Transfusion Transmission of HIV

1. Past & Current Risk Estimates of Transfusion-Transmitted HIV Infection

2. Layers of Safety in Protection of the Blood Supply

3. Future Efforts to Reduce the Risk of Transfusion-Transmitted HIV
Landmarks: HIV & the Blood Supply

- **late 1982**: AIDS-like illnesses in hemophiliacs and blood recipients first reported
- **March 1983**, FDA memorandum:
  - Education of donors regarding persons at increased risk of AIDS
  - Specific donor history questions to detect possible AIDS symptoms or exposure to patients with AIDS
- **1983-1984**: HIV-1 discovered (HTLV-III/LAV)
Landmarks:
HIV & the Blood Supply

- **December 1984**, FDA memorandum:
  - **Educational materials** to inform donors who should refrain from donating blood
  - **History questions**
  - **Confidential Self-Exclusion**

- **March 1985**: HIV-1 Antibody EIA test
- **June 1992**: HIV-2 antibody test required
  (anti-HIV-1/2 combination EIA)
- **March 1996**: HIV-1 p24 Ag test licensed for blood donor screening
- **July 1996**: HIV-1, group O -- first case in U.S
New Test Implementation and Declining Risk of Viral Infections from Transfusion

Based on data provided by Michael P. Busch, M.D.

Source: Kathryn C. Zoon, Ph.D.
Director, CBER FDA
5th Annual FDA and the Changing Paradigm for Blood Regulation - Jan 16-18, 2002
# Risk Estimates of Transfusion-Transmitted HIV Infection

<table>
<thead>
<tr>
<th>Study Design</th>
<th>Period of Study</th>
<th>Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recipient</td>
<td>1985-1991</td>
<td>1:60,000</td>
</tr>
<tr>
<td>Seroconversion(^1)</td>
<td>(11,532 pts)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(120,301 units)</td>
<td></td>
</tr>
<tr>
<td>PCR / Viral Culture(^2)</td>
<td>1987-1992</td>
<td>1:160,000</td>
</tr>
<tr>
<td></td>
<td>(200,000 units)</td>
<td></td>
</tr>
</tbody>
</table>


## Risk Estimates of Transfusion-Transmitted HIV Infection

<table>
<thead>
<tr>
<th>Study Design</th>
<th>Period of Study</th>
<th>Risk</th>
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</thead>
<tbody>
<tr>
<td>Incidence x</td>
<td>1992-1993</td>
<td>1:450,000</td>
</tr>
<tr>
<td>Window Period</td>
<td></td>
<td>to</td>
</tr>
<tr>
<td>Model³</td>
<td></td>
<td>1:660,000</td>
</tr>
</tbody>
</table>

| Incidence x            | 1991-1993       | 1:493,000     |
| Window Period          |                 |               |
| Model (REDS)⁴         |                 |               |

## 1996 Transfusion Risks*

<table>
<thead>
<tr>
<th></th>
<th>Point Estimate</th>
<th>95% C.I.</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV</td>
<td>1:676,000</td>
<td>[1:202,000 - 1:2,778,000]</td>
</tr>
<tr>
<td>Hepatitis B</td>
<td>1:63,000</td>
<td>[1:31,000 - 1:147,000]</td>
</tr>
<tr>
<td>Hepatitis C</td>
<td>1:103,000</td>
<td>[1:28,000 - 1:288,000]</td>
</tr>
<tr>
<td>HTLV I/I</td>
<td>1:641,000</td>
<td>[1:256,000 - 1:2,000,000]</td>
</tr>
</tbody>
</table>

*per unit of blood that is negative in laboratory testing

Efforts to Further Reduce the Risk of Transfusion-Transmitted HIV

HIV Variants:
- HIV-1, Group O
- future variants

Further Narrowing of the Window Period:
- Polymerase Chain Reaction (PCR)
- Transcription-Mediation Amplification (TMA)
- Other Genetic Amplification Methods
Current Transfusion Risks*
(with minipool HIV/ HCV NAT)

<table>
<thead>
<tr>
<th>Condition</th>
<th>Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV</td>
<td>1:2,135,000</td>
</tr>
<tr>
<td>Hepatitis C</td>
<td>1:1,935,000</td>
</tr>
</tbody>
</table>

(Dodd RY, Notari EP, Stramer SL. Transfusion 2002; 42: 975-979.)

<table>
<thead>
<tr>
<th>Condition</th>
<th>Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV</td>
<td>1:1,800,000</td>
</tr>
<tr>
<td>HCV</td>
<td>1:1,600,000</td>
</tr>
</tbody>
</table>

(Busch MP, Kleinman SH, Nemo GJ. JAMA 2003; 289: 959-962.)

*per unit of blood that is negative in laboratory testing
**Annual Statistics**

**Volunteer Blood Donations:**
- ~8 million blood donors
- ~16 million units donated
- ~1.9 blood components / unit

**Transfusions:**
- ~4 million patients
- ~4-5 units / transfusion (highly variable)

**Paid Plasma Donations:**
- ~12 million units of plasma
  -- utilized for plasma fractionation and plasma derivative production
Layers of Safety

• Voluntary Donations vs. Donation Incentives

• Donor Education

• Self-Exclusion in Response to Written Material

• On-site Donor Deferral Registry (“eBDR”)

• Health History Interview (eBDR = Uniform Donor History Questionnaire [UDHQ])
Layers of Safety

- Telephone Callback
  - Postdonation Information
  - Confidential Unit Exclusion (CUE)

- Donor Deferral Registry: Central Facility

- Laboratory Testing

- Viral Inactivation (plasma derivatives)
Donor Education

- information on blood safety, AIDS epidemiology, and high-risk activities
- a language appropriate for each donor
- culturally sensitive educational format
- opportunity at each visit for the donor to:
  - consider the information
  - make an informed and private decision about whether to donate
- focus is on behavior, not on stereotypes
Donor Education

- includes a description of HIV-associated clinical signs and symptoms:
  - unexplained weight loss
  - night sweats
  - blue or purple spots typical of Kaposi’s sarcoma on or under the skin, or on mucous membranes
  - swollen lymph nodes lasting more than one month
  - persistent white spots or unusual blemishes in the mouth
  - temperature > 100.5°F for more than 10 days
  - persistent cough and shortness of breath
  - persistent diarrhea

- donors may self-defer if these conditions are present
Donor Education

• **“Window period”:** time interval early in infection during which tests for HIV may be negative although infection may still be transmitted.

• **Blood Testing:**
  - sample will be tested for HIV (and other organisms)
  - donor notified if test is positive
  - positive tests: donor permanently deferred

• **Donor Deferral Registries:**
  - confidential list

• **Alternative Testing Sites**
Health History Interview

- **Direct Questions on High Risk Behavior:**
  - clinical or laboratory evidence of HIV infection
  - men who have had sex with another man even one time since 1977
  - past or present injecting drug use
  - hemophilia or clotting disorder requiring clotting factor concentrates
  - engaging in sex for money or drugs since 1977
  - sex with any of the above during past 12 months
  - syphilis or gonorrhea during past 12 months
  - receiving a transfusion of whole blood, a blood component, or a clotting factor concentrate within the past 12 months
## Impact of HIV Testing on Transfusion Associated AIDS

<table>
<thead>
<tr>
<th></th>
<th>Before 3/85</th>
<th>After 3/85</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adults</td>
<td>8,038</td>
<td>37</td>
</tr>
<tr>
<td>Children</td>
<td>374</td>
<td>2</td>
</tr>
</tbody>
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(01/13/99)
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   -- Pathogen Reduction / Pathogen Inactivation