BLOOD GROUP

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1. Core Definition

A **blood group**, often interchangeably termed **blood type**, refers to a systematic classification of blood based on the presence or absence of inherited antigenic substances located on the surface of **red blood cells** (RBCs). These antigens are primarily complex molecules--including proteins, carbohydrates, glycoproteins, or glycolipids--whose specific configuration determines how the host body's immune system recognizes the blood cell structure. The classification system is foundational to modern medical practice, particularly in the critical field of **transfusion medicine**, as it dictates compatibility and prevents potentially fatal immune reactions that occur when incompatible blood types are mixed.

The definition relies on the critical immunological interplay between these surface antigens and corresponding **antibodies** (isoagglutinins) that are found dissolved in the blood plasma. For instance, an individual classified as Type A possesses A antigens on their RBC membranes but naturally produces anti-B antibodies in their plasma. Conversely, a Type O individual lacks both A and B antigens but possesses both anti-A and anti-B antibodies. This inherent mechanism ensures that the body mounts a rapid and often severe immune defense, known as an acute hemolytic transfusion reaction, against any foreign or incompatible red blood cells introduced into the circulation, underscoring the necessity of accurate pre-transfusion typing.

2. Etymology and Historical Development

The medical understanding of blood groups emerged at the dawn of the 20th century, following centuries of repeated, usually fatal, attempts at direct blood transfusion. Early transfusions failed because the mechanisms of blood compatibility were entirely unknown, leading to immediate agglutination (clumping) of red cells, shock, and death. The pivotal breakthrough discovery is attributed to the Austrian physician **Karl Landsteiner** in 1900.

Landsteiner, while working in Vienna, systematically observed the phenomenon of agglutination when mixing the serum and red cells of different individuals. He correctly hypothesized the existence of distinct, inherited substances (antigens A and B) on the surface of the RBCs. He successfully identified the three major groups: A, B, and C (which was later renamed O). This monumental work, published in 1901, provided the scientific basis for conducting safe transfusions, effectively establishing the field of **immunohematology** and subsequently earning Landsteiner the Nobel Prize in Physiology or Medicine in 1930. The fourth major type, AB, which possesses both antigens, was identified shortly after by his students, Adriano Sturli and Alfred von Decastello.

Further significant development came in 1937 when Landsteiner, collaborating with Alexander Wiener, identified a second major system, the **Rhesus (Rh) factor**. This discovery, named after the rhesus monkeys used in early research, proved crucial for understanding complications related not just to transfusion, but specifically to pregnancy, where incompatibility between mother and fetus can trigger severe immune responses.

3. The ABO Blood Group System

The ABO system remains the single most important classification system in transfusion practice because the antibodies present against the missing antigens (anti-A and anti-B) are typically IgM class, meaning they are large, potent, and can cause immediate, severe intravascular hemolysis if an incompatible transfusion is administered. The system defines four primary phenotypes based on the presence of A and/or B antigens:

Type A: Possesses A antigens on RBCs and naturally occurring anti-B antibodies in plasma.
Type B: Possesses B antigens on RBCs and naturally occurring anti-A antibodies in plasma.
Type AB: Possesses both A and B antigens; critically, these individuals lack both anti-A and anti-B antibodies, classifying them as **universal recipients** for red blood cell transfusions.
Type O: Lacks A and B antigens; possesses both anti-A and anti-B antibodies. Due to the absence of the A and B antigens, Type O red cells are typically considered **universal donors** (though plasma antibodies must be accounted for).

Due to the potency and immediate reactivity of the ABO antibodies, cross-matching for ABO compatibility is the mandatory first step in any transfusion procedure, defining the immediate risks and safety margin for the patient. The prevalence of these groups exhibits considerable variation worldwide, with Type O being the most common blood type globally, though regional demographics show high concentrations of Type A or B in specific ethnic populations.

4. The Rhesus (Rh) Blood Group System

The Rhesus system is the second most critical blood group system, primarily defined by the presence or absence of the D antigen, the most immunogenic of the Rh antigens. If the D antigen is present on the RBC surface, the person is classified as **Rh-positive** (Rh+), which accounts for approximately 85% of the human population. If the D antigen is absent, the person is **Rh-negative** (Rh-).

A key difference from the ABO system is that Rh-negative individuals do not naturally produce anti-D antibodies. The production of anti-D antibodies is only induced upon exposure to Rh-positive blood, a process called sensitization. This exposure typically occurs either through an incompatible transfusion or, most significantly, during childbirth when an Rh-negative mother is exposed to the Rh-positive red cells of her fetus. Once sensitized, the mother produces IgG anti-D antibodies.

