ABO BLOOD GROUPS AND HUMAN FERTILITY

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The fact that those who lack the blood group antigen A have anti-A antibody, and those who lack B have anti-B (Landsteiner, 1900, 1901), leads in a number of cases to an incompatibility between maternal serum and foetal antigens inherited from the father. Such serologically incompatible pregnancies have been thought to be a possible cause of various morbid conditions in foetus or mother (*e.g.*, Gruhzit, 1923, 1924), although Tovey (1945) considers that placental resistance to the passage of agglutinin, and the presence of ABO substance in foetal plasma, together with the low sensitivity of foetal red cells, may greatly lessen the effect on the foetus.

Hirszfeld and Zborowski (1925, 1926) found that, in the mating class Father A × Mother O, there were relatively fewer A offspring than in the reciprocal class Father O × Mother A, and also that there were relatively fewer O children from Mother A × Father O than from Mother O × Father A. Later results of Hirszfeld (1928) agreed with this, but Koller (1931) showed that the findings were not significant. An exhaustive review of the literature by Hirszfeld (1934) reversed his previous conclusions, and his further work (1938) did not confirm them. Levine (1943) assembled data apparently in support not of Hirszfeld's theory of constitutional incompatibility between a mother and a foetus of different groups but of Gruhzit's theory of serological incompatibility.

Waterhouse and Hogben (1947) analysed twelve carefully chosen family studies made between 1927 and 1944 primarily to decide between the modes of inheritance of the ABO blood groups proposed by von Dungern and Hirszfeld (1910) and Bernstein (1924, 1925). Selecting the largest reciprocal mating class—namely Father A × Mother O and Father O × Mother A—in the pooled material from these studies, they found:

(*i*) a significant shortage of families of the class Father A × Mother O as compared with its reciprocal;

(*ii*) a highly significant shortage of group A children from the class Father A × Mother O:

(*iii*) a sharp fall with increasing birth rank in the ratio of A to O children in the mating class Father A × Mother O.

They reckoned the loss at 25 per cent. of the group A children expected from the mating class Father A × Mother O, and suggested that the loss was due to early abortion.

As a result of the findings of Allan (1952a, b) of a significant excess of group B women in samples of cases of both abortion and sterility, Waterhouse and Hogben's collected material has here been analysed in terms of relative fertility by mating class. In this context the term *fertility* has been used synonymously with mean number of children per family, to avoid inconvenient periphrasis. No confusion with any more precise definition of the term is intended.

RESULTS

Hirszfeld and Zborowski (1925) coined the term "homospecific" for a pregnancy in which the mother and foetus are of the same ABO group, and "heterospecific" for one in which their ABO groups differ. In this paper the term "heterospecific" is used instead for a pregnancy in which the red cells of the foetus are not only of a different ABO group from those of the mother but would also be agglutinated by the mother's serum *in vitro*. (The term "incompatible", unqualified, begs the question when applied to reproduction.) Similarly, a mating is here called heterospecific in which the wife has specific antibodies to one or both of the antigens possessed by her husband (*i.e.*, an incompatibility between the husband as donor and the wife as recipient). It will be seen that no class of homospecific mating can have heterospecific offspring (in Levine's sense), but that (most A and B individuals being heterozygous, *i.e. AO* or *BO*) all classes of heterospecific

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mating except AB × O can have homospecific offspring. The father's group is put first, and the fathers in (for example) the mating classes B × B and B × AB are collectively termed "homospecific B fathers", while the fathers in the mating classes B × A and B × O are collectively termed "heterospecific B fathers".

The expected numbers of children in the sixteen mating classes in the Waterhouse-Hogben sample have been calculated by multiplying the expected number of families in each of the classes by 3·34, this being the overall average number of children per family in the 1,239 families in the sample. A homospecific mating is found in 793 of the families, these having an average of 3·34 children, while a heterospecific mating is found in 446 of the families, these having an average of 3·33 children. In 440 of the 793 homospecific families the father and mother are of the same group, and have an average of 3·33 children per family. The average number of children in the 840 families, homospecific and heterospecific, in which one or both parents are O is 3·37; in the 273 families with one or both parents B it is 3·34; in the 812 families with one or both parents A it is 3·33; and in the 113 families with one or both parents AB it is 3·29. Table I gives the nine homospecific mating classes in descending order of average numbers of children per family, and shows that, of the five classes of heterospecific mating with a homospecific reciprocal, three are more fertile than the reciprocal. When, however, the heterospecific mating classes are studied alone, the no less interesting fact appears that the A mothers are at the upper end of the table, the B mothers at the lower end, and the O mothers in the middle; and one is thereby led to consider the rest of the sample from this unexpected point of view.

