Acta Genet Med Gemellol 30:289-292 (1981)
The Mendel Institute/Alan R. Liss, Inc.

Received 13 July 1979
Final 10 September 1981

Short Note

Isoagglutinin Levels in Twins and Families.

A Study of the Inheritance of Naturally Occurring Antibodies in Human Serum

S. Agrawal[1], V. Bhalla[2]

[1]*Genetics Unit, Department of Medicine, K.G.'s Medical College, Lucknow;*
[2]*Department of Anthropology, Punjab University, Chandigarh*

Anti-A and anti-B titers were measured in 60 twin pairs and their families. Family data shows high correlations of antibody titer values for first degree relatives but no significant spousal correlations.

Key words: Antibody levels, Twins, Genetics

Some of the factors known to influence antibody titre are age [19], heredity [4], allergic conditions [3], environment [20], immunological tolerance [11], blood groups [10], pregnancy [21], and sex [16].

In this paper, an attempt is made to reexamine the view that anti-A and anti-B titers are under genetic control.

MATERIALS AND METHODS

Antibody titers of 60 pairs of twins and their family members were quantified by the standard technique as described by Moore et al [14]. Families with parental combinations A × B, AB × AB, AB × A, AB × B, and AB × O have not been considered as these combinations were either not represented or their number was inadequate. Twin pairs with A × B, AB × AB, AB × A, AB × B, AB × O, and unlike sexed DZ twins were also not considered for statistical analysis. The serum samples were stored at 50°C. Fresh group A and B cells collected in ACD solution from the same donor were used for titrating the antibodies. Zygosity of twins was established on the basis of ABO, MN, Rh, Kell, Duffy blood group systems, phenythiocarbamide tasting ability, ABH secretion, somatoscopic observations, and dermatoglyphics. The age of the children tested ranged from 5 to 25 years. The titers were corrected for age by correlation analysis.

RESULTS

Estimates of total variability and within and among twin-pair estimates of genetic variance have been calculated after Christian et al [5]. The mean square estimates and P values

0001-5660/81/3004-0289$01.50

are shown in Table 1. The heritability estimates (anti-A = 0.8494, anti-B = 0.6297), calculated utilizing intraclass correlation coefficients, show that variations in antibody titer have an important hereditary component. Differences in the heritability estimates of anti-A and anti-B may well be chance variations due to small sample size.

The correlation coefficients of antibody titer index were computed for MZ twins, DZ twins, offspring-midparent, sibs, and husband-wife. The antibody titer was found to be significantly correlated ($P < 0.05$) for both anti-A and anti-B in all categories of blood relatives. However, nonsignificant correlation coefficients were recorded for husband-wife combinations (Tables 2 and 3).

DISCUSSION

Observations made on experimental animals [17,18] and human subjects with immunological disorders [2,12], as well as findings of population studies [6,8,9,13,15,16,19] suggest that the quantitative nature of antibody responsiveness has an important hereditary component. Additional information to test the hypothesis of genetic participation in the

TABLE 1. Among and Within Twin-pair Mean Squares, Estimates of Genetic Variance and P Values for Anti-A and Anti-B Titers

	Mean squares						
	Within pair		Among pair				
Variables	MZ	DZ	MZ	DZ	Estimates of genetic variance		P
Anti-A	5.5	13.2	146.8	39.5	GWT	7.7	<0.05
					GAC	57.5	<0.05
Anti-B	5.0	24.5	139.2	51.0	GWT	19.5	<0.01
					GAC	53.8	<0.05

TABLE 2. Correlation Coefficients for Anti-A

	Number of pairs	r	t	P
MZ twins	12	0.9339	8.2605	<0.05
DZ twins	17	0.5611	2.6226	<0.05
Sibs	35	0.4990	3.0379	<0.05
Mid parent-child	26	0.6946	4.7309	<0.05
Husband-wife	26	0.1227	0.6057	>0.05

TABLE 3. Correlation Coefficient for Anti-B

	Number of pairs	r	t	P
MZ twins	9	0.8545	4.3525	<0.05
DZ twins	13	0.6071	2.5342	<0.05
Sibs	32	0.5053	4.1659	<0.05
Mid parent-child	23	0.7677	5.4912	<0.05
Husband-wife	23	0.1053	0.4857	>0.05

regulation of antibody responsiveness may be provided by an examination of intrafamilial patterns of antibody levels. It is evident from the results of our study that isoagglutinin levels reflect a definite familial pattern. It was observed that titers of both anti-A and anti-B are significantly correlated among blood relatives. The lowest correlation coefficients were recorded in husband-wife combinations and the highest in MZ twins, strongly indicating the existence of hereditary factors controlling the quantitative nature of antibody responsiveness. Our observations lend support to the view [7] that the titer of group-specific isoagglutinins alpha and beta are under genetic control. However, the contention [7] that higher titer is inherited recessively is not corroborated by the findings of the present study. The antibody titer would rather appear to be under the control of several genes, whose individual effects may be small but which act in a cumulative manner, producing the characteristic quantitative differences that can be measured on a continuous scale, as is also confirmed by the fact that the population distribution of the titer follows a normal curve [16].

