Case Study: Is My Baby in Danger?

"I'm pregnant!" Sofia happily exclaims to her husband Miguel.

Sofia and Miguel have been married for three years and have always wanted to be parents. Sofia is 32 years old and Miguel is 34 years old. They are both in excellent health; they like to stay active and eat a balanced diet. The first-time parents recently moved into a new house with a bedroom perfect for a nursery. They are very excited to start painting and decorating it for their new arrival. There is no preference for a boy or a girl; a healthy baby is the main priority.

At her first doctor's appointment, the doctor asks for a blood sample. This sample is tested for the presence of certain illnesses like hepatitis B, and whether the mother is immune to rubella. Her blood is also tested to determine her blood group, whether she is rhesus (Rh) positive or negative and her hemoglobin levels (1).

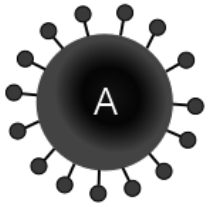
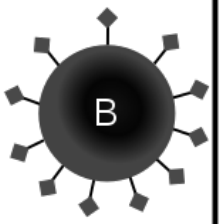
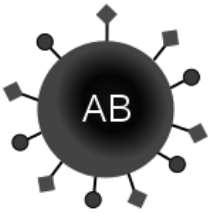
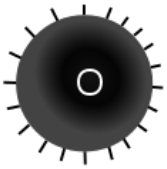
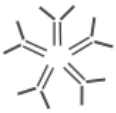
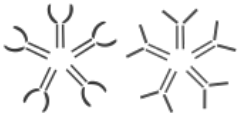
Sofia doesn't know what her blood type is; however, Miguel knows that his blood type is O^+ because he needed a blood transfusion during surgery several years ago.

Blood that is given during a transfusion needs to be similar to the recipient person's blood, so that their antibodies think nothing is amiss and that there are no invaders in the body (2). Scientists are aware of more than 20 genetically determined blood group systems; however, the ABO and Rh systems are the most important when blood transfusions are required. If incompatible blood groups are mixed, agglutination (blood clumping) will occur which may be life threatening. Nobel Prize recipient Karl Landsteiner was involved in the discovery of both the ABO and Rh blood groups, in 1901 and 1937, respectively (3).

Glycosylation is the most prevalent and diverse post-translational modification; over 70% of human proteins undergo this process. Glycosylation is the process by which sugars are added to proteins. The ABO blood type is determined by the types of sugars used to build the carbohydrates attached to proteins on the surfaces of red blood cells (2). The gene that encodes the proteins that form the basis of the ABO blood groups is located on chromosome 9 (4).

These carbohydrates have a core of 5-13 sugars, ending in the sugar fucose to form the H-antigen (2). The 'O' blood group has the H-antigen. A frameshift mutation caused by a deletion of guanine-258 near the N-terminus of the protein results in the formation of the H-antigen and the 'O' blood group (4).

Individuals that have 'A', 'B' or 'AB' blood express glycosyltransferase activities that people with 'O' blood type do not have. The glycosyltransferase activities convert the H-antigen into the A-antigen through the addition of the sugar N-acetylgalactosamine, or into the B-antigen through the addition of galactose (2,4). This small difference in the single sugar added to the H-antigen has an enormous effect, creating either the A- or B-antigen, and results in 'A', 'B' or 'AB' blood types (2).

	Group A	Group B	Group AB	Group O
Red blood cell type				
Antibodies in plasma	 Anti-B	 Anti-A	None	 Anti-A and Anti-B
Antigens in red blood cell	 A antigen	B antigen	 A and B antigens	None

(5) https://commons.wikimedia.org/wiki/File:ABO_blood_type.svg

Blood Group 'A'
If you belong to this blood group, you have A-antigens on the surface of your red blood cells. Your blood plasma has B-antibodies that work against B-antigens (3).

Blood Group 'B'
If you belong to this blood group, you have B-antigens on the surface of your red blood cells. Your blood plasma has A-antibodies that work against A-antigens (3).

Blood Group 'AB'
If you belong to this blood group, you have A- and B- antigens on the surface of your red blood cells. Your blood plasma has no antibodies that work against A- or B- antigens (3).

Blood Group 'O'
If you belong to this blood group, you have no antigens on the surface of your red blood cells. Your blood plasma has both A- and B- antibodies that work against A- and B- antigens respectively (3).

