

## THE PROPORTIONAL FREQUENCY OF GENERAL PARALYSIS OF THE INSANE AND LOCOMOTOR ATAXIA IN DIFFERENT SOCIAL CLASSES.

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*(With a Diagram.)*

IN both of these diseases, locomotor ataxia and general paralysis of the insane, the necessary antecedent is now generally recognised as syphilitic infection. Whether these two types of nervous degeneration occur at random in those so predisposed to their development, or whether some underlying factors at present unknown or only suspected operate selectively is a problem of some importance.

Different strains of the spirochaete have been noted, and Marie and Levaditi (1920) consider that the organism found in general paralysis is different from the ordinary spirochaete found in the external lesions of luetic infection. We do not, however, know whether such differences are the sign of special varieties apt to produce a particular lesion or are merely imposed by growth in a different environment.

The great differences between the sexes in the incidence and the slighter differences in the proportional frequency of each of these diseases would lead one to suspect that this development in any syphilitic is not simply a matter of chance. In the triennium 1910-12, for example, the death rate at ages 15 and over from both of these diseases combined was, for males 191 per million compared with 43.5 per million females. Mott (1902*a*), however, attributes this sexual difference in adult life to the difference in the number of individuals infected with syphilis at these ages, because, when the chance of infection is approximately the same, the incidence of parasyphilis is equal in the two sexes. This he has shown to be the case in juvenile forms resulting from congenital infection. The figures recorded for the country as a whole certainly lend some support to this view. In 1910-12 at ages 15-25 the ratio of the male to the female death rate is 1.8, against 4.4 for all ages over 15. Since it is likely that a larger proportion of deaths at ages 15-25 are cases resulting from congenital infection, from these figures it may be inferred that the total number of parasyphilitics is in a general way more an index of the number of infected individuals than of a difference in the incidence rate of parasyphilis among the total syphilitics in the two sexes. It is therefore impossible to say, in the absence of accurate statistics of the number of infected individuals, whether there is any difference in the sexes with respect to the relative

proportions of syphilitics who subsequently develop parasymphilitic lesions. The proportion of the deaths due to each of the two diseases does, however, show significant sexual difference. In males (1910–12), of all parasymphilitic deaths 24·14 per cent. were from locomotor ataxia, whereas in females only 18·70 per cent. were from this cause. The difference is 5·44 per cent. with a standard error of 1·07, so that this may be taken as representative of a real divergence between males and females.

In reference to the incidence of the two types of nerve infection, it is sometimes stated that when parasymphilitic manifestations occur, the distribution has some relation to occupational status—the syphilitic brain worker proportionately more frequently developing general paralysis of the insane, the syphilitic manual worker, locomotor ataxia. Statistical evidence in support of this hypothesis is not abundant. Mott (1902), however, considers that general paralysis is more likely to occur in persons who work with their brains rather than with their hands. The anatomical evidence which he brings forward does seem to support such a hypothesis. For example, he found that in general paralysis the gross wasting of the left cerebral hemisphere tends to be greater than that of the right. Of 24 cases of general paralysis, in 15 or 62·5 per cent. the right hemisphere was heavier than the left, whereas of 28 cases of other forms of mental disease, only 9 or 32 per cent. had the right heavier than the left hemisphere. The difference ( $30·36 \pm 13·2$ ), being more than twice the standard error, is statistically significant. This he considers as evidence in favour of the argument that stress on those parts of the nervous system which are most in use is an important element in the production of the morbid process. Clinical findings would also tend to favour this view. For instance, the histories of juvenile general paralytics show that symptoms tend to develop just after puberty when “new emotions, passions, ambitions and disappointments, associated with the awakening and development of the sexual instinct, originate a new psychological existence, wide-spreading cerebral activities and increased biochemical change.”

