Lookback studies to assess viral risks
The French experience 2000-2012

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For the French haemovigilance network-EFS

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Why perform lookback studies?

✓ **Population level**: observational approach of the transfusion infectious risk

✓ **Patient level**:
  - identify TTI in recipients and propose the infection monitoring
  - avoid secondary infections

✓ **Blood product level**:
  - evaluate transmissibility and infectivity (lowest infectious dose)
  - provide data to determine an optimal BD screening strategy
When perform lookback studies?

- Donor tested positive with a potential previous donation in the WP
- Donor who previously donated found positive after introduction of a new screening testing
- Donor identified as infected after the discovery of post transfusion infections in recipients
Donor haemovigilance network in France

Systematic and comprehensive epidemiological surveillance of all donors
- Implemented in 92 in the whole country including overseas territories
- Performed jointly by NBS (EFS), Army blood service (CTSA), National Institute of Health (InVS), 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

Goals
- Surveillance of the transmissible infection prevalence and incidence rates
- Identification of risk factors
- Estimation of residual risk

Completed by a biorepository collection of all donations archived for 5 years (3 years from 2016)
Donor–triggered lookback procedure in France

Donor Seroconversion

Local haemovigilance correspondent (blood center)

Previous donation
(Circular note 1996)

• Information for the destruction of non transfused products (including plasma stored for fractionation)

• Order to investigate the archived sample (national procedure)

• Trace recipients for testing (each transfused component is traced by hospitals (art R1221 CSP))

Positive donation

• Notification to ANSM
• Fulfill the donor questionnaire InVS
• Donor follow up by the Blood center
Lookback study in France 2000-12

Objectives

- Establish the characteristics of seroconverted donors
- Collect data on
  - Previous negative donation
  - Transfused products (including fractionated plasma products)
  - Follow up of donors
  - Follow up of recipients
- Evaluation of the overall lookback procedure
Lookback study in France 2000-12

Method

- National retrospective comprehensive study
- Donors from EFS and CTSA
- Study period: 2000 to 2012
- Inclusion criteria
  - seroconversions
    - HBV (HBsAg, DNA, excluding anti-HBc),
    - HCV (HCV Ab, RNA),
    - HIV (HIV Ab, RNA)
    - HTLV (HTLV Ab)
  - interdonation interval < 3 years (incidence cases and compatible with the storage duration of archived sample)
- Questionnaire to all the hemovigilance correspondents of blood centers
### Lookback study in France 2000-12

**Results (1)**

<table>
<thead>
<tr>
<th></th>
<th>HIV</th>
<th>HCV</th>
<th>HBV</th>
<th>HTLV</th>
<th>total</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Reported</strong></td>
<td>178 (54.3%)</td>
<td>76 (23.2%)</td>
<td>50 (15.2%)</td>
<td>24 (7.3%)</td>
<td>328</td>
</tr>
<tr>
<td><strong>Included</strong></td>
<td>169 (95%)</td>
<td>74 (98.7%)</td>
<td>50 (100%)</td>
<td>18 (75%)</td>
<td>311 (94.8%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Year of seroconversion</th>
<th>HTLV</th>
<th>HBV</th>
<th>HCV</th>
<th>HIV</th>
</tr>
</thead>
<tbody>
<tr>
<td>2000 (n=28)</td>
<td></td>
<td></td>
<td></td>
<td>13</td>
</tr>
<tr>
<td>2001 (n=34)</td>
<td>2</td>
<td>8</td>
<td>5</td>
<td>13</td>
</tr>
<tr>
<td>2002 (n=23)</td>
<td>7</td>
<td>11</td>
<td>3</td>
<td>15</td>
</tr>
<tr>
<td>2003 (n=11)</td>
<td>1</td>
<td>3</td>
<td></td>
<td>14</td>
</tr>
<tr>
<td>2004 (n=26)</td>
<td>2</td>
<td>8</td>
<td>6</td>
<td>16</td>
</tr>
<tr>
<td>2005 (n=25)</td>
<td>2</td>
<td>4</td>
<td>2</td>
<td>16</td>
</tr>
<tr>
<td>2006 (n=22)</td>
<td>2</td>
<td>3</td>
<td>12</td>
<td>14</td>
</tr>
<tr>
<td>2007 (n=18)</td>
<td>3</td>
<td>4</td>
<td>7</td>
<td>16</td>
</tr>
<tr>
<td>2008 (n=30)</td>
<td>4</td>
<td>5</td>
<td>2</td>
<td>9</td>
</tr>
<tr>
<td>2009 (n=18)</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td>9</td>
</tr>
<tr>
<td>2010 (n=32)</td>
<td>3</td>
<td>2</td>
<td>16</td>
<td>13</td>
</tr>
<tr>
<td>2011 (n=22)</td>
<td>3</td>
<td>4</td>
<td>8</td>
<td>15</td>
</tr>
<tr>
<td>2012 (n=22)</td>
<td>5</td>
<td>3</td>
<td>4</td>
<td>12</td>
</tr>
</tbody>
</table>
HIV, HCV and HBV Incidence rate in blood donors, France (1992 – 2014)

