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The Relative Aetiological Importance of Birth Order and Maternal Age in Mongolism

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I

Mongolian imbeciles are very often born last in a long family. This fact, which was pointed out many years ago by Shuttleworth (1909), has led clinicians to believe that mongolism is to some extent a product of the exhaustion of maternal reproductive powers due to frequent child-bearing (Still, 1927; Fantham, 1925). The conclusion is widely accepted with the reservation that the affected child is not necessarily born at the end of the family (Thompson, 1925). Several cases are first-born, in fact, and it is sometimes stated that the condition occurs more frequently in first and last children than in other ordinal positions. There is, however, ample evidence that mongolian imbeciles have a significantly later birth rank than normal children (Hogben, 1931).

It is also established, from large numbers of figures which have been collected, that the maternal age at the birth of mongolian imbeciles is unduly high. Though some of these imbeciles have young mothers, most of the cases (about 70%) are born after the mother has reached the age of 35 years. Thus the maternal age itself is likely to be an aetiological factor quite as important as birth order. I know of no serious attempt, however, to distinguish between the aetiological significance of these two factors: to do this is the task I have undertaken.

In an article published recently (Penrose, 1933) I have attempted to show how statistical methods may be used to disentangle the probable aetiological effects of paternal and maternal age in mongolism. The results indicated clearly that paternal age need not be considered a significant causal factor; we shall therefore not refer to it in the present discussion.

There is another factor which has been asserted by some writers to be of causal significance. The interval between the birth of a mongolian imbecile and the birth of the child which immediately precedes it is found, on the average, to be significantly longer than the corresponding interval preceding normal births (van der Scheer, 1927); that is, the mongol apparently follows a period of diminished fecundity (Jenkins, 1933). This question of length of preceding interval is intimately bound up with the main question I am considering here and it will be referred to in the course of the discussion.

The investigation of the facts, on which the present argument is based, was carried out as part of the work of the research department of the Royal Eastern Counties' Institution. It involved the accurate determination of the maternal age at the birth of all offspring in 217 sibships each containing one or more mongolian imbeciles. The birth order was also recorded with particular care: miscarriages and stillbirths were deemed to affect the ordinal number of subsequent births, but they have been excluded from the data as presented here. It is very uncertain whether they represented offspring affected or not with mongolism and I wished to include in the data only those individuals in the 217 sibships of whom it could be said with certainty that they were either mongolian imbeciles or normal. The sibships, giving the birth rank and maternal age for each known individual, are set out at the end of the paper, and a summary is given in Table I. Altogether these particulars concerning 1031 persons, 807 normal children and 224 mongolian imbeciles, are recorded. A glance at the distribution is sufficient to show that there is good reason for supposing that both the birth ranks and the maternal ages are significantly higher for affected than for normal children. About 60% of the affected children are born last and the great majority of the families are completed. We will proceed to investigate how far this displacement of affected offspring towards the end of the sibship can be attributed to the late maternal ages at which affected offspring are most frequently born.

II

The following constants were calculated from the distribution given in Table I.

	Number	Mean maternal age at birth ($\bar{q}$)	Standard deviation (σ_q)
		years	years
Affected children (M)	224	37·415	—
Normal children (N)	807	31·312	—
Total children (T)	1031	32·638	6·778

The mothers are, on the average, more than 6 years older at the births of the affected than at the births of the normal individuals. This is a highly

Table I—Scatter Diagram showing Relationship of Maternal Age to Birth Rank

(Suffixes in bold type indicate Mongols)

