Bloodline:
A Human Genetics Case Study

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Your instructor will specify how you should submit this investigation and when it is due.

Opening Scene

Oliva Keller, a senior at Granville High School, is warming up with her teammates before soccer practice. They are about to start drills when their coach walks up and announces that they have a new goalie; she gestures toward the new player and tells the team her name is Diana Morrison. Olivia exclaims, “It can’t be!” She jogs towards Diana, calling her name to get her attention.

“Olivia! Oh my gosh, it’s been forever!” Diana replies when she sees Olivia approaching.

The two girls start chatting and reminiscing, but the blast of a whistle interrupts them. Coach Hawkins shouts, “Girls! It's time to practice. You can talk more when you run two extra laps today.” The coach divides up the team and sends each group to start drills.

As Olivia jogs off to start her set of drills, her teammate Joan says, “You and Diana seem chummy. You know her?”

Olivia replies, “Yes…well, I used to. I mean, until we were 13, we were best friends, but one day my mom told me that I wasn’t allowed to see Diana anymore. Then her parents got divorced, and she and her mom moved away. I haven’t seen her since. That was before Facebook, so there wasn't a good way for us to keep in touch.”

“Why would your mom tell you not to see her anymore?” Joan asks.

“I don’t know,” Olivia says. “I guess our parents had a fight, but I never really knew for sure.”

Mid-Practice

“Okay, team,” Coach Hawkins shouts, “let’s test out our new goalie! Forwards, line up!”

The whole team glances at their new goalie.

Coach Hawkins blows her whistle, and the first player runs forward and kicks the ball. Diana jumps into the air and blocks it. The second kicker goes for a low goal kick, and Diana knocks it out before it reaches the box. The next three kickers look at each other, nod, and proceed to kick one after another. Diana slaps the first ball out of the way, grabs the second ball midair, and deflects the third ball expertly.

Joan says, “Wow, she’s pretty good. I wonder if she can block one off guard.”

“Watch this,” Olivia says. “Diana, heads up!” Olivia kicks the ball as hard as she can directly at the new goalie. Diana, confused by the sound, turns just in time for the ball to hit her directly in the face. “What’s your deal?” Diana screams, as she turns towards Olivia with a red face and a nosebleed.

“Oh, no! I’m so sorry, Diana!” Olivia says, embarrassed. Just then, Coach Hawkins blows her whistle and says forcefully, “Okay, that’s enough for today. Time for laps. Olivia gets three extra for assaulting our goalie!” The players groan, but start running.

Nothing seems out of the ordinary until the seventh lap, when Olivia hears Coach Hawkins call out, “Hey, Diana, are you okay? Diana? Somebody call 911 -- now!”

From across the field, Olivia sees that Diana has collapsed.

Emergency Room

Diana is taken by ambulance to the emergency room. Olivia and Joan follow in Joan's car. Just after they arrive at the hospital, Olivia's mother dashes frantically into the waiting room.

"Olivia! I went to the soccer field to pick you up, but you weren't there. Someone at the field said a blond girl had collapsed. I thought…" she stammers.

"Mom, I'm fine. I'm sorry I scared you. I should have called, but it's Diana," says Olivia.
"Diana?" Olivia's mother asks.
"Diana *Morrison*," Olivia replies.
"Where's Diana?" cries another woman. "I'm her mother. They told me she was here." Mrs. Morrison looks around the room and comes to a halt. She and Olivia's mother are locked a confused stare.

"What are *you* doing here?" Mrs. Morrison asks in a tense voice.
Before Mrs. Keller can answer, Olivia steps forward. "Mrs. Morrison," Olivia says, "I'm on the soccer team with Diana. We were running laps and she just collapsed."

"Was it heat stroke?" Mrs. Morrison asks, concerned. Just then, the head physician in the ER walks into the lobby and calls for the family of Diana Morrison.

Mrs. Morrison rushes over to the doctor and asks, "How's Diana? Is she okay?"

The ER doctor hesitates and then says slowly, "Mrs. Morrison, I'm so sorry. When Diana arrived in the treatment room, she was unresponsive. Even with our best efforts, we couldn't save her."