Source: InVS, INTS, EFS, CTSA
Lookback study in France 2000-12
Results (2)

Total number of SC according to the gender

<table>
<thead>
<tr>
<th></th>
<th>MALE</th>
<th>FEMALE</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV</td>
<td>131</td>
<td>38</td>
</tr>
<tr>
<td>HCV</td>
<td>26</td>
<td>48</td>
</tr>
<tr>
<td>HBV</td>
<td>40</td>
<td>10</td>
</tr>
<tr>
<td>HTLV</td>
<td>2</td>
<td>16</td>
</tr>
</tbody>
</table>

Mean age (years) according to the gender

<table>
<thead>
<tr>
<th></th>
<th>MALE</th>
<th>FEMALE</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV</td>
<td>37.5 (18-66)</td>
<td>38.1</td>
</tr>
<tr>
<td>HCV</td>
<td>41.6 (18-66)</td>
<td>43.2</td>
</tr>
<tr>
<td>HBV</td>
<td>43.1 (18-68)</td>
<td>44.4</td>
</tr>
<tr>
<td>HTLV</td>
<td>38.6 (20-63)</td>
<td>38.8</td>
</tr>
</tbody>
</table>
Lookback study in France 2000-12

Results (3)

Interdonation intervals (days)
### Lookback study in France 2000-12
### Results (4)

<table>
<thead>
<tr>
<th>Donors</th>
<th>HIV</th>
<th>HCV</th>
<th>HBV</th>
<th>HTLV</th>
<th>total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Included</td>
<td>169</td>
<td>74</td>
<td>50</td>
<td>18</td>
<td>311</td>
</tr>
<tr>
<td>Followed-up</td>
<td>167 (99%)</td>
<td>64 (86%)</td>
<td>42 (84%)</td>
<td>16 (89%)</td>
<td>289 (93%)</td>
</tr>
<tr>
<td>Information on risk factor</td>
<td>165 (99%)</td>
<td>59 (92%)</td>
<td>38 (90%)</td>
<td>16 (100%)</td>
<td>278 (96%)</td>
</tr>
<tr>
<td>Identified risk factor</td>
<td>145 (88%)</td>
<td>44 (75%)</td>
<td>22 (58%)</td>
<td>14 (87%)</td>
<td>225 (81%)</td>
</tr>
</tbody>
</table>

post donation follow up
Lookback study in France 2000-12
Results (4)

Risk factors for HIV (n=165)

- MSM: 46%
- Heterosexual: 37%
- Other: 1%
- Not identified: 14%

Part end: 32%
Part HIV pos: 21%
Part unknown status: 39%
Other: 8%

127 Men
38 Women
Lookback study in France 2000-12
Results (4)

Risk factors for HCV (n=59)
- Nosocomial: 17%
- Part HCV pos: 22%
- Part at risk: 7%
- Part with unknown status: 5%
- Not identified: 25%

Risk factors for HBV (n=38)
- MSM: 3%
- Part with unknown status: 18%
- Part at risk: 6%
- Part HBV pos: 15%
- Not identified: 42%
- Other: 9%
Lookback study in France 2000-12

Results (5)

- Lookback data available for 236 (75.9%) of the 311 included cases (lack of some records)

<table>
<thead>
<tr>
<th>Archived sample (previous donation)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Investigation on repository sample</td>
</tr>
<tr>
<td>Done</td>
</tr>
<tr>
<td>TOTAL (n=236)</td>
</tr>
</tbody>
</table>

* donation excluded from a potential contamination of the recipient (risk factor after negative donation or positive donation profile in agreement of recent infection)

3 WP HBV-DNA positives only
donations collected before 2010 (HBV ID-NAT Implementation )
No HIV, HCV, HTLV positive
### Lookback study in France 2000-12