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	Total	(N)	(M)
17	1	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	1	1	—
18	2	1	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	3	3	—
19	8_3	—	1	—	—	—	—	—	—	—	—	—	—	—	—	—	—	9	6	3
20	11_1	3	—	1	—	—	—	—	—	—	—	—	—	—	—	—	—	15	14	1
21	12_3	7	1	—	—	—	—	—	—	—	—	—	—	—	—	—	—	20	17	3
22	7_2	9_2	3	1	—	—	—	—	—	—	—	—	—	—	—	—	—	20	16	4
23	13_2	11_2	5	1	—	—	—	—	—	—	—	—	—	—	—	—	—	30	26	4
24	16_1	10	13	4	—	—	—	—	—	—	—	—	—	—	—	—	—	43	42	1
25	15	13	6	2	1	2	—	—	—	—	—	—	—	—	—	—	—	39	39	—
26	9_2	13	10_1	9	3	—	—	—	—	—	—	—	—	—	—	—	—	44	41	3
27	5_1	13_3	9_1	8_1	10	—	1	—	—	—	—	—	—	—	—	—	—	46	40	6
28	11_1	9_1	5	3	6	4_1	2	1	—	—	—	—	—	—	—	—	—	41	38	3
29	6_1	7_1	9	10	4	5	1	1	—	—	—	—	—	—	—	—	—	43	41	2
30	8	10_1	11_1	6	6	5	5	—	2	—	—	—	—	—	—	—	—	53	51	2
31	5_1	4	9_1	5_1	9	8_1	2	2	1	1	—	—	—	—	—	—	—	46	42	4
32	5_1	13_2	4_1	7	8	7_1	6	2	2_1	—	—	—	—	—	—	—	—	54	48	6
33	5	5_3	7_2	8	7_1	8	6	2	2	1	—	—	—	—	—	—	—	51	45	6
34	3	9_2	8_4	5_2	9	2	6	6	1_1	1	1	—	—	—	—	—	—	51	42	9
35	3_1	2_1	8_1	7_1	8_2	10_3	10_2	8_2	3	2	—	1	—	—	—	—	—	62	49	13
36	2_1	3_3	4	5_2	5	6	1	6_1	3	4	3_1	—	—	—	—	—	—	42	34	8
37	1	2	4_3	8_4	4_1	4_1	3_2	7_3	5_1	3	1	—	1	—	—	—	—	43	28	15
38	2_2	4	1	4_2	5	5_2	11_6	1	4_1	3_1	2	2	1	1	—	—	—	46	32	14
39	2_1	1_1	4_2	7_3	5_1	3_1	5_2	2	3_1	4_2	1	3	1	—	—	—	—	41	27	14
40	1_1	3_1	4_1	2_1	2_1	6_3	9_4	2_2	4_2	—	2	2	1_1	1_1	—	—	—	39	21	18
41	—	1	5_2	3_1	—	—	3_2	4_2	2_1	6_3	4_2	4_2	1_1	1	—	—	—	34	18	16
42	—	3_3	5_5	3_3	2_1	2_2	2_1	5_3	1	2_1	2_1	2	4_2	1	1_1	—	—	35	12	23
43	—	1_1	1_1	2_1	2_2	3_2	—	4_2	2_1	1	—	1	1	1	3_2	1	—	23	11	12
44	—	—	—	—	4_3	4_4	2	3_2	2_1	—	—	—	2_1	2_1	—	1	—	20	8	12
45	1_1	—	—	—	—	2_1	1_1	1	4_1	1_1	1_1	1	1	1	—	—	1_1	15	8	7
46	—	—	2_2	1_1	1_1	1_1	—	1	1_1	1_1	—	—	2	2_1	1	—	1	14	6	8
47	—	—	—	—	—	—	—	2_2	1_1	1	—	—	1_1	—	1_1	—	1_1	7	1	6
48	—	—	—	—	—	—	—	—	—	—	—	—	—	1_1	—	—	—	1	—	1
Total	154	157	139	112	101	87	76	60	43	31	17	16	16	11	6	2	3	1031	—	—
(N)	128	130	111	89	88	64	56	41	30	22	12	14	10	7	2	2	1	—	807	—
(M)........	26	27	28	23	13	23	20	19	13	9	5	2	6	4	4	—	2	—	—	224

significant difference, for it is more than 10 times the standard error, which is $\sigma_q \,.\, \sqrt{T/MN}$ or 0·51 years.

The following results are obtained, by making similar calculations, for birth order.

	Number	Mean birth rank* ($\bar{f}$)	Standard deviation (σ_f)
Affected children (M)	224	5·65	—
Normal children (N)	807	4·61	—
Total children (T)	1031	4·83	3·34

* The concept of mean birth rank (mean ordinal position) is a statistical fiction useful in this problem; it involves using imaginary units—fractions of a place or rank—which have no meaning except in averages. The averages given here are therefore simply shorthand description of complicated distributions.

The difference between the mean birth ranks of affected and normal children is 1·04 with a standard error ($\sigma_f \,.\, \sqrt{T/MN}$) amounting to 0·25. There is a significant discrepancy, but it is not so marked as in the case of maternal age.

In considering the question of birth order, we have not yet allowed for the effect brought about by the presence in the data of families of varying sizes. If human families were all of uniform size the expected mean birth rank, in any group of selected individuals distributed at random in respect of position, would be obtained by the ordinary methods of averaging. But human families vary in size from 1 to 20 or more pregnancies resulting from the same union. When families are selected, as they are here, by the presence of at least one affected member, the proportion of affected to normal children is greater in the small families than in the large. When the families in data such as these are pooled, the concentration of affected individuals in short sibships with low birth ranks causes the mean birth rank of affected children to be relatively nearer to the beginning of the family than it would be if we were dealing with a representative sample of the general population. Neglecting to take this consideration into account has led Pearson (1907), for example, to assert that the first-born are more likely than children occupying the later birth ranks to be affected by certain diseases, e.g., tuberculosis. Yule and Greenwood (1914) have criticized Pearson's conclusion and it is now generally accepted that, in estimating the probable number of affected children in each birth rank, the varying sizes of the families must be taken into consideration and accordingly weighted in the inverse ratio of their sizes. If more than one individual is affected in the same sibship, it is necessary to count the sibship once over for each affected member; that is to say, the sibships must be weighted directly according to the number of affected individuals they contain.

