A first study of the statistics of pulmonary tuberculosis / by Karl Pearson.

DEPARTMENT OF APPLIED MATHEMATICS
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BY

KARL PEARSON, F.R.S.
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WITH ONE DIAGRAM IN TEXT

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A FIRST STUDY OF THE STATISTICS OF PULMONARY TUBERCULOSIS.

By Karl Pearson, F.R.S.

"The germ has, perhaps, been too much with us, and the paramount importance of soil has been absurdly underrated."—Sir William Collins.

I. *Introductory.*

The most satisfactory method of studying the influence of heredity on the occurrence of special diseases undoubtedly would be to obtain a very large random sample of family histories of the general population. In this way each special disease would be represented in its due proportions and we could test by the usual statistical methods the prevalency of special types of disease in particular stocks. Unfortunately the difficulty of this method is great. I have now been two years collecting family histories and at present have only reached between 200 and 300 fairly complete histories, where 2,000 or 3,000 at least are necessary. It is extremely hard to get co-operators who are willing, or if willing, able to give perfectly frank and full family details. Still the collection goes slowly forward, and one must hope that some day it may serve the purpose for which it was designed.*

Enough, however, of these histories have now been collected to convince me that heredity plays a large part in the effective sources of tuberculous disease. The discovery of the possibility of phthisical infection has led, I think, to underestimation of the hereditary factor. Probably few individuals who lead a moderately active life can escape an almost daily risk of infection under urban conditions; but in the great bulk of cases, a predisposition, a phthisical diathesis, must exist, to render the risk a really great one. In this sense it is probably legitimate to speak of the inheritance of tuberculosis and even of the inheritance of zymotic diseases, meaning thereby the inheritance of a constitutional condition favourable to the development of such diseases should a risk be run, which cannot in the ordinary course of life be wholly avoided.† The recognised importance of modern views as

* I should be only too glad of further offers of aid in the preparation of family records.

† Again, without prejudice to fuller later investigation, my family histories, I think, show a general scattering over all stocks of zymotic diseases as a source of death, but in addition heavy incidence of these diseases in a relatively few stocks, and this not only in members living under the same environment, but among collaterals and distant ascendants.

to the nature of phthisis would be dangerous if throwing all weight on environment, they lead to the disregard of the inheritance of the diathesis as being in the bulk of cases an essential preliminary condition.

Approaching pathological inheritance from the modern statistical standpoint it is almost heartrending to notice the great amount of effort and energy wasted in the collection of data bearing on the inheritance of disease. We want to know whether the tendency to disease may be assumed to be inherited at the same rate as other physical and mental characters in the organism. If this can be shown to be reasonable, the hereditary factor can be at once assigned its due influence and position. But the data by which this preliminary inquiry can be satisfactorily answered are wholly wanting. We are told, for example, that a "family history" of tuberculosis or of cancer exists in such and such a percentage of cases, and this information is extended even to the differences of such percentages for cancer in various parts of the organism. But in 99 cases out of the 100, while a brother or a sister, an uncle or an aunt will be recorded as having cancer, no record whatever is made of the total number of brothers and sisters, or of uncles and aunts of the sufferer. No record of family history is of the least value unless the absolute number of collaterals, and their ages living or at death are taken. The like remark applies to tubercle; the same statement "no family history" is often recorded in the two cases when the mother died in childbed at twenty-five, and when she lived to a post-tuberculous age, or when no aunt or uncle existed and when none out of thirteen suffered from the disease. Luckily there has recently been an awakening in the medical profession with regard to this matter. Starting with complete family pedigrees in the case of *rare* diseases, certain physicians of distinction have introduced the custom of taking a complete family history; careful inquiries are made with regard to every ascendant and collateral that is known to have existed, and in each case it is clearly stated whether the individual was normal, abnormal or no information available. Such pedigrees often mean a very large expenditure of labour, but their ultimate value to medical science, and especially to national eugenics, is incontestable. From special and rare diseases the formation of such pedigrees is spreading and must spread to the discussion of inheritance in cases of carcinoma, pulmonary tuberculosis and the various forms of insanity.

Quite recently the Biometric Laboratory at University College has had placed at its disposal series—in each case amounting to several hundred—of such family histories in the particular cases of pulmonary tuberculosis, insanity and mental deficiency.

The present paper deals with a first series of this kind embracing 384 stocks in which cases of pulmonary tuberculosis have occurred.*

* One case had to be omitted in some part of this inquiry owing to absence of information.

II. *Material.*

The material was most kindly sent to my laboratory by Dr. W. C. Rivers, of the Crossley Sanatorium, Frodsham. The records were made by the medical men of that institution and apply in both subject and family history to cases of pulmonary tuberculosis only. The consumptives were almost wholly of the lower middle and working classes, and from Manchester (the great majority), Liverpool and their environs during 1905-6. The total number of brothers and sisters is recorded, the position of the subject in the family, and the age of the subject at probable initial onset of the disease. The number of brothers and sisters affected by the disease is stated, but neither their positions in the family nor their ages at onset are given. The family history is further extended to parents and grandparents and a statement is made of the paternal and maternal aunts and uncles known to have suffered from pulmonary tuberculosis. The total number of such collaterals is not, however, recorded.

The great value of the material is obvious, although we may hope that future records may be amplified in one or two directions. Notably it would be desirable to enter (1) the positions in the family of affected brothers and sisters, and the ages of all brothers and sisters at death or if living at time of record, (2) the total number of uncles and aunts and their ages at death or if living at time of record, (3) a special entry distinguishing between "no information" and "no disease," and (4) a record of cases of tubercle other than pulmonary, and of cancer cases in the stock.* Naturally this is the statistician's view, which will of necessity be controlled by the actual difficulties of taking the record. The present series gives much more than I have been able so far to find elsewhere and appears to be of high value. Two points must be first noted as they are essential to the right estimation of the results to be given later. First one is struck at once by the far larger number of cases of phthisis in the family histories of the women. This is associated with a fact that I have previously remarked in cancer family histories, and that has recurred in my general family pedigrees. The women know much more of the family history than the men do, and further they are much more ready to inquire about it, and to discuss it. The relative absence of tuberculous relatives in the cases of the males is not really a sexual difference; it results from no distinction being placed on the record between unaffected individuals and individuals about whom nothing is known. My own experience is that the women, especially in the lower middle and working classes, take a greater interest in and know much more than the men of the family history. They are also, if approached in the right way, more willing to reveal it, and not infrequently rather proud of a markedly pathological stock.

