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All in the Mind

Santa Clara Valley Medical Center Neurobehavior Unit, San Jose, California, July 16, 1982

The patient lay there frozen. Looking more like a mannequin than a person, he made no movement and uttered no sound. His face was expressionless and his eyes stared eerily ahead. Dr. Phil Ballard, the physician on duty, flipped through the patient's chart. He was a 42-year-old Hispanic man named George Carillo who had become catatonic two weeks earlier, shortly after being incarcerated in the San Jose jail. Since then he had been seen by a dozen or more doctors in different parts of the hospital, but it was clear that none of them had the slightest idea what was wrong.

The case notes told a bizarre story. Carillo had turned up for a court hearing intoxicated on PCP and was jailed on the spot. But in his cell, he became less and less able to function. For three days he had bounced back and forth between jail and the Valley emergency room before finally being admitted to the psychiatry unit. Within the department of psychiatry there was a specialized ward called the neurobe-

havior unit, designed to deal with unusual cases which did not seem to fit classic psychiatric classifications and where an underlying physical or "organic" cause was suspected. And so, on July 16, the mysterious case of George Carillo had been sent to them.

Ballard, who was doing a fellowship in behavioral neurology on the unit, put the chart down and looked at his patient. George Carillo hadn't moved the entire time that he had been reading the medical records. If his new patient was faking it, he sure was some actor. Ballard looked at his watch: 10:00 A.M. His boss Bill Langston would be swamped with patients in the general neurology clinic, and would not want to be dragged out. But George needed a diagnosis, and the sooner the better.

General Neurology Clinic, Valley Medical Center

That Friday morning the neurology clinic was especially busy. A dozen patients filled the small waiting room and another twenty lined the corridor outside. Bill Langston, the head of the department of neurology, was used to it. Already that day he had seen two stroke victims, one with frontal lobe syndrome, two Alzheimer's patients, a case of temporal lobe epilepsy, and three patients with migraine headaches. It wasn't glamorous or well-paid work, but it was important. For tens of thousands of poor people in Santa Clara County, some fifty miles south of San Francisco, Valley Medical Center was the only place they could go for medical treatment.

And it was interesting. Given the complexity of the brain, neurological cases are often difficult and challenging. While sophisticated imaging systems exist to image the brain, they are not sensitive enough to detect small lesions. With the exception of the nerve fiber layer in the eye, which can be seen through an ophthalmoscope, the nervous system cannot be observed directly. A dermatologist can see a rash, a cardiologist can listen to a heart, but a neurologist must localize any damage to the brain through a complex process of deduction and inference from the clinical signs

and the patient's symptoms. For example, paralysis on the right side of the face and weakness of the left arm and leg means that the lesion—whether it is a stroke, tumor, or something else—must be located at the level of the facial nucleus on the right side of the brain stem. A lesion in this location can knock out the nerve fibers that innervate the muscles on the right side of the face (which are uncrossed), and at the same time damage motor tracts that run from the right side of the brain to the left side of the body, before they have crossed to the left at the junction of the lower end of the brain stem and spinal cord.

The symptoms vary greatly from patient to patient. One of Langston's patients had been walking down the street one day when he started to hear the voice of Walter Cronkite introducing the *CBS Evening News* and wondered if he was losing his mind. Neurological evaluation revealed that his auditory hallucinations were the first sign of a brain tumor in the speech area on the left side of his brain.

For all this, Langston had a sense that his career was going nowhere fast. At age 39, married for the third time, with a baby on the way, it looked increasingly unlikely that he would achieve major recognition as a physician, much less as a researcher. For some years he had held a teaching position at Stanford, but the chances of achieving tenure were virtually nonexistent. To get tenure it wasn't enough to be a good clinician and teach, you had to do significant research and publish papers. And Langston just didn't seem to have time to do much research.

Since his early teens, Langston had been fascinated by human behavior and its underlying physical causes. When people felt hunger, anger, pleasure, or pain, what was going on in the brain? Why did one person become an alcoholic or another an obsessive-compulsive and yet another a manic-depressive? When psychiatrists spoke about such things it was often in terms of Freudian psychodynamic theory—which Langston had always found fascinating, but also somewhat circular.

