The transfusion medicine has come a long way from the landmark discovery of ABO blood group system by Karl Landsteiner in 1900 in which he described the reactions between the red cells and serum of 22 subjects. He observed that the addition of serum from some individuals would cause clumping of red cells of others and realized that this was a phenomenon with an immunologic basis. The importance of Landsteiner's work was not recognized immediately and blood grouping did not become part of universal practice until 1920s.

ABO is the most important blood group system in transfusion and transplantation practice. The ABH antigens are not primary gene products but are the enzymatic reaction products of enzymes called glycosyltransferases. The ABO system occurs as a result of polymorphism of complex carbohydrate structures of glycoproteins and glycolipids expressed at the surface of erythrocytes or other cells or present in the secretions as glycan units of mucin glycoproteins. Immunodominant structure of A and B antigens, GalNAc alpha 1>3(Fuc alpha 1->2)Gal- and alpha 1-3(Fuc alpha1->2)Gal-, respectively are synthesized by a series of reactions; the A and B transferases encoded by the functional alleles (A and B alleles) of a single gene at the ABO locus, catalyse the last step of the synthesis while the transferase coded by the O allele is nonfunctional. Therefore, the acceptor substrate (H antigen:Fuc alpha 1->2 Gal-) remains without further modification and the A and B determinants are absent. ABO genes consist of at least 7 exons and the coding sequence in the seven coding exons spans over 18 kb of genomic DNA located in chromosome 9. The function of ABH antigens remains unknown.

The transfusion of ABO incompatible units is the major cause of transfusion-induced fatalities worldwide. There is universal shortage of blood in all parts of the world including India. Group O RBCs contain neither A nor B antigens and can be transfused safely into recipients of any ABO blood group in most of the cases. Therefore, it is called as universal group. All the blood banks therefore maintain large inventories of group O RBC units. There is a great demand for group O blood, for example, for emergency services when the blood group is not known or when it is difficult to find out due to previous transfusions or allogenic stem cell transplantation. Therefore the attempts to have universal/stealth group of blood, which can be transfused to any patient without any immunological problem (alloimmunization). There are two types of approaches made towards making universal blood. The first is converting or degrading A and B antigens enzymatically or nonenzymatically to O group, and the second one is by masking RBC antigens using polyethylene glycol (PEG). In 1996 and 1997, four different groups of workers reported that if PEG is covalently bound to RBCs, they no longer react or give greatly diminished reactivity, with a range of antibodies to blood group antigens (e.g., ABO and Rh). Although the reported masking of RBC antigens in these initial studies appeared relatively efficient, it has not satisfied the criteria used by hospital blood transfusion services for pretransfusion compatibility testing. PEG-RBCs have additional advantages in that masking of ABO and all other blood group antigens of potential clinical significance is theoretically possible. Perfected PEG-RBCs could be used for any patient, regardless of whether untreated RBCs were incompatible with ABO or allo- or autoantibodies. However, there are many technical laboratory problems associated with it, and human studies still have not been performed.

Although it had been known since 1950s that one could cleave sugars from A and B RBCs to produce H antigen (i.e., group O RBCs), it took, another 50 yr
to apply it in a practical way. It was previously known that some bacterial enzymes, such as those from Clostridium tertium, C. welchii, Bacillus cereus and Trichomonas foetus would specifically destroy A, B, H antigens. But the major problem was the efficiency as well as quantity of these glycosidase enzymes. A recent report by Liu et al in April 2007, is a pioneering work to conclusively show the goal of use of universal red blood cell in transfusion practice is not far. I am excited but not surprised. This work certainly holds promise for future to make the subject of immunohaematology simpler and also to meet the demand of blood transfusion units. These investigators have solved one big problem by discovering two bacterial glycosidase gene families that provide enzymes capable of efficiently removing A and B antigens at neutral pH with low consumption of recombinant enzymes. The enzymes are expressed in Escherichia coli with high yield. This alpha-N-acetylgalactosaminidase functions with an unusual catalytic mechanism involving NAD+, and the crystal structure of the enzyme reveals a structural fold that has not been found previously in glycosidases. The availability of these bacterial enzymes should allow efficient and cost-effective enzymatic conversion of blood group A, B and AB RBCs to universal RBCs. It will be a good idea if these two methods can be combined to overcome the problem of ABO and other blood group incompatibility and produce universal red cell. I am reminded of a cartoon by Lublin where a unit of blood on an assembly line, undergoes pathogen inactivation, leucocyte reduction, treatment with enzymes to cleave A and B sugars from the RBCs and treatment with PEG to mask all other antigens. Automated cost-effective processes can be developed using the enzymes mentioned above for producing the universal RBCs for therapeutic purpose in the near future.

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