Blood supply and blood products: Regulatory issues in the pandemic context

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Plasma Derivatives

- No Shortage to expect: long shelf life
- No safety problems with respect to influenza: enveloped virus, susceptible to different methods of inactivation
- Provisions should be taken to ensure release of final products without delay at the manufacturers site and by the OMCL (Definition of key tasks and key personnel for the Business Continuity Plan)
Blood Components

- Occurrence of viremia has to be assumed, however, viremic persons are likely to have symptoms and would thus not donate. The risk of transmission by blood components will be negligible compared to the risk of community-acquired infection.

- Blood component availability is affected by:
  - Short shelf life of platelet concentrates (PC, 5 days) and of red blood cell concentrates (RBC, 6 weeks)
  - Disposition of donors in good health
  - Blood establishment (BE) personnel in good health
  - Need (Situation in hospitals, optimal use of blood components, logistics, personnel, …)
Blood Components

♦ FAQ to regulatory authorities with regard to a severe epidemic like flu pandemic is:
  Should donor selection criteria be eased to avoid blood shortage owing to the lack of donors - and possibly of blood bank personnel - in good health?

♦ Counter question:
  Are there other possibilities to maintain supply with blood components?
Course of Pandemic
Example from seasonal influenza 2007, Germany, weeks 40-51
(from http://influenza.rki.de/index.html?c=saisonbericht)

Due to our contact behavior infections will not disperse slowly, e.g. from north to south, but rather rapidly all over the country once a certain reproduction rate is exceeded: Compensation by cooperation between BE will be limited.
Simplified Pandemic Model

![Graph showing population dynamics with Susceptible, Infected, and Recovered categories over time.]

- $f$ (mortality)
- $\gamma$ (transmission rate)
- $\nu$ (recovery rate)
- $1/\nu$ (average infection period)
- $R_0$ (reproduction factor: $R_0 = \frac{\gamma}{\nu}$)

Estimated reproduction factor for the pandemic flu in 1918/19: $1.5 < R_0 < ...3$

Reproduction factor for seasonal influenza: $1 < R_0 < 1.3$
Request and delivery of RBC (data of a large red cross institute) in context with seasonal influenza

First half of the year: Nearly all requests delivered, accumulation possible.
Second half of the year: Refused requests till 25% of total demand, i.e., blood shortage occurs every year; the “transfusion chain” deals with it and the situation does not cause harm to patients.

Seasonal influenza without impact on blood component availability:
- Occurs in the accumulation phase,
- % infected persons (about 2.5%) lower than % refused requests (max. 25%).

$R_0^{eff} = 1.28$
Quarterly fluctuation of regular donors, observed in Germany 2000-2005

Despite considerable fluctuations in donor availability and despite the short shelf life of RBC and PC blood establishments are able to manage a save supply of blood components for transfusion.
Differences in transfusion of RBC between European countries is obvious. Use in countries above median (39.4 U RBC/10^3 inhabitants) varies from 40.1 (NO) to 70.8 (DK); no severe supply problems with impact on patient’s safety are published.
Differences in Consumption of Red blood cell concentrates in different hospitals in Germany

(Survey W. Schramm et al.: Hemotherapy in Germany; 24 hospitals evaluated for intra operative transfusion trigger in defined indications)

Transfusion trigger (minimal intra operative hemoglobin values) strongly varies between different hospitals despite comparable patient cohorts.
High potential to economize use of blood components. !Optimal use!
Request and delivery of RBC in pandemic flu

Not delivered demand 2006

Donor deferral 7 days $R_0^{\text{eff}}=2$

Donor deferral 14 days $R_0^{\text{eff}}=2$

Delivery strategy, deferral time, ... will influence degree of shortage.
FAQ asked again

🔹 FAQ to regulators:
Should donor selection criteria be eased to avoid blood shortage owing to the lack of donors - and possibly of blood bank personnel - in good health?

🔹 Answer by Blood Regulators Network (BRN):
No, there are other possibilities to maintain supply with blood components.

🔹 Exception:
In case of extreme blood shortage in pandemic phase 6 (WHO global influenza preparedness plan) distinct deviation will be possible.