The simple method, sometimes known as the Yule-Greenwood reconstruction (Thurstone and Jenkins, 1931), by means of which a good approximation is obtained to the expected number of affected children in each birth rank (Hogben, 1931) is not suitable to the present data owing to the gaps left for siblings of unknown type. It is necessary to modify the method so that we may treat each sibship separately.

Let s be the number of known individuals recorded in the sibship and let a be the number of affected individuals in this sibship. The expected number of affected individuals in each birth rank, if they are distributed at random, is a/s. In each sibship only those ordinal positions already occupied are to have expectations attributed to them. In this way a table of expectations has been made out whose precision is equivalent to the accuracy of the original data. Examples of the expectations attributed by this method to various ordinal positions in different sibships are shown below :—

Serial number of sibship	Order of birth 1st	2nd	3rd	4th	5th	6th	7th
123	0·200	0·200	0·200	0·200	—	0·200	—
4	—	—	—	—	—	—	1·000
102	0·167	—	0·167	0·167	0·167	0·333	—
198	—	—	0·500	0·500	0·500	0·500	—

Sibship No. 123 shows how gaps are left for unknown individuals (miscarriages, etc.).

In sibship No. 4 the mother had other children by different fathers; the half-sibs are purposely not recorded here.

In sibship No. 102 twins occur; two individuals occupy the same birth rank (the 6th) and the expectation at this place is consequently doubled.

In sibship No. 198 there are two affected persons, hence the total expectation is 2; the sibship is, in fact, counted twice over, once for each affected member.

The sum of the columns of expectation in each ordinal place gave, for the whole 217 families, the values shown in Table II; they are compared with the observed numbers of mongols.

These expectations, Table II, are the probable numbers of affected individuals in the 217 sibships, if the 224 affected children were distributed at random in respect of birth rank.

The mean ordinal place in family ($\bar{e}_M$) of affected individuals, if thus distributed at random, is now estimated from the expected numbers by the usual process of averaging. Thus,

$$\bar{e}_M = \frac{(1 \times 44{\cdot}99) + (2 \times 43{\cdot}40) + (3 \times 33{\cdot}09) + \ldots}{224}$$
$$= 4{\cdot}10 \text{ ordinal places.}$$

Table II

Rank	Expected number affected (e_M)	Oberved number affected (f_M)
1st	44·99	26
2nd	43·40	27
3rd	33·09	28
4th	24·46	23
5th	18·63	13
6th	15·15	23
7th	13·32	20
8th	9·65	19
9th	6·47	13
10th	4·91	9
11th	2·10	5
12th	2·45	2
13th	2·56	6
14th	1·60	4
15th	0·76	4
16th	0·17	0
17th	0·30	2

The expected number of normal individuals in each birth rank is obtained by subtracting the numerical values given above from the totals (t) in each place, thus :—

Order of birth	t		e_M		e_N
1st	154	−	44·99	=	109·01
2nd	157	−	43·40	=	113·60
etc.					

The corresponding mean value for expected positions of normals ($\bar{e}_N$) is found to be 5·04.

The differences between the observed mean values ($\bar{f}_M$ and $\bar{f}_N$) and these expected mean values ($\bar{e}_M$ and $\bar{e}_N$) indicate the real average displacements of the mongolian imbeciles and normals. The displacements $\bar{f}_M - \bar{e}_M$ and $\bar{f}_N - \bar{e}_N$ are greater than the corresponding differences of $\bar{f}_M$ and $\bar{f}_N$ from the mean value $\bar{f}$ which have already been given above. Incidentally, if all the sibships had been of the same size, each containing the same number of affected children, $\bar{e}_M$ and $\bar{e}_N$ would have both been equal to $\bar{f}$. In the present instance the total difference between the mean birth ranks of affected and normal children is really greater than it at first sight appeared to be ; it is increased by the reconstruction to 1·98, *i.e.*, $(\bar{f}_M - \bar{f}_N) - (\bar{e}_M - \bar{e}_N)$. This displacement is now more than seven times the standard error, 0·25. The effect of birth rank on the incidence of mongolism is therefore apparently of great significance, though it is not quite as marked as the maternal age effect.

III

We are now in a position to calculate the expected number of affected children occupying each birth rank on the assumption that we only know the maternal ages for these individuals and not the orders of their births. It is necessary first to calculate for any given rank the size of the deviation from M/T (the average proportion affected) which can be attributed to the effect of the maternal ages corresponding to the affected children in the given rank.

