
PROLOGUE

July 1979, State of Zulia, western Venezuela

As we glide through the waters of Lake Maracaibo, daubs of color appear in the distance like a hallucination or a Matisse painting. From our *chalana*—a large canoe fitted with an outboard motor—we make out a scattering of small houses splashed with paint and perched on stilts over the water. With my colleague Tom Chase, a neurologist at the National Institutes of Health where I work as a health sciences administrator, I have come on an exploratory mission to the remote village of Laguneta. We are searching for someone who has inherited Huntington's disease from both of their parents, called a homozygote. Known here as *el mal de San Vito* or simply *el mal*, Huntington's disease (HD) causes involuntary jerky movements of the body known as chorea, mental disturbances, and cognitive decline, leading inexorably to death over ten or twenty or more years. Just one parent with the illness can transmit it to their children, who each have a 50–50 chance of inheriting the disease.

We are hoping that an individual with a double inheritance of this malady will reveal its fundamental cause, as happened a few years earlier with a hereditary condition known as hypercholesterolemia, which causes early heart attacks and strokes.¹ We figure our best chance of finding such a “double dose” individual is to look for families in which both parents have *el mal* and then check out their children for atypically severe or unusual disease. But we have been in Venezuela for nearly a week and have not yet found such families, much less anyone whose Huntington's stands out as unique.

As we round a spit of land and enter a lagoon, the *pueblo de agua*, or village over water, comes into view. Laguneta is comprised of twenty-five

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Approaching Laguneta. (Photo © Steve Uzzell, All Rights Reserved.)

or so small houses built on stilts in the lake, most of them constructed of wood or tin covered by corrugated tin roofs, with occasional windows framed in bright green or blue. Each house boasts a wooden porch, many adorned with piles of fishing nets and mounds of dried salted fish, testimony to the major occupation in this community. Here on this porch is a pig in a pen; over there, a pet monkey; farther on, a cormorant tied by the leg. Red, green, yellow, and orange hammocks hang like butterflies, cradling infants and adults, while naked children with bellies protruding from malnutrition and parasites, heads shaved clean to keep cool and avoid lice, cling shyly to the sides of the houses or plunge into the water, twisting like tops and shrieking with joy.

We have come to Laguneta owing to the work of a Venezuelan physician, Dr. Américo Negrette, whose pioneering studies, in the 1950s and 1960s, of Huntington's disease in Venezuela laid the foundation for all that followed. Now, decades later, he welcomed us on our arrival in Maracaibo, walking us through the barrio of San Luis, on the outskirts of the city, where he once cared for many families with *el mal*. Because they love him, they open their homes to us, in San Luis and in the villages of Barranquitas and Laguneta, the three major centers of the disease in this region. Nearly half the people in Laguneta suffer from *el mal* or are at 50% risk, probably owing to little migration out due to poverty and



Family dwelling in Laguneta. (Photo © Steve Uzzell, All Rights Reserved.)

isolation, and intermarriage among the affected families, although no one knows for certain.

Three things the people here do know: That *el mal* runs in families (is hereditary), and both women and men can pass on the disease to their children, although not all children of a parent with the disease will inevitably get it. Yet they know that just one parent with *el mal* means that one or more of the kids will likely develop it too. Like my grandfather, uncles, and most recently my mother Leonore, who began showing symptoms decades ago and has been gone from this earth for a little more than a year.

As the clock ticks toward our departure, we intensify our search, hoping to find our homozygote before we must leave for home, possibly never to return.



