EDITORIAL

IN QUEST OF A UNIVERSAL DONOR BLOOD FOR TRANSFUSION

Tehseen Iqbal
Department of Physiology, CMH Multan Institute of Medical Sciences, Multan Cantt:, Pakistan

Long ago, man noticed the relationship of blood with vitality and vigour of animals and humans. Early scientists, before the knowledge of blood groups, attempted transfusion of animal blood to humans but with discouraging results. Now, modern transfusion services are an integral part of all national healthcare services. The major problems faced by the transfusion services are to match donated blood with the patient's blood and maintaining a voluntary donors' list for continuous supply of donated blood. Considering these problems, scientists are searching for a universal donor blood by attempting to remove A and B antigens from the donated blood and also trying to manufacture artificial or altered red blood cells having no antigens. Removing a terminal sugar from antigen A or B by using enzymes glycosidases are now possible. Some studies to form new red blood cells having no antigens have also become successful. Scientists used haemoglobin removed from expired blood and packed it in new envelops, artificial red blood cells, which have no blood group antigens. Successful research results and ongoing clinical trials give us hope that a universal donor blood will be available in near future.

Keywords: Artificial red blood cells, Blood group antigens, universal donor blood group
Pak J Physiol 2025;21(4):1–2, **DOI:** https://doi.org/10.69656/pjp.v21i4.1913

Many thousand years ago, man noticed the relationship of blood with vitality and vigour of animals and humans. Humans observed that when animals were wounded and sufficient amount of blood was lost, animals die or can be captured and so they developed sharp-edged weapons for hunting and wars. The earliest reported 'successful' attempts of transfusing lamb blood to humans were reported by Jean-Baptiste Denis in France and Richard Lower in England separately in 1667 but transfusing the blood of animals to humans became prohibited by law because of severe reactions. After the discovery of ABO and Rh blood group systems, human blood transfusions became safe on a large scale.[1]

With many other developments in blood collection, blood storage and transportation, modern transfusion services are now an integral part of all national healthcare services. Currently, blood transfusions are facing two important problems: matching of the available human blood for transfusion as antigens on red blood cells may cause serious reactions; a continuous supply of human blood. The continuous recruitment and retention of healthy blood donors is essential for blood banks.

Three genes control the expression of the ABO antigens: H, ABO, and Se genes. The H gene codes for the production of an enzyme transferase that attaches L-fucose to the already present RBC membrane-anchored oligosaccharide chain. If no A or B gene or enzyme is present, the H specificity remains, and the individual is of blood group O. In the presence of the A gene-encoded transferase, N-acetyl-galactosamine is attached with the terminal galactose, which forms 'A' blood group. In the presence of the B gene-encoded transferase, galactose is added to the terminal galactose and it confers 'B' specificity. If A and B genes or transferases are both present, the same RBC has both types of terminal carbohydrates, i.e., N-acetyl-galactosamine and galactose, and 'AB' is the blood type. The secretor gene (Se) controls the individual's ability to secrete soluble A, B, and H antigens into body fluids and secretions.[2]

Blood group A and B antigens differ only by a single carbohydrate attached to the H-type oligosaccharide chain of blood group O. Blood group O is considered a universal donor type. In blood group A, terminal carbohydrate attached to the H-type oligosaccharide chain is N-acetyl-galactosamine and in blood group B, terminal carbohydrate attached to the H-type oligosaccharide chain is galactose.[3] (Figure-1).

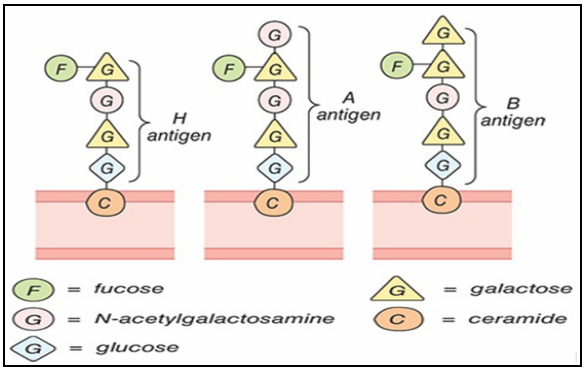


Figure-1: Chemical nature of ABO blood group antigens[3]

The process of converting blood group A or B to blood group O (universal donor) involves the enzymatic removal of specific antigens from the surface of red blood cells (RBCs). The conversion process relies on enzymes that cleave the terminal sugars of the A and B antigens, effectively transforming them into the H antigen, which is characteristic of blood group O.[4]

There are two techniques to convert blood group A and B type RBCs to universal O red blood cells. The first is the enzymatically converted group O (ECO) technique. The enzyme alpha-N-acetylgalactosaminidase can be used to remove N-acetyl-galactosamine, the A antigen, from RBCs. Similarly, the enzyme beta-galactosidase can be used to remove the terminal galactose, the B antigen from RBCs to transform them into O type.[1] Identification of novel bacterial glycosidases has greatly advanced the field. The second technique is antigen masking by using hydrogels, e.g., polyethylene glycol (PEGs) that binds to the surface of red blood cells. PEG is a flexible and biocompatible compound. Because of this coating the host's immune system cannot recognize coated RBCs after transfusion. These two methods are promising and have been extensively studied to help supply blood banks.[5]