#### Results (6)

**Recipient lookback**

Blood products were transfused for 200 donors from 236 to 231 recipients

<table>
<thead>
<tr>
<th></th>
<th>Donors</th>
<th>Transfusions</th>
<th>Recipients</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>total</td>
<td>tested</td>
<td>died</td>
</tr>
<tr>
<td>HIV</td>
<td>135</td>
<td>116</td>
<td>133</td>
</tr>
<tr>
<td>HCV</td>
<td>53</td>
<td>44</td>
<td>51</td>
</tr>
<tr>
<td>HBV</td>
<td>36</td>
<td>30</td>
<td>37</td>
</tr>
<tr>
<td>HTLV</td>
<td>12</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td>TOTAL</td>
<td>236</td>
<td>200</td>
<td>231</td>
</tr>
</tbody>
</table>

1/69 positive (HBV)
<table>
<thead>
<tr>
<th>Year</th>
<th>Donor</th>
<th>Interdonation interval (days)</th>
<th>HBV-DNA repository sample</th>
<th>risk</th>
<th>Recipient</th>
<th>Blood component</th>
<th>infected by transfusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>2000</td>
<td>M/37</td>
<td>72</td>
<td>na</td>
<td>heterosexual</td>
<td>RBC</td>
<td>No (already positive) Died before testing</td>
<td></td>
</tr>
<tr>
<td>2005</td>
<td>M/59</td>
<td>95</td>
<td>Pos &lt;6IU/ml</td>
<td>Not traced</td>
<td>RBC</td>
<td>No (test negative)</td>
<td></td>
</tr>
<tr>
<td>2006</td>
<td>M/42</td>
<td>74</td>
<td>Pos &lt;6IU/ml</td>
<td>Not identified</td>
<td>RBC Plasma for fractionation destroyed</td>
<td>YES (matched viral sequences*)</td>
<td></td>
</tr>
</tbody>
</table>

* Servant et al Transfusion 2013
Outcome of lookback: Summary

- **328 « recent » seroconversions reported (2000-2012)**
  - **311 (94.8%) investigated**
    - **278 (89.3%) information on RF**
      - **225 (81%) RF identified**
      - **33 No information**
      - **53 RF not identified**
    - **236 (75.9%) Recorded repository samples**
      - **202 (84.5%) investigated**
      - **3 (1.5%) HBV DNA pos**
      - **75 recordings not available**
      - **17 No responses**
      - **15 not done**
      - **19 no information**
    - **200 donations transfused**
      - **202 (84.5%) investigated**
      - **3 (1.5%) HBV DNA pos**
      - **80 (34.6%) died**
      - **60 (26%) no info**
      - **22 (9.5%) not investigated**
      - **1 (1.7%) HBV DNA pos**
  - **278 (89.3%) No responses**
  - **236 (75.9%) 75 recordings not available**
  - **202 (84.5%) 17 No responses**
  - **200 donations transfused 1 (1.7%) HBV DNA pos**
  - **231 recipients 1 (1.7%) HBV DNA pos**
  - **69 (30%) tested**
  - **80 (34.6%) died 60 (26%) no info 22 (9.5%) not investigated**

**Donors**

**Recipients**
Transfusion residual viral risk in France (2001-2014)

RR in France 2012-14
HIV 1/3 000 000
HBV 1/6 400 000
HCV 1/33 000 000

HIV/HCV NAT
HBV NAT
Characteristics of French blood donors who recently seroconverted for established viruses

- More than 50% infected by HIV
- 4 times more males for HIV and HBV - females more frequent for HCV and HTLV
- 46% of HIV pos males were MSM in spite of exclusion criteria
- HIV are slightly youngest
- Mean interdonation delays ranged between 5 to 18 months but very short delays was observed (28 days for one newly HIV infected donor NAT only positive no information on recipients)
In spite of experienced and standardized hemovigilance procedures, some information are not available

- 19% of seroconverted BD with follow up did not declare risk factors (12% for HIV to 42% for HBV)

  Need for improving the compliance of seroconverted donors at post donation interview?

- 24% of lookback studies: failures in archiving data

  Need for computerizing and centralizing data to perform appropriate retrospective studies?
Conclusion (3)

- Lookback procedures need an intensive work but are poorly efficient.

- Low yield of archived samples testing (0 positive since the implementation of HBV NAT) due to the low viral RR in France and the high performance of assays used for blood screening.

- Low yield of recipient lookback tracing (30% tested) and testing (no additional infection in comparison with the testing of repository sample).

Go towards a revision of recipient lookback testing strategy based on a better risk assessment?

- stage of infection of the donor, chronology of events, test results of donor archived sample,
- Targetted on the background of the recipient
AKNOWLEDGEMENTS

EFS
MF Leconte des Floris
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R Djoudi
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InVS
J Pillonel

INTS/NRC
R Caparros
L Boizeau
A Servant-Delmas

All physicians in charge of recipients
Thanks for your attention