



CHARLES FEIL—UNIPHOTO PICTURE AGENCY

What is "normal" height? Certainly the parents of these children have no reason to worry

Pediatricians fend off parents trying to send their offspring to new heights

■ To tummy tucks, breast augmentation and liposuction to whoosh away unwanted fat cells, add a new weapon in the pursuit of the ideal: Cosmetic endocrinology for short kids. Pediatricians who specialize in hormonal problems are being besieged by anxious parents to treat children slightly on the short side with a substance called human growth hormone.

A sudden abundance of human growth hormone, the result of a breakthrough in genetic engineering, has spurred these requests. Not long ago, doctors could collect barely enough of the chemical from the pituitary glands of cadavers to meet the needs of the 12,000 children in the U.S. who suffer from pituitary dwarfism, a congenital disorder that results when the body can't make enough of its own growth hormone. To treat one child for a year required more than 50 pituitary glands and cost about \$13,000. But in the fall of 1985, the Food and Drug Administration approved a synthetic version of the hormone, genetically engineered by Genentech. The price fell by about 20 percent, and the supply began to build. "When you visit pharmaceutical factories now," says Dr. Martin Press, a Yale University professor of pediatrics, "you'll find enough growth hormone in one bucketful to provide 10 years of

A shot in the arm for short kids?

treatment for all the children in the world with pituitary dwarfism."

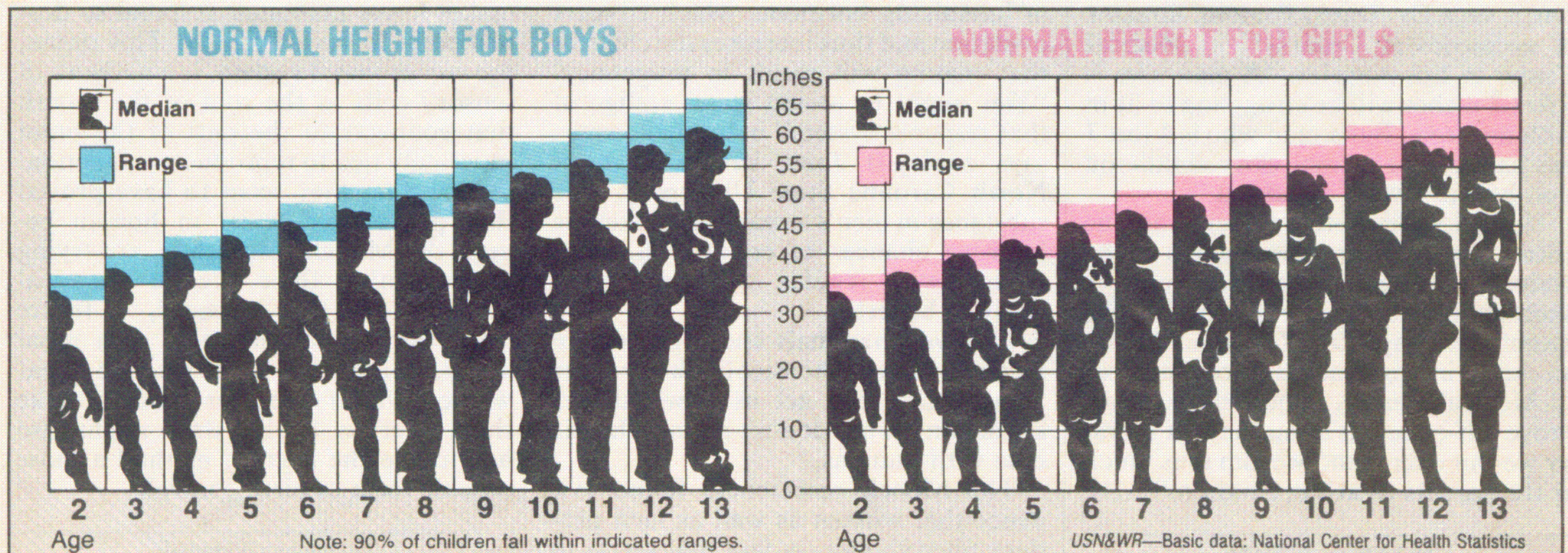
Given the sudden surplus, drug companies see an opportunity to market the hormone to short children with no medically defined growth disorder. According to the Human Growth Foundation in Bethesda, Md., 1 million children fall into the third percentile, meaning that 97 percent of their peers are taller than they are. If the line were pushed up to the 10th, 20th or even 30th percentile, the market potential would jump manyfold.

But should it? "One of the biggest questions facing us in the future is just when shortness constitutes a disease that needs to be treated," says Dr. Joseph Gertner, associate professor of pediatrics at New York Hospital-Cornell Medical Center. Doctors don't yet know which short children can safely and effectively be given human growth hormone. "Parents should not think this is a ready and easy answer to the problem of short stature," Gertner warns.

One mother, says Press, sent her 12-year-old daughter to see him because medical height charts indicated that the girl would grow no taller than 5 feet. Noting that the mother herself was 5 feet 2, Press asked the daughter: "If your mother were 2 inches shorter, would you think less of her?" The girl was taken aback, Press says, and concluded after a bit of nudging that her height was no real handicap.