The second point to be borne in mind is that pulmonary tuberculosis is a disease

* On the correlation between the existence of cancer and tubercle, see K. Pearson, "Report on Certain Cancer Statistics," *Archives of the Middlesex Hospital*, vol. ii., pp. 127-137, 1904.

the frequency of which culminates between twenty and thirty. Hence many subjects, if members of large families, have brothers and sisters who have not yet passed, perhaps even not yet reached the danger zone. Hence the number of brothers and sisters of a patient who also suffer from the disease is a minimum limit and not a real measure of the extent of the disease in the family. This is a most important point for it acts in another way on our inheritance tables and exaggerates the number of non-tuberculous * children of a tuberculous parent. The true number of non-tuberculous children to a tuberculous parent can only be reached when the family history is completed; for this reason it would be better to take the ascendants; but if we take cases of tuberculosis in the grandparental generation we find the total number of aunts and uncles unrecorded, and further, we have made a *selection* of the tuberculous individuals in the grandparental generation, namely, those in whose stocks the tuberculous diathesis was sufficiently strong for at least one grandchild to manifest tubercle. Here again we are forced to the conclusion that a random sample of the pedigrees of the general population is what is really required; but the thousands of such pedigrees needful to obtain a sufficient subsample of tuberculous stocks would alarm all but the youngest and bravest collector. We must therefore content ourselves with the fact that we have only got a lower limit to the number of tuberculous children of tuberculous parents, and endeavour to test generally the influence of increase of such number. We cannot hope accordingly to do much more at present than measure a lower limit to the intensity of hereditary influence in pulmonary tuberculosis.

III. *Preliminary Investigations.*

I first turn to the age distribution. The 167 male and 216 female cases are distributed according to age of onset as follows :—

Age.	5-7	8-10	11-13	14-16	17-19	20-22	23-25	26-28	29-31	32-34	35-37	38-40	41 43	44-46	47-49	50-52	53-55	56-58	59-61	62-64	Totals.
Men	—	—	2	9	13	26	21	19	15	14	16	13	4	5	4	3	1	1	—	1	167
Women	2	3	3	21	25	33	43	24	17	10	13	7	6	6	2	1	—	—	—	—	216

Mean age of onset: Men, 29·1 Standard Deviation: Men, 9·8
„ „ „ Women, 25·3 „ „ Women, 8·6

Thus we see that the *average* age of onset is lower in the women and more concentrated. The curves, as most age disease curves, are markedly skew, but the data are not numerous enough to justify their complete analytical treatment. The modal values of the onset are probably about twenty-four and twenty-one in the two cases, probably a little bit closer than the average values.†

* "Tuberculous" will be used throughout the remainder of this paper for those affected with *pulmonary* tuberculosis.

† The mean age of onset in cancer is earlier in women than men and again slightly more concentrated ("Report on Certain Cancer Statistics," *loc. cit.*, p. 128).

An indirect method of measuring the effect of a phthisical environment now arises. If infection really plays a large part, in the liability to phthisis, and common life, with parents or brethren suffering from phthisis, explains the apparent running of the disease in stocks, we ought, I think, to find subjects belonging to families in which one or more members (parents or brethren) were affected by phthisis attacked at an earlier age than cases in which there are no such members. Actually I reach the following results :—

MEAN AGE OF ONSET.

Sex.	All Cases.	Cases of Immediate Family History.
Males	29·1 ± ·5	27·7 ± ·9
Females	25·3 ± ·4	25·7 ± ·7

The results considering the numbers dealt with cannot be considered conclusive. At any rate no significant difference in the average age of onset can be deduced from these figures.*

Again another noteworthy point in the present figures is the comparatively few cases of both parents being tubercular. Out of 383 cases of known family history the subjects' parents were only both affected in six instances, one parent being

*Taking the 1,000 cases of male and 1,000 cases of female "acquired" phthisis given by Dr. R. E. Thompson in his *Family Phthisis*, I find Average Age of Onset: Males 29·5, Females 25·9. These are in close agreement with the above results for all cases. On the other hand if we take Dr. Thompson's tables for hereditary phthisis we find :—

	Males.	Females.
Mother only attacked	26·0	23·8
Father only attacked	26·6	24·1
Mother and brothers or sisters attacked	26·6	26·3
Both parents	24·9	22·6
Brothers and sisters, not parents	29·0	26·1

These results certainly show that the age of onset is less when one or both parents are phthisical, but are we to attribute this lowering to the greater chance of infection? It seems impossible to reconcile a large influence of infection in lowering the age, when we find the average age, in which those with a family history of mothers *and* brothers and sisters, are attacked is greater than the average age in which those are attacked when *only* mother is concerned. The fact of brothers and sisters being attacked does not lower the average age of onset at all below that of the "acquired cases". It would seem that parental phthisis lowers the age of onset, but this cannot at present be asserted to be due to infection. Inquiry ought in all cases of family history to distinguish between cases of possible infection and no such possibility. In how many of the above cases did the parents die before the offspring were attacked?

A further point is suggestive, the average age of onset of phthisis in males and females coincides very closely with their respective primes in stature and probably with their respective ages of maximum fertility.

effected in seventy-eight cases. It is difficult to consider that even those six instances are due to infection. Suppose only one-tenth of the population to suffer from tuberculosis and only eight per cent. of those that marry to suffer, then if 100 individuals who will sooner or later develop phthisis married at random, they would be likely in eight cases to have a tuberculous mate. Our statistics show that of eighty-four tuberculous married persons six had a tuberculous mate. There is clearly no need in such cases to appeal to infection from husband or wife to account for the small number of cases in which both parents suffered.

IV. *Pulmonary Tuberculosis from the Mendelian Standpoint.*

Since for cases in which one parent is tuberculous and the other not tuberculous, there may be one or more offspring tuberculous, and one or more offspring who have throughout life no evidence of tubercle at all, it is needful to consider the phthisical diathesis as a recessive character. We shall express therefore an individual who has shown evidence of tuberculosis as (RR), one who has not personally shown evidence of tuberculosis but of whom the offspring have shown it as (DR), while those in whom neither personally nor in the offspring there is any trace of tuberculosis are (DD).

Cases in which both parents show the disease must be (RR) × (RR) and on Mendelian theory all the offspring should be tuberculous.

Cases in which neither parent show the disease but it appears in the offspring should be (DR) × (DR). And cases in which one parent shows it and the other does not should be (RR) × (DR).

Now, of course, the inheritance being one of the diathesis and not of the disease, a parent treated as (DR) may really be (RR), but if some of the (DR) parents be really (RR) the effect of this should be to increase the number of tuberculous children.

The expected theoretical results are as follows :—

Matings.	Symbol.	Offspring—Per Cent.	
		Tuberculous.	Non-tuberculous.
Both parents tuberculous	(RR) × (RR)	100	0
One parent tuberculous	(RR) × (DR)	50	50
Neither parent tuberculous	(DR) × (DR)	25	75

Matings with (DD) do not concern us, as at least one of the offspring in the families recorded was tuberculous. We find :—

Matings.	Females.			Males.			Total.		
	Cases.	Offspring.		Cases.	Offspring.		Cases.	Offspring.	
		T.	N.T.		T.	N.T.		T.	N.T.
(RR) × (RR)	2	4	4	4	8	5	6	12	9
(RR) × (DR)	52	89	203	26	33	98	78	122	301
(DR) × (DR)	162	205	711	137	167	658	299	392	1,369
Totals	216	298	918	167	208	761	383	506	1,679

Treating only the totals for both sexes we have :—

Matings.	Expected to have Phthisical Diathesis.	Known to have it.
(RR) × (RR)	100 per cent.	57 per cent.
(RR) × (DR)	50 per cent.	29 per cent.
(DR) × (DR)	25 per cent.	21 per cent.