With regard to locomotor ataxia, also, Mott (1903) gives reasons for the belief that occupation does determine in some degree the site of the lesion. In 60 successive male cases of tabes dorsalis met with in hospital practice or outside the asylum, only two were not engaged in laborious occupations involving stress of the lower limbs, and individual case records would appear to show that the part of the locomotor system first or chiefly involved is that on which the stress is determined by the character of the work. Further, experiments carried out by Edinger<sup>1</sup> are quoted to favour this view. He showed experimentally that degenerative changes in the posterior column of the cord can be induced in animals rendered anaemic by a poison such as pyridin, provided these animals are daily made to use their limbs for a certain time so as to produce stress of the nervous structures concerned in locomotion. *A priori*, the statement that degeneration is more likely to occur in parts of

<sup>1</sup> Quoted from Mott (1902\*).

the central nervous system which are most in use, and that worry, anxiety and mental strain may be predisposing factors in the etiology of general paralysis of the insane seems to be perfectly reasonable. And since it also seems reasonable to suppose that these will be more frequent features of the upper occupational classes—the business and professional classes—and since such causes as mental strain, etc., are not commonly stated as influencing in any way the development of locomotor ataxia, it might be inferred that the tendency would be for parasyphilis to be more frequently a brain disease in those occupations in which mental processes feature more prominently than purely physical, whereas locomotor ataxia would be relatively more frequent in occupational groups where brawn takes precedence over brain. It should be noted, however, that it must be very difficult to cite predisposing etiological factors such as these in brain diseases. Reference to the above-quoted causes, supposed to determine in some degree the incidence of general paralysis of the insane, will show how extremely fine must be the dividing line between predisposing causes and early, but actual manifestations of the disease. No detailed body of statistics has, so far as I know, been analysed with respect to occupational status and these two diseases; and the present note, as will be seen when the data and methods are discussed, can be considered as no more than suggestive of occupational differentiation in the proportional frequency of occurrence of these two late manifestations of syphilitic infection.

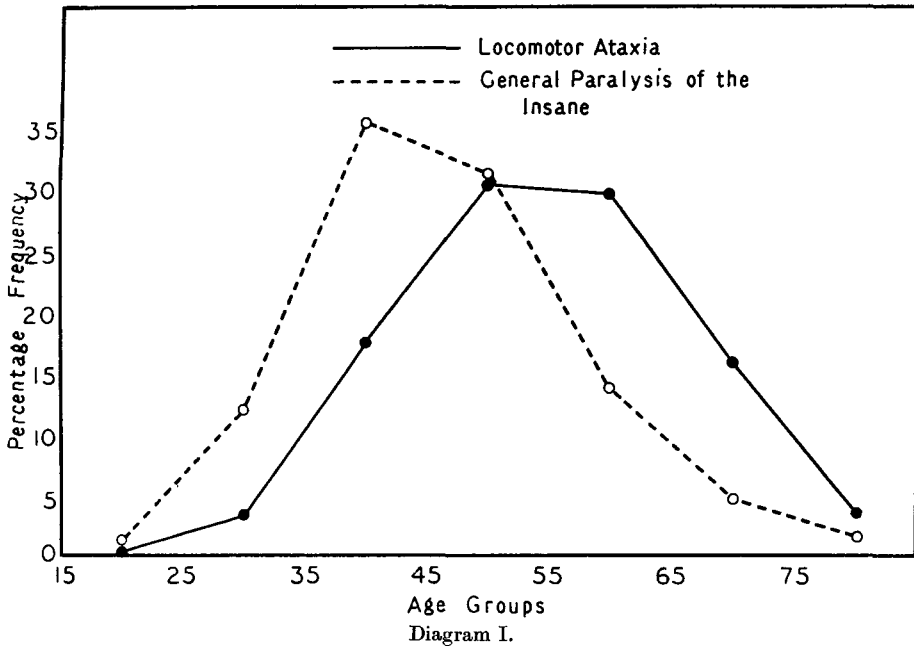
The Report on the Mortality in Occupations<sup>1</sup> gives deaths by causes for each separate occupational group and for several combined groups of social classes in the three years period 1910–12. Unfortunately both of the diseases under consideration here have been grouped together in this volume, so that an indirect method of attack has had to be planned to dissociate them. For the country as a whole the death rates at ages and the percentage frequency of deaths at ages from these two diseases are given in Table I. At ages 15 and over, general paralysis of the insane has a crude death rate almost 3½

Table I. *Showing the male death rates per million living and the percentage frequency of deaths in decennial age groups from locomotor ataxia and general paralysis of the insane in England and Wales in the triennium 1910–12.*

