

foetal infection, will not by itself prevent completely the occurrence of congenital syphilis. Other factors which will lead to the achievement of this goal will be discussed in a further communication.

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BLOOD GROUPS IN DIABETES MELLITUS

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The finding by Aird, Bentall, and Roberts (1953) of an association between carcinoma of the stomach and blood group A and by Aird, Bentall, Mehigan, and Roberts (1954) between peptic ulcer and blood group O has made it desirable to search for similar associations in other diseases. We describe here the results of independent surveys in Liverpool and in Oxford of the ABO blood group distribution among 1,333 patients suffering from diabetes mellitus and compare them with control series.

Source of Material.—The Liverpool series was drawn from patients attending the diabetic clinic of the David Lewis Northern Hospital during a five-months period and comprises 833 cases. The Oxford series consists of 500 cases chosen at random from the patients attending the diabetic clinic at the Radcliffe Infirmary. The diagnosis of diabetes had been confirmed in all patients by high fasting-blood-sugar levels or by abnormal glucose-tolerance curves. The Rhesus and MN groupings of the Oxford patients were also determined.

Control Samples and the Subdivision of the Liverpool Area

The most suitable control samples available are those for the general population, based on consecutive registration of blood donors by the National Blood Transfusion Service. The figures used are shown in Table I. They were provided by the Nuffield Blood Group Centre of the Royal Anthropological Institute.

TABLE I.—Control Samples Used. (Supplied by the Nuffield Blood Group Centre)

	O	A	B	AB	Total
*Liverpool Postal District	1,673	1,374	303	101	3,451
*Remainder of S.W. Lancashire	1,473	1,274	243	69	3,059
West Cheshire	546	521	135	45	1,247
Oxford	2,888	2,839	557	208	6,492

* Added to give a single series.

As a control series for the Oxford group of diabetic patients 6,492 blood donors in Oxfordshire and neighbouring counties were used.

The choice of controls for the Liverpool series was not so straightforward. The patients' homes were situated as follows: Liverpool postal district, 533; remainder of S.W. Lancashire, 80; West Cheshire, 199; North Wales, 10; elsewhere in the United Kingdom, 11. The Nuffield Centre figures given in Table I do not show any significant difference between the Liverpool postal area and the rest of S.W. Lancashire; hence these patients could be added together, the control figures used being the sum of the first two lines of Table I. The available Nuffield Centre figures for North Wales (making no distinction of racial origin) are very similar to those of S.W. Lancashire, so the 10 patients have been added to that series. The 11 patients coming from outside the areas named were mostly from N.W. Lancashire, and they too have been added.

West Cheshire must be kept separate, as the control frequencies are quite different. Hence the whole material available for this paper has been divided into three series, the areas being S.W. Lancashire, West Cheshire, and Oxford.

It will be noted that the Liverpool controls are slightly lower in blood group A than those of the rest of S.W. Lancashire, though the difference is not significant. The numbers in the control series are fairly equal, whereas many more patients are drawn from the Liverpool postal district. Hence, addition of the two control series, which seems desirable in the interests of simplicity and numbers, has the effect of slightly reducing the difference between diabetics and controls which is described in this paper.

Results

The basic data, with subdivisions by area, sex, and age at onset of diabetes mellitus, are shown in Table II. If men and women of all ages are compared with the controls of Table I, the findings may be summarized as shown in Table III. The control figures are weighted according to the numbers of diabetic men and women drawn from each area. The one striking difference is that compared with the controls the men show a higher proportion of patients of group A and a lower proportion of patients of group O. On the other hand, there is no such difference in the women.

The relative differences in groups O and A, for which considerable numbers are available, were examined first. The method recommended by Aird *et al.* (1954) for examining the differences in blood-group proportions and the homogeneity of the areas was used, and the comparison is shown in Table IV. The relative increase in blood group A in men is shown to be fairly highly significant. A direct comparison of the men and women patients also yields a significant difference. The women are closely similar to the controls. The three areas are perfectly homogeneous.

The men patients are lower in blood group B than are the controls, but the numbers are small and the difference is not significant.

