23.4 CLINICAL APPLICATION

Old Before Their Time

The segmental progeroid syndromes are inherited disorders that cause a person to live a lifetime in just a few years. They were once called progerias, but the newer terminology reflects the fact that they do not hasten all aspects of aging. Most of these disorders, and possibly all of them, are caused by cells' inability to adequately repair DNA. This enables mutations that would ordinarily be corrected to persist. Over time, the accumulation of mutations destabilizes the entire genome, and even more mutations occur in body cells. The various changes that we associate with aging occur.

The segmental progeroid syndromes vary in severity. People with Rothmund-Thomson syndrome, for example, may lead a normal life span, but develop gray hair or baldness, cataracts, cancers, and osteoporosis at young ages. The child in figure 23G, in contrast, shows the extremely rapid aging of Hutchinson-Gilford syndrome. An affected child appears normal at birth but slows in growth by the first birthday. Within just a few years, the child becomes wrinkled and bald, with the facial features characteristic of advanced age. The body ages on the inside as well, as arteries clog with fatty deposits. The child usually dies of a heart attack or a stroke by age 13, although some patients live into their twenties. Only a few dozen cases of this syndrome have ever been reported.

Werner syndrome becomes apparent before age 20, causing death before age 50 from diseases associated with aging. Young adults with Werner syndrome develop atherosclerosis, type 2 diabetes mellitus, hair graying and loss, osteoporosis, cataracts, and wrinkled skin. They are short because they skip the growth spurt of adolescence.

Not surprisingly, the cells of segmental progeroid syndrome patients show aging-related changes. Recall that normal cells growing in culture divide about 50 times before dying. Cells from progeroid syndrome patients die in culture after only 10 to 30 divisions. Understanding how and why these cells race through the aging process may help us to understand genetic control of normal aging. ■

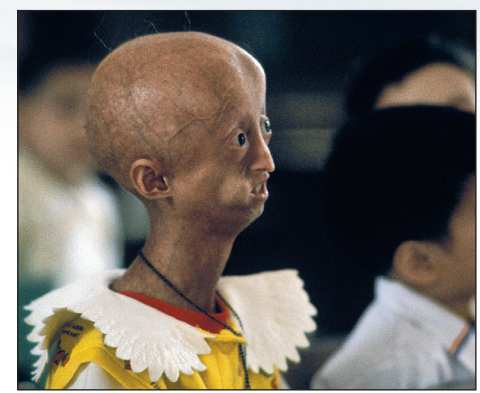

FIGURE 23G
Segmental progeroid syndromes. This child has Hutchinson-Gilford syndrome, which is extremely rare.