The hope for a cure for kids with progeria may have a fringe benefit: It could extend all human life as well.

By Herbert Burkholz

A bunch of kids are making plans for the third day of their vacation at the sprawling River Ranch in Lake Wales, Florida. Five-year-old Jesus Piedra, from Mexico, has his eyes on one of the golf carts that tool around the grounds of the ranch. "Could I drive it?" he asks his father in Spanish. "You drive, and I'll sit behind you and help," his father agrees. Then the idea is translated into English for some of the other children.

"Can I come, too?" says Courtney Arciaga, a five-year-old from Bonita California. "But after horseback riding?"

There are 16 children in all, sitting with their parents, making similar plans. The kids, who come from seven different countries, range in age from three to 19; and, based only on their interests, demeanor and liveliness, they seem much like any other group of kids on vacation. They are, however, very different. They look like little old men and women. Their faces are pinched and withered, their heads are bald, they have wrinkled skin, stiff joints and atherosclerosis, and all of them suffer from severe cardiovascular problems. They are victims of the condition called progeria.

Taken from the Greek for "prematurely old," progeria is a rare genetic disease that appears to accelerate the child from infancy to old age, and then to death, within a few short years. The average age at death is 13, the usual cause a heart attack or stroke.

Until recently, there was no help for these children, much less a cure. But an advance in the use of human growth hormone has opened up a window to the future for progeria children. No one is claiming a cure yet, but for the first time there is a glimmer of hope, and along with that hope have come new insights into the process of aging itself. For those who study aging, the same research that may someday give progeria children a better and longer life may also lead to a means of extending human life in general.

A RARE INSIGHT INTO AGING

Progeria was first described in 1886 by Drs. Jonathan Hutchinson and Hastings Gilford, and since that time there have been roughly 100 cases reported around the world. The condition is extremely rare. There are fewer than 20 known progeria children alive today, and for the past nine years the Sunshine Foundation, a philanthropic organization, has gathered them together for a week of fun. The gathering has two purposes: It allows the children to mingle for a while with their only true peers, and it allows the physicians who specialize in the field to examine the children in one place and monitor their condition.

"There are tears through the whole week," says Sue Arciaga, Courtney's mother. "The last hour is a real emotional time because you're not sure who is going to come back next year. You just hug and hug so tight, and hope that they're going to come back."

This year the physicians at the gathering are W. Ted Brown, M.D., Ph.D., chief of the division of human genetics at the North Shore Hospital–Cornell University Medical College in Manhasset, New York, and Franklin DeBusk, M.D., a teaching pediatrician at the University of Florida College of Medicine in Gainesville. Watching the children play, DeBusk makes the point that progeria is not an exact model of the aging process. "The children have no old-age mental problems," he says, "nor do they have the usual eye and ear ailments that come with aging. They don't get old-age arthritis, and they don't have a consistent problem with blood lipids or cholesterol."

Despite this, Brown and DeBusk agree that if progeria is not an exact model of aging, it is an excellent work-
ing model, the best available, and nothing proves the point better than what they call the hyaluronic acid factor. Hyaluronic acid is a molecule found in the connective tissues of animals. Though the acid’s function is not completely understood, in limited experiments the progeria children have been shown to excrete more than ten times the normal amount for their age. Similarly limited tests show that the excretion level of hyaluronic acid in normal people increases with age—and the levels excreted in the progeria children are higher even than those found in the elderly. From this follows the theory that 1) an excess output of hyaluronic acid may be a normal characteristic of aging that occurs in progeria at an accelerated rate, and 2) that the disease may be caused by a cell defect that prevents the normal regulation of hyaluronic acid in the body.

“Our assumption is that this defect has a genetic origin,” Brown explains, “just as aging has a genetic component. We feel that these kids are born with a mutated gene that’s involved in the longevity process, and our goal is to determine what that gene is.”

THE MIRACLE OF HUMAN GROWTH HORMONE

Pinpointing the gene, however, is a long-term goal. More immediately, there is the work with the rapidly aging kids—like little Jessica Davis, from Scottsdale, Pennsylvania. The daughter of Donald and Rachel Davis, Jessica weighed a conventional six pounds, ten ounces at birth, and like all progeria children she displayed no signs of abnormality then. But her weight and growth soon leveled off, and today, at the age of six, she weighs only 18 pounds and stands 31 inches tall. Her features are birdlike, her skin is paper thin, she wears a frilly bonnet to conceal her baldness and she has already suffered several mild strokes. But despite her appearance, she is brash, bright and witty, shows all the enthusiasms of a typical six-year-old and dreams of being a ballerina someday.

