EDITORIAL

Prenatal screening for cystic fibrosis in the United States – time to re-evaluate implementation policies

In October, 2001, the American College of Obstetricians and Gynecologists (ACOG) released guidelines for prenatal and preconceptional carrier screening for cystic fibrosis (CF).[1] These guidelines, developed in partnership with the American College of Medical Genetics, set forth recommendations as to how screening practice should be conducted and provided a list of 25 mutations to be included in the screening panel. For practical purposes, this document served as a new standard of practice and launched prenatal screening for CF into the routine of medical practice in the United States. Subsequently, the number of tests for CF mutations in pregnant women (and their partners) rose precipitously[2], although as yet there is no assessment of the impact of CF screening on the health care system (for example, number of women screened, number of women's partners participating, number of high risk couples identified, decisions about amniocentesis and pregnancy termination). Even without these data, however, considerable insight has accumulated that can be put to use in reshaping and improving certain aspects of screening service delivery.

Pilot trials in the United States and Europe that set the stage for introduction of screening for CF used either a two-step ("sequential") or a one-step ("couple") model.[3] The two-step model called for the pregnant woman to be offered testing first, and then asked to have her partner come for testing if she were found to carry a mutation. The one-step model called for the two partners to be approached at the outset, with testing only being started after both had submitted samples. One partner's sample (usually the woman's) was tested first; if no mutation was found, the screening process was complete. A philosophical difference existed between these two models in that an important focus of the two-step model was individual carrier identification and counselling, while the one-step model considered the couple as a screening unit from the beginning and restricted counselling to couples where both were carriers (and, hence, needed to consider diagnostic testing). With the one-step model, women could receive information about individual carrier status, but only if they specifically requested it. The conclusion drawn collectively was that both models performed satisfactorily in the context of the trials, and both were able to identify the same proportion of high risk couples and affected fetuses, given a standardised set of CF mutations to be included in the screening panel.[3] The ACOG guidelines, however, recommended against use of the one-step model.

An unanticipated problem has now been documented by one CF laboratory in the United States which has instituted the two-step model for delivering this screening service.[4] That laboratory is successful in obtaining the necessary information about pregnant women to complete the first step of screening test interpretation, but is only able to obtain samples from 42 percent of partners of those women in whom a CF mutation has been identified. In some of these instances, the partner is known to be unavailable or unwilling to be tested, but samples from other partners often appear to be sent to other laboratories, because either a different physician is involved in ordering the test, or the sample is rerouted due to constraints imposed by insurance coverage. This, in effect, breaks the chain of continuity for the screening process in spite of programmatic-driven efforts to overcome this obstacle. The opportunity for errors in making the final interpretation, in which results of CF mutation testing for the pregnant woman and her partner must be combined is, therefore, increased. This type of problem is likely to be widespread, given the way in which medical practice is currently structured in the United States.

A more serious problem has arisen as a result of failure by some CF laboratories to implement programmatic components that include either of the two models used in the past trials. Instead, the laboratory's testing service is being offered in the absence of a formal model. In many cases, the laboratory is not able to determine whether a sample submitted for CF testing is for prenatal screening, for carrier testing, or for diagnostic purposes.[4] Under those conditions, an appropriate interpretation for the couple often is not possible. From a strictly legal perspective, the laboratory is only responsible for issuing a report that identifies whether or not a CF mutation is present in the submitted sample. From the ethical standpoint of assuring that the pregnant woman and her partner as a couple receive a complete and accurate screening interpretation, however, the laboratory is the logical entity to assume responsibility for coordinating the screening process.

Now that these problems with implementation have become clearly defined, prenatal CF screening services in the United States will need to be reevaluated and restructured to better meet the needs of screened couples. The one-step model[5] has recently been revisited as a way of overcoming many, and possibly all of the problems.[6] One prime feature of the one-step model requires that the laboratory have samples from both partners in hand before any testing is begun.[6] Treating the couple as the screening unit from the outset allows both partners to decide whether to be tested before the process is begun and assures that interpretation of screening results will be made in the proper context. False starts are also minimised (that is, the woman is found to be a carrier, but the partner decides not to be tested, or is unavailable). The down side is that more work will be required by health care providers and laboratories at the beginning of the screening process. Controversial issues about how to convey screening results, especially carrier status, would best be decided locally or regionally. Innovative approaches, such as supplying the couple with cards (similar to credit cards) embossed with information about carrier status, might help to merge philosophical views. Paramount to any change will be two considerations: the couple, rather than the individual, is the screening unit; and the laboratory-based CF screening service

is the logical coordinating entity for assuring the best possible product to the couple.

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