diphtheroid cystitis. In these cases the bacilli were present in too great numbers to have come merely from the urethra, which in other cases very frequently contains some diphtheroid bacilli. If further observations confirm the testimony of these ten cases, we shall be bound to conclude that in tabes there is in the urinary tract an infective focus comparable to that which occurs in the respiratory or alimentary tract in general paralysis. The bacilli are invading, and therefore produce toxic effects far greater than those that result from the simple passage of the disintegrating bacilli through the urinary tract.

There is evidence that the general paralytic defends himself, and often with prolonged success, by manufacturing specific bacteriolytic anti-bodies. It seems therefore worth while to produce such anti-bodies in suitable lower animals and to use them as therapeutic agents. This method of treatment is at least going to be given a trial at the Royal Edinburgh Asylum.

(1) Delivered at the Royal College of Physicians, Edinburgh, on January 24th, 26th, and 29th.

The Prognosis in Dementia Paralytica. (1)

By GEORGE GREENE, M.A., M.B.Cantab., Assistant Medical Officer, Claybury Asylum.

THE difficulty of informing the relatives of patients suffering from dementia paralytica on the probable duration of the disease led the writer to inquire into those symptoms and signs which appeared to be of value in prognosis.

Text-books on insanity give little information concerning the subject, beyond stating that the affection usually lasts less than three years. This statement, as will presently be shown, is of little value, since some patients die within a few weeks after the onset of the disease, whilst others survive for many years.

The subject will be dealt with in the following order :

(1) Variations in the course of the disease at different periods of life.

(2) The influence of sex.

(3) The effect of alcohol.

(4) Variations in the course of the disease according to the associated mental state.

(5) The evidence to be obtained from an examination of the fundus oculi, pupil, and pupil reflexes.

(6) The effect of epileptiform convulsions.

(7) The prognosis in the degenerate as compared with that in the highly developed individual.

(8) The special features of the juvenile cases.

(9) The special features when associated with tabes dorsalis.

(10) The types of patients in whom remissions occur.

(1) *Variations in the Course of the Disease at Different Ages.*

The duration of dementia paralytica bears a distinct relation to the age at which the symptoms of the disease first make their appearance. The adjoined table illustrates the variations in the duration of dementia paralytica according to the different ages at which the disease occurs. The table is based upon records obtained from 500 cases of general paralysis.

In many instances, because of the extreme difficulty of obtaining reliable information concerning the patient's condition previous to admission, the age at onset of the disease is reckoned as beginning from the date at which the patients entered the asylum. Unless otherwise stated, this remark also applies to other places in this paper where reference is made to the duration of general paralysis.

It will be seen, on examination of the table, that the longest expectation of life is in those subjects in whom the disease begins at an early age, whilst the more rapid forms of the disease usually occur towards middle life. Thus, from the age of fifteen up to thirty-five years the duration of the disease steadily diminishes. After this age has been passed, however, the duration slightly increases as the fifth decade is reached, to sink again as old age approaches.

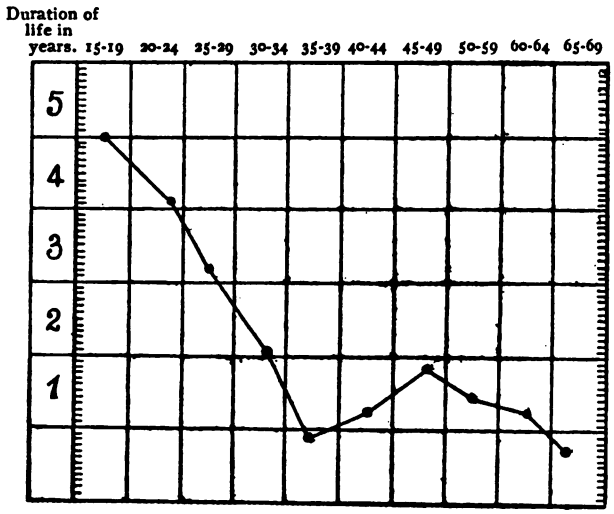
It is probable that the relatively long duration of the disease in young subjects is due chiefly to two causes. First, many are of the juvenile type, in which a high degree of degeneracy is frequently present. (It will be shown that degenerates live longer than highly-developed subjects.) Secondly, owing to their youth, they have been exposed in only a minimum degree to the various forms of stress, in consequence of which their neurones are less likely to have been damaged, and the patient

is thus left in a condition better fitted to withstand the invasion of the disease.

That the shortest duration of life should occur when the onset of the disease begins between the ages of thirty-five and thirty-nine is what might naturally be expected, since, at this period of life, the individual is most likely to be undergoing the greatest mental and bodily strain. The neurones of a subject liable to become a victim to general paralysis are thus reduced to a more or less unstable state, so that he is in a poorer condition to withstand the devastating effects of such a disease.