The Davises were reluctant, at first, to have their daughter used as the subject of a scientific experiment, for they guard her privacy fiercely. This is an attitude common to all progeria parents, one of many that they share. Since there are so few of them, and since they are all in the same boat, they often feel closer to each other than to members of their own families. “Everyone here [in Florida] seems like part of your family,” explains R.C. Arciaga. Courtney’s father. “As soon as something happens to one of the other families, we all know about it. It’s like a little chain—everyone calls one another.” Last June, despite the desire to keep her out of the spotlight, Jessica became the second progeria child to be treated with a genetically engineered version of the human growth hormone. In its natural state, this hormone is secreted in the pituitary gland at the base of the brain, and it stimulates the production of a compound called insulin-like growth factor-1 (IGF-1), a protein that promotes tissue growth and organ health. Until recently, the only source of the hormone was human cadavers, which severely limited its use, but in 1980 genetic engineers at both Eli Lilly & Co. and Genen-
Kids suffering from progeria are like living laboratories of the aging process.

Tech Inc. perfected a method for producing a recombinant form of the hormone, thus making it available to researchers.

By then, progeria specialists were aware that the growth-hormone levels in children with the condition were normal for their age, but that their IGF-1 levels were extremely low. The normal level of growth hormone should stimulate the production of an equally normal level of IGF-1, and the inescapable conclusion was that the growth hormone in the children somehow was not able to do its job.

Since the natural hormone was not working to produce IGF-1, Fima Lifshitz M.D., chief of North Shore Hospital’s division of pediatric endocrinology, metabolism and nutrition, and his colleagues decided to try the man-made version on the children. They were looking for more than its known ability to treat short stature, hoping that it would increase the IGF-1 level, and that IGF-1 would have other beneficial effects on the children’s bodies, particularly their metabolism.

“These children have a very high metabolic rate,” Brown explains, “and that’s most unusual, not seen except in children who are hyperthyroid. Jessica, for example, burns up her fat stores at double the normal rate.”

The first child to receive the treatment was four-year-old Kevin Brown (no relation to the physician) of Elyria, Ohio. The treatment began in November 1969, and the results were soon obvious, Kevin’s metabolic rate began to fall, his IGF-1 level began to rise and, most dramatically, he grew an inch and a half in six months, as compared to the half inch annually that is typical of progeria children (an inch for normal kids). He also began to grow hair and gain weight, and at his next examination, the physicians will look for changes in the ratio of his muscle mass to fat. an indication of whether his internal organs are now aging less rapidly. (With age, fat tends to accumulate around internal organs.) The attitude among the researchers has been one of professionally guarded optimism. but Brown, who is overseeing Kevin’s treatment, clearly believes that he is on the right track. It was alter the results with Kevin that Jessica’s parents agreed to have her join the program, for if Brown is right, then a treatment and maybe, ultimately, a cure for progeria is in sight for the first time.

REVERSING THE AGING PROCESS

This guarded optimism turned to genuine excitement last summer when The New England Journal of Medicine published a study on the use of growth hormone at the other end of the age spectrum. After a clinical test of 21 men with low IGF-1 levels, ranging in age from 61 years to 61 years, Daniel Rudman, M.D., and colleagues at the Medical College of Wisconsin in Milwaukee determined that treatment with the recombinant version of the growth hormone could at least temporarily reverse many of the effects of aging in the body. In the study, regular injections of the hormone substantially reduced the excessive fat tissue and the atrophying of muscles that are commonly found in elderly men. The subjects came out of the program with leaner bodies and stronger skin and spines. By many standards, their apparent age had dropped by 20 years. The experiment had been designed to test the theory that much of the frailty of aging comes from a drop in the production of the natural growth hormone in the body, which tends to decline after age 30, and by age 60 may be reduced by as much as 60 percent. In the study, the man-made equivalent appeared to compensate for that loss, and to restimulate the release of IGF-1, thus promoting tissue growth. After six months of treatment, the skin of the men involved had regained a youthful thickness; and although there had been no overall weight loss, they had averaged an 6.6 percent increase in lean tissue and a 14.4 percent drop in fat tissue. Much of the added bulk had arisen in the muscles, while the rest had helped to rebuild such vital organs as the heart, the kidneys and the gastrointestinal tract. Although the study involved only men, Rudman believes the treatments were likely to have the same effect on women.

“It’s exciting news,” Brown says. “They’ve clearly shown there is some relationship between the growth hormone we’ve been using on the kids and the aging process in general.”