An Anomaly of Inheritance in the MNSs Blood Groups

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THERE IS AN IRREGULARITY in the inheritance of the MNSs groups in the family Baet (Fig 1). A Ns × MNSs mating produced three Ns offspring, three MNSs, and one MNs (II-5). That the MNSs typings are correct is substantiated by the agreement of various examples of MNSs antisera, both in our own laboratory and in that of Dr. T. E. Cleghorn (Fig. 1), and by absorption studies (Table 1).

The family is Caucasian; the first three children were born in The Netherlands, the rest in Manitoba. So far as the parents know, they are not blood relatives. They have no relatives in Canada, nor have any of their relatives visited here. The family came to our attention because the proposita (II-7) had trisomy 18. Dr. Irene Uchida, Director, Department of Genetics, Children's Hospital, Winnipeg, made the chromosomal diagnosis and provided the primary specimens for blood grouping. The karyotypes of the parents and of the children other than the proposita were normal.

Dosage and absorption studies with anti-M and anti-S as well as full blood grouping and serum typing were done on these specimens. For verification we later obtained second specimens from I-1, I-2, II-1, II-3, and II-5. These enabled us to confirm our typings, to repeat the reaction times with anti-M and anti-S, and to measure the reaction times with anti-s as possible evidence of zygosity (Table 2). Aliquots of these samples were also sent to Dr. T. E. Cleghorn. A summary of the results is given in the legend of Fig. 1.

DISCUSSION

The family history, the blood groups, serum types, red cell enzymes, and serum enzymes are all consonant with the assumption that II-5 is the child of I-1 and I-2. If this assumption be granted, the MNSs anomaly may be explained by any one of several genetic mechanisms: suppression, deletion, mutation, or recombination. No one of these can be proved or disproved, but we favor recombination.

Because anti-M and anti-N differ so much from anti-S and anti-s, both in mode of their production and in the way in which they react, we believe the chemical structure of M and N may differ basically from that of S and s. The little evidence on the structure of M, N, M^g, S, and s leaves unanswered the question of whether there exists a basic difference between the antigens (Springer and Ansell, 1958; Mäkelä and Cantell, 1958; Springer and Stadler,