In striking contrast was the way scientists studied behav-

ior in animals. As a boy, Langston had watched programs on public television showing experiments in which rats would push a lever that electrically stimulated a certain area of their brain thought to induce a feeling of pleasure. The rats would push this lever rather than one that provided food, to the point of starvation. Langston had been intrigued by such experiments. These scientists were attempting to dissect the neurological basis of behavior, to discover the physical basis of pleasure and hunger. Perhaps such experiments on animals would eventually shed light on why people behave the way they do.

Langston had gone to medical school and, after toying with the idea of going into psychiatry, specialized in neurology, thinking that clinical neurology was a sound background for doing research into human behavior and the brain. But somewhere along the line, he had become virtually a full-time clinician. Now his days were so filled with the practice of medicine that he had little time to even think of research, let alone carry it out. Despite his expertise in diagnosing and treating patients, he felt unfulfilled. From time to time he wondered whether he should have studied basic science rather than medicine and set out to discover something new. He had always wanted to make a difference, but now it just didn't seem to be in the cards.

Langston was just about to start on a new patient when a call came through from Phil Ballard. "You must come and see this patient who was just admitted to the neurobehavior unit, Bill, you're just not going to believe it!" Langston listened impatiently as Phil outlined the case and how the psychiatrists had decided that the case belonged on Langston's neurobehavior unit. It sounded interesting, but not exactly urgent. Phil Ballard was insistent. "Absolutely. I'm telling you you must come right now. The psychiatrists don't know what to make of him."

Langston started to walk to the neurobehavior unit. In a sense, this unit was Langston's research. Two years before, he had set up this small unit in the psychiatry department to diagnose and treat unusual cases. It was well known that

from time to time cases turned up in psychiatry that were not truly psychiatric patients. These patients' disorders were caused by specific and sometimes irreversible damage to their brains, and therefore they needed to be seen by a neurologist. While these patients needed to be properly diagnosed and treated, they also offered a research opportunity. Such cases might give Langston a way of linking behavior to physical changes in the brain.

To date, the unit had admitted some interesting cases. There had been a young college student who had begun preaching in class and then aggressively approaching female classmates. He proved to have Wilson's disease, a rare disorder of copper metabolism. There was a patient who had started hallucinating wildly and drinking water from a toilet bowl, who turned out to have a herpes encephalitis, a viral infection that affects the temporal lobe of the brain. In both instances, abnormal behavior had resulted from organic changes (lesions) in their brains. Langston liked to call such cases experiments "of nature" rather than of science. Neurologists could not study humans the way neuroscientists studied rats in the laboratory, by stimulating or removing parts of the brain and observing the change in behavior. They had to wait for cases to arise naturally. But when they did arise, they offered scientists a small window into how the brain operates and controls behavior.

Wilson's disease, viral encephalitis, and today a frozen man. Langston felt sure that important insights would be gleaned from these and other experiments of nature transferred to his unit, but they hadn't yielded any breakthroughs yet.

Yet the minute Langston walked into the room and saw the mystery patient, he understood why Phil had called him out of the clinic. George Carillo lay propped up in bed staring straight ahead. His mouth was slightly open and drooled continuously. His arms were bent at his side with the elbows outward, as if frozen midway through a motion. He made no sound.

Langston also immediately understood why the psychia-

trists had not been sure what to make of George. The zombie-like appearance did look like catatonia. Langston took George's arms and very gently pulled them toward him. They were very stiff. Langston held the arms straight out in front of George's body and let them go. They just stayed there fixed in space where he had left them. After thirty seconds they began to fall slowly and over the next three or four minutes returned to George's side. Next Langston lifted one of George's arms above his head and let go. Again it stayed there for thirty seconds or so before slowly falling under gravity. Langston had seen this before. It was called "waxy flexibility" and it was a legendary sign of catatonia. He saw why some of the psychiatrists had opted for this diagnosis.

He turned his attention to George's face. It was totally expressionless—more like a mask than a face. The eyes stared eerily ahead without blinking. Langston gently tapped the forehead between the eyebrows. This will cause anyone to blink, even someone in a catatonic state—it is an involuntary reaction to the stimulus of tapping. However, with repeated tapping most people stop blinking. But George didn't. The failure to stop blinking is known as Myerson's sign and is typically seen with damage to an area of the brain known as the basal ganglia.

