Chapter 9: PKU and Pregnancy

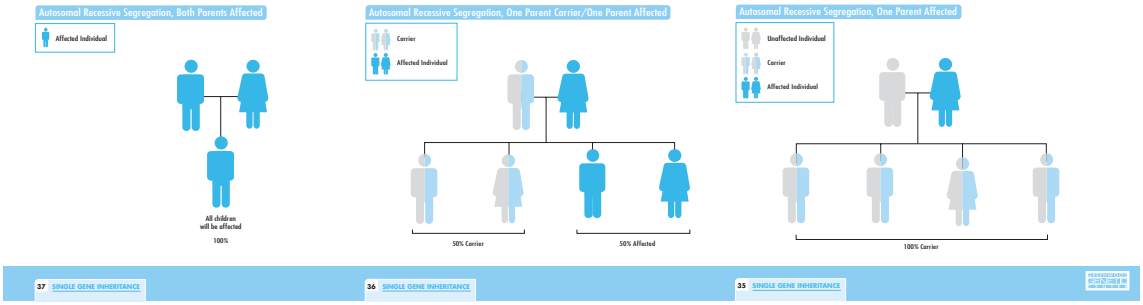
A Parent's Perspective

"Having PKU during pregnancy seemed like the biggest issue I would deal with; I was so wrong. There are worse things to deal with. PKU is manageable and if you follow your diet and stay in control, what seems scary becomes second nature." -Nicole, NJ

What to Expect

Women may experience a variety of emotions about having a child, both before and during pregnancy. Most parents feel concerns at one time or another about their ability to conceive, the health of a developing fetus, and how they will care for an infant. These feelings are all normal. For women with PKU, emotions around pregnancy may be heightened by worries about how their PKU disorder impacts the health of a developing fetus. With proper precautions and adherence to diet and treatment, women with PKU can have a normal pregnancy and a healthy baby

It is unlikely that an individual with PKU will have a child that also has PKU, although the child will always at least be a carrier. Testing to see if a partner carries the PKU gene is available. The partner must be a carrier in order for an individual with PKU to have a child with PKU. In a family where one child has PKU, prenatal testing may be available. However, because the treatment of PKU is so successful, it is rarely requested.



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PARENT 1	PARENT 2	CHILD
PKU	Non-PKU Non-PKU carrier	100% chance of being a carrier of PKU
	Carrier	50% chance of having PKU 50% chance of being a carrier
	PKU	100% chance of being affected with PKU

A Parent's Perspective

"At times the PKU diet may seem hard or even impossible to follow, but once you hold that perfect baby in your arms, you realize it wasn't hard at all!" - Laryssa, NY

PKU and Pregnancy

Maternal PKU Syndrome
While having a child with PKU may be a concern for individuals with PKU, an even more serious concern may be the effect a woman's PKU may have on her fetus. High Phe levels during pregnancy can result in miscarriage or cause Maternal PKU Syndrome (MPKU).

MPKU affects the fetus and is believed to be caused by high, uncontrolled Phe levels, which may include:

- Heart problems
- Small head size
- Physical deformities
- Slow development
- Brain damage[61]

A Parent's Perspective

"It's important to remind yourself on a regular basis that you CAN do this, that you ARE doing it, and that, at the end, you'll have a beautiful, perfect, healthy baby in your arms! That outcome makes anything you face totally |worth it!" -Kerry, NY

Studies show that the later a woman with PKU gains control of her Phe levels during pregnancy, the more likely it is that the child will have:

- behavioral problems such as aggressive "acting out" behaviors[62]
- attention issues
- difficulty developing friendships
- lower intelligence

It has also been found that timing of when the mother gains control of her Phe levels is connected to the child's intelligence quotient (IQ), with earlier control being related to higher IQs[63].

