Role and missions of a National Reference center for blood borne agents: the French example

Virginie Sauvage, PhD
Département des Agents Transmissibles par le Sang,
Centre National de Référence pour les Hépatites B et C et du VIH en Transfusion,
Institut National de la Transfusion Sanguine, Paris

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National Institute of Blood Transfusion

3 missions: research, reference, education

Staff: ~150 people

6 departments:
- National reference center for blood groups
- Platelets immunology
- Human genetics
- Education (Universities and training)
- Research unit in red blood cells
- Blood-borne agents

Partnership for research and education with 5 French Universities (P5, P6, P7, Jean Monnet Lyon/St Etienne, La Réunion)

90% Public funding
Department of blood-borne agents

Staff: 14 people (+ temporary students)
- 4 researchers
- 8 technicians
- 1 secretary
- 1 head
Department of blood-borne agents

4 units:

1- Expert laboratory
   - diagnostic and characterization of viral infections (HIV, HBV, HCV, HTLV, Parv B19)

2- National reference center for HIV, HBV, HCV in blood transfusion
   - surveillance of epidemiology and viral diversity in BD population
   - evaluation of infectious transfusion risks
   - surveillance of the performance of tools used for blood screening (virus)

3- Emerging infections with impact on blood safety
   - metagenomics

4- Molecular mechanisms of viral infections transmissible by transfusion
   - HBV infectivity at the entry into the hepatocyte
   - OBI etc..
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French population: 64 million people
2014 1.6 million donors: 4% of people (18-65 years)
22% FTBD
Sex ratio =1; 33% < 30 years
3 million donations
Mandatory and systematic viral blood testing in France

1971   HBsAg
1985   anti-HIV-1 Ab EIA
1988   anti-HBc Ab + ALT (abandoned in Dec 2003)
1989   anti-HIV-1/-2 Ab EIA
1990   anti-HCV Ab EIA
1991   anti-HTLV-I Ab EIA
2001   NAT  HIV-1 / HCV
2010   NAT-HBV (started in 2005 for Army and Overseas Areas)
Blood screening in France: organization

1 national establishment (EFS) since 2000

- 4 blood centers (2500-3000 donations/day) + 3 overseas (50-100 donations/day)

1 blood center in army service

(50-100 donations/day)
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Donor haemovigilance network in France

Systematic and comprehensive epidemiological surveillance of all donors
- Implemented in 1992 in the whole country including overseas territories
- Performed jointly by NBS (EFS), Army blood service (CTSA), National Institute of Health (SPF), NRC (INTS), French national drug safety agency (ANSM)

Electronic questionnaires (since 2010)
- Quarterly
  - N donations, status of blood donors (FTBD, RBD)
  - For each positive (Syp, HIV, HBV, HCV, HTLV) donor: gender, age, status, ethnicity, risk factors
- Annual: Whole blood donor population:
  - total number of donors, distribution according to gender and age

National centralization of data (EFS, SPF, INTS)

Bio Collections (since 2010)
- Biorepository collection of all donations archived for 5 years (3 years from 2016) EFS
- Plasma collection of French blood donors positive HIV, HCV, HBV, HTLV (since 2000) INTS

Goals
- Surveillance of the transmissible infection prevalence and incidence rates
- Identification of risk factors
- Estimation of residual risk
### HIV, HTLV, HCV, HBsAg positive rate in French BD (2014)

<table>
<thead>
<tr>
<th></th>
<th>FTBD</th>
<th>RBD</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>N donations</strong></td>
<td>449 671</td>
<td>2 363 499</td>
<td>2 813 170</td>
</tr>
<tr>
<td><strong>HIV</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N</td>
<td>19</td>
<td>17 a</td>
<td>36</td>
</tr>
<tr>
<td>p. 10 000</td>
<td>0.42</td>
<td>0.07</td>
<td>0.13</td>
</tr>
<tr>
<td><strong>HTLV</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N</td>
<td>25</td>
<td>5</td>
<td>30</td>
</tr>
<tr>
<td>p. 10 000</td>
<td>0.56</td>
<td>0.02</td>
<td>0.10</td>
</tr>
<tr>
<td><strong>HCV</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N</td>
<td>120</td>
<td>7</td>
<td>127</td>
</tr>
<tr>
<td>p. 10 000</td>
<td>2.7</td>
<td>0.03</td>
<td>0.45</td>
</tr>
<tr>
<td><strong>HBsAg (or DNA+)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N</td>
<td>255 b</td>
<td>1 c</td>
<td>256</td>
</tr>
<tr>
<td>p. 10 000</td>
<td>5.7</td>
<td>0.004</td>
<td>0.91</td>
</tr>
</tbody>
</table>

* a 1 NATpos / Ac neg
* b 2 NAT pos/ HBsAg neg / anti-HBc neg
* c 1 NAT pos/ HBsAg neg / anti-HBc neg

Source: SPF, INTS, EFS, CTSA
HIV-1 genotype distribution in French blood donor population from 2004 to 2015 (n=348)

13 HIV-2/1697 HIV 1992 - 2015 (0.77%)
HBV genotype distribution in French blood donor population from 2005 to 2014 (n=2323)

6% harboring S mutations
HCV genotype distribution in French blood donor population from 2000 to 2014 (n=1954)
HIV and HCV NAT in France

