The Blue People of Troublesome Creek

Pedigree Challenge ●■● Newsome Biology

Group: _____ Date: _____ Block:_____

Condition of Interest: Methemoglobinemia

Methemogloninemia in humans is a blood disorder in which an abnormal amount of methemoglobin is produced. Hemoglobin is the protein in red blood cells (RBCs) that carries and distributes oxygen to the body. Methemoglobin is a form of hemoglobin. It results in decreased availabitlity of oxygen to the tissues. Symptoms are proportional to the methemoglobin level and include skin color and blood color changes.

The Troublesome Family: Background Information

In 1820 a French orphan named Martin Fugate settled on the banks of eastern Kentucky near Troublesome Creek. He married his American redheaded sweetheart named Elizabeth Smith. They had 7 kids and lived happily ever after. However…four of their kids were **blue!**

Six generations later in 1975, Martin's great-great-great-great grandson, Ben Stacy was born blue, and was immediately rushed from the maternity ward to the nearest city hospital by ambulance. There he stayed for two days receiving tests but no one could explain why baby Ben was blue. Then, Ben's grandmother brought up the "Blue Fugates of Troublesome Creek." That's when Ben's father admitted that his grandmother, Luna Fugate was a blue Fugate. After this information was revealed, doctors concluded that Ben Stacy was blue due to an inherited condition known as methemogloninemia. Over time, the blue appearance of Ben's skin diminished as he aged. Today he is a normal looking man, though his fingernails still have a tinge of blue.

Decades before Ben's birth, the legend of the "Blue Fugates of Troublesome Creek" caught the attention of a hematologist (*someone who studies blood*) from the University of Kentucky named Dr. Madison Cawein. Dr. Cawein decided to investigate the Blue people of Troublesome Creek. At the time, no one knew much about them-least of all why these people were blue. He worked closely with a local nurse who was also interested in finding out more about the blue people. However, as soon as Dr. Cawein spotted a blue person from afar, they would soon disappear. Most of these people were older and were born at their childhood homes, not in a hospital. Their condition went undetected and they were very private, not wanting to be seen by any outsiders.

Then, one day, seemingly out of nowhere, two blue people walked into the medical clinic. As Cawein once put it, "They were bluer than heck." The pair of blue people that showed up to the clinic was a brother and sister, Patrick and Rachel Ritchie. They were very embarrased about their appearance. Dr. Cawein examined them and ruled out heart and/or lung disease. They seemed perfectly healthy other than their blue skin. Finally he asked them if they had any blue relatives. Come to find out they had quite a few blue relatives that were deceased or living in the hills near Troublesome Creek. Dr. Cawein decided to chart out their family.

After doing it, it was quite apparent that this was an inherited condition. Also, many of the family members married cousins, aunts and uncles (yes, I said incest) because there weren't any railroads or ways coming and going out of Troublesome Creek. The Blue People of Troublesome Creek did not have much opportunity to mix with others for many generations. So, they married the girl next door, even if that happened to be their cousin. Now the question was what exactly caused their blue skin? Dr. Cawein took many samples of the Ritchie's blood and brought it back to his lab at the University of Kentucky.

Again, hemoglobin is responsible for carrying oxygen in your bloodstream (oxygen bonds with the iron, giving your blood a red color). Hemoglobin is actually converted into a slightly different molecule called **methemoglobin.** Methemogloblin is bluish or purplish in color, not red. The methemogloblin gives oxygen-depleted blood a purple hue,

which appears blue through the skin as seen in veins. This is because methemoglobin has a slightly different ion of iron different than that of hemoglobin, and it does not effectively bond with oxygen.

If all of our hemoglobin were converted to methemoglobin, it would be useless. However, the conversion is a natural process that happens over time. So, how is it that all our hemoglobin doesn't just turn into methemoglobin? An enzyme known as **diaphorase** is responsible for converting methemoglobin back into hemoglobin. Dr. Cawein suspected that the blue people perhaps didn't have the enzyme diaphorase, which would mean that their (red) hemoglobin was turing (blue) methemoglobin and not turing back into (red) hemoglobin, like in normal people. Rachel and Patrick Ritchie must have spead the word about their blue family because of their 76-year-old uncle, Zach Fugate (who happened to be Patriarch of the Blue Clan), as well as Zach's 84-year-old Aunt Bessie, who also agreed to give blood. Cawein studied the blood of the blue Fugates and found that none of them had the enzyme diaphorase just as he thought! **#science!**

After more research, Dr. Cawein discovered a piece of older medical literature from the late 1800's in which a doctor by the name of E.M. Scott had researched a explained a condition known as "methemoglobinemia," in which patients lacked the enzyme diaphorase and were, in fact, blue. That condition perfectly described the Blue Fugates of Troublesome Creek, and a diagnosis was finally reached. They had accumulated so much of this molecule in their blood, that it overwhelmed the normal red hemoglobin. Instead of showing through as pink as it does in most Caucasians, it showed through as blue, similar to the blood that you may see in your veins.

Now, Dr. Cawein just needed a cure, and suddenly he thought of a molecule called methylene blue. We use methylene blue to dye cells in the classroom. It's looks just like a little bottle of blue ink. And yes, Dr. Cawein was suggesting that the Blue Fugates allow him to inject blue dye into them, and assured them that it would turn them a normal color. They thought he was crazy, trying to fight blue with blue, but decided to give it a try. Within minutes, the Blue Fugates were slowly turning a normal color. Methylene blue serves as an electron donor, which is required to turn methemoglobin back into hemoglobin. It brought many of the Blue Fugates to tears of joy, including old Aunt Bessie, who finally after 84 years was now no longer blue!