TABLE I

ORDER OF FERTILITY OF ABO MATING CLASSES

No. Observed		Homospecific Mating Classes (Father first)	Average No. of Children per Family		Heterospecific Mating Classes (Father first)	No. Observed	
Families	Children					Children	Families
8	30	B × AB	3·75	—	—	—	—
17	62	B × B	3·65	4·00	AB × A	80	20
225	779	O × O	3·46	3·56	B × A	210	59
28	96	A × AB	3·43	3·47	B × O	229	66
244	835	O × A	3·42	3·28	A × O	686	209
189	599	A × A	3·17	3·13	AB × O	72	23
54	171	O × B	3·17	3·11	A × B	196	63
19	56	O × AB	2·95	2·33	AB × B	14	6
9	24	AB × AB	2·67	—	—	—	—

For this purpose, it is helpful to combine those mating classes in which the father or the mother is of any one group and specificity—*e.g.* B × B and B × AB—and when this is done the descending order of fertility of homospecific fathers is found to be B-O-A. The picture grows still clearer when the A and B parents of both specificities are taken alone, as in Table II.

TABLE II

ORDER OF FERTILITY OF A AND B PARENTS

Homospecific Parents			Heterospecific Parents	
Ratio of No. of Families Observed to No. Expected	Group of Parent	Average No. of Children per Family	Group of Parent	Ratio of No. of Families Observed to No. Expected
1·04	B Father	3·68 3·67	A Mother	0·95
1·04	A Mother	3·31 3·51	B Father	1·04
0·90	B Mother	3·28 3·24	A Father	1·00
0·95	A Father	3·20 3·04	B Mother	1·05

If now the B parents of both sexes and both specificities are placed in descending order of fertility, as in Table III, and the A parents are placed alongside, the second pattern of reciprocity stems only partly from the first.

TABLE III

ORDER OF FERTILITY OF A AND B PARENTS

Group B Parents				Group A Parents		
Children			Specificity of Parent	Children		
Ratio of No. Observed to No. Expected	Range from Observed to Expected	Average No. per Family		Average No. per Family	Range from Observed to Expected	Ratio of No. Observed to No. Expected
1·15	+12	3·68	Homospecific Father	3·20	−66	0·91
1·09	+37	3·51	Heterospecific Father	3·24	−29	0·97
0·89	−30	3·28	Homospecific Mother	3·31	+39	1·03
0·96	−9	3·04	Heterospecific Mother	3·67	+13	1·05

On the other hand, when the AB and O parents of both sexes and both specificities are placed in descending order of fertility, as in Table IV (overleaf), and the O parents are placed alongside, the outcome is parallelism. When the homospecific O and AB parents are placed in descending order, as in Table V (overleaf), alongside the heterospecific O and AB parents, the result is again reciprocity.

TABLE IV

ORDER OF FERTILITY OF AB AND O PARENTS

Group AB Parents				Group O Parents		
Children					Children	
Ratio of No. Observed to No. Expected	Range from Observed to Expected	Average No. per Family	Specificity of Parent	Average No. per Family	Range from Observed to Expected	Ratio of No. Observed to No. Expected
0·86	−27	3·39	Heterospecific Father	—	—	—
1·00	+1	3·22	Homospecific Mother	3·46	+10	1·01
1·93	+12	2·67	Homospecific Father	3·40	+63	1·04
—	—	—	Heterospecific Mother	3·31	−23	0·98

TABLE V

ORDER OF FERTILITY OF AB AND O PARENTS

Homospecific Parents			Heterospecific Parents		
Ratio of No. of Families Observed to No. Expected	Group of Parent	Average No. of Children per Family		Group of Parent	Ratio of No. of Families Observed to No. Expected
0·98	O Mother	3·46	—	—	—
1·02	O Father	3·40	3·39	AB Father	0·85
1·04	AB Mother	3·22	3·31	O Mother	0·99
2·42	AB Father	2·67	—	—	—