Our guide cuts the motor, and we glide up to one house in the center of the village. People freeze and gape at us in silence. Tom, six-feet-two, thin, and pale, and I—*la catira* they would call me, the blonde—with my long hair and blue eyes, arrive in this place like visitors from another galaxy. A woman catches my eye as she sits cross-legged on the porch. She had been cleaning fish, but seeing us, she stops. She wears a gray cotton

dress that hangs straight down from her shoulders. Her long black hair is pulled back into a ponytail. She has brown eyes, a strong jaw, and when she finally smiles, a few scraggly teeth. At first, she remains totally still. Then her strained effort gives way to a series of jerky movements. I know this woman; I know how she will get up with a lurch, walk with a wide gait to resist her movements, slur her words that I might not understand but I will know what she is saying anyway. She will move her mouth and face and eyes against her will so that they speak for her. She will even feel the same as my mother to hug, with her muscles constantly working to escape my grasp, even as she won't let go.

Our Lady of Laguneta holds me in her spell. The continuous movement accompanying her words has a hypnotic effect as she greets us. We describe our project, and she tells us about her thirteen children and her husband who had been at risk but has recently died of pneumonia, leaving her to raise her brood alone. Crestfallen, we explain that for our research, we need to find someone with two *living* parents with *el mal*. As we thank her and start to leave, she tells us, almost as an afterthought, "I have a sister...". That sister lives with her husband and children in a house a little farther along the grove of houses in the lagoon. She gestures toward them. "Go talk to them, they'll help you," she says.

At her sister's house, there are more hammocks, more children scurrying about. We climb out of our *chalana* onto the porch. Inside the house we meet the sister, a chain-smoking woman with sharp features, elegant bearing, and obvious chorea. She eyes us with a mixture of curiosity and suspicion. We introduce ourselves by way of her sister and tell her why we have come. The woman smiles and her reserve dissolves in the warmth of that smile. Then we see a white T-shirt moving in a hammock strung up at the other end of the room; clearly the man inside that T-shirt has Huntington's as well. He gets up out of the hammock to greet us. Soon he, too, is in the familiar state of standing still and moving at the same time. At first, we think they are brother and sister, but no, they are married, with fourteen children, at least one of whom has likely inherited the faulty gene from both parents.

We have finally found the family we were looking for. I should have felt elated. Instead, I am overcome by feelings of sadness, as I realize that most of these beautiful children will develop the disease, inheriting

either one or two copies of the faulty gene. Satisfaction and sorrow are intertwined within me like the two strands of the double helix. My thoughts of Venezuela will be forever etched with memories of these bright, vivacious kids, many of whose lives will fade and be cut short due to the cruelty of a single dominant gene.



The children, timid at first, grow braver and give in to their curiosity as they crowd around us. The woman's smile fades slightly as she puts her hands on the shoulders of a teenage girl, her daughter. "One is already sick," she says. We talk to the children, and they agree, albeit with trepidation, to let Tom draw their blood while I caress them and speak to them in my pidgin Spanish. After a while, a man poles up to the house in his *chalana*. He is the chain-smoker's brother and the chieftain of the town, we are told. As I discover later, he is also one of the most intelligent men I've ever met. He appears to be in the very early stage of *el mal*, with slight jerky movements and a hint of unsteadiness but no other signs of anything amiss. He wants us to meet his son. He poles away and brings back an angelic boy of five or six, with enormous blue-green eyes, curly light brown hair, freckles, and a slow, incandescent smile like a Cheshire cat's. The chain-smoker introduces her nephew. I think he has Huntington's, Tom says to me in English. The child has been ill since age two and now moves as if through glue. We watch him carefully as he walks like a little old man, falling, taking another step, falling again. He is certainly the youngest case of Huntington's that we have encountered so far.



Always in my heart. (Photo © Steve Uzzell, All Rights Reserved.)

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His aunt tells us who does and does not have *el mal* in their family, weaving together a complex family history going back multiple generations, a history that will eventually become crucial to our project. She and her husband also agree to donate blood. That night we return to Maracaibo and the next day, we will leave for home, carrying with us, along with precious blood samples, bittersweet memories of our first visit to this haunted place and the children whom we cannot forget. Especially that little boy who will die in the throes of uncontrollable seizures at the age of 11, but not before making his contribution to the world in a way that will surprise us all.