration (Marchi reaction) with multiplication of the neurilemma nuclei in leg and arm nerves and slight affections in the left phrenic.

The following table correlates the state of the knee-jerks

with the changes found in the posterior tibial nerves and spinal tracts in the nine cases examined :

No	Knee-jerks.	Axonal-like Betz cell.	Axonal-like fore-horn cells.	Neuritis.	Changes in spinal cord tracts.
1	Absent	Present	Lumbar only	Present	Marked recent degeneration in posterior columns and slighter changes in pyramidal tracts.
2	Absent	Absent	Absent	Present	Marked degeneration in posterior columns only.
3	Absent	Absent	Absent	Not examined for	No tract degeneration.
4	Absent	Present	Lumbar only	Not examined for	Marked degeneration of posterior columns and pyramidal tracts.
5	Absent	Present	Absent	Not examined for	No tract degeneration.
6	Exaggerated	Present	Absent	Present	Slight degeneration in posterior columns and pyramidal tracts.
7	Well marked	Present	Absent	Present	No tract degeneration.
8	Normal	Absent	Absent	Not examined for	No tract degeneration.
9	Exaggerated	Absent	Absent	Absent	No tract degeneration.

It will be observed that in two cases an exaggerated or well-marked condition of the knee-jerks was associated with extensive old neuritis ; on the other hand the general tendency is for absent knee-jerks to be associated with changes in the exogenous fibres of the posterior columns.

Spinal ganglia.—Several (five or six) of the cervical and lumbar spinal ganglia were examined in three cases :

(1) Associated with well-marked degeneration of the exogenous fibres of the posterior columns the chief change noted in the cells was that resembling axonal reaction—marked central chromatolysis ; the cells were plump but pallid, nucleus eccentric. In the Nissl preparations not much pigment was noted in the larger cells, but with osmic acid they were found to contain a rather large amount of nearly black (? fatty) pigment. The small cells were heavily pigmented, this pigment showing in the Nissl preparations. There was marked proliferation of the connective-tissue covering of the nerve-cells and many clumps of small dark cells, representing probably the sites of degenerated nerve-cells. In the Marchi preparations

there did not appear to be any degenerative changes in the myelin fibres either within the ganglia or at either pole, nor did the anterior roots appear affected, but vacuolation of the cells was noted.

(2) Also associated with posterior column degeneration the ganglia cells were affected but in divers ways; some showed axonal characters, many were shrunken (especially in the cervical ganglia) and darkly stained and distorted; some were loculated and with invading nuclei which appeared to have partially destroyed them. The cells were heavily pigmented, this pigment appearing of a nearly black colour with osmic acid. There were many collections of dark nuclei representing probably the sites of degenerated ganglia cells. Marchi preparations showed no degeneration in the myelin fibres.

(3) This case was not associated with tract degeneration in the cord. The majority of the cells were plump, closely fitting their connective-tissue coverings; they were very pale, with only a few scattered grains of chromatoplasm and no peripheral ring of flakes. The nucleus was pale, sometimes crenated, and appeared as if solid; it was central and surrounded by a wide perinuclear space. There was a large amount of pigment. The small cells were paler than normal and with general chromatoplasm. No vascular or connective changes were noted.

Liver.—In 6 of the cases the liver was cirrhotic, and in 2 of these it had a typical hob-nailed form. In one of the cases of delirium tremens it was cirrhotic. Marked fatty infiltration was ascertained in 2 by microscopic examination, and was probably present in 2 others which were not examined microscopically. Endarteritis was present in 1.

Kidneys were granular or showed evidence of more or less marked interstitial changes in 8, and it should be observed that none of the 4 in which this organ was stated to be healthy were subjected to microscopical examination. In all 4 of the cases of delirium tremens they appeared natural, but only one of these was examined microscopically.

Very marked endarteritis was noted in 2 of the cases of alcoholic insanity.

Heart.—Excessive deposition of fat was noted in 2. In 8 the aorta was atheromatous (but in 3 only to any marked degree). Cole found, microscopically, fatty degeneration of the

heart muscle in 2 of his 3 cases, and noted also in 2 cases extensive fatty degeneration without loss of transverse striation of the voluntary muscles.

Pathology.

The only distinguishing feature in the pathological anatomy of alcoholic insanity appears to be degenerative changes in the nerve-fibres, peripheral and central. I have given reasons which tend to show that the condition of the Betz and anterior horn-cells, on which considerable stress has been laid by previous observers, has no direct relation to either alcohol or to the secondary toxins which its abuse may engender in the system. The accumulation of free nuclei or satellite cells around the nerve-cells and also in the peri-adventitial spaces is also in no wise peculiar to this form of insanity, although it may reasonably be regarded as a response on the part of the leucocytes, the adventitial or glia elements, whichever they may be, to a toxin either directly alcoholic or more probably a secondary toxin, the result of a general perversion of metabolism. The fatty degeneration of the nerve-cells and the dark staining may also probably be similarly accounted for.

