

TECHNOLOGICAL BREAKTHROUGHS IN MEDICINE

Public hearing of 27 January 2011

*organised on behalf of the OPECST
by Mr Claude Birraux, deputy, President of the OPECST*



On 27 January 2011, Mr Claude Birraux, a deputy and President of the OPECST (Parliamentary Office for Scientific and Technological Assessment), organised a public hearing on technological breakthroughs in medicine, the idea for which had been suggested to the Opecst by Professor Jean-Michel Dubernard, a member of the board of the High Health Authority (HAS).

This public hearing set out to analyse, through examples concerning cell therapies, medical acts and medical devices, the conditions for the success of some of these technological breakthroughs, but also the failures that have hindered the development of some others.

In his preliminary remarks, Mr Laurent Degos, former president of the High Health Authority (HAS), declared that the whole issue raised by technological breakthroughs resulted from the ignorance in which society finds itself when faced with the result of a product or a practice, while placing great hope in its benefits and while being ready to assume its risks.

Referring to transplants and grafts, he noted that they would not have been practised without the perseverance of medical players, since it took no less than 263 liver transplants before a transplant patient survived more than a week.

Several other participants also emphasised such difficulties of an experimental nature

which form the first obstacle met by any technological breakthrough. Mrs Marina Cavazzano-Calvo, director of the biotherapy department at Hôpital Necker, stated for instance that gene therapy for children affected by X-linked severe combined immunodeficiency had had to be suspended from 2002 to 2010. Four of the ten children treated indeed developed a leukaemia, whereas this had not happened in mice and was in no way predictable following all the pre-clinical trials.

For his part, Mr Philippe Menasché, director of the 'Cell therapy in cardiovascular pathology' unit at Hôpital européen Georges Pompidou, recalled that he had started working more than fifteen years ago on cell therapy for heart failure without having

obtained any success, owing to several difficulties related to the characterisation of cell therapy products, cell amplification and keeping injected cells alive.

In vitro fertilisation has also been the result of very lengthy experimentation. Mrs Jacqueline Mandelbaum, Head of the histology, reproduction biology department/centre for the study and preservation of human oocytes and sperm (CECOS) at Hôpital Tenon, recalled that in vitro fertilisation first began by experiments in 1880 in Vienna on the mammalian embryo conceived in vivo. In 1944, the first in vitro insemination tests of human oocytes took place, but unsuccessfully. The first births did not arrive until 1959. At last, in 1978, after in vitro fertilisation tests on animals, then on the human embryo, and following clinical tests, at last Louise Brown was born, the seventy-fifth human-being conceived by this technique worldwide.

Referring to legislation-related obstacles, certain provisions of French law and Community law have been criticised. For instance, the ban by the bioethics Act of 6 August 2004 of any research on embryonic stem cells – except by way of dispensation and for a limited time – has prevented, according to Professor René Frydman, any research on oocyte vitrification.

While Mrs Jacqueline Mandelbaum did not consider oocyte vitrification to be a technological breakthrough strictly speaking, she did feel it was a technical improvement helping to preserve fertility. There was no reason, to her mind, to fail to authorise it given the experience acquired in animals and man.

In any case, Mrs Marina Cavazzano-Calvo felt that the limit on research on embryonic stem

cells for therapeutic purposes, laid down by the bioethics Act of 2004, would further accentuate the delay incurred by France, which she assessed at fifteen years, to which could be added ten additional years of delay due to maintenance of the dispensatory system.

Nevertheless, Mr Jean-Baptiste Vialatte, a deputy and member of the OPECST, pointed out that several members of the National Assembly special committee tasked with considering the new bill on bioethics had expressed very great mistrust for the pharmaceutical industry with respect to the use of embryonic stem cells, fearing in particular a merchandisation of human body products.

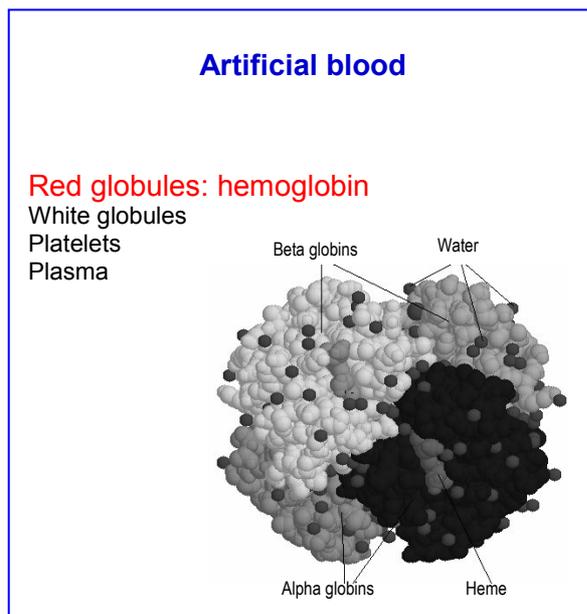
As for the Community framework, either it suffers from insufficient harmonisation as is the case with cell therapy practices, or else it introduces a regulatory regime running counter to French law, as illustrated by the fact that gene therapy cell products are classified as medicinal products by the regulation of 13 November 2007 on advanced therapy medicinal products.