Age groups	Death rates per million		Percentage frequency	
	Locomotor ataxia	General paralysis of the insane	Locomotor ataxia	General paralysis of the insane
15–	0·3	6·4	0·19	1·15
25–	5·8	74·6	3·15	12·00
35–	38·4	269·2	17·30	35·72
45–	93·3	324·8	30·48	31·25
55–	142·8	225·2	29·90	13·87
65–	135·5	136·6	15·76	4·67
75–	80·7	114·5	3·22	1·34
15 +	43·5	147·8	100·00	100·0

<sup>1</sup> Mortality of Men in Certain occupations in Three Years 1910, 1911 and 1912. *Supplement to the Seventy-Fifth Annual Report of the Registrar-General for England and Wales.*

times as heavy as that from locomotor ataxia; but this relationship does not hold good for the separate age groups. Under 45 years, the general paralysis death rate is about nine times as high as that from tabes, whereas after that age they become more nearly alike. In other words, the deaths from general paralysis of the insane occur at an earlier age than those from locomotor ataxia. This will be seen more clearly in the columns showing the percentage frequency of deaths at ages, which are graphically represented in Diagram I.



The mean ages at death are as follows:

General paralysis of the insane	= 46.41 ± 0.10 years,
Locomotor ataxia	= 54.69 ± 0.23 years,
Difference	= 8.28 ± 0.25 years.

And since the two distributions are roughly symmetrical, the modal (or most common) ages at death are practically the same as the mean ages.

There is thus a significant difference of over eight years in the average age at death from the two diseases.

The above finding suggests a method of surmounting the difficulty imposed by the limited nature of the data at our disposal. What has been done may be explained briefly as follows: If the proportion which these two diseases bear to one another in the male population of the country as a whole were exactly the same in different units of the country, the frequency distribution of deaths at ages from the two diseases combined should be the same, provided that differences in the age distribution of the populations at risk are the same. It follows from this, then, that if we apply the death rates from each of the two

diseases in the country generally to the age distribution of any occupational sub-group, the distribution of the sum of the two groups of deaths should, apart from chance fluctuations, be similar to that actually observed in any period of observation, provided that there is no correlation between the proportional frequency of these two diseases and differences in the type of occupation. On the other hand, if it be found that the distributions are more divergent than can reasonably be attributed to chance, an excess of deaths at early age groups in the actually observed over the "expected" deaths may reasonably be claimed as due to an excessive proportional frequency of deaths from general paralysis; and an excess in the older ages (or, what is the same, a defect in the younger age groups) of the actual over the expected may be taken as indicative of excessive frequency of deaths from locomotor ataxia in that occupational group. The tacit assumption for this argument to be at all valid is that the age distribution of the deaths from these two diseases is the same in any sub-unit we choose to consider as in the country as a whole. This is a point on which we have no statistical evidence, so that it must simply be taken for granted.

For the purpose of this investigation, three distinctive social (or occupational) groups have been considered, namely:

(1) Upper Social Classes (Class I of the Mortality in Occupations Report), in which mental processes may be considered as taking precedence over muscular work;

(2) Skilled workmen (Social Class III), a happy combination of both mental and physical labour in proper proportions, and

(3) Unskilled workmen (Social Class V), in which mental work is probably least of all.

Table II contains the comparison between the actually observed deaths in decennial age groups from the two diseases combined and the deaths which would have occurred had the proportional distribution been similar in these classes to that in the population at large.

Table II. *Showing the percentage frequency distributions of the expected and observed deaths from locomotor ataxia and general paralysis combined in decennial age groups in different social classes.*

Age groups	Upper classes		Skilled workmen		Unskilled workmen	
	Expected	Observed	Expected	Observed	Expected	Observed
15-	0.97	0.33	0.89	0.48	0.76	0.76
25-	9.94	5.72	10.81	10.11	9.58	13.21
35-	31.00	28.81	32.26	31.58	32.20	34.26
45-	31.64	34.75	31.21	29.92	31.87	31.61
55-	17.51	18.95	17.30	18.21	17.81	14.54
65-	7.06	8.97	6.28	7.62	6.63	4.55
75-	1.88	2.47	1.25	2.08	1.15	1.07
15+	100.00	100.00	100.00	100.00	100.00	100.00

In the upper social classes we note that the observed deaths are in defect of the expected at ages under 45, and in excess above that age. Among skilled

workmen the same tendency is manifest, but in a much less noticeable degree. In the lowest social classes an exactly opposite type of relationship is seen to exist.