We turn our attention to the first born and we find, from Table I, that the mean maternal age for first-born children (q_1) is 26·071 years.

In order to find the most probable *proportion* of affected to total first-born children, based on the knowledge of this mean maternal age, we use a regression which can be obtained from the distribution of affected and normal (M and N) given in the upright columns on the extreme right in Table I. The most probable deviation at any given maternal age, q, from (M/T) or 224/1031, the mean proportion affected, is given by multiplying $q - \bar{q}$ by b, where

$$b = r_{mq} \cdot \frac{\sigma_m}{\sigma_q}.$$

The correlation r_{mq} is a simple biserial,

$$r_{mq} = \frac{(\bar{q}_{\mathrm{M}} - \bar{q}_{\mathrm{N}}) \cdot m}{q} \quad \text{and} \quad \sigma_m = \sqrt{\mathrm{MN}}/\mathrm{T}.$$

Substituting the values which are already known, we find that $b = 0{\cdot}0226$.

Since $q_1 = 26{\cdot}071$,

$$b\,(q_1 - \bar{q}) = (0{\cdot}0226)\,(26{\cdot}071 - 32{\cdot}638)$$
$$= -\,0{\cdot}1483.$$

From this fraction we obtain the expected numerical deviation in first born affected individuals by multiplying it by the total number of first-born children, 154.

Thus, $$(-\,0{\cdot}1483)\,(154) = -\,22{\cdot}84.$$

The standard error of this expected deviation is

$$\sigma_m \cdot \sqrt{1 - r_{mq}{}^2} \cdot \sqrt{154}, \text{ i.e., } \pm\,4{\cdot}75.$$

Returning now to the figures given when the results of the reconstruction were compared with the observed numbers of mongols in each birth rank, § II, we ascertain the following facts :—

Total first-born children (t_1)......................	154
Observed number affected (f_{M1})	26
Number of first born estimated by reconstruction of the data on the assumption that affected children are distributed at random with respect to birth order (e_{M1})	44·99

Since the families in the data are not uniform in size, the average values, $t_1 \, . \, \mathrm{M/T}$, $t_2 \, . \, \mathrm{M/T}$, etc., do not represent the expected numbers of mongols in each rank if birth order is random. The average $t_1 \, . \, \mathrm{M/T}$ has to be replaced by e_{M1} or 44·99. The deviation due to the effect of maternal age must be added to e_{M1} to obtain the expected number of first-born mongols. We therefore add $-22 \cdot 84$ to 44·99 and the result, 22·15, differs from the observed number, 26, by 3·85. This difference is less than the standard error, 4·75, and is insignificant.

Table III—Results of Analysis by First Method

I	II	III	IV	V	VI	VII	VIII
1	154	26	44·99	−22·84	22·15	+3·85	4·75
2	157	27	43·40	−14·80	28·60	−1·60	4·80
3	139	28	33·09	−5·28	27·81	+0·19	4·52
4	112	23	24·46	−0·46	24·00	−1·00	4·05
5	101	13	18·63	+1·75	20·38	−7·38	3·85
6	87	23	15·15	+4·69	19·84	+3·16	3·57
7	76	20	13·32	+5·59	18·91	+1·09	3·34
8	60	19	9·65	+6·97	16·62	+2·38	2·97
9	43	13	6·47	+5·64	12·11	+0·89	2·51
10	31	9	4·91	+4·34	9·25	−0·25	2·13
11	17	5	2·10	+2·53	4·63	+0·37	1·58
12	16	2	2·45	+2·75	5·20	−3·20	1·53
13	16	6	2·56	+3·52	6·08	−0·08	1·53
14	11	4	1·60	+2·66	4·26	−0·26	1·27
15	6	4	0·76	+1·54	2·30	+1·70	0·94
16	2	0	0·17	+0·49	0·66	−0·66	0·54
17	3	2	0·30	+0·91	1·21	+0·79	0·66
Mean birth rank (or corresponding deviation from mean birth rank)	4·83	5·65	4·10	+1·55	5·65	0·00	0·17

I. Birth rank.
II. Total children in each rank, t_1, t_2, t_3, etc.
III. Observed number of mongols, f_{M1}, etc.
IV. Expected number of mongols, based upon reconstruction, e_{M1}, etc.
V. Expected deviation in number affected, based on mean maternal age, in a given birth rank, $b\,(q_1 - \bar{q})\,t_1$, etc.
VI. Expected number of mongols, $e_{\mathrm{M1}} + b\,(q_1 - \bar{q})\,t_1$, etc.
VII. Difference between observed and expected numbers, $f_{\mathrm{M1}} - e_{\mathrm{M1}} - b\,(q_1 - \bar{q})\,t_1$, etc.
VIII. Standard error of expected numbers, $\sqrt{\mathrm{MN}}/\mathrm{T} \, . \, \sqrt{1 - r_{mq}{}^2} \, . \, \sqrt{t_1}$, etc.

