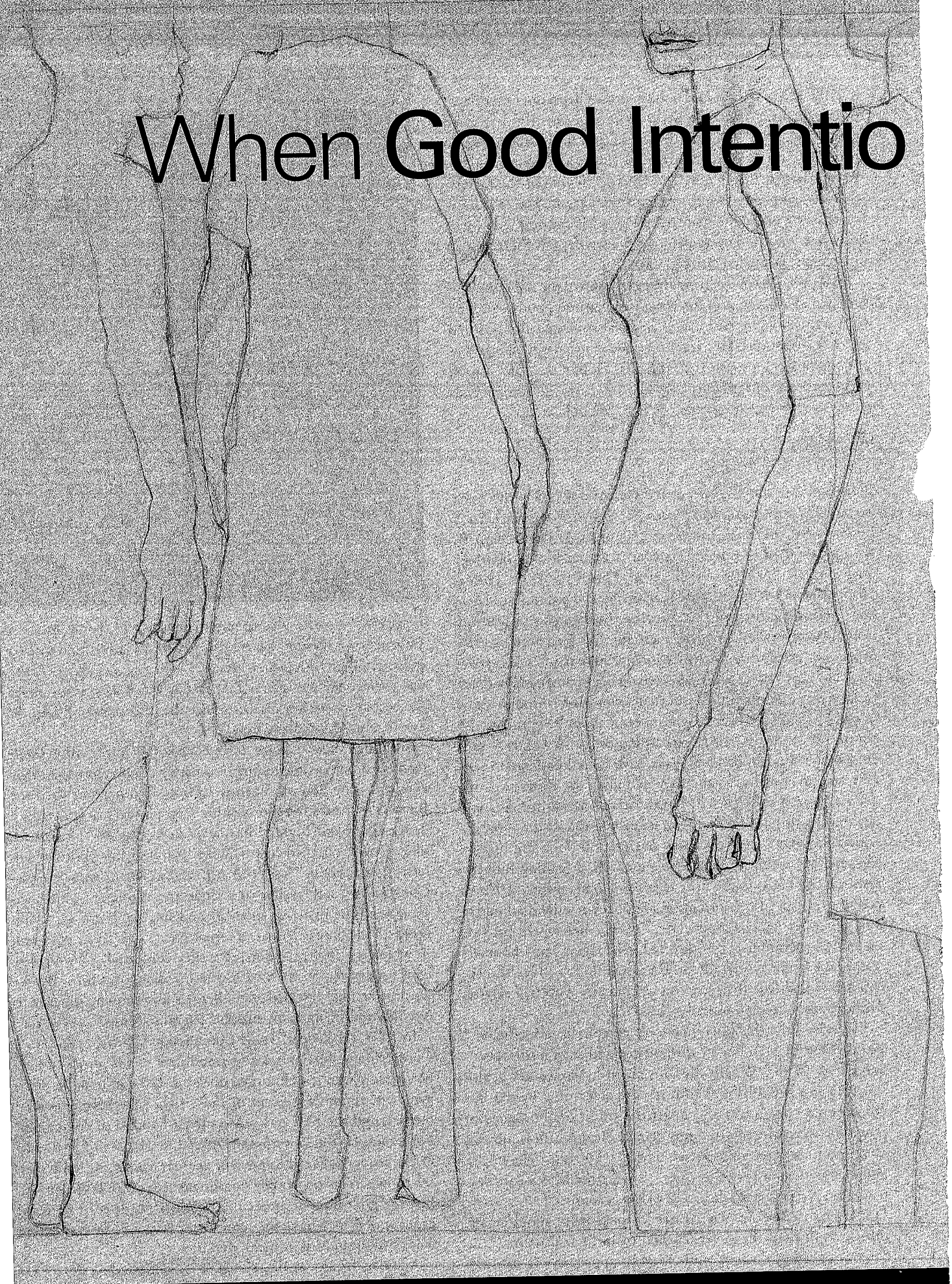