The women patients show a rather high proportion of group AB. This has been examined in two ways. First, a direct comparison has been made with the controls in regard to the percentage of group AB. With the method of Aird *et al.* (1954), χ^2 for the difference is 3.25 and so does not attain the 5% level of significance. χ^2 for the heterogeneity of the three areas is 2.88, which is not significant, but does to some extent reflect the fact that the excess of those of group AB is confined to two of the areas. Secondly, if the figures are added together, irrespective of area, Fisher's test for unreasonableness of group proportions (Dobson and Ikin, 1946) gives an expected number of those of group AB of 25.804 against the 38 observed, χ^2 for one degree of freedom being 3.99, which just exceeds the 5% level of significance. It may be concluded that, while the women are rather high

in the proportion of AB blood, there is no clear indication that this might not be due to the accidents of sampling.

It is shown later that subdivision of the males raises the possibility that the excess of group A may not be the same in all types of diabetes. To give every chance for differences to emerge, should they be present, alternative comparisons can be made by adding the two groups which are in excess—namely, A and AB—and also the two groups which are reduced—namely, O and B. Thus the percentage now examined is that of persons who possess gene A. The results for the totals are shown in Table V. This comparison shows much the same differences as the previous comparison involving groups O and A only, but the significance of the difference between the men patients and the controls is increased.

TABLE II.—Basic Data. Blood Groups of Diabetic Patients by Area, Sex, and Age at Onset

Age	Men				Women			
	O	A	B	AB	O	A	B	AB
<i>South-West Lancashire</i>								
0-9	1	2	2	0	2	3	0	0
10-19	3	10	1	0	8	6	1	0
20-29	12	15	2	1	8	10	2	0
30-39	16	15	5	0	16	11	3	0
40-49	21	14	2	4	25	26	5	2
50-59	24	22	5	3	62	50	15	7
60-69	9	16	2	2	52	43	10	8
70+	5	7	0	0	16	15	6	1
Total	91	101	19	10	189	164	42	18
<i>West Cheshire</i>								
0-9	3	5	2	0	3	3	0	0
10-19	1	3	1	0	3	4	2	0
20-29	5	6	0	0	2	4	0	1
30-39	3	4	0	0	4	1	0	1
40-49	5	7	1	1	10	8	1	0
50-59	6	9	0	0	19	12	1	0
60-69	5	8	1	0	12	14	2	0
70+	2	4	0	0	3	6	0	1
Total	30	46	5	1	56	52	6	3
<i>Oxford</i>								
0-9	4	1	0	0	0	1	0	0
10-19	7	7	1	2	5	8	0	4
20-29	6	15	1	2	12	5	2	3
30-39	7	7	3	1	5	19	3	0
40-49	13	14	2	0	17	9	0	1
50-59	13	23	1	0	49	41	11	2
60-69	18	17	1	1	43	40	3	4
70+	6	7	1	0	8	19	2	3
Total	74	91	10	6	139	142	21	17

TABLE III.—Group Percentages: Diabetic Patients and Controls

Group	Men (484 Cases)			Women (849 Cases)		
	Control*	Disease	% Inc. or Dec. on Control	Control*	Disease	% Inc. or Dec. on Control
O	46.12	40.29	-12.6	46.26	45.23	-2.2
A	42.01	49.17	+17.0	41.98	42.17	+0.5
B	8.87	7.03	—	8.80	8.13	—
AB	3.00	3.51	—	2.97	4.48	—

* Weighted.

TABLE IV

	Weighted Diff. in A/(O+A+B+AB)%	χ^2 for Diff. (D. of F. = 1)	χ^2 for Heterogeneity (D. of F. = 2)
(Diabetic ♂)-(controls) ..	+7.23	8.84	0.78
(" ♀)-(") ..	+0.63	0.11	0.08
(" ♂)-(diabetic ♀) ..	+6.60	4.80	0.79

TABLE V

	Weighted Diff. in (A+AB)/(O+A+B+AB)%	χ^2 for Diff. (D. of F. = 1)	χ^2 for Heterogeneity (D. of F. = 2)
(Diabetic ♂)-(controls) ..	+7.67	11.04	0.69
(" ♀)-(") ..	+1.70	0.93	0.31
(" ♂)-(diabetic ♀) ..	+5.91	4.33	0.60

