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STUDIES ON THE HEREDITY OF THE HUMAN BLOOD GROUPS II. THE A-B-O GROUPS [1]

by

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In a previous paper [1] was summarized the investigations by the senior author and his collaborators on the heredity of the M-N types during the period 1929 to 1952. The purpose of the present paper is to summarize the studies on the heredity of the A-B-O groups carried out during the same period of time.

In table 1 are presented previously unpublished studies on the heredity of the A-B-O groups, carried out during the years 1949 to 1952. It will be seen that no exceptions were encountered to Bernstein's theory of inheritance. In table 2 are summarized those families in which the subgroups of A were determined. It will be noticed that table 2 lists a total of only 625 children as compared with 649 children in table 1. The reason for this is that the subgroups of A cannot be determined reliably in newborn infants, so that such children had to be omitted from the calculations. To date all attempts to produce anti-A_1 serum of high titer and specificity have been of no avail. The reagents which have been available for these tests have rarely exceeded 10 units in titer, and lack the high avidity and specificity exhibited by satisfactory anti-A and anti-B reagents. Therefore, even though no exceptions to the genetic theory were encountered in the present study, the subgroups of A are not considered by us to be sufficiently reliable to be applied in medicolegal problems of disputed parentage.

In table 3, we have summarized all the studies on the heredity of the A-B-O groups carried out in this laboratory during the period 1929 to 1952. Among 3,398 children there were only two contradictions to Bernstein's theory, both of which were apparently due to illegitimacy. Of special interest are the families in which one or both parents belong to group AB. In the mating $O \times AB$ half the children would be expected to belong to group A and half to group B; the deviation, 13.7±4.9 percent, is less than three times its probable error and therefore not significant statistically. In the mating $A \times AB$ 50 percent of the children would be expected to belong to group A, while in the mating

B × AB 50 percent would be expected to belong to group B; the actual observed frequencies agree closely with the expected value. In the mating AB × AB, the number of children tested is too small to permit statistical analysis. All in all the observations in this large number of families agree satisfactorily with Bernstein's multiple allele theory of inheritance.

Comment

While tests for the four A-B-O groups have been applied in courts of law for more than 3 decades in problems of disputed paternity, tests for the subgroups of A are not considered sufficiently reliable for medicolegal use. The subgroups of A have been known since 1910, so that this position is not based merely on lack of experience or lack of in-

Table 1 - Heredity studies on the A-B-O groups (1949-1952)

Parental combination	Number of families	Number of children of types				Total
		O	A	B	AB	
O × O	78	122	0	0	0	122
O × A	134	88	120	0	0	208
O × B	55	34	0	42	0	76
A × A	61	18	71	0	0	89
A × B	45	17	21	16	18	72
B × B	6	1	0	8	0	9
O × AB	22	0	10	27	0	37
A × AB	18	0	13	6	6	25
B × AB	7	0	3	5	3	11
Totals	426	280	238	104	27	649

formation. As has been pointed out, the main difficulty has to do with the testing sera, because the best anti-A_1 sera that have been produced to date have all been of low titer, specifity and avidity. As a result, when testing the blood of newborn infants where the agglutinability of the red cells is low, the reactions are generally indistinct and blood of subgroup A_1 may fail to react with the anti-A_1 reagent. Even in older children and adults difficulty in determining the subgroups of A may be encountered, especially when testing blood of group AB. In the presence of agglutinogen B the agglutinability of the cells by anti-A_1 serum is reduced, so that blood of subgroup A_1B may be mistaken for subgroup A_2B. The difficulties are further magnified by the existence of bloods giving reactions intermediate between A_1 and A_2, namely, the so-called subgroup $A_{1,2}$. Blood of subgroup $A_{1,2}$ is especially difficult to distinguish from subgroup A_2B. Blood of the intermediate subgroup $A_{1,2}$ is rare among Caucasoids, but is not infrequent among Negroids.