Questions:

1. What is a frameshift mutation?
2. What is an antigen?
3. What is an antibody?
4. What is the name given to a protein that has a carbohydrate attached?
5. Fill in the following chart about blood donors and blood recipients.

Blood Type	Can Donate Blood To	Can Receive Blood From
A		
B		
AB		
O		

The blood type story is not complete. In addition to the ABO blood groups, there is the Rh factor blood grouping system. Many people have the Rh factor, an antigen, on the surface of their red blood cells. Those that have this antigen are Rh^+ and those that do not have it are Rh^-. Unlike the ABO blood typing system, people that are Rh^- do not naturally have Rh antibodies in their blood plasma. However, an Rh^- person can develop Rh antibodies in their blood plasma if they receive Rh^+ blood (3). This is not only problematic during blood transfusions but also during pregnancy. If a pregnant female is Rh^- and her male partner is Rh^+, there is a chance that the baby will be Rh^+. If the baby is Rh^+, the mother's body may produce antibodies which will attack the baby's red blood cells (1). A person with Rh^+ blood can receive Rh^- blood without any problems (3). 15% of the population is Rh^- (6).

A few days later, Sofia and Miguel go to her follow-up appointment with her doctor to find out her blood test results. Sofia is immune to rubella, her hemoglobin levels are normal and she is negative for all the illnesses she was tested for. Sofia breathes a sigh of relief.

"There is one thing that is of concern." Dr. Singh tells her. "Your husband is blood type O^+ and you are blood type A^-."

"What is the problem doctor?" Sofia asks with concern evident in her voice.

"The minus part of your blood type is the Rh factor; in your case, you don't have it. Since most of the population has it, including your husband, there is a good chance your baby will have it too" Dr. Singh explains.

"Oh no! What does this mean? Is my baby in danger?" Sofia starts to tear up. Miguel puts a reassuring arm around her shoulders.

"Since this is your first pregnancy, the potential danger to your baby is much less than it may be in subsequent pregnancies. There is a medication called RhoGAM that you can take. Its antibodies destroy any of the baby's Rh positive blood cells that may enter your blood before your immune system has a chance to make antibodies that work against

their Rh factor. Unlike other antibodies that you will pass on to your baby, the antibodies in RhoGAM cannot cross the placenta so your baby cannot be harmed by them." (6)

"Are you sure our baby won't be harmed?" Miguel asks.

"Yes. This medication has been in use since the 1960s and has allowed women who are Rh negative to carry Rh positive babies safely. (6) Please don't worry. Miguel, I will make sure your wife and your baby are both safe" Dr. Singh informs them.

