question the utility of MSAFP testing for women undergoing second-trimester amniocentesis for genetic reasons.

When we began performing genetic amniocentesis in 1980, we agreed with Elias et al. that there was no need to perform MSAFP testing on these patients since they were having amniotic fluid AFP (AFAFP) testing performed and AFAFP testing was far more accurate in evaluating the neural-tube status for the fetus than was MSAFP. However, in 1984 we began to perform routine MSAFP testing on such patients on a study basis to evaluate whether this test could provide any information that might prove predictive of high-risk pregnancy. In the first year, 19 out of approximately 500 of our prenatal genetics patients had high MSAFP results with normal AFAFPs. We did a careful follow-up of these 19 patients and found that 11 of them had a significant complication of pregnancy such as prematurity, pregnancy hypertension, SGA babies, placental problems, etc. Since this time, we have been providing MSAFP to between 700 and 1,100 genetic amniocentesis patients per year and have found a similar percentage of patients were correctly identified as high-risk pregnancies. The private obstetric practices in the Baltimore-Washington area to whom we provide prenatal genetics services have given us positive feedback on our accurate identification of this high-risk group of pregnancies. Our laboratory supervises over 10,000 MSAFP tests per year, including tests from several other obstetrical genetics groups in our area who have also begun to offer this service to their obstetrical genetics patients with results similar to ours. The high-risk pregnancies identified by having high MSAFPs and normal AFAFPs in our obstetrical genetics patients present obstetrical management problems that are not different from those of the much larger group of patients (approximately 110 out of 10,000 patients screened) identified as high risk by the routine MSAFP testing which is currently recommended by the American College of Obstetricians and Gynecologists for pregnancies. We should also point out that the additional cost for MSAFP before an amniocentesis is small in comparison to the significantly higher cost of the prenatal genetic testing which these obstetrical genetics patients are undergoing anyway.

We agree that there is no consensus in the obstetrical community on the optimal methods for surveillance for this high-risk pregnancy group. Obstetricians do routinely attempt to identify high-risk pregnancies such as women with previous pregnancy loss, intrauterine growth retardation, gestational and nongestational diabetes, and medical complications of pregnancy. In these high-risk pregnancies there is also often no general agreement on the optimal obstetrical management. However, the obstetrical community does feel that management of these high-risk pregnancies using closer clinical monitoring, nonstress tests, and more aggressive induction of labor is justified and may result in reduced morbidity and mortality for these patients (Baskett et al. 1987).

We hope that our study results will eventually help lead to the development of better monitoring techniques and protocols for the high-risk pregnancies which MSAFP screening may identify and thus will contribute to saving the lives of a significant number of fetuses in our future population.

MARK R. GEIER* AND JOHN L. YOUNG†
*Molecular Medicine, Inc.; and †Genetic Consultants, Bethesda, MD*

## References

Garver KL (1989) Update on MSAFP policy statement from The American Society of Human Genetics. Am J Hum Genet 45:332–334

Elias S, Simpson JL, Golbus MS (1990) Re: update on MSAFP policy statement from the ASHG. Am J Hum Genet 46:847

Baskett et al. (1987) Fetal Biophysical Profile and Perinatal Death. Obstet Gynecol 70:357

---

*Am. J. Hum. Genet. 47:741–742, 1990*

## Some Issues in the Study of Birth Defects and Recurrence Risks in Live Births and "Stillbirths"

*To the Editor:*

The interesting paper by Rasmussen et al. (1990) reports a surprisingly high proportion of false negative reports by mothers in response to queries regarding the presence of birth defects in their offspring. The sensitivity for all defects by their methods is only 61%, and much lower for some particular disorders.

The authors imply that, in view of their results, use of family history data obtained only through maternal interviews will falsely lower recurrence-risk estimates.

