169. Family Study of the Original Australian Rhnull

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When Vos et al.1) discovered the first Rhnull blood with no detectable Rh antigens in an Australian aborigine, Mrs. Elsie Nelson, in 1961, the genetical background was not known, as she had no parents, sibs, nor children; she had delivered two babies who died in their early lives, and she had suffered one miscarriage.

The second case was found in an American Caucasoid woman by Levine et al.2) in 1965, and the third in a Japanese boy by Ishimori and Hasekura3) in 1966.

Through family studies, the American case and the Japanese case revealed two different genetic bases for Rhnull phenotypes. The Japanese case was explained by the homozygosity of amorphic Rh alleles, Rh(- - -/- - -). The heterozygotes of Rh(- - -) in the family could be recognized by apparent non-maternity or non-paternity of the children receiving the silent genes, e.g. the phenotype of the brother of the propositus was Rh2Rh2 (ccDEEF) and the mother was Rh1Rh1 (CCDeeF).4) The terms Rh for genotype and rh for phenotype were first proposed by Wiener.5)

On the other hand, the American case was not explained by this simple Mendelian inheritance, as the propositus was able to transmit an R1 (CDe) gene from one of her parents to her child. A suppressing gene, X°r, was postulated to prevent Rh genes from expressing themselves at all in a homozygote X°rX°r. Also, X°r heterozygotes were found to be distinguished by their weaker expressions of Rh antigens compared with normal bloods by quantitative haemagglutination tests.6) This type of Rhnull is called rh (zero rh) by Wiener7) and Rh:-29m or rhm (m standing for membrane anomaly) by Rosenfield.8)

In a hope of finding out if the original Rhnull in Australia was one of these cases, or of a different genetical background, the authors made a field trip to Western Australia to test the relatives and tribal relatives of the propositus.

Blood samples were obtained from most of the close relatives of the propositus, members of the “Darlot mob” who are close tribal

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relatives, and other aborigines living in the Leonora-Laverton-Mt. Margaret area, who might share ancestry with the propositus.

Samples were tested in the field for the ABO and the Rh blood groups. The results are shown in the Table.

The blood samples were brought back to the Flinders University and were titrated against saline agglutinating Rh antisera (Ortho Diagnostics).

The following five cases were found to give weaker agglutination reactions for all Rh antigens (Fig. 1):

Table I. The ABO and Rh blood groups of the Western Australian aborigines in the tribe containing the original Rhnull propositus

<table>
<thead>
<tr>
<th>ABO groups</th>
<th>No.</th>
<th>Rh groups</th>
<th>No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>O</td>
<td>36</td>
<td>Rhnull (propositus)</td>
<td>1</td>
</tr>
<tr>
<td>A1</td>
<td>73</td>
<td>Rh1Rh1 (CCDee)</td>
<td>30</td>
</tr>
<tr>
<td>A2</td>
<td>3*</td>
<td>Rh1Rh (CcDee)</td>
<td>7</td>
</tr>
<tr>
<td>B</td>
<td>0</td>
<td>Rh2Rh2 (ccDEE)</td>
<td>17</td>
</tr>
<tr>
<td>A1B</td>
<td>1*</td>
<td>Rh2Rh (ccDEe)</td>
<td>11</td>
</tr>
<tr>
<td>A3B</td>
<td>0</td>
<td>Rh2Rh0 (CcDEe)</td>
<td>39</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Rh2Rh1 (CCDEe)</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Rh2Rh2 (CcDEE)</td>
<td>3</td>
</tr>
<tr>
<td>Total</td>
<td>113</td>
<td>Total</td>
<td>113</td>
</tr>
</tbody>
</table>

Rh gene frequencies in the sample except the Rhnull propositus: $R^1=0.4955$, $R^2=0.3884$, $R^0=0.0804$, $R^*=0.0357$.

* It is presumed that these are due to white admixture, since, in full-blood Australian aborigines of this area, only blood groups O and A1 occur. The A2 groups were found in a man, known to be a half-caste, and two of his children. The woman with group A1B was known to be a half-caste.

Fig. 1. Pedigree of Mrs. Elsie Nelson. R2R0 = Rh1Rh1(CCDee), R2R2 = Rh2Rh2 (ccDEE), R2R1 = Rh1Rh2(CcDEe), R2R0 = Rh2rh(ccDEe), R2R1 = Rh2Rh1(CcDEe), R2R2 = Rh2Rh2(CcDEE).

* The information is not positive that I-6 is a sib of I-5; it may be a sib of I-4 instead.
1) III-11, R₁R₂, a first cousin of the propositus
2) IV-5, R₁R₂, a half first cousin
3) III-17, R₂R₉, a second cousin
4) II-12, R₈R₉, the mother in law
5) II-21, R₅R₇, an aunt in law.

The last one is of special interest, as she has sisters of R₁R₁ and R₅R₇, i.e., the R₁R₁ sisters (II-19 and II-21) possess the identical Rh genes, yet express the antigens on the red cells with different degrees of agglutinability. This difference was more evident by Wilkie & Becker-type of quantitative haemagglutinations9 (Fig. 2).

These results indicate the participation of a suppressing gene independent of Rh genes, and gives evidence that Mrs. Elsie Nelson’s phenotype is due to X₀rX₀r homozygosity, as the American case.

American Rhnull cases were known to suffer from haemolytic anaemia which is attributed to some defects of red cell membrane

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Fig. 2. Wilkie & Becker-type of quantitative haemagglutinations, using anti-Rh₀(D) and anti-hr''(e). The comparison of two sisters with the identical Rh genotypes: II-21 cells show suppressed agglutinability.
structure shared by the precursor substance of Rh antigens.\(^8\),\(^10\) Schmidt and Vos\(^10\) have reported that the Australian propositus had normal haemoglobin levels and reticulocyte count.

Sufficient haematological tests on her blood were not made this time; still, the fragility of her cells was noticed as the supernatant plasma of her blood was coloured pink after an overnight's storage in a refrigerator, and also a marked haemolysis was seen when her cells were ficinized for Rh grouping. On the blood film of the propositus, stomatocytosis was observed suggesting a membrane anomaly of red cells, as was seen in American cases\(^11\) (Fig. 3).

A more detailed report on this investigation has been submitted to the Australian Journal of Experimental Biology and Medical Sciences.\(^12\)

Acknowledgment. We wish to thank Dr. Fukuoka of Tokyo Medical and Dental University for confirming the stomatocytosis of the propositus.

References

4) T. Ishimori and H. Hasekura: A Japanese with no detectable Rh blood: A Japanese with no detectable Rh blood group antigens due to silent Rh alleles or deleted chromosomes. Transfusion, 7, 84–87 (1967).


7) A. S. Wiener: Personal communication.


11) R. E. Rosenfield: Personal communication.