National Institutes of Health

Fact Sheet — *Progeria*

Thirty Years Ago

- Thirty years ago, virtually nothing was known about progeria, and due to the rarity of the disease, little research was done until the 1990s.
- Progeria is an extremely rare genetic disease of childhood characterized by dramatic, premature aging. The condition is estimated to affect one in 8 million newborns worldwide. Hutchinson-Gilford progeria syndrome (HGPS) is the most severe form of the disease.
- As newborns, children with progeria usually appear normal. However, within a year, their growth rate slows and they soon are much shorter and weigh much less than others their age. While possessing normal intelligence, affected children develop a distinctive appearance characterized by baldness, aged-looking skin, a pinched nose, and a small face and jaw relative to head size. They also often suffer from symptoms typically seen in much older people: stiffness of joints, hip dislocations and severe, progressive cardiovascular disease.
- Some children with progeria undergo coronary artery bypass surgery and/or angioplasty in attempts to ease the life-threatening cardiovascular complications caused by progressive atherosclerosis. However, there currently is no treatment or cure for the underlying condition.
- Death occurs on average at age 13, usually from heart attack or stroke.

Today

- In 2003, NIH-funded researchers discovered that Hutchinson-Gilford progeria is caused by a tiny mutation in a single gene, known as lamin A (*LMNA*). In laboratory tests involving cells taken from progeria patients, researchers found that the mutation responsible for Hutchinson-Gilford progeria causes the *LMNA* gene to produce an abnormal form of the lamin A protein which destabilizes the patient's cells.
- A genetic test for Hutchinson-Gilford progeria syndrome is currently available. In the past, doctors had to base a diagnosis of progeria solely on physical symptoms, such as skin changes and a failure to gain weight, that were not fully apparent until a child's first or second year of life. This genetic test now enables doctors to diagnose a child at a younger age and initiate treatment early in the disease process.
- A new mouse model of progeria has been developed that is helping scientists test experimental therapies for progeria and also explore cardiovascular disease in general.
- Researchers published cell culture and mouse model studies that support a potential drug treatment for children with Progeria. Farnesyltransferase inhibitors (FTIs), originally developed for cancer, are capable of reversing the dramatic cell structure abnormalities that are the hallmark of cells from children with Progeria.
- A clinical trial using FTIs is being planned, just a few years after the gene was discovered.

Tomorrow

The NIH is poised to make major advances in the treatment of progeria, as well as in the field of aging and in heart disease.

- NIH-funded researchers are exploring the possible role of the wild-type *LMNA* gene in the aging process. They are collecting and analyzing DNA from a cohort of about 600 centenarians to determine whether there is something unique about their *LMNA* gene sequence that promotes longevity.
- Research studies on progeria examined the damage the mutant protein does to blood vessel cells of humans and mice. The discoveries offer increased hope for a cure for progeria and may also provide key insight into the cause of adult heart disease.

- Laboratory research is now ongoing, in preparation for clinical trials using Farnesyltransferase inhibitors as possible therapeutics for progeria.