Probably the increase in the duration of the disease after

Ages at which the Disease commenced.



the age of forty-five years is an indication that the individuals in whom the onset of the malady occurs subsequently to this period are possessed of relatively stable neurones in virtue of which they are enabled to fight for a longer time against the ravages of the disease. Further, at and after this time of life most individuals have passed the period of greatest strain. The gradual decline in the duration of life after the onset of the disease in subjects of the age of fifty years and upwards is, perhaps, the result of the increasing effects of such senile changes as arteriosclerosis and the like, which may tend to accelerate the progress of the malady.

(2) *The Influence of Sex.*

The sex of the patient is one of the most important factors to be taken into consideration in any attempt to estimate the duration of life in a subject of dementia paralytica.

Females affected with the disease, on the whole, live considerably longer than males. In 128 female cases the average duration of the disease was twenty-three months, whilst in 400 male cases the average duration was only fifteen months.

The following observations appear to afford some explanation of this difference in the expectation of life in victims of the disease in the two sexes.

The female general paralytics as a class present more of the ordinary stigmata of degeneracy than do the male, and they have a smaller and simpler type of brain from the point of view of the female average than have the males considered from the standpoint of the male average. Females on the whole are much less exposed to the various forms of mental and bodily stress than are males, and therefore have not these devitalising factors to contend against.

Lastly, it is frequently asserted that epileptiform convulsions tend to hasten the progress of the disease; and although this statement is not in accordance with the writer's experience, still as the matter has some bearing upon the point under discussion, attention may be directed to the rule that the female general paralytic is much less liable to such seizures, both with regard to number and severity, than is the male.

(3) *The Effect of Alcohol.*

It is well known that the subjects of general paralysis are frequently addicted to the excessive consumption of alcohol. In many instances it is difficult to ascertain the precise part which alcoholic excess plays in the genesis of the disease, since it is often doubtful whether the abuse of alcohol has hastened its onset or whether the tendency to drink is merely a part of the loss of self-control so often present in the early stage of the disease. These conditions may occur separately or in some cases they may be associated.

It is often noticed that general paralytics in whom the abuse of alcohol has been a recently acquired vice rapidly improve when they are placed under conditions which exclude

intoxicating liquors. This amelioration is the more marked if the case be an early one in which mental symptoms due to alcoholism preponderate over those due to paralysis.

It is chiefly the last-mentioned class of cases in which it would appear that alcohol has hastened the onset of the disease. In a large proportion of such cases, when once the alcoholic stimulant has been withdrawn, the improvement is often very rapid, the patient quickly passing from a restless, noisy and confused state into apparent convalescence.

These cases usually run a chronic course, remaining in a more or less unstable condition; but in some instances they improve sufficiently to be eventually discharged, and they constitute a large percentage of the sum of remissions.

Although, as stated above, general paralytics in whom recent drinking has been a prominent feature improve as a rule when removed to an asylum, an amelioration is much less frequent in those subjects who for years have been heavy drinkers. Even in the latter class of cases there is occasionally an improvement in the mental symptoms after intoxicants have been discontinued, but the majority of such cases run an average course. It is probable that the chronic alcoholic is less likely to improve, because his neurones have been permanently damaged by the prolonged use of a poison which, in the case of the recent drunkard, has only acted long enough to produce a temporary disturbance. The one is a destructive lesion, the other merely a derangement from which, under favourable conditions, recovery may ensue.

Taken as a whole, the alcoholic cases of dementia paralytica generally soon show some improvement and run a somewhat longer course than the average of all cases of the disease.

Of 25 cases in which a history of recent drunkenness was obtained, 19 showed an improvement in three weeks, whilst in an equal number of cases in which there was no history of alcohol, only 12 showed an amelioration in the same time. The average duration of life after the onset of the disease was in the former cases four months longer than in the latter.

(4) *Variations in the Course of the Disease according to the Associated Mental State.*

The prognosis in dementia paralytica varies according to the associated mental state.

By different authors almost every form of insanity has been described in conjunction with the physical signs of the disease, but it is intended to discuss here only those mental states which appear to have a direct relation to the ultimate course of the malady.

The following mental states will be especially considered: early dementia, mania, melancholia, exaltation of ideas, and fixed and systematised delusions.

Early dementia.—General paralytics in whom a marked degree of dementia is an early and prominent symptom are nearly always characterised by an extremely acute course. The rapidity in the progress of the disease is, moreover, much accelerated when dementia is associated with a dull, apathetic state, bordering upon stuporose melancholia, a condition in which the patient remains in the same position thoughout the day, regardless of his surroundings. This type of general paralysis constitutes a large proportion of those rapidly fatal cases which die within a few months or less after admission into an asylum. The patients quickly exhibit a condition which resembles that usually seen in the terminal stage of the disease, excepting that they are well nourished and show little signs of progressive paralysis.

