Anti D and Early Abortion

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Disclosures

- None.
# Rh Negativity Rates

<table>
<thead>
<tr>
<th>Population</th>
<th>Rh(D) Neg</th>
<th>Rh(D) Pos</th>
<th>Rh(D) Neg Alleles</th>
</tr>
</thead>
<tbody>
<tr>
<td>Basques</td>
<td>21%-36%</td>
<td>65%</td>
<td>~ 60%</td>
</tr>
<tr>
<td>Britain</td>
<td>17%</td>
<td>83%</td>
<td></td>
</tr>
<tr>
<td>China</td>
<td>&lt;1%</td>
<td>&gt;99%</td>
<td></td>
</tr>
<tr>
<td>Europeans</td>
<td>16%</td>
<td>84%</td>
<td>40%</td>
</tr>
<tr>
<td>India</td>
<td>0.6%-8.4%</td>
<td>99.4%-91.6%</td>
<td></td>
</tr>
<tr>
<td>Moroccans</td>
<td>9.5%</td>
<td>90.5%</td>
<td></td>
</tr>
<tr>
<td>Moroccans (High Atlas)</td>
<td>~29%</td>
<td>71%</td>
<td></td>
</tr>
<tr>
<td>Subequatorial Africa</td>
<td>1%-3%</td>
<td>99%-97%</td>
<td></td>
</tr>
<tr>
<td>United States</td>
<td>15%</td>
<td>85%</td>
<td></td>
</tr>
</tbody>
</table>
Hemolytic Disease of the Newborn

First exposure: Birth of first Rh⁺ infant

1. During birth, Rh⁺ fetal erythrocytes leak into maternal blood after breakage of the embryonic chorion, which normally isolates the fetal and maternal blood.

2. Maternal B cells are activated by the Rh antigen and produce large amounts of anti-Rh antibodies.

Second exposure: Rh⁺ fetus

3. Rh antibody titer in mother’s blood is elevated after first exposure.

4. Rh antibodies are small enough to cross the embryonic chorion and attack the fetal erythrocytes.
International Policies on Anti D

- Most countries recommend testing and treating all Rh-negative pregnant women with anti D.

- The Netherlands and Sweden only test and treat >7 weeks LMP for induced abortions and >10 weeks LMP for spontaneous abortions.

- Women On Web only tests and treats patients >12 weeks LMP for medication-induced abortions.
Evidence for Anti D

- Do Rh-negative women with an early spontaneous abortion need Rh immune prophylaxis?

Visscher RD, Visscher HC

- The only randomized, double-blind, controlled study to evaluate the benefit of anti D in the first trimester of pregnancy found that the incidence of alloimmunization was zero, with (0/19) or without (0/38) anti D treatment.
Evidence for Anti D cont’d

- **Do Rh-negative women with first trimester spontaneous abortions need Rh immune globulin?**
  Hannafin B, Lovecchio F, Blackburn P

  “Given the lack of supporting evidence, it would seem reasonable to forgo administration of RhIG to Rh-negative women with a first trimester threatened or spontaneous abortions in whom the clinician is certain the gestational age is less than 14 weeks.”
What volume of blood is in an 8-week fetus?

- **Rh-prophylaxis in early abortion.**
  Fiala C, Fux M, Gemzell Danielsson K

  - Less than **0.33 cc**
What volume of blood is in a 12-week fetus?

- **Rh-prophylaxis in early abortion.**
  
  Fiala C, Fux M, Gemzell Danielsson K
  

- 4.2 cc
How much blood causes clinically significant antibodies?

- **Experimental studies on Rh immunization.**
  Stern K, Davidsohn I, Masaitis L

  - Over 7.5 cc
Why do we care?

- **Risks** with Anti D (in the past)
- **Costs** of testing and treating
- **Shortages** of Anti D
- **Privacy** outside abortion clinics
- **ACCESS:** especially for telemedicine
Women On Web
~8000/year

Willow Women’s Clinic
~200/year
Can we safely stop testing for Rh status and immunizing Rh-negative women having early abortions? A review of Rh alloimmunization in Canada and the Netherlands.

