

Multiple Alleles: Modeling of Blood Groups and its Applications

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Abstract

It is well known that the gene which determines blood group in humans have three different alleles A,B and Rh factor, which gives sixteen possibilities of genotypes. The aim is to investigate the transmission of blood groups from parents to their offspring. Considering Rh factor allele with A, B and O alleles, we construct a modeling table for genotypes and blood groups of the off-springs. Finally we derived a table from which we can deduce the possible blood groups for the father when we know the blood group of mother and her child. The last result can also used in certain disputed legal cases to decide the parents of a born child.

Keywords and Phrases: Rh factor, Modeling table for genotypes, blood groups of the off-springs.

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(1) Introduction and Historical environments of ABO-Blood groups:

We all have observed that offspring tends to have physically traits in common with their parents. In humans, similarity in hair color, eye color, height and physique is often quite clearly seen in families. On other hand, It is also possible that the traits of offspring are generally not completely predictable from observing those of the parents. A child might have a trait, such as hemophilia, that neither parent exhibits, though such a trait might occur more commonly within one family than other. Thus, despite patterns of inheritance, chance also appears to be involved. Creating a mathematical model of heredity requires both of these aspects. The hereditary units which are transmitted from one generations to the next (inherited) are called genes. The genes reside in a long molecule called DNA. Each gene occupies a specific position; loci, on a chromosome. Each locus can be occupied by one of several variant genes called alleles. Except for the sex chromosomes, it follows that there are two genes at every locus. If the two alleles are identical, then the person is homozygote

otherwise a heterozygote. Genotype may not be observable, what observable is person's phenotype.. An allele is an alternative form of a gene (one member of a pair) that is located at a specific position on a specific chromosome. These DNA codings determine distinct traits that can be passed on from parents to offspring. The process by which alleles are transmitted was discovered by Gregor Mendel and formulated in what is known as Mendel's law of segregation.

The main objectives of the work is to determine the inheritance pattern of dominant/co-dominant/recessive genes and using the blood grouping systems to demonstrate the transmission of dominant/recessive and co-dominant alleles from parents to the offspring.

Consider the gene which is of great interest to humans is the ABO blood group gene, has three alleles. The ABO locus resides on the long arm of chromosome number 9 at band "q34". This locus determines detectable antigens on the surface of red blood cells. There are three alleles: A, B and O, which determine an Antigen A, a B Antigen and the absence of either antigens respectively. Each allele has two chromosomes, so the presence of three different alleles means that there are six possible genotypes. For the ABO gene, the three alleles are the I^A , I^B and i alleles (common symbol is the letter "I," which stands for "immunoglobulin, a form of antibody found in blood Plasma."). We typically call these alleles "A," "B," and "O," blood groups. As the symbols above should suggest, the i allele (the "O" allele) is recessive to both the I^A and I^B alleles (the "A" and "B" alleles). The I^A and I^B show co-dominance. This means that in an individual who is heterozygous for these two alleles, the phenotypes of both alleles are completely expressed, thus producing blood type AB.

Thus we have the following:

Genotype	ii	$I^A I^A$ or $I^A i$	$I^B I^B$ or $I^B i$	$I^A I^B$
Phenotype	Type O	Type A	Type B	Type AB

Experiments with blood transfusions and the transfer of blood or blood components into a person's blood stream have been carried out for hundreds of years. Many patients have died due to blood transfer until 1901. In 1901, the Austrian Karl Landsteiner[5] discovered human blood groups and hence blood transfusions became safer.

Mixing blood (of different blood group) from two individuals can lead to blood clumping or agglutination (clotting). The clumped red cells can crack and cause toxic reactions. This can have fatal (causing death or deadly) consequences. Karl Landsteiner discovered that blood clumping was an immunological (Pertaining to the body's natural defence) reaction which occurs when the receiver of a blood transfusion has antibodies against the donor blood cells. Karl Landsteiner's work made it possible to determine blood types and thus paved the way for blood transfusions to be carried out safely. For this discovery, he was awarded the Nobel Prize in Physiology or Medicine in 1930.

The differences in human blood are due to the presence or absence of certain protein molecules called antigens and antibodies. The antigens are located on the surface of the red blood cells and the antibodies are in the blood plasma. Individuals have different types of antigens and antibodies and different combinations of antigens and antibodies. The blood group you belong to depends on what you have inherited from your parents.

There are more than 20 genetically determined blood group systems known today, but the ABO and Rh systems are the most important ones used for blood transfusions. Not all blood groups are compatible with each other. Mixing incompatible blood groups leads to blood clumping or agglutination, which is dangerous for individuals. Nobel Prize Winner Karl Landsteiner was involved in the discovery of both the ABO and Rh blood groups. Landsteiner had made a rule which gave the idea about different types of blood group.