On several occasions, George's eyes slammed shut and would not reopen. "Try and open your eyes, please, Mr. Carillo," Langston asked whenever this happened. He had no idea whether George could understand him or not, but thought it better to presume competence on the part of his patient. For a while nothing happened. Then, after some thirty seconds, George slowly opened his eyes. This condition is called "eyelid apraxia," and it is very rare—so rare, in fact, that it is not definitively associated with any known neurological disease. Langston had no idea what it meant in George's case.

While Langston had been examining George, the room had filled up with physicians—mostly psychiatrists, but also several neurology residents. George had created quite

a stir in the psychiatry department, and there was an ongoing debate as to whether his condition was psychological or physiological in origin. The psychiatrists had become convinced that George's condition was organic or neurologic in nature, whereas the neurology house staff had concluded with equal vehemence that his condition was entirely psychiatric. It was now up to Langston to make the final pronouncement.

The waxy flexibility indicated catatonia, a psychiatric condition. But the Myerson's sign and the eyelid apraxia pointed toward a neurological cause. Langston continued his examination of George's face. The upper part of the face was unusually oily, a condition known as seborrhea. Seborrhea, like Myerson's sign, is seen with certain diseases of the basal ganglia.

Langston gently took George's arm, holding the wrist in one hand and supporting the elbow in the other. Slowly he tried to bend the arm. It was very stiff. Langston had to apply considerable pressure to make the joint move, and when it did it moved in fits and starts, like a ratchet wheel. Langston relaxed. He was now certain that George had a neurological disorder. He had seen several cases of catatonic schizophrenia on the neurobehavior unit and they didn't show any "cogwheel rigidity."

It appeared as if George had incurred damage to the basal ganglia area of his brain. But how? The blood and urine tests had ruled out tranquilizers as the cause, and there was no evidence of infection.

The most important element of any medical diagnosis is the history—the tale of the patient's illness, life, work, and previous illnesses. But with George they were stuck: not only could he not speak, but it was highly likely that his memory and reasoning abilities were also impaired, that his mind was as frozen as his body. They would have to proceed cautiously and hope for a break.

George was now officially admitted to the neurobehavior unit and put under close observation. Several times a day, nurses repositioned him in bed so that he wouldn't develop

bedsores. They washed him and fed him. Despite his external appearance, his internal organs appeared to function normally. If food and water was administered in small teaspoons into his mouth, he was able to swallow it. He also seemed to have control over his bladder and bowels.

For seven days George lay there without speaking or moving. Then one morning Phil Ballard noticed him moving his fingers ever so slightly. The movements were slow and looked as if they could be voluntary. On a long shot, Phil gently wrapped the fingers of George's right hand around a pencil and slipped a yellow notepad under it.

"Write your name," Phil said. Unexpectedly and very slowly, the pencil started to move. After a minute it was clear that their patient was trying to write something, perhaps the first letters of a name: *"G . . . e . . . o . . .* Five minutes later he had completed a name, *George Carillo.* After half an hour, there were three more sentences on the page of paper: *I'm not sure what is happening to me. I only know I can't function normally. I can't move right. I know what I want to do. It just won't come out right.*

Langston and Ballard were astonished. Trapped inside this frozen body was a normal mind. Langston thought of the awful process George had been through: being prodded, pricked and scraped, having ammonia stuck under his nose, feeling pain but being unable to scream, hearing questions but being unable to respond. Never had there been a better illustration of the warning all doctors are taught from the beginning of medical school: No matter how bad a patient's mental status seems, whether it be deep coma or utter confusion, never carry on clinical discussions at the bedside on the assumption that the patient can't hear you. Langston could only wonder what discussions George must have listened to during those fateful emergency room trips. But at least now they had a window to his mind, a way of getting a case history, and so by question and slow answer they painstakingly gathered evidence.

George told them that about two weeks earlier he had started feeling stiff and that his girlfriend, Juanita Lopez,

was having the same problem. Probing for clues, Langston asked him to write down any medicines he was on. In reply, he didn't write down the name of any prescribed medicine. Rather, he wrote down the word "heroin." Langston looked at Ballard and smiled. "No, George, I don't mean street drugs, I mean medications that doctors prescribe." George showed no reaction.