Inquiry into the previous histories of these cases usually shows that the onset of the disease has been sudden, the patients having for the most part followed their occupations in a perfectly normal and satisfactory manner up to a period of a few weeks previous to their coming under treatment.

Of 25 cases at Claybury Asylum who were admitted with or passed into this condition within their first month of residence, 15 died within six months, 8 died within a year, whilst only 2 survived over the latter period.

Mania.—General paralysis with mania runs a variable and inconstant course. In many instances the maniacal symptoms rapidly disappear, but the patients retain their delusions, which may persist for a longer or shorter period before dementia supervenes. In others both the maniacal symptoms and delusions persist until a time when the patients begin to lose bodily strength and become demented, the disease then terminating in the usual manner.

In some cases both the delusions and maniacal symptoms disappear within a few months of the onset of the malady, the

patient afterwards remaining for a variable period in an extremely unstable condition, although he may slowly improve and eventually regain his mental equilibrium. On the whole general paralysis with mania runs a little longer course than the average of all cases, the average duration of fifty cases of this type being sixteen months.

Melancholia.—Melancholia is the predominant mental symptom in 20 *per cent.* of all cases of general paralysis.

In some instances the depression is so marked that the paralytic nature of the affection is not suspected until the patient has been under observation for several months or, in exceptional cases, even for years. In those subjects in whom general paralysis is not at first suspected the disease usually runs a relatively long course; and it not infrequently happens that they are discharged as recovered from what was believed to be pure melancholia, only to return again after a short time, when they are then discovered to be really suffering from dementia paralytica. The subjects of melancholia in whom the physical signs of paralysis are difficult to elicit usually live for a considerable length of time. The above-mentioned type, however, only forms a small proportion of the melancholic subjects of general paralysis. In the majority of cases with melancholia the disease is more rapid than the average, as melancholia is often associated with deficient appetite and loss of weight, conditions which accelerate the course of the complaint. The great majority of cases of general paralysis in whom melancholia is the predominant mental symptom prove fatal within a year.

In estimating the prognosis in melancholic general paralytics the state of the bodily health must be taken into consideration, since it frequently happens that an exacerbation of any bodily affection to which the patient may be subject is followed by a marked deterioration in his mental condition. For instance, many general paralytics with a mild degree of melancholia become acutely depressed after an attack of bronchitis or slight coryza. In this way an unjustifiably grave prognosis may be made, which is subsequently rectified by amelioration of the mental symptoms as the bodily affection improves. On the whole, however, the duration of general paralysis associated with melancholia is shorter than the average duration of the disease accompanied by other mental states.

Exaltation of ideas.—The presence of exaltation of ideas

gives little help in estimating the probable duration of the disease. The expectation of life in subjects presenting this symptom is on the whole a very variable one, and no definite statement can be made beyond this, that it is unusual for such cases to run an extremely acute course. In many instances, more especially if the onset of the malady has been associated with mania, the accompanying delusions of exaltation gradually become less prominent and may ultimately disappear, when the patient may pass into a quieter and less confused condition. From this point the patient may slowly pass into dementia, or may relapse into an excitable and exalted condition. Other patients remain in a chronic state of exaltation which persists until the final stage of the disease is reached. In some instances exaltation of ideas is followed by melancholia, which, in its turn, is succeeded by the rapid onset of paresis and death.

From the foregoing remarks it is evident that, in estimating the prognosis in those general paralytics in whom exaltation of ideas is the most prominent symptom, the mental symptoms alone are of little value. It is, therefore, essential, in order to elicit a correct conclusion, to consider the other aspects of the case.

Fixed and systematised delusions.—As regards the duration of life, the presence of fixed and systematised delusions in the course of general paralysis is usually a favourable sign. In a fair proportion of such cases the delusions show an early tendency to wane and disappear. This amelioration in the mental symptoms is occasionally followed by a remission of the disease, lasting for several months before the patient relapses. In the majority of such cases, however, the delusions persist, and are often associated with periodical attacks of excitement, during which exacerbations the physical signs of the disease become more apparent. It occasionally happens that patients who are at first thought to be suffering from monomania or chronic delusional insanity eventually prove to be general paralytics.

There is frequently a strong resemblance between general paralytics with fixed delusions and cases of chronic delusional insanity. In the former, on account of the delay in the appearance of the signs of paralysis, the disease makes relatively slow progress, whilst the latter, from the extreme chronicity of their

course, tend to accumulate and fill our asylums. The more limited and systematised the delusions in these subjects the more chronic is the course of the disease. For example, a general paralytic with only one fixed delusion has a much better expectation of life than one who has numerous varied delusions which change from day to day.

Of 48 cases of general paralysis with fixed and systematised delusions, only 16 died within a year and 21 lived over two years, the average duration of the disease in the 48 cases being twenty-four months.