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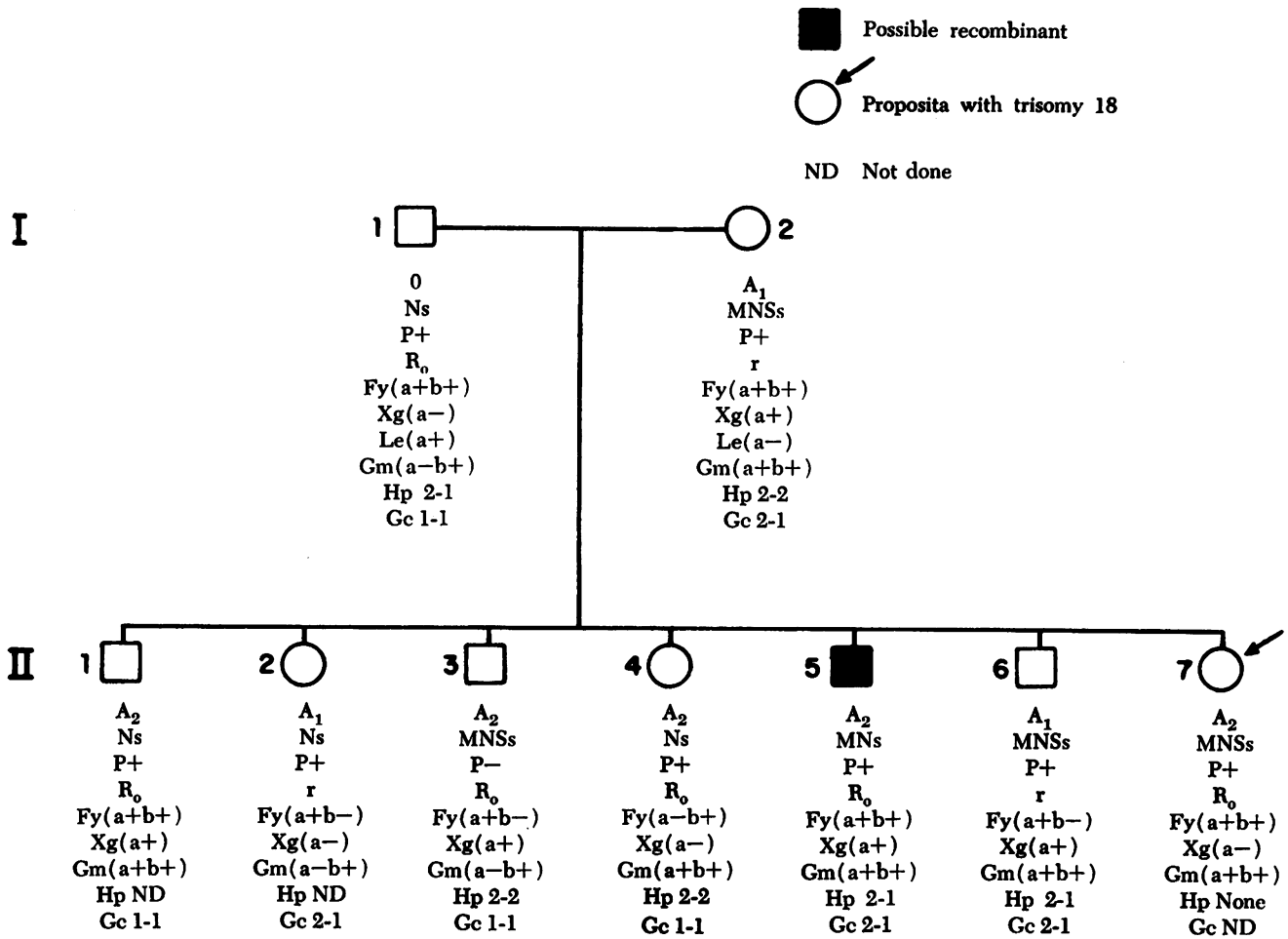

(See figure legend on facing page.)

TABLE 1. ABSORPTION STUDIES

Each serum was absorbed three times with cells from persons as indicated.
+ = positive, the number indicating the reaction time in minutes (capillary method).
− = negative.

Cells	Type	Anti-M absorbed by			Anti-S absorbed by		
		I-1 Ns	I-2 MNSs	II-5 MNs	II-4 Ns	II-5 MNs	II-6 MNSs
I-1	Ns	−	−	−	−	−	−
I-2	MNSs	+3	−	−	+18	+18	−
II-1	Ns	−	−	−	−	−	−
II-2	Ns	−	−	−	−	−	−
II-3	MNSs	+3	−	−	+18	+18	−
II-4	Ns	−	−	−	−	−	−
II-5	MNs	+3	−	−	−	−	−
II-6	MNSs	+3	−	−	+18	+18	−

1961; Stadler and Springer, 1962). If M and N differ basically from S and s, this could be considered an indication that they are controlled by two pairs of genes. If so, although the loci may be closely linked, they should be separable by crossing over.

If there *are* two loci, crossing over cannot be frequent; otherwise, the ratio of *MS* to *Ms* would be the same as that of *NS* to *Ns*. Instead, they are about 1:1.1 and 1:5. The published family data are so scant they do not weigh heavily against the possibility of crossing over. Our own data on Caucasians consist of just over 400 families tested with anti-M, -N, -S and -s. Of these, only 78 are of such MNSs type as to be potentially informative about recombination. Among the 290 children, 244 are informative, and II-5 is the only possible recombinant who could be recognized. If recombination does occur, this gives some measure of its frequency and also of the volume of material which must be studied to establish its occurrence. Families of at least three generations will be required for direct proof, although statistical evidence

