THE RELATION OF THE BLOOD GROUP OF THE INDIVIDUAL TO BLOOD DISEASES AND NEOPLASMS

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It is unfortunate that unless some obvious difficulties can be surmounted little or no conclusions can be drawn from any work of this nature. In the first place it is necessary to have accurate diagnosis; secondly, to examine and test a very large series of cases; and, thirdly, the tests must be free from error, either in the technique employed or in the interpretation of the results. The results themselves must be carefully tabulated and recorded.

It is readily understood that such work as this can only be undertaken at large treatment centres, and that the observers must have sufficient time, amounting to years, and infinite patience. Alternatively, small groups of observers from the medical field of the entire world could collect their results and by pooling their material get sufficient data from which to draw conclusions. It is in the latter respect that this small contribution is offered. Perhaps some indication of the probable direction of the results is here presented.

The Auto-agglutination Factor

The blood grouping itself, and especially in so far as Group AB (Moss I) is concerned, must be done accurately. Factors such as the presence of auto-agglutination may mask the true group of the individual case. To eliminate such possible error all cases showing doubtful grouping were retested, often several times. The blood cells of the patient before testing against the stock sera were washed thoroughly in normal saline. In such cases, also, the cells of known groups were tested against the patient's sera. This precaution was taken particularly in the case of patients whose blood fell into Group AB (Moss I). In some few cases even with all these precautions the blood group was indeterminate.

In the cases which showed auto-agglutination—notably those suffering from gross anaemia, either of a primary nature or secondary on a neoplastic state—under the aforesaid conditions, it was proved, usually without difficulty, that the patient was either a true Group AB (Moss I) or alternatively some other group.

Case 1.—W. C., a male suffering from a leukaemic condition of his blood, was an auto-agglutinator with apparent agglutination in the stock sera. The cells after being thoroughly washed showed no agglutination in the stock sera, the patient of course falling into Group O (Moss IV).

Case 2.—Mrs. C., suffering from pernicious anaemia, was also an auto-agglutinator and apparently a Group AB (Moss I), but turned out to be a Group A (Moss II) on washing her cells. This was confirmed by testing known cells against her serum, and was reconfirmed easily when the patient recovered later from her severe anaemic condition as the auto-agglutination formerly present had disappeared.

It was noted in those patients who recovered from their severe anaemic condition that the auto-agglutination which had been present invariably disappeared. Their blood groups were then readily determined. It was also observed in those cases in which this phenomenon of auto-agglutination had disappeared on recovery or improvement, and in which the original sera, stocked when the auto-agglutinating properties were evident, had been kept, that the washed cells taken from the patients after their recovery showed neither agglutination in the fresh sera taken simultaneously nor in the original sera. This was noted in Case 2 above and also in Case 3.

Case 3.—Mrs. S., suffering from a haemolytic anaemia, was a marked auto-agglutinator and a Group AB, proven after taking the customary precautions. Following splenectomy the patient's condition improved, and she lost the power of auto-agglutination. She was regrouped, and was found to be a true AB. Fresh blood cells taken after the improvement did not agglutinate either in her fresh serum, taken simultaneously, or in her original serum, taken when she showed the auto-agglutination.

This auto-agglutination, due to pseudo-agglutination—that is, to a deformation and exaggeration of the rouleau-forming power of the blood—and essentially related to the sedimentation time of the red blood corpuscles as has been already definitely established, is obviously from the observations in Cases 2 and 3 mainly a corpuscular phenomenon, and only secondarily related to the patient's sera. The fresh cells taken from the blood of the patients, whose condition had improved sufficiently for the auto-agglutination to have entirely disappeared in the fresh sera taken simultaneously, were apparently not agglutinated in the original sera stocked when the phenomenon was evident—a fact that would indicate the cellular origin of the phenomenon. On the other hand it was noted, in the same cases which showed this auto-agglutination and in which the cells were thoroughly washed several times in saline, that they reacted accordingly to the true group of the individual in the stock sera A, B, O, when, previously unwashed, they were apparently agglutinated in all three stock sera, thus giving the impression that the group was an AB; also that the same washed cells were again auto-agglutinated in the sera of the corresponding patients. From this it may be observed that:

(*a*) The unwashed cells were apparently agglutinated in all three stock sera.

(*b*) Washed, they were not agglutinated in any of the stock sera if an O—and only in the appropriate sera if an A or B, and in all of course if the patient happened to be a true Group AB.

(*c*) The same washed cells on retesting against the corresponding auto-agglutinating patient's serum showed again this auto-agglutination.

This latter occurrence would lead one to believe that the serum had at least some part in the phenomenon in those cases. On the other hand, it has been shown that on diluting this serum through increasing dilutions the auto-agglutination became negligible in comparison with the continued agglutination in a genuine agglutinating serum, progressively diluted on a similar scale.

Analysis of the Blood Disease Categories

For the purpose of this work the blood diseases were observed in three categories and the individual blood group tabulated in the appropriate category. Other blood conditions such as haemophilia, purpura, polycythaemia, agranulocytosis, etc., were grouped also, but as so few cases of these were obtainable they were not included. In the latter diseases the groups of those tested were, with the exception of one B, entirely A's or O's.

