BLOOD GROUPS IN DIABETES MELLITUS.

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Since shortly after the discovery of the ABO groups there has been considerable interest in blood group distribution in various diseases. The majority of the earlier studies dealt with small series or with rather heterogeneous groups of diseases. It has only recently been shown that group A is significantly more frequent and group O less frequent among patients with gastric carcinoma than among the general population in the same localities (Aird *et al.*, 1953) while there is an increased proportion of group O in those with peptic ulceration (Aird *et al.*, 1954). Pike and Dickins (1954) have reported an increase in group O among patients with toxaemia of pregnancy. McConnell *et al.* (1954) have found no abnormal distribution among patients suffering from bronchial carcinoma when all histological types were included though an excess of group A was present in those with oat-cell tumours.

When we started this investigation we were unable to find any reports of the blood group distribution in diabetes mellitus. This condition seemed to us to be particularly suitable for study as there is usually little doubt about the diagnosis and there is also a well recognised familial incidence. It seemed possible that some difference in blood group distribution might emerge between the young, non-obese, insulin-deficient patients and the older, obese, insulin-resistant patients. Since then McConnell (1955) has reported his findings in a series of diabetic patients ; he found a significant increase in the proportion of group A among the young diabetics. Further analysis of his figures (McConnell, personal communication) has shown that this preponderance of group A is present in all male diabetic patients regardless of age at onset, the females showing a normal distribution.

The results of our investigation of the ABO and Rh(D) groups in 817 diabetic patients are presented.

MATERIAL AND METHODS.

The series comprises all the known diabetic out-patients attending the Metabolic Clinic of this hospital between 12th November, 1954 and 12th April, 1955. The diagnosis was based on a typical history supported by a single blood sugar determination taken at random on the patient's first visit to the Clinic, and by a glucose tolerance test whenever necessary.

Capillary blood was obtained from each patient at the first visit between the above dates ; it was taken directly into saline. Groupings were carried out within three hours or after storage overnight at 4°C., the cells being washed and resuspended immediately before the tests were made. ABO and Rh(D) groups were determined as described by Mollison(1951) with appropriate known cells as controls. Results

were read macroscopically and microscopically. In two cases in which there was doubt about the result of the anti-D test venous samples were obtained and were re-examined here and at the Regional Transfusion Centre ; both proved to be examples of the weak antigen D^u.

The following data were obtained about each patient : sex, presence or absence of a family history of diabetes and of obesity ; weight and age at the time of diagnosis of diabetes.

A patient was considered to have a family history of diabetes if any consanguineous relative was known to be diabetic. No rigid definition of a family history of obesity was possible : the records were completed in accordance with the patient's answers to simple questions as to the build of known relatives.

Classification by weight was based on tables of average weight (Dunlop *et al.*, 1949). The weight at the time of diagnosis of diabetes has been used throughout. Patients who were more than 20 per cent above ideal weight for sex and height were regarded as obese, those between 5 per cent and 20 per cent as intermediate, and those less than 5 per cent overweight as non-obese.

RESULTS.

The results for the whole series are shown in Table 1 together with figures for new donors in this area and for all patients whose ABO and Rh(D) groups were determined for the first time in this hospital during 1953 and 1954.

The diabetic series as a whole did not differ significantly from the donors in respect of ABO and Rh(D) blood groups. In the major divisions used (Table 2) the only significant abnormality was found in the non-obese patients, who showed a reduction in group B (7.1%) when compared with the donors (11.0%), X^2 being 6.12 for one degree of freedom.

Subdivision and combination of the data revealed significant abnormalities in various categories. It was found that these abnormal results occurred only when group O was compared either with another group or with the total for all the other groups. Where the former comparison reached a significant level the latter was also abnormal and therefore in Tables 3 and 4 only the comparisons between group O and the total for all the other groups is shown, Yates's correction being used throughout in the calculation of X^2. No disproportionate number of Rh(D) negatives was found in any category.

DISCUSSION.

For comparison we have used the donor figures throughout. Aird *et al.* (1954) have pointed out the fallacies of using a hospital series as a control group and our findings confirm this. Our series of hospital patients differs significantly ($X^2=9.63$ for three degrees of freedom) from the donor series for the ABO groups. This is due to an increase in group O and a decrease in group B among the hospital patients. The former is possibly due to the number of patients with peptic ulcers included in the population of a general hospital ; the latter may be due to the ' protective ' element postulated by Aird (1955). There is no significant difference in the Rh(D) groups.