(5) *The Evidence to be obtained from an Examination of the Fundus Oculi, Pupil, and Pupil Reflexes.*

The Argyll Robertson pupil is present in about 28 *per cent.* of all cases of dementia paralytica.

Except in tabetic general paralysis, the presence of pupils which do not respond to light is usually associated with a course of more than average rapidity. Pupils which are inactive to light occur most frequently in patients in whom the accompanying mental state is one of well-marked early dementia.

Sluggish reaction of the pupils to light is present in about 50 *per cent.* of all cases of the disease. This sign is not such a bad prognostic indication as the presence of the Argyll Robertson pupil; subjects exhibiting it, as a rule, run a variable course, although the average duration of the disease is longer than when the pupils are fixed to light.

The pupils react normally to light in 22 *per cent.* of all cases; and, taken as a whole, it is this class of case, so far as we may judge from the pupillary signs alone, in which as regards duration of life the prognosis is most favourable.

A comparison of 50 cases of each of the three above types showed that in the subjects with fixed pupils the average duration of life was 11, with sluggish 15, and with normal pupils 23 months respectively.

Inequality of the pupils occurs in about 20 *per cent.* of all cases of dementia paralytica, and, as a rule, when this sign is present the disease is a little more rapid than in the average of other cases. Instances occasionally occur in which from day to day, or even during the same day, the pupils show wide and

rapid variations in size. Thus in some patients one pupil may be larger in the morning and the other in the evening, or *vice versâ*. When this is the case the disease nearly always runs a very rapid course, usually terminating fatally within a few months of its onset.

These rapid oscillations in the size of the pupils are usually seen in the early stage of the disease, although they do also occur later; but in these instances also the condition generally appears a short time before death.

Hippus occurred in three patients, and in all these the disease terminated fatally within a month after the first appearance of the symptom. In two of these cases the total duration of the disease was under five weeks.

It would appear from the foregoing remarks that the alteration in the dimensions of the pupils may be taken as an index of the amount of active degeneration of cerebral tissue which is taking place.

Optic neuritis may occur at any period of the disease, but it is much less frequently observed in the early than the later stages. Optic neuritis does not appear to have any special prognostic indication.

Optic atrophy was present in the early stages of the disease in three subjects, one of whom lived fourteen months, another thirty months, whilst the third has survived for three and a half years and is still alive.

Judging from these three cases alone, it would seem that the prognosis of general paralysis, like that of tabes, is more favourable as regards the relative duration of life when the disease is associated with the early onset of optic atrophy.

(6) *The Effect of Epileptiform Convulsions.*

Contrary to the opinion frequently expressed, the study of the cases included in this series shows that the occurrence of epileptiform convulsions in the course of dementia paralytica does not appear to have any general bearing upon the prognosis of the disease. From an examination of seventy-four cases of general paralysis in which the presence or absence of convulsions was carefully noted, the following deductions were made:

(*a*) There was little difference in the duration of the disease

between those subjects in whom convulsions occurred frequently and those in whom they were few or altogether absent.

(*b*) In a few subjects the disease terminated fatally within a few months or even weeks from the onset of the disease without the occurrence of a single convulsion.

(*c*) Convulsions, although often preceded by an elevation of temperature, with restlessness and excitement, are frequently followed by a temporary amelioration in the mental symptoms.

(*d*) In chronic cases of dementia paralytica periodical successions of convulsions often occur.

(*e*) That a convulsion *per se* is seldom directly responsible for producing a fatal issue.

(7) *The Prognosis in the Degenerate as compared with the Highly Developed Individual.*

The standard of mental and bodily development is one of the most important factors in estimating the prognosis in dementia paralytica.

It is usual for general paralytics presenting congenital physical defects to outlive those of their fellows who are of a more highly developed type, and in whom stigmata of degeneracy are absent.

This statement is supported by the *post-mortem* statistics, which show that in subjects with a large and well-constructed brain the disease usually terminates more quickly than in those in whom the brain is small and relatively poorly developed. It would appear that on the one hand the greater the degree of intelligence and the more highly the subject is organised, the more rapid is the disease, and that, on the other hand, the less the degree of intelligence and the less highly the subject is developed, the longer is the affection in coming to its invariably fatal termination. The basis for the foregoing assertion is founded on the following two sets of statistics. The first relate to the standard of mental and bodily development shown by clinical examination, the second to the *post-mortem* records of the condition of the brain as regards its development.

The compilation of the first set of statistics was made from the examination of 118 patients suffering from general paralysis.

In each case notes were made concerning both the standard

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of mental development and the presence or absence of the various stigmata of degeneracy. Of these 118 patients, 20 had subsequently to be excluded from the classification because they died from some intercurrent affection before the terminal stage of paralysis had been reached. The remaining 98 cases, however, were divided into three classes, as follows:

Class A.—Those with slight or no visible stigmata of degeneracy, and of average or above mental powers.