The potential damage high Phe levels during pregnancy can cause to your child can be very frightening. To prevent damage from occurring to the fetus, it is extremely important that you plan your pregnancies by:

- Meeting with your PKU team 3-6 months before pregnancy
- Fine tune your diet with formula and Phe intake
- Increase Phe level monitoring to 2-4 times per month
- Keep Phe levels in the range of 2-6 mg/dL for 2-3 months prior to conception

It's important to use birth control until you are able to lower your Phe to the recommended level for pregnancy. Following the recommended diet to ensure that Phe levels are low when you become pregnant – and stay low throughout your pregnancy – is the only way to ensure your fetus develops safely.

Contact your PKU team if you are thinking about planning a pregnancy. They can provide guidance on achieving and maintaining safe Phe levels before and during pregnancy. They can monitor your Phe levels closely to ensure that your levels are safe before conception. Any questions you have about your treatment during your pregnancy can be addressed by your PKU team.

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[61]Acosta PA, Yannicelli S. PROTOCOL 2 – Maternal Phenylketonuria (MPKU) Nutrition Support of Pregnant Women With Phenylketonuria (PKU) With PHENEX™-2 Amino Acid-Modified Medical Food *The Ross Metabolic Formula System Nutrition Support Protocols 4th Ed.* Colombus Ohio, 2001:12-27
[62]Ng TW, Rae A, Wright H, Gurry D, Wray J. *Maternal phenylketonuria in Western Australia: pregnancy outcome and developmental outcomes in offspring.* J Paediatr Child Health 2003;39 358-63
[63]Maillot F, Lilburn M, Baudin J, Morley DW, Lee PJ. *Factors influencing outcomes in the offspring of mothers with phenylketonuria during pregnancy: the importance of variation in maternal blood phenylalanine.* Am J Clin Nutr 2008:700-5

PKU and Pregnancy

If you become pregnant unexpectedly, contact your clinic team immediately. The PKU team can help you reduce your Phe levels which will improve the outcomes for your child. Also, if you are not already on diet, immediately go back on diet and take the medical formula as prescribed.

Treatment

The amount of natural protein and phe that each woman with PKU can have varies widely depending on the severity of her PKU and how rapidly the fetus is growing. During periods of rapid fetal growth, phenylalanine tolerance increases because the fetus has a higher demand for phenylalanine in order to build its body tissues. This will allow you to eat more natural protein. Frequent monitoring of blood phenylalanine levels show if a woman is getting the right amount of phenylalanine. If your level is less than 2mg/dL you may be able to tolerate more phenylalanine from natural foods. If your level is greater than 6 mg/dL you are most likely getting too much phenylalanine and/or not enough formula. Your dietitian will advise you about adjusting your diet[64].

Formula will remain the most important part of your diet throughout pregnancy, since it is your main source of protein. It provides all the amino acids needed for a woman and her developing baby, minus phenylalanine which cannot be properly metabolized in PKU. Formula also provides calories, vitamins and minerals, and increases your feeling of fullness. During pregnancy with PKU there is no way other than formula to provide sufficient protein for proper fetal growth and development.

For many women, especially those who are returning to diet for pregnancy, drinking the formula may be a major challenge. Taking the time prior to pregnancy to find a formula you enjoy drinking is important.

Formula is best used by the body and baby when you drink it throughout the day; usually three or four servings are recommended. Your formula prescription will be designed specifically for you by your metabolic doctor and dietitian to meet your changing needs.

Sometimes formula may be difficult to tolerate, especially during the early weeks of pregnancy when nausea and vomiting are common. Since formula is critical to your success, contact your metabolic clinic and Ob/Gyn if nausea and vomiting are prolonged[65].