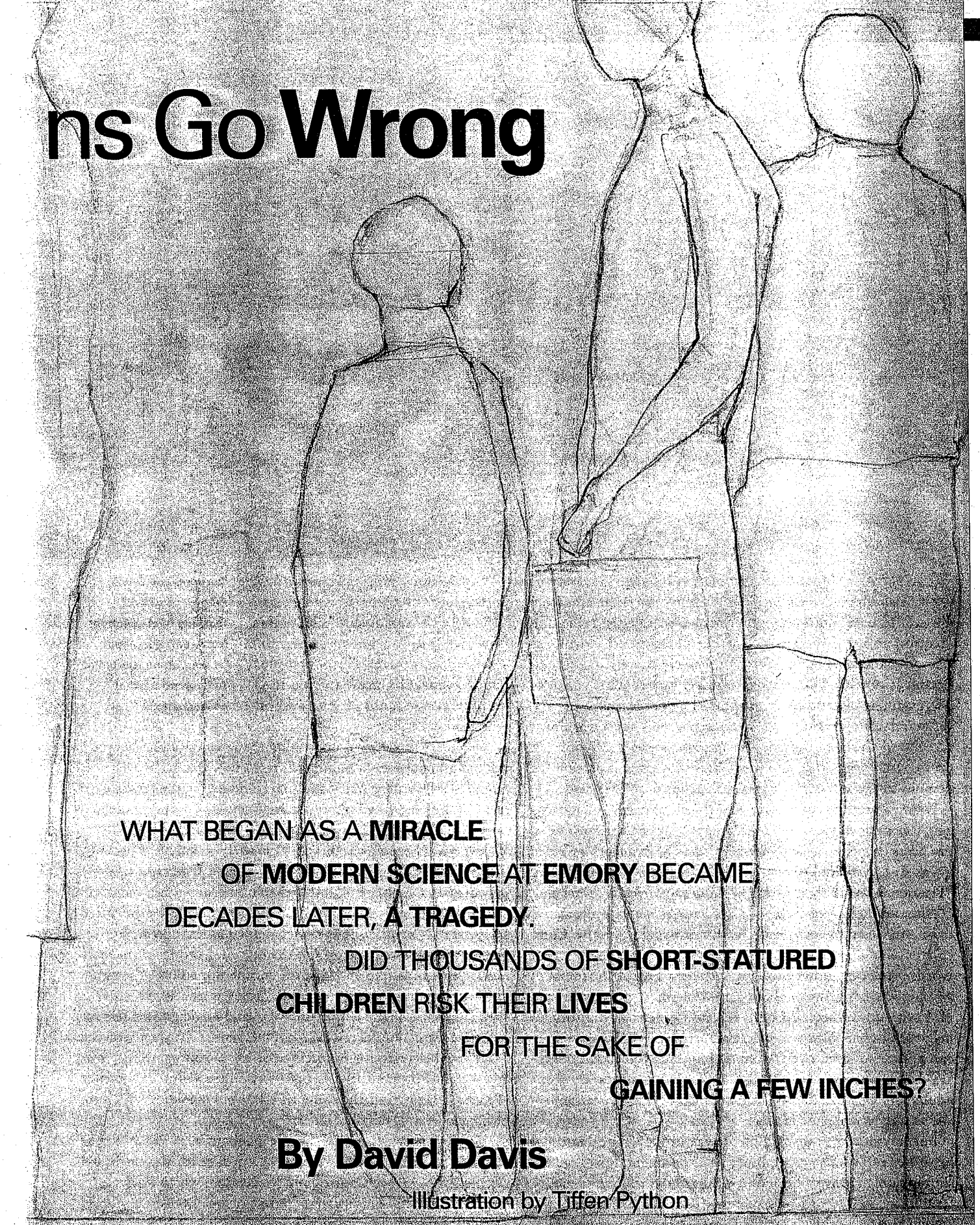
When Good Intentio