Subdivision by Age at Onset

A distinction is often drawn between diabetes in the young and in the middle-aged and old respectively. Furthermore, Harris (1949, 1950) found evidence of a genetic difference when division was made at age 30. If the figures of Table II are divided at age 30 and differences in the percentages of those possessing gene A are examined the results are as shown in Table VI. The excess of gene A is somewhat

TABLE VI

	Weighted Diff. in (A+AB)/(O+A+B+AB)%	χ^2 for Diff. (D. of F. = 1)	χ^2 for Heterogeneity (D. of F. = 2)
(♂ under 30)-(Controls) ..	+11.92	6.95	0.20
(♂ over 30)-(") ..	+6.28	5.61	1.38
(♂ under 30)-(♂ over 30) ..	+5.37	1.06	1.01

higher in the men under 30, but the difference is not significant. The men over 30 as well as the men under 30 differ significantly from the controls. The percentage difference between women under 30 and women over 30 is +4.61; χ^2 for the difference is 0.76 and for heterogeneity 0.20.

If the figures are divided at age 40 such differences as there are between patients under and over 30 almost vanish. For the men the weighted mean difference is reduced from +5.37 to +0.07 and for the women from +4.61 to +0.05. Once again men under 40 and men over 40 differ significantly from the controls, χ^2 for the weighted mean differences being respectively 4.38 and 6.90.

Thus the excess of gene A in men applies to cases both of earlier and later onset. The excess is somewhat greater in younger subjects, but the difference is not significant on the numbers in the present series.

Subdivision by Insulin Requirement

As an alternative to division by age, those on insulin therapy may be compared with those not receiving insulin. The results are shown in Table VII. The differences in both

TABLE VII.—Subdivision of Diabetic Patients by Insulin Requirements

	Men				Women			
	O	A	B	AB	O	A	B	AB
<i>On Insulin</i>								
S.W. Lancs ..	59	63	13	6	87	88	22	6
W. Cheshire ..	21	32	4	1	35	31	5	1
Oxford ..	51	69	9	5	105	110	13	14
Total ..	131	164	26	12	227	229	40	21
<i>Not On Insulin</i>								
S.W. Lancs ..	32	38	6	4	102	76	20	12
W. Cheshire ..	9	14	1	0	21	21	1	2
Oxford ..	23	22	1	1	34	32	8	3
Total ..	64	74	8	5	157	129	29	17

sexes are smaller than those shown by division at age 30, which have already been shown to be much below the level of significance. It is therefore unnecessary to present a detailed analysis. If simple unweighted averages of the differences in the three areas are taken, the difference in the percentage possessing gene A between men on insulin and men not on insulin is only 0.43, as against a corresponding figure of 3.55 for division at age 30. In the women the insulin figure is 1.18 as against 5.38.

Subdivision by Family History

Neither at Liverpool nor at Oxford was a genetic study carried out, and relatives were not examined. At both centres, however, patients were asked whether any relatives were affected. When the patients were divided into those who had an affected relative of any kind and those who had no known affected relative, as shown in Table VIII, the result for the women was entirely negative, as with the previous

comparisons; the simple unweighted difference in the percentage of those with gene A was only 1.14.

The men, however, gave a very different result. The percentage unweighted difference was 7.67, which greatly exceeded the difference found when division was made by onset before and after 30 years. In Table VIII, therefore, the results for the men are set out in more detail. With such small numbers no more than a single comparison is justified.