The same calculation and comparison has been made for other birth ranks. The figures are shown in Table III. The fit between observed and expected values in columns III and VI is satisfactory. There is no indication that any birth rank is more frequently occupied by a mongol than would be expected from the mere consideration of the maternal ages at which these children are born. Although the observed number of first-born mongols is slightly in excess of expectation, the excess is not significant. Primogeniture is therefore not likely to be an aetiological factor.

IV

There are certain inaccuracies in the statistical treatment I have so far employed here. It has been assumed that the reconstruction is entirely independent of maternal age. This is, however, not necessarily true, for the smaller families might be concentrated more at the low or high maternal ages. In section III it was tacitly assumed that the regression of incidence of mongolism on maternal age is adequately represented by a straight line: this assumption is inaccurate. Moreover, no allowance has been made for the possible effect of the reconstruction upon the sampling errors given in Table III. To avoid these sources of ambiguity the data have been subjected to analysis by an entirely different method which was suggested by Professor R. A. Fisher.* By use of this new process we are able, after a single complex reconstruction, to compare the observed number of mongols in any given birth rank with the number which is to be expected on the hypothesis that the probability of a mongol child depends upon maternal age (in some manner unknown prior to the data) but not, given age, upon birth rank.

Let us suppose that there are a number of families containing only two children born at the maternal ages of 32 and 42, respectively, and that one child in each family is a mongol. Call p_{32} and p_{42} the probabilities that a mongol is born at these maternal ages. The frequencies of families which have the mongol at age 32 to those which have the mongol at 42 will be in the ratio

$$\frac{p_{32}}{1-p_{32}} : \frac{p_{42}}{1-p_{42}},$$

or, say, $x_{32} : x_{42}$ where x is proportional to $\frac{p}{1-p}$. In any such family the expectation that the child born at 32 is a mongol is $\frac{x_{32}}{x_{32}+x_{42}}$. In general, for families containing only one mongol the expectation that any given child is the affected one is $x/S(x)$ where $S(x)$ is the sum of the values of x for the different maternal ages represented in the family. For families containing more than one mongol the corresponding expressions are more complicated. Given a series of x values, the expectation that each recorded child in the data is a mongol can be calculated. These expectations are then summed up in two ways. In the first place, the assigned values of x will be correct when the

* Only a brief account of the method is given here; a full description is to appear in the 'Annals of Eugenics.'

number of mongols observed at any given maternal age tallies with the sum of the expectations attributed to each child at that maternal age. Secondly, when the correct x values have been ascertained, the sum of the expectations for all the children in any given birth rank can be compared with the number of mongols actually observed in that birth rank.

In order to simplify the arithmetic, maternal ages for each five consecutive years were grouped together. The following x values for these groups were estimated by a method of successive approximation :—

	Maternal age group	x values
A	15 to 19	22
B	20 to 24	10
C	25 to 29	6
D	30 to 34	19
E	35 to 39	88
F	40 to 44	296
G	45 to 49	558

It will be seen that the probability of the birth of a mongol child is lowest between the maternal ages of 25 and 29 and that it rises rapidly after the age of 35. Table IV shows the results of calculating the expectation of mongolism for each child recorded in the data. The x values have been chosen so that the sum of the expectations (in the vertical columns) agrees sufficiently closely

Table IV—Results of Analysis by Second Method

Birth order	A	B	C	D	E	F	G	Calculated total	Observed total
1	2·92	7·33	4·44	2·34	4·94	1·00	1·00	23·97	26
2	0·03	4·23	4·90	6·84	4·45	6·35	—	26·80	27
3	0·03	1·12	1·78	5·84	7·94	12·11	1·94	30·76	28
4	—	0·19	1·48	3·30	11·32	6·00	1·00	23·29	23
5	—	—	0·76	3·05	6·04	6·65	0·54	17·04	13
6	—	—	0·26	2·30	7·99	8·89	2·21	21·65	23
7	—	—	0·18	1·37	8·55	8·06	0·94	19·10	20
8	—	—	0·02	0·80	4·57	9·55	2·43	17·37	19
9	—	—	—	0·63	4·07	4·83	3·25	12·78	13
10	—	—	—	0·09	2·11	5·02	1·90	9·12	9
11	—	—	—	0·02	0·83	3·24	0·42	4·51	5
12	—	—	—	—	0·85	2·55	0·55	3·95	2
13	—	—	—	—	0·37	3·42	1·86	5·65	6
14	—	—	—	—	0·11	1·86	1·57	3·54	4
15	—	—	—	—	—	1·32	0·91	2·23	4
16	—	—	—	—	—	0·61	—	0·61	0
17	—	—	—	—	—	—	1·65	1·65	2
Calculated total	2·98	12·87	13·82	26·58	64·14	81·46	22·17	224·02	—
Observed total	3	13	14	27	64	81	22	—	224

with the total number of mongols observed in each of the maternal age groups. The expectations, added horizontally, give the expected numbers of mongols in each birth rank. The discrepancies between observed and expected values are not great, but there is a slight excess of first-born mongols, as in the results which were obtained by the earlier method of analysis, given in Table III. In calculating the standard error of these differences it was found convenient to group the birth ranks, and the following results were obtained :—