ns Go Wrong



WHAT BEGAN AS A **MIRACLE**
OF **MODERN SCIENCE** AT **EMORY** BECAME,
DECADES LATER, **A TRAGEDY.**
DID THOUSANDS OF **SHORT-STATURED**
CHILDREN RISK THEIR **LIVES**
FOR THE SAKE OF
GAINING A FEW INCHES?

By David Davis

Illustration by Tiffen Python

Author David Davis (above, as a child) received hGH injections for three years. When he was 22, he learned of the potential lethal consequences.

On a blustery November day, Emory University hums with brisk vitality. Red-cheeked students hurry to and from class, alternately discussing the just-concluded presidential election and the upcoming Ben Harper concert, while the school's handsome buildings exude a steely power. The combination is potent: The school, at once, bursts with youthful energy and is steadied by the anchor of higher learning.

I stand at the entrance to the library and let it all wash over me. I need all the help I can get: I've journeyed 2,500 miles to do research here, to see if knowledge gleaned will placate the demons inside me. My very future depends on what I find.

Let me start at the beginning. Shortly after I was born 38 years ago, it became obvious that I wasn't growing at the same rate as my peers. I was so little that when I was 8, strangers assumed I was 4. I answered to, variously, "Shrimp," "Shorty" and "Pipsqueak." And those were the names my *friends* called me.

After administering a slew of tests, my pediatric endocrinologist confirmed the obvious. I wasn't growing normally. Clinically, I was diagnosed as a hypopituitary dwarf—in other words, my body didn't produce sufficient growth hormone. I would probably grow to about four-foot-something, marooned in a stunted netherland between adolescent and adult. In height-conscious America, where actors stand on boxes so they can appear to loom over romantic interests, the consequences are dramatic: Study after study shows that significantly short adults fare worse than their peers in income and education levels, as well as marriage rates.

But, my doctor informed me, I was in luck. The National Institutes of Health was running an experimental program to supply human growth hormone, primarily produced at Emory University School of Medicine, to hypopituitary dwarfs. By taking thrice-weekly injections of this human growth hormone, I could be made to grow.

I took those shots, injected into the muscle of my upper arm, from 1974–1977. And, lo and behold, they worked. I didn't become Dikembe Mutombo, or even Chipper Jones, but I eventually grew to five-foot-four. Call me Spud Webb, without the dunking ability.

The scars of growing up smaller than everyone else lingered, as did all of the jeers I endured, but I was able to live a "normal" life. I went on dates and played on my high school soccer team. At college, I edited the school newspaper and graduated Phi Beta Kappa. The future was, finally, bright.

But what began as a miracle of modern science has become, decades later, a tragedy of modern science. The growth elixir produced at Emory has resulted in numerous deaths, both in the United States and abroad, due to a rare malady called Creutzfeldt-Jakob disease. Better known as the human equivalent of mad cow disease, CJD is one of a group of diseases called transmissible spongiform encephalopathies—meaning, literally, that it eats sponge-like holes in the brain. CJD is always fatal, usually within one year, and no diagnostic test for it exists. And, despite the fact that Dr. Stanley Prusiner won the 1997 Nobel Prize for Medicine for his work regarding "prions" (pronounced PREE-ons)—the infectious agent that Prusiner theorizes is the cause of CJD—no one knows for sure what causes this horrible illness.

What's known is this: CJD can incubate in the body for as long as 30 years before striking. According to Atlanta-based Centers for Disease Control and Prevention, which tracks CJD in the U.S., this means that many former hGH recipients, including myself, remain at risk.

All of which brings me to Emory on this beautiful fall day.

FIFTEEN YEARS AFTER THE OUTBREAK OF CJD,
I STILL DON'T KNOW HOW I'M SUPPOSED TO FEEL.
SHOULD I CONSIDER MYSELF UNLUCKY
TO HAVE PARTICIPATED IN THIS EXPERIMENT,
OR AM I LUCKY TO BE ALIVE AND
A FEW INCHES TALLER?
SHOULD I LAUGH AT THE IRONY OF TAKING
HUMAN GROWTH HORMONE INJECTIONS TO
"CURE" ME, ONLY TO DISCOVER THAT THEY MIGHT KILL ME?
HOW DO I MOVE ON?

As the leading producer of human growth hormone from 1963–1977, Emory was ground zero for this medical experiment gone awry. And while I'm no expert—I'm a sportswriter, ferchristsakes—I figure that maybe, just maybe, by coming here, I'll find answers to the questions that have plagued me for years. What went wrong? Could this have been prevented? Did thousands of children risk their lives for the sake of gaining a few inches?

What follows is a cautionary tale, one that sullies the most powerful health agency in the United States and the medical community alike. And now that events have ended up in the hands of lawyers, our nation's depository for shattered dreams, it's likely that few of the victims will find justice or peace.

THE STORY OF the hGH experiments begins in 1950, with the arrival of Dr. Alfred Wilhelmi at Emory University School of Medicine. At the time, a golden age of scientific and medical research was dawning. The Nuclear Age promised—and delivered—so much: widespread use of the polio vaccine, the understanding of the structure of DNA, the first successful kidney transplant, birth control pills. Funded in part by a U.S. government flush with post-war greenbacks, these breakthroughs changed the way the world lived.