The first category had the largest number of cases, and mainly consisted of pernicious anaemia. Of the 228 cases tested seventeen were of the achrestic and eighteen of the aplastic type of anaemia.

In the latter two types of anaemia two of Group AB were noted, one to each type, and in the aplastic type one

Diseases	Moss : IV			III		II		I	
	International Grouping : O			B		A		AB	
	No. of cases	Abs.	%	Abs.	%	Abs.	%	Abs.	%
(a) *Blood Diseases :*									
(i) Pernicious anaemia	193	80	41.45	25	12.95	75	38.9	13	6.7
Achrestic „	17	9	—	—	—	7	—	1	—
Aplastic „	18	11	—	1	—	5	—	1	—
Category (i), total cases	228	100	43.85	26	11.4	87	38.15	15	6.6
(ii) Haemolytic anaemia	65	30	46.2	6	9.2	26	40	3	4.5
Categories (i) and (ii), total cases	293	130	44.36	32	10.92	113	38.56	18	6.14
(iii) Leukaemias	24	12	50	3	12.5	8	33.3	1	4.2
Total blood diseases, categories (i), (ii), and (iii)	317	142	44.8	35	11	121	38.2	19	6
(b) *Neoplasms :* (i) Carcinomata	92	49	53.3	9	9.8	30	32.6	4	4.3
(ii) Sarcomata	15	9	—	—	—	6	—	—	—
(iii) Intracranial group of neoplasms and a few others Cerebellar tumours	16	7	—	2	—	7	—	—	—
Cerebral tumours	196	99	50.5	18	9.2	75	38.3	4	2
Meningioma	18	9	—	1	—	7	—	1	—
Acoustic and other neuromata	23	11	—	2	—	9	—	1	—
Other tumours and spinal tumours	40	16	—	3	—	20	—	1	—
Total	293	142	48.46	26	8.87	118	40.27	7	2.38
Pituitary tumours	61	29	47.6	3	4.9	26	42.6	3	4.9
Total category (iii)	354	171	48.3	29	8.2	144	40.7	10	2.8
Total categories (i), (ii), and (iii)	461	229	49.7	38	8.3	180	39	14	3
Normal for the hospital, calculated from 1,927 consecutive cases grouped	1,927	939	48.72	148	7.68	792	41.1	48	2.49

Group B was found. Fifteen of Group AB and twenty-six of Group B were included in this series of 228 cases. The remainder were 100 Group O and eighty-seven Group A. The percentages of this series were thus: O, 43.85; B, 11.4; A, 38.15; AB, 6.6. The cases of pernicious anaemia alone numbered 193, and showed 41.45 per cent. of Group O, 12.95 per cent. of B, 38.9 per cent. of A, and 6.7 per cent. of AB.

It is seen that Groups O and A approach one another very closely, Group A remaining roughly about the normal 41 per cent. and, if anything, a degree or two under (the normal figures for the hospital are given in the table). Group O is well below the normal, 48 per cent. It is also noted that the rarer Groups AB and B are higher in numbers and percentages than normal—Group B almost twice and Group AB thrice the normal percentage. It was also noted clinically that in the latter groups the severest manifestations of the blood diseases often were generally evident. From this high incidence of the Groups AB and B in the blood diseases dealt with in this article one would like to make the statement that people falling into those blood groups are more susceptible to those diseases than people in the other groups, but, of course, to do so and to eliminate the element of coincidence would require much more intensive examination of a very large series of cases—into the thousands or tens of thousands if possible.

In the second category only sixty-five cases were available. This category included those diseases diagnosed as haemolytic anaemias of various types, acquired or hereditary (acholuric jaundice, etc.), with corresponding blood abnormalities, and with or occasionally without an enlarged spleen. A similar type of percentage chart to the above was again observed, but the similarity was not so marked. The figures were 46.2 per cent. of Group O, 9.2 per cent. of B, 40 per cent. of A, and 4.5 per cent. of AB.

The third category, and the smallest, included the leukaemias (lymphatic, myelogenous, and monocytic types, chronic or acute). In all only twenty-four cases were available. Among those were three of Group B and one of Group AB. The proportions were 50 per cent. of Group O, 12.5 per cent. of B, 33.3 per cent. of A, and 4.2 per cent. of AB.

The latter percentages are strikingly like those given by the series of carcinomata grouped. On this observation one would like to conjecture some association between those two classes of disease—but of course that would be ridiculous on such small evidence. A point which should perhaps be made here is that in the hospital in which this work was done the proportion of cases of blood diseases may be higher than in the average general hospital.

The Neoplasms

The neoplasms were also treated in three categories; the last, the biggest, was included because of the large numbers of cases of intracranial tumours available which were grouped, in the majority pre-operatively.

The first category included the carcinomata, and ninety-two cases were grouped. There were 53.3 per cent. of Group O, 9.8 per cent. of Group B, 32.6 per cent. of Group A, and 4.3 per cent. of Group AB.

The second category included the sarcomata, but only fifteen cases of the latter were available. These were nine of Group O and six of Group A.

