

Gene Therapy Returns

GENE THERAPY—REPAIRING MALFUNCTIONING cells by mending their DNA—offers an elegant solution to diseases caused by a single flawed gene. Since the first human study began in 1990, however, the field has struggled with technical challenges and setbacks such as the death of a volunteer in a trial. But this year, gene therapy turned a corner, as researchers reported success in treating several devastating diseases:

- **Leber's congenital amaurosis (LCA)**, a rare form of inherited blindness that strikes in infancy. Researchers in the United States and the United Kingdom injected one eye of LCA patients with a harmless virus carrying a gene coding for an enzyme needed to make a light-sensing pigment. In the first completed trial, the light sensitivity of all 12 partially blind patients improved. Four children gained enough vision to play sports and stop using learning aids at school. (Another team using a similar approach gave full color vision to squirrel monkeys born with red-green colorblindness.)
- **X-linked adrenoleukodystrophy (ADL)**, a brain disorder that usually kills boys before they're teenagers. The disease involves a flaw in



Success. Blind patients regained some vision after treatment to repair an enzyme-making gene.

a gene that makes a protein that helps maintain the myelin sheath around nerves. A French team inserted a corrective gene into the blood cells of two 7-year-old boys with ADL, and some of the cells began making the missing protein and apparently migrated into their brains. Two years later, the progressive brain damage typical of ADL has stopped. The trial is also the first to carry the gene into cells with a disabled HIV virus, which should be less likely than older vectors to cause cancer.

- **"Bubble boy" disease:** severe combined immunodeficiency (SCID) due to a lack of an enzyme called adenosine deaminase. In January, Italian researchers gave an update on an 8-year-old trial for children with the disease. Eight of 10 patients no longer need enzyme-replacement therapy and are living normal lives. None suffered serious side effects from the therapy. (Gene therapy for a related disease, X-linked SCID, restored the immune systems of 19 infants but caused leukemia in five of them, one of whom died.)

Clinical results for other genetic diseases are expected out soon, and more trials using the new, safer vectors are gearing up.