As Emory's newly appointed chair of the School of Medicine's biochemistry department, Dr. Wilhelmi was an acknowledged medical luminary. Born in Lakewood, Ohio, he graduated from Western Reserve University, *summa cum laude*, in 1933. That same year, he put aside his plans for medical school to attend Oxford University in England on a Rhodes Scholarship, where he earned his Ph.D. in biochemistry. Upon returning to the States, he joined the faculty at Yale University's department of physiological chemistry.

Dr. Wilhelmi's specialty was endocrinology, or the study of the mechanisms that regulate the body's hormonal system. The pituitary gland, located at the base of the brain, is perhaps the most well-known gland within the endocrine system. The small, oval-sized mass of tissue controls such functions as sexual development and reproduction, as well as the body's metabolism. The pituitary gland also secretes growth hormone—the substance that, literally, makes us grow.

Because each pituitary gland generates limited amounts of growth hormone, scientists were unable to collect enough hormone for research purposes. It was this shortage that Dr. Wilhelmi's work addressed. Through the extraction, isolation and purification of bovine pituitaries, Dr. Wilhelmi pioneered a practical way to produce sufficient growth hormone for researchers to use.

"Scientists needed purified hormone in large quantities to conduct experiments," says Dr. Jack Kostyo, chair of Emory School of Medicine's department of physiology from 1968–1979. "[Dr. Wilhelmi] sacrificed his individual career by concentrating on the production of hormones for others."

With his penchant for tweeds and his Oxfordian mannerisms, Dr. Wilhelmi brought a touch of old-school decorum to the sleepy campus. He and his wife, Dr. Jane Russell, settled in Decatur, with Siamese cats as their companions. The couple bore no children, and they devoted themselves to endocrinology and their garden.

"He was very elegant, very genteel," says Dr. Albert Parlow, who worked in Emory's physiology department from 1962–1965. "He had the capacity to articulate that was second to none. He made Demosthenes sound like a tyro orator."

As Dr. Wilhelmi continued to mine the pituitary gland—work funded in part by grants from the National Institutes of Health—Tufts University professor Dr. Maury Raben first reported substantive results injecting short-statured children with growth hormone extracted from the pituitaries of human cadavers. Dr. Raben's breakthrough, announced in a letter to the editor in the *Journal of Clinical Endocrinology and Metabolism* in 1958, was greeted with euphoria by worried parents. This, in turn, produced a new problem. There simply wasn't enough hGH to treat every patient, and the potential for a black market was ripe.

To alleviate the shortage, Dr. Wilhelmi and others established the National Pituitary Agency (NPA) as a collaborative venture with the National Institutes of Health, which funded the program, and the College of American Pathologists, which supplied the pituitaries after autopsy. After collecting the pituitaries, the NPA shipped them to Dr. Wilhelmi, Dr. Raben and Cornell University's Dr. Brij Saxena.

The three processed the pituitaries to create human growth hormone, and sent this back to the NPA. The agency then dispatched the hormone to pediatric endocrinologists around the country. This was distributed, free of charge, to needy children like myself.

[Continued on Page 158]

When Good Intentions Go Wrong

Continued from Page 71

From 1963 until 1977, processing tens of thousands of pituitary glands annually, Dr. Wilhelmi produced the bulk of the hGH that was distributed to approximately 3,500 American children. (Because of imperfect record keeping, it is impossible to determine exactly how many children received Dr. Wilhelmi's hGH.) According to one published estimate, the children who received hGH during the entire period of the program grew, collectively, more than one mile.

Dr. Wilhelmi's reputation grew even as he was showered with honors. He chaired the endocrine study section at the National Institutes of Health. In 1960, he shared the Endocrine Society's Upjohn Scholar award with his wife. From 1968–1969, he served as president of the Endocrine Society, and he was later awarded that group's Distinguished Leadership award. After Dr. Wilhelmi retired as chair of Emory's biochemistry department in 1977, he received the school's Thomas Jefferson Award for his "gifted teaching" and "brilliant research in biochemistry and physiology."

If the story ended here, Dr. Wilhelmi would have been remembered as a medical hero. However, in May 1984, a young man named Joe Rodriguez complained to his mother about experiencing occasional dizziness. By June, he staggered when he walked and had difficulty speaking. In November, six months after displaying symptoms, Rodriguez was dead. He was 20 years old.