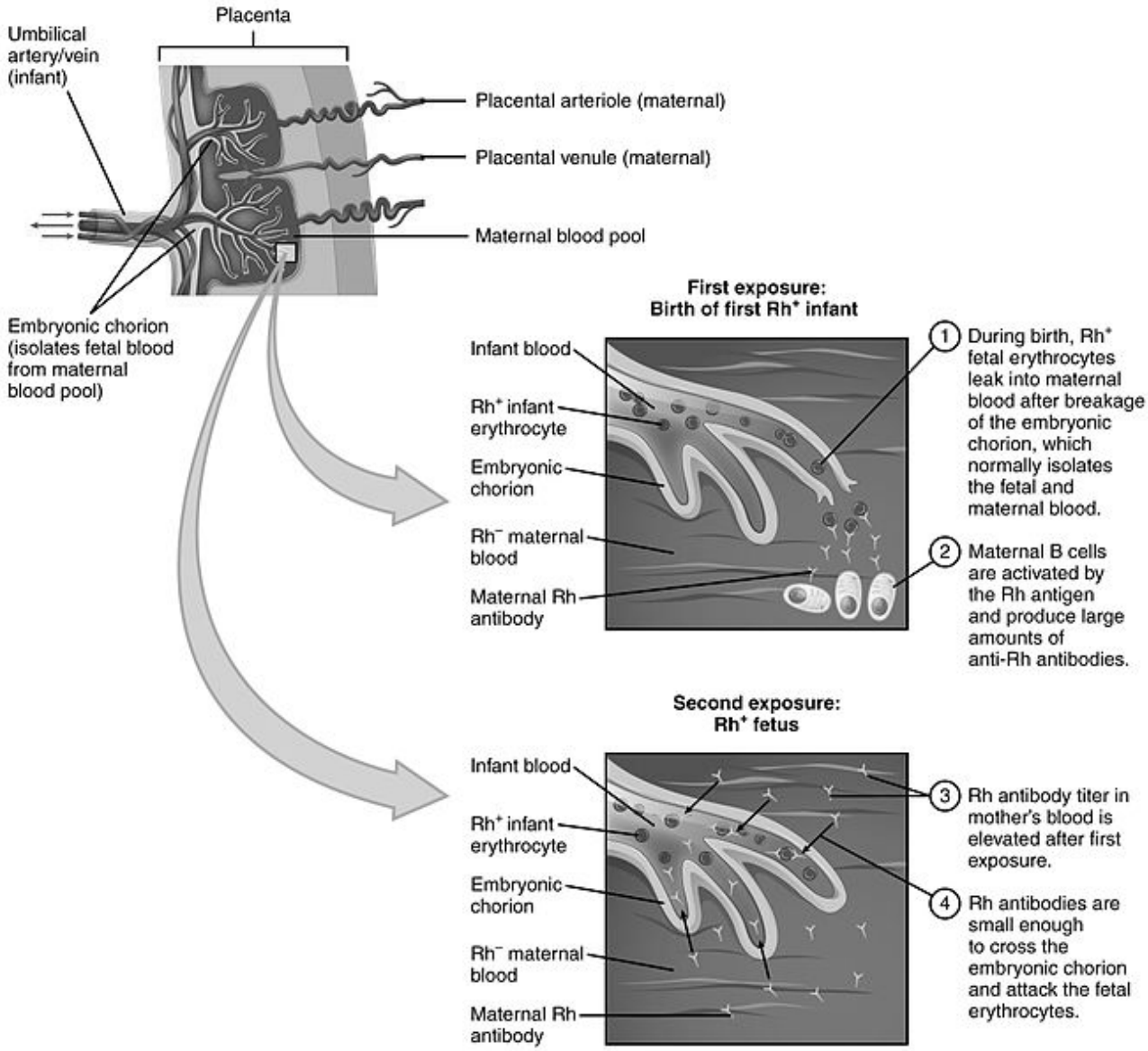
"Will I get RhoGAM today?" Sofia asks.

"No. It is too early to receive it since you are only two months along. It is administered between weeks 26 and 28 of pregnancy. If your baby is found to be Rh positive at birth, you will receive another dose of RhoGAM within 72 hours of your delivery." (7) Dr. Singh tells them.

"Thank you, doctor, for explaining everything so clearly. I am so relieved to hear that my baby won't be harmed due to my blood type" Sofia says.

"Everything will be fine. Don't be stressed about it. It is not good for you or for your baby. Please schedule your next appointment at the reception desk on your way out." Dr. Singh says.

"Thank you for everything doctor." Miguel says while shaking his hand.



(8) https://commons.wikimedia.org/wiki/File:1910_Erythroblastosis_Fetalis.jpg

6. There are actually 8 blood types, instead of 4 if you consider the Rh factor. List the 8 blood types.
7. What is the universal donor blood type?
8. What is the universal recipient blood type?

There are three gene alleles that control blood type: I^A, I^B and i. 'I' stands for immunoglobin, for the type of white blood cell that would be triggered to attack. I^A and I^B are co-dominant genes, meaning that when they are both inherited, they are both fully expressed. The recessive form of the allele is 'i' (9).

9. What is the difference between co-dominance and incomplete dominance?

10. Complete the following chart for the possible genotypes for each blood type. Although each blood type can come with or without the Rh factor, focus on just the ABO blood typing system.

Blood Type	Possible Genotypes
A	
B	
AB	
O	

Sofia has type A blood and Miguel has type O blood.

11. What are the possible genotypes for Sofia's blood type?

12. What is the only possible genotype for Miguel's blood type?

13. If Sofia is homozygous dominant for type A blood, what is the probability that their child will have type A blood or type O blood? Use a Punnett square to help you determine the answer.

14. If Sofia is heterozygous for type A blood, what is the probability that their child will have type A blood or type O blood? Use a Punnett square to help you determine the answer.

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