The neuritic lesion is evidently, as Cole points out, a degeneration of the nerve-fibre and not an inflammatory condition. He, however, believes that the primary changes are the result of pathological processes "which partially impair the vitality of the whole neuron, leading first to decay of its remotest parts," and that these changes are due not directly to alcohol, but to secondary toxins, and he points to the changes noted in the large nerve-cells as an evidence of this change in the neurons.

I would suggest that alcohol itself exerts a prejudicial effect, not primarily or necessarily on the cell bodies, but on the myelinated branches of specially susceptible nerve-cells. The almost universal opinion of physiological chemists now is that alcohol has invariably a paralysing influence on the nervous system (Schmeideberg, Binz, Bunge, Dixon, etc.). As Bunge (28) puts it, "the stimulating action which alcohol appears to exert on the psychical functions is also only a paralysing action." The cerebral functions first to suffer are judgment and reason, and as a consequence emotional life comes into free play unhampered by the guiding strings of reason." These results

appear to me to be best explained by the view that the paralysing influence is exerted on the nerve-fibres and not on the nerve-cells (see p. 43 and diagram). This prejudicial effect may be exerted directly on the nerve-fibre, or perhaps by a vicious combination of alcohol with the myelin sheaths or perhaps by both combined. I am led to this conclusion by the absence of any constant or characteristic lesion in the cells themselves, and to the frequency with which in the presence of well-marked neuritic changes one fails to discover any morbid character whatever in the nerve-cells. But although I regard this to be the essential and primary lesion, I believe that subsequently in the course of the disease secondary toxins come into play to complicate the pathological process, and that these are essential for the onset of delirium tremens. But the alcoholic lunatic is no exception to the rule which obtains in all other cases of so-called acquired insanity: he is born, not made.

This hypothesis harmonises with the clinical features of alcoholic insanity better than the idea of a primary change in the nerve-cell body itself. In a large majority of cases rapid improvement up to a certain point occurs after admission to an asylum and therefore immediately following deprivation of alcohol; but in a certain proportion there are anomalous features about some of the symptoms, such as alterations in the knee-jerks and the accession of delirium tremens some time after admission to an asylum, which point to the interaction of a morbid agency other than alcohol.

And, moreover, in regard to the relationship of the axonal-like Betz cells and the neurotic lesions, if, as some hold, the cell change is a genuine axonal reaction, we should expect to find evidence of lesions in the pyramidal tracts in all the cases where this form of cell occurs, and equally, if the cell change were due, as Cole and others believe, to a toxic action directly exerted on the cell body, we should expect to find secondary changes in the axons forming the pyramidal tracts; but these conditions are not fulfilled, and often where we find affected cells we find no evidence of change in the medullated axons, and *vice-versâ*. And on both suppositions we are driven to invoke another morbid agency to account for either the cell or fibre changes, a disadvantage which is avoided by the assumption that the appearances observed in the cells are not

the result of acquired morbid agencies, but of an inborn defect in the cerebral structure.

A more extended examination of the spinal ganglia than has hitherto been made will be necessary before we shall be in a position to make definite assertions as to the relation of the changes in the posterior columns of the cord and the cells of the spinal ganglia. In my three cases the evidence, so far as it goes, would seem to show that there is *some* connection, for in the two cases where the cells showed axonal-like characters there was found a degeneration in the exogenous fibres of the posterior column, but in the third case where the cells did not show this character the posterior columns were intact. But after experimental division of the posterior roots, although according to Köster (29) palpable changes are found in the cells of the ganglia, these do not take the form of axonal reaction.

Although I cannot claim to have shown that neuritic changes were present in all my cases of alcoholic insanity, seeing that 4 out of 12 failed to show any evidence of this nature in the parts examined, yet as alcohol seems to be very capricious in the selection of the part it will affect, and in view of the generally positive results following more extended investigation of the tissues, I am inclined to impute my failure to a lack of thoroughness in the histological examination. Thus in no less than 3 of my negative cases the peripheral nerves were not examined. Wehrung, in this connection, states that neuritis has been found in *all* the cases (Korsakow's disease) in which it has been looked for.

Many other views have been advanced to account for the pathogenesis of polyneuritic psychosis. Korsakow himself attributed the disease to the action of noxious substances in the blood allied to Bouchard's poisons.