Now to predict the genotypes and phenotypes of Blood Groups of the offspring, we use the **Punnett Square**, a useful tool to do genetic crossings. For this we have to determine the genotypes of the parent organisms and then cross mating should be written and then represent it in p-square.

The **Punnett square** is a diagram that is used to predict an outcome of a particular cross or breeding experiment. It is named after Reginald C. Punnett, who devised the approach, and is used by biologists to determine the probability of an offspring having a particular genotype. The Punnett square is a summary of every possible combination of one maternal allele with one paternal allele for each gene being studied in the cross. In this example, both organisms have the genotype Bb . They can produce gametes that contain either the B or b allele. (It is conventional in genetics to use capital letters to indicate dominant alleles and lower-case letters to indicate recessive alleles.) The probability of an individual offspring having the genotype BB is 25%, Bb is 50%, and bb is 25%. It is important to note that Punnett squares give probabilities only for genotypes, not phenotypes. The way in which the B and b alleles interact with each other to affect the appearance of the offspring depends on how the gene products (proteins) interact.

	Maternal	
	B	b
Paternal	B	BB Bb
	b	Bb bb

(2) Basic Mathematical Model for Inheritance of Genetic Characteristics of ABO Blood Groups.

It is known from the earlier studies that **there** may be a number of alleles corresponding to a given locus. The most important and elementary example is the gene determining blood groups which has three allele A , B , O , giving rise to nine possibilities, (A,A) , (A,B) , (A,O) , (B,A) , (B,B) , (B,O) , (O, A) , (O,B) , and (O,O) . There are however only six genotypes (A,A) , $(A,B)=(B,A)$, $(A,O)=(O, A)$, (B,B) , $(B,O)=(O,B)$, and (O,O) . Since A and B dominate over O , there are only four Phenotype groups namely $\{ (A,A), (A,O), (O,$

A)), { (B,B), (B,O), (O,B)}, { (A,B), (B, A) } and {(O,O)}. These are denoted by A, B, AB and O respectively. i.e.,

Phenotype	{ (A,A), (A,O), (O,A) }	{ (A,A), (A,O), (O, A) }	{ (A,B), (B, A) }	{(O,O)}
Blood Group	Type A	Type B	Type AB	Type O

From the following table, we can deduce the possible blood groups for the father when we know the blood groups of mother and child

Father Mother		A		B		AB	O
		(A,A)	(A,O)	(B,B)	(B,O)	(A, B)	(O, O)
A	(A,A)	(A, A) A	(A,A), (A,O) A	(A, B) AB	(A, B), (A,O) AB, A	(A, B), (A, A) AB, A	(A,O) A
	(A,O)	(A,A), (A,O) A	(A,A), (A,O), (O,O) A, O	(A, B), (B,O) AB, B	(A, B), (A,O), (B,O) AB, A, B	(A, A), (A, B), (A,O), (B,O) AB, A, B	(A,O), (O,O) A, O
B	(B,B)	(A, B) AB	(A, B), (B,O) AB, B	(B,B) B	(B, B), (B,O) B	(A, B), (B,B) AB, B	(B, O) B
	(B,O)	(A, B), (A,O) AB, A	(A, B), (A,O), (B,O), (O, O) AB, A, B, O	(B, B), (B,O) B	(B, B), (B,O), (O,O) B, O	(A, B), (A,O), (B,O), (B,B) AB, A, B	(O,O), (B,O) B, O
AB	(A, B)	(A, B), (A, A) AB, A	(A, A), (A, B), (A,O), (B,O) AB, A, B	(A, B), (B,B) AB, B	(A, B), (A,O), (B,O), (B,B) AB, A, B	(A, A), (A, B), (B,B) AB, A, B	(A,O), (B,O) A,B
O	(O, O)	(A,O) A	(A,O), (O,O) A, O	(B, O) B	(O,O), (B,O) B, O	(A,O), (B,O) A,B	(O,O) O

Table 1.1

Let us derive from table 1.1, the Possible Blood groups of father in terms of blood groups of mother and child:

CHILD → MOTHER	A	B	AB	O
A	A, B, AB, O	B, AB	B, AB	A, B, O
B	A, AB	A, B, AB, O	A, AB	AB, O
AB	A, B, AB, O	A, B, AB, O	A, B, AB	Nil
O	A, AB	B, AB	Nil	A, B, O

Table 1.2

This table is used in certain disputed legal cases whether a certain child born of a certain mother can be the child of a given male. From the last table, we easily derived that a mother with blood group O cannot produce a child with blood group AB and a mother with blood group AB cannot produce a child with blood group O.

