

Before, Between & Beyond Pregnancy

The National Preconception Curriculum and Resources Guide for Clinicians

Annotated Articles Guiding Preconception Care of Women with PKU

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Platt LD, Koch R, Hanley WB, et al. 2000 The International Study of Pregnancy Outcome in Women with Maternal PKU: Report of a 12-year Study; Am J Obstet Gynecol; 182; 326-333

The Maternal PKU Collaborative Study began recruiting women who intended pregnancy or who were already pregnant in 1984 with a goal of including 200 mom-baby dyads. The intention was to initiate diet control before conception and maintain maternal phenylalanine (phe) levels between 120 and 600 micromolar. In 1988, four years into the study, the treatment plan was revised to maintain phe levels between 120 and 360 micromolar/L, as data showed a clear benefit in achieving these lower levels.

In 1992, the study was extended to include samples of 40-50 offspring whose mothers had control established either before conception or prior to week 10 of gestation as well as offspring of mothers with mild hyperphenylalaninemia (MHP). 100 normal control women were included. Sample acquisition was completed in 1995 with the last birth in 1996 and included 576 pregnancies with 414 livebirths and 162 spontaneous and elective abortions (28%) which is similar to the general population. 53 women had untreated non-PKU MHP and 361 women were prescribed diet therapy. 129 (36%) of the women began diet treatment before pregnancy, 180 (50%) started during the first trimester, 44 (12%) started during the second trimester, and 4 (1%) started during the third trimester. 4 (1%) patients refused treatment throughout. Consistent blood phe levels <600 micromolar occurred within 2 weeks of dietary therapy in only 27%. 393 (95%) of the pregnancies that resulted in live birth were to those women on a phe-restricted diet by 8 weeks; however, only 125 (30%) had control by 10 weeks. Control was defined by phe

levels consistently less than 600 micromolar. 61 women had control prior to conception, and 64 women had control established within the first 10 weeks. 34% of these 125 women had levels <360 micromolar.

From 1985 to 1995, mean maternal IQ increased from 80 to 88, mean maternal age increased from 21 to 23, and the number of maternal subjects who graduated from high school and attended college increased with a commensurate increase in the number of subjects with higher socioeconomic status over the 10 year period.

For psychological/intelligence testing:

Performance was best in offspring of control subjects followed by those with preconception control of their phe level and those with non-PKU MHP. Scores were lower in women who conceived prior to diet therapy, but were better than expected among women who achieved control before 10 weeks. Scores decreased substantially when dietary control was delayed beyond 20 weeks gestation. Similar patterns were seen at ages 1-2 on the Bayley Scales of Infant Development, at age 4-5 on the McCarthy Scales of Children's Abilities, and on the Wechsler Intelligence Scale for Children-Revised which was given after age 6, with an almost linear decrease in performance across the above groups. Microcephaly was similarly distributed.

For congenital heart defects (CHD):

At the time of publication, 31/414 (7.5%) were born with CHD. Of note, in a subsequent publication, 3 more children had been diagnosed with CHD. Of the 31 infants with CHD, 6 (19.4%) died. Also at the time of this publication, no infant born to a mom with non-PKU MHP or a preconceptionally treated mom was affected with CHD.

The authors again stress the importance of preconception dietary phe restriction, with attainment of phe levels <360 by 8-10 weeks resulting in substantially lower occurrence of congenital heart defects. Cognitive status seems to be even more sensitive with optimal intellectual performance in offspring of mothers well controlled prior to conception.

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