TABLE VIII.—Subdivision of Diabetic Patients by Family History

Relatives Affected	S.W. Lancashire				W. Cheshire				Oxford			
	O	A	B	AB	O	A	B	AB	O	A	B	AB
Men												
2 parents ..	0	1	0	0	0	0	0	0	0	2	0	0
1 parent ..	7	13	3	0	1	10	0	0	7	10	0	0
1 parent and 1 sib ..	0	0	0	0	0	0	1	0	1	1	0	0
2 sibs ..	0	0	1	0	0	0	0	0	0	1	0	0
1 sib ..	2	5	1	3	2	1	0	0	3	6	0	0
1 child ..	2	0	0	0	0	0	0	0	1	0	1	0
Total—1st degree relatives ..	11	19	5	3	3	11	1	0	12	20	1	0
More distant only ..	5	9	1	1	4	6	1	0	8	5	2	1
None ..	75	73	13	6	23	29	3	1	54	66	7	5
Women												
Any relative ..	33	38	11	5	18	15	1	2	41	38	6	4
None ..	156	126	31	13	38	37	5	1	98	104	15	13

TABLE IX

	Weighted Diff. in (A+AB)/(O+A+B+AB)%	χ^2 for Diff. (D. of F.=1)	χ^2 for Heterogeneity (D. of F.=2)
(1st degree relative affected) —(controls) ..	+17.00	10.63	1.15
(Remainder)—(controls) ..	+5.75	5.11	0.21
(1st degree relative affected) —(remainder) ..	+11.06	3.68	0.55

Hence males with an affected first-degree relative have been compared with the remainder, including those with only a more distant relative affected. It will be seen that this last group shows little difference from the remainder, and the result is practically the same whether they are included or not. Comparison is also made with the controls. The results are shown in Table IX. Both groups, those with and those without a first-degree relative affected, differ significantly from the controls, though the difference is much greater with the former group. The direct comparison yields a difference which nearly, though not quite, attains the 5% level of significance. As in previous comparisons, the three areas are perfectly homogeneous.

The basis of classification employed can provide at best only an imperfect genetic separation, and the size of the difference which has emerged with such small numbers suggests the possibility that the excess of gene A might, if real, be confined to a type of diabetes mellitus which is genetically distinct from other forms of the disease.

A More Detailed Search for Associations with Age

Apart from division into younger and older subjects, which would naturally be made in diabetes mellitus, a general examination of age distributions is desirable in any disease in which there may be associations with the blood groups. Table X shows the mean ages of onset for patients of the four blood groups, separately by sex and area. The means have been calculated from the figures of Table II, which are given in 10-year groups. Ages are, of course, recorded in completed years, so half a year is added throughout.

The most general approach is to look at the figures for each sex as a whole, distinguishing the contributions to variation of age attributable to blood groups, to areas, and to interaction of blood groups and areas, the mean squares

TABLE X.—Mean Ages, by Blood Group, Sex, and Area

	O	A	B	AB	Total
Men:					
S.W. Lancs	45.44	44.21	39.21	50.00	44.55
W. Cheshire	43.00	43.26	27.00	45.00	42.20
Oxford ..	46.49	46.76	43.00	30.00	45.88
Total ..	45.46	45.00	38.53	42.65	44.65
Women:					
S.W. Lancs	52.94	52.32	55.24	59.44	53.21
W. Cheshire	49.11	49.81	43.33	45.00	49.02
Oxford ..	53.27	53.52	52.62	45.59	52.93
Total ..	52.50	52.43	53.41	52.11	52.53

TABLE XI.—Variation of Age. Analysis of Variance. (Years)²

Variation of Age Due to	Degrees of Freedom	Mean Square	Variance Ratio	P
Men				
Blood groups ..	3	778.6	2.25	0.1-0.05
Areas ..	2	197.5	0.57	>0.2
Interactions ..	6	392.6	1.14	>0.2
Individuals ..	472	345.8		
Women				
Blood groups ..	3	58.7	0.22	>0.2
Areas ..	2	835.3	3.16	0.05-0.01
Interactions ..	6	371.8	1.41	>0.2
Individuals ..	837	264.3		

being compared with the mean square for individuals. The procedure adopted is that described by Snedecor (1946, section 11.12) for securing unbiased estimates of the mean squares when subclass numbers are disproportionate. The results are shown in Table XI. The results for the women can be dismissed briefly. There is a significant difference between areas, the patients from West Cheshire being rather younger than those from the other areas. This difference is irrelevant, however, and there is no suggestion of any significant variation of age due to blood groups.