Class B.—Those with moderate stigmata of degeneracy and with mental powers a little below average.

Class C.—Those with marked stigmata of degeneracy associated with feeblemindedness or defective intelligence.

The annexed two tables will show the number of cases which came under each of these three classes, the approximate duration of life in each case, the average duration of life in each class, and the percentage of deaths occurring between certain periods. All dates are reckoned from the time the patients were admitted into the asylum.

TABLE I.

Showing the number of cases placed under each class, the approximate duration of life in each subject, and the average duration of life in each class.

Class A.—Fifty-eight cases. Those with slight or no signs of degeneracy and average or above mental powers:

23	died	between	1	and	6	months	after	admission
16	„	„	7	„	12	„	„	„
10	„	„	13	„	24	„	„	„
9	lived	over	24			„	„	„
Average duration			11			„	„	„

Class B.—Twenty-four cases. Those with moderate stigmata of degeneracy and with mental powers a little below average:

9	died	between	1	and	6	months	after	admission
7	„	„	7	„	12	„	„	„
4	„	„	13	„	24	„	„	„
4	lived	over	24			„	„	„
Average duration			14			„	„	„

Class C.—Sixteen cases. Those with marked stigmata of degeneracy associated with feeblemindedness and defective intelligence:

2	died	between	1	and	6	months	after	admission
2	„	„	7	„	12	„	„	„
5	„	„	13	„	24	„	„	„
7	lived	over	24			„	„	„
Average	duration		23			„	„	„

In Class A, B, and C three, two and three cases respectively are still alive. Their duration of life has only been reckoned up to the present time, so that the figures quoted at the bottom of each class represent an average which is a little too low.

TABLE II.

Showing the percentage of deaths occurring between certain periods after admission in the three classes :

	Classes A	B	C
Percentage of patients dying between 1 and 6 months after admission	40	37	13
„ „ „ „ 7 „ 12 „ „ „	28	29	13
„ „ „ „ 13 „ 24 „ „ „	17	16	30
„ „ living over 24 „ „ „	15	16	44

From table II the following deductions may be made. In Class A, representing subjects with high development, a large proportion—nearly 40 *per cent.*—died within six months after admission ; whereas in Class C, representing the degenerate type, only 13 *per cent.* died within a short time. Again, in Class C 44 *per cent.* lived over two years, whilst in Class A only 15 *per cent.* survived beyond this period.

Concerning Class B little need be said but to point out that in it the figures represent a very fair mean between the other two classes.

Although the foregoing tables demonstrate that general paralysis runs a more rapid course in subjects of high intelligence than in those of a degenerate stamp, the following statistics further the belief and place it on a still more definite basis.

Records were collected from the *post-mortem* books at Claybury Asylum of the brain-weights and the complexity of the convolutions in 100 cases in which the diagnosis of general paralysis was confirmed by the autopsy. These 100 cases were then divided into the four following groups :

Group I.—Brains over 1300 grm., with average or above average development and cerebral complexity.

Group II.—Brains under 1300 grm., with average or above average development and cerebral complexity.

Group III.—Brains under 1300 grm., with under-development and simple convolutional pattern.

Group IV.—Brains under 1200 grm., with under-development and simple convolutional pattern.

The brains in these cases were weighed immediately after removal from the cranium, with the membranes attached and before any appreciable amount of fluid had drained away. By this method a fairly correct estimate of the brain-weight previous to disease was obtained, for the thickening of the membranes and the amount of cerebro-spinal fluid compensate, to a greater or less extent, for the atrophy of the brain associated with the terminal stage of the disease.

In classifying the individual brains under one or other group, the cerebrum was viewed as a whole and a general estimate made of the convolutional pattern in addition to obvious signs of under-development. Special attention was paid to the Sylvian angle, the intra-parietal fissure, and the presence of superficial and deep annectants. The calcarine fissure was also carefully examined, with special reference to the distance it extended towards or round the occipital pole, which affords one of the criteria of the degree of development of the parietal lobe.

The annexed two tables will show the number of cases which come under the several groups, the approximate duration of life in the asylum of each patient, the average duration of life in the asylum of patients in each class, and the percentage of deaths occurring between certain periods, dating from the time each patient came under observation.

TABLE III.

Showing the number of cases placed under each group, the approximate duration of life in each case, and the average duration of life in each group.