Now this table shows—what we might expect on any theory of heredity—that the percentage of tuberculous offspring rises steadily according as they have no, one or both parents tuberculous; but except in the last case the percentages show no approximation to the expected Mendelian values. Nor is this absence of agreement in itself to be at all insisted on, for it must be remembered that it is the inheritance of the diathesis and not that of the actual disease with which we are concerned.* The numbers of persons in the three cases we should expect on the Mendelian hypothesis to have the phthisical diathesis are 21, 212 and 435 respectively. Thus in the case of both parents being tuberculous 43 per cent. of the offspring with the diathesis escaped infection; in the case of one parent being tuberculous 42 per cent.

* Possibly a better comparison with Mendelian theory can be made by using the statistics of Dr. Thompson (*Family Phthisis*, p. 45). He gives the data for eighty families with *completed* family history, not very extensive statistics it is true, but the best available. Dr. Thompson gives no cases of non-parental incidence with details as to number of brothers and sisters affected, *i.e.*, we cannot supply (DR) × (DR). But we have from the sixty-eight available families :—

	Tuberculous.	Non-tuberculous.
One parent affected (DR) × (RR)	132	141
Both parents affected (RR) × (RR)	43	21

Here the "one parent affected" group has risen from 29 to 48 per cent., a near approach to the Mendelian 50 per cent. But the "both parents affected" class has only risen from 57 to 67 per cent. and is still a long way from the Mendelian 100 per cent. It is remarkable that in these statistics of completed family history, as well as in those cited in the text, the approach to Mendelism in the partial parental affection is considerably greater than in the (RR) × (RR) cases.

One important point arises out of the statistics here dealt with. In stocks in which at least one parent is tuberculous, the offspring are tuberculous and non-tuberculous in the ratio of 175 to 162; in other words when the family history is completed at least 50 per cent. of such stocks will be tuberculous.

escaped infection, and in the case of neither parent being tuberculous 14 per cent. escaped infection up to the time of the record. Now if these percentages had been approximately equal the divergence between the expected and the known percentages would not be remarkable; they would merely show that a large percentage of those with the diathesis had escaped infection at the time of the record; but the remarkable point is that three times as many escape the disease where one or two parents exist as centres of infection as escape when no such parental centres are present.

The average age of onset being for males twenty-nine and females twenty-five it is clear that most parents are either dead or through the danger zone at the time of the record, and in the working-class population of a town like Manchester it may reasonably be doubted if many (RR)'s who have lived to forty or fifty years of age would not have met with infection enough to convert the potentiality into actual pulmonary tuberculosis. A few (RR)'s may have been classified as (DR)'s, but it is unlikely that the difference between 14 and 42 per cent. can be introduced in this way. Thus the group which at first sight gives the closest approach to the Mendelian percentage, namely 21 instead of 25 per cent., is the one which on the whole is most unfavourable to it.

Of course the present discussion is based on the assumptions (1) that the diathesis of pulmonary tuberculosis is a "recessive" character, and (2) that when tuberculous and non-tuberculous stocks cross the latter is dominant in the hybrid. If, however, diverse constitutions be attributed to the hybrids, so that they may sometimes be classed with (RR) and sometimes with (DD), other than the simple Mendelian percentages cited above may be reached. The great value, however, of the simple Mendelian theory, *i.e.*, that it allows of the latency of the recessive character through several generations, is lost when the idea of dominance is suspended.

V. *Pure Statistical Theory of Inheritance of Tuberculosis. Parental Heredity.*

On the whole it does not seem probable that any simple Mendelian theory will throw light on the inheritance factor in pulmonary tuberculosis. That such an inheritance factor really exists is sufficiently marked by the increasing percentage of tuberculous offspring as we pass from neither parent to one parent and then to two parents affected. If we approach the matter now from the purely statistical standpoint we can arrange our records as follows :—

Male Pedigrees. Parent.			Female Pedigrees. Parent.		
Offspring.	T.	N.T.	Offspring.	T.	N.T.
T.	$49 + y$	361	T.	$107 + y$	509
N.T.	$108 - y$	x	N.T.	$207 - y$	x

Here the numbers represent the data actually given by the Crossley Sanatorium records. Each child is entered twice, once with each parent; x represents the number of non-tuberculous children (male or female) of non-tuberculous parents which are clearly not provided by the records, but which would be associated with this amount of tuberculous material had we reached the record of it from a random sample of the general population.

To explain the other unknown, y, we note that 108 and 207 are the number of non-tuberculous offspring of the tuberculous parents at the time of taking the record, y is the further number which possess the tuberculous diathesis, and might, or probably would, exhibit pulmonary tuberculosis if the family history were completed. There would of course be a similar corrective factor for the non-tuberculous parents, who might posterior to the date of the record develop tubercle. But this correction will not, I think, be of much significance, because (1) in the case of the parents their history is in a much larger number of cases completed and (2) the great bulk of parents have at the time of the record passed through the danger zone, *i.e.*, they are forty-five years of age or older.*

The general effect of this correction would be to increase the number in the first quadrant, and so intensify the hereditary influence. I shall not, however, make any attempt to allow for it.

To determine y we must appeal to the only data that I know to exist, namely, Dr. Thompson's record of families with completed tuberculous history (see footnote, p. 9). This shows us that slightly more than half the offspring of a tuberculous parentage are tuberculous. Accordingly we have for the two cases:—

$$49 + y = 108 - y, \text{ or } y = 30, \text{ say,}$$

$$\text{and } 107 + y = 207 - y, \text{ or } y = 50.$$

Thus our two tables may be written in the following form:—

MODIFIED TABLES, CORRECTION FOR COMPLETED FAMILY HISTORY.

Male Pedigrees. Parent.				Female Pedigrees. Parent.			
Offspring.	T.	N.T.	Totals.	Offspring.	T.	N.T.	Totals.
T.	79	361	440	T.	157	509	666
N.T.	78	x	$78 + x$	N.T.	157	x	$157 + x$
Totals	157	$361 + x$	$518 + x$	Totals	314	$509 + x$	$823 + x$

It remains to determine what value shall be given to x in order that these tables should represent random samples of the general population. To judge by the

* As already indicated there is the possibility that the parents recorded as "non-tuberculous" have died of other diseases before getting wholly across the danger zone. For this reason the age of relatives at death should always form part of the family history.

death rate, hardly fewer than 10 per cent. of the inhabitants of this country are affected by pulmonary tuberculosis. This fact is occasionally forgotten, when great stress is laid on the occurrence in a family history of one or more cases. Very few families of average size would escape such incidence if the disease were distributed at random ; the evidence for inheritance must therefore lie on a reduced incidence in certain stocks and a marked increase in other stocks. Assuming that our offspring are a normal sample of the population we must have :—

$$440 = \tfrac{1}{10}(518 + x), \text{ or } x = 3882 \text{ for the first case,}$$

$$\text{and } 666 = \tfrac{1}{10}(823 + x), \text{ or } x = 5837 \text{ for the second case.}$$

We can then throw our tables into the following final forms, which represent on the basis of our hypotheses random samples of the general population classed into tuberculous and non-tuberculous groups, after completed family history.

