Perspectives on self-sufficiency of blood-derived therapies. Global evolution and realities.

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Vice President Global Access PPTA
The Rome Declaration on Achieving Self-Sufficiency in Safe Blood and Blood Products, based on Voluntary Non-Remunerated Donation

- The exploitation of donors
- The undermining of blood services
- The risk of transfusion transmissible infection
- Blood as a public enterprise
Self-sufficiency

Confounders

• Should transfusion components and plasma therapies have the same framework?

• Is blood a public asset of a tradable commodity?

• Should blood donation be compensated?
<table>
<thead>
<tr>
<th>Blood components</th>
<th>Plasma protein therapies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Derived from individual donors</td>
<td>Derived from plasma pools (&gt;60 K donors)</td>
</tr>
<tr>
<td>Minimally processed; Relatively labile</td>
<td>Intensively manufactured; relatively stable</td>
</tr>
<tr>
<td>Delivered from the NFP sector</td>
<td>Delivered from the FP sector</td>
</tr>
<tr>
<td>Mostly – acute applications</td>
<td>Mostly – chronic situations</td>
</tr>
<tr>
<td>Minimally regulated</td>
<td>Strongly regulated</td>
</tr>
<tr>
<td>- GMPs</td>
<td>- GMPs</td>
</tr>
<tr>
<td>- No efficacy assessment</td>
<td>- Standards</td>
</tr>
<tr>
<td>- Evidence base?</td>
<td>- Efficacy assessment</td>
</tr>
<tr>
<td>- Common sense?</td>
<td>- Post market oversight</td>
</tr>
<tr>
<td>- Etc etc</td>
<td>- Etc etc</td>
</tr>
<tr>
<td>Historical use</td>
<td>Historical AND evidence based use</td>
</tr>
</tbody>
</table>
Clinical need – Plasma protein therapies

• Assessing plasma sufficiency requires assessment of clinical need
• The plasma industry has gone through successions of demand drivers
  – Albumin
  – Factor VIII
  – Immunoglobulin
• In the established economies the driver is Ig
“The average potential usage of Ig for the treatment of CVID and XLA was estimated at 72 g/1,000 population, which is higher than the estimated Ig usage in CVID and XLA of 27–41 g per 1,000 population in the US.”
Australia Ig issues

Australian NBA 2014 [link to report]

[Chart showing trends in grams of IgG issued to AHPs from 2003-04 to 2012-13, with data points indicating a rise from $A57/g to $A63/g]
Australia Ig issues

94% of usage is level 1 – 2A
Australian fractionation landscape
The driver and the motor

Ig usage

Plasma for fractionation

www.pptaglobal.org
Plasma – How Much?
Theoretical estimate -

- On the basis of
  - Usage of 150 g/10000 population
  - Ig yield of 5 g/L of plasma – Best obtainable – generally 3 to 4 g/L

- Ig needs can be met through 30L of plasma/1000 population

- This will also generate 6 IU/per capita FVIII
Plasma – From where?

- Options for plasma procurement
  - Recovered from blood donations
  - Sourced from plasmapheresis
- If recovered
  - Assume 95% of donations are packed, each donation 250ml of plasma

➤ Need to collect 126 units of whole blood per 1000 population!
Blood and red ink: Hospitals perform fewer transfusions and blood banks feel the pain

By Alan Bavley, The Kansas City Star

May 04---In 2008, the Community Blood Center of Greater Kansas City was riding a 14-year national boom in blood demand.

Its donors provided a record number of units of red blood cells for area hospital patients that year, and the blood center opened a gleaming new state-of-the-art laboratory about a mile from its midtown headquarters to swiftly test donor blood for infections.

But all that was about to change.

As the Great Recession took hold that year, people started worrying about their jobs and health insurance, and they canceled elective surgeries.

More important, hospitals across the country -- including St. Luke's Hospital and the University of Kansas Hospital -- had been changing policies and technology to safely minimize the need for blood transfusions, both to cut costs and to diminish risks to patients.

Research had been mounting for years that most hospital patients stayed healthier when they received little or no transfused blood. They faced less risk of infection, lung complications, even death.

From 2008 to 2011, transfusions nationwide dropped 8.2 percent, according to the most recent data from the Department of Health and Human Services. And the numbers are still trending lower, blood banking experts say, as more hospitals develop "patient blood management" programs.

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Red cell issues - Australia
• RCC usage is plunging in the established economies
• Recovered plasma production is decreasing
• Recovered plasma is more difficult to control than source plasma
• Most of the indications for red cell transfusion in emerging economies are best met through WB ()
• Tying the blood service to the generation of plasma for fractionation is inimical to mainstream transfusion demands
### Plasma Production: The Top Ten Country Plasma Production