The existence of the subgroups of A has also been responsible for errors in tests

for the four common A-B-O groups. The agglutinability of group AB cells by anti-A serum is lower than that of group A cells, and this is especially noticeable in subgroup A_2B. Thus, it is not unusual for blood of subgroup A_2B to be incorrectly classified as group B, especially if the serum (or plasma) is not tested for its isoagglutinin content to confirm the blood grouping tests. Two cases have come to our attention in which men were incorrectly excluded as the fathers of children, because of such an error. In both cases the putative father was reported to belong to group B, the mother to group O, and

Table 2 - Heredity studies on the subgroups A

Parental combination	Number of families	Number of children of group						Total
		O	A_1	A_2	B	A_1B	A_2B	
$O \times O$	78	122	0	0	0	0	0	122
$O \times A_1$	99	73	75	7	0	0	0	155
$O \times A_2$	30	15	0	25	0	0	0	40
$O \times B$	55	34	0	0	42	0	0	76
$A_1 \times A_1$	40	12	41	2	0	0	0	55
$A_1 \times A_2$	18	5	12	7	0	0	0	24
$A_2 \times A_2$	3	1	0	3	0	0	0	4
$A_1 \times B$	37	14	13	1	12	17	0	57
$A_2 \times B$	8	3	0	3	4	0	1	11
$B \times B$	6	1	0	0	8	0	0	9
$O \times A_1B$	19	0	9	0	24	0	0	33
$O \times A_2B$	3	0	0	1	3	0	0	4
$A_1 \times A_{1,2}B$	1	0	0	0	1	0	0	1
$A_1 \times A_1B$	10	0	7	0	4	2	2	15
$A_1 \times A_2B$	2	0	1	0	0	0	1	2
$B \times A_1B$	6	0	2	0	3	3	0	8
$A_2 \times A_1B$	5	0	5	0	1	0	1	7
$B \times A_2B$	1	0	0	0	2	0	0	2
Totals	421	280	165	49	104	22	5	625

the child to group A. However, on retesting the blood specimens we found that both men belonged to group AB, subgroup A_2B, and the children to the subgroup A_2. In one of these cases, a tragedy was narrowly averted by the timely discovery of the error. It should be pointed out that ordinary clinical pathologists who had undertaken to perform these tests were responsible for the errors made in these two cases, and this serves to demonstrate once more how important it is that these test be carried out only by qualified specialists.

An interesting sidelight is the recent application of the blood tests by the United States Immigration Department. As a result of the war in Asia, there are many Chinese refugees in Hong Kong trying to enter the United Stated, who claim to have parents in the United States who are citizens. Limiting the tests merely to the A-B-O and M-N systems,

in as many as 35 percent of the cases it has been possible to exclude paternity or maternity, and an official of the department estimates the number of fraudulent applications for entry into the United States to be as high as 85 percent. In connection with this work, the importance of permitting only qualified experts to perform the tests again became evident. In two cases where previous investigators had excluded parentage, the people involved requested another examination, and we found that errors had been made in the M-N tests so that there actually was no exclusion of parentage.

Table 3 - Heredity studies on the A-B-O groups [2] (1929-1952)

Parental combination	Number of families		Children of groups				Total
			O	A	B	AB	
O × O	278		632	(1) [3]	0	0	633
O × A	535		493	705	0	0	1198
O × B	188		167	0	200	0	367
A × A	251		96	415	0	0	511
A × B	141		67	81	70	75	293
B × B	29		15	0	45	0	60
O × AB	74 {	Number	0	49	86	0	135
		Percent	0	36.3 ± 4.9	63.7 ± 4.9	0	
A × AB	69 {	Number	0	78	25	47	150
		Percent	0	52.0 ± 2.7	16.7	31.3	
B × AB	21 {	Number	(1)	12	25	7	45
		Percent	0.2	26.6	56.6 ± 4.8	16.6	
AB × AB	4 {	Number	0	1	1	4	6
		Percent	0	16.7	16.7	66.6	
Totals	1590 {	Number	1471	1342	452	133	3398
		Percent	43.3	39.5	13.3	3.9	100.0

Summary and conclusions

The results of studies on the heredity of the A-B-O groups in a new series of 426 families with 649 children are presented. No exceptions were encountered to the multiple allele theory of heredity of the A-B-O groups and subgroups of A. During the period 1929 to 1952, a total of 1590 families with 3398 children have been tested for the A-B-O groups and only two contradictions to the Bernstein theory of inheritance were encountered, both apparently due to illegitimacy. Statistical analysis reveals a satisfactory agreement between the observed frequencies of blood groups in the children and those

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[2] This table includes all the previous studies made by the authors and their collaborators, together with the results of the present study.

