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Future of Plasma Fractionation

Pessimistic View
Magdy El Ekiaby
Devil advocate!!!!!!!
Elements of plasma fractionation

Source or recovered plasma collection, testing and storage

Cold Chain Transport

Fractionation Plant

- Competent local medicinal regulatory agency
- An array of legislations supporting blood collection activities, storage, manufacture and cross border movement of raw material & finished products
Challenges of Plasma for Fractionation as a Raw Material!
Recovered Plasma

**Global Blood Collection:** Around 92 million blood donations are collected annually: Approximately half of these blood donations are collected in high-income countries, home to 15% of the world’s population.

**Blood Screening:** In 39 countries, blood donations are still not routinely tested for transfusion-transmissible infections.

**Blood Processing:**
Only 31% of the blood collected in low-income countries is separated into blood components.
Demographic Challenges in Developed countries

- Progressive increase in aging in EU countries will reduce donor population
- New life style of young people with frequent travel to endemic areas with specific infectious agents reduces their frequency of blood donation
- Emerging new pathogens such as vCJD with banning of UK plasma
- National self sufficiency of plasma fractionated products from NBTS in Europe is becoming a history!!

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EU 25 average: 23.4% in 2005, 24.9% in 2025, 35.7% in 2050

Note:
(i) Based on the assumption of net immigration 2005-2050 amounting to almost 4.0 million people.
(ii) Greek part of Cyprus only.
Source: Eurostat, Europop 2004 (base scenario)
Demographic and Epidemiologic Challenges in developing countries

- Majority of blood donors are family replacement first time donors
- High prevalence of transfusion transmitted infectious agents
- High residual risk even when implementing NAT blood screening
69% of blood collected in low income countries is not processed into components

- 45 million units of blood are collected in developing world

- These donations need to be:
  - Tested according to international standards
  - Processed into components
  - Plasma further processed into safe plasma products

- With realities mentioned in WHO report, it looks that a lot of work need to be done to process these blood donations and qualify its plasma for fractionation
Source Plasma from Paid Donors, Ethics

- WHO, ISBT and IFBDOs advocate and promote voluntary non-remunerated blood donors

- IFBDO Statutory goals:
  - To promote the regular, anonymous, voluntary, non-remunerated gift of blood in all countries of the world.
  - To work towards meeting the needs for high quality human blood and blood products in every country, in co-operation with the competent entities.
  - To ensure that ways and means are applied guaranteeing the safety of both the donor and the receiver.
  - To combat all forms of marketing and gain with respect to blood and blood derivatives, under the principle that the human body is unalienable.
  - To participate in all studies, activities, discussions or events related either to the organization of blood transfusion and blood donor associations or to knowledge and research in blood transfusion techniques.
Plasma as a raw material is a permanent challenge!!!!
The World of CFCs

Today and Tomorrow!!!!!
2000’s – Advancing on All Fronts

SD Cryo Biosimilars

Current Therapy

Long-Lasting Products Gene Transfer

Sources: Vox Sanquinis 2006; NEJM 2012
- Only 9 countries use almost 60% of Global FVIII production*
- Recombinant FVIII represent almost 80% in these countries and close to 90% of global recombinant market*

*WFH Global Survey 2010
Australia, Canada, Japan, France, Germany, South Korea, Switzerland, UK and USA
Deep look into today reality

- The main consumers of recombinant CFCs are also the same main producers of plasma for fractionation.
- This means that there should have been a surplus of plasma derived CFCs available to developing countries at an affordable price.
- Contrary to this reality, fractionators are not so far processing the unused cryoprecipitate paste in these countries, most probably due to lack of cost efficiency and complexity of legal and regulatory aspects.
And if this is true in well regulated countries

Then it should be even more challenging to start a new fractionation industry in emerging world!!!!!!!!!!!
Tomorrow
Strategies.1

Half-life extension

PEGylated Liposomes

PEGylation
- Random
- Site specific

Fusion protein
- Fc fragment
- Albumin

Modification of amino acid sequence

Peyvandi F.
Alternative Therapeutic strategies
- inhibitors of coagulation to increase the hemostatic efficacy

Inhibition of TFPI
- antibodies (anti-TFPI)
- synthetic inhibitors (aptamers)

Bispecific antibody (ACE910) against activated factor IX (FIXa) and factor X (FX)