These findings strongly suggest that, judging by the Waterhouse-Hogben sample, heterospecificity does not, of itself, lower fertility, and one or two further points may reinforce the argument. For example, 84 per cent. of the AB fathers in the sample, 83 per cent. of the B fathers, 56 per cent. of the A fathers, and none of the O fathers, are heterospecific, and—presuming A and B offspring to be equally, or almost equally, sensitive—this would lead one to expect the descending order of fertility of all fathers in the sample to be O-A-B-AB, but in fact it is B-O-AB-A. Similarly, 57 per cent. of the O mothers in the sample, 49 per cent. of the B mothers, 15 per cent. of the A mothers, and none of the AB mothers are heterospecific, and this would lead one to expect the descending order of fertility of mothers in the sample to be AB-A-B-O, whereas in fact it is O-A-AB-B. It is certainly possible that, if heterospecific parents did lose offspring, they would make up the loss by more pregnancies, as do parents who lose (full-term) offspring from Rh-incompatibility (Glass, 1949), or from hereditary acholuric jaundice (Race, 1942); and it is probable that, since all types of heterospecific mating except AB × O can give rise to homospecific offspring, many of these extra offspring would live. But if this did happen the chances would be small that heterospecific matings would have, as in the present sample, so nearly the same overall average number of children per family as homospecific parents; and there would still remain the question why heterospecific A fathers and B mothers were unable to make up the loss while heterospecific B fathers and A mothers more than made it up.

If, then, heterospecificity has no effect on fertility, some other reason must be sought for the curious differences of fertility found in the sample. Now Table VI shows that four of the eight mating classes with a higher than average number of children per family have a group B father, and also that all four classes with a B father are more fertile than any of the four classes with an A father—an event which would occur by chance 1 in 70 times (Fisher, 1951). It can also be seen that, in seven of the eight types of parent, some mating classes show an excess, and some a shortage, either of families or of children; whereas all four of the mating classes with a B father show an excess both of families and of children. Thus, to judge by this one sample, the B father, as such, is the most fertile type of parent among Caucasians, and may be provisionally regarded as a norm by whom all other types of parent may be judged, the descending order of fertility of all types of parent being shown in Table VII. The B father is also the type of parent with the

TABLE VI

ORDER OF FERTILITY OF ABO MATING CLASSES

Ratio of No. Observed to No. Expected		Major Mating Classes (Father first)	Average No. of Children per Family		Minor Mating Classes (Father first)	Ratio of No. Observed to No. Expected	
Families	Children					Children	Families
1·01	1·08	B × A	3·56	4·00	AB × A	0·97	0·81
1·06	1·10	B × O	3·47	3·75	B × AB	1·23	1·10
0·98	1·01	O × O	3·46	3·65	B × B	1·11	1·02
1·14	1·17	O × A	3·42	3·43	A × AB	1·17	1·14
0·97	0·96	A × O	3·28	3·13	AB × O	0·84	0·89
0·93	0·88	A × A	3·17	2·95	O × AB	0·65	0·74
0·87	0·82	O × B	3·17	2·67	AB × AB	1·93	2·42
1·08	1·01	A × B	3·11	2·33	AB × B	0·57	0·82

smallest *range* of fertility in the sample—from 3·75 for B × AB to 3·47 for B × O—the ascending order of width of range being B father, A father, O mother, O father, A mother, B mother.

TABLE VII

DESCENDING ORDER OF FERTILITY OF PARENTS
(INCLUDING MATING CLASSES B × B, O × O, A × A,
AND AB × AB)

Families				Children		
No. Ob-served	Range from Ob-served to Ex-pected	Ratio of No. Ob-served to No. Ex-pected	Group of Parent	Ratio of No. Ob-served to No. Ex-pected	Range from Ob-served to Ex-pected	No. Ob-served
150	+6	1·04	B Father	1·10	+49	531
542	+9	1·02	O Father	1·04	+62	1,841
523	−10	0·98	O Mother	0·99	−13	1,766
512	+12	1·02	A Mother	1·03	+52	1,724
58	−3	0·94	AB Father	0·93	−16	190
489	−11	0·98	A Father	0·94	−95	1,577
64	+3	1·04	AB Mother	1·00	+1	206
140	−4	0·97	B Mother	0·92	−39	443