Birth order	Observed number of mongols	Expected number of mongols	Difference	Standard error
1st	26	23·97	+2·03	2·68
2nd or 3rd	55	57·56	−2·56	3·85
4th, 5th, or 6th	59	61·98	−2·98	4·07
7th to 10th	61	58·37	+2·63	3·41
11th to 17th	23	22·14	+0·86	1·84
Total	224	224·02	—	—

The agreement between the theoretical number of mongols and the observed number is satisfactory, and the excess of first born affected children is not significant.

V

If we accept that order of birth is not a significant aetiological factor in mongolism, it becomes very doubtful whether the length of the interval preceding the birth can be considered to be of aetiological significance either. If order of birth is not causal, it makes no difference whether a mother aged 40, bearing an affected child, has previously had only one child, born 20 years earlier, or whether the gap has been filled by 10 pregnancies. The present data, however, give opportunities for testing directly the hypothesis that the interval preceding the birth of a mongolian imbecile is unduly long.

If we take only those cases which are last born and which immediately succeed a normal child in the sibship, we shall find that the interval between these two, ultimate and penultimate, births is very long in comparison with intervals between two normal children in the sibships. This is to be expected if maternal age is the significant aetiological factor, for, during an interval between births, the maternal age increases but the birth rank does not rise correspondingly. The longer the interval, therefore, the more likely will it be that an offspring is affected. If, however, instead of taking affected children who are born last, we select those who both succeed immediately and are immediately followed by a normal child, a comparison may be made of the intervals before and after the birth of affected offspring. Sibships 8, 20, 21, 30, 33, etc., contain cases fulfilling this condition. There are in all 37 instances of this in 36 sibships. The mean intervals between consecutive births are shown below.

Mean interval between normal and mongol immediately following, $2\cdot78 \pm 1\cdot33$ years.

Mean interval between mongol and normal immediately following, $2\cdot95 \pm 1\cdot82$ years.

The difference between the two means is $0\cdot17$ years with a standard error $\pm 0\cdot37$.

The observed difference is not significant, but it actually shows the interval succeeding the mongolian imbecile to be *greater* than that preceding it. This is probably due to the fact that, normally, as maternal age increases, intervals in the sibship tend slightly to lengthen. The large interval or period of diminished fecundity found in certain instances preceding the birth of a mongolian imbecile is, according to this analysis, unlikely to be of causal significance.

VI

In this paper data from the investigation of the family histories of 224 mongolian imbeciles are presented. Statistical analysis, by two entirely different methods, shows that the numbers of imbeciles in each birth rank are very close to those which are to be expected on the assumption that the incidence of mongolism depends upon maternal age and not upon birth order. This conclusion applies also to the number of first-born children found to be affected. Aetiological significance can therefore not be attributed to birth order with any reasonable degree of probability. Neither is there any evidence that the long interval which sometimes precedes the birth of an affected child is of causal significance.

These findings are comparable with Wright's observations concerning the relative effects of birth order and maternal age in the production of certain characteristics in the guinea pig (Wright, 1926); here, too, birth order was found to be of no significance.

I wish to thank all those who have taken part in preparing the material presented in this paper and particularly my assistants, Miss D. E. Newlyn, Dr. M. Gunther, and Mr. R. A. Green. I am indebted to the Medical Research Council and the Darwin Trust for financial assistance.

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APPENDIX

Data giving Birth Ranks and Maternal Ages at Births of 1031 *Individuals in* 217 *Sibships*

The serial numbers of the sibships and sexes of the affected individuals are given in the first two vertical columns.

The maternal ages at the births of the sibs are given at the top of the page.

Affected individuals (M) given in bold type.

Normal individuals (N) given in ordinary type.

Maternal Age.

