Normal Child by a Gestational Carrier of a Phenylketonuria (PKU) Mother-An Alternative to Diet

PiNian Chang* and Robert O Fisch
Emeritus Department of Pediatrics, University of Minnesota, Minneapolis MN, USA

Abstract
PKU mothers have a high incidence of spontaneous abortion. The consequences of untreated pregnancies are severely detrimental to their offspring. It manifested by intrauterine growth retardation with microcephaly, congenital malformations and abnormal intellectual development. Infants' pathology is independent of fetal genotype, but is directly correlated with excessive phenylalaninaemia of the mother throughout pregnancy. PKU mothers can produce healthy infant if they maintain a very restricted and controlled diet prior conception and during pregnancy. However to maintain a well-controlled diet prior to conception and during pregnancy is not possible in most cases, and significant mental and/or physical disability can result in children born due to either the delay or the not well controlled dietary treatment. We, previously, described the first child born using, non-PKU, gestational carrier with a PKU mother's egg and the husband's sperm. In this report, we present the normal developmental outcome of this infant at 4 years 7 month of age. We suggest that doctors who take care of PKU females could suggest gestational carriers as an alternative therapy for MPKU.

Introduction
Maternal phenylketonuria (MPKU) is a well-established teratogenic syndrome of children born to mothers with phenylketonuria (PKU). The ill effects of MPKU include mental retardation, intrauterine growth retardation with microcephaly, spontaneous abortion, and congenital heart disease [1-4]. As many of the female PKU patients, grow into adulthood with good metabolic control, normal intelligence and good quality of life. The importance of having unaffected offspring becomes an important issue. The MPKU collaborative study has clearly demonstrated the fact that healthy birth outcomes occurred when maternal metabolic control was attained before or very early in pregnancy and maintained through pregnancy [5,6]. However this is not a simple task for many MPKU patients. More importantly, many of the PKU patients of child bearing and rearing age do not keep regular contacts with the PKU centers. In a recent survey of long term follow ups [7], Lee et al. [8] also suggested that the lack of appropriate resources to care for pregnant women with PKU may compromise the outcome of the pregnancies. Therefore, it would be very difficult to attain good metabolic control before pregnancy starts. Clarke et al. [9] suggested the need to explore novel and non dietary approaches to the treatment of MPKU. In 1993, Fisch et al. [10] recommended in vitro fertilization using gestational mother as an alternative therapy for MPKU. Subsequently, a normal male infant was born using gestational carrier for a PKU mother [11]. In this report, we present the developmental outcome of this infant at 4 years 7 month of age.

Method
The child was brought to the Pediatric Psychology Clinic for physical measurements, individual testing and parental interview. The following instruments were used.

Achenbach child behavior checklist (CBCL)
The CBCL asks the caregiver to rate the frequency and intensity of a variety of behaviors. Scores are summarized as T-Scores with 40-60 representing the average range. Scores above 70 are considered clinically significant [12].

Stanford-Binet intelligence scales–fifth edition
The Stanford-Binet Intelligence Scales is a measure of general intellectual functioning. It provides estimates of the individual's general verbal and non-verbal abilities, as well as, abstract reasoning, knowledge, quantitative reasoning, visual-perceptual and working memory abilities. Scores are presented as standard scores with 85 to 115 representing the average range [13].

Maternal history
The mother of this child was born in 1975, she was considered as a "classical" PKU patient because her Phenylalanine (Phe) level was 2448 µ/l at 28 days of age when the diet was initiated. Diet was discontinued prior to 7 years of age. Her Phe level at the time of procedure was 1278 µ/l. The mother's last IQ score was 97 and she completed high school. Her gynecological history reveals one elective termination of pregnancy of 6 weeks' gestation, and right salpingectomy for ruptured right tubal pregnancy. She did not follow any diet. She has a close friend (22 years old who had a normal child) who agreed to become a gestational carrier.

Child's developmental status
Age: Four years and seven month.
Physical measurements
Height: 114 cm at the 95th percentile.
Weight: 20.5 kg at the 89th percentile.
mothers who are untreated for PKU have congenital abnormalities or developmental delay [22]. Considering all the factors that influence the concentration on Phe and tyrosine, i.e., daily amount of amino acid, protein and calories, disease, body temperature, activity, it is no wonder that children born to mothers treated for PKU are more likely reported to have abnormalities [23]. We do not have any data regarding PKU women who gave birth to children without being treated for PKU during pregnancy, or do we have the results of the outcome of the birth. But, we do know that the number of the PKU patients’ clinic visits decrease by age, and only one-third of clinics are providing care for patients beyond 18 years of age [14]. Therefore, there is a need for new approaches to try to reduce the birth of abnormal children of PKU mothers. We believe the use of gestational carrier is an alternative and should be suggested. Serious efforts have to be made to inform parents, the PKU patients as well as their future husbands and their families of the damaging consequences of maternal PKU. We also believe this information can also be given to patients at a younger age. Obviously, to find a volunteer woman who is willing to carry out someone else pregnancy is not an easy task either. But, the female member of the father’s family can be possible candidates. Gestational carrier also require financial commitment, it is an expensive treatment for the PKU mothers. The insurance companies currently not only pay for mothers with PKU but also pay for the future medical expenses of their handicapped children. In this paper, it is clearly shown that the use of gestational carriers can have normal developing offspring, both physically and intellectually. However, there has no mention of this approach as a viable alternative in the medical literature. It is important that all PKU patients need to be made aware of the use of gestational carrier as a viable option for a heath offspring. We want to thank the young woman who gives life for friendship.