GENERAL POPULATION, RANDOM SAMPLES.

Male Pedigrees, Parent.				Female Pedigrees. Parent.			
Offspring.	T.	N.T.	Totals.	Offspring.	T.	N.T.	Totals.
T.	79	361	440	T.	157	509	666
N.T.	78	3,882	3,960	N.T.	157	5,837	5,994
Totals	157	4,243	4,400	Totals	314	6,346	6,660

The exact hypotheses on which these tables are based must be realised. In the first place these results are deduced from the Crossley Sanatorium records ; these naturally give "incomplete" family histories, *i.e.*, they contain only the number of cases of pulmonary tuberculosis at the time when a patient was in the sanatorium. I have assumed that the history as to parents is approximately complete, because the average age of the patient is such that the parent will be usually through the danger zone. The actual Crossley records only show 156 tuberculous offspring out of 481 offspring of affected parents, *i.e.*, about 32 per cent. But this is certainly below the correct value when the history is completed. If we take the data of Dr. Thompson, we find more than 50 per cent. are ultimately affected. The first correction is made on this basis of a final 50 per cent. In the next place an estimate has to be made of the non-tuberculous offspring of non-tuberculous parents. This can only be done by judging by the death rates from pulmonary tuberculosis the number of the population affected ; this is certainly more than 8 per cent. and probably less than 13 per cent. I have taken 10 per cent. as a round number to start work with ; 1 or 2 per cent. either way will not make a substantial difference in the result. Of course a reduction to 5 per cent. would much intensify the strength of heredity, just as raising to 15 per cent. would weaken the intensity. What we shall obtain from our tables will be an approximate value to the intensity of the heritage.

The tables have been worked out as fourfold tables of normal distribution, the assumption made of course being that the modal frequency of pulmonary tuberculosis is not among the very slight or very severe cases. This is generally in accordance with Dr. Thompson's statistics for degree of acuteness and of hæmoptysis,* which, I think, suffice to show no clustering at one end of the range and justify the use of the fourfold table method for approximate results, and will provide at any rate a first approximation, which is all we can venture to hope for at present, to the intensity of tuberculous heredity.

For the male pedigrees, the equation for the correlation coefficient is

$$1{\cdot}044{,}264 = r + 1{\cdot}155{,}432\, r^2 + {\cdot}241{,}046\, r^3 - {\cdot}032{,}869\, r^4$$

which gives in the nearest second decimal : $r = {\cdot}59$.

For the female pedigrees, the equation for the correlation coefficient is

$$1{\cdot}091{,}844 = r + 1{\cdot}072{,}139\, r^2 + {\cdot}192{,}622\, r^3 + {\cdot}024{,}362\, r^4$$

which gives to the nearest second decimal : $r = {\cdot}62$.

Thus while the male pedigrees give a slightly lower intensity of inheritance than the female, both practically give ·6 for the value of the coefficient of parental heredity. Before drawing any conclusion, I will endeavour to ascertain the effect of modifying the values of x and y.

Clearly a lower limit to the intensity would be found by putting $y = 0$. This gives :—

Male Pedigrees. Parent.				Female Pedigrees. Parent.			
	T.	N.T.	Totals.		T.	N.T.	Totals.
T.	49	361	410	T.	107	509	616
N.T.	108	3,582	3,690	N.T.	207	5,337	5,544
Totals	157	3,943	4,100	Totals	314	5,846	6,160

* *Loc. cit.*, pp. 52, 53, 62, 63. He gives the following data :—

		Acquired Phthisis.		Hereditary Phthisis.	
		Males (1,000).	Females (1,000).	Males (1,000).	Females (1,000).
Clinical Course.	Acute	288	425	320	445
	Sub-acute	441	326	382	296
	Chronic	271	249	298	259
Hæmoptysis.	Copious	279	170	272	180
	Moderate	146	116	171	144
	Slight	306	368	285	344
	Nil	269	346	272	332

For the male pedigrees we find—

$$\cdot 464{,}608 = r + 1\cdot 134{,}724\, r^2 + \cdot 228{,}679\, r^3 - \cdot 017{,}452\, r^4,$$

whence the correlation coefficient = ·33, to two decimal places.

For the female pedigrees we have :—

$$\cdot 667{,}718 = r + 1\cdot 047{,}991\, r^2 + \cdot 179{,}317\, r^3 + \cdot 038{,}549\, r^4,$$

whence the correlation coefficient = ·44.

The average of these values = ·385. This value is itself higher than has been found for the inheritance of cephalic index from mother to offspring, or in some shorter series for stature from parent to child. But it is somewhat smaller than the values obtained for long series of stature or pigmentation in man. The male pedigree results show the reduced correlation to be expected from less complete records. We see accordingly that parental inheritance lies between ·4 and ·6, approaching the upper limit, if we suppose the family histories when completed to give as great a tuberculous percentage as that observed by Dr. Thompson.

Lastly, let us ask what effect it would have on the intensity of parental influence if we supposed 13 per cent. and not 10 per cent. of the community to suffer from tuberculosis. Our tables now become :—

Male Pedigrees. Parent.				Female Pedigrees. Parent.			
	T.	N.T.	Totals.		T.	N.T.	Totals.
T.	79	361	440	T.	157	509	666
N.T.	78	2,867	2,945	N.T.	157	4,300	4,457
Totals	157	3,228	3,385	Totals	314	4,809	5,123

From these tables we find—

Equation from male pedigrees :—

$$\cdot 842{,}527 = r + \cdot 946{,}738\, r^2 + \cdot 081{,}783\, r^3 + \cdot 023{,}793\, r^4,$$

giving $r = \cdot 55$.

Equation from female pedigrees :—

$$\cdot 885{,}075 = r + \cdot 869{,}594\, r^2 + \cdot 061{,}995\, r^3 + \cdot 077{,}276\, r^4,$$

giving $r = \cdot 58$ to nearest second place of decimals. It will thus be seen that an increase of 3 per cent. in the amount of tuberculosis in the general population from which the Crossley Sanatorium patients are drawn would lower the correlation coefficients by ·04. An increase in the percentage of tuberculous offspring of tuberculous parents from the one in three of the incomplete family records to the one in two of Dr. Thompson's complete family records * raises the correlation from about ·4 to ·6. We may, I think, accordingly conclude with safety that the intensity of the inheritance factor in pulmonary tuberculosis is greater than ·4 and less than ·6.

* This is the increase which is essential also on the Mendelian hypothesis, see p. 8.