Group I.—Sixty cases. Brains over 1300 grm., with average or above average development and cerebral complexity:

27	died	between	1	and	6	months	after	admission.
14	„	„	7	„	12	„	„	„
11	„	„	13	„	24	„	„	„
8	lived	over	24			„	„	„
Average		duration	12			„	„	„

Group II.—Eleven cases. Brains under 1300 grm., with average or above average development and cerebral complexity:

4	died between	1	and	6	months	after	admission.
3	„ „	7	„	12	„	„	„
2	„ „	13	„	24	„	„	„
2	lived over	24			„	„	„
Average	duration	13			„	„	„

Group III.—Fifteen cases. Brains under 1300 grm., with simple convolutions and under-development:

4	died between	1	and	6	months	after	admission
3	„ „	7	„	12	„	„	„
3	„ „	13	„	24	„	„	„
5	lived over	24			„	„	„
Average	duration	19			„	„	„

Group IV.—Fourteen cases. Brain under 1200 grm., with simple convolutions and under-development:

2	died between	1	and	6	months	after	admission.
2	„ „	7	„	12	„	„	„
4	„ „	13	„	24	„	„	„
6	lived over	24			„	„	„
Average	duration	27			„	„	„

TABLE IV.

Showing the percentage of deaths occurring between certain periods after admission in these four groups:

	Groups I	II	III	IV
Percentage of patients dying between 1 and 6 months after admission	45	36	27	14
„ „ „ „ 7 „ 12 „ „ „	23	27	20	15
„ „ „ „ 13 „ 24 „ „ „	19	18	20	28
„ „ living over 24 „ „ „	13	18	23	43

These two Tables (III and IV) give very similar results to those seen in Tables I and II. Inspection of Table IV shows that of Group I, which represents the highly-developed subjects, 45 *per cent.* died within six months after admission, whereas in Group IV, representing the degenerate subjects, only 14 *per cent.* died within that period. Again, in Group IV, 43 *per cent.* lived over two years, whilst in Group I only 13 *per cent.* survived over that period. Groups II and III show a very fair mean between Groups I and IV.

Tables I and III are of interest apart from their bearing upon the prognosis of dementia paralytica. It is frequently asserted that the malady affects almost exclusively individuals possessed of high intelligence and more than average cerebral development—indeed, that those having the best minds amongst our town population are much the most liable to fall victims to the disease. This conclusion may have arisen from the rule that the individual with higher mental powers, when he becomes affected by the disease, generally becomes the noisy, turbulent and exalted patient, who presents the more vivid clinical picture as compared with the individual less mentally gifted, whose clinical manifestations are less impressive and therefore rather more apt to be overlooked. A careful study of a large number of cases shows, however, that the disease is not very prone to affect individuals with the higher cerebral development.

On reference to Table I, compiled from ninety-three cases, it will be seen that 57 *per cent.* of the cases occurred in subjects who would be considered of average, or above average, intelligence, whilst in the remaining 43 *per cent.* individuals defective in this respect fell below a moderate average standard, for as many as 17 *per cent.* exhibited a very well marked degree of mental insufficiency. Again, Table III, compiled from the study of the cerebral development in 100 consecutive patients upon whom autopsies were made, shows that in 60 *per cent.* the brain reached or was above a moderate average development as regards weight and complexity. In 40 *per cent.* the cerebrum fell below this standard, and in 14 *per cent.* was much below it both in relation to weight and development.

A satisfactory explanation of the result that the degenerate general paralytic, after being attacked by the disease, as a rule lives longer than his more highly-developed brother, is somewhat difficult.

Many as are the opinions on the causation of general paralysis, they may be condensed into two opposing views. According to the first of these views, (2) general paralysis is due to a premature primary decay of the neurones occurring in a potential lunatic, who has become syphilised and exposed, to a greater or less extent, to the various forms of stress—drink, worry, and the like. From this point of view stress does no more than determine the period of onset of the disease, and toxines, from whatever source derived, although they may hasten the

progress of the malady, have likewise but a secondary effect. The essential factor in the genesis of the disease is declared to be the possession by the individual of neurones of inherited defective durability, even though these may be well developed. Upholders of the second view deny the existence of any primary decay of the neurone itself owing to defective durability, but assert that its destruction is effected through the influence of toxins of syphilitic or other origin, acting either directly on the neurone or chiefly upon the walls of the minute cerebral blood-vessels, whereby changes in these are brought about and interference with the nutrition of the nervous elements produced.

That the syphilitic toxin or toxines may produce profound changes in the walls of the cerebral blood-vessels there is indisputable pathological evidence, but the statement that such toxins induce any primary decay of the neurone itself, at least in instances of acquired syphilis in the adult, is a mere assumption ([3]). The second of the two views above outlined is supported by quite insufficient evidence, whilst the first appears to be in accordance with the facts as at present known.

