THE ORGANIZATION OF RARE BLOOD PROCUREMENT IN FRANCE AND THE EUROPEAN COLLABORATION

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- Frequency < 4/1000 in the general population
- Lack of expression of a high incidence antigen (public antigen)
  - No antigen expressed: Rh nul, JK (a-b-)
  - Low incidence antigen expressed: Lu(a+b-), Kp(a+b-)
- Rare combination of common antigens: ddCcEe, ddccEE...

RARE BLOOD GROUP: DEFINITION (Décret n°95-195 - 16/02/95)

- D-C+E-c-e+ 4/10.000
- D-C-E+c+e+ 1/10.000
- D-C+E+c-e+ < 1/10.000
- D-C+E+c-e- extremely rare
- Rhnul extremely rare
- Kp(b-) c 4/10.000
- Ko c 5/100.000 (Ile de la Réunion)
- Jk(b+) Afro-Caribbean 1/1000
- Fy(a-b-) Afro-Caribbean 70%
- S-a-b+ Afro-Caribbean 1/1000
- Jk(a+b-) extremely rare (Melanesians)
- Lu(b-) 2/1000
- Yb- 2/1000
- Bombay extremely rare (Ile de la Réunion)
- Ge2 2/10.000 (mediterranean region)
- Tj(a+) extremely rare
- Co(a+) 2/1000
- Vel 4/10.000
- Jk(a-) extremely rare
- Co(a-b-) extremely rare

ORGANIZATION OF TRANSFUSION IN FRANCE

- ETABLISSEMENT FRANCAIS DU SANG (EFS)
- 17 regions, 8000 professionals (1400 EFS Ile de France)

DONATION
- MANDATORY TESTS
- PREPARATION
- STORAGE
- DISTRIBUTION

- Immuno-hemato analyses
- Research
- HLA
- Cellular therapy
- Therapeutic activities
- Formation, Expertise...

2,000,000 RBC units/year

- MANAGMENT OF RARE BLOOD TRANSFUSION IN FRANCE

250 RBC units transfused per year

- Official Agreement between EFS (BNSPR) and INTS (CNRGS)

BNSPR (National Bank of rare blood units): A. Fialaire-Legendre
Transfusion Center of the Mondor Hospital, Créteil: F. Noizat-Pirenne
EFS Ile de France: director P. Bierling

CNRGS (Blood Group National Reference Center): PY Le Pennec
INTS: National Institute of Blood Transfusion: director P. Bouger (Research, Reference, formation)

17 Regional EFS in France
- management of donation
- preparation
- mandatory tests
- Management of transfusion

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**TRANSMISSION OF RARE BLOOD**

Marseille: 1 patient needs rare blood

EFS Alpes-Med calls the CNRGS and ships blood samples: > 4H

- CNRGS performs analyses: > 1H and asks samples of rare units to BNSPR for compatibility testing: > 2H

- CNRGS performs compatibility testing and asks BNSPR to deliver compatible rare units: > 1H

- BNSPR thaws the rare units: 2H

- BNSPR organizes shipment of rare units with EFS Alpes-Med: > 5H

At least 15 hours to get rare blood unit

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**Transportation remains the main problem**

- By plane: product ready 4H before take off
- By train: product ready 2H before departure, only TGV
- By car: no delay before departure

For long distance: Canada (Kuhne and Nagel)
The product is sent frozen in Carboglace
The transportation cost: paid by the receiving institution

**DONATION OF RARE BLOOD**

For a new donor:

- EFS Alpes-Med sends tubes to the CNRGS for confirmation of the rare blood and registration of the donor in the national file
- EFS Alpes Med sends the unit to the BNSPR for freezing.
- The unit is registered at the BNSPR and at the CNRGS

The CNRGS sends a rare blood card to the donor

For a known donor:

- The unit is sent directly for freezing to the BNSPR and registered

**RARE BLOOD DONATION / DIFFERENCES WITH STANDARD BLOOD DONATION RULES**

- Blood donation
  - Age
  - Frequency
  - Donor pathology

- Preparation
  - No leuco-depletion

- Mandatory tests (Arrêté - 28/12/95)
  - HIV destruction
  - Other markers: specific agreement

**FREEZING METHODS FOR RED BLOOD CELLS**

(approved by the French Regulatory Authority AFSSaPs)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cryoprotector</td>
<td>Glycerol (cf 40%)</td>
</tr>
<tr>
<td>Storage</td>
<td>-80°C &gt; 10 ans</td>
</tr>
<tr>
<td>Thawed-washed units</td>
<td>1 h</td>
</tr>
</tbody>
</table>
| Post wash storage period   | 24 h (open system) at +4°C
                          | 7 days (closed system) at +4°C in SAGM
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**FREZING METHODS FOR RED BLOOD CELLS**
(approved by the French Regulatory Authority AFSSaPs)

