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I08 Development of transfusion medicine in Europe – A challenge for physicians, scientists and politicians

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Modern transfusion medicine in Europe has successfully handled the major threats to a safe blood supply by “classical viral” transfusion-transmitted pathogens like HCV and HIV. However, this was only managed by utilizing major financial and expert resources.

Today, European harmonisation of optimal use of blood components in clinical hemotherapy, uniform quality standards for blood donations, testing and component production as well as an increasing cost pressure in clinical care are tasks, which need our full attention. Modern cellular therapies and regenerative medicine are novel treatment options, which can only be handled by a close cooperation between clinicians and transfusion medicine specialists.

Future challenges comprise proactive measures like pathogen inactivation for all blood components in order to diminish threats to blood safety by (re-)emerging pathogens, an adequate blood supply bearing in mind the ongoing ageing of most European populations and political decisions regarding a potential open “blood market” in Europe, which in our opinion should not be supported by the European Union.

Keywords: Blood safety; Optimal use of blood; European regulations; Future challenges in transfusion medicine

Introduction: When Karl Landsteiner (1868–1943) published his discovery of ABO-blood groups in 1901, transfusion medicine started a course of tremendous development which has not yet ended. Sadly, as it is the case with most technical and scientific changes, World Wars I and II sped up the transition of transfusion medicine into modern high-tech medicine. While traumatology, surgery and internal medicine as well as gynecology and obstetrics expanded their approach to diagnostics and therapies of complex diseases, novel fields of modern medicine emerged: Transplantation medicine and hematopoietic stem cell transplantation in hematology/oncology and modern pediatrics are relatively recent developments. In parallel, the need for safe blood components grew. For example, the Heidelberg University clinics performed 25 transfusions in 1927. 80 years later, transfusions of red blood cell concentrates at a comparable sized institution have multiplied by more than the factor 1000.

History: When after World War II the needs of modern medicine called for well organized blood donor services, most European governments handed this task over to their respective national Red Cross organizations. With increasing demand for blood components, encouragement and mobilization of the healthy population to donate blood became one of the prominent tasks of these new organizations in the 50s of the last century. The aging of most European populations nowadays demands great efforts to provide blood donations from healthy volunteers since most surgical procedures on elderly patients require more blood products than the same procedure on young people does.

Providing an adequate amount of safe blood components is vital for modern societies in Europe and it remains to be decided, whether this important task will be handled by the national Red Cross organizations, hospitals, private pharmaceutical companies, governmental organizations or even possibly a combination of those.

For hemophilia patients, who in former times died in early adulthood due to bleedings or other complications, the introduction of self-treatment at home with factor VIII or factor XI concentrates helped these patients to achieve a normal life expectancy. However, most of the hemophiliacs treated suffered from hepatitis B or hepatitis C in the last decades of the last century. In the 80s of the last century, the first AIDS scandal helped to accelerate the development of heat-inactivated factor VIII concentrates. Later on, in the 90s of the last century, a second AIDS scandal in blood products shocked Germany: Following this, public authorities were closed and the Paul-Ehrlich-Institute took over responsibility for granting marketing authorizations for blood and plasma products. New institutions like the “Arbeitskreis Blut” at the German Ministry of Health with experts from transfusion medicine, hemostaseology and patient care were established and new laws like the transfusion law were inaugurated as well.

Since then, safety of blood products has become one of the highest priorities in Germany as well as in most other European countries.
Quality and safety of blood components have increased dramatically since the beginning of the 90s of last century: Registration of blood donor services as pharmaceutical companies, manufacturing licenses and marketing authorizations for blood products, in-line filtration of whole blood donations in order to diminish leucocyte contamination of the final blood components, quality control and quality management as well as inspections by governmental authorities and blood donor services themselves, look-back measures and notification requirements are all examples of the measures implemented during the last 20 years which have contributed to increasing product quality and safety. Medical histories taken by a doctor from every blood donor, a medical examination and the exclusion of donors with an increased risk of transmitting blood borne diseases are well established measures to reduce the risk of pathogen transmission by blood transfusion. Laboratory blood donor screening nowadays includes serological markers like HBsAg, Anti-HBc, Anti-HCV, Anti-HIV I/II, Anti-CMV and TPHA-testing as well as pool-PCR-testing for HCV, HIV and HBV (HBV-PCR-testing is not mandatory in Germany).

The combination of all these measures led to a dramatic reduction in the risk of transfusion transmitted HCV or HIV infections in Germany: The observed frequency of transfusion associated viral infections for 1997 to 2006 for ELISA- and pool-PCR-negative blood products from unpaid donors of the German Red Cross was as follows [1]: For HCV, 1 in about 30 million blood donations tested and HIV 1 in about 30 million blood donations tested. However, the introduction of HCV- and HIV-PCR in blood donor screening causes high costs per prevented infection: In Germany, the cost per prevented HCV- or HIV-infection by blood transfusions are approx. EUR 3.5 to 4 million per prevented infection. Compared to the global situation, with over 75 million units of blood donated every year around the world, less than 50% of WHO countries test for HIV, HCV or HBV on a regular basis in their transfusion organizations. Therefore, unsafe transfusions and medical treatment account for approx. 8–16 million HBV infections/year, 2–4 million HCV-infections/year and approx. 100,000 HIV-infections/year globally [2].