It remains finally to enquire how great weight must be attached to these differences—whether they are simply differences which might well have occurred by chance or whether they may be taken as representative of real divergences. The significance of these differences may be evaluated in one or both of two ways. The difference in the average ages at death in the expected and observed distributions may be considered with regard to their probable errors, or the two distributions may be compared *en bloc* by means of the  $\chi^2$  test. Both of these methods have been adopted and the results are in good agreement with one another. These are contained in Table III.

Table III. *Showing the significance of the differences between the expected and observed age distributions of the deaths from locomotor ataxia and general paralysis combined in different social classes.*

	Upper classes	Skilled workmen	Unskilled workmen
Expected mean age ...	48.35 ± .28	47.70 ± .19	48.09 ± .22
Observed mean age ...	50.30 ± .25	48.64 ± .21	46.39 ± .18
Difference ...	1.95 ± .38	0.93 ± .28	1.70 ± .29
$\chi^2$ ...	17.98	8.08	18.38
<i>P</i> ...	.012	.327	.010

It will be observed from these figures that in the upper and lower occupational groups the differences are almost certainly statistically significant. The odds against the differences being due to random sampling are too great for this to be the explanation. Among Class III (skilled workmen), however, the differences observed may quite readily be the result of chance; so that in this group the distribution may be considered as approximating to that of the general population.

An even more significant result is found if, instead of comparing each social unit with the average or general male population, we compare the two extremes of occupation. This has been done by applying the death rates from the two diseases combined in Class V to the age distribution of the population in Class I, and the expected and observed distributions of deaths compared. The mean ages of the resultant distributions and their difference are as follows:

$$\begin{aligned} \text{Expected} &= 46.59 \pm 0.23 \text{ years,} \\ \text{Observed} &= 50.30 \pm 0.25 \text{ years,} \\ \text{Difference} &= 3.72 \pm 0.34 \text{ years.} \end{aligned}$$

Comparing the two distributions as a whole, the value of  $\chi^2$  found = 58.45, and the corresponding value of  $P < .0000001$ . Such enormous odds against the distributions being similar must be considered as significant proof of occupational differentiation of the proportional frequency of occurrence of the two types of syphilitic nervous disease, although it gives no clue to the cause of this relationship.



It must be concluded, then, that general paralysis of the insane is relatively more frequent in the lower social units of the population than in the upper classes. The conclusion is apparently contradictory to general belief, but a definite statement such as this can scarcely be made from a cursory examination of such a gross body of statistics. In interpreting these results, the following points must be borne in mind.

In the first place it may be that the general impression is really wrong, and that factors such as mental worry or overstrain form part of the early symptomatology of general paralysis and not factors in the etiology of the disease. Owing to the amount of selection of cases admitted, statistics derived from public institutions are always apt to afford a totally biased view of the incidence of disease with respect to social class. Whether such selection is as stringent in a mental as in a general hospital cannot be determined, but in the diseases under consideration, and more especially with general paralysis, it is likely that most of the cases end their days in such an institution, so that a fairly representative sample of the total population may be got.

