Journal of Medical
Screening

Editorial

National Institutes of Health consensus development conference statement on genetic testing for cystic fibrosis

On 14–16 April 1997 an independent consensus development panel of medical and health policy experts was convened by the National Institutes of Health "to provide healthcare providers, patients, and the general public with a responsible assessment of the optimal practice for genetic testing for cystic fibrosis (CF)".[1] The panel performed its task commendably. This is the first time that American national guidelines have been developed for the clinical genetic use of a DNA test. The recommendations are likely to aid in developing guidelines for other DNA based genetic testing.

The panel concluded that testing should be offered to (*a*) adults with a positive family history of CF; (*b*) partners of individuals with CF; (*c*) couples currently planning a pregnancy; and (*d*) couples during early pregnancy, as a screening test for CF in the fetus. It was also recommended that health insurers provide reimbursement for this testing. Cystic fibrosis testing was not recommended for newborns (owing to lack of evidence of efficacy), or for carrier identification in the general population (primarily because interest in testing has been shown to be limited).

Cystic fibrosis is one of the most common genetic diseases in white people and currently affects more than 30 000 Americans. About 1000 new cases are diagnosed each year, usually within the first year of life. Lung, pancreatic, and intestinal complications can range from mild to severe. Although some individuals with CF lead productive lives into their thirties (and beyond), there has been little lifespan extension between 1990 and 1995. Thirty one years is the current median age at death, and 90% die from the lung damage. New experimental treatments include inhaled DNASE (which breaks down viscous DNA from neutrophils), inhaled proteases (to decrease mucus viscosity), and pharmacological stimulation of ion transport (to decrease viscosity of secretions). Double lung transplantation extends life but is not curative. Although the feasibility of gene therapy is under investigation, this potential "cure" is not expected in the near future. The panel appropriately emphasised the need for active research on improved treatments for affected individuals, further improvements in molecular diagnosis of CF, and better understanding of the pathophysiology.

The CF gene was identified in 1989, but the initial enthusiasm for applying this knowledge to population screening was dampened by the discovery that many different mutations can cause CF; more than 600 have now been identified. The ΔF508 mutation accounts for 30% to 70% of CF alleles in most populations, and 15 to 20 other mutations collectively account for 2% to 20% of the remaining alleles. Considering this background, the panel concluded that laboratories should offer white populations of northern European heritage prenatal screening capable of approaching identification of 90% of CF carriers (leading to an 81% detection rate of CF fetuses).

Prenatal screening of couples in most white populations using nine mutations (ΔF508, G551D, G542X, 621+1G–T, W1282X, N1303K, R553X, 3849+10kbC–T, 1717G-A) could detect about 85% of parent carriers and about 66% of CF fetuses. This test panel would detect more than 90% of Ashkenazi Jewish CF carriers and more than 80% of their CF fetuses. However, 20 to 30 mutations would have to be included to approach the 90% carrier detection level recommended by the panel. Cost effectiveness of the use of larger test panels using current technology is of concern.

Issues arising out of variations in the prevalence of CF mutations in different populations may lead to re-evaluation of some of the panel's recommendations. For example, the option of prenatal screening for fetal CF was recommended for all racial/ethnic subpopulations. However, given the considerable variability in CF prevalence and in testing sensitivity, CF screening may not be universally feasible. For example, the birth prevalence of CF in white American subjects of northern European heritage (1:2500) is 13 times higher than in Asian American subjects (1:32 000). Furthermore, the current operational maximum percentage of CF alleles that can be tested for in white subjects is 90%; in Asian Americans it is 30%. This means that the prenatal fetal CF detection rate for white subjects would be 81%, but would be only about 9% for

Asian Americans. If testing were to cost $75 per couple, the cost for each CF fetus detected prenatally would be about $240 000 for white couples, and about $26 675 000 (over 100 times higher) for Asian American couples. A similar situation is encountered in prenatal screening for Tay-Sachs disease. The relatively high prevalence of Tay-Sachs disease among Ashkenazi Jews justifies the cost of screening, but this is not true for the non-Jewish population, where the prevalence is much lower.

Prenatal couple based screening for the risk for fetal CF has been shown to be feasible and probably cost effective. Prenatal couple carrier testing, though more expensive and logistically more complex, may also be cost effective. It is appropriate to offer screening to couples during early pregnancy in conditions where test panel(s) of CF mutations can be cost effectively provided and where appropriate genetic counselling and the availability of prenatal diagnosis can be assured for couples who are found to be at high risk.

RICHARD A DOHERTY

Foundation for Blood Research
PO Box 190
Scarborough
Maine 04070 0190
USA

1 National Institutes of Health consensus development conference statement. *Genetic testing for cystic fibrosis.* 3 June 1997.

(http://odp.od.nih.gov/consensus/statements/cdc/106/106_stmt.html)