## Artificial Red Blood Cells Timothy Alberg, Biomedical Engineering Program University of Rhode Island

Blood has many functions in the human body. It consists of oxygen carrying blood cells, lymphatic white blood cells, adhesive platelets, and plasma. It carries oxygen, waste, hormones, and CO<sub>2</sub> to the appropriate places in the body. Blood transfusions occur when a patient has suffered massive blood lose. Whole blood can be used for these transfusions, but there are some limitations and problems with whole blood. Whole blood must be stored in a refrigerated room, and it has a shelf life of about one month. Another problem arises with the transmittance of blood borne illnesses such as hepatitis and HIV. For years researchers have been searching for a substitute for whole blood, which has led to many companies developing many different types of artificial blood.

There are several goals that most artificial blood researchers strive for while making their blood substitutes. First, it must be easy to manufacture to meet the high demand for blood around the world. Second, the blood substitute must be storable in room temperature. Third, the shelf life of the product should last anywhere between one to three years. Fourth, Blood types (A, B, O, and AB) should not matter with artificial blood. Fifth, it should be safe for the recipient, and not cause any health risks. Blood borne illnesses should not be of concern with blood substitutes. And six, it must be able to transport oxygen to the parts of the body where it is needed.

Artificial blood is divided into two categories, volume expanders, and oxygen therapeutics. Perfluorocarbons or PFC are biologically inert materials that have a greater ability to dissolve oxygen than blood plasma does. In 1966, Leland C. Clark Jr. demonstrated the ability of fluorocarbons to hold oxygen gas by submersing mice in liquid fluorocarbon. These mice were able to breath for an extensive period of time, which led to more research. The first PFC, Fluosol-DA, was made by Ryoichi Naito of the Japanese Green Cross. This perfluorocarbon was the first of many that used emulsifiers to make fluorocarbons water soluble. Perflubron, a fluorocarbon emulsified with perfluorodecyl bromide and egg yolk phospholipids, was created after many experiments with fluosol. This PFC was found to carry three times the amount of oxygen than fluosol, and the amount it can carry/release is directly related to oxygen partial pressure. PFC's carry more oxygen than the plasma portion of blood, and they increase the volume of the blood allowing the remaining blood to circulate until real blood can be transfused into the body.

The other type of artificial blood is Hemoglobin-Based Oxygen Carriers, or HBOC. These are based off of the hemoglobin protein found in blood. Hemoglobin outside of the RBC has a short

half-life, a stronger affinity for oxygen, and breaks apart into elements that are toxic to the body, specifically the renal system. Researchers had to find a way to modify HBOC's so they would not be small enough to fit in-between capillaries, bind to nitric acid, and causes hypertension in the capillaries. Robert Winslow of the Sangart Company developed the MP4 HBOC, a fluid consisting of hemoglobin coated with polyethylene glycol. This increased the viscosity of the blood substitute by making the HBOC bulkier, and gave it a greater affinity for oxygen (compared to other HBOC's in testing) allowing the oxygen to be released in the capillaries, rather than the arteries. HBOC's do diffuse more oxygen than RBC's, making them more effective oxygen carriers while they are in use by the body. Since HBOC's are significantly smaller than RBC's, testing needs to be done to make sure they have no adverse affects on the organs and tissues of the body, including the brain. This is why HBOC's are oxygen therapeutics.

Currently, PFC's and HBOC's can be used to treat patients who have lost most of their blood, until real blood is available to them. Only small amounts of both are needed to temporarily replace the blood that is lost. Other research has shown that PFC's and HBOC's aid in the removal of cancerous cells, creating a double effect for them. Currently one of the larger problems with these is their half-life inside of the human body, and dosage amount. PFC's have a high retention period in the body (one week) and thus patients have to wait until this period is over to avoid damaging their spleens and livers. HBOC's are known to cause high blood pressure, and bind to nitric acid, causing capillary problems in the body. However, despite these issues, PFC's and HBOC's suit most of the needs and requirements in order for it to be used by people. They do not have a membrane, so blood typing is not an issue, they can be stored in room temperature for about three years, they can be produced in mass amounts, and they are disease/virus free.

## Sources

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