It is not a dogmatic step from this result to assert that the tubercular diathesis is inherited at the same rate as I have found physical characters in man are inherited, namely, somewhere about ·46 to ·50. What we need to supplement the present investigation are more extensive records for the "completed" family history of tuberculous stocks. We may note here an interesting point: if we take the 50 per cent. of tuberculous offspring demanded by the Mendelian theory in the case of tuberculous parentage,* we can hardly reach a correlation less than ·5. Such a value is inconsistent with the one-third which a simple Mendelian theory demands. This fact coupled with the number of non-tuberculous offspring found in cases where both parents are tuberculous leads me to believe that if pulmonary tuberculosis has a Mendelian inheritance, the principle of dominance does not apply or applies only—to use a Mendelian phrase—"with a complication".

The main result of this investigation is not, however, a question of one or other theory being applicable; it is the all-important genetic fact that the diathesis of pulmonary tuberculosis is undoubtedly inherited and that the intensity of this inheritance is comparable with that found for normal physical characters in man. A theory of infection does not account for the facts, and there is an anti-social disregard for national eugenics in the conduct of medical men who can write to the public press that the marriage or even intermarriage of members of tuberculous stocks is of no social detriment, provided they live with a good supply of fresh air. I am inclined to think that the risks run, especially under urban conditions, are for tuberculosis as for a number of other infectious diseases so great, that the constitution or diathesis means almost everything for the individual whose life cannot be spent in self-protection.

TABLE OF PARENTAL INHERITANCE.

Condition.	Source of Statistics.	Computer and Locus.	Minimum Value.	Maximum Value.	Probable Value.
Pul. Tuberculosis	Crossley Sanatorium	K. Pearson, this Memoir	·40	·60	·50
Insane Diathesis	Dr. O. Diem's Data	K. Pearson, *British Med. Journ.*, 1905, p. 1176	·30†	?	—
Hereditary Deafness	Dr. Fay's Data	E. Schuster, *Biometrika*, vol. iv., p. 466	·45	·62	·54
Insane Diathesis	Dr. Urquhart's Data	D. Heron Unpublished results	?	·65	—
Character.					
Stature	Pearson, Family Records	Lee and Pearson, *Biometrika*, vol. ii., p. 378	·49	·51	·51
Span			·45	·46	·46
Forearm			·41	·42	·42
Eye Colour	Galton, Family Records	Lee and Pearson, *Phil. Trans.*, 195 A, p. 106	·44	·55	·50

* Really slightly greater as a few cases of both parents tuberculous actually do occur.

† This should be really compared with the ·33 and ·44 of this memoir as being based on "incomplete" family histories.

The foregoing table reproduces what has been biometrically deduced at present regarding the inheritance of pathological conditions and compares the results with those for certain physical characters. The pathological states dealt with are very diverse but there appears no ground, after comparing the upper and lower parts of the table, for asserting that the pathological conditions are inherited with a less intensity than normal physical characters, or even in broad outlines for supposing that environment influences the one more markedly than the other.

VI. *Fraternal Heredity.*

As a general confirmation of the above result, that the tuberculous diathesis is inherited, and sensibly at the same rate as normal physical characters in man, we may consider the fraternal resemblance. The matter is not so straightforward as the parental correlation, and as the assumptions made are rather greater I have confined myself to the more reliable female pedigrees. Taking every pair of siblings * from these pedigrees we find :—

		First Sibling.		
		T.	N.T.	Totals.
Second Sibling.	T.	288	1,214	1,502
	N.T.	1,214	4,808	6,022
	Totals	1,502	6,022	7,524

Now this table contains only sibships in which one member at least is tuberculous, and these sibships deal only with "incomplete" family records. We have first to complete the family records and secondly to allow for non-tuberculous sibships, before we have a random sample of the general population. The above is based upon 216 families containing 1,217 offspring of whom 300 or nearly one-fourth were tuberculous. We have seen that if one parent at least be tuberculous, then 50 per cent. of the offspring in completed histories show tuberculosis. I think we shall probably underestimate the amount of the disease if we suppose that, when family histories are completed, one-third of the offspring of all families having at least one tuberculous member will on the average be tuberculous. I base this estimate on the following considerations: There were 8 offspring with both parents tuberculous, 292 offspring with one parent tuberculous and 916 with neither parent tuberculous. Dr. Thompson's statistics for completed family history show that of the first two classes $292 + 8 = 300$ individuals in all would give $300 \times 175/337 = 156$ tuberculous members. We may suppose the third class to give the Mendelian quarter at least or 229 tuberculous members. Hence the proportion of tuberculous $= 385/1217 = \cdot 32$ or nearly one-third.

* Pair of siblings = a pair of offspring from the same parents.

Accordingly we shall have, on completed family history, actually 406 instead of 300 tuberculous individuals in our total of 1,217 individuals. I have now distributed the 106 additional tuberculous individuals among the 216 families, so as to give as nearly as possible the ratio of one tuberculous to every three members. This process is of course only approximate, but there results the following table, which represents, as far as we can reach it without actual observation, the number of pairs of each class of siblings in 216 tuberculous families with completed family history.

		First Sibling.		
		T.	N.T.	Totals.
Second Sibling.	T.	441	1,302	1,743
	N.T.	1,302	4,479	5,781
	Totals	1,743	5,781	7,524

This table represents the sibships of 406 tuberculous individuals, but such a number of individuals in the community would correspond to a total of 4,466 individuals, supposing 1 in 11 of the community tuberculous,* or to 4,060 non-tuberculous individuals. Of these 812 are already accounted for as siblings to the tuberculous; we have therefore 3,248 individuals without tainted stock. But if, as we shall see, tuberculous stocks are at least as fertile as the non-tuberculous, we have the simple rule of three sum—If 1,217 individuals give rise to 7,524 pairs of siblings, how many will 3,248 provide? The answer is 20,080. We must accordingly add into the above table 20,080 pairs arising from non-tuberculous families to reach a random sample of the general population. We obtain the following table which leads to the equation :—

$$\cdot 779{,}940 = r + 1\cdot 168{,}800\, r^2 + \cdot 298{,}195\, r^3 + \cdot 042{,}736\, r^4$$

and this gives fraternal correlation = ·48.

FINAL TABLE FOR FRATERNAL CORRELATION, MODIFIED FOR COMPLETION OF FAMILY HISTORY AND BY INCLUSION OF UNTAINTED STOCKS.

		First Sibling.		
		T.	N.T.	Totals.
Second Sibling.	T.	441	1,302	1,743
	N.T.	1,302	24,559	25,861
	Totals	1,743	25,861	27,604

* We have seen that the percentage lies between 8 and 13.