A little research revealed that George's girlfriend, Juanita Lopez, 30 years old, had been living with George before he was incarcerated and was now staying with her sister. But when Langston called Juanita's family, they seemed reluctant to talk to him. They did, however, confirm that Juanita was sick.

After days of cajoling and pleading, Langston managed to convince Juanita's family to bring her in to Valley Medical Center to be examined. Langston was shocked at what he saw. She sat completely motionless, like a wax doll. Her face was acned and, like George's, expressionless. Her eyes hardly blinked. She drooled continuously. For two weeks now her family had been taking care of her in this condition. In the morning they would get her up, bathe, dress, and feed her, then put her in a chair for the duration of the day. In the evenings this process was repeated in reverse before they put her back to bed. In short, she required the type of total body care that is usually found only in hospitals. The family was desperate for help.

They confirmed that shortly after Juanita returned from George's place on July 1, she had frozen up completely. They had taken her to a local hospital but, thinking she was high on PCP, the hospital had turned her away. Her family, worried that the police might then arrest her, had decided to keep the matter to themselves. Langston could sense the relief they felt now that they had brought her in. He could also sense their expectations that he would make her better. But Langston knew he could do little until they discovered the cause of the strange symptoms.

Juanita's clinical history matched George's. Whatever had gone wrong, the symptoms for both of them began on

July 1. Like detectives at the scene of a crime, Langston and Ballard searched for clues. The obvious place to start looking was George's apartment. The cause of the mysterious paralysis might be something in their common environment—something that they both ate; a furnace leak of carbon monoxide or some other chemical. At this stage, Langston didn't want to rule out anything.

There was a very well-known neurological disease which seemed to fit their physical signs and symptoms in every detail: Parkinson's disease. Between 500,000 and 1 million Americans have this disease, including one of every hundred people over the age of 60. Parkinson's sufferers freeze up and have difficulty moving. Their limbs exhibit cogwheel rigidity and their speech becomes soft and slurred. Advanced cases have expressionless "reptilian" faces (as they are called) and oiliness of the skin. But Langston had two problems with this diagnosis: Parkinson's disease doesn't strike people overnight, and it hardly ever affects the young. It usually occurs after the age of 50, and comes on very gradually, so gradually that most patients have symptoms for one to two years before they go to a doctor. But the Valley Medical Center cases were young—Juanita was barely 30—and their symptoms had developed in days rather than years. Langston no longer thought about his career rut. He had a first-class medical mystery on his hands.

The weekend after Juanita came in, Phil Ballard decided to take off for a weekend break. He drove thirty miles south on Highway 17 to Santa Cruz, where he had been invited to a party. The host was Dr. Jim Tetrud, a Watsonville neurologist in private practice. As the evening wore on, the two neurologists began talking about the subject that drove their professional lives, the study of the human brain. Phil was on the verge of describing the mysterious cases he had seen at Valley Medical Center, but before he could, Jim Tetrud told Phil an equally astonishing tale of two patients he had seen that week in the Watsonville Community Hospital.

Two brothers, David and Bill Silvey, had been found lying

frozen in their apartment, unable to move or talk. On discovering them, their mother had called an ambulance which took them to the Watsonville Community Hospital. The admitting physician, seeing no obvious medical reason why two apparently healthy young men in their twenties should be frozen, listed a diagnosis of catatonic schizophrenia.

The family's private physician, Dr. Sean Murphy, was bothered by the diagnosis. Two brothers developing a rare condition like catatonia at the same time? He decided to ask Dr. Tetrud to take a look at David and Bill. Both brothers had a long history of drug abuse and apparently had been taking drugs continuously for more than a week before they froze up, so initially Tetrud suspected that the symptoms were caused by intoxication. Tetrud gave them Benadryl and later Cogentin to unfreeze them, but the medicines were totally ineffective.

"It's incredible," Jim Tetrud said to Ballard, "but it's almost as if these young men have advanced Parkinson's disease."

Phil Ballard couldn't believe what he was hearing. "Did you say they were drug addicts? What was their favorite drug of abuse?"

"Oh, heroin, I think," said Tetrud.