Memorial Service (a few days later)

Olivia and her parents attend a memorial service for Diana. When they arrive, Olivia sees Diana's mother being comforted by several of her daughter's friends. Olivia starts to approach Mrs. Morrison to give her condolences, but at the sight of Olivia, Mrs. Morrison bursts into tears.

Olivia's teammate Joan walks up and asks Olivia, "What was that about?"

Olivia explains to Joan, “Diana and I used to do everything together. It was almost like we were sisters. Play dates, sports, camping, vacations…our birthdays are even a few days apart, so our parties were combined, and we made it into this whole big deal every year.”

“So what happened?” Joan asks.

“It just ended,” Olivia explains. “I remember waking up one night to find my Mom rocking me and crying and crying. I asked her what was wrong, but all she would say was that she loved me. After that, everything changed. Diana’s mom and dad split up. We stopped hanging out with them, and then Diana and her mom moved.” Olivia shrugs. “My mom told me to forget about Diana, to make new friends.”

Olivia looks up just as her father heads toward Mrs. Morrison. They speak briefly, and then hug. Olivia notices that they part slowly, and she looks toward her mother in confusion. Her mother meets her gaze for an instant, but then quickly looks away.

Answer all questions in your lab manual.

Question 1: What do you think is going on between these two families? (You don't have to know for certain. What is your suspicion?)

Question 2: You know about the A, B, and O alleles for ABO blood type and the Rh-factor alleles, +/-. If you had access to the blood types of the members of these two families, how could you use that information to test your suspicion?

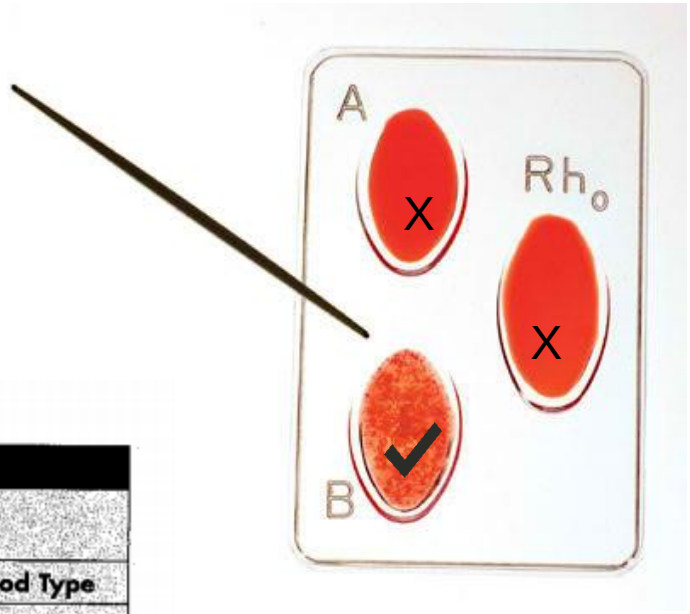
Question 3: Following the instructions in the lab manual, a lab technician has provided you with data on the blood types of the following characters in this case study: Diana Morrison, Mr. Morrison, Mrs. Morrison, and Mr. Keller (Olivia's father). The lab technician's results are on the next page, and you can use them to determine the blood types of those individuals. Copy the results (checks and Xs) into Table 8-1 on p. 95, and fill in the last column (Blood Types). You can use the illustration on the next page as a guide for interpreting the results.

3.

Table 8-1. Blood Types Determined by Agglutination Tests

Blood Sample	Check the Wells in Which Clumping Occurred			Blood Type
	A	B	Rh	
Example	X	✓	X	B–
1 (Diana Morrison)	✓	X	✓	
2 (Mr. Morrison)	X	✓	✓	
3 (Mr. Keller)	✓	✓	X	
4 (Mrs. Morrison)	X	X	✓	

agglutination=clumping



This blood sample is Type **B-** (because there is clumping in the "B" well, but not in the "A" or "Rh" wells).

Question 4: Based on the blood types that you just determined, is it possible for Mr. Morrison to be Diana's biological father? Construct one or more Punnett squares to support your answer.