The clinical importance of the Rh system is magnified in obstetrics. While the first Rh-positive pregnancy may proceed without complications, the maternal anti-D antibodies produced during that initial exposure can cross the placenta in subsequent pregnancies and attack the red blood cells of an Rh-positive fetus. This leads to **Hemolytic Disease of the Newborn** (HDN), also known as erythroblastosis fetalis, a condition that can range from mild fetal anemia to severe jaundice, hydrops fetalis, brain damage, or intrauterine death. The introduction of prophylactic administration of Rh immunoglobulin (RhoGAM) has been transformative, effectively preventing maternal sensitization and drastically reducing the incidence of HDN.

5. Genetic Inheritance and Alleles

Blood groups are strictly inherited traits, following Mendelian laws of genetics. The ABO system is controlled by the ABO gene located on chromosome 9. This gene has three principal alleles: IA, IB, and i. The IA and IB alleles are **codominant**; thus, an individual inheriting both (genotype IAIB) expresses both A and B antigens, resulting in Type AB blood. The 'i' allele, which codes for the O type, is **recessive**, meaning it only expresses the O phenotype (lacking A and B antigens) when two copies are inherited (genotype ii).

The Rh system is controlled primarily by two linked genes, *RHD* and *RHCE*, found on chromosome 1. The presence of the *RHD* gene leads to the expression of the D antigen (Rh-positive status). In most Rh-negative individuals, the *RHD* gene is entirely deleted, representing a homozygous recessive condition. Understanding these genetic mechanisms allows for accurate prediction of potential blood types in offspring and provides essential tools for geneticists, forensic scientists, and for counseling prospective parents regarding the risk of HDN.

6. Other Major Blood Group Systems

The ISBT recognizes over 30 distinct blood group systems, each defined by a set of antigens determined by a specific gene locus. While ABO and Rh systems are critical for initial screening, several other systems are significant in specialized medical settings, especially for patients requiring chronic transfusions who are prone to developing alloantibodies against less common antigens. Recognizing these antibodies is crucial for preventing delayed hemolytic transfusion reactions (DHTRs), which, while less immediate than ABO reactions, can still be clinically serious.

Kell System: This system is highly immunogenic, ranking third in clinical significance after ABO and Rh. Anti-Kell antibodies are frequently IgG class and are capable of causing both severe transfusion reactions and HDN.
Duffy System: The antigens of the Duffy system are structurally significant as they serve as receptors for the *Plasmodium vivax* malaria parasite. Intriguingly, individuals who are completely deficient in the Duffy antigen (the Fy(a-b-) phenotype) exhibit a natural resistance to this form of

malaria, illustrating a powerful example of evolutionary selection pressure impacting blood group distribution.

Kidd System: Antibodies in the Kidd system (Jka and Jkb) are notoriously difficult to detect because they often decrease rapidly in titer following sensitization, only to cause severe, delayed hemolytic transfusion reactions several days after the transfusion is complete.

MNS System: This complex system is characterized by numerous antigens. Antibodies developed against MNS antigens are often cold-reacting, meaning they are active at temperatures below normal body temperature, though some MNS antibodies can be clinically significant and cause transfusion complications.

7. Significance and Impact

The classification of blood groups represents one of the most fundamental and high-impact discoveries in the history of medicine. Its primary significance lies in establishing the safety and efficacy of blood transfusions, transforming what was once a deadly gamble into a routine, life-saving intervention necessary for surgery, trauma care, and managing conditions like severe anemia and hemorrhage. The rigorous process of blood typing and cross-matching ensures that transfused blood is immunologically compatible, thereby preventing the catastrophic consequences of massive **hemolysis**, disseminated intravascular coagulation, and acute renal failure.

Beyond immediate clinical relevance, blood typing is indispensable in research. The observed differences in blood group prevalence across global populations have provided invaluable data for the study of **human population genetics**, helping to trace ancient migration routes and patterns of human evolution and mixing. Furthermore, research continues to explore potential correlations between specific blood types and susceptibility to certain diseases. For example, individuals with Type O blood have been consistently observed to have a lower risk of cardiovascular diseases and certain types of gastric ulcers, while Type A individuals may exhibit higher susceptibility to certain bacterial or viral infections, showcasing the profound biological influence of these surface antigens.

Further Reading

Blood Type (Wikipedia)
Karl Landsteiner - Biographical (Nobel Prize)
The Rhesus System (NCBI Bookshelf)
International Society of Blood Transfusion (ISBT)