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Editorial

Blood group reckoning: Unraveling the mystery of blood group antigens

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Way back in 18th century there was a myth surrounding the blood groups. It was thought that all individuals contain the same type of 'red-colored' blood and therefore could be transfused to one another without any difficulty. But when this misunderstanding led to disastrous consequences (following such blood transfusions), it made scientists all over the world to reconsider this belief. This led to an increase in the number of experimentations that later proved that blood was different for each individual and they could be classified into various blood types depending on the different forms of surface antigens present on the red blood cells **[1]**.

Blood groups

A significant contribution to classification of blood types into ABO system (also known as ABH system) was made by Karl Landsteiner, an Austrian biologist, physician and immunologist. He was awarded the Nobel Prize in Physiology and Medicine for the same in 1930 **[2]**.

He had identified, through a series of experiments, 3 blood types: A, B and C; the C group was later renamed as O. Almost a year later was the fourth blood group, AB discovered. From 1927 onwards, many types of blood group antigens were discovered as given in **Table 1**. According to International Society of Blood Transfusion (ISBT), till the year 2018 a total of 36 blood group systems are present comprising of 346 RBC antigens **[3]**.

Table 1: Major blood groups, year of report, discoverer/s **[4]**

Blood group	Year	Reporter (s)
ABO system	1901	Landsteiner K
MNS system	1927	Landsteiner K, Levine P
P system	1927	Landsteiner K, Levine P
Secretor /Non–secretor (SS)	1932	Schiff F, Sasaki H
Factor Q	1935	Imamuras S
Rhesus (Rh)	1940/41	Landsteiner K, Wiener A
Lutheran (Lu)	1945	Callenders S, Race RR, Paykoc Z
Lewis (Le)	1946	Mourant AE
Kell (K)	1946	Coombs RR, Mourant AE, Race RR
Factor S/s	1947	Walsh RJ, Montgomery C
Duffy (Fy)	1950	Cutbush M, Mollison PL
Kidd (Jk)	1951	Race RR et al
Diago (Di)	1954	Levine P et al
Yt System	1956	Eaton BR et al
Auberger (AU)	1961	Salmon C et al
Xg	1962	Mann JD et al
Dombrock (Do)	1965	Swanson J et al

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Distribution and physiological role of blood group antigens (agglutinogens)

The ABO blood group antigens are not only present on RBC membrane but also in tissues like salivary glands, lungs, liver, pancreas, kidney and testis; and also in body fluids like saliva, semen and amniotic fluid. This created a mystery surrounding the existence of blood group antigens. Though many of RBC cell surface antigens serve as the basis for blood grouping, tissue matching, paternity tests and also to understand the inheritance patterns of an individual; these antigens also have some physiological functions. Rh antigens are transmembrane protein channels and act as ammonia transporter, Lewis antigen is α3/4-fucosyltransferase enzyme, Kell antigen is endothelin-3-converting enzyme, Duffy antigens are chemokine receptors, etc **[5]**.

Blood group antigens and microbiome

The communities of microorganisms, both useful and harmful, occupy considerable space in our gastrointestinal system. Bacteria present in human fecal matter secrete enzymes that digest the blood group antigens lining the gastrointestinal tract **[6]**. These bacteria are now found to be correlated with the blood group type of the host organism. The blood group of an individual is known to program the gastrointestinal system in terms of both the digestive secretions and mucosal lining features **[7]**.

Blood group antigens as energy source for microbes

These antigens are predominantly found lining the gastrointestinal tract. Those foodstuffs that have blood group type antigens are favored by the microbes inhabiting the gut. The fecal bacteria produce enzymes that degrade the antigens of ABO blood group and use it as a source of energy **[8]**.

Composition of intestinal microbiota depends on host blood group

Not only does the mucosa of the intestinal epithelium acts as the first layer of host defense system, it also acts as a medium between the host and the microorganisms.

Development of blood group antigens and antibodies

ABO blood group antigens develop during the late second trimester of intrauterine life where as blood group antibodies are absent throughout the intrauterine life and are inconspicuous at birth. Antibodies (agglutinins) start appearing during second week after birth as a result of exposure to the microbes and food having antigenic epitopes homologous to ABO blood group antigens. But this mechanism does not explain why corresponding agglutinins to one's blood group are not developed.

Blood groups and susceptibility to diseases

Mere presence or absence of particular blood group antigen does not significantly contribute to occurrence of any disease in the population. O blood group individuals with no A and B antigens often live a normal life. Many older and newer studies have shown that there exists an interesting association between blood antigens and disease predisposition especially infections. Advances in molecular biology and molecular diagnostics have opened new vistas for research in probing the role of blood group antigens in disease states. Most plausible mechanism implicated in pathophysiology is close resemblance of certain bacteria with blood group antigens which confuses the host immune system that do not identify the bacterial antigen as non-self, resulting in the individual being susceptible to that infection **[9]**. Blood group B and AB are at 60% greater risk of Escherichia coli infection, A individuals have higher risk of Helicobactor pylori, O individuals are prone to severe form of diarrhea caused by Vibrio cholera **[5]**.

O blood group is associated with gastric and duodenal ulcers, A group is associated with gastric cancer and B group is associated with esophageal cancer **[5]**.

On the other hand particular blood group confer immunity to certain diseases like O blood group are protected against severe acute respiratory syndrome (SARS) caused by coronavirus, severe form of malaria and cerebral malaria. Absence of Duffy antigen confers resistance against Plasmodium vivax infection **[5]**.

We need to revisit the structure and functions of antigens present on blood cells thereby understanding the role of blood groups in health and disease. Hence, this reckoning of blood groups will unravel the mystery of blood group antigens.

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