Tips for Staying on Diet and Drinking Formula During Pregnancy

- *Mix formula with lemon or straw berry sorbet for a treat.*
- *Add a splash of seltzer for carbonation. Bubbles may help the formula go down easier.*
- *Increase the amount of water in your formula to meet additional fluid needs and prevent dehydration.*
- *Food cravings are sometimes common to pregnancy. Make a list of foods you desire and match with foods you can have. For example; low protein cakes, muffins, and chips.*
- *Keep a journal of your food and formula intake. It is the best way for you & your metabolic team to examine and control your diet.*

[64] Maltzman, S, : *My PKU Toolkit A Transition Guide to Adult PKU Management*. New Jersey : Applied Nutrition Corp. 2007:56-57
[65]Maltzman, S, : *My PKU Toolkit A Transition Guide to Adult PKU Management*. New Jersey : Applied Nutrition Corp. 2007:56

PKU and Pregnancy

Controlling Phe

As your needs and the needs of your developing baby change each trimester, your PKU team may adjust your diet or medical formula as necessary, keeping a close watch on Phe levels to ensure they stay in the safe range. Both Phe and tyrosine blood levels are monitored closely throughout pregnancy. Tyrosine supplements may be prescribed if your level is low. It is important during pregnancy that you:

- *Take your medical formula consistently.* Drinking your formula as it is prescribed will help you get the caloric intake your body requires each day. Eating a small amount of low protein bread, pasta or crackers 15 minutes before you take your medical formula may help settle your stomach so you can drink it more easily.
- *Drink formula in small, frequent doses to help with formula tolerance.*
- *Eat regular small frequent meals.* Gaining or maintaining weight will help keep Phe levels in the safe range. Losing even a little weight at this time can make your blood Phe levels higher. Eating small frequent meals will also help prevent heartburn.
- *Maintain frequent blood tests.* Your clinic team will advise you if Phe levels need to be monitored more closely so that your diet and formula can be adjusted as needed.
- *Keep track of your Phe intake.*

Phe levels may start to drop in the 2nd and 3rd trimester due to increased growth of the fetus. You may be able to start eating more Phe in your diet. Your dietitian will monitor your Phe levels and make recommendations about the best way to increase your Phe intake.

Common Difficulties during Pregnancy

Many women feel sick to their stomach during pregnancy, especially in the first trimester, which may make it difficult to hold down your medical formula and food. Heartburn and constipation may also be a problem. These tips may help:

- Eat small amounts of prescribed food hourly while awake.
- When you wake up, eat some prescribed low-protein crackers.
- Drink fluids, especially water, between meals.
- Avoid fried or spicy foods and unpleasant smells.
- Eat only lightly seasoned foods
- Try plain fruits with skins and vegetables (raw vegetables may help with constipation).
- Eat some prescribed food before preparing meal.
- Sit up straight while you're eating, chew carefully and eat slowly.
- Go for a walk after eating.
- Avoid stooping or lying down after eating to reduce heartburn.
- For constipation, try having high fiber cereal in the morning and drinking prune juice.
- Daily exercise is always healthy, and continues to be during pregnancy. It can help with constipation and make you feel better overall[66].

[66] Acosta PA, Yannicelli S. PROTOCOL 2 – Maternal Phenylketonuria (MPKU) Nutrition Support of Pregnant Women With Phenylketonuria (PKU) With PHENEX™-2 Amino Acid-Modified Medical Food *The Ross Metabolic Formula System Nutrition Support Protocols 4th Ed.* Colombus Ohio, 2001:41

PKU and Pregnancy

Kuvan® during Pregnancy

In a small number of women with PKU studied, Kuvan® (sapropterin dihydrochloride) has been found to help control Phe levels during pregnancy[67]. There have been no harmful effects of the fetus reported with Kuvan use. However, the number of pregnancies exposed is too small to be certain that there are no adverse effects. Additional studies are needed on the safety and effectiveness of using Kuvan during pregnancy[68].

Blood Phe Monitoring and Health Assessments

High levels of Phe at any time during your pregnancy may harm your baby. Your fetus will be monitored with ultrasound examinations throughout your pregnancy to ensure that development is on track. It is essential that you follow your diet and take the medical formula as prescribed before and throughout your pregnancy to control your Phe levels and to ensure that you have enough tyrosine in your blood[69].