In an autopsy performed at the University of California, San Francisco, pathologists discovered that Rodriguez's brain displayed classic signs of Creutzfeldt-Jakob Disease. CJD is exceedingly rare: According to the CDC, approximately one person per million in the U.S. contracts CJD, resulting in one death in every 10,000 persons. But what *really* surprised the pathologists was Rodriguez's youthfulness: CJD afflicts older people almost exclusively. How could such a young man die from this?

Rodriguez's former pediatric endocrinologist, Dr. Raymond L. Hintz, provided a clue when he recalled that Rodriguez received hGH injections, starting when he was 3, for 14 years. Perhaps, theorized Dr. Hintz, hGH concocted from the diseased brain tissue of cadavers was the problem.

In February 1985, Dr. Hintz wrote the NIH, NPA (now known as the National Hormone and Pituitary Program, or NHPP) and the Food and Drug Administration warning that there might be a deadly link between hGH and CJD. In an article he later wrote for the *Journal of Clinical Endocrinology and Metabolism*, Dr. Hintz recalled that his initial letter was met with disdain because no major problems had ever been reported in the 22-year-old program. "Many of my other pediatric endocrinologists clearly felt that I was an alarmist, and they did not hesitate to tell me so," he wrote.

Within weeks of Dr. Hintz's warning, however, as pediatric endocrinologists scrambled to locate their now-adult patients, it was discovered that two other hGH recipients died from CJD in the U.S.—one in Buffalo and another in Dallas—even as reports of one case in England emerged. In April, the U.S. program was halted. Almost immediately, the NIH sent letters to the parents of hGH recipients, warning them about the problem.

THE MANY DOCTORS I interviewed believe with a heartfelt passion that their work saved the lives of thousands of short-statured children. They feel that their participation in the program ranks as the finest achievement of their careers. But close examination of the program—which I have done both as a recipient and a journalist—leads me to a different conclusion: that despite their best intentions, the growth hormone experiments were so flawed as to be a disaster waiting to happen.

The most fundamental error involved the formation of the National Pituitary Agency. Because the NPA was established and run by experts in the field—including Dr. Wilhelmi—apparently no one believed it was necessary for outsiders to periodically review the program for most of its life. And what began as a clinical trial developed, pro forma, into an established therapeutic program, with funding (and blessings) provided by the National Institutes of Health.

Said one San Francisco–based endocrinologist: "There may have been a certain amount of hubris in this. Most physicians thought hGH was perfectly safe." >>>

According to sources that worked alongside him, Dr. Wilhelmi's vaunted reputation—and the fact that he supplied physicians, gratis, with much-needed hGH—shielded him from criticism. These sources state that Dr. Wilhelmi's method for processing human pituitaries produced sub-standard growth hormone because he routinely skipped a crucial step in the purification process called gel filtration, or "size-exclusion chromatography," that others in the field employed as early as the mid-1960s.

The filtration process of size-exclusion chromatography separates large molecules of protein from the growth hormone, including chunks of viral protein. This generates a cleaner product, one that yields a higher percentage of growth hormone. By not incorporating this step, Dr. Wilhelmi sacrificed quality for quantity. His hGH was often as little as 50 percent pure and it provoked antibodies in a significant percentage of hGH recipients. As the NIH's Dr. Mortimer Lipsett noted in the *Los Angeles Times* in 1985, soon after the outbreak of CJD, "Before 1978 the material was no more than 35 percent hormone, the rest of it being contaminating protein."

"[Wilhelmi's] product had a reasonable degree of hormonal purity, but it wasn't chemically pure," says a former colleague who spoke on the condition of anonymity because of pending litigation. "[Dr. Wilhelmi] knew the product was crude, but he felt it was good enough."

Biochemistry professor Dr. Leo Reichert, who worked at Emory 1960–1979, disagrees with this characterization, stating that Dr. Wilhelmi didn't employ gel filtration so as to increase the amount of usable hGH. "As long as the 50-percent-pure material didn't cause any problem, it seemed like a good idea to use the less purified material so that twice as many kids could benefit from it."

Whatever his reasoning, the hGH that Dr. Wilhelmi produced was sub-standard. In 1977, Dr. Albert Parlow took over the U.S. production of hGH from Dr. Wilhelmi and included size-exclusion chromatography in the purification process. To date, says Dr. Parlow, no U.S. hGH recipient who took growth hormone exclusively after 1977 has contracted CJD. (It should be emphasized that, after the 1985 CJD outbreak, hypopituitary dwarfs began to receive

synthetic hGH, which doesn't carry the risk of CJD.)

