Maternal Phenylketonuria

Prior to newborn screening and the availability of dietary treatment for phenylketonuria, most patients with classic phenylketonuria developed profound mental retardation and rarely reproduced.\cite{1,2} Newborn screening for phenylketonuria has been routinely available throughout the United States for approximately 25 years. Many infants who were identified as having elevated blood phenylalanine concentrations received dietary treatment. In most cases they have attained normal intelligence. A significant number of women who are no longer being treated have entered or are approaching their reproductive years. When diet is discontinued, elevated blood phenylalanine concentrations and other biochemical changes of classic phenylketonuria again become evident.

Children born to mothers whose blood phenylalanine concentrations exceed 0.6 mM (10 mg/dL) have an extremely high incidence of microcephaly and mental subnormality due to the teratogenic effects of phenylalanine and its metabolites.\cite{1-8} The incidence of other congenital anomalies, such as congenital heart defects, is also increased. When blood phenylalanine concentrations are less than 0.6 mM (10 mg/dL), the effect on offspring appears to be less severe and less constant. The outcome of such pregnancies is being investigated in a collaborative study sponsored by the National Institutes of Health.\cite{1-7} Additional data will become available soon.

All women with persistent phenylalanine elevations should be counseled prior to pregnancy about the possible adverse effect of their condition on their offspring. These women should also be counseled about the risk that their child might have phenylketonuria (approximately 1/120). Reproductive options should be discussed.

Women who decide to proceed with pregnancy should be advised that dietary treatment may improve the outcome for their child.\cite{2-4,7-9} There is increasing evidence that dietary treatments instituted prior to conception and maintained throughout the pregnancy may reduce the fetal morbidity associated with maternal PKU. Unfortunately, many women with hyperphenylalaninemia are unaware of the risks to their children and are no longer under the care of specialists who are aware of these risks.\cite{10} A major goal is to identify these women prior to pregnancy.\cite{1,2,11} The problem of maternal phenylketonuria therefore should be discussed with all women of childbearing age including adolescents and young adults with phenylketonuria. Pediatricians, internists, family practitioners, obstetricians, and health department and family planning clinic personnel should be advised of the dangers to future offspring of women who have elevated blood phenylalanine concentrations.

RECOMMENDATIONS

1. To optimize pregnancy outcome for women with PKU, the pediatrician should refer all young women with hyperphenylalaninemia to appropriate treatment centers where careful monitoring by a physician and nutritionist will allow for adequate maternal and fetal nutrition. This referral should antedate pregnancy.

2. Women who have given birth to children with microcephaly and retardation, without a known etiology, should have a blood screening test for hyperphenylalaninemia.

3. In cooperation with newborn screening programs and physicians caring for children with phenylketonuria, state health departments should develop a plan to establish and/or maintain contact with women identified as having elevated blood phenylalanine concentrations so that these women are kept informed about the implications of their condition and available treatment.

4. Further studies of hyperphenylalaninemic pregnancies are needed to define the optimal treat-
ment. Physicians are encouraged to refer women contemplating pregnancy to the National Maternal PKU study. (Dr Felix de la Cruz, National Institutes of Health, 301-496-1383)

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REFERENCES
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