When the eight types of parent are separated according to sex (Table VIII), it is seen that, while the descending order of fathers is B-O-A or B-AB-A, the order of mothers, though A-AB-B, is not A-O-B but O-A-B. Now, in this context, the fact that O mothers are less fertile than B fathers would suggest that the non-reciprocity of mothers with the B-O-A order of fathers is due not to O mothers but to A mothers; and that this is indeed so is clear from Table VI. Here it is seen that all four types of B father are more fertile than three of the four types of B mother, the exception being the mating class B × B, and that all four types of A father are less fertile than three of the four types of A mother, the

TABLE VIII

ORDER OF FERTILITY OF FATHERS AND MOTHERS
(INCLUDING MATING CLASSES B × B, O × O, A × A,
AND AB × AB)

No. Expected		Group of Father	Average No. of Children per Family		Group of Mother	No. Expected	
Fami-lies	Chil-dren					Chil-dren	Fami-lies
144	482	B	3·54	3·38	O	1,779	533
533	1,779	O	3·40	3·37	A	1,672	500
61	205	AB	3·28	3·22	AB	205	61
500	1,672	A	3·22	3·16	B	482	144

exception being the populous class A × A. In other words, it is clear that the classes B × B and A × A, which could (other things being equal) have resembled the mother's side or neither side in respect of fertility, decidedly resemble the father's side, and that this distorts the sample as a whole. This effect can be eliminated—relatively, at least—by leaving these classes out of the sample along with AB × AB and O × O; when this is done there emerges the almost perfect reciprocity of Table IX. Given this order of fertility of fathers, its reciprocal, like its parallel, would occur in mothers by chance once in 24 times.

TABLE IX

ORDER OF FERTILITY OF FATHERS AND MOTHERS
(EXCLUDING MATING CLASSES B × B, O × O, A × A,
AND AB × AB)

No. Expected		Group of Father	Average No. of Children per Family		Group of Mother	No. Expected	
Fami-lies	Child-ren					Child-ren	Fami-lies
128	426	B	3·53	3·48	A	993	297
58	193	AB	3·39	3·31	O	1,010	302
302	1,010	O	3·35	3·31	AB	193	58
297	993	A	3·26	3·10	B	426	128

Moreover, this notable pattern leads, though not of necessity, to the even more striking pattern of Table X, where the descending order of blood groups of the four types of parent of more than average fertility is reversed in the parents of less than average fertility. This type of pattern might be thought to be due to the blood-group incidence,

TABLE X

DESCENDING ORDER OF FERTILITY OF PARENTS
(EXCLUDING MATING CLASSES B × B, O × O, A × A,
AND AB × AB)

Families				Children		
No. Ob-served	Range from Ob-served to Ex-pected	Ratio of No. Ob-served to No. Ex-pected	Group of Parent	Ratio of No. Ob-served to No. Ex-pected	Range from Ob-served to Ex-pected	No. Ob-served
133	+5	1·04	B Father	1·10	+43	469
323	+26	1·09	A Mother	1·13	+132	1,125
49	−9	0·85	AB Father	0·86	−27	166
317	+15	1·05	O Father	1·05	+52	1,062
298	−4	0·99	O Mother	0·98	−23	987
55	−3	0·95	AB Mother	0·94	−11	182
300	+3	1·01	A Father	0·99	−15	978
123	−5	0·96	B Mother	0·89	−45	381

but if that were really the cause, in whole or in part, the smallest samples—those of the AB parents—would be at the ends instead of very near the mean, and would, along with A and B, have a much more even sex distribution. It seems more likely that this pattern, together with that of Table X, gives some provisional support to the theory of Ford (1948) that the ABO blood groups are a system of balanced polymorphism, like sex—all the more so as such a system is believed to be invariably the outcome of a balance of opposed selective agencies, as, e.g., maleness and femaleness. (It has been shown by Fisher (1930) that genes of *neutral* survival value must be rare). But that the ratio of the ABO genes may not, in fact, be stable is suggested by the high fertility of B × B and the low fertility of A × A, especially as the difference between these two classes is even greater in the much larger sample of Hirszfeld (1934), as analysed by Allan (1953).