As Jim Tetrud sketched out the symptoms of David and Bill Silvey, it was as if he were describing George and Juanita. Yet these were two different people from a completely different location. Ballard got on the phone to Langston and repeated what Tetrud had said. When he had finished, Langston asked him, "Do the Silveys have any relationship with George and Juanita?"

"No, Bill, as far as we know they have never met."

Langston paused. "We'll have to check on Monday that there's no connection, but assuming that's true, assuming they didn't know each other and had never visited each other's apartment, then there's only one connection between the four cases, isn't there?"

"Yes," said Phil, "they are all heroin addicts."

After hearing about the Silvey brothers, Langston found

it impossible to relax. Four young people's lives had been destroyed in a tragedy that seemed to hinge on drugs. His mind filled with a far-fetched theory. Perhaps something was not right about this particular batch of heroin, and when injected into the bloodstream it had passed into the brain, damaging it so as to produce the symptoms of advanced Parkinson's disease. As far as Langston knew, no such substance had ever been encountered before. There were drugs that caused transient parkinsonism—neuroleptics like chlorpromazine and haloperidol—but George's emergency room doctors had tested his blood and urine for these and found nothing.

As Langston wrestled with the medical mystery, a chilling thought crossed his mind: If the heroin was to blame, northern California might have a major public-health disaster on its hands. They had seen cases in San Jose and cases fifty miles away in Watsonville. What if this batch of heroin was being sold all over northern California? Two things needed to be done immediately. First, Langston needed samples of the heroin that the four addicts had used to send for chemical analysis. Second, he had a duty to warn the public that there was a poison on the streets, and that anyone using heroin was in grave danger. Otherwise there might be an epidemic of frozen addicts.

Langston had never had any dealings with the press, and consequently had no idea how to get a message out to the public. The medical director of Valley Medical Center referred him to the hospital's public relations firm, PRx, which in turn put out a brief release to local newspaper and television reporters. PRx, which generally had a hard time generating any interest in Valley Medical Center among the local media, was astonished. There were so many inquiries for further details that PRx decided to hold a press conference the next day and get Langston to speak.

By ten o'clock the next morning, interest had spread to the television stations from the San Francisco Bay area. The administrative conference room of the hospital, which had been hastily converted to a press room, was packed

with cameras and reporters. As he had no idea how to talk to the press, Langston spoke as if they were medical students and he was conducting morning rounds. He made a brief statement, answered a few questions, and left, glad he had gotten the message out.

Sound bites from the press conference made the nightly news on four of the northern California stations, which meant that, at that time of year, approximately twenty million people heard about the story. Even though drug addicts weren't known for their patronage of the nightly news, it was likely that a sizable fraction either saw or were told about the broadcast.

In San Jose, a physical therapist named Jan Bartell happened to be watching. As she looked at the videos of George Carillo, she became increasingly agitated. She wrote down Langston's name and resolved to call him the next morning.

For several weeks she had been making home visits to a young woman named Connie Sainz with a very unusual "mental" condition. About six weeks earlier Connie had frozen up. Over a couple of days Connie had become a total invalid and now she couldn't walk, talk, or do anything for herself. Connie had spent two weeks on a Stanford Medical Center psychiatric ward undergoing tests, but had been discharged when doctors decided that her "paralysis" was hysterical in nature. In such patients the paralysis usually went away without intervention, and home-based care seemed the appropriate solution.

But Connie was not doing well, and after seeing the television pictures of George Carillo, Jan began to wonder whether Stanford's doctors might have made a terrible mistake. The patient on TV looked uncannily like Connie. He had the same reptilian stare, the same flat facial expression, the same paralysis. The next day she called Langston at Valley Medical Center and told him everything. Langston was very excited and asked Jan to bring Connie and her family in immediately. The press conference had already brought totally unexpected results.

Even though Langston had seen four cases of this drug-

induced state, he was still shocked when he saw Connie. Just 21 years old, this young woman was a tragic sight. She had bedsores from lying in the same position for six weeks, and a crushed nerve in one of her legs. She couldn't do anything for herself. She found eating difficult and had to be hand fed. She couldn't move her arm to pick up a cup of water. She couldn't stand up by herself. When Langston put his head close to her chest he could just hear a whimper, but otherwise she could not talk. Sometimes Connie's eyes would close in reaction to a noise or a doctor's hand that was examining her. If she was left to herself, it took her forty seconds to reopen them. Her symptoms closely matched those of George, Juanita, and David and Bill.