This value is very close to what has been already determined for the intensity of fraternal inheritance in man. It must be remembered that here we have mixed siblings of both sexes. The correlation between brothers and sisters for stature, span, cubit and eye colour gives a value slightly under ·5 for adults.* Mr. E. Schuster, dealing with deaf mutes, obtains a value about ·7 and nearly as high a value has been obtained for pigmentation in horses; but the bulk of values† are lower than this and cluster not far from ·5 to ·55. The three assumptions made in the deduction are (1) the final value of the tuberculous contingent in families with neither parent tuberculous; (2) the distribution among the families of this "later than record" contingent, and (3) the total percentage of those who suffer at any time from pulmonary tuberculosis in the community. We can appreciate the effect of modifying (1) by simply supposing the table on p. 16, which represents the tuberculous contingent at the time of record, to represent the final state of affairs; we shall then get a minimum limit to fraternal correlation. Repeating the same argument as before we have 300 tuberculous and 917 non-tuberculous. In the general community, if we take 1 in 11 tuberculous to give round numbers, 300 tuberculous correspond to 3,000 non-tuberculous, or to an addition to our table of 3,000 − 917 = 2,083 non-tuberculous individuals from non-tuberculous sibships. But these 2,083 would give $\frac{7,524}{1,217} \times 2,083 = 12,878$ sibling pairs. Thus our table becomes—

		First Sibling.		
		T.	N.T.	Totals.
Second Sibling.	T.	288	1,214	1,502
	N.T.	1,214	17,686	18,900
	Totals	1,502	18,900	20,402

This gives—

$$\cdot 446,483 = r + 1\cdot 050,312\, r^2 + \cdot 201,895\, r^3 + \cdot 070,797\, r^4$$

leading to $r = \cdot 33$.

It is safe to say that the fraternal correlation is considerably above one-third, because 1 in 4 is undoubtedly too small a tuberculous contingent for completed records.

Again as to (3), if we go to the opposite extreme and make 1 in 8 of the community tuberculous, or say 13 per cent., we find that the correlation is only reduced

* Huxley Lecture. *Biometrika*, vol. iii., p. 140.

† See table in "Inheritance of Coat Colour in Shorthorns," *Biometrika*, vol. iv., p. 454.

to about ·43.* Thus, although our assumptions appear large, a very considerable latitude in their numerical application does not widely modify the correlation. I think we may safely assert that there is nothing in the degree of fraternal resemblance to oppose the result reached from the somewhat more certain parental data, and this result is that:

The tuberculous diathesis is inherited in the same way and with the same intensity as the physical characters are inherited in man.

VII. *Fertility of Tuberculous Stocks.*

The result reached in the previous section is of such importance from the standpoint of national eugenics, that it is desirable to consider in more detail the nature of the fertility in stocks tainted with pulmonary tuberculosis.

The distribution of the 381† tuberculous families, which may be practically considered as completed, is as follows:—

Size of family	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	22	Total
Number of families	15	34	43	42	62	59	40	29	22	14	6	6	3	4	1	1	381

Accordingly the mean family contains 5·68 offspring. For the male pedigrees the mean size is 5·80 and for the female pedigrees 5·59. Mr. Schuster finds the mean size of families containing at least one deaf mute to be from American statistics 6·08, and from English statistics for probably completed families 6·19.‡ If we compare such results with those for the general population, we must be cautious about three points: (1) when we say that these families are probably complete, we mean that no sensible further additions are likely to be made after the date of record, because the average age at onset is twenty-five for women and twenty-eight for men; (2) barren marriages by the nature of the case are excluded; and (3) many of these marriages will not necessarily have lasted throughout the whole fertile period. While artizans' marriages usually begin early, they may terminate by the death of one or other of the pair before the end of fecundity.

I have reduced statistics of the fertility of the normal population available of three kinds: (*a*) those including sterile marriages; these are incomparable and need not be considered; (*b*) marriages which in each case have lasted fifteen years at

* The fourfold table is then:—

441	1,302	1,743
1,302	18,773	20,075
1,743	20,075	21,818

with the same meanings for the compartments as before.

† Three individuals were not placed in their sibships.

‡ *Biometrika*, vol. iv., pp. 477 and 482.

least and where neither husband nor wife was more than thirty-five at the time of marriage.*

A first series of such, 417, chiefly middle class cases, gives : Mean size = 6·40 ± ·10

A second series of such, 788, chiefly middle class cases, gives : Mean size = 6·68 ± ·07

Next : (*c*) Marriages which were completed by death or by extending beyond the fertile period, barren marriages being excluded :—

First series, 4,390, chiefly middle class cases, gives : . . Mean size, 4·52.

Second series, 204, middle class cases, gives : . . . Mean size, 4·65.

Third series, 378, middle class cases, gives : . . . Mean size, 4·70.

I add :

Danish,† fertile marriages, professional classes, 15 years at least (1,605 cases) 5·18.

Danish,† *all* marriages, working classes, 25 years at least (2,934 cases) 5·26.

New South Wales,‡ fertile marriages, all classes, 15 years at least (86,140 cases) . . . . . Mean size, 7·10.

Now I have found that the exclusion of the barren marriages does not, in most cases, raise the mean size of families more than about ·5 of a child. The Danish industrial classes have a mean size of family (gross fertility) of 5·26, and this number is identical with that given by Powys for the artizan classes in New South Wales.§ We may, I think, safely say that the fertile marriages of the artizan class in this country, even if they have lasted fifteen years at least, will not give a greater average gross fertility than six offspring. The educated and professional middle classes give a gross fertility for all completed marriages of under five offspring ; only when we take the fairly stringent selection of marriages begun at or before thirty-five years for both husband and wife and lasting at least fifteen years does the average gross fertility rise to 6·5. Now in the tuberculous and deaf mute stocks no selection of marriages lasting fifteen or more years has been made, no selection of age at entering on the marriage has been made, yet we find in both these cases a fertility of 5·7 to 6·2. We are forced to conclude that these pathological conditions do not tend to reduce the fertility, but that such stocks appear to be quite as fertile and in all probability are more fertile than normal stocks of the same class in the community at large.

It would thus appear that fewer offspring are not born to stocks tainted with pulmonary tuberculosis. The fact, however, that tuberculosis is a disease of youth and early middle life distinctly lowers the marriage rate of such stocks and thus reduces the total number of offspring born to them. From the Crossley Sanatorium records we find :—

Both parents tuberculous : . . . . Mean size of family = 3·50

One parent tuberculous : . . . . . Mean size of family = 5·42

Neither parent tuberculous : . . . . Mean size of family = 5·82

* Unpublished material.

† Pearson, *Chances of Death*, vol. i. *Reproductive Selection*, pp. 62-102, *passim*.

‡ Powys, *Biometrika*, vol. iv., p. 250. § *Loc. cit.*, p. 285.

Thus, to use Mendelian terminology, it is the (DR)'s and not the (RR)'s which constitute from the eugenic standpoint the gravest source of danger to the community. Without exogamy the endogamy of the tuberculous would lead to their extinction. The like result is not so marked, I think, in insanity statistics, where the evil so frequently manifests itself after the reproductive period.

VIII. *On the Distribution of Pulmonary Tuberculosis in Tuberculous Families.*

I now turn to an exceedingly important point, the question whether order of birth has any influence on liability to tuberculosis. This, if any limitation of natural fertility is taking place, is not only of importance from the eugenic standpoint, but clearly must have very considerable bearing on any Mendelian theory. Breeders are apt to assert—it is difficult to say on what definite evidence—that late offspring occasionally differ in a marked manner from earlier offspring even in pigmentation characters.