Inhibition of APC and antithrombin (AT)
- aptamers and RNAi silencing
Tomorrow

- Long acting CFCs are close to reach markets in the next few years

- The CFCs trend making countries may soon embark on using these new products in prophylaxis with the hope to reach a trough level of 10-15% and a bleed free world

- It will be logic for major CFCs manufacturers to transfer current recombinant technology to major consumers of emerging markets such as Russia, Brazil, India and China

- In such a scenario, these countries can become self sufficient and also can distribute regionally at affordable prices
Does this scenario sound logic?!
It looks that there is a good margin for price reduction.
Affordable Treatment For All

The 80:20 Challenge

Source: Guh et. al. (CDC) *Haemophilia* 2011
A Paradigm of Scarcity

- Treatment protocols dictated by scarcity of treatment products
- Constraints on utilization distort true demand
- Understanding unconstrained demand is vital
  - Production planning
  - Health policy planning
- Today, supply constraint should not be a factor
Time for a 21st Century Paradigm
A new Business Model

• Accelerating innovation of treatment products presents the opportunity to accelerate global access
• A 21st century business model is required
  A new paradigm based on high-volume, low margins
• Payers expect the optimization, innovation and efficiencies achieved in manufacturing will be passed on in final product pricing
Technology, knowledge and capacity exist to dramatically improve global access

- The technology, knowledge and capacity exist to dramatically improve global access to clotting factor concentrates.
- It is now a moral imperative for governments, regulators and industry to rise to the challenge by:
  - Promoting free trade
  - Adopting market-based business solutions
- The production, pricing and marketing strategy of companies bringing new products to market present the opportunity to significantly and favorably impact the cost–benefit equation
So, which industry can be more responsive to the future business model?

Plasma or recombinant industry??!!!
Innovation; Mini-Pool Fractionation (Bio-similar)

- A new concept to provide large transfusion centers in developing countries to have access to safer plasma components
- It is based on validated single use medical devices to concentrate and virally inactivate plasma proteins
- The technology is like plug and play!!
- It helps to use domestic plasma
- It is cost effective for developing countries
- So far two medical devices are commercially available
- Already used in Egypt and several developing countries are in progress
Medical Devices
- Pharmaceutical grade SD/F cryoprecipitate

- Possibility of FI, FVIII, VWF & FXIII dose labeling
Solvent-detergent filtered (S/D-F) fresh frozen plasma and cryoprecipitate minipools prepared in a newly designed integral disposable processing bag system

M. El-Ekiaby,1 M. A. Sayed,2 C. Caron,3 S. Burnouf,4,5 N. El-Sharkawy,7 H. Goubran,8 M. Radosevich,6 J. Goudemand,3 D. Blum,4,5 L. de Melo,9 V. Soulié,9 J. Adam9 & T. Burnouf5 1Shabrawishi Hospital Blood Bank, Giza, Egypt, 2Fayoum University, Fayoum, Egypt, 3Laboratoire d’hématologie, Hôpital Régional et Universitaire Lille, 4INSERM, U837, 5Université Lille-Nord de France, IMPRT, Jean-Pierre Aubert Research Centre, 6Human Protein Process Sciences, Lille, France, 7National Cancer Institute, 8Faculty of Medicine, Cairo University, Cairo, Egypt, and 9V.I.P.S. SA Virus Inactivation of Plasma Systems, 2013 Colombier, Switzerland
ORIGINAL ARTICLE

Pharmacokinetic study of minipooled solvent/detergent-filtered cryoprecipitate factor VIII

M. EL-EKIABY,* H. A. GOUBRAN,†† M. RADOSEVICH,§ A. ABD-ALLAH,* A. EL-EKIABY* and T. BURNOUF§†

*Shabrawishi Hospital Blood Bank, Giza, Egypt; †Saskatoon Cancer Centre, University of Saskatoon, Saskatoon, Canada; ‡Faculty of Medicine, Cairo, Egypt; §Human Protein Process Sciences, Lille, France; and *College of Oral Medicine, Taipei Medical University, Taipei, Taiwan
Eventually!!!

- Fractionation industry played a major role to provide safe and effective medicines; particularly in the last 3 decades
- Progressive innovations particularly in the recombinant technology is currently complementary to fractionated products, but may prevail in the next 2 decades
- Advances in gene and stem cell therapies may provide safer and permanent alternatives to fractionated plasma products in the future
So, with all these new innovations to come:

Will plasma fractionation have the same role, more contribution or less contribution to the world of CFCs??!!!!