FIG. 1. Family (Baet) with an irregularity in the inheritance of the MNSs groups. For Rh phenotypes, all bloods were tested with anti-C, -C^w, -c, -C^x, -D, -E, -e, -f, -E^w. All were K− k+ Kp(a−b+); Lu(a−b+); Jk(a−b+). All children were Le(a−). I-1, I-2, and II-5 were Mi(a−), Vw−, Be(a−), Bi(a−), Bu(a−), Wr(a−), Ra−, Go(a−), Inv(a−), Tf C, Gm(x−c−). All were tested with six anti-M (three human and three rabbit), two anti-N, five anti-S (three saline-active and two indirect Coombs), and two anti-s (indirect Coombs) sera. I-1, I-2, II-1, II-3, and II-5 were tested with two other anti-s (saline-active) for dosage. These five persons were MNSs typed by Dr. T. E. Cleghorn, who used five anti-S sera in his typing. Tests with all sera were in agreement with the results given in the Figure.

Dr. Cleghorn also found that none of the five carried the following antigens: Sw^a, Tr, Bp, Ls, Hut, Mu, Hi, St^a, Ri^a, Vr, Cl^a, Ny^a, Mt^a, Wb, Bx, Finlay, Peacock, Orriss, Yahuda, By, Evans, Levay, Hunt. Dr. Bette Robson, Human Biochemical Research Unit, King's College, confirmed the Hp and Tf typings and further reported that two serum cholinesterase systems and three red cell enzyme systems (acid phosphatase, 6-phosphogluconate dehydrogenase, and a new system under investigation) were all in agreement with the legitimacy of II-5.

TABLE 2. REACTION TIMES WITH ANTI-s (CHEI)

Blood Sample	Minutes
10 S− s+ controls	9 to 12
9 S+ s+ controls	19 to 25
I-1 S− s+	12
I-2 S+ s+	22
II-1 S− s+	12
II-3 S+ s+	25
II-5 S− s+	11

The family was also studied for dosage with anti-M and anti-S. M+ persons gave a single dose reaction with anti-M, S+ persons a single dose reaction with anti-s.

may be obtained from two-generation families, if large enough numbers are studied.

Two observations are congruent with the hypothesis that crossing over does occur between the *MN* and *Ss* loci and that II-5 is a recombinant. First, two other possible recombinants have been reported. Shapiro (1956), in studying the inheritance of He (Henshaw), found one family in which the phenotypes could be interpreted as evidence that crossing over had occurred during oögenesis with consequent recombination in the MNSs system. Shapiro did not obtain evidence that the putative father was not the true father and did not seek evidence to establish the probability of his being the true father; the case was dismissed as due to illegitimacy. We reported a possible example of recombination (Lewis, Chown, and Kaita, 1963), but in that case crossing over would have had to occur during spermatogenesis. Illegitimacy was considered the more probable explanation.

Second, the reaction of the cells of II-5 with anti-s, as given in Table 2, does not differ from that of *ss* cells. Assuming from this reaction that the boy is *ss*, the genotypes of the family are given in Table 3. We have studied many families with the particular anti-s used in this case and consider it reliable as an indicator of dosage. The reaction recorded for II-5 is not absolute proof that he is *ss*, but the reaction is consistent with such an interpretation and therefore with his being a recombinant.

SUMMARY

The blood groups, serum types, and red cell and serum enzymes are recorded for a family in which the father is Ns, the mother MNSs, three offspring Ns, three MNSs, and one MNs. The family history and observations on genetic systems other than MNSs agree with the assumption that the MNs child is legitimate. Possible genetic explanations are gene suppression, dele-

TABLE 3. PRESUMPTIVE MNSs GENOTYPES OF BAET FAMILY

I-1	*Ns/Ns*
I-2	*MS/Ns*
II-1,-2,-4	*Ns/Ns*
II-3,-6,-7	*MS/Ns*
II-5	*Ms/Ns*

tion, mutation, and recombination. Reasons for supporting recombination as an explanation are given.

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