BLOOD SUBSTITUTES IN 2010

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The basic principles of modified hemoglobin based blood substitutes have been available since the 1960's (Chang, 1964, Bunn & Jandl, 1968). Unfortunately there was no interest in this until HIV contaminated blood raised its ugly head in 1989. For many years, donor blood brought with it a high incidence of HIV infection. This urgent need for blood substitutes led a number of companies to carry out the impossible task of research and development in the absence of basic knowledge in this area. Granting agencies then started for a short time to support the badly needed basic research in blood substitutes. Unfortunately, this did not last long since it was thought that blood substitute was a simple product that could be easily developed by the industries themselves without the need for basic research. This resulted in much setbacks and delays in this area as developers and researchers started to realize the need for the nonexistent basic knowledge. As a result, it took 20 years to reach the present status of first generation blood substitutes that are still not approved for routine use (Alayash et al 2007, Buehler et al 2004,Chang 2007, Jahr et al 2008, Liu & Xiu, 2008, Moore et al 2009, Mozzarelli 2010, Tsuchida et al 2006, Winslow, 2006 Yu et al, 2010, and others). In any case, it was too late for the large number of patients infected with HIV contaminated blood until screening tests were implemented, as least in some countries that can afford this. This led to a false sense of security and a repeat of the earlier lack of interest in blood substitutes. The present economical crisis around the world also did not help. Again, people seem to feel that there is no need to develop blood substitutes until we need it. They seem to forget that it took more than 20 years to come to the present status of first generation blood substitutes that have not yet been approved for clinical use. It will take many more years for basic research and development to come out with a perfect blood substitute. In the meantime if another HIV-like disaster should suddenly appear, are we willing to repeat our mistake? Even at present, there are urgent needs for blood substitutes in major surgery, mass disaster, war and other situations, especially where donor blood is not readily available. Furthermore, millions of people are living in regions where there are major problems related to HIV, malaria and other contamination in donor blood.

It will be important to consider both the present and the future as follows:

(1) For the present, we need to carry out careful risk/benefit analysis of available HBOC for specific conditions and specific locations in the world. This includes more narrow indications and the exclusion of patients and conditions with arteriosclerosis, diabetes and other endothelial dysfunctions especially in situations of oxidative stress. There are also potential ways to prevent adverse effects (Yu et al, 2010) including new generations of blood substitutes in development (Buehler et al 2004,Chang 2007,Tsuchida et al, 2006 and others). What is also important is that one country's regulatory standard should not be automatically applied to all countries around the world. The risk/benefit will be different in countries with unsafe blood (HIV, malaria and other parasites, etc). The risk/benefit is also different in critical situations as in natural or man-make disasters when there is insufficient blood supply

(2) For the future, it will be important to intensify basic research for basic information and R&D into new improved blood substitutes. Past experience shows that it is an impossible task to develop safe and effective products in the face of minimal basic knowledge in this area. The biannual

series of International Symposium on Blood Substitutes (ISBS) has been organized for many years to bring together molecular biologists, biochemists, chemists, clinicians, physiologists, those in R&D and others. The most recent ones included the 2007 XI ISBS organized by Professor Liu and Professor Xiu of the Peking Union Medical College in Beijing, China. The 2009 XII ISBS was organized by Professor Mozzarelli of Parma University in Parma, Italy. Professor Zapol of MGH, Harvard Medical School will be organizing the XIII ISBS to be held at the MGH of Harvard Medical School, 27-29 July, 2011 (Please see www.artcell.mcgill.ca for a link to his URL when it is ready). We therefore have all the major researchers and developers around the world interacting closely to move this area forward. All we need now is for granting agencies around the world to give priority to support blood substitute related research in order to avoid another future major disaster like the one we had with HIV contaminated blood in 1989.

(This has been posted on www.artcell.mcgill.ca)

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