In whatever way the destruction of the nervous elements is brought about, there seems to be little doubt that, excluding those lesions which are directly and obviously due to syphilis, the neurones first affected are those which are onto-genetically and phylogenetically the latest developed ([4]). It has been proved that the pyramidal layer of nerve-cells is the last to be laid down in the process of onto-genetic development, and that the distinction between the cerebral cortex of the highly intellectual individual and that of the ament lies in the greater depth of the pyramidal layer in the former as compared with the latter ([5]). Thus the more highly intellectual subject, as compared with one who is more or less an ament, is provided with a greater number of these later developed, but relatively unstable, neurones, and accordingly is furnished with a larger amount of material less able to withstand the process of the disease. Destruction of these neurones in large numbers at quite an early stage of the malady may lead to the accumulation of degeneration products, such as neurin and cholin, which, by their irritative properties, cause proliferation of the neuroglia and of the elements of the vascular walls, with consequent impairment of the nutrition of the neurones. Hence more neurones become rapidly attacked in a secondary destructive process, followed in its turn by a

further accumulation of degenerative products and a further injurious effect upon the nutritional supply of the nervous structures. Thus a vicious circle, which is constantly enlarging, is early and rapidly established.

In the ament it is presumed that, owing to the relatively smaller number of highly unstable neurones present, such a vicious circle is formed more slowly and with greater difficulty, so that the ament, if secondary effects could be altogether excluded, might survive until the primary process of decay had affected his lower neurones. Naturally one would not expect to meet with such an extreme case, but almost all degrees are found between the limits above sketched.

The explanation thus suggested of the increased rapidity of the disease in the individual with the greater cerebral development is supported by pathological evidence. In the case of the ament in whom the disease has run a slow course it is found that there is a comparative absence of active neuroglial and vascular change, and that the destruction of the nervous elements is almost entirely of a primary nature, a state which presents a decided contrast to the appearance of the cerebral cortex in a case which has proceeded rapidly to a fatal termination, in which there is much active proliferation of the neuroglia and of the elements of the vascular walls, together with striking evidence of secondary acute destruction of large numbers of neurones.

(8) *The Special Features of the Juvenile Cases.*

The course of juvenile general paralysis is relatively very long as compared with that in adults. Few juvenile subjects die within two years of the onset of the disease, whilst this period is considerably exceeded in many. The average duration of the disease in nineteen cases was five years, the shortest being ten months and the longest nine and a half years. It would seem that the comparative longevity in the juvenile cases as compared with that in adults is in part due to the high degree of degeneracy which is nearly always present in these subjects. The comparative absence of the various forms of mental and bodily stress is also another factor which influences the duration of the disease.

In juvenile subjects the prognosis appears to be worse when

epileptiform convulsions occur, although convulsions in juvenile subjects are usually neither so frequent nor so severe as in adults. When they do occur, however, the disease is likely to be more rapid, and this rapidity of progress is especially marked if the convulsions occur early in the disease. Various forms of mental disorder may accompany the malady, but attacks of mania or excitement are relatively rare. The majority of juvenile cases are of an imbecile type, but delusions of diverse characters are not infrequently associated. The usual course for the disease to follow is a steadily progressive dementia, gradually terminating with emaciation, paresis, and death.

A remission, or even a temporary amelioration resembling a remission, did not occur in any of the nineteen cases.

From the study of the above cases, and from the fact that the writer has been unable to obtain evidence of a remission occurring in any other case of juvenile general paralysis, it would seem probable that remissions do not occur in this form of the disease.

(9) *The Special Features when associated with Tabes Dorsalis.*

Ataxic symptoms are associated with general paralysis during some period of this disease in about 10 *per cent.* of all cases. In a large proportion of these cases the ataxic symptoms do not make their appearance until an advanced stage of general paralysis has been reached. These cases will not be discussed here, as when the tabetic symptoms are first apparent the patients are already on the verge of a fatal termination; thus it is difficult to say in what manner the course of general paralysis is influenced thereby. In other instances general paralysis does not appear until the tabetic symptoms have existed for many years. In these subjects the onset of general paralysis usually brings about an early and rapidly fatal termination.

In a small proportion of cases (probably about 2 *per cent.*) the symptoms of tabes dorsalis and general paralysis appear almost simultaneously. These cases, in which general paralysis and tabes dorsalis appear together thus early, have several characteristic features.

The duration of life is much above the average, in 22 cases being two years and nine months, or more than twice the average length of life in the non-tabetic forms of the disease.

The subjects affected were for the most part of a relatively older age than is usual in this disease, the youngest subject affected being 34, whilst the majority were over 40 years of age. A slowly progressive dementia, not infrequently associated with a mild degree of melancholia, was the predominant mental feature in nearly all cases. Delusions were seldom well marked, and when present were usually of a mild, persecutory nature, and bore a relation to the associated melancholia.

Exaltation of ideas was present in only 1 out of the 22 cases. From the foregoing remarks there is reason to believe that if the symptoms of dementia paralytica appear at a time when the tabetic symptoms have only recently appeared the duration of the disease is usually long, whilst if the symptoms of general paralysis do not appear until tabes has been established for several years or more the disease usually runs a rapid course.