Another process, however, by which an ABO balance might be maintained can be discerned in Table XI, from which the balance is seen to be largely due to a balance of reciprocal classes of mating. In this connection it is relevant to note that, just as in the mating class A × O the ratio of A/O children falls with rising birth-rank, so in the mating class O × A, if the children above the fifth birth-rank are ignored, rising birth-rank gives a steady fall in the ratio of O/A children. When he saw this in August, 1951, the writer accepted the suggestion put to him six months before by a colleague, Dr. William Hamilton, that the data point to direct genetic action, but this two-fold decline also hints at some environmental factor.

TABLE XI

COLLECTIVE FERTILITY OF COMPARABLE ABO MATING CLASSES

No. Expected		Classes of over Average Fertility (Father first)	Combined Observed Average No. of Children per Family	Classes of under Average Fertility (Father first)	No. Expected	
Families	Children				Children	Families
214·36	715·96	O × A	3·36	A × O	715·96	214·36
24·60	82·16	AB × A		AB × O	86·21	25·81
24·60	82·16	A × AB	3·35	O × AB	86·21	25·81
7·29	24·35	B × AB		AB × B	24·35	7·29
62·11	207·45	B × O	3·33	O × B	207·45	62·11
230·24	769·00	O × O	3·33	A × A	678·85	203·25
·58·27	194·62	B × A	3·33	A × B	194·62	58·27
16·67	55·68	B × B	3·31	AB × AB	12·42	3·72

Hogben (1939) has said:

Several things point to the importance of studying the influence of the uterine environment upon the characteristics of individuals. One is the high incidence of certain conditions amongst first-born children. Another is the high incidence of various malformations among women approaching the end of the child-bearing period.

And Ford (1948), writing of the effect of maternal age upon the penetrance of the genes in the offspring, has said:

It is thought that a number of conditions, some of them in part genetic, are expressed with greater frequency in children as maternal age advances.

DISCUSSION

It has been shown that, in the present sample, all four types of A father are less fertile than all four types of B father. Now, the four types of A father—A × AB, A × B, A × O, and A × A—can have, together, offspring of all four ABO groups, viz.:

(i) B offspring, whose B gene is always inherited from the mother;

(ii) O offspring, with an O gene from the mother and another from the father;

(iii) AB offspring, with a B gene from the mother and an A gene from the father;

(iv) A offspring, all of whom, in the classes A × B and A × O, get their A gene from their father, and a large majority of whom, in the classes A × A and A × AB, get an A gene from their father.

But the only type of offspring common to these four classes are A offspring. Indeed A offspring and A fathers are the only relevant characters shared by these classes, suggesting that one or other or both of these characters must be the cause of their sub-mean fertility. This idea is made the more plausible by Waterhouse and Hogben's demonstration that the loss of offspring in the mating class A × O is a loss of A, not of O, offspring, and by the fact that a large majority of the offspring of the mating class A × A are also A. If, however, high mortality of A offspring, as such, were a basic cause of sub-mean fertility, the mating classes AB × A, B × A, and O × A would also be short of A children; and Waterhouse and Hogben have shown that there is no such shortage—relative, at any rate, to O children—in the mating class O × A, which is the largest, and the least fertile, of the three—no relative shortage, in other words, of A children whose A gene has come from their mother. This would suggest that the basic cause of the sub-mean fertility of A fathers is the fact that they, themselves and not their children or their wives, are A. If this were found to be the truth, it would be interesting to see whether men with two A genes were less fertile than those with one.

In the present sample, also, if the mating class B × B is left out, all three types of B mother are less

fertile than all three types of A mother (and all three types of B father). In the same way then, as with A, and in spite of the fact that the shortage of children in the mating class O × B is, as Waterhouse and Hogben have pointed out, a shortage of B children, one is led to think that the basic cause of the sub-mean fertility of B mothers, other than those with a B husband, is the fact that they themselves, and not their children or their husbands, are B. As with A fathers, it would be interesting to see whether B women with two B genes are less fertile than those with one.

Genetic action by *both* the parents in the mating class A × B might explain why that class is even less fertile than the classes O × B and A × O. On the other hand, the effect on AB offspring might be modified by the union of an A and B gene in these offspring. This would tally with the fact that AB parents are near the middle of the scale, if the class AB × AB is set aside, though it is notable that there is then a shortage of families with AB mothers. It is possible, too, that the parallelism shown in Table IV between O and AB parents, unlike the reciprocity of A and B parents shown in Table III, might be due to the fact that the genotype *AB* is doubly dominant, and *OO* recessive, while in most of the world A and B individuals are mainly heterozygous (*AO* or *BO*), not homozygous (*AA* or *BB*).

