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AN ASSOCIATION BETWEEN BLOOD GROUP A AND PERNICIOUS ANAEMIA

A COLLECTIVE SERIES FROM A NUMBER OF CENTRES*

For several years studies on pernicious anaemia have been in progress at the centres contributing to this report. The nature and purposes of the studies vary, but in all of them the ABO blood groups of the patients have been determined. Realizing that with so rare a disease it would be unlikely that any single centre could obtain enough data within any reasonable time for testing the existence of blood-group associations, we decided to compare our data and pool the results. This was done nearly a year ago, when we discovered that the combined data pointed fairly strongly to a higher incidence of pernicious anaemia in persons of group A than in those of group O. Though we had hoped to build up a larger total, we think that a brief interim account should now be given, setting out the evidence for the association with blood group A and postponing a more detailed analysis till later. It is to be hoped that others will be able to supplement the data and either confirm or disprove a finding for which, however, the evidence is tolerably strong.

It is interesting that Buchanan and Higley (1921) gave results for no fewer than 457 cases of pernicious anaemia. In retrospect the percentage frequencies of O and A—41.4 and 44.2 respectively—do suggest an excess of group A. Their own statement covering all the diseases studied was, however: "There is no relationship between blood groups and any disease in which sufficient data are available to justify a conclusion."

Results

The basic data are given in Table I. In London and Glasgow there seemed to be large differences between different hospitals. This is very striking if the figures for the Southern General Hospital and the Royal Infirmary at Glasgow are compared. Lest real heterogeneity should be obscured, the data from hospitals in these areas have been kept separate so far as possible. In London the fairly large series for Hammersmith and the Kingston General Hospital are both high in A, the remainder showing no excess. The remainder consist of several very small series, which have been added together. Seven results from Birmingham, which has very much the same ABO frequencies as London, have also been added.

Except for Sheffield the control series used have all been described in previous publications: those for London and Newcastle by Aird, Bentall, Mehigan, and Roberts (1954); for Oxford by McConnell, Pyke, and Roberts (1956); for Cambridge by Bennett and Walker (1956); for Glasgow by Peebles Brown, Melrose, and Wallace (1956). The control series for Sheffield was kindly provided by the Nuffield Blood Group Centre of the Royal Anthropological Institute; it is based on a count of consecutively registered blood donors.

For the analysis we have added a series of 111 cases from Copenhagen, as recorded by Køster, Sindrup, and Seele (1955). It is useful to be able to include additional published series, but in this instance it is especially important that the Copenhagen figures should be added, because they lower the significance of our finding. The Copenhagen figures

TABLE I.—*Basic Data*

	Pernicious Anaemia				Controls			
	O	A	B	AB	O	A	B	AB
London:					4,578	4,219	890	313
Hammersmith	48	75	7	4				
Kingston	23	42	1	2				
Composite*	19	18	4	1				
Oxford	112	120	18	8	2,888	2,839	557	208
Cambridge	51	49	8	2	1,571	1,501	255	111
Sheffield	47	58	10	8	1,451	1,318	249	93
Newcastle	55	45	7	2	6,598	5,261	1,321	392
Glasgow:					3,177	1,906	637	178
Southern General	63	35	9	3				
Royal Infirmary	72	61	22	5				
Total	490	503	86	35				

* This composite number includes 7 patients obtained from the records of Birmingham United Hospitals in the course of the survey of another disease, and the remainder of the group comprise 35 patients suffering from pernicious anaemia who have presented, since the collection of data was begun, at Balham Hospital, the Central Middlesex Hospital, the North Middlesex Hospital and Whipps Cross Hospital.

TABLE II.—*Summary of Group Frequencies in Patients and Controls (including Copenhagen)*

	Pernicious Anaemia		Corresponding Weighted Controls (%)
	No.	%	
O	534	43·6	47·2
A	550	44·9	40·3
B	100	8·2	9·3
AB	41	3·3	3·2
Total	1,225		

* This report is an analysis of studies made by the following workers: I. Aird, H. H. Bentall, and J. Bingham (Department of Surgery, Postgraduate Medical School of London, Hammersmith Hospital); E. K. Blackburn, Mary S. Mackay, and H. T. Swan (Department of Haematology, Royal Infirmary, Sheffield); Sheila T. Callender and M. A. Denborough (Nuffield Department of Clinical Medicine, Radcliffe Infirmary, Oxford); E. H. Hemsted (Royal Berkshire Hospital, Reading); D. P. Mollin, Barbara Anderson, John Selwyn (Department of Haematology, Postgraduate Medical School of London); D. N. Phear and G. A. Gresham (Department of Pathology, Addenbrooke's Hospital and University of Cambridge); Joan S. Sneath (Blood Group Research Unit, Lister Institute, London); C. C. Ungley (Royal Victoria Infirmary, Newcastle); John Wallace (Western Scotland Blood Transfusion Service, Glasgow); J. S. Adams (Department of Medicine, Royal Infirmary, Glasgow); and J. Buchanan and G. H. Shaw (Southern General Hospital, Glasgow). The data supplied have been analysed by J. A. Fraser Roberts (Burden Mental Research Department, Stoke Park Colony, Bristol, and London School of Hygiene and Tropical Medicine).

for pernicious anaemia are: O, 44; A, 47; B, 14; AB, 6; and for the corresponding controls: O, 5,804; A, 6,299; B, 1,557; AB, 644.