It would thus appear on the one hand that the association of tabes with general paralysis is of favourable import so far as the prognosis of the latter disease is concerned, but on the other hand that the presence of general paralysis is unfavourable as regards the prognosis of tabes.

Taken as a whole, tabetic general paralytics are characterised by comparative longevity and a steadily progressive course usually free from maniacal attacks and exacerbations, but eventually slowly terminating in paresis, dementia, and death.

(10) *The Types of the Disease in which Remissions occur.*

An arrest in the symptoms of general paralysis sufficiently complete and lasting to enable the patient to be discharged is an occurrence of comparative rarity.

A definite history of a remission was obtained in only 4 out of 200 subjects who died in Claybury Asylum; 3 *per cent.*, however, of all general paralytics admitted during two consecutive years eventually became sufficiently recovered for discharge. The smaller percentage of recoveries in the first instance is accounted for by the exclusion of those patients who had a remission, were discharged, and then died elsewhere than in Claybury.

Examination of previous histories of general paralytics not infrequently shows that many of these patients have had a

short and passing attack of mental aberration occurring some months or years previous to admission. These short attacks of mental disorder, in which the mind has perhaps been affected for a few days or weeks only, should, however, be regarded as prodromal symptoms, rather than as a definite manifestation of the disease afterwards followed by a remission.

The following is a summary of the chief results obtained from an analysis of 20 cases of dementia paralytica in which a definite remission occurred. The observations refer to the condition of the patient on the first occasion of his detention in an asylum.

In 13 cases the associated mental state was melancholia, in 5 mania, and in 2 confusion of ideas bordering on dementia. That such a large proportion of the patients (namely 65 *per cent.* of the cases) who subsequently had a remission of the disease should have exhibited melancholia as their prominent mental state is of interest, and is all the more remarkable when it is remembered that melancholia is present only in 20 *per cent.* of all cases of general paralysis. In 4 of these 13 cases the patients were admitted on the first occasion suffering from what was then believed to be pure melancholia—*i.e.*, unassociated with general paralysis. In due course, however, they were discharged recovered, only to return afterwards with definite paralytic symptoms.

Auditory hallucinations were present in 8 cases, exaltation of ideas in 2, fixed and systematised delusions in 6, and varied delusions occurred in the remainder. The very high proportion of cases with aural hallucinations is here the chief point of interest, since, taking all cases of dementia paralytica together, only 6 *per cent.* are subject to delusions of this character.

In 7 cases a history of recent drinking was obtained. In 17 cases the pupils were equal, in 3 unequal, in 1 fixed to light, in 10 the reaction to light was sluggish, and in 8 normal. Slight irregularity of the pupils was present in 2 cases. In 14 of the cases the patients recovered within six months, 5 within nine months, and the remaining 1 within eighteen months.

Summary.

From the foregoing remarks it seems that the chief indications of favourable import, so far as the prospect of a remission

is concerned, are the presence of melancholia, auditory hallucinations, equal pupils which respond to light, and a history of recent drunkenness, but it would appear that there is little prospect of a temporary recovery if the disease continues for a period over six months without showing signs of amelioration.

(*a*) The expectation of life is best in young subjects. From the age of fifteen up to thirty-five the duration of the disease steadily diminishes. From thirty-five to forty the acutest forms occur ; after the latter age the duration again rises, but only to sink as old age approaches.

(*b*) Females live nearly twice as long as males.

(*c*) Subjects in whom the abuse of alcohol has been a recently acquired vice usually pursue a favourable course.

(*d*) The early onset of dementia is a very unfavourable symptom. Few melancholic subjects survive over a year. Subjects with mania and exaltation of ideas pursue a variable course ; the presence of fixed and systematised delusions is usually an indication that the course of the disease will be protracted.

(*e*) Pupils inactive to light, sluggish reaction to light, rapidly alternating pupils, and hippus are all unfavourable signs. Normal reaction to light and the early appearance of optic atrophy are favourable signs as to duration.

(*f*) Epileptiform convulsions have little or no general bearing on the course of the disease.

(*g*) The degenerate lives longer than the highly-developed subject.

(*h*) The disease in juvenile subjects pursues a long and chronic course, slowly terminating with a steadily progressive dementia.

(*i*) The association of early tabes with early general paralysis is an indication that the course of the latter disease is likely to be lengthened.

In conclusion, I have to offer my best thanks to Dr. Robert Jones, Dr. Mott, and Dr. Watson for their kindness in supplying me with the necessary material for the compilation of the above figures.

(1) Read at the Quarterly Meeting of the Medico-Psychological Association, in London, November 16th, 1905.—(2) Bolton, "Histological Basis of Amentia and Dementia," *Archives of Neurology*, 1903.—(3) Ford Robertson.—(4) Watson, "Juvenile General Paralysis," *Archives of Neurology*, 1903.—(5) Bolton, *loc. cit.*—(6) Watson, *loc. cit.*