<table>
<thead>
<tr>
<th>Country</th>
<th>Plasma production L/1000 population</th>
<th>Donor status</th>
</tr>
</thead>
<tbody>
<tr>
<td>United States</td>
<td>66</td>
<td>Uncompensated and compensated</td>
</tr>
<tr>
<td>Austria</td>
<td>56.6</td>
<td>Uncompensated and compensated</td>
</tr>
<tr>
<td>Czech Republic</td>
<td>33</td>
<td>Uncompensated and compensated</td>
</tr>
<tr>
<td>Germany</td>
<td>31.6</td>
<td>Uncompensated and compensated</td>
</tr>
<tr>
<td>Australia</td>
<td>21.5</td>
<td>Uncompensated</td>
</tr>
<tr>
<td>Netherlands</td>
<td>18.8</td>
<td>Uncompensated</td>
</tr>
<tr>
<td>Denmark</td>
<td>17</td>
<td>Uncompensated</td>
</tr>
<tr>
<td>France</td>
<td>16.3</td>
<td>Uncompensated</td>
</tr>
<tr>
<td>Sweden</td>
<td>16.1</td>
<td>Uncompensated</td>
</tr>
<tr>
<td>Belgium</td>
<td>15.5</td>
<td>Uncompensated</td>
</tr>
</tbody>
</table>
No evidence of donor poaching

Czech Blood Collection Regions
Presence/absence of plasma centers*

*Source: Ústavu zdravotnických informací a statistiky České republiky 2009
Plasma collection in Italy

12.5 L/1000 pop

Total Collection

Plasmapheresis

4.4 L/10^3 population (35%)
“The Government pursued the goal of self-sufficiency in factor VIII during the 1970s and most of the 1980s, in line with WHO and Council of Europe recommendations. The primary aim of this goal was to reduce the reliance on expensive imported concentrate.....”
UK developments

- **1999** – All plasma for fractionation to be imported
  - First attempts from VNRD sources, quickly abandoned for USA compensated sources

- **2004 – 05** – all FFP for transfusion to children ≤ imported from USA

- **2008** – Scottish Protein Fractionation Centre closed down
  - “Scottish Government decided that it would be less expensive to obtain fractionated blood products from outside Scotland”
  - No offers to purchase the PFC

- **2013** – 80% of English Bioproducts Laboratory sold to Bain Capital
Can fresh components cross borders?

- **Euroblood Program**
  - Swiss, Dutch and German red cells for USA
  - At one time – 40% of NY blood supply
  - Stopped because of vCJD risk

- **UK importation of FFP**
  - Started because of vCJD risk

- **Swiss program for Greece**
  - 28,000 pa red cells for thalassemia
  - Stopped because of ……..
Swiss Red Cross Cuts Donor Blood Supply To Greece After Failing To Pay Bills

By FRANK JORDANS 02/26/13 11:35 AM ET EST [AP]

BERLIN — The Swiss Red Cross is slashing its supply of donor blood to Greece because the financially stricken country has failed to pay its bills on time, the head of the group’s transfusion service said Tuesday.
Albumin usage

NB – Taking out outliers in the South shows usage more conformant to EU levels (and decreasing) Grazzini G., Calizzani G. SIMTI 2014
Self-Sufficiency gone bad: The French Blood Scandal

- France – early 1980s – Fiercely for self-sufficiency
- French blood service – its own fractionator and regulator
- French blood donors – all voluntary – but included prisoners
- Delayed introduction of heat treatment for FVIII until French technology was available
- Delayed introduction of AIDS test until French (Pasteur) test was available
- Stocks of unheated, untested product given knowingly to haemophiliacs
- THOUSANDS of haemophiliacs and transfusion recipients infected with HIV
- Trials and jail sentences
The bureaucrat's answer

“I never refused importation but I did not insist on imports. Our ambition was self-sufficiency”

Jacques Roux, French Director General of Health early ‘80’s.

Sentenced four years (suspended) jail.
Self-Sufficiency gone bad:
Ireland – The road to hell……

- Irish blood service late 1970s – its own fractionator and regulator
- Made FVIII, FIX, anti-D – NO LICENSES
- Anti-D program for self-sufficiency
- Used chromatographic method to get better yields than Cohn – no viral clearance/inactivation
- Used donors from plasma-exchange programs – no medical scrutiny
- One donor was HCV positive – infected many batches
- OVER FIVE HUNDRED WOMEN INFECTED WITH HCV
- Inquiries, dismissals, reforms
- **Ireland no longer has a self-sufficiency policy – or a fractionation capacity**
Self-Sufficiency – Single Supplier?

- Self-Sufficiency in plasma – should it result in reliance on one manufacturer?
- Dangers of monopoly – pressure on regulator
- French regulator – lower standard for domestic products
Developments in the government fractionation sector

- Canada – Closed down fractionation facility after the Krever report
- Australia – privatized its facility in 1994
- Scotland – closed down its facility in 2006
- Finland – Closed down its facility in 2004
- Denmark – Stopped fractionating in 2002
- Switzerland (Red Cross NFP) – sold in 2000
- England – Privatized and sold 2013
Conclusions

• Sufficiency of plasma for fractionation is driven by Ig needs, 80% of which are obtained from the commercial sector
• Governments previously aligned to self-sufficiency and public fractionation have moved away from these activities
• Sufficiency of plasma therapies requires efficient apheresis, which requires donor compensation and free cross-border commerce
• Whole blood collection, and hence recovered plasma production, is dropping as the need for red cells decreases
• Extremist adherence to self-sufficiency, leading to unregulated monopolies, has harmed vulnerable patients
• Continued differentiation between the blood transfusion and plasma therapy sectors is desirable for good, evidence-based, medical practice