In dealing with quantitative characters, such as the synthesis of immunoglobulins, it is impossible to completely isolate the role of the genotype from that of the environment. It has been argued [1] that the environment (in the form of antigenic stimulation) determines which type of antibody will be made, but that heredity plays a significant role in determining how much antibody should be made. There seems to be an innate genetic potential, which determines the optimum level of isoagglutinins that can be reached in an individual, subject to his receiving adequate antigenic stimulation. Variations in antibody level would thus be a combined effect of the hereditary and environmental factors that come into play.

REFERENCES

1. Allansmith M, McClallan B, Butterworth M (1969): The influence of heredity and environment on human immunoglobulin levels. J Immunol 102:1504–1510.
2. Barth WF, Asofasky R, Liddy TO, Tanka Y, Rowe DS, Fahay JL (1965): An antibody deficiency syndrome. Am J Med 39:319–334.
3. Callende ST, Sheila TE, Race RR (1946): Cited by Prokop O and Uhlenbruck G.
4. Carlinfenti E (1948): The predisposition of immunity. J Immunol 59:1–7.
5. Christian JC, Kang KW, Norton JA (1974): Choice of an estimate of genetic variance from twin data. Am J Hum Genet 26:154–161.
6. Furuhata J, Matsunaga E (1952): Studies on the heredity of the group specific isoagglutinins in human normal serum. V. Proc Jpn Acad 28:456-458.
7. Furuhata J, Eguchi N (1955) : The change of agglutinin titer with age. Proc Jpn Acad 31:555–557.
8. Grundbecher FJ (1976): Genetics of anti-A and anti-B levels. Transfusion 16:48–55.
9. Hollingsworth JW, Hamilton HB, Beebe GW, Yamasaki M (1961): Blood group antibody levels in Hiroshima. Blood 17:462–473.
10. Ichikawa Y (1959): A study of the isoagglutinin titer in the Sera of Australian subjects (white). Jpn J Med Sci Biol 12:1–7.
11. Jakobowicz R, Crewford H, Graydon JJ, Pinder M (1959): Immunological tolerance within the ABO blood group system. Br J Haematol 5:232–244.
12. Leonhardt T (1957): Familial hypergammaglobulinemia and systemic lupus erythematosus. Lancet 2:1200–1203.
13. Linhard J (1953): Taux des isoagglutinines anti-A at anti-B chez les noirs Africians de la région de Dakar. Rev Hamatol 8:171–182.
14. Moore BPL, Humphreye P, Lowett MCA (1972): Serological and immunological methods: The Technical Manual of the Canadian Redcross Blood Transfusion Service. Canadian Redcross Society, Toronto-5.
15. Renkonen KC (1946): Sind die Isoagglutinintiter erblich bendingt? Acta Path Microbiol Scand 23:549–551.
16. Roy S, Bhalla V (1979): Blood group isoagglutinin levels in males and females. J Ind Anthropol Soc 14:167.

17. Sang JH, Sobey WR (1954): The genetic control of responses to antigenic stimulus. J Immunol 72:52–65.
18. Scheibal JF (1943): Hereditary differences in the capacity of guinea pigs for the production of diphtheria entitoxin. Acta Path Microbiol Scand 20:465–484.
19. Thomsen O, Kettel K (1929): Die Starke der menschlichen Isoagglutinine und entsprechenden Blutkorperchenrezeptoren in verschliedenen Lebensaltern. Z Immunitatsforsch 63:67–93.
20. Tovey LDA, Taverner JM, Longstera GH (1970): The effect of environment on ABO antibodies. Vox Sang 19:64–72.
21. Zuelzer WW, Kaplan E (1954): ABO heterospecific pregnancy and hemolytic disease. Am J Dis Child, 86:158–192.

Correspondence: Dr. S. Agrawal, C-272, Nirala Nagar, Lucknow, UP, India.