Letters to the Editor

INHERITANCE OF FACTOR XIII

To the Editor: Lorand et al. (1970) have correctly pointed out that definitive evidence for sex-linked inheritance of Factor XIII deficiency would be provided by the demonstration of heterozygosity in mothers but not in fathers of affected males. They applied a method for detecting heterozygotes to four families with only affected males and to two families with affected females. In all cases both parents showed evidence of heterozygosity. Their conclusion that, "These findings support the concept that congenital FSF (Factor XIII) deficiency is transmitted as an autosomal recessive trait" is correct but incomplete, because they fail to mention that the data do not exclude sex-linked inheritance in some cases. Their paper is incomplete also in that they offer no explanation for the peculiar distribution of consanguinity among the parents of the two sets of families, one with affected daughters, the other with affected sons only (Ratnoff and Steinberg 1968).

TABLE 1

CONSANGUINITY PREVALENCE AS A FUNCTION OF THE PRESENCE OF AFFECTED FEMALES

AFFECTED FEMALES	CONSANGUINITY		TOTAL
	Yes	No	
Yes	12	10	22
No	1	15	16
Total	13	25	38

At the time of our original publication we were aware of 21 families, each of which had at least one affected child. We are now aware of an additional 17 families (some of them have been summarized by Lorand et al. 1970). The total data are presented in table 1. Analysis by Fisher's exact test for a 2×2 table gives (for a single-tail distribution) $P = .002$ that the observed difference in the frequency of consanguinity could have arisen by chance, if the samples came from the same universe.

Twenty of 89 sibs of affected female probands (single selection only) are affected, $p = .23 \pm .04$. Among families with only affected males, 3 of 12 male sibs and none of 14 female sibs are affected. The data from these families are too few to permit distinction between alternative hypotheses. The combined data for both sets of families do not differ significantly from expectation on the basis of autosomal re-

cessive inheritance ($p = .20 \pm .04$), but the standard error is large and most of the data come from families with affected females.

The highly significant difference in the frequency of consanguinity between the two sets of families remains to be explained. We submit that the simplest explanation is that a portion of the pedigrees represents sex-linked inheritance.

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To the Editor: Of course, we agree with Steinberg and Ratnoff that there appears to be a highly significant difference in the frequency of consanguinity among the parents with and without affected females in families with inherited fibrin-stabilizing factor (Factor XIII) deficiency. This, indeed, could suggest an X-linked mechanism in addition to an autosomal recessive one. Clearly, quantitative biochemical evidence will have to be sought along the lines given in our paper (Lorand et al. 1970) and we plan to extend our data in this regard. Up until now, we have found reduced fibrin-stabilizing factor levels in all four fathers from nonconsanguineous families with only affected males (families A, B, E, and F) and, thus, there is no evidence so far to suggest an X-linked mode of inheritance; however, it still remains an attractive hypothesis.

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