Question 5: Based on the blood-types you determined, is it possible that Mr. Keller had an affair with Mrs. Morrison and is Diana's biological father? Construct one or more Punnett squares to support your answer. You will not need to know the blood types of Olivia Keller or Mrs. Keller to answer this question, but if you're curious, Olivia is type A-, and Mrs. Keller is type O+.

Mercy Hospital, several days later

A nurse is reminiscing with a colleague:
“So many babies have been born at this hospital, but I will always remember the day that Diana Morrison was born. The charge nurse ordered me to go to Mrs. Morrison’s room and try to get her up and walking. When I got to the room, she was talking to Mr. Keller about the baby. I was fresh out of nursing school, and I didn’t think it was any of my business. Anyway, what could I do? A few days later, Olivia Keller was born, and I watched both mothers bonding with their babies, cradling them and talking to them.”

“All these years later, I recognized Diana’s name when the paramedics brought her in.”

The nurse sighs.

“The autopsy just came in,” she continues. “Diana’s death was due to a blood clot. That news made me think about all of this again. I pulled the girls’ medical records, and they confirmed my suspicions. I’m determined to contact the families because the blood clot that killed Diana sounds like it could be an inherited condition. It could affect someone else in her biological family. They have to be told.”

Inherited Blood Disorders

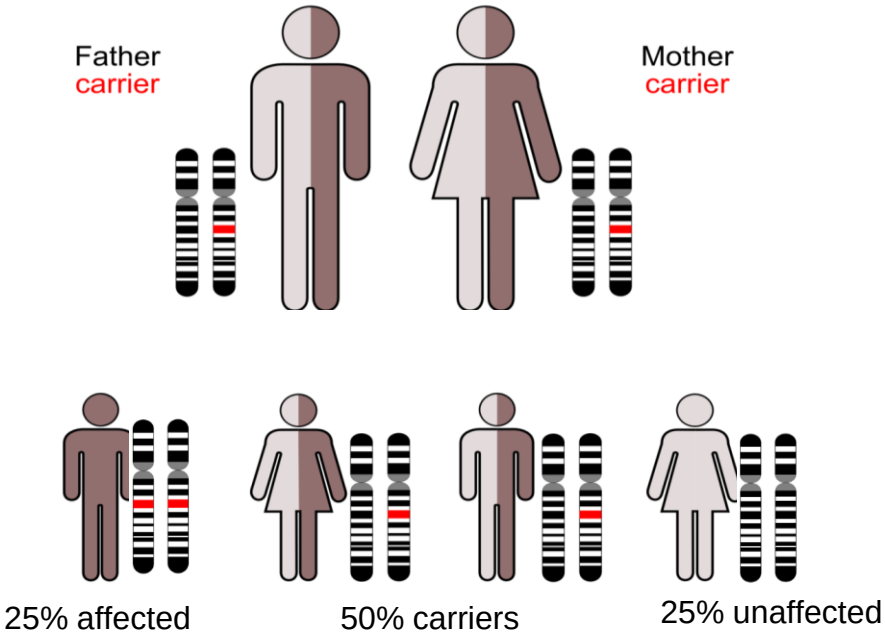
Hemophilia is a group of inherited disorders that lead to problems with *factors* (proteins in blood plasma) that normally stop the bleeding when a blood vessel is broken. Hemophiliacs don't bleed more intensely than other people, just longer. For a hemophiliac, even a minor injury can result in blood loss that lasts days or weeks.

Hemophilia A, which occurs when a clotting factor is absent, accounts for about 90% of all cases of hemophilia. Hemophilia A is a sex-linked trait. The responsible gene is on the X chromosome.

Hemophilia B, which occurs when a clotting factor is deficient, is also a sex-linked trait. Again, the responsible gene is on the X chromosome.

Hemophilia C also involves a deficient clotting factor, but it is inherited as an autosomal recessive trait (the responsible gene is not on a sex chromosome). This form of hemophilia is the subject of the next set of questions.

Hemophilia C: Autosomal recessive



Question 6: Using **H** and **h** for the dominant and recessive alleles for Hemophilia C, construct a Punnett square on your data sheets to illustrate the parents shown on this page and their predicted offspring.