[3] These contradictions to the laws of heredity are apparently due to illegitimacy.

predicted under the theory of multiple alleles. While the A-B-O groups are reliable for medicolegal application in cases of disputed parentage, the subgroups of A should not be applied in such cases. The reason for this is that it has been impossible up to now to prepare anti-A_1 reagents of satisfactory titer, avidity, and specificity, comparable to anti-A and anti-B reagents which are available. As a result, subgrouping tests, particularly of newborn babies, do not give entirely reliable results.

References

1. WIENER, A. S., DI DIEGO, N., and SOBOL, N.: *Studies on the heredity of the human blood groups.* I. The M-N types. Acta Genet. Med. et Gemellol., (1953) 2: 391-398.

RIASSUNTO

Vengono presentati i risultati di studi che riguardano l'eredità dei gruppi A-B-O sopra una serie di 426 famiglie e con 649 figli. Non si verificano eccezioni alla teoria dell'eredità degli alleli multipli dei gruppi A-B-O e dei sottogruppi di A. Durante il periodo 1929-1952 un totale di 1590 famiglie comprendenti 3398 figli furono sottoposte alle ricerche per i gruppi A-B-O; non si riscontrarono che due contraddizioni alla teoria di Bernstein e ciò si deve probabilmente ad illegittimità. L'analisi statistica indica un sufficiente accordo delle frequenze dei gruppi sanguigni presso i figli con quelle previste dalla teoria degli alleli multipli. Benchè i gruppi A-B-O diano sicurezza per l'applicazione medicolegale in casi di discendenza contestati, i sottogruppi di A non devono essere utilizzati in tali casi perchè finora non è stato possibile preparare dei reattivi anti-A di titolo, avidità e specificità sufficienti, tali da essere paragonati ai reattivi anti-A e anti-B attualmente disponibili; di conseguenza le determinazioni dei sottogruppi, in particolare presso i neonati, non danno risultati del tutto sicuri.

RÉSUMÉ

On présente les résultats d'études concernant l'hérédité des groupes A-B-O sur une série de 426 familles ayant 649 enfants. Il n'y a pas eu d'exceptions à la théorie d'hérédité des allèles multiples des groupes A-B-O et des sous-groupes de A. Pendant la période de 1929 à 1952, un total de 1590 familles ayant 3398 enfants ont subi les épreuves pour les groupes A-B-O; il n'y a eu que deux contradictions à la théorie Bernstein, et celles-ci probablement à cause d'illégitimité. L'analyse statistique indique un accord suffisant entre les fréquences notées des groupes de sang chez les enfants et celles prédites d'après la théorie des allèles multiples. Quoique les groupes A-B-O soient sûrs pour l'application médicolégale en cas de parentage contesté, les sous-groupes de A ne doivent pas être employés dans de pareils cas, parce que jusqu'ici, il a été impossible de préparer des réactifs anti-A de titre, d'avidité, et de spécificité suffisants, comparables aux réactifs anti-A et anti-B actuellement disponibles. Par conséquent, les épreuves de sous-groupement, en particulier chez les nouveaux-nés, ne donnent pas de résultats absolument sûrs.

ZUSAMMENFASSUNG

Die Resultate des A-B-O Gruppen–Vererblichkeitsstudien in einer neuen Serie von 426 Familien mit 649 Kindern werden vorgeführt. Es wurden keine Ausnahmen zur Mehrallelentheorie der Vererbung in A-B-O Gruppen und A-Untergruppen vorgefunden. Während der Jahre 1929-1952 wurden insgesamt 1590 Familien mit 3398 Kindern auf A-B-O Gruppen untersucht. Es wurden jedoch nur zwei Widersprüche zur Bernstein Vererbungstheorie vorgefunden, beide scheinbar auf Unehelichkeit zurückzuführen. Die statistische Analyse zeigt eine befriedigende Uebereinstimmung zwischen der beobachteten Blutgruppenhäufigkeit in Kindern und derjenigen die durch die Mehrallelentheorie vorausgestellt wurde. Jedoch, während die A-B-O Gruppen für medizinisch-rechtliche Fälle bestrittener Paternität zuverlässig sind, sollten die A-Untergruppen in solchen Fällen nicht angewendet werden. Der Grund dafür ist das es bis jetzt unmöglich gewesen ist, Anti-A1 Reagenzien befriedigender Avidität, Titer und Spezifität herzustellen, im Vergleich zu den Anti-A und Anti-B Reagenzien, die zur Verfügung stehen. Deswegen geben Untergruppenuntersuchungen, besonders mit neugeborenen Kindern, noch keine vollständig zuverlässigen Resultate.