

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.



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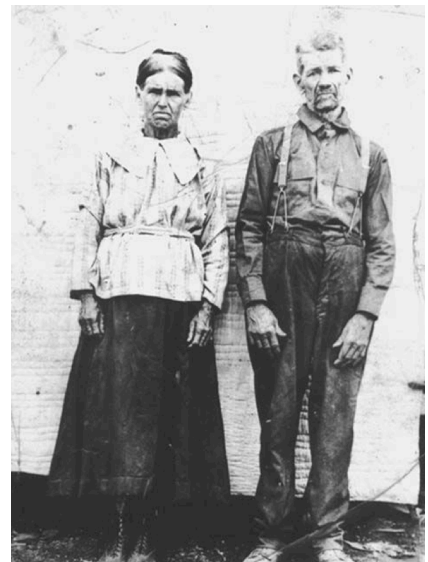
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Part II—Pieces of the Family Puzzle

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 descendants 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.

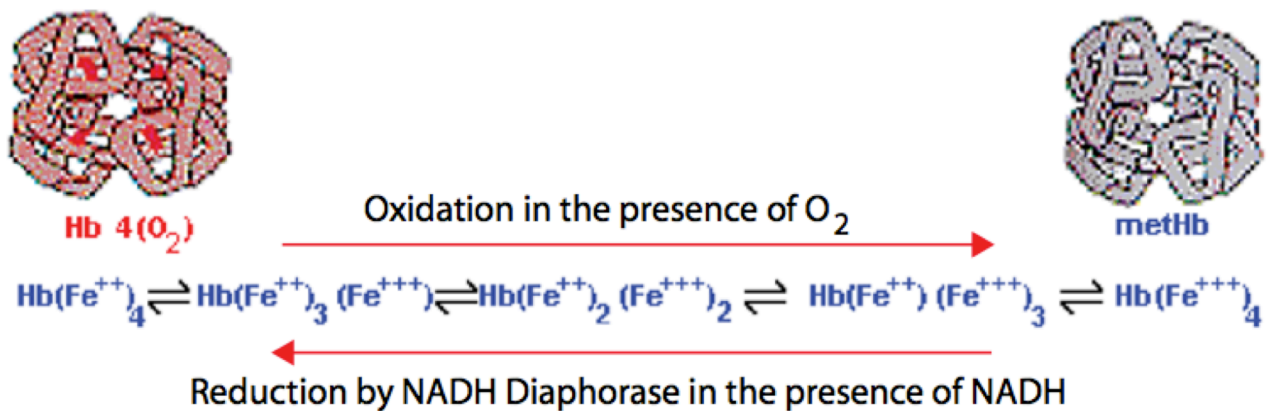
Zachary, one of Martin and Elizabeth's blue sons, married Elizabeth's sister. (Because of the isolation in this region, it was not uncommon to simply marry someone from next door. As the generations passed, this led to sometimes marrying a cousin or other relative as the family continued to grow.) They 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.

Part III—A Different Shade of Blue

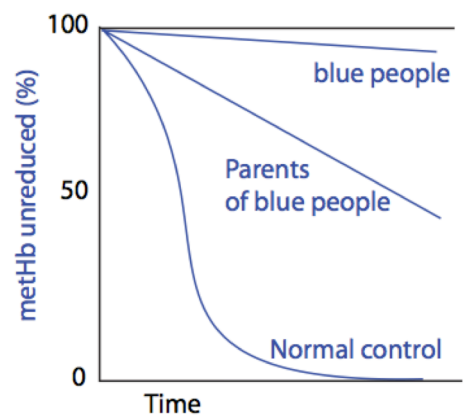
The mutation you have evaluated is located in the gene that codes for the enzyme called NADH diaphorase (or NADH dependent methemoglobin reductase). It is found in large concentration in red blood cells (RBC), where the enzyme functions to return hemoglobin to a normal oxygen binding state after it has 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 I.

Figure I. Oxidation and Reduction



The graph at right 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.



Those Old Kentucky “Blues”

(by **Celeste A. Leander**, Departments of Botany and Zoology, University of British Columbia **Robert J. Huskey**, Department of Biology, University of Virginia)

Directions: This is an “interrupted” case study. You will be given a number of pieces of paper—one at a time—that have some information and “clues” to the case. Each of these “clues” also has some questions that it will ask you to consider and answer. Please answer the questions on this sheet **THOROUGHLY** and with **DETAIL** in **COMPLETE SENTENCES** (where appropriate).

Part I—“Blue People”

1. What type of molecules give organisms (and parts of organisms such as leaves, skin, hair, eyes, blood etc...) their color?
2. Name and describe three of these molecules that you are familiar with (think about “Survival of the Sickest”—Chapter 1-Ironing It Out and Chapter 3-The Cholesterol Also Rises; Photosynthesis, etc...). Explain...1. What organisms produce this molecule, 2. Where it would be found, and 3. Its function (what does it do?).
 - a. What color would these molecules be? Why (Explain what light is doing)?
3. Which of these molecules do you think is giving these people their blue color? Explain why you think it is these molecules.
4. How could you test to see if you are right?

Part III—“A Different Shade of Blue”

7. Study Figure 1 carefully. Describe what is happening to the iron in hemoglobin when it is oxidized and explain how that contributes to the “blue” color of the pigment in this state.

8. What is the function of NADH Diaphorase? What would happen if this enzyme was not functional? Describe at least two ways that a “blue person” What are some possible ways that a “blue person” could have a non-functioning NADH Diaphorase (In other words, explain what could cause a non-functioning enzyme? Come up with at least two ways)!

9. Study the graph in Figure 2 carefully.
 - a. Explain, in your own words, what the graph is showing.

 - b. Place “alleles” on each of the lines that might help you express the “genetics” of each line.

10. Now that you have this information about the methemoglobinemia, what do you think the inheritance pattern might be? How is this different from your “answer” to question 6?

11. Given what you know, how do you think methemoglobinemia might be treated? What type of molecule do you think you could give the patients? Why might this work?

12. Look up the treatment for methemoglobinemia (<http://en.wikipedia.org/wiki/Methemoglobinemia> and/or <http://emedicine.medscape.com/article/204178-treatment#aw2aab6b6b2>). What two molecules have been used successfully? What do they do?