Question 7: Mrs. Morrison and her parents and sister have normal blood clotting, but she has a brother with Hemophilia C (autosomal recessive). What is the probability that Mrs. Morrison is a carrier? Explain how you know.

Question 8: Suppose you were counseling someone (not necessarily the family pictured) about the likelihood of inheriting an autosomal recessive condition. How would you explain to them the circumstances under which a child could be born with a trait like Hemophilia C?

Pedigree symbols

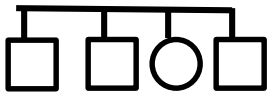
Pedigrees are representations of family relationships.
They can be used to determine inheritance patterns.

male

female

mating

offspring (in birth order)

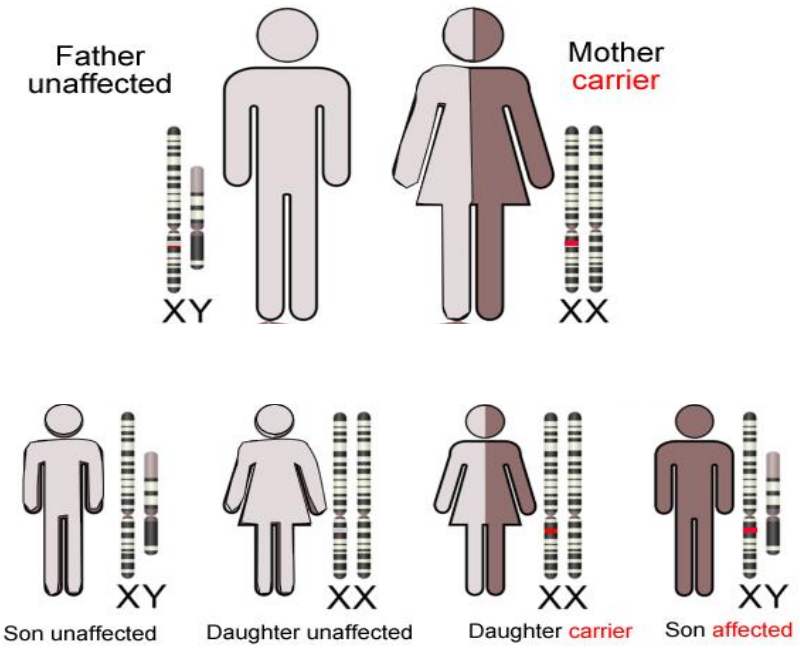


affected individuals (have the trait of interest)

carriers

Question 9: Use the blank pedigree in your lab manual to depict the autosomal recessive inheritance pattern from question 6. You are simply demonstrating your ability to translate information into the form of a pedigree. *This pedigree is not intended to represent the Keller family or the Morrison family. There is no connection between this trait and biological sex. You do not need to re-draw the key to the symbols used in the pedigree.*

Hemophilia A: Sex-linked Recessive



These parents will not have a daughter with Hemophilia A, but the probability of a son having Hemophilia A is 50%.

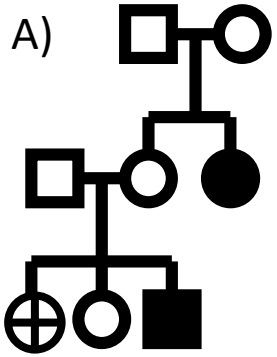
Question 10: Use X^H for the dominant allele and X^h for the recessive allele for the Hemophilia A gene. Construct a Punnett square to represent the parents shown above and their predicted offspring. (For example, the genotype of a male who does not have Hemophilia A is X^HY.)

Question 11: Use the blank pedigree in your lab manual to show the sex-linked inheritance pattern for Hemophilia A (using the image on the previous page and your Punnett square). As on the previous pedigree, this pedigree does not represent the Kellers or the Morrisons; you're simply demonstrating that you can represent information correctly in a pedigree. Do not re-draw the symbol key.

