Deferral of Donors with Non-Human Tissue Transplants in Germany

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Since the occurrence of variant Creutzfeldt-Jakob disease (CJD) the transmission of infectious agents from animals to humans with possibly deleterious consequences is again a hotly debated topic. As a consequence, transplantation of animal *organs* to humans (xenotransplantation) was tightly regulated or halted in most countries where they could be performed. In principle, the same transmission would be possible by transplantation of animal *tissue*. Infection of blood donors with animal-infecting agents might go undetected for a long time and would provide a source of recirculation of the agent within the population, possibly even triggering a new epidemic. That is why the Bundesärztekammer and the Paul-Ehrlich-Institut in their Guidelines for Procurement of Blood and Blood Constituents and for the Application of Blood Products (<http://link.springer.de/link/service/journals/00103/bibs/0043007/00430555.htm>) excluded patients with xenotransplants for lifetime from further donations, irrespective of the quality of the inactivation process. It might be argued that 'transplantation' only covers the transfer of viable cells [1] and that for non-viable tissues the designation implant would be more appropriate, but as the transfer of dura mater is also called a transplantation in the same guidelines, it might as well be argued that xenotransplantation in the sense of the guidelines covers the transfer of all animal material into humans.

In Europe, non-viable tissue transplants from non-human species are regulated by the Council Directive 93/42/EEC, put into practice in Germany by the Medical Devices Act (Medizinproduktegesetz: www.dimdi.de/germ/mpg/mpg-gesetz.htm). These products get access to the market by being certified by a notified body of one of the member states of the European Union. A list of notified bodies accredited in Germany can be found under www.dimdi.de/germ/mpg/fr-mpgdt.htm.

The number of animal tissues and tissue derivatives applied in humans contains

- heart valves,
- pericardium (as a replacement or fortification of connective tissue structures, including dura mater replacement),
- vein segments for vessel prosthesis,
- bone as substantia spongiosa, substantia compacta, bone matrix with collagen type 1 as main constituent, anorganic bone matrix and ceramics of hydroxylapatite, and
- collagen to cover or close wounds and as cornea protection.

Contrary to organs, most tissues can be treated physically (heat) and/or chemically in order to reduce or eliminate possible infectivity. The degree to which this reduction of infectivity is achieved varies for the different tissues. The evaluation of these inactivation steps is part of the certification process by the notified body. This evaluation, however good it might be, can only demonstrate a very low residual risk and therefore 'reasonable safety', but it is impossible to demonstrate a residual risk of zero. This is all the more true if details of the infection process are only partially understood as this is the case for BSE and new variant CJD. After all, the suitability of an animal material recipient for blood donations is outside the scope of the certification process for that material.

So if there is a non-zero risk of infections transmissible by blood transfusion what should be done with blood donor applicants who received animal material?

The first question is whether *all* donors with xenotransplants of tissue, irrespective of species and inactivation procedure, should be deferred or, in other words, whether the transfer of *any* animal tissue into a human is indeed a xenotransplantation in the sense of the blood donor guidelines. In our opinion, blood donor applicants who received nonvirus-inactivated animal material should be deferred for lifetime. If the material has undergone inactivation procedures, we have a situation in which the transfusion of blood of such donor applicants holds a very low risk of virus transmission but, if it actually occurs,

possibly very serious consequences. The decision to defer or not defer these donor applicants should take into account i) details of the inactivation procedure, ii) whether we can afford the number of persons to be excluded, and iii) the difficulty to explain to a donor applicant that very likely everything is all right but he has to be excluded nevertheless. One has to keep in mind that e.g. France excludes even all blood donor applicants who have received a human blood transfusion from further blood donations for fear that an unknown agent might recirculate.

It is highly likely that many donors do not know that they have received a xenotransplant. It is therefore of utmost importance that the flow of information is clarified for those per-

sons who are finally to be excluded. Producers of animal material to be applied in humans should give attention to recipient information in the package insert with respect to blood transfusion. Treating physicians should be obliged to inform their patients. Finally, donor questionnaires should specifically ask for the different kinds of tissue transplant.

References

- 1 WHO Working Party on Biotechnology: OECD/WHO Consultation on Xenotransplantation Surveillance: Summary Report. DSTI/STP/BIO(2001)11/FINAL. siehe unter www.oilis.oecd.org.