Sources of Funding

The Minnesota PKU Foundation.

References

1. Mabry CC, Denniston JC, Nelson TL (1963) Maternal phenylketonuria. N Engl J Med 269: 1404-1408.
2. Fisch RO, Walker WA, Anderson JA (1986) Prenatal and postnatal developmental consequences of maternal phenylketonuria. Pediatr 37: 979-986.
3. Fisch RO, Doeden D, Lansky LL, Anderson J (1989) Maternal phenylketonuria: detrimental effects on embryogenesis and fetal development. Am J Dis Child 118: 847-858.
4. Stevenson RE, Huntley CC (1967) Congenital malformation in offspring of phenylketonuric mothers. Pediatrics: 40: 33-45.
5. Koch R, Hanley W, Levy K, Matalon R, Rouse B, et al. (2003) The maternal phenylketonuria project: a summary of progress in the United Kingdom. Pediatrics 112: 1553-1556.
6. Waisbren SE, Azen C (2003) Cognitive and behavioral development in maternal phenylketonuria offspring. Pediatrics 112: 1544-1547.
7. Fisch RO, Matalon R, Weisberg S, Michals K (1997) Phenylketonuria: current dietary treatment practices in the United States and Canada. J Amer Coll Nutr 16: 147-151.
8. Lee PJ, Lilburn M, Baudin J (2003) Maternal phenylketonuria: experiences from the United Kingdom. Pediatrics 112: 1553-1556.
9. Clarke JT (2003) The maternal phenylketonuria project: a summary of progress and challenges for the future. Pediatrics 112: 1584-1587.
10. Fisch RO, Tagatz G, Stassart JP (1993) Gestational carrier- a reproductive haven for offspring of mothers with phenylketonuria (PKU): an alternative therapy for maternal PKU. J Inher Metab Dis 16: 957-961.
11. Stevenson RE, Huntley CC (1967) Congenital malformation in offspring of phenylketonuric mothers. Pediatrics 40: 33-45.
12. Fisch RO, Stassart JP (2004) Normal infant by a gestational carrier for phenylketonuria mother: alternative therapy. Molecular Genetics and Metabolism 82: 83-86.
13. Achenbach, Thomas M (2003) Child Behavior Checklist, University of Vermont, 2001. Riverside Publishing, Standard Binet Intelligence Scale (5th edn.).

14. Fisch RO, Matalon R, Weisberg S, Michals K (1991) Children of fathers with phenylketonuria: an international survey. J Pediatr 118: 739-741.

15. Fisch RO, Burke B, Bass J, Ferrara TB, Mastrid A (1996) Maternal phenylketonuria – chronology of detrimental effects on embryogenesis and fetal development: pathological report, survey, clinical application. Pediatr Pathol 5: 449-461.

16. Lipson A, Buehler B, Bartly J, Walsh D, Yu J, et al. (1984) Maternal phenylalaninemia fetal effects. J Pediatr 104: 216-220.

17. Rohr F.J., Doherty LB, Waisbren SE, Bailey IV, Ampola MG, et al. (1987) New England maternal PKU project: prospective study of untreated and treated pregnancies and their outcomes. J Pediatr 110: 391-398.

18. Bessman SP (1979) The justification theory: the essential nature of nonessential amino acid. Nutr Rev 37: 209-220.

19. Weglage J, Finders B, von Teeffelen-Heilhoff A, Ulrich K (1993) Treatment of phenylketonuria: wish and reality. Monatsschr Kinderheilkd 141: 670-674.

20. Fisch RO (2000) Comments on diet and compliance in phenylketonuria. Eur J Pediatr 159: S142-144.

21. Weglage J, Wiedermann D, Finders B, Wilken B, Schubert D, et al. (1993) School performances and intellectual outcome in adolescent phenylketonuria. Acta Paediatr 82: 582-586.

22. Magee AC, Ryan K, Moore A, Trimble ER (2002) Follow up of fetal outcome in cases of maternal phenylketonuria in Northern Ireland. Arch Dis Fetal Neon 87: 141-143.

23. Farquhar DL, Steven F, Westwood A (1985) Preliminary report on inverse diurnal variation of phenylalanine: implication in maternal phenylketonuria. Hum Nutr Appl Nutr 39: 224-226.