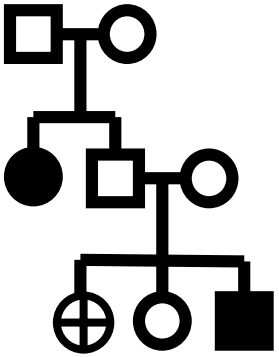
Question 12: In question 8, you learned that Mrs. Morrison's brother had Hemophilia C. Suppose that, instead, Mrs. Morrison's brother had suffered from Hemophilia A (sex-linked recessive). In that case, what would be the probability that Mrs. Morrison is a carrier? Assume that her parents and sister have normal clotting. Explain your answer.

Question 13: Remember that Mrs. Morrison's brother had hemophilia, but her sister and parents did not. It turns out that *her mother's sister* died very young, apparently of a massive hemorrhage. Which of the following is an accurate pedigree of Mrs. Morrison's family? Explain how you ruled out the other two pedigrees.

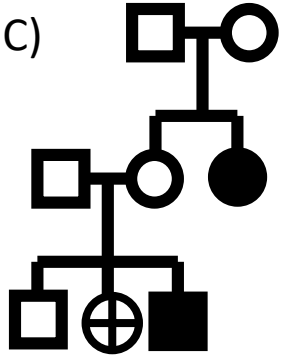
A)



B)



C)



⊕ = Mrs. Morrison

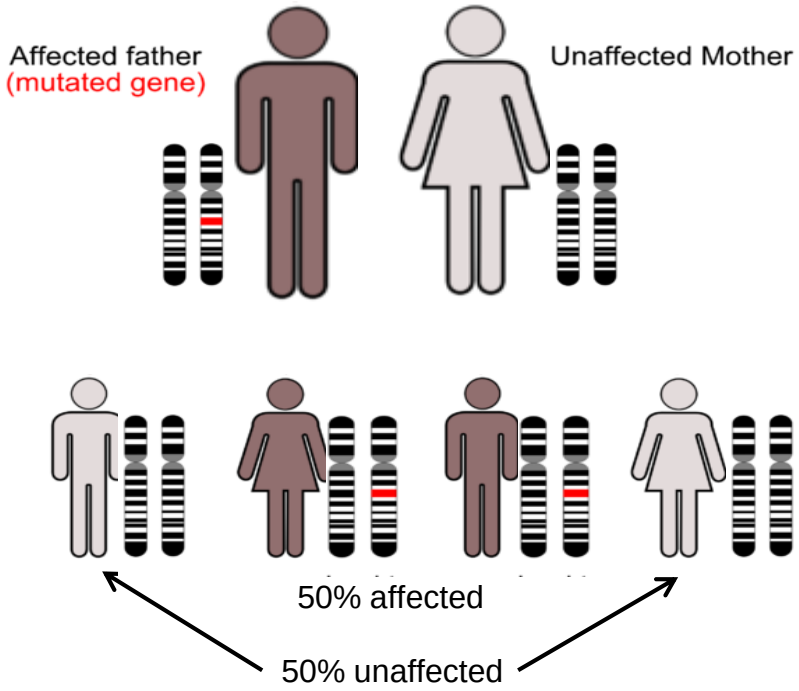
Other Inherited Blood Disorders

Hemophilia causes a lack of blood clotting, but Diana apparently died from overactive blood clotting (hypercoagulation).

The most common inherited disorder that produces hypercoagulation is Factor V Leiden, which follows an **autosomal dominant** inheritance pattern (like Huntington's Disease). About 5% of Caucasians in North America are affected by it. A dominant mutation of a gene located on chromosome 1 causes the body to produce too much of a clotting factor. This leads to deep vein thrombosis, pain, strokes, and heart attacks. Miscarriages and pulmonary embolisms can also result.

The autosomal dominant inherited pattern is shown on the next page.