Yet Connie's story, as told to him by her family, touched Langston in a way that the others' had not. She came from a poor but educated Hispanic family in Greenfield, a small town in California's central valley surrounded by miles of hot, dusty fields. Until 1982, Connie had had a fairly normal life. She had finished high school and gone to work. Though not married, she had one son. And she had managed to avoid drugs. But then she had met Toby.

Toby Govea, soft-spoken with gentle eyes and a sweet smile, was a dealer who had repeatedly been in trouble with the law. Drugs were an everyday activity in Toby's family—he routinely shot up with his father, brothers, and sisters. Whereas a middle-class family might discuss the day's events while the parents sip martinis, Toby's family would chat as they shared heroin, PCP, or cocaine. Toby not only used heroin, he sold it on a large scale, and to support his habit he robbed stores.

Toby later claimed that he had urged Connie not to use the drugs he was selling, but if he did she ignored his advice. One day in June 1982, perhaps saddened because Toby had been taken off to the Salinas jail, she started fixing with some new heroin that Toby had been selling. She used it every day for a week. Then she heard from a friend that Toby had fallen ill with a strange freezing disease. After a few days, she became listless and apathetic, moving less and

less. Then her body became twisted and contorted, her limbs moving into strange positions in fits and starts, at times jerking violently. After the movements stopped, Connie began to stiffen up and soon couldn't move or talk. Her face lost all expression and became like a mask. By the tenth day she looked more like a marble sculpture than a young woman. Connie's sister Stella had been so worried that she had taken Connie to Stanford Medical Center. But whatever was wrong with her, Stanford hadn't discovered it.

As Langston subsequently discovered, Toby was transferred to Stanford as well. Like Connie, he was frozen, but also had a pronounced parkinsonian tremor. Stanford's neurologists didn't know what to make of him, but in the course of his examination it was discovered that he had been briefly treated in prison with phenothiazene, a class of neuroleptics that can induce temporary parkinsonism. Since they had no other ideas about what was wrong with him, they concluded that neuroleptics were the cause of his bizarre condition.

As a Stanford faculty member, Langston was deeply chagrinned when he heard this story. One of the neurologists treating Toby was a former student of his. But that wasn't the end of it. The neurologists in this case went so far as to make a videotape of Toby, which was then placed in the Fleischman Library (an innovative video teaching library for medical students at Stanford) as a classic example of phenothiazene toxicity. To this day, if a medical student goes to this audiovisual medical teaching library to learn about phenothiazene-induced parkinsonism, he or she will see Toby. It is somewhat painful to read the message at the end of the tape: "This is a case of phenothiazene toxicity. Since the medication has been discontinued, he will eventually return to normal." But Toby did not have phenothiazene toxicity, nor would he ever be normal again.

As July turned to August, Langston knew of six cases: George, Juanita, David, Bill, Connie, and Toby. Three were now being treated at VMC, two in Watsonville, and one at Stanford, but he had assumed de facto responsibility for all

of them. The mystery of their condition was consuming an enormous amount of his time and energy. But it was to solve this kind of fascinating mystery that he had gone into neurology in the first place.

Because the key to the mystery centered on the heroin, Langston and his colleagues now focused on obtaining samples for analysis. By coincidence, the day after the Silveys were taken to the hospital, the Watsonville police had raided their apartment. They didn't find the Silveys, but they did find several bindles of heroin. When Langston contacted them, they were very cooperative and sent a squad car up to San Jose with sirens blazing to deliver the sample to Valley Medical Center. A search of George's apartment had turned up a gram of heroin in his refrigerator. For completeness, Langston would need a sample of the batch that Connie and Toby had taken.

Langston sent samples of the heroin to various toxicology labs in northern California for analysis, and tried to get on with his life while he waited for the results. Every day he called the labs to get a progress report. They told him that whatever it was, it wasn't heroin; it was a synthetic concoction bearing no relation to the opium poppy. It didn't make a lot of sense to Langston that addicts would call a synthetic substance heroin if it wasn't heroin. So what exactly was this synthetic substance? The labs were not sure.