WHO global influenza preparedness plan
The role of WHO and recommendations for national measures before and during pandemics
Details on BRN statement: http://www.who.int/bloodproducts/brn/en/

Blood Regulators Network

The World Health Organization (WHO) Blood Regulators Network (BRN) was established in 2006 and is comprised of leading international regulatory authorities that have responsibility for the regulation of blood, blood products and related in vitro diagnostic devices (IVD).

The Expert Committee on Biological Standardization (ECBS) recognized the need for a global network of regulatory authorities in the blood field and recommended that WHO promote cooperation of experienced regulatory authorities in risk assessment and information-sharing through the establishment of a "peer regulators group".

The BRN provides a forum for the exchange of information and opinion among members on blood-related issues. The Network focuses on the scientific assessment of current and emerging threats to the safety and availability of blood and blood products, assessment of the impact of new blood-related technologies, and also explores opportunities for regulatory cooperation and collaboration where possible.

BRN PUBLICATIONS

:: Donor Selection in Case of Pandemic Situations [pdf 15kb]

RELATED LINKS

:: BRN Members
Donor selection in case of pandemic

General aspects

- Make sure that blood transfusion services are alerted appropriately and included in national pandemic information systems.

- Develop a stochastic scenario which estimates
  - the degree of affection of donors and
  - blood bank personnel,
  - possibilities to attenuate the situation,
  - the critical need of transfusion, and
  - the win in blood supply due to any relaxation of donor selection and testing.
Donor selection in case of pandemic

- **No changes** in information to be provided to prospective donors of blood or blood components - special information on hygiene measures may be added; donor vaccination should be recommended (in line with information by health authorities).

- **No changes** in information to be obtained from donors.

- Without extreme necessity, **no changes** should be permitted in donor screening for infectious parameters, i.e. test panels and test procedures.

- **No changes** in any of the serological assays.

- Without extreme necessity, **no changes** should be permitted with respect to permanent or temporary donor deferral criteria issued to avoid serious danger for donors’ health and to avoid transmission of infectious diseases by transfusion.
Donor selection in case of pandemic

- As standard procedures in BE are well implemented, familiar to the employees and running more or less smoothly, any changes in the standard procedures bear the danger of making mistakes, while it is doubtful whether they would really improve the situation.

- Moreover, it may be difficult for the blood bank personnel to understand that hitherto strictly observed standards would be discounted. Therefore, any deviations from donor selection criteria should be clearly communicated to the blood bank staff as a measure in exceptional circumstances.
Donor selection in case of pandemic

- It is conceivable, under the responsibility of a qualified healthcare professional and in appreciation of the effective risk situation, to apply less restrictive criteria for individual donations as follows:
  - raised upper age limit, preferably for regular donors
  - lowered haemoglobin level for females and males
  - shortening of donation intervals for platelet aphaeresis provided that critical parameters are within ranges harmless to donor health.
Donor selection in case of pandemic influenza

Particularities

- National authorities should advise their BE on the time interval for donor re-entry after cessation of symptoms according to the state of knowledge.
- Donors should be asked for intensive contact with flu patients (sick-nursing) within the last 7 days.
- To minimize contagion between donors, donation dates should be arranged in a way to avoid gathering.
Influenza Virus

Arbeitskreis Blut, Untergruppe «Bewertung Blutassoziierter Krankheitserreger»

1 Current Knowledge about the Pathogen

1.1 Characteristics of Influenza Viruses

Influenza viruses are members of the family Orthomyxoviridae. This family represents enveloped viruses the genome of HA are obviously more stable (loss of infectivity at pH <4.5) than viruses with cleaved HA (loss of infectivity at pH <5) [2]. The most outstanding characteristic of influenza viruses is their rapid evolution which leads to its great variability. This is the case especially with influenza A viruses. According to the
Further Considerations in Case of Pandemic

- Deadlines for reporting (other than notifications of severe adverse reactions) which fall within the pandemic period may be temporarily suspended by the responsible authorities.

- Depending on the availability of personnel, cancelling of autologous donations could be considered, as this kind of donation has a lower degree of standardization and therefore may be too time consuming and error-prone in case of staff shortage.
Thanks for data submission to …

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- C. Kamp, Biostatistik Paul-Ehrlich-Institut