Now the position in the family of each tuberculous member is given in the present records. If we consider the community as a whole, it will be built up of families in all stages of development. There will be some in which both eldest and youngest siblings have passed through the tuberculous zone, some in which the eldest have and the youngest have not, and some in which the eldest are in it, and the youngest have not reached it. Each one in his lifetime passes through the danger zone, and we might expect, out of the totals that pass through, the same percentage would be attacked, whether they happen to be elder or younger siblings. In other words, if we take the Crossley Sanatorium population at a given date we might expect that as far as position in family is concerned it would be drawn indifferently from all parts of the family.* Taking the 381 families of which the record of birth position is available I find that there was the following distribution of birth position among the 2,164 members :—

TUBERCULOUS STOCKS, NUMBERS OF EACH CLASS OF SIBLING.

Siblings' order	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22
Number of cases	381	366	322	289	247	185	126	86	57	35	21	15	9	6	2	1	1	1	1	1	1	1

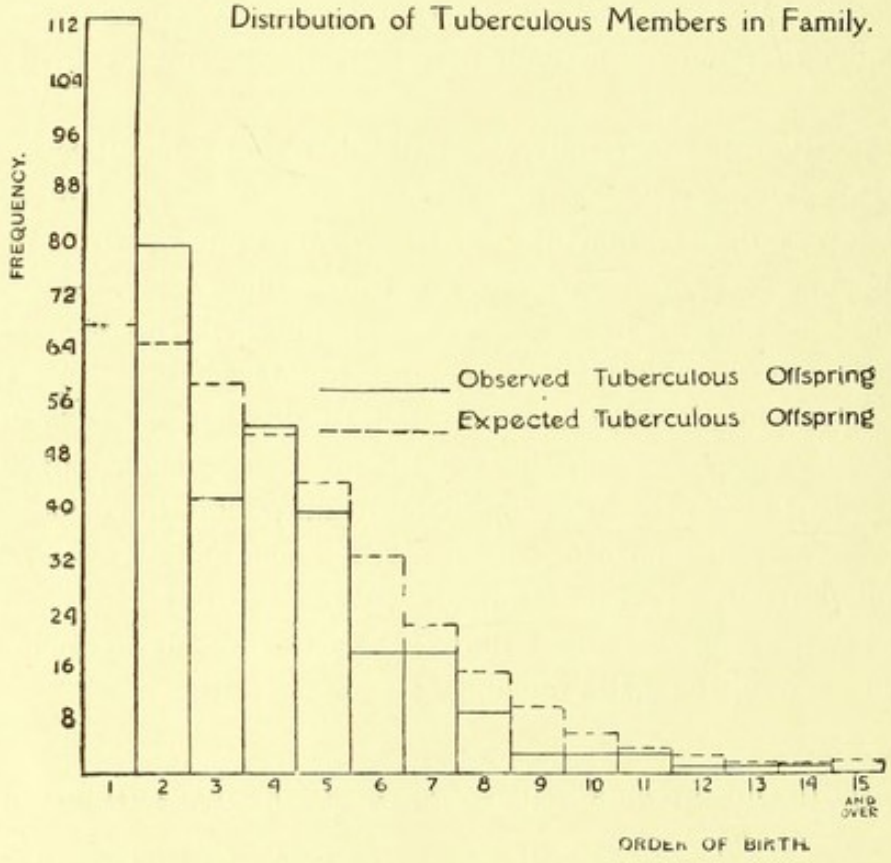
If we take the actual 381 tuberculous patients we find they were distributed as follows :—

* Thus while a certain number of families exist with young siblings, in which the elder alone are likely to suffer, there are others in which the elder are dead or past the danger zone and which only the younger are likely to suffer. I have taken out the actual patients and not all the tuberculous siblings of the family.

TUBERCULOUS PATIENTS.

Siblings' order	1	2	3	4	5	6	7	8	9	10	11	12	13	14	Above 14
Number of cases, observed	113	79	41	52	39	18	18	9	3	3	3	1	1	1	0
Number of cases, calculated	67·1	64·4	58·5	50·9	43·5	32·6	22·2	15·1	10·0	6·2	3·7	2·6	1·6	1·1	1·6

It will be obvious on mere inspection of this table, or of the accompanying graph, that the excess of elder born and defect of younger born is most marked. Testing by the usual process for goodness of fit,* we find $\chi^2 = 59{\cdot}61$ and conclude that the probability of such a distribution of elder and younger members of a family occurring by random selection lies between one and two in the ten million trials.



To further test the matter I considered only the cases of parental heredity, amounting to 83. In the families due to tuberculous parents there occurred 443 offspring distributed as follows :—

TUBERCULOUS STOCKS FROM TUBERCULOUS PARENTS.

Siblings' order	1	2	3	4	5	6	7	8	9	10	11	12	13
Number of cases	83	82	74	61	52	34	19	15	11	6	3	2	1

* *Biometrika*, vol. i., p. 155.

If we distribute the 83 patients in these proportions we have the following table :—

TUBERCULOUS PATIENTS.

Siblings' order	1	2	3	4	5	6	7	8	9	10	Above 10
Number of cases, observed	28	18	6	16	8	2	2	2	0	0	1
Number of cases, calculated	15·5	15·4	13·9	11·4	9·7	6·4	3·6	2·8	2·1	1·1	1·1

The irregularity at three is due probably to the smallness of the numbers, but there is the same general result, excess of elder members and defect of younger members attacked. The χ^2 for goodness of fit = 24·34 and the probability of a divergence in a random sample of this magnitude is measured by ·007. We must conclude that there is a real significance in this preponderance of older siblings even among the tuberculous offspring of tuberculous parents. In order to give additional confirmation to this investigation I have taken the following 7,670 fertile families from the industrial class in New South Wales,* which were *completed* at the time of the record. The total children were 46,325, or the average 6·05 was only slightly in excess of that of our tuberculous stocks. The result gives a slightly less number of elder members than the tuberculous families in the table provide (" number of cases, calculated " on p. 22); the difference is to some small extent due to the ·3 of a child marking increased size of family. But the general correspondence between the distribution of elder and younger siblings in the New South Wales industrial classes and in the tuberculous families is sufficient to indicate that the great redundance of elder members among those actually suffering from tuberculosis is not due to any special constitution of the tuberculous families.

DISTRIBUTION OF SIBLINGS.