A brief summary of the findings is given in Table II. The percentage group frequencies for the controls are based on figures weighted according to the numbers of patients drawn from each area. It will be seen that in the disease series as compared with the controls A is increased and O and B are both reduced, though, of course, the number with B is very small.

The method of analysis is that of Woolf (1955). It is rather similar to that used by Aird *et al.* (1954), but the work is carried out in terms of relative incidences instead of differences in proportions. It is natural to think of diseases in terms of incidence, and the results come out in a form which has a direct and simple meaning. For example, from Table I, the Sheffield results show 47 with O and 58 with A in the disease series, compared with 1,451 and 1,318 respectively in the controls. Thus the relative incidence of pernicious anaemia in persons of group A, as compared with persons of group O, is simply $(58\times1,451)\div(47\times1,318)=1.3586$. Woolf's method also has the advantage that series drawn from populations with very different gene frequencies can readily be combined. When such differences are not very large, as in this country, the two methods give closely similar results, but this would not necessarily be so if data from different parts of the world were being compared. The method of combining areas in the analysis is the same.

Table III gives the relative incidence and χ^2 for groups A and O.

TABLE III.—*Relative Incidence of Pernicious Anaemia in Persons of Group A Compared with its Incidence in Persons of Group O*

	Relative Incidence	χ^2
London:		
Hammersmith	1·70	8·05
Kingston	1·98	6·90
Composite	1·03	0·01
Oxford	1·09	0·41
Cambridge	1·01	0·00
Sheffield	1·36	2·35
Newcastle	1·03	0·02
Glasgow:		
Southern General	0·93	0·13
Royal Infirmary	1·41	3·83
Copenhagen	0·98	0·01
		21·71

The combined weighted relative mean incidence of pernicious anaemia in persons of group A is 1.20 compared with 1 in group O. The total χ^2 of 21.71 is partitioned as follows:

	D. of F.	χ^2	P
Difference from unity	1	8·84	0·0029
Heterogeneity	9	12·87	0·17

Thus the probability of getting so great a departure from equality by chance is 1/340.

There is no evidence of any heterogeneity. Although the results look so different for the different series, ranging from an incidence in Group A at Kingston Hospital which is practically double that in group O to an actual slight excess in group O at the Southern General Hospital, Glasgow, and also at Copenhagen, such fluctuations are only to be expected with samples of this size.

Group A is also increased as against group B. If A is compared with O and B added together, the analysis shows:

	D. of F.	χ^2	P
Difference from unity	1	10·63	0·0011
Heterogeneity	9	15·28	0·087
Total	10	25·91	

The probability of getting so great a difference by chance is thus reduced to 1/900, and once again the 10 areas are not significantly heterogeneous at the 5% level.

Further analysis must await more detailed comparisons, we hope on larger numbers. For the moment we simply give in Table IV a brief comparison by sexes, which shows that the excess of A appears in both. This refers to the British data only, as the Copenhagen figures were not broken down by sex. The differences in the control figures are due to the differing proportion of men and women at the various centres.

TABLE IV.—*Comparison of Sexes. Totals for British Series*

	Men			Women		
	Pernicious Anaemia		Corresponding Weighted Controls	Pernicious Anaemia		Corresponding Weighted Controls
	No.	%	%	No.	%	%
O	167	42·7	47·4	323	44·7	48 0
A	180	46·0	40·4	323	44·7	39·7
B	34	8·7	9·0	52	7·2	9·2
AB	10	2·6	3·1	25	3·4	3·1
Total	391			723		

Summary

The combination of data from a number of centres shows with fairly high significance that pernicious anaemia is commoner in persons of Group A than in persons of Group O, and also perhaps, though the numbers are small, than in persons of group B. The greater incidence in group A appears in both sexes.

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In the recently published Annual Report of the General Board of Control for Scotland for the year 1955 (H.M.S.O., price 1s. 6d.), it is stated that more people are seeking psychiatric help at an earlier stage of mental illness. During 1955 the total number of patients under treatment for mental illness in Scotland was 21,242, 80 fewer than at the end of 1954, but the number admitted to hospital was 9,168, 657 more than in 1954. Of that number 2,583 were certified patients and 6,585 were voluntary patients, the latter figure being an increase of 723 over the previous year. On the other hand, the number of discharges both of certified and of voluntary patients increased substantially, the figures being 1,481 and 5,718 respectively. 241 patients were allowed out on probation from mental hospitals during the year: of these, 123 were discharged at the end of their probation period, 95 were sent back to institutions, 22 were transferred to guardianship in private dwellings, and 3 died. Seven deaths occurred from suicide among hospital patients and 52 died as a result of accidents. The total number of certified mental defectives was 8,065, or 207 more than at the end of 1954. Of that number 5,513 were patients in institutions and 2,552 were under guardianship. The Board comments that all but one of the mental hospitals in Scotland were built more than 50 years ago, but much is being done to make these institutions more cheerful.