To meet the current shortage of blood supplies, many approaches are being experimented. Many promising attempts to create artificial blood proved unsafe on clinical trials. By far the greatest number of research efforts have focused on manipulating the structure of haemoglobin so that it can be effectively and safely administered as a substitute for whole-blood transfusions. Some scientists attempt to synthesize chemicals that act as haemoglobin. Genetically engineered haemoglobin is also under research. One promising strategy encapsulates haemoglobin within liposomes-membrane-wrapped containers. A more recent strategy under development is a water-soluble, synthetic plastic version of haemoglobin. The newest technique being explored is using haemopoietic stem cells to "grow" a supply of transfuseable red blood cells. Synthetic O_2 Carriers are also being researched. Some researchers also attempted to increase the life of red blood cells.[6]

The researchers at the University of Maryland, School of Medicine in Baltimore extracted haemoglobin from expired blood and enclosed it in a bubble of fat, essentially creating artificial red blood cells. The scientists then freeze-dry the artificial red blood cells into a powder form which is shelf-stable for years. The powder can also be easily transported. Freeze-dried artificial blood developed in the lab can be reconstituted with water and infused when required. This artificial blood is still to be tested in clinical trials.[7]

Recent developments are reported from USA and Japan. Both of them used the same approach. The artificial blood is made from haemoglobin extracted from expired donor blood and encased in a protective synthetic shell. At Maryland scientists developed synthetic blood called ErythroMer. ErythroMer is a powder-based product that, when mixed with water, transforms into a liquid that can deliver oxygen to tissues when transfused. The product still needs to be tested on humans.[8] Japanese researchers have started clinical trials in March 2025, to explore the effectiveness and safety of a universal artificial blood. Their approach involves extracting haemoglobin from expired donor blood which is then encased in a protective shell to create stable, virus-free artificial red blood cells. Unlike donated blood, these artificial cells have no blood type, eliminating the need for compatibility testing and making them invaluable in emergencies. Notably, donated blood has a shelf life of just 42 days, while this artificial blood can be stored for up to two years at room temperature. The researchers are hopeful for wider clinical use by 2030.[9] In view of ongoing research we can hope to see a universal donor blood group for transfusion to all blood types.

REFERENCES

1. Transfusion Medicine History. Accessed from: https://www.aabb.org/blood-biotherapies/blood/transfusion-medicine/transfusion-medicine-resources/transfusion-medicine-history on 11 Oct 2025.
2. Garcia K. The 100th Anniversary of the First Blood Bank. Accessed from: https://stanfordbloodcenter.org/100th-anniversary-first-blood-bank/ on 11Oct 2025.
3. Barret KE, Barman SM, Boitano S, Brooks HL. Blood as a circulatory fluid & the dynamics of blood & lymph flow. In: Ganong's Review of Medical Physiology 26th ed. McGraw-Hill Education; 2019.
4. Olsson ML, Hill CA, de la Vega H, Liu QP, Stroud MR, Valdinocci J, *et al*. Universal red blood cells--enzymatic conversion of blood group A and B antigens. Transfus Clin Biol. 2004;11(1):33–9.
5. Guamba E, Cevallos A. Recent advances on the development of a universal blood type. Revis Bionatura 2022;7(1):32.
6. Sherwood L. Human Physiology: From Cells to Systems. 9th ed. Boston, MA: Cengage Learning; 2016.
7. Scientists are developing artificial blood that could save lives in emergencies. Accessed from: https://www.npr.org/sections/shots-health-news/2025/07/24/nx-s1-5477632/artificial-blood-hemorrhage-emergency-medicine on 17 Oct 2025.
8. Zizaza N. Synthetic, shelf-stable blood developed by Maryland scientist could save lives in emergencies. Aug 8, 2025. Accessed from: https://www.cbsnews.com/baltimore/news/maryland-synthetic-blood-scientist-medicine-health-innovation/ on 5 Nov 2025.
9. Singh A. Universal artificial blood for all types in clinical trials, could save millions. Jun 6, 2025. Accessed from: https://www.ndtv.com/science/universal-artificial-blood-for-all-types-in-clinical-trials-could-save-millions-8600351 on 21 Jul 2025.

Address for Correspondence:

Dr Tehseen Iqbal, Professor of Physiology, CMH Multan Institute of Medical Sciences, Multan Cantt:, Pakistan.
Cell: +92-333-6144799
Email: prof.tehseeniqbal@gmail.com

Received: 16 Nov 2025 **Reviewed:** 19 Nov 2025 **Accepted:** 20 Nov 2025

Conflict of Interest: None **Funding:** None