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Reply to Sham

To the Editor:

We thank Dr. Sham for his thoughtful comments on our paper and regret our incorrect statement that Sham and Curtis (1995) recommended separate analyses for fathers and mothers. We agree that heterozygous parents can be treated independently under the hypothesis of no linkage or no association and that, in general, they are not independent when there is linkage and association. We agree further with Dr. Sham that we did not study the consequences of stratification in our simulations. As we mentioned in our Discussion, we were thinking more of admixture as a source of association when linkage is absent.

We differ from Dr. Sham in standing by our statements concerning the distribution of $T_{m\text{het}}$. We had noticed, as he has, that the variance of the statistic may be greater than that for a χ^2 variable, but our simulations focused on the whole distribution. The statements in our paper were therefore based on percentiles rather than just the variance. We made explicit mention of the significance level and power being well approximated by χ^2 theory in our simulations at that time.

We have now performed simulations for populations from which samples had the degree of sparseness and imbalance shown in the example of Dr. Sham. We have found that power levels for Monte Carlo (MC)–$T_{m\text{het}}$ were very similar to those obtained under the assumption of χ^2. We also found the power of MC-$T_{m\text{het}}$ to be very similar to that of the Sham and Curtis likelihood ratio test, and it may even be greater under some circumstances.

There is theoretical interest in the statistic T_m because power of the test can be predicted from a noncentral χ^2 distribution for which the noncentrality parameter may be estimated. However, we stress that we did not advocate use of the T_m statistic, even when it is used with a Monte-Carlo procedure.

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Family Cell Lines Available for Research—An Endangered Resource?

To the Editor:

Diabetes continues to be a major health problem that is continuing to grow not only in the United States, but worldwide, at an escalating cost to the patient as well as to society. The cost to the individual is tremendous, and a shortened life span is the outcome regardless of whether expert care to delay late complications is available. The genetic factors that control the insulin-dependent type of diabetes, type 1 diabetes, are still not understood. Genomewide scanning has confirmed HLA as a major genetic factor for type 1 diabetes and a number of potential loci for contributing genes (Davies et al. 1994; Todd et al. 1996). This task was in part accomplished and progress accelerated by investigator-supported initiatives to establish large collections of DNA and cell lines from multiplex type 1 diabetes families. Some 5 years ago, emerging new human genome technologies were available, but there was a shortage of families with type 1 diabetes to be analyzed for genetic linkage or association between the disease and polymorphic markers on human chromosomes.

In a letter to the editor (Lernmark et al. 1990), the availability of cell lines and DNA from the Human Biological Data Interchange (HBDI), a not-for-profit orga-