No variance ratio is significant in the men, but the ratio of 2.25 for blood groups is not very much below the 5% level of significance, which is 2.62. Table X shows that the chief contribution to the variation due to blood groups is that male diabetics of group B are considerably younger than those of the other groups, this being true of all three areas. The numbers are small, but a direct comparison of group B with the other groups has been made. The results, pooling the three areas, are shown in Table XII. An ordinary

TABLE XII.—Proportion of Male Diabetics of Group B by Age. All Areas

Age	Numbers			% B
	B	O+A+AB	Total	
0-19 years ..	7	49	56	12.50
20-39 ..	11	115	126	8.73
40-59 ..	11	179	190	5.79
60+ ..	5	107	112	4.46
Total ..	34	450	484	7.02

$2 \times n$ comparison gives a χ^2 of 4.70 for 3 degrees of freedom, which is not significant at the 5% level. The figures do, however, suggest a trend, the proportion of men diabetics of group B falling as age advances. Using a more sensitive procedure due to Fisher (Holt, 1948), which assesses the significance of a trend, χ^2 is 4.43 for one degree of freedom, so there is some slight evidence that it may be real. We would lay little stress on this finding, however. It is one comparison out of many, selected after inspection of the figures; and, while it would be desirable to examine the point further when more data become available, it cannot be regarded for the present as more than somewhat suggestive.

The outstanding conclusion is that, with this one possible exception, there is no evidence, so far as the present series goes, of any association between the age of onset of diabetes mellitus and ABO blood-group frequencies.

The Oxford Series

Rhesus and MN groupings recorded for the 500 patients in the Oxford series show no significant departure from the proportions to be expected in the area.

TABLE XIII.—*Rhesus and MN Groupings for 500 Diabetics (Oxford)*

	Rh Pos.	Rh Neg.	M	N	MN
Whole series	401	99	123	112	265
Males (181)	142	39	44	46	91
Females (319)	259	60	79	66	174
Under 40 (131)	107	24	33	30	68
Over 40 (369)	294	75	90	82	197
On insulin (376)	295	81	88	89	199
Not on insulin (124)	106	18	35	23	66

Whole series: Rhesus-negative, 19.8%; M, 24.6%; N, 22.4%; MN, 53.0%.

Discussion

The Liverpool investigation was largely prompted by the infrequency of duodenal ulcer in patients suffering from diabetes mellitus (Joslin, 1947). A preliminary analysis (McConnell, 1955) suggested that there was a significantly increased frequency of blood group A in young diabetics and that possibly this applied to all diabetics of the insulin-sensitive type. Opinions differ on whether diabetes mellitus is one disease or a syndrome with several causes. The genetical basis of the condition is still so uncertain that division into the two main clinical types is not sufficient and a more detailed analysis is desirable. This has modified the original tentative conclusions. The outstanding difference that has emerged is that between the sexes. There is fairly strong evidence that diabetic men show an excess of group A, whereas diabetic women show no significant difference from the control series.

The original preliminary finding was due to the fact that any series of diabetic subjects is likely to contain much the same numbers of young men and young women, but a big excess of older women. This, coupled with some non-significant excess of group A in the younger women, made it appear that the excess was a feature of young subjects. Further analysis has, as already described, shown that the underlying difference is due to sex and not to age.

One possible age association which has emerged is a suggestion of a decreasing proportion of diabetic men of group B as age advances. The numbers are very small, however, and we would merely suggest that this is a point to be looked at when more figures are available.

Subdivision of the material has been made in three ways: by age of onset of the disease; by insulin requirement; and by family history. In the women the same negative result emerges as for the series as a whole.

In the men the excess of group A is almost the same in those receiving and those not receiving insulin. When division according to age of onset is made at 30 years the excess of group A is greater in the younger subjects; but the difference is non-significant, and both groups differ significantly from the controls. The excess of group A is, however, much greater in those with a first-degree relative known to be similarly affected, and although the numbers are small this difference nearly attains significance at the 5% level. It is possible, therefore, that the excess of group A in men may be characteristic of a particular kind of diabetes mellitus rather than of the disease as a whole.

