

## THE RELATIVE EFFECTS OF PATERNAL AND MATERNAL AGE IN MONGOLISM.

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It has long been known that mongolian imbeciles are frequently born to elderly parents, and practically every observer, who has recorded any large number of cases, has come to the conclusion that either the age of the parents at the birth of the child or ultimogeniture is an aetiological factor<sup>1</sup>. The present communication is not concerned with the problem of how far order of birth may be an accessory causative factor, but is confined to consideration of the relative effects of paternal and maternal age.

In the human species ages of the parents are so closely correlated that it is difficult to separate the effects of the two elements. Hitherto attempts to do so, in mongolism, have only demonstrated that the maternal age is of more aetiological importance than the paternal age. For example, a serious attempt to solve the problem was made in 1927 by Van der Scheer<sup>2</sup>, who compared the relative percentages of 316 mongolian imbeciles born at various maternal ages with the percentages of normal children born to mothers of equivalent ages in a very large series of families gathered from the general population. The resulting ratios showed a very marked increase in the incidence of these defectives as the age of the mother increased, and also a similar, though not quite so marked, rise of the incidence with increasing paternal age.

In studying the effects of parental age on certain characteristics in inbred stocks of guinea-pigs, Wright<sup>3</sup> was able to demonstrate that the age of the dam was an essential factor in the production of white coat colour and also of polydactyly. He found, for example, the correlation of age of dam and proportion of white in the offspring to be  $+0.190 \pm 0.015$ . The correlation of age of dam and proportion of polydactylous

<sup>1</sup> Thurstone, L. L. and Jenkins, R. L.: *Order of Birth, Parent-Age and Intelligence*, pp. 73-5 and 110-13, Univ. of Chicago Press, 1931.

<sup>2</sup> Van der Scheer, W. M.: "Beiträge zur Kenntnis der Mongoloïden Missbildung," *Abhand. a. d. Neur., Psychiat. und Psychol.* Heft 41. Berlin: S. Karger, 1927.

<sup>3</sup> Wright, S.: "Effect of age of parents upon characteristics of the Guinea-pig," *Amer. Naturalist*, 60 (1926), pp. 552-9.

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offspring was  $-0.370 \pm 0.018$ . In the case of white coat colour, the ages of the dam and sire were identical, and so no conclusion as to their relative effects could be reached. But in respect of polydactyly, which, it is to be noted, was most frequent when the dam was young, the use of the technique of partial correlation enabled him to show that the effect of the age of the sire was negligible, after eliminating the effect of the age of the dam.

The present writer has attempted a similar treatment of 150 families of the human species containing mongolian imbeciles among the children. Every family included was visited personally and, among other things, the ages of the parents at the birth of each child was carefully recorded: miscarriages and all individuals in whom a diagnosis of normality or mongolism could not be made with certainty were excluded. No obvious disparity was observed between the ages of the parental pairs, which were distributed in a manner resembling that found by pooling all married couples in the general population, thus:

	150 families	Census (1911)	Census (1921)
	%	%	%
Husband older	94 62.8	62.9	63.5
Husband and wife, same integral age	26 16.7	13.1	12.5
Wife older	31 20.7	24.0	24.0

The following results were obtained from the data summarised in Table I:

- (i) Correlation between maternal age and incidence of mongolism  
=  $+0.362 \pm 0.032$ .
- (ii) Correlation between paternal age and incidence of mongolism  
=  $+0.294 \pm 0.034$ .
- (iii) Correlation between paternal age and maternal age  
=  $+0.829 \pm 0.012$ .

The partial correlation between maternal age and mongolism, found by eliminating paternal age, is  $+0.221$ , and that between paternal age and mongolism, found by eliminating maternal age, is  $-0.011$ . Since the families contain 727 children, the standard deviation of these partial coefficients is less than 0.04. The result suggests that the age of the father is insignificant as an aetiological factor. But the partial correlation technique involved is open to certain objections, partly on account of the hypothetical nature of the variable mongol-normal. It is not, however, necessary to use this technique to demonstrate the various points, and the following method is at once clearer and more precise.

TABLE I.  
Summary of data.

150 Families

Paternal age (p)	Maternal age (r)																				Normal (N)	Mongol (M)									
	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36											
17	1																					1									
18	1	1																					2								
19	1	1	2																				6								
20		1	1	1																			8								
21		2	2	2	1																		10								
22		1	1	3	3	4																	27								
23			1	1	5	6	2																24								
24				1	1	4	4	1															28								
25					2	2	2	2	1														25								
26					1	1	3	3	3	4													31								
27						1	1	2	2	4													28								
28							1	1	1	1	2												39								
29								1	1	1	1												26								
30									1	1	1	1											30								
31										1	1	1	1										33								
32											1	1	1	1	1								27								
33												1	1	1	1	1							32								
34													1	1	1	1	1						21								
35														1	1	1	1	1					26								
36															1	1	1	1	1				33								
37																1	1	1	1	1			17								
38																	1	1	1	1	1		10								
39																		1	1	1	1	1	9								
40																			1	1	1	1	11								
41																				1	1	1	11								
42																					1	1	15								
43																						1	13								
44																							4								
45																							7								
46																							6								
47																							4								
48																							4								
49																							1								
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57																							1								
58																							1								
59																							2								
(N)	1	2	5	8	13	11	22	31	25	31	22	30	36	32	35	27	35	21	21	22	31	16	10	9	6	5	8	4	8		
(M)																															154