There are several reasons, however, why the results are not pertinent to recurrence-risk estimates. First, the authors used a *compound* question which asked initially only about the presence or absence of a health problem *or* a birth defect in a child. Only if the response was "yes" was there any follow-up question. Thus any

recent health problem might submerge recall of an earlier diagnosed *birth defect,* as they note.

Second, the query asked only about a diagnosis in the *first year of life.* A mother might be aware of a defect but believe it was diagnosed later in life, subsequent to the end of the first year. (This factor, incidentally, may also account for some of the few false positive replies especially with regard to positional defects of the legs. Some cases in controls may have been diagnosed after the first year [e.g., after the child began to walk] and thus not be in the authors' registry. Or, some mothers may have correctly recalled the presence of a problem, but not that the age of formal medical diagnosis was after one year of age.)

In any event, the methods used by the study are not representative of those used in eliciting family histories in genetic clinics, the usual source of recurrence-risk estimates.

Third, *neither* the study *nor* the control populations are representative of those families in which a recurrence of a defect has occurred. This is pertinent because a mother with an earlier child with a malformation is far more likely to recall the presence of a malformation in a later child, and recall it more accurately, than a mother with no such earlier affected child.

For the reasons above, the applicability of the results of the study to *recurrence*-risk estimates appears remote. (This is not to deny the value of validating the diagnosis of a defect reported in a history.)

On a separate matter, the "cases" of the study included stillbirths and live births, but the "controls" only live births, undermining the strict comparability of the two groups. It is quite unlikely there was as good ascertainment of significant defects, at least of internal organs, in "stillbirths" as in the live births in the same population group. (Non-autopsied stillbirths would dilute the rates here.) Thus the true "sensitivity" of the investigation for defects in stillbirths is likely to be significantly lower than the 56% Rasmussen et al. estimated on the basis of defects *of which they had knowledge.*

The differences in ascertainment and diagnosis of defects in live-borns and stillborns are so vast that the results on these categories should always be presented separately. And the precise definition of stillbirth used should always be specified because of the many different definitions of this term in current use (see, e.g., Hook 1982).

ERNEST B. HOOK

## References

Hook EB (1982) Incidence and prevalence as measures of the frequency of birth defects. Am J Epidemiol 116:743–747

Rasmussen SA, Mulinare J, Khoury MJ, Maloney EK (1990) Evaluation of birth defect histories obtained through maternal interviews. Am J Hum Genet 46:478–485

---

*Am. J. Hum. Genet. 47:742–743, 1990*

## Reply to Dr. Hook

We thank Dr. Hook for his insightful comments. In response to his first criticism, we had to limit our question to birth defects diagnosed in the first year of life because the maternal responses were compared with data from the Metropolitan Atlanta Congenital defects Program (MACDP) registry, which ascertains only birth defects recognized in the first year of life. We agree that this limitation may be responsible for some of the differences between maternal responses and registry data; however, we believe this restriction is likely to produce more false positives, which represent a small number in our study (about 2% of controls gave a false positive response). We consider the scenario depicted by Dr. Hook, in which the mother is aware of the presence of a defect but believes that it was diagnosed after the first year of life and therefore does not mention it, to be less likely.

Dr. Hook also warns that both our study and control populations are unlikely to represent families with a recurrence since these families would be more likely to accurately recall a birth defect. We are unaware of any evidence to oppose or support his statement; however, we look forward to the availability of more data in this area.

Dr. Hook also notes that data on stillbirths and live births should be presented separately. Actually, we did present separately the overall sensitivity and specificity for live births and stillbirths (fetal death at >20 weeks gestation or >500 grams) (see Rasmussen 1990, table 2) and the difference between the two groups was not statistically significant because of the small number of stillbirths in our data set. For this reason, we did not present sensitivity and specificity for live births and stillbirths for the 66 individual defect categories.

Dr. Hook's final point is that stillbirths are likely to be poorly ascertained by MACDP and that the true sensitivity among stillbirths is probably lower than what