EDITORIAL

Couple screening to avoid thalassemia: successful in Iran and instructive for us all

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The recent report by Samavat and Modell[1] describing thalassemia screening in Iran is worthy of admiration and even a bit of envy from anyone who has been involved with planning and implementing screening programmes. Beginning 20 years ago, government policy makers in Iran developed a nationwide, fully integrated primary health care system that also recognized the importance of targeted education and data collection. Emphasis was initially placed on communicable diseases, but once this group of disorders was brought under control the focus broadened to include non-communicable diseases as well. The Ministry of Health and Medical Education subsequently chose thalassemia as the index disorder to examine the feasibility of disease prevention in this latter category. Table 1 summarizes the key features of the screening design.

This is a good example of couple screening.[2] In addition, the classic criteria for a worthwhile screening programme are satisfied,[3] though perhaps the offer of screening should be mandatory rather than screening itself. The disorder being screened for has serious medical consequences and it occurs sufficiently often to have an important societal impact. A remedy is available to couples with positive test results: avoidance of the disorder's occurrence in the next generation. The screening methodology is inexpensive and reliable. Diagnostic testing, when needed, is readily available, as are services for termination. A nationwide system is in place to deliver screening services and also to provide education.

In addition to reducing the thalassemia birth rate by 70%, a remarkable consequence of the introduction of thalassemia screening has been the revision of Iran's abortion policy, demonstrating how effective an integrated screening service can be when it encourages policy adjustment, based on systematic feedback by the recipients of testing. When couple screening was initiated in 1997, abortion was not permitted in Iran. Premarital testing avoided the serious dilemma associated with couples' learning of their risk for the first time during pregnancy, without having termination as an option. Couples' choices were limited to going forward as they would have without testing, postponing marriage (or, at least, childbearing), or separating and finding other partners. It quickly became apparent, however, that those being tested wanted to have prenatal diagnosis available. This pressure led to ethical discussions by Muslim scholars and others, resulting in a *fatwah* that allowed abortion during the first 15 weeks after the last menstrual period, when the fetus was diagnosed with thalassemia. Once this revised policy came into effect, the health community was able to notify at-risk couples who had been identified earlier, so that they, too, could avail themselves of this new and important option.

When the medical disorder being screened for is inherited in an autosomal recessive manner, it makes logical sense to classify the couple as a screening unit from the outset. Under that condition, further action is called for only when both partners carry the mutation; otherwise the screening test is negative. This can have a large effect on reducing the number of people who need special action on the basis of the result. It is reduced by the square of the prevalence of the mutation in the population in question; if the carrier rate is 5%, only 0.25% of couples need special action. There are no important health implications for an individual carrier. A similar approach to thalassemia screening has been used successfully in several areas of the Mediterranean.[4,5] By contrast, there has been considerable resistance to using the couple model for preconceptional and prenatal cystic fibrosis screening in the USA, even though a prospective intervention trial found it to be both practical and acceptable.[6] In that country, the prevailing view is that emphasis should be placed on identifying and counselling individual carriers, rather than restricting the focus to situations where both partners are carriers.

The different philosophy about how screening for recessively inherited genetic disorders should be conducted in the USA has led to the use of a 'sequential' model. Screening is initiated when the woman comes for medical care and opts for cystic fibrosis testing. When a mutation is identified, she is counselled and her partner is sought and counselled. The partner is then tested and, if a mutation is found, the couple receives further counselling. In practice this testing sequence has been associated with a high drop-out rate among partners of carrier women, either by refusal to participate or by unavailability, thereby invalidating the purpose of screening.[7] As a further complication, samples submitted for cystic fibrosis testing often lack sufficient information to determine whether they are for screening or other purposes. In other words, no model is being used and no programmatic methodology is in place to assure that screening takes place in an orderly fashion. The couple model would avoid these pitfalls by requiring that both

Table 1 Key features and screening sequence of Iran's national couple screening programme for thalassemia

Screening is mandatory
It is performed as part of pre-marital blood testing
Red cell indices are the initial test (usually mean cell volume or mean cell haemoglobin to identify microcytosis)
The man's indices are measured first
If microcytosis is found, the woman's indices are measured
If both partners show microcytosis, haemoglobin A_2 is measured
If haemoglobin A_2 is elevated in both, genetic counselling is provided
If haemoglobin A_2 is not elevated, iron is prescribed and indices re-measured
If microcytosis persists, further counselling is provided

partners agree to testing and submit samples at the outset, even though the second partner's sample is tested only if a mutation is found in the first partner's sample. In couple screening, information about individual carrier status is provided only if requested.

Once in place, a screening service relies on systematic feedback to guide modifications and improvements. The revision in Iran's abortion policy is one such example. In the USA, however, some important problems that relate to 'sequential' cystic fibrosis screening have not been extensively documented, due to the unavailability of a monitoring system. On the one hand, difficulties with certain of the original mutations in the recommended cystic fibrosis screening panel have become obvious because of dilemmas in interpretation faced by laboratories and counsellors. These have been highlighted and dealt with by the American College of Medical Genetics subcommittee charged with providing guidance.[8] On the other hand, there is no mechanism to document problems that lead to an inefficient expenditure of health resources, such as male partners dropping out of the screening process. We must learn from examples such as the Iranian programme reported by Samavat and Modell, where so many aspects of the screening process have been handled so well.

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