(3) Chronological Background of Rh factor Blood group:

The ABO blood group isn't the only aspect of our blood type chemistry. There are about a dozen known genes which affect "blood type" activity. Because the ABO blood type has been known the longest, and has such a powerful effect, it is the one we focus on. The others genes also work in the same way, though certainly all of them not all have three alleles. The other aspect of blood type which is of most interest to us is the Rh factor[1]. Genetically, this is much simpler than the ABO system. It has only two alleles, one dominant (Rh-positive) and one recessive (Rh-negative). However, this facet (feature) of our blood type has some serious implications when we reproduce.

In 1939, Levine and Stetson described a hemolytic (the breaking down of red blood cells with oscillation of hemoglobin) transfusion reaction in an Pregnant woman following delivery of new-born child. There was woman who required transfusion of blood. Her husband, who had the same ABO type, was selected as her donor, after transfusion the recipient, demonstrated the classic symptoms of severe hemolytic transfusion reaction. Subsequently an antibody was isolated from the mother's serum (blood plasma) that react both at 37°C and 20 °C with the father's red cells. It was postulated that the fetus (developed or mature egg) and the father possessed a common factor that the mother did not have. While the mother carry the fetus, the mother was exposed to this factor and subsequently built up an antibody that reacted against the transfused red cells from the father and resulted in hemolytic transfusion reaction. The antibodies responsible led to the discovery of the Rh blood group.

Although it is much more complicated, the Rh blood factor can be explained by a pair of alleles on homologous chromosome pair, one of a pair of chromosomes that match up at meiosis and are identical in morphology and arrangement; a chromosome with the same gene sequence as another, each derived from one parent. The dominant Rh positive gene (+) produces the Rh antigen, a glycoprotein component of the RBC membrane. Like the type O gene, the recessive Rh negative gene (-) does not produce an antigen. The significance of the Rh blood group is related to the fact that the Rh antigens are highly immunogenic (capable of producing body's natural defence). The "Rh" Locus Reside on the short arm of chromosome number 1 at band "p36". This locus determines detectable antigens on the surface of red blood cells.

Anti-Rh (immune-type) antibodies can readily pass through the placental capillary(very thin blood tubes) membranes. A serious potential problem called maternal-fetal blood incompatibility or Rh Disease could occur with a pregnant Rh negative mother who carries an Rh positive fetus. Leakage of fetal red blood cells (RBCs) into the mother's system through minute injury in the placenta may cause her to produce anti-Rh antibodies. This could occur during the latter months of pregnancy or when the baby is delivered. Because of the time interval involved in producing a concentration (titer) of antibodies, the first Rh positive child may not be adversely affected. However, a subsequent Rh positive child may be at risk because the mother's anti-Rh can pass through the placenta, thus entering

the fetal circulatory system and clumping fetal RBCs. RhoGam injection, a serum containing anti-Rh antibodies, is now given to Rh negative woman within 72 hours after giving birth to their Rh positive baby. The RhoGam enters the mother's circulatory system and destroys any residual fetal positive RBCs that may be present in her system. This prevents her from producing anti-Rh antibodies. RhoGam must be given after each Rh positive baby. In this scenario of erythroblastosis fetalis, a life-threatening blood disorder, the fetus must be Rh positive, the mother Rh negative and the father Rh positive.

Almost always, an individual has the same blood group for life, but very rarely an individual's blood type changes through addition or suppression of an antigen in infection malignancy or autoimmune disease. An example of this rare phenomenon is the case of Demi-Lee Brennan^[11] an Australian citizen, whose blood group changed after a liver transplant Another more common cause in blood-type change is a bone marrow transplant Bone-marrow transplants are performed for many Leukemias and lymphomas, among other diseases. If a person receives bone marrow from someone who is a different ABO type (e.g., a type A patient receives a type O bone marrow), the patient's blood type will eventually convert to the donor's type

From the above data and using the Punnett square method we have made the following table of possible genotypes and blood groups of offspring when the blood groups of parents are known.

(4) Mathematical Modeling of Multiple Allele ABO-Blood Groups with Rh factor:

Using Punnett Square method, here is a table of possible genotypes and blood groups of offspring when blood groups of Parents are known:

Blood-Group	You Can Give Blood To	You Can Receive Blood From
A+	A+ AB+	A+ A- O+ O-
O+	O+ A+ B+ AB+	O+ O-
B+	B+ AB+	B+ B- O+ O-
AB+	AB+	Everyone
A-	A+ A- AB+ AB-	A- O-
O-	Everyone	O-
B-	B+ B- AB+ AB-	B- O-
AB-	AB+ AB-	AB- A- B- O-

Table 1.7

Based upon the above table, Rh positive recipients can theoretically receive positive or negative blood, and Rh negative donors can theoretically give to Rh positive and Rh negative recipients. Therefore, the "universal donor" is O Negative, while the "universal recipient" is AB Positive.

