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COVER: Spectacular view of islands west of Baja California is not a photograph but an image taken from orbit by the synthetic-aperture radar (SAR) aboard the new Seasat ocean-monitoring satellite. Light areas are not clouds but effects of wind and rain on the sea surface, such as the fan-shaped feature (below center) which may result from winds blowing off the island above it. See p. 89. (Image: JPL)

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SCIENCE NEWS OF THE WEEK

Prenatal Examination of Human Genes

The era of recombinant DNA — with all its promise and controversy — grew from the discovery of enzymes that cut DNA molecules at specific sites. These "restriction" enzymes snip long chains of genetic information into segments that can be separated by size and then identified. Now medical scientists report the first clinical application of those same techniques. They can be used to detect prenatal human gene abnormalities. By cutting, separating and identifying DNA segments taken from amniotic-fluid cells, investigators have diagnosed delta beta-thalassemia trait in a fetus.

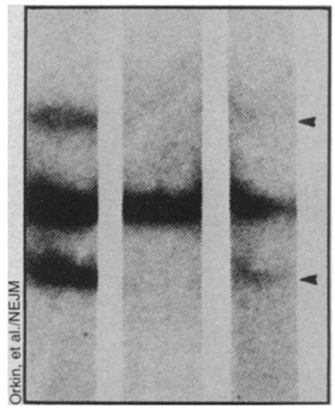
The new technique is reported in the July 27 NEW ENGLAND JOURNAL OF MEDICINE by Stuart H. Orkin of Children's Hospital Medical Center in Boston and colleagues at Harvard Medical School, Yale University School of Medicine and Haceteppe University in Ankara, Turkey. They used a restriction enzyme to clip the entire set of genes from human cells into thousands of fragments. On a gel the fragments were spread into a smear with the shortest at one end and the longest at the other.

The key to the procedure is finding a probe that will pick out sequences of interest. "If you had the right probe, you could look for any gene," Orkin told SCIENCE NEWS. Currently probes for the hemoglobin genes are the easiest to construct.

Orkin's probes are radioactively labeled DNA segments of the same sequence as the genes being studied. That DNA is constructed on the template of messenger RNA, the cytoplasmic representative of a gene. Red blood cells, which predominantly synthesize hemoglobin, provide ample globin messenger RNA. In more versatile liver cells, for example, isolating a specific messenger RNA from all the others would be a formidable task, Orkin points out.

The radioactively labeled probes bind specifically to those fragments containing pieces of globin gene DNA. When the DNA-containing gels are exposed to photographic paper (autoradiography), only the globin bands appear. The researchers compared normal patterns with those from patients having rare blood abnormalities known to be due to deletions of the globin genes. They found an absence of alpha genes in patients with alpha-thalassemia and an absence of particular fragments that hybridize with beta-gene probe in delta beta-thalassemia and in hereditary persistence of fetal hemoglobin.

Amniotic fluid cells were the source of DNA in another experiment. A Turkish couple, both carriers of delta beta-thalassemia, requested amniocentesis. Orkin and colleagues grew the amniotic fluid cells for six weeks and then analyzed the DNA to confirm the results of other tests. The beta-gene bands were present in reduced amounts on the gel; therefore the baby was just a carrier of the trait.



According to DNA analysis, the fetus examined has one copy of normal gene (gene at right). Gene probe binds to three bands of normal DNA fragments (left), but to only one band of DNA from patient with both genes abnormal (center).

Yuet Wai Kan and colleagues at San Francisco General Hospital have previously diagnosed deletions in fetal alpha-globin genes by binding probes to DNA in solution. Orkin says that his procedure requires a smaller amount of fetal DNA and that visual representation of the gene deletion on a gel avoids problems of nonspecific binding and probe purity.

At present prenatal diagnoses of most beta-thalassemias and sickle-cell anemia require measurement of globin synthesis by fetal blood samples. Although the analysis is rapid, the test is done only in a few medical centers because taking blood from a fetus is a much more difficult procedure than sampling amniotic fluid. The high risk to the fetus makes physicians eager to find a different procedure, Orkin says. He sees the gene-visualizing technique to be especially promising for diagnoses in developing countires where hereditary blood diseases are more common than in the United States. Amniotic fluid samples could be sent for analysis to international centers specializing in particular syndromes.

Orkin views his procedure as a prototype for diagnosis of a wide range of hereditary diseases. For instance, sickle cell anemia is a likely candidate for a similar prenatal detection method. The abnormality of that DNA is known, and among the available restriction enzymes there is one that should recognize that abnormality. The major limit now, Orkin says, is the void of information about the bases of genetic diseases. "We need much more groundwork," he concludes. □