That the group O fathers and mothers are in the centre of the scale, at least when O × O is omitted (Table IX) might be expected from the partial reciprocity of the classes A × O and O × A, B × O and O × B, AB × O and O × AB, but the fact that the class O × O has a shortage of families, and a lower average number of children per family than any class with a group B father, hints at selection against the O gene. More support for this hypothesis can be got from classes A × O and O × A, apart from the fact that all the A offspring of these two classes have at least one O gene, and by virtue of the fact that A × O and O × A are only partially reciprocal. Thus if the 114 A × O families in which the father is known to be heterozygous are joined with the 135 families in which the mother is known to be heterozygous, the four kinds of mother-child combination give the following average numbers* of children per family:

(*i*) 2·23 for O ex O;

(*ii*) 2·06 for A ex A;

(*iii*) 2·01 for O ex A;

(*iv*) 1·83 for A ex O.

* The overall average for these 135 O × A families is 4·07, and for the 114 A × O families 4·06.

Of the remaining 95 A × O and 109 O × A families, there is a small number whose children are all of group O, and in these the average number of children is 0·49 for O ex O and 0·44 for O ex A. Thus, in both types of A × O and O × A family, there are fewer O children from A mothers than from O mothers. On the other hand, the average number of O children per family is 1·59 for both the 66 B × O matings and the 54 O × B matings.

If there were, in fact, selection either for or against any of the O, A, and B genes, the first question that would arise concerns the form such selection might take—the stage or stages, from conception onward, in the life-history of the off-spring, at which selection might occur or be most severe. Other questions would concern the influence, if any, that might be exerted by other genes, such as the blood-group genes for Secretion, Lewis, and Rhesus; the possibility of differential selection against the sub-groups of A or the still obscure sub-groups of B; and the possibility that certain ABO mating classes are more prone than others to give rise to twins or triplets. In the meantime, however, whether there is, in fact, selection against the O, A, and B genes, or whether, on the contrary, the pattern of fertility found in this sample is due to chance, is a question which only further investigation can answer. The Waterhouse-Hogben sample was taken from several scattered Caucasian sources, and as the authors pointed out, is not entirely homo-genous. This being so, the ideal source of a large enough sample to test the hypothesis would, at first sight, be a city, but few large cities, even in Britain, have homogeneous populations. Nor would the environs of cities be in very much better case, for the detailed surveys of Northern England by Roberts (1951), and of Wales and the Marches by Mourant and Watkin (1952), have uncovered strikingly different ABO blood-group distributions even in neighbouring valleys and villages.

Firmer evidence could be claimed if populations whose ABO blood-group distribution was very different from the Caucasian showed a pattern of fertility—given samples with roughly the same average family size—which essentially fitted the hypothesis. For example, in populations with a much higher A-gene frequency and a much lower B-gene frequency (*i.e.* in populations with a higher proportion of homozygous A husbands and wives, and a lower proportion of homozygous B husbands and wives) one might find that A, not B, parents were at the extremes; but there are very few such peoples. Indeed the frequency of the A-gene falls fairly steadily, while that of the B-gene rises, from Western Europe to Eastern Asia (Hirszfeld and Hirszfeld,

1919); and thus, as the Waterhouse-Hogben sample is composed of European and White American individuals, one would expect, other things being equal, to find its pattern of fertility maintained, and the range from B father to B mother widening, as one passes from West to East. In this connexion Huxley (1942) says that:

Genetic polymorphism deserves the most intensive study, especially in cases where the ratios of the types are geographically graded, since here we may hope not only to measure the intensity of the selective forces at work, but to discover also something as to their nature.

SUMMARY

(1) In a composite sample of 1,239 families with 4,139 children, Waterhouse and Hogben found a highly significant shortage of group A offspring in the mating class Father A × Mother O as compared with the reciprocal class Father O × Mother A, and an appreciable shortage of group B offspring in the mating class Father O × Mother B as compared with the reciprocal class Father B × Mother O.