Analysis Questions:

1. What is hemoglobin? _____

   _____

2. What molecule does hemoglobin decay into over time? _____
3. What is the role of the enzyme diaphorase? _____

   _____

4. Explain why the Blue People of Troublesome Creek were blue in as much detail as possible: _____

   _____

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5. What is the cure for methemoglobinemia, and ***what does it do?*** _____

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6. What is the reason that methemoglobinemia was isolated to Troublesome Creek area of KY? (In other words, why was the disorder only prevelent in KY; why didn't other states see cases?)_____

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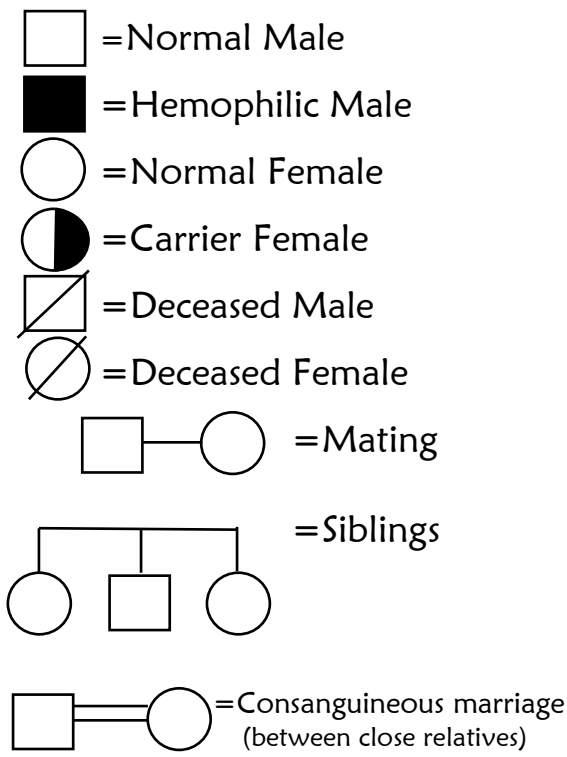
Your Task: Draw The Pedigree for This Family

You will have **43 individuals** and **7 generations** shown in this pedigree. Determine which females are likely carriers and indicate them using the key. You must include the following in your poster.

- Roman numerals to indicate generations.
- Family member names for all individuals whose names are provided.
- A **title** for your chart.
- Key (as shown below) on your chart.
- A list of the **total** number of known female carriers and male individuals with methemoglobinemia.

Pedigree Key



You are required to draw a **rough draft** before you start your poster-this will help you determine spacing and ensure accuracy. The rough draft will be stapled to this sheet and submitted. Count how many individuals you will have in each generation in order to space them neatly. **A ruler must be used to draw straight lines.** Neatness is a part of this grade.

The Family Tree:

Martin Fugate married Elizabeth Smith, who had red hair and was described to be "as pale as Mountain Laurel." It is unknown as to whether or not Martin Fugate was blue or not. Together they has seven children: Elenor, Charles, John, Zachariah, William, Hanna, and Levi. John, Zachariah, Hanna and Levi were blue. Zachariah married a woman with the last name Ritchie (her first name is unknown, but she was **actually Zachariah's aunt**), she was normal. Together they had 6 children, 4 sons and 2 daughters. 2 of the sons were blue.

One of their sons was named Levy, Levy was NOT blue, and he also married a Ritchie woman named Mahala. He and Mahala had 8 children, 4 boys and 4 girls. Only 1 of their children were blue, her name was Luna. Luna married a man by the name of John Stacy. Together they had 13 children. 6 boys and 7 girls. **NONE** of their children were blue. One of their sons was named Bill. Bill married Mary Ritchie. They has a son named Alva who was not blue either. Alva married a woman named Hilda Godsey. Alva and Hilda are Ben Stacy's parents. Ben was born blue, but outgrew his bluish tint without medical intervention, suggesting he is a carrier of methemoglobinemia.

***Because many of the names or birth orders are unknown, it is ok to list boys and girls on the pedigree the way they are mentioned in the "family tree" part.**

The Grade Breakdown: The Grading Rubric

5- Advanced Mastery: The pedigree is completed with creativity and no mistakes. Roman numerals are listed for all 7 generations, all 43 individuals are shown and named. The pedigree is complete with neatness and legibility, has good space utilization, a title and a key.

4- Mastery of The Standard: The pedigree is completed with creativity and 1-2 mistakes. Roman numerals are listed for all 7 generations, a minimum of 40 individuals are shown and named. The pedigree is complete with neatness and legibility, has good space utilization, a title and a key.

3- Approaching Mastery: The pedigree is completed with little creativity and 3-5 mistakes. Roman numerals are listed for majority of the generations, and a minimum of 35 individuals are shown and named. The pedigree is complete with neatness and legibility, has good space utilization, a title, and a key.

2- Developing Mastery: The pedigree is completed with very little creativity more than 5 mistakes. Roman numerals are not listed for the generations, and a minimum of 30 individuals are shown and named. The pedigree is complete with very little neatness and thought and is hard to follow. There is not a good use of space utilization, a title, and a key.

0.1- Not Yet: The pedigree is less than half way completed. Roman numerals are not listed for the generations, and only 20 or less individuals are shown and not all family members are named. The pedigree is complete with very little neatness and thought and can not be followed. There no use of space utilization, no title, and a key.

M- Missing: The pedigree was not completed at all, or was completed but not submitted. This assignment will also be "missing" if the student refuses to work/join a group to complete the assignment.