Siblings' order	1	2	3	4	5	6	7	8	9	10	11	12	13	14	Over
N.S.W. Industrial classes (46,325)	7,670	7,003	6,184	5,442	4,708	3,986	3,266	2,593	1,927	1,405	908	546	311	167	209
N.S.W. Industrial classes (for 381 cases)	63·1	57·6	50·9	44·8	38·7	32·8	26·9	21·3	15·8	11·6	7·5	4·5	2·6	1·4	1·7
Tuberculous families (for 381 cases)	67·1	64·4	58·5	50·9	43·5	32·6	22·2	15·1	10·0	6·2	3·7	2·6	1·6	1·1	1·6
Actual distribution, 381 patients	113	79	41	52	39	18	18	9	3	3	3	1	1	1	0

I think we may fairly conclude that no population giving such a distribution of elders and youngers as that of the tuberculous patients could in practice possibly arise from families of the average size of the tuberculous stocks by random

* Powys, *Biometrika*, vol. iv., p. 284.

sampling.* Mr. Heron has recently found that in stocks tainted with insanity the heritage is more likely to be shown by elder than younger siblings. That the result is not due to some special constitutional weakness in the elder members of families, and holds for all diseases, appears to be demonstrated by the fact that Miss Beeton and I have shown † that older siblings live on the average four to five years longer than younger siblings. The conclusion therefore must be that, in certain cases at least of constitutional defects, which are inherited, the earlier members of the family are more likely to suffer than the later. It is difficult to reconcile this result with any simple Mendelian theory; it would seem necessary to combine such a theory with what amounts in result to a selective action on the gametes. I have already pointed out ‡ that such action would not only modify the Mendelian proportions, but also the parental correlations. Further, this selective action would vary with the environment, *i.e.*, the changing constitutions of the parents. Such direct action of the environment on the gametic cells is one which it would from the standpoint of national eugenics be of the greatest importance to study.

IX. *General Conclusions.*

Although this investigation does not profess to be more than preliminary, and its results need confirmation when much more numerous data are available, still certain general conclusions appear to be highly probable.

(*a*) What I have spoken of as the diathesis of pulmonary tuberculosis is certainly inherited, and the intensity of inheritance is sensibly the same as that of any normal physical character yet investigated in man.

Infection probably plays a necessary part, but in the artizan classes of the urban populations of this country, it is doubtful if their members can escape the risks of infection, except by the absence of the diathesis, *i.e.*, the inheritance of what amounts to the counter-disposition. The probably earlier age of onset, at least in certain cases of family history, as compared with those cases without family history, cannot at present be definitely asserted to be due to parental infection. In the statistics we are dealing with, the bulk of the parents must have passed the

* In order to allow for environmental influence of tuberculous parents, I excluded the 83 families, and worked out the data for the 298 patients without parental history (mean sibship, 5·77). The following table gives the numbers compared with a standard population and proves that the result is not due to very large sibships with non-tuberculous parents and small sibships with tuberculous patients :—

Siblings' order	1	2	3	4	5	6	7	8	9	10	11	12	13	14	Over 14
Standard population N.S.W.	49·3	45·0	39·8	35·0	30·3	25·6	21·0	16·7	12·4	9·0	5·8	3·5	2·0	1	1·3
298 Tuberculous patients	85	61	35	36	31	16	16	7	3	3	2	1	1	1·1	0

For goodness of fit, supposing the sample random, $\chi^2 = 59{\cdot}94$ and the odds are more than a million to one.

† *Biometrika*, vol. i., pp. 53-57. ‡ *Phil. Trans.*, 203 A., p. 86.

danger zone before the onset to the offspring (average age: 29 for males and 25 for females) and further, many such offspring will already have left in the artizan classes the immediate home environment. The earlier age of onset in the children is probably associated with the same tendency to earlier inheritance noted in cases of cancer and defective vision and possibly in gout, rheumatic fever and diabetes, where the question of infection hardly arises.

I feel fairly confident that for the artizan class the inheritance factor is far more important than the infection factor, because in a very large proportion of cases it does not lie in the power of the individual to maintain in the stress of urban life a wholly safe environment.

(*b*) There is no reduced fertility in the case of tuberculous stocks, in fact their fertility is as great as that of any other class in the community, and markedly greater in artizan tuberculous stocks than in any class of brain workers.

Tuberculosis having a mean age at onset, perhaps twenty years earlier than cancer, is from the eugenic side more self-destructive than cancer. Strange as it may appear, from the statistical standpoint, the marriage of the actually tuberculous is less productive of evil than the marriage of those of tuberculous stock, *i.e.*, the Mendelian (DR)'s tend more to perpetuate the evil than the manifest (RR)'s, for the latter if segregated would relatively cease to be owing to their reduced period of reproduction being associated with a much smaller fertility, and their offspring being more frequently affected and at an earlier age.

(*c*) In general, whether we deal with all tuberculous stocks, or only with those having no parental history, the elder offspring, especially the first and second, appear subject to tuberculosis at a very much higher rate than the younger members.

If this special incidence on the earlier born be found to be true for other forms of pathological heritage, we have a very serious factor of national deterioration introduced by the growing limitation of the family. It is further conceivable that any class, which reproduces itself largely from elder children, *e.g.*, the peerage, as far as the father is concerned, would tend on the average to more rapidly degenerate. The substantiation in other cases of this pathological weighting of elder children, which appears true for the cases of tuberculosis and insanity, would be a eugenic fact of the greatest importance. The limitations of the family may not only be an evil, if it leads to a smaller relative output of the mentally and physically better stocks, but even in the case of feebler stocks, it may lead to a relatively larger proportion of the more affected individuals being added to the community.

It is, of course, unfortunately too true that we want far more data on the inheritance of pathological characters than we have at present, if definite rules for social conduct are to be preached with earnestness and effect. But the attitude taken by one medical writer on this subject may even in the light of our present knowledge be considered demonstrably false.

"It is evident," he writes, "from the knowledge we possess as to the great "extension of the disease in this country that the promiscuous proscription of mar- "riage for any one whose family is tainted with a suspicion of phthisis would result, "if such advice was obeyed, in a considerable limitation of the population, which "would in the end lead to the catastrophe of national degeneration, however much "in these hard times some diminution in the overcrowding may be earnestly desired "by some; and it would also tend to discourage marriage among a class of persons "who, from their amiable and intellectual disposition, are especially qualified for "marriage and likely to procreate intellectual and amiable offspring."

The correlation thus asserted between amiability and intelligence on the one hand and tuberculous taint on the other rests, as far as I know, on no statistical evidence yet published, and the assertion that the "catastrophe of national degeneration" would follow a limitation of the marriages of tuberculous stocks seems very wide of the mark.

The one certain rule of racial fitness is the preservation of the dominant reproductivity of the mentally and physically fitter stocks. In less civilised communities than our own this is roughly provided for by the struggle for survival within the race and between races, and by the fight against organic environment and against physical environment. As far as statistical facts as to inheritance, fertility and survival in civilised communities are at present known and available, the dominant reproductivity of the mentally and physically fitter stocks appears likely to be more and more weakened by (1) the lessened intensity of the intraracial struggle and (2) the differential limitation of the family.

Can we consciously do what in the past was unconsciously achieved; can we preserve this dominant reproductivity of the mentally and physically fitter stocks? If this is to be done at all, we must patiently continue to collect data as to disease, inheritance, and fertility in man. There must be a healthy co-operation between medically and statistically trained minds, and when the evidence is, as I believe it will be in the near future, overwhelming, then there must be a united effort of both to influence public opinion in favour first of a few simple rules of conduct for those social by nature, and then, if necessary, a further united effort in favour of legislation to restrain those anti-social by inheritance or nurture.

In conclusion, I have to thank Dr. W. C. Rivers, not only most heartily for his material, but further for the help he has given me at various stages of this enquiry.

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