In the opinion of the French school it is due to an auto-toxin arising from hepatic inadequacy, especially when there is also an interference with the renal functions. Ascherson unfavourably criticises this latter view, because he only found *clinical* evidence of liver affection in 64·5 *per cent.* of cases and definite cirrhosis in 16 *per cent.*, and the kidneys were sufficiently affected to cause albuminuria in only 20 *per cent.*, and symptoms pointing to joint lesions of both in only 16 *per cent.* But of his cases only 5 came to autopsy, and among these the liver was cirrhotic in 2, fatty in 2, and normal macroscopically

in 1 ; the kidneys were fatty and cloudy in 1, granular in 1, and healthy in 3. In reference to Ballet's contention that hepatic inadequacy sufficient to give rise to mental symptoms may exist in the absence of macroscopical changes in the liver, he cites a case of Korsakow's disease in which the liver was found to be healthy both to the naked eye and the microscope, and in which the kidneys were but slightly diseased. These are weighty objections, but they appear, with the single exception of the last quoted instance, to rest entirely on macroscopical examination. Unfortunately I only made microscopical examinations of the liver and kidney in 6 of my cases, but in all these the liver was found to be affected (in 4 cirrhotic and in 3 also fatty), and in 5 the kidney showed interstitial changes, and in 1 only it appeared natural. Of the remaining 6 in which the liver and kidney were not examined by the microscope, in 2 both organs appeared healthy ; in one the liver appeared healthy, whilst there was evidence of interstitial changes (adhesions of capsule) in the kidney. In 2 the liver was cirrhotic (hob-nailed) and the kidneys granular ; in the remaining 1 the liver had appearances indicating fatty changes and the kidneys were cystic. So that in no less than 10 (83 *per cent.*) there were appearances of disease in these organs either separately or conjointly. In my opinion even where a microscopical examination of a tiny piece of such a large organ as the liver fails to show any change, to conclude thereform that the organ in its entirety is healthy is a very bold assumption. S. Cole, in all three of his cases, also found changes in these organs ; fatty infiltration or degeneration and cirrhosis of the liver ; fatty changes alone or in combination with slight interstitial changes in the kidneys, although in two of the cases this organ appeared natural to the naked eye.

Wehrung supposes that in Korsakow's disease there is the production of an antitoxin the result of prolonged alcoholic abuse, and he attributes the delay which so often occurs after a bout of drinking before mental symptoms appear to the time occupied for the neutralisation of the alcohol by the antitoxin ; only when this is accomplished can the excess of antitoxin exert its own influence upon the cortical structures. Tansi (31) practically adopts this view in discussing the cause of delirium tremens, but in the opinion of Hertz (quoted by Tansi) it is the result of renal insufficiency—a symptom of alcoholic nephritis.

Bonhöffer (30) in all cases of polio-encephalitis hæmorrhagica superior (by which term Wermeke in 1881 described certain paralyses of the eye movements, accompanied by delirium, with acute onset and fatal termination, the symptom-complex arising on the basis of chronic alcoholism), found neuritis and amnesia (Korsakow's disease). But he believes that alcohol alone is insufficient to cause the occurrence of the syndrome and that there is *always* an additional toxic cause, and that the syndrome in the great majority of cases is ushered in by delirium tremens.

According to him senile and arterio-sclerotic changes often produce the syndrome in a very pure form, but here it is preceded by apoplectic or minor attacks. He finds it also (but rarely) in general paralysis.

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EXPLANATION OF PHOTO-MICROGRAPHS.

FIG. 1.—Nerve-cells in the upper part of the third (pyramidal) layer from frontal convolution, in a state of fatty degeneration. × 600. Notice also the breaking up of the myeline fibres into a beaded condition. The section from which this photo-micrograph was taken was from a case of acute delirium not of alcoholic origin, but precisely similar appearances are met with in alcoholic cases.

FIG. 2.—Large pyramidal cells from the ascending frontal convolution in a case of alcoholic insanity. To show the marked increase of satellite cells around the nerve-cells (× 400). Many, if not all, these bodies represent mesoglia cells, and by special methods their cell-body and branches can be shown, the latter to a large extent embracing the body of the nerve-cells.

FIG. 3.—Longitudinal section of the right posterior tibial nerve in a case of alcoholic insanity, showing recent degeneration of the myeline, which is darkly stained and broken up into beads (× 100).

FIG. 4.—Transverse section of posterior tibial nerve in a case of advanced general paralysis, showing a fairly healthy condition (× 100) in contrast with—

FIG. 5.—Transverse section of posterior tibial nerve from a case of alcoholic insanity, showing marked neuritic change characterised by disappearance of myeline fibres (× 100).

The Systematic Estimation of the Leucocytosis in Certain Cases of Insanity: with Special Reference to the Toxæmic Theory.[1]

By S. CARLISLE HOWARD, M.D., Assistant Medical Officer, London County Asylum, Horton, Epsom; formerly Assistant Medical Officer, District Asylum, Murthly, Perth.

SURVEYING insanity as a whole, one recognises as a fundamental fact that insane persons belong to a class who start life with a "deficient grade of organisation" of the nervous system called "hereditary predisposition." Some authorities hold that this is the *sine quâ non* of insanity, but such a view, I consider, is not strictly accurate. It is certainly not borne out by statistics. All observers, using even indifferent discrimination, must have noticed cases in which no hereditary factor could be traced, but in which much self-abuse had occurred—either in the form of alcoholic, sexual, and other excesses—or where