The main finding—an excess of male diabetics of group A—seems to be supported by fairly strong evidence. Comparing the proportions in male diabetics and controls respectively of those who possess gene A, χ^2 for the difference is 11.04 for one degree of freedom, corresponding to a probability of one in 1,120. Moreover, the same difference emerged in both our independent investigations, and the three areas into which the material has been divided in this paper are perfectly homogeneous. Nevertheless, we do not regard

the difference as securely proved, and put it forward tentatively only. While sex differences may indeed emerge in the future in connexion with studies on blood groups and disease, such differences could hardly have been anticipated, and the finding is a peculiar one. It might be mentioned, however, that it is not quite unique. Maxwell and Maxwell (1955) report a deficiency of group AB amongst hypertensive men. They are cautious in their conclusions, and consider that it is probably a chance effect. Aird, Bentall, and Roberts (1955), however, commenting on their figures, point out that the evidence is at least strong enough to justify further investigation. Aird *et al.* (1953), in a study on gastric carcinoma, collected data from a large number of hospitals, and sex was not distinguished. In 1,000 of these patients, however, for whom sex had been recorded, Aird *et al.* (1954) point out that almost the whole of the excess of group A was due to the men, though on these numbers the sex difference was not significant.

We have an additional reason for caution. We have compared results with Dr. J. Craig and Dr. I. Wang, who have carried out a similar investigation on diabetes mellitus at the Victoria Infirmary, Glasgow (Craig and Wang, 1955). They do not find an excess of group A in either male or female diabetics. If their series of 276 male diabetics were to be considered a fourth area and added to the three of this paper, χ^2 for the combined weighted mean difference in the proportion of those with gene A would be reduced from 11.04 to 6.77. χ^2 for heterogeneity of areas is naturally increased—from 0.69 for 2 degrees of freedom to 4.96 for 3 degrees of freedom. This last figure is not significant at the 5% level, so it cannot be said that the Glasgow findings contradict ours. Nevertheless a probability of 1 in 1,120 has been increased to 1 in 110. It may be odd for a χ^2 of 11 for one degree of freedom to vanish with the addition of further data, but such things are not unknown in biometrical work.

The data of this paper can support no more than tentative and provisional conclusions. There does seem a case, however, for further investigation, and we trust that new series will be forthcoming which will establish or disprove the apparent excess of group A in men suffering from diabetes mellitus.

Summary

The frequencies of the ABO blood groups have been studied in 1,333 patients in Liverpool and in Oxford suffering from diabetes mellitus and comparisons made with control series.

In the men there is a considerable excess of those of group A, the difference from the controls being fairly highly significant. The findings at both centres are in agreement and the three areas into which the material has been divided are perfectly homogeneous for the difference. It is suggested, however, that the evidence does not justify more than a tentative conclusion and that confirmation is required.

The women diabetics do not differ significantly from the controls.

Subdivision of the diabetic patients by age of onset of the disease, by insulin requirement, and by family history gives negative results in the women. In the men there is some suggestion that the excess of group A is greater in those with a close relative similarly affected.

Rhesus and MN groupings of the 500 patients in the Oxford series do not differ significantly from the proportions to be expected.

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FURTHER OBSERVATIONS ON ABO BLOOD-GROUP FREQUENCIES AND TOXAEMIA OF PREGNANCY

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In a previous paper (Pike and Dickins, 1954) a comparison was made of the frequencies of the ABO blood groups of toxæmic and non-toxæmic women in 3,651 consecutive deliveries. The toxæmic mothers showed a higher frequency of group O than the remainder, the difference being fairly highly significant. It was realized, however, that larger numbers were needed, and the hope was expressed that other series would be studied at other hospitals.

As a first step the original material was re-scrutinized, with stricter criteria for the diagnosis of toxæmia. Ninety-three women were transferred from the toxæmic series to the non-toxæmic on the following grounds: (1) that the arterial pressure had reached 140/90 in labour only; (2) that the prescribed level of arterial pressure was attained by the systolic or diastolic reading only and not by both; and (3) that the history of toxæmia in a previous pregnancy, though probable, was not beyond all doubt. The modified figures, with the addition of cases over a short further period, were described briefly by one of us (Dickins, 1955). The significance of the difference was reduced, but the evidence remained fairly strong.

