78. B_x , Another Allele of the ABO Locus and its Heredity

By Hideo YAMAGUCHI,^{*)} Yasuto OKUBO,^{*)} Fumio
HAZAMA,^{*)} and Shizuo OYAMA^{**)}

(Comm. by Tanemoto FURUHATA, M.J.A., May 9, 1964)

Since June 1962, the authors have examined about 80,000 blood specimens and typed them at the request of the welfare authorities of the Prefectural Office of Osaka. Among the samples were 18 weak B and 6 weak A bloods, besides some A_2 group bloods. We have in the literature several examples of the so-called B_x or B_m blood type, all from the Japanese people.¹⁾⁻⁶⁾

However, the genetics of this blood type has not been determined. In this paper we present 3 families including 18 individuals either of B_x or of AB_x blood type that were discovered in the course of this work. All the families are natives of Osaka and its suburbs, Japan.

Serological Findings. To ordinary blood typing procedures the B_x blood appears as of the group O missing anti-B antibody, and AB_x blood appears as of the group A devoid of anti-B antibody. So, we made various attempts, such as treatment with enzymes (bromelin and ficin) and indirect Coombs' test to enhance the affinity of the cells to anti-B, using several high-titered sera. But the cells were not agglutinated.

As was to be expected, the B_x and AB_x cells absorbed much less anti-B than did normal B red cells, but the eluates from the B_x cells contained more antibody than did eluates prepared from the normal B blood. This paradoxical finding of greater activity of eluates prepared from the weak B blood had been pointed out by Levine *et al.*⁷⁾ This effect did not occur to the eluates from the AB_x cells. Only one of the 39 O-group sera (anti-A+B) tested, agglutinated these cells on the slide test.

The B_x cells showed nearly the same activity as normal O cells with anti-H (eel and *Ulex europaeus* extract), though the AB_x reacted at a slightly lower titre. Similar observation has been made by several investigators on the weak B and A cells.⁵⁾⁻⁸⁾

All the sera from the B_x individuals contained normal anti-A antibody, but neither anti-B nor any atypical antibody was detected. The sera from the AB_x group blood were devoid of antibody of any kind.

Tests for the B-substance in sera on some of the picked-up

^{*)} The Osaka Red Cross Hospital, Osaka Red Cross Blood Bank.

^{**)} Public Health Centre of Tondabayashi, Osaka.

materials indicated that the B_x and AB_x sera contained this substance in a somewhat smaller quantity, compared with the normal B group serum.

The B_x and AB_x individuals secreted in saliva as much B-substance as did the normal B individuals. The H-substance level in saliva of the B_x and AB_x individuals was as high as in the normal O-group individuals. The saliva of the non-secretors of the B_x individual (II-5 and III-1 of M. Family) contained a small amount of both B- and H-substance, indicating that the gene responsible for B_x is independent of the secretor gene.

From the above findings, it seems safe to conclude that the B_x (and AB_x) phenotypes reported here are to be classified serologically as a variant B belonging to the 2nd category of weak B (Race and Sanger, 1962)⁹⁾ in which no anti-B is present in serum but B- and H-substance are found in saliva.

In case it is preferable to designate this weak B in analogy to weak A, it may be better to use B_m , provided that the suffix "m" does not mean "modifying".

Pedigree Studies. 1) M. Family (Fig. 1): This is the largest of the 3 families and includes 13 individuals either of B_x or of AB_x type. In this family the B_x -gene was transmitted through 2 or 3 generations. There are two matings between AB_x and O individuals (II-1 $\times$ II-2 and II-6 $\times$ II-7) in which the genotypes of the progeny may be reasonably inferred.

Fig. 1. M. Family. Probable genotypes are shown in brackets.

II-5 has 8 children of whom 4 (III-8, 9, 10 and 12) exhibit the B_x phenotype, though their genotypes are unknown. It seems nearly certain that II-5 is B_xO , because she has two O children. From the fact that II-1 is AB_x , II-3 AB , II-5 B_xO , and II-7 AB_x respectively, the genotypes of their parents (I-1 and I-2) may be assumed as BB_x (I-1) and AO (I-2). A cousin of II-1-8, II-12, is also B_x .

Two of the B_x individuals (II-5 and III-1) were found to be non-secretors.