In the second place it may be argued that we have taken no account of the juvenile cases resulting from congenital infection—these are not distinguished in official statistics—and that the sole result of this investigation is an indirect statement of the fact that congenital syphilis is more common in the lower than in the upper social classes. But it may be pointed out that cases of juvenile general paralysis and tabes are relatively uncommon, and that although congenital syphilis very probably is higher in the lower than in the upper social classes, the much higher infantile and child mortality in the former may leave about equal numbers to survive to the age at which parasyphilitic manifestations usually occur. Again, on inspection of the death curve, if these juvenile cases were really of such importance as to vitiate or fully explain the result found, it would be reasonable to expect some discontinuity in the frequency distribution of the deaths at ages—some evidence of bimodality would be present. But as shown in Diagram I the curve seems perfectly smooth, and shows no significant evidence of discontinuity at any point. There seems no reason to suppose otherwise than that it forms the frequency distribution of a homogeneous group of cases. An unsuccessful attempt was made, however, to obtain a rough indication of the proportion of juvenile cases. A homogeneous death rate usually follows a course capable of being expressed by some relatively simple equation. Although the mere fact that a series of death rates at ages can be adequately described by a simple function does not necessarily give to the equation any ulterior meaning, it is reasonable to suppose that if a group of deaths does form a homogeneous series, the extrapolate from a curve fitted to part of it should agree fairly accurately with the observed deaths. Since most of the deaths from juvenile general paralysis and locomotor ataxia take place before the age of 30, it was decided to use the values of the death rates at later ages as the basis for curve fitting. If the curve is continuous, extrapolate and observed should, within

the limits of error, be equal; if a compound of two separate death rates, extrapolate should be in defect of the observed. The further procedure would be to deduct from the observed deaths the number to be expected if the curve fitted to the death rates at later ages adequately describes the whole series. The residual deaths would then be taken to represent those resulting from congenital infection, and further should on Mott's conclusions be approximately equal in the two sexes. The foundation on which it was proposed to determine the proportion of juvenile cases is obviously an unstable one; but no better line of approach was apparent. The method adopted in fitting the curves was that of successive approximation. A parabola of the third order fitted to the actual death rates in males at ages 30 and over fits the observed points fairly closely, but predicts negative rates for the three preceding quinquennial age groups, 15-20, 20-25, and 25-30, whereas for locomotor ataxia the prediction is greatly in excess of the observed. A further attempt was made by fitting a parabola to the logarithms of the rates instead of to the actual values. In this case the predicted values for general paralysis of the insane are in excess of the observed, whereas with locomotor ataxia, extrapolate and observed agree very closely. Curves fitted to the female death rates give, in the case of third order parabolas, all negative values for the younger ages in both general paralysis of the insane and locomotor ataxia. Fitted to the logarithms of the rates, a cubic predicts rates equal to the observed. Obviously the two methods give entirely different answers. The use of actual death rates for curve fitting and extrapolation leads to the conclusion that *all* the deaths under 30 years of age are juvenile, whereas a curve fitted to the logarithms of the rates would suggest that juvenile cases are of negligible importance. Since the results are so obviously discrepant, it may be concluded that by this method it is impossible to arrive at even a rough approximation to the proportion of deaths from these two diseases resulting from congenital infection; so that an answer to the question as to how far the (possibly) greater prevalence of congenital syphilis in the lower than in the upper social classes will explain the differential prevalence of parasyphilis with respect to social status can only be given by more detailed statistics than are at present available.

Thirdly, we must recognise the importance of other factors influential in the genesis of the two types of nerve infection which may counterbalance or even completely outweigh the influence of occupation. For example, the importance of alcoholism in the development of general paralysis of the insane has been stressed by Mott (1902) who regards it as a powerful adjuvant to the toxic effects of the specific virus, whereas, with respect to locomotor ataxia, alcoholism is regarded as of importance, not in favouring the onset of the disease, but in accelerating its progress.



## CONCLUSIONS.

An examination of the statistics relating to broad groups of social class in England and Wales as a whole suggests that general paralysis of the insane is proportionately more frequent in the lower than in the upper occupational classes. If, as is commonly believed, excess of mental work is a factor of importance in the etiology, its influence must therefore be more than counter-balanced by other more important predisposing factors, which must be more frequent in the lower social classes.

## REFERENCES.

- MARIE and LEVADITI (1920). “La paralysie générale est due à un tréponème distinct de celui de la syphilis banale.” (Abstract, *Ann. Malad. Vénér.* 15, 554.)
- MOTT, F. W. (1902). “Observations upon the Etiology and Pathology of General Paralysis.” *Arch. Neurol.* 1, 166–203.
- (1902). “Notes of Twenty-two cases of Juvenile General Paralysis, with Sixteen Post-mortem examinations.” *Ibid.* 1, 250–32.
- (1903). “Tabes in Asylum and Hospital Practice.” *Ibid.* 2.

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