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Hypothesis

- We expect no significant difference in the rate of Rh alloimmunization in women between Canada and the Netherlands.
Methods


- Policies
  - Canada: all women tested and treated
  - Netherlands: >7 weeks for induced abortions and >10 weeks for spontaneous abortions

- Data collected:
  - Induced and spontaneous abortion rates
  - Number of births
  - Rh negativity rate
  - Clinically significant perinatal antibodies – outcome measure
Defining Clinically Significant Perinatal Antibodies

- Antibodies are considered clinically significant in causing HDFN if:
  1) they are predominantly IgG antibodies (and can therefore cross the placenta).
  2) the antigen is present on fetal red blood cells.
  3) the antibody is known to bind to the fetal antigen resulting in anemia. (This can be due to either hemolysis of fetal red cells or fetal bone marrow erythroid suppression.)
  4) the titre of the antibody is above 16.
Methods cont’d

- Population comparison:
  - Total fertility rate
  - Total number of pregnancies
  - Number of births
  - Number of induced and spontaneous abortions
## Results: Table 1

<table>
<thead>
<tr>
<th>Country</th>
<th>Induced abortions</th>
<th>Estimated spontaneous abortions</th>
<th>Births</th>
<th>Abortion rate</th>
<th>Total fertility rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Canada</td>
<td>912 435</td>
<td>844 196</td>
<td>3 764 763</td>
<td>1.9</td>
<td>1.62</td>
</tr>
<tr>
<td>Netherlands</td>
<td>316 583</td>
<td>390 336</td>
<td>1 793 390</td>
<td>1.2</td>
<td>1.73</td>
</tr>
</tbody>
</table>

- **Total fertility rate**: average number of children that would be born alive to a woman during her lifetime
- **Abortion rate**: the number of abortions per 1 000 pregnancies
Results: Table 2

<table>
<thead>
<tr>
<th>Country</th>
<th>Rh negativity rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Canada</td>
<td>13.0%</td>
</tr>
<tr>
<td>Netherlands</td>
<td>14.5%</td>
</tr>
</tbody>
</table>
Results: Table 3

<table>
<thead>
<tr>
<th>Country</th>
<th># pregnant women tested</th>
<th># women with clinically significant perinatal antibodies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Canada</td>
<td>1 964 229</td>
<td>8 272</td>
</tr>
<tr>
<td>Netherlands</td>
<td>1 816 457</td>
<td>7 316</td>
</tr>
</tbody>
</table>

- **Canada**: 4.21/1 000 (95% CI 4.12 to 4.30)
- **Netherlands**: 4.29/1 000 (95% CI 4.18 to 4.39)
Results: Figure 1

Cumulative incidence (per 1000)

Netherlands: 4.0, 4.1, 4.2, 4.3, 4.4, 4.5
Canada: 4.0, 4.1, 4.2, 4.3, 4.4, 4.5

Cumulative incidence (per 1000)
Sources of Error

- Not all induced abortions are reported
- Spontaneous abortions are not reported
- How many women were tested and treated?

In Canada:
- Only 6/13 provinces and territories reported
- Before 2014, only # of antibodies, not # women with antibodies were reported (requiring estimates)
- 2006-2009 fiscal years instead of calendar years reported
Possible Confounders

- Different abortion rates, fertility rates, and rates of medical vs. surgical abortions
- Possible difference in compliance with policy
- Missing data
Study Strengths

- Almost 2 million women from each country
- 10 years of data
- 10 years after policy change in the Netherlands
- Both countries use same definition of clinically significant antibodies
Conclusion

- The anti D policies in the Netherlands are safe for women.
But what about 12 weeks?

- Fetal blood volume = 4.2 cc
- Minimum amount of blood needed for significant antibodies = 7.5 cc
- No evidence that anti D is needed
Thank you!

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