Blood Phe monitoring is also especially important while planning and throughout your pregnancy. In addition to monitoring your Phe levels, your clinic will also monitor your nutritional status to ensure you have the nutrients required to support you and your developing fetus throughout your pregnancy. Other assessments may include

- Complete blood count (test for anemia)
- Metabolic profile (chemistry panel)
- Prealbumin
- B12
- Selenium
- Total cholesterol
- Ferritin
- Folate

If your PKU team finds that your diet isn't providing enough of certain nutrients, supplements will be recommended.

Special Considerations

Parenting with PKU

Congratulations! You're the parent of a beautiful newborn baby! Like all parents, this is an exciting and stressful time. It may be even more stressful for a mother with PKU. Many women with PKU think that once the baby is delivered, relaxing their diet is acceptable. Many mothers report that they no longer use their medical food once their child is born[70].

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[67]Koch R. Maternal phenylketonuria and tetrahydrobiopterin Pediatrics 2008:1367-8
[68]Trefz FK, Blau N. *Potential role of tetrahydrobiopterin in the treatment of maternal phenylketonuria.* Pediatrics 2003:1566-9
[69]Acosta PA, Yannicelli S. PROTOCOL 2 – Maternal Phenylketonuria (MPKU) Nutrition Support of Pregnant Women With Phenylketonuria (PKU) With PHENEX™-2 Amino Acid-Modified Medical Food *The Ross Metabolic Formula System Nutrition Support Protocols 4th Ed.* Colombus Ohio, 2001:35
Rohr F, Munier A, Sullivan D, Bailey I, Gennaccaro M, Levy H, Brereton H, Gleason S, Goss B, Lesperance E, Moseley K, Singh R, Tonyes L, Vespa H, Waisbren S. *The Resource Mothers Study of Maternal Phenylketonuria: preliminary findings* J Inherit Metab Dis 2004:145-55

PKU and Pregnancy

However, high Phe levels result in a variety of issues that may impair your ability to properly parent your child. It has been shown that home environment has a direct impact on a child's development. Controlling your Phe levels may help you provide your child with the stimulating environment that helps a child thrive[71,72]. Diet for life is recommended and important for your health and may help with your ability to parent.

Increased Phe levels are associated with:

- *Lower IQ*
- *Thought disorders*
- *Mood disorders, like depression*
- *Learning difficulties*
- *Mental processing issues*
- *Personality disorders*
- *Anxiety*
- *Behavioral problems*[14]

You may also be concerned about the potential for Maternal PKU Syndrome, and whether your baby has PKU. Newborn screening will be done to determine whether your child has PKU. Even if your baby does have PKU, he or she can still be breastfed (see Chapter 4 for more information on breastfeeding and managing PKU for an infant).

Mothers with PKU can breastfeed their child. If you maintain your diet, breastfeeding will not result in your baby being exposed to high Phe levels. In fact, breastfeeding may even keep your Phe levels a little lower.

Working closely with your PKU team to ensure that your Phe levels remain controlled is important, and if your baby has PKU, that his or her Phe levels are also controlled. Your PKU team is there to support and guide you, especially at this important time in your life.

[71]Waisbren SE, Hanley W, Levy HL, Shifrin H, Allred E, Azen C, Chang PN, Cipcic-Schmidt S, de la Cruz F, Hall R, Matalon R, Nanson J, Rouse B, Trefz F, Koch R. *Outcome at age 4 years in offspring of women with maternal phenylketonuria: the Maternal PKU Collaborative Study.* JAMA 2000:756-62

[72]Waisbren SE, Chan P, Levy HL, Shifrin H, Allred E, Azen C, de la Cruz F, Hanley W, Koch R, Matalon R, Rouse B. *Neonatal neurological assessment of offspring in maternal phenylketonuria.* J Inherit Metab Dis. 1998:39-48

[14] American Academy of Pediatrics Committee on Genetics Policy Statement: maternal phenylketonuria. Pediatrics 122 (2008) 445-449