Based on the Table 1.6 we get impossible blood group of father when mother's blood group and child's blood group are known:

Mother's blood group	Child's blood group	Impossible blood group of father
A+	B+,B-,AB+,AB-	A+,A-,O+,O-
A+	O+,O-	AB+,AB-
A+	A+,A-	Nil
A-	B+, AB+	A+,A-,O+,O-, B-, AB-
A-	B-, AB-	A+,A-,O+,O-
A-	A+	O+,O-
A-	A-	Nil
A-	O+	A-,O-, B-, AB-, AB+
A-	O-	AB+,AB-
B+	AB+,AB-, A+,A-,	O+,O-, B+,B-,
B+	B+,B-,	Nil
B+	O+	AB+,AB-, O-
B+	O-	AB+,AB-
B+	AB+, A+	O+,O-, B+,B-, AB-, O-
B-	A-	O-, B+,B-,
B-	B-	Nil
B-	AB-	O+,O-, B+,B-
B-	O+	B-, AB-, A-
B-	O-	AB+,AB-
AB+	A+,A-, B-	Nil
AB+	O+,O-,	All
AB+	B+	O+,O-, AB-

AB+	AB+	O-
AB+	AB-	O+,O-,
AB-	A-, B-	Nil
AB-	B+, A+	A-,O-, B-, AB-,
AB-	AB+	A-,O-, B-, AB-, O+
AB-	AB-	O+,O-,
AB-	O+,O-	All
O+	A+,A-,	O+,O-, B+,B-
O+	B+	A+,A-,O+,O-
O+	AB+,AB-	All
O+	O+,O-	AB+,AB-
O-	A+	A-,O-, B-, AB-, O+
O-	A-,	O+,O-, B+,B-
O-	B+	A+,A-,O+,O-, AB-
O-	B-	A+,A-,O+,O-
O-	AB+,AB-	All
O-	O+	A-,O-, B-, AB-, AB+, B+
O-	O-	AB+,AB-

Table:1.7

(6) Conclusions: From the all above Tables, we can conclude the followings:

- 1) In Various legal cases, if we want to know the father of a child, after determining the blood group of mother and child, we can get the possible blood group of father. This can help us determine the child's father in criminal cases.
- 2) From the above Table no. 1.7 it becomes clear that if we have the particular blood group, we come to know whom we can give the blood and from whom we can receive. Tables 1.7 also concludes that O- is Universal donar and AB+ is universal acceptor
- 3) While getting married in INDIA, people match their horoscope but now it has become necessary to match the blood groups for the good health of next generation and mother. Rh type mother-fetus incompatibility occurs only when an Rh+ man gives birth to a child with an Rh- mother. Since an Rh+ father can have either a DD or Dd genotype .Only the Rh+ children (Dd) are likely to have medical complications. When both the mother and her fetus are Rh- (dd), the birth will be normal.

When the first time an Rh- woman becomes pregnant, there usually are not incompatibility difficulties for her Rh+ fetus. However, the second and subsequent births are likely to have life-threatening problems. The risk increases with each birth. Nutrients and the mother's antibodies regularly transfer across the placental boundary into the fetus, but her red blood cells usually do not, except in the case of an accidental rupture. Normally, anti-Rh+ antibodies do not exist in the first-time mother unless she has previously come in contact with Rh+ blood. Therefore, her antibodies are not likely to agglutinate the red blood cells of her Rh+ fetus.

Placental ruptures do occur normally at birth so that some fetal blood gets into the mother's system, stimulating the development of antibodies to Rh+ blood antigens. As

little as one drop of fetal blood stimulates the production of large amounts of antibodies. When the next pregnancy occurs, a transfer of antibodies from the mother's system once again takes place across the placental boundary into the fetus. The anti-Rh⁺ antibodies that she now produces react with the fetal blood, causing many of its red cells to burst or agglutinate. As a result, the newborn baby may have a life-threatening anemia because of a lack of oxygen in the blood. The baby also usually is jaundiced, fevered, quite swollen, and has an enlarged liver and spleen.

Serum (Rho-GAM injection) containing anti – Rh⁺ antibodies into the mother around the 28th week of pregnancy and again within 72 hours after the delivery of an Rh⁺ baby. This must be done for the first and all subsequent pregnancies Rho-GAM is also routinely given to Rh⁻ women after a miscarriage, an ectopic pregnancy, or an induced abortion to avoid complication.

So people are suggested to match their blood group before getting married !!!!

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