Did Dr. Wilhelmi's hGH cause all of the U.S. CJD cases? We know that he supplied the majority of the hGH produced in the U.S. But an NIH spokesperson, Jane DeMouy, says that incomplete record-keeping by pediatric endocrinologists—as well as the routine disposal of records at the NIH—makes it impossible to determine which batch of hGH each recipient received. Thus, says DeMouy, no one can determine how many CJD cases were caused by hGH prepared by Dr. Wilhelmi.

This much is known. According to the *New England Journal of Medicine*, the initial source of Joe Rodriguez's hGH was identified as "Wilhelmi preparation." And, according to a paper published in *Pediatrics*, NIH investigators who examined Dr. Wilhelmi's own notes in 1988 determined that one batch of glands produced in 1966 had in fact found its way into at least one lot received by every U.S. patient with Creutzfeldt-Jakob disease.

Further, *Atlanta* Magazine has learned that Emory recently settled a lawsuit brought by the families of two New Zealand hGH recipients who died from CJD. The terms of the settlements are confidential, but previous litigation (McKenzie et al. vs. Emory University) established that, beginning in 1964, New Zealand pediatric endocrinologists sent approximately 50,000 pituitary glands to Emory. Of the approximately 175 hGH recipients in New Zealand who received Dr. Wilhelmi's product, at least five patients have died from CJD.

FOR 22 YEARS, SHORT-STATURED CHILDREN RECEIVED EXPERIMENTAL PRODUCT. "THIS WAS A NOVEL UNDERTAKING WITH NO ESTABLISHED GUIDELINES," SAYS EMORY'S DR. LEO REICHERT. "THERE'S RISK INVOLVED WITH ANY EXPERIMENTAL DRUG INVOLVING HUMAN SUBJECTS."

"We can't understand why we have such a high proportion," said one New Zealand lawyer involved in the McKenzie case. "All we know is, we got bad batches of hGH from Emory."

DR. WILHELMI'S sub-par processing method wasn't the only flaw in the system. The NPA's guidelines for the collection of pituitaries were perfunctory: The agency didn't ban pituitaries from patients with chronic, degenerative neurological diseases. Thus, pathologists unwittingly harvested contaminated pituitaries.

In addition, despite a bank of growing knowledge about the transmissibility of CJD, during the 1960s, '70s and early '80s, prior to 1985, no one ever warned the 8,000 U.S. hGH recipients, or their parents, about the possible risk of transmission. This remains the most controversial aspect of this case: When should doctors have recognized the risk of CJD?

Pediatric endocrinologists argue that their field of expertise doesn't encompass CJD, a rare neurologic disease

affecting the elderly. True enough, but it's likely that scientists—including Dr. Wilhelmi, who worked with human tissue taken from the brain—would have known about the dangers of CJD as early as 1968.

That year, in *Science* magazine, NIH researchers demonstrated that CJD was transmissible among monkeys. The following year, transmissibility of CJD from humans to chimps was established. In 1974, writing in the *New England Journal of Medicine*, Dr. Philip Duffy warned about CJD after a case involving a corneal implant from a diseased cadaver.

Los Angeles Times reporter Emily Green has investigated the connection between CJD and hGH for two decades, beginning in Great Britain. She wrote that British investigators questioned the NIH about the risk of CJD as early as 1978. According to Green, visiting pathologist Colin Masters answered that query, writing that "It would be reasonable to expect that the pituitary gland and/or surrounding tissue taken from a case of CJD disease would be contaminated with the virus."

But Masters admits that he didn't warn others at the NIH about this, telling Green that "Presumably the people who were running the pituitary programs should have been aware of the warnings that were being sounded in the medical press."

Dr. Wilhelmi confirmed in correspondence that he had thought about such risks. But he believed his product was safe. "The question of virus in our hGH preparations has come up from time to time, especially since we use rather gentle methods in the isolation," he wrote one colleague in 1973. "We don't have advice or opinion from an array of experts. Our main evidence of low hazard is that, in years of use of substantially more than a kilogram of clinical grade hGH, no patient seems to have caught anything."

Perhaps the many flaws in the system—the lax rules for the extraction of pituitaries from contaminated cadavers; Dr. Wilhelmi's sub-par processing method that didn't neutralize the agent causing CJD; the failure to heed warnings about CJD published in the most prestigious medical journals; the carelessness of NIH not to inform hGH recipients of the possible danger of CJD—would have been rectified if human growth hormone were approved by the Food and Drug Administration and thus subject to FDA regulations.