Serial number	Sex	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42	43	44	45	46	47	48
1	f											4		5		6		7		8		10		11	12		13		**14**				
2	m					**1**		2				3		4																			
3	m			**1**		2			3																								
4	m																					**7**											
5	m					1		**2**																									
6	m, f								2		4			6							8		**9**			**10**							
7	m					1	2		3		4		5			6			7		8		9				**11**						
8	m															1	2		3		**4**		5		6								
9	m																4		5											**7**			
10	m					1							2														**3**						
11	f															**1**	2						3										
12	f							1	2		3			5		6			8			9					12					**13**	
13	f																2		**3**														
14	m														2				**3**														
15	f										2											**3**											
16	f																				1		2		3			**4**					
17	m							1		2		3			4			5		6			**7**							9			
18	f			1			3					4			5	6		7		8				9			**10**						
19	m	1	2	3	4							5									10	11		12			**13**						
20	m, f									1	2	3				4		**5**		6			**7**										
21	f									1		**2**		3													5						
22	m								1					2		3				4		5						**6**					
23	m																			**1**													
24	m																1		**2**	3		4								**6**			
25	f																								**1**								
26	f							1		2				3					5				**6**										
27	f								1		2		3					5		6												**8**	
28	f												1		2				4						7			**8**					
29	m											1		2		3								**5**						6			
30	m									1						2								**3**		4			5				

31	f					2		3					5			6				7									**8**						
32	m																									**1**									
33	f				1			2			3			4		5												7		**8**				9	
34	m																									1				**2**					
35	m										1			3			5					6			**7**					9					
36	m																														**2**				
37	f																																		**4**
38	f										1								**2**																
39	m													1								2				**4**									
40	m																1						**2**												
41	f															1			2											**3**						
42	m						3										5									7				8					**10**
43	f							1		2	3			4			**6**	7		8				9											
44	m						**1**	2		3		4		5						6															
45	m							1			2			3			4		5			6			**7**										
46	m			1							4	5		6					7									**8**							
47	m																			1					2					**4**					
48	m	1				2		3			5		6			7		8	9			10						12		**13**		14			15
49	m												1					2					3			4						**5**			
50	m													1				2							**4**										
51	m									1		2		3		4						**5**	6												
52	m																					1			2						4				**5**
53	m																		1				**2**						3						
54	f							1					**2**																						
55	f				**1**			2			3																								
56	f																		3	**4**					5			7							
57	f					2		3			4	5		6			7		8			9							**11**					12	
58	f									1	2							3												**4**					
59	m						1			2			3				5	**6**				7		8											
60	m			1			2			3	4							5	6			**7**			8	9			10						
61	m																		1			**2**				3									
62	f	1				**2**					3																								
63	f			1	2		3			6		7	8			9				11		12			14					**15**	16				
64	m																	1		2		4		5				**6**							
65	m					1	**2**							4																					

Maternal Age—(*continued*)

Serial number	Sex	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42	43	44	45	46	47	48
66	m																				**1**					2							
67	f												1		2					3				5		**7**				8			
68	f														1		2									**4**							
69	f									1		2			3								4					**5**					
70	f										**1**	2				3		4															
71	f				1		2						4				5		7			**8**				10							
72	f		1						3									4		5			6		**7**								
73	m					**1**		2			3													**4**									
74	f											1											2		**3**								
75	m														3		4		5		6		**7**			8							
76	m												1		2			3				4						**6**					
77	m							1	2			3			4		5		6			7		8		**9**							
78	m																	6		7		8	9			**10**							
79	f												2			3		4	5					**6**					7				
80	f								1				2		3	4		5					**6**										
81	f																										**2**						
82	m																							12		**13**							
83	m							1		2		**4**		5				6															
84	m																		**3**		5		6		7								
85	m			**1**			2		3		4	5																					
86	m										1					2				3		**4**		5									
87	f											**2**																					
88	f			1		2	3		4			5			6		7			9			**10**		11								
89	f																	1	**2**						3								
90	f													2		3				**4**													
91	f							2	3		5				7	8				10	11		12		**14**			15			17		
92	m														1			**2**															
93	f													**1**																			
94	f					1										2					4			5					**6**				
95	m																												**8**				

96	m								1		2			3		4		5			6		7							8			**9**	
97	m							1		2		4				5				6	7	**8**										9		
98	m					2																				**4**								
99	m							1		2		3			4	5	6							**7**										
100	m					**1**					5				6			7				8				9		10						
101	m															1		2				3	4							**5**				
102	m					1					3			4			5																	
103	m	1			3						5			7		8				{6 **6**						**9**								
104	m															**1**	2									3								
105	m					1			2											3		4		5									**6**	
106	m															2												**3**						
107	m			1		2			3		5			6		7		**9**			10		11					13						
108	f					1			2	3		4				6				7	8			**9**				11				13		
109	m							1	2												4							**5**						
110	m																										**12**		13			14		
111	m				1			2																		**7**								
112	f				3	4					6					7				**8**			10			11								
113	m									1		2															**3**							
114	f																						**1**											
115	m													1			**2**						3											
116	m										**1**					3						4												
117	f									1					2			**3**																
118	m		2		3										5					7							**11**							
119	f		**1**			2																												
120	m	1	2						**3**			4			5		6			7		8												
121	m																	1				2		**3**										
122	m																												**9**					10
123	m											1				2		3		4						**6**								
124	f													2			3				**4**													
125	m				2					4				5			7	8				10					**12**						13	
126	m		1		2	3			4	5						6	7			8	9			**10**										
127	f																1	2		**3**				4										
128	m								2					3			4			5		6					**7**						8	
129	m			1					3					5				8				**9**		10										
130	m														2		**3**																	