Ian Irwin of Stanford's Drug Assay Laboratory successfully isolated a pure extract from the synthetic heroin and fed it into a gas chromatograph/mass spectrometer, an instrument that uses a stream of electrons to shatter molecules into little pieces. The way the molecules break apart and the pattern formed by the fragments form a molecular fingerprint. Chemical compounds have fingerprints every bit as unique as the ones people have. To a chemist, a chemical like codeine, cocaine, or salt is completely recognizable by its chemical fingerprint. The fingerprints of some forty thousand known chemical compounds were stored in a database in Washington, D.C. Irwin's strategy was to first

fingerprint the new heroin and then screen it against the forty thousand compounds to look for a match. But after considerable time and effort, no match could be found. He could not identify what was in the synthetic heroin.

Meanwhile, the condition of the six addicts was deteriorating. They were invalids, unable to wash, dress, or feed themselves. George and Juanita had become so ill that Langston began to fear for their lives. His biggest fear was that one of them might develop a pulmonary embolism—a blood clot that forms in the leg and passes into the lungs, where it blocks an artery and causes sudden death. Any patient who is bedridden and completely inactive is at high risk of this. Langston was also worried about infection. Some of the patients, notably Connie, had developed serious bedsores. If these open sores were not kept clean they might become infected; if the patient became septic (blood-borne infection) it could easily be fatal.

To make matters even worse, these patients had all lost a lot of weight and were very debilitated and vulnerable to infection. If one of them developed pneumonia, they might not be strong enough to fight it. Remarkable though it was, these six young people appeared to be dying of Parkinson's disease.

Parkinson's is one of the two great neurodegenerative diseases of aging (the other, Alzheimer's, entails progressive loss of memory and other mental faculties). Past victims of Parkinson's are thought to include Mao Ze-dong, Francisco Franco, and Adolf Hitler. It has been known for more than fifty years that the symptoms of Parkinson's result primarily from the death of nerve cells in a small area at the base of the brain called the substantia nigra, which means "black substance." These cells produce a brain chemical called dopamine—a so-called neurotransmitter, which nerve cells use to communicate with each other—that is essential for normal control of movement. Without dopamine, the *thought* of lifting an arm can't be transferred into the *act* of lifting an arm. In Parkinson's disease, nerve

cells (or neurons) in the substantia nigra die. As the number of neurons diminishes, so does the production of dopamine, and the motor system begins to shut down.

As parkinsonian patients become more and more disabled, they become highly susceptible to what physicians call "intercurrent illnesses," such as pneumonia and sepsis. After a period of being bedridden, the advanced Parkinson's disease patient can succumb to an infection or a pulmonary embolism. Langston now feared the same fate for his patients.

In the late 1960s neurologists began treating their Parkinson's patients with a new drug called L-dopa. The cells in the brain use this chemical to make dopamine. By being given the chemical precursor L-dopa, the remaining cells in the brain can be induced to make more dopamine, partially reversing the deficiency and giving patients back voluntary control of their muscles. As there was nothing to lose, on July 28, Langston administered the drug to George and Juanita and waited.

The effect was miraculous. Within hours, George and Juanita unfroze and came back to life. Within days they could walk normally, move normally, speak normally, and feed and wash themselves. As a medical student Langston had read Oliver Sacks's moving book *Awakenings,* in which L-dopa awakens a group of patients afflicted with a rare form of parkinsonism known as post-encephalitic parkinsonism. What Langston was seeing was scarcely less remarkable. The frozen addicts could now talk about the private hell they had all endured for weeks—the psychobabble, the mistaken diagnoses, the frustration, the fear, the pain, and the sadness. The four other patients, including Connie, proved equally responsive to L-dopa.

George told of how he had endured being prodded and scraped. Connie wept as she recounted the tale of her misdiagnosis at Stanford and how she had to listen to all the earnest theorizing about her mind, and how, despite the pain from the crushed nerve in her leg, she had been unable to cry out.

Here were six patients whose symptoms modeled, down to the last detail, one of the major unsolved degenerative diseases of the aging brain. What did it mean? In the weeks ahead it would become clear that what had started as a drug tragedy was to open a new chapter of medical research which would offer hope to Parkinson's disease sufferers throughout the world.