The analysis of this family indicates that the B_x blood type is due to an allele at the B locus and the genotypes B_xO and AB_x are manifested as of the B_x and AB_x type respectively. The phenotype of the genotype BB_x remains to be shown.

2) I. Family (Fig. 2): The propositus, II-4 has 3 children of phenotypes B(III-3), AB_x(III-4), and B(III-5). Her husband, II-3 is of the AB group, so, she had been suspected to belong to either B_xO or BB_x. Her sister, II-2 who has the normal B blood, married to a B group husband (II-1) and gave birth to 2 children (III-1, 2) both of the B_x phenotype. Since this B_x-gene should have been derived from the mother, she probably has the B_x-gene, even though she presented herself as a normal B individual, with nothing abnormal in her saliva.

Fig. 2. I. Family.

Although this pedigree is less extensive than M., it is a valuable one, as every example showing interaction of the B_x-gene against A-, B- or O-gene is represented, and it is demonstrated that the BB_x genotype is manifested as B phenotype, B_x-gene behaving as a recessive to the B-gene.

3) K. Family (Fig. 3): This family includes only one B_x member, (III-1). The course of transmission of this gene could not be followed in this pedigree, in spite of our effort using all available means to clarify this point. There was nothing striking other than that concerning the ABO system.

Four conjectures were made of the blood type of this individual, following some previous authors:— i) an allele of ABO,⁷⁾ ii) a recessive modifying gene of B,¹⁰⁾ iii) a new mutation, and iv) environmental effect on the manifestation of the normal ABO-genes, for instance, leukaemia.¹¹⁾⁻¹³⁾

Fig. 3. K. Family.

The last possibility was ruled out because, although we had kept the proband under observation for about 2 years, there were no changes in his blood nor in any other health condition.

If II-1, the proband's uncle, whose blood sample has not been available, has the B_x -gene, the third possibility would be ruled out.

For the present, it seems more reasonable to assume the first possibility — the proband has a rare allele of ABO system. The genotype of the proband's mother, II-3 is probably BB_x , though she appeared to have normal B blood.

Throughout these 3 families, the serological findings of all the B_x (and AB_x) individuals are nearly identical, if not exactly so. Accordingly, it seems to be warranted to conclude that the B_x and AB_x bloods reported here are due to another allele at the ABO locus.

Acknowledgements. The authors wish to offer their thanks to Dr. T. Furuhashi, Dr. T. Komai for their kind discussion and revision of this report and also to Dr. R. Kimura for his constant encouragement.

References

- 1) Yokoyama, M., Stacey, S. M., and Dunsford, I.: *Vox Sang.*, **2**, 348 (1957).
- 2) Yokoyama, M., Barber, M., and Dunsford, I.: *Juntendo Med. J.*, **5**, 273 (1959).
- 3) Hashimoto, Y., Ukai, A., Kano, S., Shirai, T., Ono, S., and Yokoyama, M.: *J. Jap. Soc. Blood Trans.*, **7**, 160 (1960).
- 4) Murakami, S., Tokunaga, E., Nagao, M., and Asanuma, T.: *J. Jap. Soc. Blood Trans.*, **8**, 181 (1961).
- 5) Kitahama, M.: *J. Jap. Soc. Blood Trans.*, **9**, 38 (1962).

- 6) Nakajima, H., Shikura, I., and Akabane, J.: J. Jap. Soc. Blood Trans., **9**, 39 (1962).
- 7) Levine, P., Celano, M., and Griset, T.: Proc. 6th Cong. Int. Soc. Blood Trans., 132 (1958).
- 8) Weiner, W., Lewis, H. B. M., Moore, P., Sanger, R., and Race, R. R.: Vox Sang., **2**, 25 (1957).
- 9) Race, R. R., and Sanger, R.: Blood Groups in Man. 4th ed. Blackwell Scientific Publications, Oxford (1962).
- 10) Kitahama, M., Yamaguchi, H., Okubo, Y., and Hazama, F.: to be published.
- 11) Renton, P. H., Stratton, F., Gunson, H. H., and Hancock, J. A.: Brit. Med. J., i, 294 (1962).
- 12) Bartova, A., Novotony, Z., and Slepicka, J.: Blood, **14**, 566 (1962).
- 13) Hart, Mia van der, Veer, Marga van der, and Loghem, J. J. van: Vox Sang., **7**, 449 (1962).