Those Old Kentucky Blues: An Interrupted Case Study

by

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Part I—"Blue People"

Ruth had never been as astonished as she was the day she encountered the first of the "blue people" from Troublesome Creek. The blue woman simply walked into the rural health clinic where Ruth was a nurse. Ruth suspected the woman was having a heart attack, but the woman wasn't concerned at all.

"I'm one of the blue Combses," she explained to Ruth, as if it was all perfectly logical. "And my mother-in-law is a Fugate."

As their conversation continued, Ruth learned from her patient that there were, in fact, many blue people living in the isolated community around Troublesome Creek.

Questions

1. Why might these people be blue? Generate at least two hypotheses.
2. How might you test your hypotheses?

Lorenzo ("Blue Anze") and Eleanor Fugate, circa 1915. Lorenzo was a son of Zach Fugate. Courtesy of Mary Fugate.

Part II—Pieces of the Family Puzzle

So began an adventure that lasted nearly a decade. Ruth and a physician, Dr. Cawein, who had heard rumors of blue people in the region, spent the next summer fighting off bugs and dogs as they trudged through the region piecing together a family tree of the reclusive Fugates, a large clan living in the valleys and hollows of the Appalachian Mountains in eastern Kentucky. Several of the relationships that Ruth and Dr. Cawein established have since been challenged by modern-day descendents of Martin Fugate. Nevertheless, the major lineages that they were able to establish helped to answer some of Ruth's questions.

The Fugate clan in the Troublesome Creek region could be traced back to the arrival of Martin Fugate, an orphan from France, in 1820. Legend has it that Martin may have been blue, but reports vary. For this case, we'll assume that Martin is blue. Martin settled in the area and married the pale, red-headed Elizabeth Smith. Over the years, they had at least seven children. Four of them reportedly were blue.

Zachary, one of Martin and Elizabeth's blue sons, married Elizabeth's sister. (Because of the isolation in this region, it was not uncommon to simply marry someone from next door. As the generations passed, this led to sometimes marrying a cousin or other relative as the family continued to grow.) They had several children. One of their sons was Levy. Levy married a girl from the Ritchie clan, another prominent family in the region. Together, they had eight children, including Luna. Luna is legendary for having had nearly purple skin.

Luna was courted by and married John Stacey. Together they raised 13 children. None of them were blue. One of Luna and John's children had a son, Alva Stacey. Alva and his wife, Hilda, came from separate branches of the extensive clan. Alva remembered his maternal blue grandmother and also tells the story of his infant son, Ben, who had caused quite a stir at the hospital when he was born with a blue tinge. Ben's blue color faded soon after birth, and he now reports only his fingernails and lips turning blue at times. Ben has since gone on to graduate from the Eastern Kentucky University in Richmond, Kentucky. He married soon after graduation and has moved to another state.

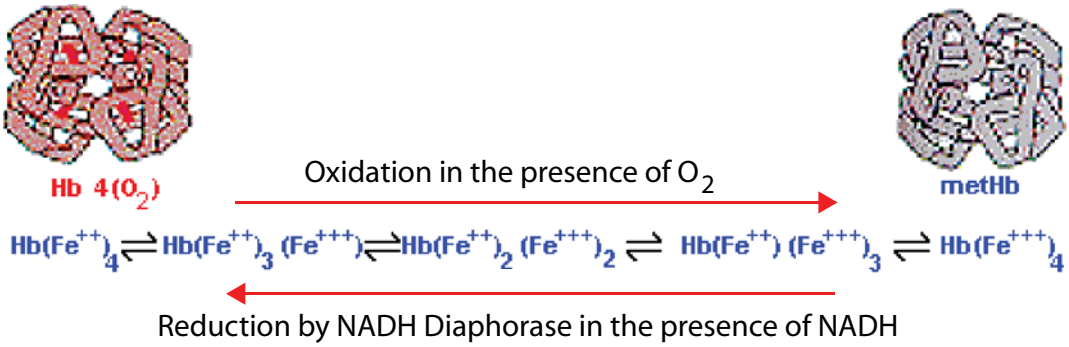
Questions

1. Construct a family tree (pedigree) from the information provided.
2. Evaluate your pedigree. Can you decide if "blueness" is a heritable trait?
3. If so, what pattern of inheritance do you suspect? If not, what other hypotheses might you suspect? Explain your answer.
4. Provide allele designations for each person in the pedigree.

Part III—A Different Shade of Blue

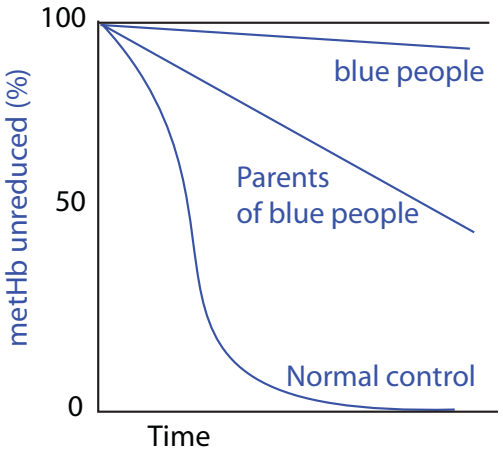
The mutation you have evaluated is located in the gene that codes for the enzyme called NADH diaphorase (or NADH dependent methemoglobin reductase). It is found in large concentration in red blood cells (RBC), where the enzyme functions to return hemoglobin to a normal oxygen binding state after it has been oxidized to methemoglobin (metHb). MetHb cannot bind oxygen or carbon dioxide (because iron, the oxygen binding part of the heme group, is in the ferric state and binds water instead of oxygen), and gives the blood a blue tint. This oxidation process is slow, but requires enzyme mediated reduction to return to hemoglobin as shown below in Figure 1.

Figure 1. Oxidation and Reduction



The graph below in Figure 2 shows enzyme activity over time in people that are blue, people that are not blue but may have blue children, and people that are not blue and never have blue children.

Figure 2. RBC NADH Diaphorase Activity



Red blood cell extracts from three different groups assayed for ability to reduce metHb to Hb.

Questions

1. What are the three lines on the graph in Figure 2 telling us?
2. Provide genotype designations for each line on the graph in Figure 2.
3. After evaluating the data above, what can you say regarding pattern of inheritance for this scenario?
4. Compare your conclusions on pattern of inheritance with those from Part II. Is one perspective more correct than another? Explain.

References

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