(2) The other mating classes in the Waterhouse-Hogben sample yield some evidence against the possibility that the above loss of group A offspring is caused by the action of maternal anti-A haemagglutinin, the average number of children per family being 3·33 for the 446 heterospecific (*i.e.* serologically incompatible) matings in the sample, and 3·34 in the 793 homospecific matings.

(3) On the other hand, the data give grounds for believing that the shortage of A offspring in the mating class Father A × Mother O is part of a shortage of offspring of A fathers generally, the four types of mating with an A father being less fertile than the four types of mating with a B father. They also give grounds for believing that the shortage of group B offspring in the mating class Father O × Mother B is part of a general shortage of offspring of group B mothers, other than of group B mothers with a group B husband. There are also signs of a loss of group O offspring.

(4) The descending order of fertility of parents in the sample (omitting the symmetric mating classes B × B, O × O, A × A and AB × AB) is B-AB-O-A for fathers, and A-O-AB-B for mothers, the overall descending order being B father, A mother, AB father, O father, O mother, AB mother, A father, B mother. It is suggested that this provides evidence in support of Ford's theory that the ABO groups form a system of balanced polymorphism. Against

this theory is the high fertility of B × B and the low fertility of A × A.

(5) It is also suggested that confirmation, modification, or contradiction of the findings would be obtained from a homogeneous population with the same descending order of ABO gene frequency (namely, O-A-B) as that of the diverse Caucasian populations of which the Waterhouse-Hogben data form a sample, or from peoples in whom the descending order is A-O-B or O-B-A.

ADDENDUM

Since this paper went to press it has come to my notice that, in matings with a history of at least two abortions, Sjöstedt and others (1951) found a significant excess of group B wives, other than those with a group B husband. This observation led the authors to remark, "One may have some doubt as to whether the current notion of ABO incompatibility is the right one in the present context".

REFERENCES

Allan, T. M. (1952a). *Lancet*, 1, 102.
—— (1952b). *Ibid.*, 1, 370.
—— (1953). *Ibid*, 1, 650.
Bernstein, F. (1924). *Klin. Wschr.*, 3, 1495.
—— (1925). *S. indukt. Abstamm.-u. VererbLehre*, 37, 237.
Dungern, E. von, and Hirszfeld, L. (1910). *Z. ImmunForsch.*, 6, 284.
Fisher, R. A. (1930). "The Genetical Theory of Natural Selection". Clarendon Press, Oxford.
—— (1951). "The Design of Experiments", 6th ed. Oliver and Boyd, Edinburgh.
Ford, E. B. (1948). "Genetics for Medical Students", 3rd ed. Methuen, London.
Glass, B. (1949). *Amer. J. Obstet. Gynec.*, 57, 323.
Gruhzit, O. M. (1923). *Ibid.*, 5, 400.
—— (1924). *Ibid.*, 7, 588.
Hirszfeld, L. (1928). "Konstitutionsserologie und Blutgruppenforschung". Springer, Berlin.
—— (1934). *Ergebn. Hyg. Bakt.*, 15, 54.
—— (1938). "Les groupes sanguins". Masson, Paris.
—— and Hirszfeld, H. (1919). *Lancet*, 2, 675.
—— and Zborowski, H. (1925). *Klin. Wschr.*, 4, 1152.
—— —— (1926). *Ibid.*, 5, 741.
Hogben, L. (1939). "Nature and Nurture", 2nd ed. Allen and Unwin, London.
Huxley, J. S. (1942). "Evolution. The Modern Synthesis". Allen and Unwin, London.
Koller, S. (1931). *Z. Rassenphysiol.*, 3, 121.
Landsteiner, K. (1900). *Zbl. Bakt.*, 27, 357.
—— (1901). *Wien klin. Wschr.*, 14, 1132.
Levine, P. (1943). *J. Hered.*, 34, 71.
Mourant, A. E., and Watkin, I. Morgan. (1952). *Heredity*, 6, 13.
Race, R. R. (1942). *Ann. Eugen., Lond.*, 11, 365.
Roberts, J. A. Fraser (1951). *Man*, 51, 94.
Sjöstedt, S., Grubb, R., and Linell, F. (1951). *Acta path. microbiol. scand.*, 28, 375.
Tovey, G. H. (1945). *J. Path. Bact.*, 57, 295.
Waterhouse, J. A. H., and Hogben, L. (1947). *British Journal of Social Medicine*, 1, 1.