### In vitro specifications (for one unit)

- Hematocrit: 50 – 80%
- Hemoglobin: > 35 g
- Residual extracellular hemoglobin: ≤ 1.2% of total hemoglobin
- Residual extracellular glycerol: ≤ 1 g

### In vivo results

- Freeze thaw wash recovery: 90.4 ± 2.3%
- Survival at 24h: 83.6 ± 6.9%

**FREEZING ACTIVITY**

<table>
<thead>
<tr>
<th>Year</th>
<th>Total number of frozen units</th>
<th>Nb of frozen units/year</th>
</tr>
</thead>
<tbody>
<tr>
<td>2000</td>
<td>4967</td>
<td>1413</td>
</tr>
<tr>
<td>2005</td>
<td>519</td>
<td>1247</td>
</tr>
<tr>
<td>2006-2007</td>
<td>407</td>
<td>112</td>
</tr>
</tbody>
</table>

**PHENOTYPIC repartition (%)**

- FY: -1 -2: 50%
- Rare RH: 17%
- U: -11%
- KEL: -2: 7%
- YT: -1: 7%
- VEL: -4%

**STORAGE REGULATION**

Between 2002 and 2007: 2426 units were destroyed for storage regulation

To reach the mandatory requirements for the entire stock (NAT)

To ameliorate the phenotypic/genotypic characteristics of the units

- Fy(a-b-): frozen only if
  - homozygozytes in JK, MNS
  - RH:-20 and/or KEL:-7

**CHARACTERISTICS OF STORED UNITS**

- Age of units:
  - < 5 years: 58%
  - 5 - 10 years: 25%
  - 10 - 15 years: 9%
  - > 20 years: 3%

- Units frozen in the close system: 1630 (29.5%)

- Units with NAT on donation: 3571 (64.6%)
- Units with NAT on donor: 4638 (83.3%)

- Units with biological abnormalities: 116 (1.1%)
- 68% AChEBs: 28% Pau+ syphilis

- Non leucodepleted units: 47 (0.9%)

- Units with CI in donors:
  - 100 units: 60 donors (75% from transfused donors and 43% from travelers in malaria area)

**DATA IN THE NATIONAL FILE**

- For all individuals with a rare blood group: donors and recipients
  - Personal data
    - identity, birth-date, address
  - Immuno-hematological data
    - rare blood group, full phenotype, antibodies in the serum
  - Pathology
  - Donations
    - number of units available, unit number identification, date of donation, marker requirements
  - Transfusions
    - Identification number of units received, identity of donor, date of transfusion
REMAINING PROBLEMS IN THE ORGANIZATION OF RARE BLOOD TRANSFUSION

- Need to upgrade the mandatory tests and requirements
  - The nucleic acid test (NAT) since 2001
  - Leuco-depleted blood since 1998
- Delay between request and supply: thawing, shipment
- Risks management implementation because of
  - Positive mandatory tests
  - Storage for long term duration: development of donor pathologies with units in the BNSPR

EUROPEAN AND INTERNATIONAL COLLABORATION

Since 2002: 16 units have been shipped to different regions
  - The Netherlands, Belgium, Switzerland, Canada
Request to the CNRGS if units available:
  - Management of the shipment with BNSPR and receiving institution
  - Depending on the distance:
    - Frozen units: thawing procedure as to be the same as in France
    - Thawed units: have to be transfused before 24H
  - Authorization for the exportation, signed by the EFS director
  - Price: the same, will probably increase

Last collaboration in August 2008:

One unit needed in Switzerland for a child with the McLeod phenotype

The unit was not available at the BNSPR

A donor of the CNRGS file, living in Bordeaux, has been asked to give blood at the regional center of the EFS

The unit has been shipped to Paris at the BNSPR, then to Switzerland

France participates to the Rare Donor Working Party

ISBT Working party: concerned by quality of shipment and international requirements: a form has to be completed:
  - The form is packed by the shipper and completed by the receiving facility
  - The form is sent by FAX to the IBGRL
  - Phenotype of units
  - Number of units
  - Condition of the units at arrival
  - Expected time respected
  - Infectious disease: Tests performed and documented
  - Billing document in order
  - Transfusion outcome

French donors are not on the International Panel

Because of the Official Agreement BNSPR and CNRGS are the only institutions allowed to manage rare blood.
In France, the rare donor panel is not available for the French users.

An institutional collaboration in Europe has to be made at the European Council
  - First meeting: July 10, 2008
  - France was represented by Dr A. Falilaire-Legendre
  - Discussions were on transportation and possibilities to organize a European rare blood file

CONCLUSION

- The existence of a national file of rare individuals at risk for transfusion allows a better follow up of the patients
- The existence of a large number of frozen units
  - Makes easier the answer to emergency cases
  - Allows a better prevention of the allo-immunization for the rare phenotype and the most common immunogenic antigens
- European collaboration has to be developed
- France can share its experience with other countries

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