Ashkenazi Jewish genetic disease carrier screening

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To the Editor:

We read with interest and much concern the recent recommendation of the College regarding carrier screening in individuals of Ashkenazi Jewish (AJ) descent (*Genet Med* 2008;10: 54–56). Specifically, we felt that Recommendation 4, "if only one member of a couple is of AJ background, testing should still be offered," is quite problematic. As stated in the Guidelines, the cumulative probability of being a carrier for one of the conditions in the panel is between 20 and 25%. One in 4 or 1 in 5 couples where only one member is of AJ descent will be identified as at increased risk to have an affected child and offered testing for that specific condition for the non-AJ partner. The screening of the non-AJ partner for the mutations that occur in the AJ population is an exercise in unknown probabilities (Table 1). Since the frequency of those mutations that occur more often in the AJ population is unknown in non-AJ populations, there is no way to revise a couple's risk after screening the non-AJ member for the AJ mutations.

Counseling a couple that the non-AJ member does not carry any of the AJ mutations does not provide much solace (or information) regarding their risk for a child with one of the AJ genetic conditions. In the case of cystic fibrosis (where gene frequencies are known in various populations) and in the case of Tay-Sachs disease (where enzyme analysis is informative regardless of ethnicity) the Practice Guidelines do provide useful information that would aid a family in their decision-making process. Even without testing the non-AJ member, counselors can be reassuring to those couples where the AJ member is a carrier for Dysautonomia, Bloom syndrome, or Mucolipidosis IV, as these conditions are either extremely rare or unreported in non-AJ populations. So the question remaining (with the exception of cystic fibrosis and Tay-Sachs screening) is what do we accomplish by the implementation of these Guidelines in couples where only one member is of AJ descent?

Table 1
Probability of having an affected child if Ashkenazi Jewish partner is a carrier

Disease name	Carrier frequency in non-AJ	AJ partner is carrier/Risk for affected child	AJ partner is carrier/Non-AJ screen negative
Dysautonomia	1 confirmed non-AJ patient reported	Extremely small	Extremely small
Tay-Sachs	~1/300	1/1,200	? <1/1,200
Canavan	~1/500	1/2,000	? <1/2,000 mutations in non-AJ are diverse and private
Fanconi anemia (C)	~1/300 (all types)	1/1,200	1/1,200 since the AJ mutation is not found in non-AJ populations
Niemann-Pick (A)	~1/300	1/1,200	? <1/1,200
Bloom syndrome	Very rare	Extremely small	Extremely small
Mucolipidosis IV	No non-AJ patients reported	Extremely small	Extremely small
Gaucher type I	~1/200	1/800	? <1/800