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The MNSs Chromosome

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For 25 years after their discovery the MN groups remained apparently simple, then, in 1947, with the discovery of S, they took a turn for the complex and now the system seems as elaborate as Rh. First slide (table I). This is how we think of the chromosome in September 1958.

Table I

The MNSs Chromosome, 1958

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M and N you know are allelic genes and so are S and s; and their combined inheritance is well worked out. Most of the other symbols on this slide represent very rare genes that produce no less rare antigens: but they are important, out of all proportion to their rarity, because of the glimpse they give us of the complexity of the loci.
I am going to speak of three recent additions to the knowledge of this chromosome - that is about M, about Vw and its associated Mia, and about Vr.

First M. The antigen Ms is evidently very rare: so far it has been found only in a selected Boston family and no further example was found in testing 2500 random Bostonians. Next slide (table II). Here is part of the Boston family.

Table II

The antigen M, part of the pedigree from Allen, Corcoran, Kenton and Breare, 1958

You will see that tests with anti-M and anti-N exclude the father from paternity of his son - for the father reacts like an N while his son reacts like an M. On the other hand, the presence of the very rare antigen M in father and son virtually proves that the father is the father. The explanation is simple, once it is realized that M is an allele of M and N. The father is of the genotype M/jV and the son M/M; and neither anti-M nor anti-N reacts with the antigen M. The extremely rare homozygote M/M probably exists somewhere in the world, and if he were found his blood would be negative with anti-M and with anti-N.

Now Vw and Mia: in 1954 van der Hart, Bosman and van Loghem found a new antigen which at first appeared to be of the private type; it was called Vw. But a study of the family of the propositus was brilliantly informative, because the gene responsible for Vw was seen to be travelling, without exception, on an Ms chromosome. So Vw was clearly part of the MNSs system. Then the story became more involved when it was found that the members of the family who had the Vw antigen also had the very rare antigen Mia; so it was assumed that Mia and Vw were synonymous. (The Mia of Levine, Stock, Kuhmicel and Bronikovsky had not previously been realized to belong to the MNSs system.)

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But Mia and Vw are not quite the same. In collaboration with Dr. Wallace and Dr. Mohn we found that only about half the samples of Mi(a+) blood are Vw +, the other half are Mi(a+) Vw-.

Table III

In white people the gene responsible for the
Mi(a+) Vw + antigen usually travels on an Ns chromosome (no exception yet found)
Mi(a+) Vw antigen usually travels on an MS chromosome
(one exception: travelling with Ns)

Next slide (table III). The gene responsible for the Mi(a+) Vw + reaction usually
travels on an Ms chromosome: while the gene responsible for the Mi(a +) Vw reaction usually travels on an MS chromosome. The pedigrees are typical examples of the inheritance of the two types of reaction. In these pedigrees the fathers MNSs contribution is written first.

In the left hand pedigree the father has given his Mi (a +) Vw + to three of his children (marked in black) and to each of the three he has given also Ms. On the other hand to two of the children he has given his MS chromosome and neither of them has received his Mi (a +) Vw +.

In the right hand pedigree we see that the gene responsible for the Mi(a +) Vw reaction has travelled with the fathers MS.

The latest contribution to the MNSs system comes from Holland, where a new antigen called Vr has been found. One in about 400 Dutch people have Vr. Next slide (table IV). This summarized pedigree shows that Vr belongs to the MNSs system. The father is heterozygous for the new gene because he has four children lacking the antigen. We can see where the fathers MNSs genes have gone, and his contribution to each of the nine children is written first. Vr has travelled to all the five children who have received their fathers Ms chromosome. The four children who have received their fathers Ns chromosome lack Vr. In the two other families so far tested Vr is also travelling on a Ms chromosome; but though Ms seems to be the chromosome of choice, at any rate in Europeans, exceptions will doubtless be found.

Serological tests showed that Vr, like Mia and Vw, can hardly be an allele of M or N or of S or s, and that is all that can be said at present.

Next slide (table I). Here again is the 1958 MNSs chromosome. Though it is clear that Hu, He, Mi3-, Vw and Vr are not alleles of M or N or of A or r there is yet no evidence of their relationship to each other, and there probably won't be for a long time because of the extreme rarity of the antigens.

The versatility of the region of chromosome responsible for the MNSs antigens appears to equal that of the region responsible for Rh, and we feel that continued work on the MNSs system and on the Rh system, such as that described by Dr. Rosenfield, will within a few years lead us to a deeper understanding of the structure of blood group genes.

References