The original series comprised deliveries from March, 1951, to April, 1954. A second series, comprising deliveries at the same hospital from May, 1954, to December, 1955, has now been analysed. The second series does not confirm the original result, and it must now be concluded that we have no acceptable evidence that toxæmic and non-toxæmic mothers differ in their ABO frequencies. Some mystery remains, however—a mystery we cannot explain—as to why the original series gave the result it did. The Table shows the results for the original period, with the amended figures on re-scrutiny, and the later series.

ABO Frequencies in Toxæmic and Non-Toxæmic Women: Numbers and Percentages

	Toxæmic				Non-Toxæmic			
	O	A	B	AB	O	A	B	AB
<i>Basic Data</i>								
1. March, 1951–April, 1954	290	203	34	14	1,416	1,342	263	89
2. No. 1 on re-scrutiny	237	170	30	11	1,469	1,375	267	92
3. May, 1954–Dec., 1955	106	116	29	11	695	670	115	43
Total 2+3	343	286	59	22	2,164	2,045	382	135
<i>Corresponding Percentage Frequencies</i>								
1.	53.6	37.5	6.3	2.6	45.5	43.2	8.5	2.9
2.	52.9	37.9	6.7	2.5	45.9	42.9	8.3	2.9
3.	40.5	44.3	11.1	4.2	45.6	44.0	7.6	2.8
2+3 . . .	48.3	40.3	8.3	3.1	45.8	43.3	8.1	2.9

If groups O and A only are compared the series as originally published gave a χ^2 for the difference between toxæmic and non-toxæmic mothers of 9.09 for one degree of freedom. If group O is compared with the total of the other three the χ^2 was 11.75 with one degree of freedom. The effect of the transfer of the 93 mothers on re-scrutiny is to lower these figures to 6.18 and 7.82 respectively, the second figure corresponding to a probability of less than 1 in 100. The new series (3 in the Table) shows an excess of A in the toxæmic mothers, but the difference from the non-toxæmic mothers is far below the level of significance ($\chi^2 = 0.77$ for the OA comparison).

When the whole material is combined the excess of group O in the toxæmic mothers is not significant. χ^2 is 2.17 for the OA comparison, and 1.72 when group O is compared with the total of the other groups. The two series are, however, significantly heterogeneous. With due regard to correct weighting, χ^2 for heterogeneity, with one degree of freedom, is 4.75 for the OA comparison and 8.48 for the comparison of group O against the other groups. Thus the material taken as a whole shows no significant excess of O in toxæmic women. The results for the two periods, however, do not agree, the discrepancy being fairly highly significant.

We have tried to find reasons for the discrepancy, but without success. Exactly the same criteria were applied in the diagnosis of toxæmia of pregnancy. The frequencies amongst all women grouped in the area and those delivered in hospital do not differ and there has been no secular change in either. For example, dividing women grouped from mid-1948 to the end of 1955 into 15 half-yearly periods, the total in groups O and A is 10,844. The relative proportions of O and A are perfectly homogeneous, χ^2 being only 8.26 for 14 degrees of freedom ($P = 0.87$). The two series of toxæmic women are homogeneous within themselves, the first for high O and the second for low O. If each is divided into four periods the χ^2 's for heterogeneity within the two series, with 3 degrees of freedom, are as follows: for the OA comparison 6.73 for the first series, 3.68 for the second; for the O versus (A+B+AB) comparison, 5.44 and 1.73. All these values are non-significant at the 5% level. We have also subdivided the toxæmic patients into those with pre-eclamptic toxæmia of pregnancy and those with essential hypertension in pregnancy according to criteria described previously (Dickins, 1955). Both types show high O during the first period and low O during the second.

When it was originally thought that there was an excess of group O in toxæmia it was decided to reinvestigate the question of ABO heterospecific pregnancy as a possible explanation (Richardson, 1955). During both the original period of high O and the later period the proportion of heterospecific pregnancies corresponded closely to what would be expected on the basis of the gene frequencies. The total number of pairs of mothers and babies tested was 236. In all pregnancies which were ABO compatible a