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Having already calculated the correlation coefficient (iii) from Table I, the following two regression equations are easily obtained:

(iv) Regression of father's age ( $p$ ) on mother's age ( $q$ ) (based on 727 products):

$$P = (0.944)q + 4.304. \text{ (Standard deviation of } P = 4.315^1.)$$

(v) Regression of mother's age on father's:

$$Q = (0.726)p + 7.120. \text{ (Standard deviation of } Q = 3.787^2.)$$

The following mean ages of fathers and mothers were also obtained from the pooled families:

Mean age in years of mother at birth of

$$154 \text{ mongols } (qM) = 37.253 \pm 6.553$$

$$573 \text{ normals } (qN) = 31.249 \pm 6.242$$

Mean age in years of father at birth of

$$154 \text{ mongols } (pM) = 39.383 \pm 7.786$$

$$573 \text{ normals } (pN) = 33.830 \pm 7.253$$

It will be seen in the first place that the difference between the mean ages of the mother at the births of mongols and normals respectively is 6.004 years and the standard error of this difference equals

$$\sqrt{\frac{(6.553)^2}{154} + \frac{(6.242)^2}{573}} \text{ or } 0.589.$$

It is obvious that maternal age is of significance because the difference is ten times the standard error.

From the regression equation (iv) we find that the most likely paternal age at the birth of mongols (given the maternal age as fixed) is 39.471, *i.e.*  $0.944qM + 4.304$ . Similarly, the most likely paternal age of normals (given the maternal age as fixed) is  $0.944qN + 4.304$  which is 33.803. The expected difference between the father's average for mongols and for normals is, therefore, 5.667 years and the actually observed value ( $pM - pN$ ) is 5.553 years. The standard error of the expected mean value of the father's age for mongols will be  $4.315/\sqrt{154}$  or 0.348, and the corresponding error for normals will be  $4.315/\sqrt{573}$  or 0.180. The standard error of the difference between these two expected mean paternal ages is, therefore,  $\sqrt{(0.348)^2 + (0.180)^2}$  or 0.392 year. The difference between the expected 5.667 years and the observed 5.553 years is 0.115 year, which

$$^1 \sigma_p = \sigma_p \sqrt{1 - r_{pq}^2} = 7.711 \sqrt{1 - (0.829)^2} = 4.315.$$

$$^2 \sigma_q = 6.769 \sqrt{1 - r_{pq}^2} = 3.787.$$

is less than half the standard error and therefore quite insignificant, since it is very likely to be due to random sampling.

By using the regression equation (v) in a similar way—this time keeping paternal age constant—we find that the expected difference between average maternal age for mongols and for normals, respectively, is 4.032 years (see Table II). The observed difference (which has already

TABLE II.

*Summary of numerical results.*

Mean age	Observed value (a)	Expected value (b)	Difference (a - b)
$pM$	39.333	$39.471 \pm 0.348$	-0.088
$pN$	33.830	$33.803 \pm 0.180$	+0.027
$pM - pN$	5.553	$5.668 \pm 0.392$	-0.115
$qM$	37.253	$35.712 \pm 0.305$	+1.541
$qN$	31.249	$31.680 \pm 0.158$	-0.431
$qM - qN$	6.004	$4.032 \pm 0.341$	+1.972

been discussed) is 6.004 years. The difference between observed and expected mean values is 1.972 years, with a standard error, worked out again in the same way as above, of 0.341 year. The difference is nearly six times the standard error and therefore the odds are enormously against its being due to sampling.

There can be little doubt, judging from these results, which confirm those obtained by the partial correlation technique, that the father's age is an insignificant factor in the aetiology of mongolism, the emphasis being entirely on the age of the mother. This conclusion helps to justify the method of analysis of sibships containing mongolian imbeciles applied by the present writer in a previous article<sup>1</sup>.

Though the material on which this argument is based may appear at first sight to be small in quantity, I believe it to be very accurate. In human genetics it is extremely difficult for one person to investigate a sufficient number of families to give significance to such results in a reasonable time. I have been fortunate in having had the assistance of Miss D. E. Newlyn and Dr M. Gunther, who collected a great part of the material. I also wish to thank Dr G. F. Cobb for his kind assistance in supplying several family histories, and the Essex and Suffolk Voluntary Associations for Mental Welfare and also the London County Council for supplying us with accessory information. I am also much indebted to Miss H. L. Brown and Miss J. Bedwell for their help in analysing the

<sup>1</sup> "On the interaction of heredity and environment," *J. Genetics*, 25, No. 3, 407-22, April, 1932.

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data. I have also to thank the Medical Research Council and the Darwin Trust for financial assistance.

In this paper 150 sibships, containing each at least one mongolian imbecile, have been analysed with respect to the relative aetiological importance of paternal age and maternal age. The results indicate that paternal age is not a significant factor, while maternal age is to be regarded as very important.