

# Blood substitutes

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Blood substitutes have long been sought after, and artificial oxygen carriers may soon become a reality. Despite increased safety of allogeneic blood in terms of transmission of infectious diseases [1], avoiding allogeneic blood transfusions remains an important goal in perioperative and intensive care medicine. This is because allogeneic blood transfusions may cause immunosuppression with an increased incidence of postoperative infections [2,3] and may adversely affect outcome in intensive care [4], and thus they remain a public concern [5].

Artificial oxygen carriers are promising substances to avoid allogeneic blood transfusions and related side effects. In addition, artificial oxygen carriers may be effective anti-ischaemic agents in a variety of diseases and conditions that are characterized by compromised tissue oxygenation. Artificial oxygen carriers may be grouped into haemoglobin-based oxygen carriers (HBOCs) and perfluorocarbon emulsions. The biological efficacy of both groups has been documented in a variety of animal experiments [6,7], and phase III trials are ongoing at present to prove their clinical efficacy.

In HBOCs (see article by Baron J-F, this issue of *Critical Care*), the haemoglobin is either human (outdated human blood), bovine or from a genetically engineered source [7]. All haemoglobin solutions tested contain modified haemoglobin to improve oxygen off-loading, by decreasing oxygen affinity, and to reduce side effects. At present, haemoglobin solutions in clinical trials are aqueous solutions, but the production of micro-encapsulated haemoglobin particles (neo red cells) might be a future option

[8,9]. Comparison between HBOCs is difficult because there are very few studies that directly compare different products. It appears though that larger haemoglobin molecules, in particular haemoglobin polymers with a small residual haemoglobin monomer fraction, are better tolerated; this is probably due to a reduced penetration of these relatively large molecules into the vessel wall [10].

In the group of perfluorocarbon emulsions, only perflubron emulsion is in phase III testing. It has been shown recently that treatment with perflubron emulsion in conjunction with pure oxygen ventilation was more effective than retransfusion of autologous blood in reversing physiologic transfusion triggers [11]. With perflubron emulsion patients thus may tolerate lower haemoglobin levels, and perflubron emulsion may be used to modify the acute normovolemic haemodilution (ANH) into 'augmented ANH' (see article by Spahn DR, this issue of *Critical Care*). In this way, the added oxygen unloading capacity of the perflubron emulsion is utilized to compensate very low intraoperative haemoglobin values. Because of retransfusion of the ANH blood at the end of the procedure, the patient's are supported by their own blood in the postoperative period.

Comparing HBOCs and perfluorocarbon emulsions is difficult. First, there are no studies that directly compare the two groups of artificial oxygen carriers. Second, the practical use of these substances will be relatively different once they are on the market. Haemoglobin solutions might be used relatively similar to a conventional blood transfusion and haemoglobin measurement may still be used to assess the oxygen transport capacity. When used to avoid allogeneic blood transfusions, perfluorocarbon emulsions will be used preferentially in the concept of 'augmented ANH', and physiologic transfusion triggers [12] will be used primarily to assess the adequacy of oxygen delivery.

Despite a longer than expected final development phase, HBOCs as well as perfluorocarbon emulsions will eventually be released for general clinical use and will substantially alter standard clinical practice.

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