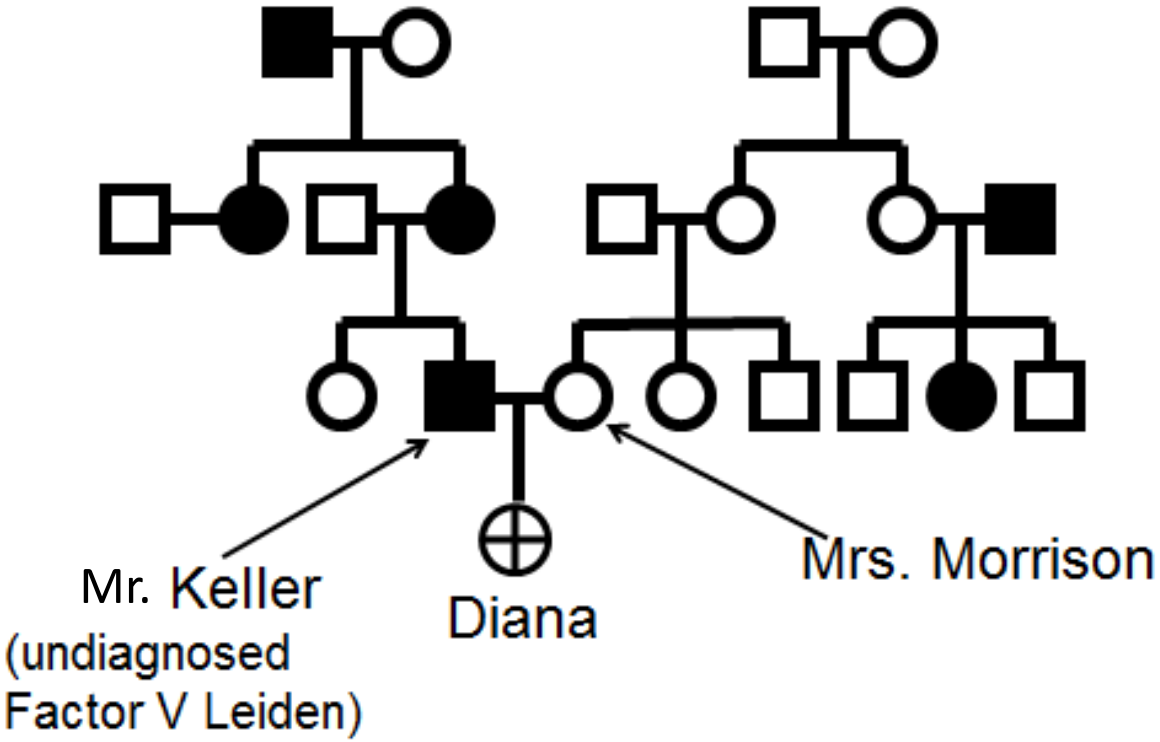
Autosomal dominant



Question 14: Using ***B*** (uppercase) for the dominant allele and b (lowercase) for the recessive allele for Factor V Leiden, construct a Punnett square to show the parents from this page and their predicted offspring.

Question 15: Mr. Keller (Diana's biological father) investigates his family medical history when he is made aware of concerns about Factor V Leiden. Mrs. Morrison looks into her family history, too.

Mrs. Morrison's aunt's husband and cousin died of heart attacks, but her mother and sister are fine. Mr. Keller's aunt had multiple miscarriages; his mother suffered from deep vein thrombosis; and his grandfather died of a heart attack. Based on this information, do you think Mr. Keller or Mrs. Morrison is more likely to be the source of Diana's Factor V Leiden mutation? Explain why.



The End

Additional Information

Online Mendelian Inheritance in Man has excellent descriptions of the human genetic disorders mentioned in this case: http://www.ncbi.nlm.nih.gov/sites/entrez?db=OMIM

Information about thrombophilia can be found at: http://www.fvleiden.org/

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Graphic of autosomal recessive inheritance patterns.
Author: Armin Kübelbeck
http://commons.wikimedia.org/wiki/File:Autorecessive_en_01.png

Picture showing the inheritance of a recessive allele on an X-chromosome.
Author: Armin Kübelbeck, modified to English by Peggy Brickman
http://commons.wikimedia.org/wiki/File:X-chromosomal-rezessive-Vater.png

Picture showing the inheritance of a dominant allele on an autosome.
Author: Armin Kübelbeck http://commons.wikimedia.org/wiki/File:Autodominant_en_01.png