01/07/2001 - 31/12/2014 = 37 million donations tested with NAT

2001-2010 : MPX24 Roche + MPX8 TMA ID
2010-2014 : ID-NAT Ultrio

<table>
<thead>
<tr>
<th>RNA</th>
<th>Ab</th>
<th>HIV (n=462)</th>
<th>HCV (=2688)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pos</td>
<td>pos</td>
<td>428 (92.6%)</td>
<td>1798 (66.9%)</td>
</tr>
<tr>
<td>Pos</td>
<td>Neg</td>
<td>21 (4.6%)&lt;sup&gt;1&lt;/sup&gt;</td>
<td>14 (0.5%)&lt;sup&gt;3&lt;/sup&gt;</td>
</tr>
<tr>
<td>neg</td>
<td>Pos</td>
<td>13 (2.8%)&lt;sup&gt;2&lt;/sup&gt;</td>
<td>876 (32.6%)</td>
</tr>
</tbody>
</table>

<sup>1</sup> 2 with another marker

<sup>2</sup> 5 HIV-2, 7 low VLs, 1 HIV-1gO

<sup>3</sup> 2 with another marker
## HBV NAT in France

2005 - 31/12/2014 = 13.5 million donations tested with ID- NAT (Ultrio)

<table>
<thead>
<tr>
<th>HBV</th>
<th>(n=1359)</th>
</tr>
</thead>
<tbody>
<tr>
<td>NAT+/HBsAg+/HBc+</td>
<td>1231 (90.6%)</td>
</tr>
<tr>
<td>NAT+/HBsAg-/HBc+</td>
<td>34 (2.5%)</td>
</tr>
</tbody>
</table>
| NAT+/HBsAg-/HBc-   | 12 (0.8%)  
| (4 HBsAb pos)      |
| NAT-/ HBsAg+/HBc+  | 75 (5.6%) |
## Characteristics of NAT Yield cases in France (2001-14)

<table>
<thead>
<tr>
<th>Yield cases</th>
<th>HIV (n=21)</th>
<th>HCV (n= 14)</th>
<th>HBV (n=12)</th>
</tr>
</thead>
</table>
| **BD status** | 17 RBD  
(Median interdonation: 108 days range: 28-284)  
4 FTBD | 10 RBD  
(Median interdonation: 143 days range: 77-1515)  
4 FTBD | 6 RBD  
(Median interdonation: 221 days range 56-1393)  
6 FTBD |
| **Sex ratio** | 19 M / 2 F  
33.6 years (19 - 50) | 8 M / 6 F  
41.6 years (23 - 64) | 6 M / 6 F  
28.3 years (18 - 57) |
| **Risk factors** | | | |
| **males** | 10 MSM (10RBD)  
6 heterosexual  
3 unknown | 1 partner HCV  
1 endoscopy  
4 unknown  
2 not investigated | 1 MSM  
1 partner HBV  
1 partner from endemic area  
3 not investigated |
| **females** | 2 partner from endemic areas | 5 partner HCV  
1 professional exposure | 1 partner HBV  
3 partner from endemic area  
1 piercing  
1 not investigated |
| **Mean VLs** | 5.5 log cp/ml (1,6-6,4) | 7 (1.39-7.7) log IU /ml, | <6 – 456 IU/ml |
| **Genotypes** | 15 gtB, 3 gtC, 3 gtCRF02. | 8 gt1a, 1 gt1b, 2 gt3a ,1 gt4a | 2 gtA, 1gtB, 1gt D, 5 gtE, 3nt |
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HIV/HCV/HBV /HTLV Residual risk in France

2012-2014 (global 1/1.9 millions de dons)

HBV: 1/6.4 M (1 / 2 years)
HIV: 1/ 3.0 M (< 1/year)
HCV: 1/33 M (1 / 11 years)
HTLV: 1/9 M (1 /3 years)

(MF without leucoreduction)
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Biobanks: unique tool for ensuring blood safety

1. Plasmas from French blood donors collected from HIV, HCV, HBV, HTLV national surveillance
   (n >8000, volumes >100 ml each)

2. Plasmas from African blood donors
   (n = 16 000)

3. At-risk populations
   - Hemodialyzed
   - Multiply-transfused patients

4. BOTIA (blood and organ transmitted infectious agents)
   Paired donor-recipient samples
   (France n = 200 recipients, > 12 000 archived samples)
Quality Control in Francophone Africa, 2010
17 participating countries- 51 centers- 60 panels tested
Quality Control in Anglophone Africa, 2011
12 participating countries- 43 centers- 43 panels tested
Role of a national reference center for infectious disease in transfusion

1- National expertise
   - diagnostic and characterization of viral infections
   - independent expertise in lookback studies

2- Surveillance of epidemiology and viral diversity in BD population
   - Identification of emerging variants compromising the blood safety
   - Constitution of panels for the study of diagnostic devices and proficiency studies
   - Evaluation of donor selection procedures
   - Evaluation of residual risks

3- Research programs
   - OBI
   - metagenomics…

4- Trainings
Acknowledgments

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  slaperche@ints.fr

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  pcappy@ints.fr

- Research programs:
  - Daniel Candotti, PhD, dcandotti@ints.fr
  - Camille Sureau, PhD, c sureau@ints.fr
  - Virginie Sauvage, PhD, vsauvage@ints.fr

- Staff:
  - Rémi Caparros
  - Laure Boizeau
  - Johanna Gomez
  - Micheline Thauvin
  - Clémence Hamon
  - Christine Portal
  - Quentin Lucas
  - Catherine Jourdain
  - Secretary: Lucilia Lopez
National surveillance of blood donors: organization

Anonymous questionnaires
- Donor status
- Demographic data
- Risk factors

Data base
- QUED

Epidemiological Surveillance

Viral diversity

Plasma bags

Plasma collections