Neither has the institutional framework been deemed favourable to researchers, who have to face what has been termed the thousand-layered administration, the procedural jungle or the assault course, owing, in particular, in certain cases, to the obstruction set in place by the French health products safety agency (AFSSAPS) or, as stated by President Claude Birraux, the administrative nature of the French health system. Mrs Cavazzano-Calvo regretted she had had to carry out in Italy some projects which she was not allowed to develop in France for want of financial, logistic and human means.

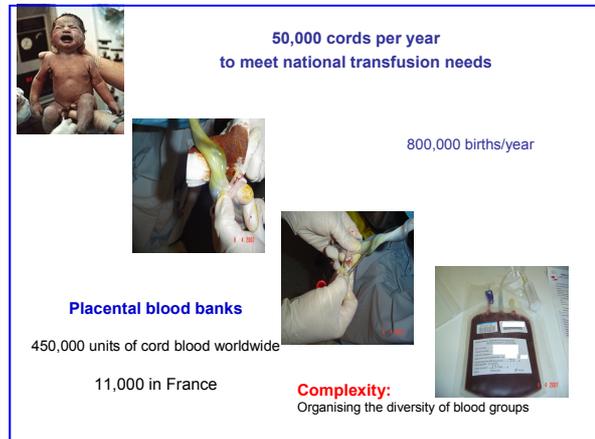
⁽¹⁾ Agence française de sécurité sanitaire des produits de santé

Similarly, Professor Ugo Amaldi, a particle physics specialist at the CERN (European Organization for Nuclear Research) and inventor of hadrontherapy – which treats inoperable and radioresistant cancers – decided to open a hadrontherapy centre in Italy and no longer in France owing to the refusal he received from the French ministries on the grounds that the *Etoile* project was already under way in the Rhône-Alpes region, which prevented them from supporting a second one.

Finally, **factors of an economic and financial nature** are also to be blamed for the failure or late development of certain technological breakthroughs. Several participants criticised the absence in France of biotechnology companies capable of supporting gene therapy – except for Généthon – or else the disappearance of companies producing surgical instruments. Others deplored that the issue of the funding of the beginning of the transition to the clinical phase has still not been solved, or that the real takeoff of their research – like that on artificial blood undertaken by Mr Luc Douay,



medical and scientific director of the French blood establishment of the Ile-de-France (EFS-IdF) – did not occur until the US Army took an interest in it.



As for **favourable conditions for the success of technological breakthroughs**, Mr Philippe Menasché insisted in particular on the scientific quality of French research teams, as well as on one of the specificities of France, namely the lack of compartmentalisation between the hospital system and the university system.

As for Mr Luc Senesbé, medical and scientific director of the French blood establishment of the Centre region (EFS-région Centre), he mentioned the need for high adaptability on the part of all the players of research, research-development and at the regulatory authorities, and better assessment of all aspects of the risk/benefit ratio.

Presenting his work on the *artificial heart*, Professor Alain Carpentier, chair of the Academy of Sciences (AdS), stated that it was completed thanks, in particular, to the relationship he established with Jean-Luc Lagardère, which allowed him to create an economic interest group – the GIE Carmat, Carpentier-Matra – which has since become

the company Carmat SAS. Mr Alain Carpentier mentioned the techniques which, to his mind, have allowed him to enjoy a considerable technological lead over foreigners: use of valvular bioprostheses, which he invented forty years ago, and which have allowed him to overcome the hemocompatibility obstacle – i.e. the tendency of blood to coagulate on contact with a foreign body – and prevent immunological rejection; housing of the artificial heart entirely in place of and instead of the diseased heart, using the model of onboard electronics as in aeronautics – unlike existing artificial hearts comprising a control and regulation console separate from the patient; and taking advantage of the progress of medical imagery to make simulations, for instance the virtual incorporation of an artificial heart inside a human body.



In the **public hearing conclusions**, which he presented on 28 June 2011 to Opecst, President Claude Birraux first mentioned some of the recommendations concerning French law and Community legislation.

Regarding the repeal of the **ban regime on embryonic stem cell research**, he recalled that both French Parliamentary Chambers had expressed their desire not to carry it out during the debate on the bill on bioethics, finally maintaining the principle of a ban with dispensations, even if oocyte vitrification has been formally authorised.

Referring to Community legislation, President Claude Birraux desired that debates take place on some of the problems recalled during the public hearing: the classification of gene therapy cell products under the medicinal products regime, and the disparities in cell practices, despite efforts by the European Medicines Agency to make them uniform.

President Claude Birraux pointed out that **Europe** could however act as a very useful level of reforms to establish a coordinatory structure with a view to the development of costly systems, or else to set up a procedure ensuring the quality of the assessment by structures tasked with authorising research, such as AFSSAPS.

On the institutional level, President Claude Birraux deemed it necessary to study two proposals: the first would reexamine the possibility of a **grouping of the bodies concerned**, such as the National Consultative Ethics Committee (CCNE), the Biomedicine Agency (ABM), and AFSSAPS which is being restructured following the Médiateur affair. The second would consist in setting up a **one-stop-shop** procedure, separate from the regulatory bodies, for innovations in the health field.

Last, he desired that the players of the administration and of industry should drop their overcautiousness. They should now see the need for innovation no longer only as a negative factor in terms of costs but as a positive factor regarding the care delivered, which requires a redefinition of the relationship between the relative medical value of an innovation on the one hand, and its benefits and costs on the other hand.