Genetic diseases

Problems of prenatal testing

Washington

NEW techniques for prenatal diagnosis of genetic diseases are sharpening the debate in the United States over when the Food and Drug Administration (FDA) should approve for commercial use test kits that might lead a woman to prefer an abortion to the possibility of bearing a handicapped child. Methods based on analysis of fetal DNA promise to increase greatly the number of diseases for which prenatal diagnosis is possible, but the anti-abortion lobby is firmly opposed to any test used in a "search and destroy" mission. And the anti-abortion lobby cannot be dismissed as part of the lunatic fringe: President Reagan has made clear his opposition to abortion under any circumstances.

Prenatal testing for some easy-to-detect conditions such as Down's syndrome and Tay-Sachs disease has been carried out for several years. Although in some instances a good argument can be made that tests have increased, rather than decreased, births of healthy but potentially affected children, the strength of anti-abortion sentiment suggests that the arguments will have to be fought anew as each new test becomes available. Furthermore, the spread of chorionic villus testing, which allows fetal cells to be obtained earlier in pregnancy than by amniocentesis, could make easier those abortion decisions based on tests for inherited conditions: the National Right to Life group is already challenging use of the technique.

FDA spokesmen are wary of speculating about the regulatory passage of future commercial kits, but it is clear that any company wishing to market a new prenatal diagnostic will have to go to unusual lengths to provide data on false positive rates before approval can be expected; a false positive result could lead to the unnecessary abortion of a healthy fetus. Industry spokesmen hope that FDA will restrict itself to questions of safety and efficacy, disregarding the thorny risk/benefit issue, with its attendant questions about the quality of life of a handicapped child. But some recent FDA decisions — on putative cancer therapies, for example — suggest that FDA does indeed consider it part of its job to scrutinize possible benefits as well as safety.

In 1983, after seven years of foot-dragging, FDA eventually approved unrestricted use of test kits to detect elevated concentrations of α-fetoprotein (AFP) in amniotic fluid or serum, indicative of neural tube defects such as spina bifida. That decision reversed FDA's earlier position, in which it had sought to specify the testing protocol and interpretation of results for AFP kits. Although it is pointed out in defence of FDA's delay that there are good reasons to be wary of uncritical use of AFP tests, few tests would claim to be 100 per cent efficient — in any case, numbers matter little to those whose opposition to abortion is based on religious grounds; it remains to be seen whether future tests will experience similar delays.

Many prenatal diagnostic tests, such as those for sickle cell anaemia and phenylketonuria, are now being performed in university medical centre research programmes, approved by institutional review boards but not by FDA for unrestricted use. Commercial reference laboratories, in contrast, use only FDA-approved reagents. The limits of FDA's authority to regulate experimental tests are "somewhat cloudy", according to an official in FDA's compliance division: although there is no question that an experimental test can be used for evaluation in conjunction with an established technique, or if it presents no significant risk, established tests are sometimes lacking, and abortion decisions are being taken on the basis of experimental tests. There is at least one published case of an abortion resulting from incorrect experimental diagnosis of a haemoglobinopathy.

For some of the genetic conditions that can now potentially be diagnosed by analysis of linked fetal DNA markers, such as retinitis pigmentosa, Duchenne muscular dystrophy and Huntington's disease, testing of relatives is necessary (but not always sufficient) to arrive at probabilistic estimates that a given fetus is affected by an inherited disorder. As long as this sort of specialized knowledge is required for testing, work will be restricted to experimental medical centres and so remain effectively beyond FDA's purview, even though such testing is offered as a commercial service.

But the goal of much current research is to produce probes that will identify a mutant gene directly, or, even better, the gene product. Recently, for example, a direct gene probe for prenatal detection of phenylketonuria has been obtained. When simpler tests become available error rates will fall, and commercial kits will be feasible. One of the greatest hopes is for a test for cystic fibrosis, the commonest lethal genetic disease in the United States. The gene responsible for the disease has not yet been identified, but development of a test is "at an advanced stage", according to Integrated Genetics Inc. of Massachusetts. Although the eventual FDA approval for AFP test kits is hailed as a precedent for future tests, the industry knows that it will have to work harder in future to satisfy FDA demands. **Tim Beardsley**

Geology

New Chinese institute

A NEW Chinese research institute, the Xian Laboratory of Loess and Quaternary Geology (XLLQG), has been set up in Xian, Shaanxi Province. The laboratory is an independent unit, attached to Academia Sinica, and is engaged in the study of the characteristics and formation processes of loess and other Quaternary sediments in China. On the basis of the geological and biological records of the Quaternary period, the workers at the institute will try to reconstruct the history of the environmental changes of the Quaternary, and to understand the effect of human activities on future developments. This reconstruction of the pattern of environmental change is the single most important task facing Quaternary investigators, and those involved with XLLQG will be well placed to make significant contributions.

Xian is in the middle reaches of the Yellow River with the great Loess Plateau and widespread deserts to the north and west. To the east, Xian faces the North China Plain, and to the south, across the Qin Ling mountain, is the Red Basin of Sechuan Province with temperate and subtropical landscapes. The continuous loess-palaeosol series which began to be deposited 2.4 million years ago (see *Nature* **300**, 431; 1982) provides one of the best available indicators of Quaternary climatic changes, and contains abundant traces of early humans and Quaternary vertebrates.

Several research projects are already under way; these include investigations on the composition, physical characteristics and micromorphology of loesses and palaeosols and their relation to environmental changes and engineering construction; processes and mechanisms of recent dust falls and loess sedimentation and the relation of loess accumulation and loess erosion; the evolutionary history of human fossils on the Loess Plateau and the migration of fauna and flora during the Quaternary; loess-palaeosol sequences and their meaning to palaeoclimate since 2.4 Myr BP, and the sequence pattern and its development in northern China; and the recent climatic change (over about the past 2,000 years) and its relevance to human activities on the Loess Plateau and in northern China.

The first director of the new institute is Liu Tungsheng, with An Zhisheng as deputy director. Liu says he expects XLLQG to be a laboratory of international character. It is hoped that scientific and technical cooperation between China and other countries will not be limited to the exchange of research workers, but will also include joint ventures. This idea is fully supported by Academia Sinica and the new institute should provide a chance for investigators from all over the world to work in one of the really classic loess regions. **Ian Smalley**