That never happened. For 22 years, short-statured children received experimental product. "This was a novel undertaking with no established guidelines," says Emory's Dr. Reichert. "There's risk involved with any experimental drug involving human subjects."

To date, 22 U.S. hGH recipients have contracted CJD. Worldwide, the number of cases exceeds 125 (there have been many more cases in England and France, where scientists processed their own brand of hGH). It's also possible, CDC officials acknowledge, that other recipients contracted the disease, but died from different causes before symptoms developed.

In 1994, Dr. Wilhelmi died at the age of 84. Emory officials refused to allow this reporter to examine Dr. Wilhemi's private papers—described in the university's computer data bank as measuring "13 linear feet of paper"—that are stored in the library's special

refused to allow the agency to perform an autopsy on his wife.

I VIVIDLY REMEMBER the day my parents called me into the dining room to tell me about the CJD outbreak. Understandably, they were devastated by the news, though they tried to hide their fears by telling me that much was still unknown. My mother is a pediatrician, and she emphasized that the odds were extremely high that I would ever contract this.

At the time, I was 22 years old. I was just out of college and thought I knew everything. Let me correct that: I *knew* I knew everything. I was sure this wouldn't affect me.

I was wrong. Consciously or not, I've wrestled with the specter of CJD—that at any moment I might succumb to a gruesome disease—ever since. There were times when I ignored it and chose to party myself into oblivion. I've stared

"THERE'S A SENSE OF SADNESS NOW," LIZ SAYS. "I'VE ALWAYS DREAMED THE TYPICAL AMERICAN DREAM: JOB, CHILDREN, HUSBAND. IT HASN'T WORKED OUT THAT WAY."

deeply into it and scared myself into bouts of depression. I've been so angry that I could scarcely find my voice.

On several occasions, I've asked the NIH to send a letter—which I agreed to pay for—to the thousands of surviving U.S. hGH recipients. In the letter, I proposed forming a support group so that we could communicate and commiserate with each other.

The NIH has repeatedly refused this entreaty. DeMouy says, "We have to protect [patients'] confidentiality. . . . Not all hGH recipients have expressed a desire to talk about this."

I've managed to contact several hGH recipients on my own. When we talk on the phone, we connect on a deep level, as if we've survived cancer or another illness together. While I did research in Atlanta, I met with one former hGH recipient. Liz (she asked that her real name not be used) is perky and, of course, petite. She lives with her two dogs in a well-appointed home about 20 minutes from downtown, where she works as a legal secretary for a Fortune 500 firm.

Over dinner and then lunch the next day, we bond like long-lost siblings. "I never had a normal social life," she says, echoing my own memories. "Kids always teased me, saying the meanest things and pushing me when I walked down the hallways. It was awful."

She remembers hearing about human growth hormone and thinking it was her salvation. "It was like a dream," says Liz, who was treated at Emory by pediatric endocrinologist Dr. Daniel Rudman. "Everyone had built this up for years. I thought maybe I'd grow to five feet tall so I could shop in stores for clothes and not have to sew everything."

Liz heard about the specter of CJD from a hGH recipient she met while being treated at Emory. She remembers feeling shock, which soon turned to fear. "The NIH couldn't track me down, so when I heard about it sheer terror came over me," she says. "I just couldn't believe it. It opened up everything again—all the memories of growing up, all the injections, the whole experience."

She says living with the uncertainty is perhaps the worst part of this ordeal. "I don't sit and dwell on it," she says, "but it's always in the back of my head. You hope you don't carry it. I just wish they knew more about this because it's sad that we live in limbo.

"There's a sense of sadness now," she continues. "I always dreamed the typical American dream: job, children, husband. It hasn't worked out that way."

I agree with her. It hasn't worked out the way it was supposed to. And 15 years after the outbreak of CJD, I still don't know how I'm supposed to feel. Should I consider myself unlucky to have participated in this experiment or am I lucky to be alive and a few inches taller? Should I laugh at the irony of taking human growth hormone injections to "cure" me only to discover that they might kill me? How do I move on?

I know this. I'm tired. I'm tired of being angry. I'm tired of being a "victim." I'm tired of being tired. I just want to live a "normal" life.

I don't have much experience in that. I'm not sure I know how to begin. All I can do is make peace with my past and allow myself to have a future. And maybe, I'm big enough to do both.