shoved up on the continent and rocks called blueschists that are metamorphosed at the unique high pressures and low temperatures of subducting ocean crust, for example. Most geologists no longer see this as an insurmountable problem. The resemblance of features common to both early Proterozoic and recent orogens is so strong that some differences are allowable, they say. In addition, notes Bowring, some features such as blueschists are so rarely preserved even in young orogens that their absence in older ones, subject far longer to erosion, might not be surprising. Careful searches by Precambrian geologists, keeping in mind how features would change with age, might reveal additional familiar features, he and others note.

Being familiar with modern examples that might turn up in the Proterozoic does seem to help. Gregory Harper of the State University of New York at Albany recently discovered an ophiolite in Wyoming that is at least 2.65 billion years old. It is metamorphosed, missing typical underlying mantle rocks, and is sliced up and severely stretched, but Harper's field experience on younger ophiolites let him recognize the mounded lava flows of underwater eruptions, the dikes feeding lava to the sea floor, the rock of frozen magma chambers, and other characteristic ophiolite features. Given a clear Archean example, says Harper, there is a strong possibility that ophiolites older than 1 billion years can be found in the rocks of the Proterozoic.

As further proof of the collisional nature of the Penokean orogen, as the Great Lakes crustal addition is called, Bruce Nelson and Donald DePaolo of the University of California at Los Angeles have determined the time at which its rock separated from the mantle as magma and became part of the crust. Using isotopes of the rare earth elements neodymium and samarium, they found that the average mantle separation age is 2.1 to 2.3 billion years, too young to be Archean crust but older than the 1.9-billion-year age of the collision. Either the collision mixed old Archean crust with newborn island arc magma, or island arc formation had been going on for hundreds of millions of years.

Farther outboard of the growing continent, the movement of continent and sea floor was about to add a far larger area of young crust to proto–North America, according to Hoffman and Bowring's story. M. E. Bickford of the University of Kansas, Van Schmus, and Isidore Zietz of the Phoenix Corporation in Falls Church, Virginia, have identified two orogens that appear to span the midsec-

New Sickle Cell Test

A new method has been developed for the prenatal diagnosis of sickle cell anemia that is faster and more sensitive than the ones currently in use. The method, which was devised by researchers at Cetus Corporation in Emeryville, California, works by combining two novel techniques for amplifying and analyzing specific DNA segments and may be generally useful for the diagnosis of genetic diseases. Moreover, the individual techniques have the potential for much wider application in molecular biology.

Sickle cell anemia is a hereditary disease caused by the alteration of a single nucleotide in the beta-chain gene, which encodes one of the two proteins of the adult hemoglobin molecule. Individuals who inherit two copies of the mutant gene get sickle cell disease. Persons who inherit just one copy do not have the full-blown disease but can pass the defective gene on to their children.

Current methods for diagnosing sickle cell anemia and other diseases that are caused by gene mutations often use restriction enzymes that cut DNA at very specific sites to detect changes either in the defective gene itself or in DNA that is closely linked to the gene. For example, the sickle cell mutation abolishes a site in the beta-chain gene that would ordinarily be cut by the enzyme designated *Dde*1. Consequently, digestion of the mutant and normal genes with the enzyme produces fragments of different sizes that can be separated and then detected by a method called Southern blotting.

The new method for diagnosing sickle cell anemia, which is published on p. 1350 of this issue of *Science*, also requires restriction enzymes. The improvements devised by the Cetus group include first the "polymerase chain reaction" protocol for amplifying the number of copies of the target DNA sequence and thus increasing the sensitivity of the analysis, and second, the "oligomer restriction" technique for determining whether the target DNA carries the mutation.

The polymerase chain reaction, which was conceived by Kary Mullis and Fred Faloona of Cetus, is a method for copying simultaneously both strands of a specific gene segment, in this case a 110–base pair sequence containing the sickle cell mutation site of the beta-chain gene. By repeating the reaction 20 times—each repetition requires only 5 minutes—the researchers obtain about a 220,000-fold amplification of the sequence.

Once the beta-chain gene segment is amplified, it is analyzed for the presence or absence of the *Dde*1 restriction site by the oligomer restriction technique that was devised by Randall Saiki and Henry Erlich of Cetus and Norman Arnheim of the University of Southern California. In this procedure, a short, radioactively labeled DNA segment (the oligomer) is used as a probe for the restriction site. Ultimately it is restriction fragments released from the probe that are detected, and not fragments of the gene itself. An eight-nucleotide fragment is produced if the beta-chain gene is normal; if the gene carries the sickle cell mutation, there is a three-nucleotide fragment.

The Cetus workers have shown that the new method can readily determine whether an individual carries two copies of the sickle cell gene, one copy, or none at all. According to Erlich, the analysis takes only 1 day to complete once they have isolated the DNA from the test cells, compared to 5 to 6 days for current methods. Basically each step of the analysis is faster than similar steps in the current procedure.

Moreover, 20 nanograms of DNA—about one-fiftieth of the one microgram or so that is now required—is sufficient for analysis by the new method, although more time may be needed with such small samples. Finally, all the steps of the procedure except the final separation of the restriction fragments are test-tube operations and amenable to automation.

Small sample size can be a problem, especially when DNA must be obtained from fetal cells for prenatal diagnosis. The virtue of the polymerase chain reaction is that it can amplify the beta-chain DNA and potentially any DNA that might be in short supply. In addition to being used for genetic diagnosis, the method might aid in diagnosing infectious diseases or in forensic medicine, Erlich suggests. As he points out, "If there isn't enough specific target available, you can just make more of it."—**JEAN L. MARX**