European measures to increase safety and quality of blood transfusions: Starting in the 90s of the last century, the Council of Europe published recommendations on the suitability of blood and blood donors and the screening of blood donations in the European Community (Council recommendation 98/463/EC of June 1998). Directive 2002/98/EC of the European Parliament and of the Council of January 2003 setting standards of quality and safety for the collection, testing, processing, storage and distribution of human blood and blood components (and amending directive 2001/83/EC) was the key directive of the European Commission which has now been implemented into the transfusion laws of most countries. Later directives like directive 2004/33/EC, directive 2005/61/EC dealing with look-back and notification of serious adverse reactions following blood transfusion, directive 2005/62/EC regarding common standards and specifications for a quality system in blood donation services in Europe as well as further technical directives and recommendations show that the European Union is active in the field of procurement of safe and adequate blood components. Further directives regarding tissues and cells, in-vitro diagnostics and the CE-marks of medical devices are additional examples of the European Union thoroughly regulating this vast and rapidly developing field of modern medicine.

Proactive measures to reduce threats to a safe blood supply from (re-)emerging pathogens: Apart from the "classical" hepatitis viruses, HI virus and bacteria as potential transfusion transmitted pathogens, new threats from (re-)emerging pathogens have developed over the last few decades: Variant Creutzfeldt-Jacob Disease (vCJD) caused by prions [3,4], viral infections like Severe Acute Respiratory Syndrom (SARS), Avian Influenza, West-Nile-Virus and Chikungunya fever are all examples of (re-)emerging pathogens (see also Table 1). These pose an acute and more dangerous threat to safe blood transfusions than the "classical" viral pathogens such as hepatitis viruses and HIV, which today are almost negligible transfusion risks as has already been described above. The new threats from (re-)emerging pathogens require constant hemovigilance and acute decisions regarding new test procedures for these pathogens or the introduction of pathogen inactivation measures for blood products as they become available in Europe.

Increasing costs and economic pressure on the European health care systems: Modern medicine in Europe has to deal with an ageing population and a decline in (altruistic) blood donations while facing an increasing cost pressure on the health care systems in Europe at the same time. Clinical hemotherapy and transfusion medicine have to deal with these backgrounds: Questions arise, whether it is more suitable to establish smaller, hospital-based blood donor services which are able to work closely with the hospital staff versus bigger entities working like pharmaceutical companies, which are able to reduce costs through economies of scale.
Research and development: Modern clinical transfusion medicine and hemotherapy are essential parts of today's medicine. Close cooperation and scientific networking with industrial and clinical partners in tissue transplantation, cell therapy and other new fields of medicine are vital to the future of our field. However, funding for R&D, competition with the pharmaceutical industry regarding blood donor screening and new blood substitutes, as well as growth factors like erythropoietin or thrombopoietin provide some examples of the more problematic fields in this competition.

Many experts are calling for a trend to "bloodless medicine". However, evidence of any true benefit from "bloodless medicine" is lacking. Growth factors like erythropoietin show adverse events like a potential increase in tumor growth and their use has not led to the mortality reduction hoped for in several patient populations.

Optimal use of blood products is a worthwhile goal to aim for; however, the risk of undertransfusion in some patients has to be taken into account. In some European countries, strategies to reduce allogenic blood transfusion led to less advertising for healthy volunteer blood donors which finally resulted in the dramatic reduction in blood donations now endangering the blood supply in these countries.

Future challenges in transfusion medicine: Medical: Maintaining and increasing blood transfusion safety: With the successful containment of the "classical" viruses like hepatitis and HIV by transfusion, the focus has shifted to sources of lower risks to blood transfusion safety: Screening of blood donations for prions, bacterial screening (especially in platelet concentrates), pathogen inactivation of all blood products and testing for new and emerging pathogens [5] are examples of ongoing challenges in transfusion medicine.

Transplantation medicine: Transplantation of solid organs and hematopoietic stem cells require complex diagnostic and procedural logistics: HLA-testing, stem cells apheresis and storage as well as new cell therapies like stem cells in acute myocardial infarction and chronic heart diseases are examples of the vast developments in this field [6,7].

New blood products and regenerative medicine: Hematopoietic stem cells from bone marrow are nowadays almost completely replaced by peripheral hematopoietic stem cells obtained via apheresis procedures. Umbilical cord stem cells are a promising source of hematopoietic stem cells also in adult patients nowadays. Cellular therapeutics and gene therapy as well as immunotherapy are novel tools which will help to bring regenerative medicine and cellular therapy to a new blossom.

A challenge for politicians: Competition is an important factor for the success of the European economy as well as in the scientific world. However, blood donations are gifts from healthy donors to patients who require them. The buying and selling of blood donations or a blood market should not be promoted by the European Union. On the other hand, politics has to define the framework within which competition in the health care market in Europe takes place. Harmonization of blood donation and hemotherapy in Europe, reimbursement of blood donors, calculation of costs and pricing, Europe-wide blood product distribution including regions with different epidemiological backgrounds for blood borne diseases and different levels of quality management are examples of currently unsolved problems which require the close attention of European politicians as well as experts in the field of transfusion medicine.
Conflict of interest statement: Both authors declare that they have no conflicts of interest.

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