trisomy in 2 to 5 percent of tissue samples taken from fetuses during prenatal testing. "That's pretty high," she says. She suggests that most of those surviving to birth somehow lose their extra chromosome during development. If the disappearing chromosome originally came from the parent who contributed only one, then the child may harbor cells that are uniparentally disomic.

Along similar lines, Engel notes that about half of all fetuses spontaneously aborted during the first trimester show chromosomal abnormalities, and that many of these defects result from errors during meiosis. This, along with evidence from mice, suggests to him that the chance of a person ending up with uniparental genetic duplication is higher than many scientists suspect.

"Maybe sometimes it doesn't carry any bad effect with it," Engel says. Unless the disomy encompasses a mutant gene that requires a duplicate presence to cause disease, as in the case of CF, "you may have perfectly normal people with no problem," he suggests.

Well, *almost* no problem. Many geneticists suspect that even when no particular disease gene gets involved, uniparental disomy can have subtle effects. These influences have their roots in the phenomenon of genetic imprinting.

Geneticists have found that certain otherwise identical genes show differences depending upon which parent – male or female – contributed the genes. In biologists' jargon, the gene from one parent gets "imprinted" with a molecular marker indicating whether it has come from the mother or father. In these cases, it's critical that a child receive both imprinted and nonimprinted versions of that gene for proper development; two paternal versions or a pair of maternal ones simply won't do.

So in some cases, uniparental disomy may leave a fetus viable but with subtle abnormalities resulting from the lack of mixed maternal and paternal genes. Hall and others suggest, primarily on the basis of mouse studies, that human uniparental disomy involving chromosomes that normally bear imprinted genes can result in mild developmental problems, including short stature and learning disabilities.

Indeed, these geneticists suspect that the short stature of Beaudet's CF patient stemmed from her lack of certain imprinted genes. Geneticists already know that certain genes on paternal copies of chromosome 7 are normally imprinted in mice, and without that paternal complement of imprinted genes, development proceeds abnormally.

Every time nonimprinted DNA substitutes for imprinted DNA, "you'd expect to get someone with short stature," Beaudet says. "And if [the nonimprinted DNA] includes the CF gene, then you'd have cystic fibrosis too."

That kind of thinking has spurred Hall and her colleagues to begin looking for hidden cases of uniparental disomy among healthy, short-statured people – especially those showing subtle behavioral problems like those seen in mice with imprinting abnormalities. "We're looking for kids with abnormal growth patterns and [abnormal] behavior," she says. "We've started looking at some of these individuals and testing them for uniparental disomy."

In addition, Hall, Engel and others expect that as geneticists analyze DNA from people with inherited disorders of unknown cause, they will begin to find uniparental disomy at the roots.

"There's a sense that [uniparental disomy] might be more common than has been thought, and that the mechanism may explain a few or a number of syndromes that thus far have no explanation," Engel says. "As in Prader-Willi, there are some syndromes where there usually is a tiny chromosomal deletion, and some of the cases don't show such a deletion. One might envision that disomy might explain these rare syndromes."

Among the unexplained, inherited abnormalities that Engel mentions as candidates are Beckwith-Wiedemann syndrome, Miller-Dieker syndrome and Silver-Russell syndrome. Each involves variations of growth retardation and congenital anomalies.

But in order to peg these or other syndromes to uniparental disomy, researchers need to perform detailed analyses of the DNA base sequence on all 23 pairs of human chromosomes, studying both the person in question and his or her parents. And although the number of DNA probes grows every month, the current selection still leaves large chromosomal regions essentially unmappable.

Ultimately, as more and more human chromosomes bare their secrets to genetic probes, prenatal testing may routinely include searches for uniparental disomies. In coming years, Engel predicts, "molecular probes will detect these and tell us more about their frequency."

While Engel looks forward to learning those details, he says he also hopes researchers and parents will not become obsessed with genetic analyses of every developing fetus. "To tell the truth," he says, "I think that would take all the beauty out of human procreation." □

News of the week continued from p.7

Shuttles grounded by two sets of leaks

It proved a double blow to proud NASA. As astronomers pondered the consequences of an apparently misshapen mirror that significantly reduced the Hubble Space Telescope's ability to explore the distant heavens, engineers at Kennedy Space Center in Florida discovered yet another hydrogen leak in a space shuttle. A month ago, the space agency delayed the flight of Columbia because of such a leak. This time, Atlantis revealed a similar and possibly related leak.

NASA, which had already postponed Columbia's mission until at least August, reacted to this second potentially lethal problem by indefinitely suspending flights by the three shuttle craft. William B. Lenoir, NASA's chief of space flight, said the shuttles would remain grounded until engineers found, understood and fixed the leaks.

No one ventured a specific date when the shuttle fleet might fly again.

Liquid hydrogen and liquid oxygen serve as the propellants for the shuttle orbiter's three powerful main engines that help drive the craft into space. The two supercold fluids fill the huge external fuel tank that clings to the underside of the astronaut-carrying orbiter and flow through a complex system of pipes and valves to the main engines. The fuel mixture is highly explosive.

Hydrogen has no scent or color, and spotting hydrogen leaks requires special detectors. It is far more difficult to locate a leak and repair it than to simply confirm that one exists. Engineers have been conducting tests of each craft's external tank and its piping, as well as of the "umbilical" connecting hoses and the fittings used to fill the tanks.

The leak studies now focus on four themes, Lenoir says. One involves a detailed analysis of how the pieces that make up the propellant-storage and delivery components were made. A second concentrates on how this equipment was handled, assembled and shipped. A third line of investigation is devoted to step-by-step data analysis of the system, checking to make sure engineers haven't overlooked some possible leak source. And the fourth, reminiscent of the Challenger investigation, creates and follows "fault trees" designed to anticipate subtle flaws – in design, fabrication or other aspects – that might trigger equally disastrous consequences.

Columbia had been scheduled for a May launch to carry Astro-1, a four-telescope observatory that will study the sky from the shuttle's cargo bay rather than from a "free-flying" satellite like the Hubble Space Telescope. Atlantis had been scheduled to deploy a classified satellite for the Department of Defense.

– J. Eberhart