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The Role of Xg^a Blood Group Incompatibility in Fetal Loss

Twin study *

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The Xg blood group system is unique in that it is the only blood group antigen which is controlled by a gene residing on the X chromosome. There are six possible mating types in X-linked dominant inheritance, such as the Xg system represents. One of these types is of particular interest in this presentation, even though it amounts to only 6% of possible matings, assuming the usual western Caucasian gene frequency of the Xg system. In this mating type, an Xg(a+) father, whose X chromosome is designated as +, mates with an homozygous Xg(a—) mother (Fig. 1). The offspring of such a mating, if female, will be incompatible with their mother, since they have received their father's Xg(a+) X chromosome. Male offspring are of course compatible, since they receive their mother's Xg(a—) X chromosome and their father's Y chromosome. It follows that any biologically significant materno-fetal incompatibility with respect to the Xg system might lead to preferential loss of daughter conceptions.

The present paper deals with data collected during the course of a study of twin pairs who were participating in an ophthalmologic investigation. The twins were classified as MZ or DZ on the basis of their blood types (ABO, MNS Rh, Kell, Duffy, etc.), physical likenesses, and dermatoglyphic findings. The results expected of Xg^a testing, assuming random mating and no selection, were calculated by Li's method (1955), using the gene frequency of 0.65 for the Xg^a allele.

Fig. 2 illustrates the observed findings compared to the expected ones (in parentheses). As many as 221 sets of twins were judged to be MZ. When the MZ twins were ♂♂, the observed numbers of Xg(a+) and Xg(a—) sets conformed very closely to the expected values; when they were ♀♀, there was a slight deficiency in the observed numbers of Xg(a+) twins and a slight excess of negative twins. As many as 38 sets of twins were DZ ♂♂. Here again, the observed results were almost identical to the numbers predicted, assuming random mating and no selection. When the twins were DZ ♀♀, disparities from the expected values were encountered. There was a deficiency in the twin pairs where both twins were Xg(a+); an equivocal excess in the number of sets in which both twins were negative; and a definite excess in

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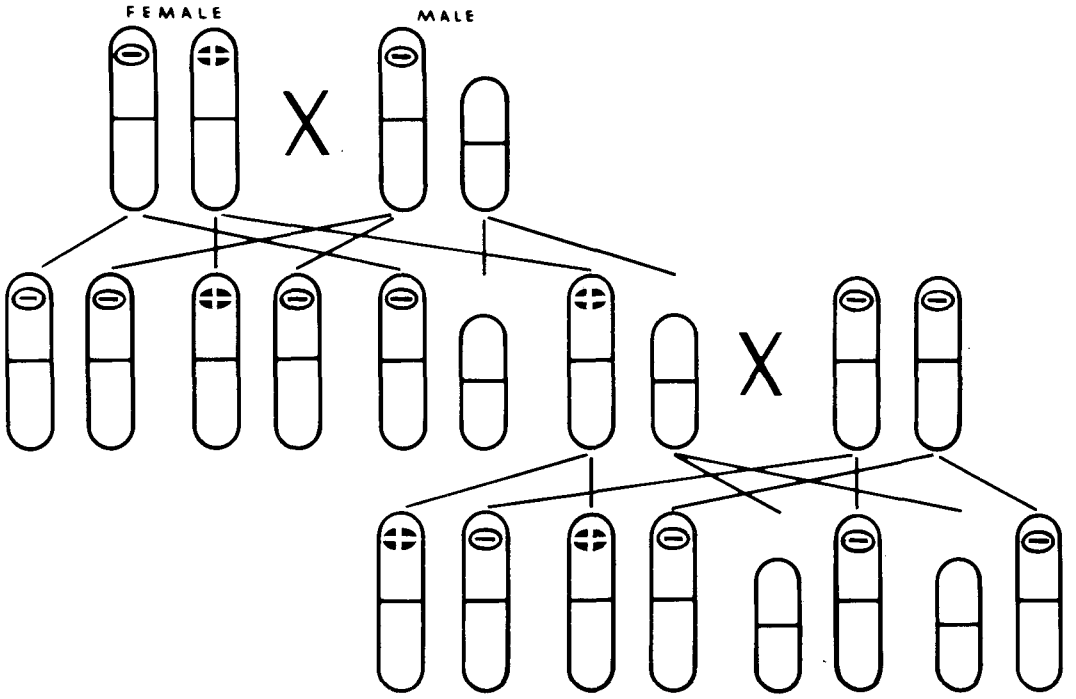

Fig. 1. Diagram illustrating the X-linked mode of inheritance of the Xg blood group system.

MZ N. = 221

	BOTH	
	$Xg^{a}+$	$Xg^{a}-$
♂♂	(66) 67	(37) 36
♀♀	(98) 104	(20) 14

DZ ♂♂ N. = 38

	♂	
Xg^{a}	+	−
+	(19) 20.4	(9) 8.6
−		(10) 9.6

DZ ♀♀ N. = 48

	♀	
Xg^{a}	+	−
+	(32) 39.9	(10) 3.8
−		(6) 4.3

DZ ♂♀ N. = 44

	♂	
Xg^{a}	+	−
+	(23) 26.8	(6) 11.9
−	(5) 1.8	(10) 3.5

Fig. 2. Observed (in parentheses) and expected Xg^{a} blood types of 221 MZ and 130 DZ twins.

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sets where one twin was positive and one negative. The latter situation, of course, cannot occur unless the mother is heterozygous for the Xg^a gene and such twins cannot be the offspring of an incompatible mating of the type discussed earlier.

As many as 44 twin sets were DZ ♂♀. Here, there appears to be a definite disparity from expected values. In every cell of the diagram, there is a deficiency of Xg (a+) females and an excess of Xg(a—) females. There is a deficiency of sets where both twins are Xg(a+); an excess of sets with a positive male and a negative female; a deficiency of sets with a negative male and a positive female; and an excess of sets where both twins are Xg(a—).

We believe that the simplest explanation for these results is that materno-fetal incompatibility for the Xg^a blood group antigen is producing selective loss of female offspring. There is prior evidence to support this hypothesis.

We have previously reported two studies dealing with the sex ratio of the offspring of the incompatible mating type of Xg(a+) fathers with Xg(a—) mothers. The first was a series drawn from obstetrical cases (Dewey et al, 1965). The second was ascertained by studying a large Amish kindred from Adams County, Indiana (Jackson et al, 1969). In both of these series, there was a very high sex ratio observed in the offspring of the incompatible matings. When the two series are combined, one finds that the incompatibly mated parents produced 234 boys and only 160 girls (Tab. I). Furthermore, the sex ratio is even higher in offspring born after the birth of the first girl than it was before the first female was born. This suggests that a sensitization may have taken place as a result of the birth of an Xg(a+) female child; subsequent female children would therefore be more liable to selective loss.

Tab. I. Sex ratio in the offspring of Xg^{a+} father × Xg^{a-} mother matings

	After birth of first daughter		Total	
	♂	♀	♂	♀
1965 report (12)	63	26	121	38
Amish study (13)	85	56	113	82
Total	148	82	234	160

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