The third category included the intracranial group and some others. The tumours were either non-malignant types—that is, meningioma, acoustic tumours, pituitary adenoma, non-malignant glioma, etc.—or occasional malignant types.

A few spinal tumours, etc., of various types, and others were also included. There were 354 cases of known intracranial neoplasms grouped, sixty-one of which were pituitary tumours and were dealt with separately.

The latter pituitary group gave 47.6 per cent. of Group O, 4.9 per cent. of Group B, 42.6 per cent. of Group A, and 4.9 per cent. of Group AB.

The percentages of the larger remainder were 48.46 of Group O, 8.87 of Group B, 40.27 of Group A, and 2.38 of Group AB.

The combined percentages of the whole 354 cases were 48.3 of Group O, 8.2 of Group B, 40.7 of Group A, and 2.8 of Group AB.

Conclusion

In conclusion it was noted that of all the cases grouped in the hospital over the same period, in the instance of the blood diseases:

(*a*) 15.12% of all Group O were blood diseases
(*b*) 15.27% „ „ A „ „ „
(*c*) 23.65% „ „ B „ „ „
(*d*) 39.58% „ „ AB „ „ „

Similarly in the case of the neoplasms it was noted that:

(*a*) 24.38% of all Group O were neoplasms
(*b*) 22.72% „ „ A „ „
(*c*) 25.67% „ „ B „ „
(*d*) 29.16% „ „ AB „ „

It will be seen by these figures that only 31.26 per cent. of Group AB and 50.68 per cent. of Group B were diseases other than blood diseases or neoplasms, in comparison with 60.5 per cent. of Group O and 62 per cent. of Group A. It will be also observed how the neoplasms remained a steady 22 to 29 per cent. of each group, whereas in the blood diseases the A's and O's were about 15 per cent. and the B's and AB's were again strikingly high in comparison—23 per cent. and 39 per cent. respectively.

Summary

1. Before any conclusions can be formed as to the relation of the blood group of the individual to a particular disease the facts and figures from a very large selection of cases must be examined.

2. This is only feasible if the observer or observers have the necessary time to spend on the laborious testing of these cases, which must be very accurately diagnosed to be of any statistical value.

3. It is more feasible, however, for a multitude of observers to note their findings regarding this relation of the blood group to the cases of any diseases at their disposal or to those of a particular disease in which they are interested, and, having collected their notes, to submit them to a common group of statisticians who could file the material. When sufficient data had been collected conclusions of probable interest and possible value might be derived from them.

4. For contrast as well as control purposes, cases from the two classes of diseases chosen for this article were blood-grouped. Some interesting figures were noted.

5. Whereas for general purposes the total percentages of blood groups of the cases of neoplasms grouped were roughly within normal limits, it was noted, on the other hand, that there was a strikingly high incidence of blood diseases in the blood groups B and AB. It was also noted that many of the severest cases of the blood diseases fell into those latter blood groups.

6. Several cases in which auto-agglutination was present were grouped, and it was interesting to note one or two points about this phenomenon.

7. One would have liked to have more time to spend, and a larger number of cases at one's disposal, in order that some definite ruling as to the ultimate direction of those figures could be established.

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Clinical Memoranda

Pre-eclamptic Symptoms following Successful Hormone Treatment of Sterility

The following case appears to be sufficiently interesting to warrant being placed on record.

The patient was a married woman of 26, suffering from menstrual irregularity, the cycle being lengthened to forty-two days. The flow when it appeared was excessively scanty and lasted only one or two hours. The condition was accompanied by signs of hormone deficiency such as vasomotor instability and psychic depression, and by sterility.

On examination keloid scars were observed on the knee and abdomen. The uterus was found to be normal in size, but the right ovary was very tender and had prolapsed. The distribution of bodily hair was normal, but during the last six months the patient had inclined to the male type: the breasts had become smaller and the female fullness about the hips had been lost. She had marked sexual frigidity. Her weight was decreasing.

It was decided to treat the patient with the follicular hormone progynon-B oleosum (Schering) according to the following scheme: an injection of 10,000 I.B.U. to be given on the first day after menstruation had ceased, followed by one on the seventh and the thirteenth, and, finally, on the nineteenth day the injections to be supplemented by oral administration of one dragée four times daily during the intermenstruum. It was decided to allow an interval in injection treatment until the next menstruation was over and then to repeat the course.

The previous period had been on March 6, 1936, and lasted for about three hours. Following treatment a period was obtained on April 12 lasting one and a half days, followed by another on May 25 which lasted three days. On June 23, 1936, the patient had a perfectly normal period, and she stated that it was the first she had had for some years. Treatment was also successful in producing normal development of the breasts, the patient becoming more feminine in appearance. The frigidity disappeared. The sterility was also overcome, and the patient became pregnant in July. Treatment was then suspended. On March 13, 1937, the patient complained of a swollen face and headaches. There was no albumin in the urine, and the blood pressure was normal.

On March 15 her condition became much worse. There was marked swelling of the face and ankles, and traces of albumin in her urine, and for the first time she complained of spots before the eyes, with difficulty in vision: clinically a typical late pre-eclamptic picture. Her headaches were worse,