Maternal Age—(*continued*)

Serial number	Sex	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42	43	44	45	46	47	48
131	m															1			**2**							3							
132	f													2		3			5									**8**					
133	m														2			3			5			6		7		8				**9**	
134	m									2				4		5										**10**							
135	f																						7	8		9		10		**11**			
136	m															5		6		7		**8**	9			10							
137	f							1					2		3			4		5	6		7		**8**								
138	f					I				2		3			4						5			6			**7**						
139	m, m														1		2		3			**4**			5		**6**		7				
140	f							I				2			3									4					**5**				
141	m											**1**	2																				
142	f				**1**					2																							
143	m									1												2					**3**						
144	m, m										3							6		7	8				{9 **9**					**10**			
145	f						**1**	2	3	4		5		6		7		8															
146	m										**1**	2																					
147	m				2				3	4		5										**6**											
148	m							2		3		4			6		7			**8**	9												
149	m																					5			**6**		7						
150	m																2			3					4				**6**				
151	f		I		2		3		4		5				7	8		9			10		11						16			**17**	
152	m																									4		**5**					
153	f						1				2			3					**4**														
154	f										1			3				4			6			7					**8**				
155	m									1		2							4						**5**								
156	f						4			6			7	8		9		10					13							**17**			
157	m																				**11**		12	13		14							
158	m									3			6		7					8		10				12		**15**					
159	f														**3**			4					5										
160	f									1	2		3		4				5	**6**				7									

161	m															1														**2**					
162	f													1									**2**												
163	m																		1							**2**			3						
164	f																					5		6		**7**									
165	m																	1				3	5		6					**8**					
166	m							1			2							5							**7**					8					
167	m							1		2										**3**															
168	f																											2		**4**					
169	m																					4		**5**				6							
170	f										1			**2**																					
171	f															1		**2**				3													
172	m												1			2		**3**																	
173	m							1			2		3					4				5										**6**			
174	m			1	2												6			7									**8**		9				
175	m											**2**		3								4													
176	m			1									4			5		6		7			**8**												
177	f, f						**1**	2									**4**			5															
178	m			1		2		3			4						6					9													
179	m									I			2			3			4			**5**													
180	m							1		2		3		4			5		6				8	9						12		13			**14**
181	m											2				3						5						**7**			8				
182	m	1			3		4			5			**6**					7		8															
183	f										1		2			3		4		5			6		7				8			{9, **9**			
184	m																													**3**					
185	m			2				4				5		6								8			10				11			**13**			14
186	m																		3						**4**										
187	m						1			2		3		4				6		8			9			**10**			12						
188	m																					1		**3**		4					6				
189	m												1			2		3					4		5				7					**9**	
190	m											4						5				**6**													
191	m						1					**3**	4					5				7													
192	f																								**1**										
193	f												I	2									3	**4**											
194	m				2							5		**7**				9		10			11			12		**13**							
195	m									1								**2**																	

Maternal Age—(*continued*)

Serial number	Sex	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42	43	44	45	46	47	48
196	m						1			3			7				**9**																
197	m					1		2	3		4		5		6							**7**											
198	m, f															**3**			4				5						**6**				
199	f								1	2							4	5							**7**								
200	f																					1			2			**3**					
201	m														1		2		3			**4**											
202	f												1						2								**3**						
203	m						**1**																										
204	m													1								**3**											
205	f												1			3	4				5				6							**8**	
206	m			**1**																													
207	f																													**1**			
208	f															1				4		6	7				**8**						
209	f																		1						**2**								
210	m									1		2									3			**4**									
211	m														9	10						13						14				**15**	
212	f												1		**2**	3																	
213	m											4			5		6			**7**													
214	m																		2		3						**6**						
215	m				1		2			3										8		9		10		11		12			13		**14**
216	f															5	6	7			10						14	**15**					
217	m, m																		2												{**3** **3**		
		1	3	6	14	17	16	26	42	39	41	40	38	41	51	42	48	45	42	49	34	28	32	27	21	18	12	11	8	8	6	1	—
		—	—	**3**	**1**	**3**	**4**	**4**	**1**	—	**3**	**6**	**3**	**2**	**2**	**4**	**6**	**6**	**9**	**13**	**8**	**15**	**14**	**14**	**18**	**16**	**23**	**12**	**12**	**7**	**8**	**6**	**1**