## THE BLUE PEOPLE OF TROUBLESOME CREEK

Six generations after a French orphan named Martin Fugate settled with his redheaded American bride on the banks of eastern Kentucky's Troublesome Creek, his great-great-great-great grandson was born in a modern hospital not far from where the creek still runs.

The boy inherited his father's lankiness and his mother's slightly nasal way of speaking. What he got from Martin Fugate was dark blue skin. "It was almost purple," his father recalls.

Doctors were so astonished by the color of Benjy Stacy's skin that they raced him by ambulance from the maternity ward in the hospital near Hazard to a medical clinic in Lexington. Two days of tests produced no explanation for skin the color of a bruised plum.

A transfusion was being prepared when Benjy's grandmother spoke up. "Have you ever heard of the blue Fugates of Troublesome Creek?" she asked the doctors.

"My grandmother Luna on my dad's side was a blue Fugate. It was real bad in her," Alva Stacy, the boy's father, explained. "The doctors finally came to the conclusion that Benjy's color was due to blood inherited from generations back."

Benjy's blue skin was a legacy of a recessive gene found across generations of the Fugates—also known as the "blue people" in the hills and hollows around Troublesome and Ball Creeks. 162 years preceding Benjy's birth, Martin Fugate (who emigrated to Kentucky in 1820) first introduced such a body discoloration to his family line. No mention of Martin's skin color is made in the early histories of the area, but family lore has it that Martin himself was blue. He managed to find and marry a woman who carried the same recessive gene. Of their seven children, four were reported to be blue.

The Fugates clan kept multiplying. Fugates married other Fugates. And they married the people who lived closest to them. All lived in isolation from the world, bunched in log cabins up and down the hollows, and so it was only natural that a boy married the girl next door, even if she had the same last name. Martin Fugate's blue children multiplied in this natural isolation tank.

Stacy recalls that his father-in-law, Levy Fugate, was "part of the family that showed blue. "It run in that generation who lived up and down Ball [Creek]," he says. "They looked like anybody else, 'cept they had the blue color."

In 1960, a doctor named Madison Cawein who worked at a medical clinic at the University of Kentucky's Lexington began hearing rumors about the blue people. "I'm a hematologist, so something like that perks up my ears," Cawein says. He would drive back and forth between Lexington and Hazard and scour the hills looking for the blue people he'd heard rumors about.

"They were bluer'n hell," Cawein says. "Well, as you can imagine, I really examined them. After concluding that there was no evidence of heart or lung diseases, I said 'Aha!' I started asking them questions: 'Do you have any relatives who are blue?' Then I sat down and we began to chart the family."

The doctor suspected methemoglobinemia, a rare hereditary blood disorder that results from excess methemoglobin. Methemoglobin is a nonfunctional form of the red hemoglobin that carries oxygen.

Cawein began drawing blood samples from the blue people and tested first for abnormal hemoglobin. The results were negative. Stumped, he turned to medical literature for a clue. It wasn't until he came across E. M. Scott's 1960 report in the *Journal of Clinical Investigation* that the answer began to emerge.

Scott had discovered hereditary methemoglobinemia among indigenous Alaskans. It was caused, Scott speculated, by an absence of the enzyme diaphorase from their red blood cells. Scott also concluded that the condition was inherited as a simple recessive trait. In other words, to get the disorder, a person would have to inherit two genes for it, one from each parent. Somebody with only one gene would not have the condition but could pass the gene to a child.

Scott's Alaskans seemed to match Cawein's blue people. If the condition were inherited as a recessive trait, it would appear most often in an inbred line.

"So I brought back the new blood and set up my enzyme assay," Cawein said. "And by God, they didn't have the enzyme diaphorase," he said, astonished. "I looked at other enzymes and nothing was wrong with them. So I knew we had the defect defined.''

Once he had the enzyme deficiency isolated, methylene blue sprang to Cawein's mind as the "perfectly obvious" antidote. Cawein knew from earlier studies that the body has an alternative method of converting methemoglobin back to normal. Activating it requires adding to the blood a substance that acts as an "electron donor." Many substances do this, but Cawein chose methylene blue because it had been used successfully and safely in other cases and because it acts quickly.

Cawein packed his bag and prepared to reveal his big discovery. He went over to the Ritchie's house and injected each of them with 100 milligrams of methylene blue.

"Within a few minutes. the blue color was gone from their skin," the doctor said. "For the first time in their lives, they were pink. They were delighted." The drug's effects are temporary, as methylene blue is normally excreted in the urine. So, the doctor gave each blue family a supply of methylene blue tablets to take as a daily pill.

Benjy Stacy is one of the last of the blue Fugates. A few weeks after his birth, Benjy lost his blue tint, and now he is about as normal looking a seven-year-old boy as you could hope to find. His lips and fingernails still turn a shade of purple-blue when he gets cold or angry, a quirk that intrigued medical students so much that, after Benjy's birth, they would crowd around the baby and try to make him cry to see his lips and nails turn blue. "Benjy was a pretty big item in the hospital," his mother says with a grin.

Because Benjy was intensely blue at birth but then recovered his normal skin tones, Benjy is assumed to have inherited only one gene for the condition. With Fugate blood on both his mother's and his father's side, the boy could have received genes for the enzyme deficiency from either direction. Such people tend to be very blue only at birth, probably because newborns normally have smaller amounts of diaphorase. The enzyme eventually builds to normal levels in most children and to almost normal levels in those like Benjy who carry one gene.

As coal mining and the railroads brought progress to Kentucky, the blue Fugates started moving out of their communities and marrying other people. The strain of inherited blue began to disappear as the recessive gene spread to families where it was unlikely to be paired with a similar gene.

*Adapted from Trost, C. (1982). The Blue People of Troublesome Creek: The story of an Appalachian malady, an inquisitive doctor, and a paradoxical cure. Science 82. https://web.archive.org/web/20180309180709/http://www.indiana.edu/~oso/lessons/Blues/TheBlues.htm*

## References


*Cawein, Madison and E.J. Lappat, "Hereditary Methemoglobinemia" in Hemoglobin, Its Precursors and Metabolites, ed. by F. William Sunderman, J.B. Lippincott Co., Philadelphia PA, 1964.*

*Cawein, Madison, et. al. "Hereditary diaphorase deficiency and methemoglobinemia". Archives of Internal Medicine, April, 1964.*

*Scott, E.M. "The relation of diaphorase of human erythrocytes to inheritance of methemolglobinemia", Journal of Clinical Investigation, 39, 1960.*