TABLE 1.

Distribution of ABO and Rh(D) groups among diabetic patients, donors and hospital patients.

(Percentage distribution is indicated in italics.)

	O	A	B	AB	Rh(D) neg.	Total
Diabetic patients	411 *50.3*	296 *36.2*	80 *9.8*	30 *3.7*	133 *16.3*	817
Donors	3853 *51.9*	2485 *33.5*	817 *11.0*	263 *3.5*	*263 *17.3*	7418
Hospital patients	1430 *55.1*	841 *32.4*	245 *9.4*	81 *3.1*	441 *17.0*	2597

* Control series for Rh(D) based on 1518 donors.

TABLE 2.

Distribution of ABO and Rh(D) groups among 817 diabetic patients when divided according to sex, to family history of diabetes or of obesity, to weight at onset and to age at onset.

(Percentage distribution is indicated in italics.)

	O	A	B	AB	Rh(D) neg.	Total
Male	151 *54.7*	92 *33.7*	23 *8.3*	9 *3.3*	41 *14.9*	276
Female	260 *48.1*	203 *37.5*	57 *10.5*	21 *3.9*	92 *17.0*	541
Family history of diabetes	98 *46.7*	81 *38.6*	22 *10.5*	9 *4.3*	47 *22.4*	210
Family history of obesity	211 *48.0*	161 *36.6*	52 *11.8*	16 *3.6*	69 *15.7*	440
Obese	104 *46.8*	83 *37.4*	28 *12.6*	7 *3.2*	32 *14.4*	222
Intermediate	73 *45.9*	58 *36.5*	21 *13.2*	7 *4.4*	34 *21.4*	159
Non-obese	234 *53.7*	155 *35.6*	31 *7.1*	16 *3.7*	67 *15.4*	436
Aged thirty or under at onset	73 *57.0*	41 *32.0*	9 *7.0*	5 *3.9*	18 *14.1*	128

TABLE 3.
Categories (I to V) in which group O is significantly DECREASED compared with total for other groups.
(Percentage distribution indicated in italics.)

Category	O	A	B	AB	Total	X^2
I	177 *46.5*	141 *37.0*	49 *12.9*	14 *3.7*	381	4.15
II	248 *47.2*	199 *37.9*	59 *11 2*	19 *3.6*	525	4.16
III	213 *46.8*	172 *37.8*	54 *11.9*	16 *3.5*	455	4.31
IV	130 *45.8*	107 *37.7*	39 *13.7*	8 *2.8*	284	3.92
V	34 *39.5*	37 *43.0*	12 *14.0*	3 *3.5*	86	4.76

Category I Overweight (obese and intermediate) patients.
Category II All patients with a family history of diabetes, obesity or both.
Category III Patients over thirty at onset with a family history of diabetes, obesity or both.
Category IV Overweight (obese and intermediate) patients with a family history of diabetes, obesity or both.
Category V Overweight (obese and intermediate) patients with a family history of diabetes.

TABLE 4.
Categories (VI to XI) in which group O is significantly INCREASED compared with total for other groups.
(Percentage distribution indicated in italics.)

Category	O	A	B	AB	Total	X^2
VI	116 *59.5*	63 *32.3*	11 *5.6*	5 *2.6*	195	4.04
VII	76 *63.3*	32 *26.7*	8 *6.7*	4 *3.3*	120	5.69
VIII	64 *68.1*	22 *23.4*	5 *5.3*	3 *3.2*	94	9.06
IX	21 *72.4*	5 *17.2*	2 *6.9*	1 *3.4*	29	4.07
X	43 *66.2*	17 *26.2*	3 *4.6*	2 *3.1*	65	4.66
XI	75 *62.5*	35 *29.2*	6 *5.0*	4 *3.3*	120	4.86

Category VI Non-obese patients with no family history either of diabetes or of obesity.
Category VII Males with no family history either of diabetes or of obesity.
Category VIII Non-obese males with no family history either of diabetes or of obesity.
Category IX Non-obese males thirty or under at onset with no family history either of diabetes or of obesity.
Category X Non-obese males over thirty at onset with no family history either of diabetes or of obesity.
Category XI Non-obese males with no family history of obesity.

