Experiments on Rh-negative male volunteers injected with Rh-positive cells showed that Rh immunisation could not be prevented by injecting 195 anti-Rh antibody, although about 60 percent of the cells were eliminated. When 75 antibody was substituted for 195, the way was clear for preventing Rh haemolytic disease. In addition, the Kleinhauser technique enabled the size of any anti-Rh haemolysin to be determined. [The SCV indicates that this paper has been cited in over 200 publications.]

**Experimental Prevention of Rh Immunisation by Injecting Anti-D**

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About 1 in 7 marriages are between Rh-negative women and Rh-positive men, and yet in about 1 in 20 of such unions the woman is the only one immunised. There are three principal reasons for this. First, the husband may be heterozygous (which occurs in about 20 percent of cases); this is protective. R.E. Race and R. Sanger were the first to suggest this, since they thought that the naturally occurring maternal 195 anti-A or anti-B would eliminate any fetal cells before they had time to stimulate the production of Rh antibodies. This suggestion was responsible for our trial of 195 anti-D given to Rh-negative male volunteers who had been injected with Rh-positive cells. However, this failed since only about 50 percent of the injected cells were eliminated, and controls and "treated" were immunised in equal numbers. The result was quite different when we switched to the 75 ("incomplete") Rh antibody, which inactivated (by "coating") all the injected red cells, and the male volunteers were fully protected. Trials followed in women using incomplete anti-D gamma globulin, which were again successful. Other countries joined in the work and the excellent results are shown in the table.

**Table**

<table>
<thead>
<tr>
<th>Location</th>
<th>Control Immune</th>
<th>Control Not Immune</th>
<th>% Immune</th>
<th>Treated Immune</th>
<th>Treated Not Immune</th>
</tr>
</thead>
<tbody>
<tr>
<td>Liverpool</td>
<td>25</td>
<td>8</td>
<td>22</td>
<td>15</td>
<td>9</td>
</tr>
<tr>
<td>Germany</td>
<td>7</td>
<td>4</td>
<td>3</td>
<td>45</td>
<td>9</td>
</tr>
<tr>
<td>Columbia, NY</td>
<td>14</td>
<td>4</td>
<td>10</td>
<td>20</td>
<td>10</td>
</tr>
<tr>
<td>Long Beach, CA</td>
<td>14</td>
<td>3</td>
<td>11</td>
<td>21</td>
<td>10</td>
</tr>
<tr>
<td>Connell, NY</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>100</td>
<td>0</td>
</tr>
<tr>
<td>Edinburgh</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Totals</td>
<td>63</td>
<td>15</td>
<td>48</td>
<td>22</td>
<td>66</td>
</tr>
</tbody>
</table>

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Surprisingly, the results were not quite as good with our "low risk" trial, in women with no or very few fetal cells. This turned out to be because a few women are immunised during pregnancy, and, although we kill all cells if they are eliminated, the antibodies cannot be detected by standard procedures, and the women enter the trial as non-immunised. To overcome this problem, antenatal anti-D got rid of almost all the failures of prophylaxis.

The effect of anti-D on Rh baby deaths has been monitored since 1977 by the Research Unit of the Royal College of Physicians of London and more recently by the Department of Community Health in the University of Liverpool (Professor Peter Pharoah and Dr. Ruth Hussey). The deaths were ascertained from the Office of Population Censuses and Surveys (OPCS) and amplified from the case notes kindly lent to us by the obstetricians. We found that the number of deaths from haemolytic disease due to anti-D fell progressively from 106 in 1977 to 27 in 1984. It thereafter remained approximately constant for three years but fell again in 1988 (30 deaths). Interestingly, the number of deaths due to anti-c has remained approximately constant—three to four per year, except in 1984, when it was five; in 1987, when it was 9; and in 1988, when it was 1. One might have expected these deaths to have dropped since improved obstetric care is thought to be rescuing more hydrops fetalis babies than in earlier years.

The number of deaths registered on the death certificates as due to HDN but found by us to have some other cause fell progressively—the number was 43 in 1977 but only 1 in 1988—clearly due to our frequent discussions with the OPCS resulting in more accurate death certification.

The failure rate remains antenatal anti-D given at the 20th week of pregnancy (which occurs in about 1 in 7 pregnancies) and this can probably only be reduced by the wider application of antenatal anti-D, which at present is only given in a few centres in this country, principally because of shortage. However, with the coming of monoclonal anti-D, this will be overcome, as will the current fear of jaundice and AIDS. Nevin Hughes-Jones informs me that first testing of monoclonals in male volunteers has resulted in excellent clearance of the coated cells. The future looks bright.