Market potential

So far, the FDA permits the sale of growth hormone only as therapy for pituitary dwarfism. But early clinical evidence raises hopes for patients with Turner's syndrome, a chromosomal disorder that causes shortness in 8,000 U.S. girls. And at Yale, Stanford and the University of California at San Francisco, two-year clinical trials on children who fall below the fifth percentile for undetermined medical causes show promise. While about 35 percent of these children don't respond to growth hormone, the other 65 percent grow an average of 1 inch more a year, and the evidence suggests that they will be 2 to 2½ inches taller than they would have been without treatment. But Dr. Selma Kaplan, a pediatrician conducting the clinical trials at UCSF, cautions against being too optimistic. "The children may grow faster, but the period in which they



grow may be shortened by the premature onset of puberty," she says.

Other doctors worry about long-term side effects. Animals given large amounts of the hormone, for example, sometimes develop diabetes and joint disease. "Growth hormone has not proved harmful at low dosages," says Dr. Gordon Cutler, an endocrinologist at the National Institute of Child Health and Human Development. "But there may be the temptation to increase the dosage to dangerous levels with the hope of gaining added inches."

There are practical problems, too. For one, the hormone cannot be taken orally. "Unless a child is likely to be severely short," says Cutler, "most are not too keen about being injected three times a week." And at some \$10,000 a year, the hormone is still expensive. Insurers will cover 80 percent to treat pituitary dwarfism but won't pay to experimentally treat children who simply find themselves near the bottom of the growth charts. "Is it really worth \$100,000 over 10 years in an attempt to gain a few inches of height?" Cutler asks.

Some parents think so. "Every time an article about Genentech's plans for marketing growth hormone appears in the *Wall Street Journal*," says Gertner, "I get a lot of calls from stockbrokers who would like it for their children." Gertner also hears frequently from other doctors.

Gender gap

Parents are far more worried about sons than about daughters. The typical patient is a boy of 10 to 13 with the height of a child two or three years younger and is teased as being the class "shrimp." Most parents, says Press, "behave responsibly when they hear how much is still unknown about growth hormone. But on occasion I've had to dig my heels in and say flat out 'No' to parents who are convinced that shortness is a social and professional handicap."

Dwarfs often adjust to their height better than short people in the normal range, says Dr. David Rimoin, director of pediatrics at Cedars-Sinai Medical Center in Los Angeles. "A man who is 5 feet 3 inches will be struggling to fit in with his peers. But a man who is 4 feet 3 has had to accept since early childhood that he will always stand out."

Until doctors better understand the effect of growth hormone dosages on the body, the consensus is that only severely short children should be treated. "In the meantime," says Dr. Raymond Hintz, an endocrinologist at Stanford University Medical Center, "counseling to improve self-esteem is often the best therapy we can offer—and we aim it as much at the parents as at the children." ■

by Kathleen McAuliffe

Chemicals in male sweat can increase the chance of pregnancy

Siren song of the pheromones

■ A new study will provide grist for a decade's worth of talk-show and cocktail-party chatter, not all of it conducted in tones of sweet reason. Researchers have found that a substance exuded in the sweat of a man can help keep a woman's reproductive system in good working order.

It's the first strong proof that chemical signaling between the sexes, something scientists have long observed in lower animals, takes place in humans as well. And the evidence suggests that a woman's reproductive system may be profoundly altered by scents in the air of which she's unaware.

The experiment, which was performed by researchers George Preti and Winnifred Cutler of the Monell Chemical Senses Center in Philadelphia, exposed eight women who had irregular menstrual cycles to an alcohol solution containing an extract of male sweat. All of the subjects had been having cycles at least three days longer or shorter than the normal 29½ days. After about three months of having the solution rubbed under their noses several times a week, the women's cycles shifted closer to the norm.

The effect of a sweaty male would hardly surprise a monkey or a rodent. A chemical substance given off by male mice, for instance, will immediately stimulate a female to produce a flood of luteinizing hormone, which triggers ovulation and thus increases the chances that mating will result in pregnancy. "You might be seeing some vestige of that response system" in human beings, says zoologist John Vandenberg of North Carolina State University. The substance in men's sweat might likewise improve chances of conception, since women with regular cycles are more likely to be fertile.

In lower mammals and especially in insects, these chemicals, known as pheromones, can act as powerful sex attractants. That doesn't seem to be the case with humans.

The Monell researchers found evidence that women as well as men produce pheromones—a fact that seems to

explain a long-standing medical mystery. "It's a well-reported phenomenon that women housed together in dormitories will synchronize their menstrual cycles," says Douglas Danforth, a researcher at Eastern Virginia Medical School in Norfolk who studies human reproduction. "But it's been really hard to determine if it's chemical [induced] or behavior induced."

In a second experiment, Preti and Cutler supplied the missing proof. In one trial, 10 women were exposed to alcohol containing sweat obtained from an 11th woman over the course of her menstrual cycle. The solution was rubbed under the women's noses, as with the test of male sweat, several times a week. After several cycles, the periods of eight of the 10 women had shifted by several days so that they menstruated closer to the time the donor did. Ten additional women who were exposed to plain alcohol showed no change.

One explanation of this phenomenon is that it was originally a way of coping with a hostile environment. "You would have synchronized births," Vandenberg says. And in the face of hungry predators, "The chances of surviving are better if you have 10 births all at once

than if they are spread out."

Humans and most higher primates have lost the specialized organ that makes lower mammals respond so dramatically to sexual smells. This organ, the vomeronasal system, is a network of sensory cells in the roof of the mouth that connects to the part of the brain intimately tied to reproductive function.

Now that they seem to have proved that pheromones exist in human beings, the Monell researchers are trying to determine their precise chemical identities. If they succeed, a future drug, perhaps in the form of a nasal spray, might be developed to treat women whose irregular periods make them infertile. Such a drug might also help make the rhythm method a more reliable form of birth control. ■

by Stephen Budiansky