As diabetes mellitus is thought to be more prevalent in some races the ethnic constitution of the diabetic series must be taken into account in any consideration of the blood group distribution. Munro *et al.* (1949) have shown that there is no significant loading due to race in the patients attending this clinic.

The distribution of the ABO groups is similar to that of the donors when our patients are considered as a whole (Table 1), or when divided according to sex, family history of diabetes or of obesity, and age at the time of diagnosis of diabetes (Table 2). The only significant abnormality when divided according to weight is a reduction in the proportion of group B among the non-obese patients. In view of the small proportion of group B in any blood group study we do not feel that much emphasis can be placed on this abnormality.

Our findings differ from those of McConnell (1955 and personal communication) who, working in Liverpool, found a significant increase in the proportion of group A among the young diabetics and in male patients. We could not find such an increase ; 36.4 per cent of our young non-obese diabetics and 33.7 per cent of our male patients belong to group A compared with 33.5 per cent of the donors. We can offer no satisfactory explanation for this discrepancy unless environment plays a part in the aetiology of diabetes mellitus. It is of interest that while Aird *et al.* (1953) found a significant increase in group A among patients with gastric carcinoma in various centres this increase was much less marked in Scotland. The series reported by Wallace (1954) suggests that it is very slight indeed in the Glasgow area.

We have found abnormal blood group distribution in certain combinations and subdivisions of the main classes of patients (Tables 3 and 4). Group O is significantly decreased among all the overweight patients (category I), and among all patients with a family history of diabetes or of obesity or both (category II). The patients over thirty at the onset of diabetes (category III) are responsible for the latter observations, the younger patients showing no abnormality. In these three categories however the decrease is due to the overweight patients with this family history (category IV) since those who were overweight and without family history and those with a family history who were not overweight show no abnormality. All except two of the overweight patients with a family history of diabetes or of obesity or both were over thirty years at the onset of diabetes ; subdivision by sex gives no significant result.

In those with no family history either of diabetes or of obesity the proportion of group O is increased both among all the non-obese patients (category VI) and among the males (category VII). In both these categories the group O increase is due to the non-obese males without a family history (category VIII) as the females included in category VI and the overweight patients included in category VII show no abnormality in

blood group distribution. This increase of group O in category VIII is not connected with age as it is present in the younger (category IX) and in the older (category X) patients.

One might be justified in drawing conclusions on the basis of this increase in group O among non-obese patients without a family history in contrast to the decrease in group O among the older, overweight patients with a family history of diabetes or of obesity. We do not feel however, that in the absence of confirmation by other series, the abnormalities which we have found can be considered as more than possible factors in the natural history of diabetes mellitus.

SUMMARY.

The results of an investigation of ABO and Rh(D) blood group distribution in 817 diabetic patients are reported.

The danger of using hospital patients as the control series is confirmed.

No significant difference is present between a series of new donors in the same area and the diabetic series regarded as a whole or divided according to sex, to family history of diabetes or of obesity, to age and to weight at the time of diagnosis of diabetes.

Group O however is decreased among older overweight patients with a family history of diabetes of or obesity or both, and is increased among non-obese male patients with no family history either of diabetes of or obesity.

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REFERENCES.

Aird, I, (1955), *Proc. Roy. Soc. Med.* **48** : 139

Aird, I., Bentall, H. H. & Roberts, J. A. F. (1953). *Brit. med. J.* **1** :799

Aird, I., Bentall, H. H. Mehigan, J. A. & Roberts, J. A. F. (1954). *Brit. med. J.* **2** : 315

Dunlop, D. M., Davidson, L. S. P. & McNee, J. W. (1949). Textbook of Medical Treatment (5th Ed.), Edinburgh : Livingstone, p. 385

McConnell, R. B. (1955). *Proc. Roy. Soc. Med.* **48** : 291

McConnell, R. B. Personal communication

McConnell, R. B., Clarke, C. A. & Downton, F. (1954). *Brit. med. J.* **2** : 323

Mollison, P. L. (1951) *Blood Transfusion in Clinical Medicine,* Oxford : Blackwell pp.204 & 208,

Munro, H. N., Eaton, J. C. & Glen, A. (1949). *J. clin. Endocrinol.* **9** : 48

Pike, L. A. & Dickins, A. M. (1954). *Brit. med. J.* **2** : 321

Wallace, J. (1954). *Brit. med. J.* **2** : 534