

# Maternal Phenylketonuria (PKU)

## Information for women who have maternal phenylketonuria during pregnancy or breastfeeding

The information provided below is for readers based in the United States of America. Readers outside of the United States of America should seek the information from local sources.

### What is phenylketonuria?

Phenylketonuria (PKU) is a recessive genetic condition, meaning that you have the condition if you received two gene copies that cause the same defect, one copy from your mother and the other from your father. Normally, the two gene copies encode an enzyme called *phenylalanine hydroxylase* (PAH). This enzyme is needed to convert the amino acid phenylalanine into a different amino acid, called tyrosine, which can be utilized by the body to make proteins, and also converted into still other amino acids, by other enzymes. More than 500 mutations making the gene for PAH defective have been identified. A combination of any two defective genes for this enzyme in the same individual leads to PKU but, depending on the particular mutations, the individual may have some amount of enzyme activity. If PKU is identified early in infancy, its effects can be minimized with a special diet that limits the amount of phenylalanine that you ingest.

If you have PKU and are pregnant, probably your PKU has been controlled quite well. Also, if your partner does not carry a PKU gene, the baby, though a carrier for PKU, will not have the condition as you do. Nevertheless, the levels of phenylalanine in your blood have to be kept at a particularly low level during pregnancy (below 360  $\mu\text{mol/l}$ ). Otherwise, the concentration of phenylalanine will rise to dangerous levels in the blood of your baby. If this happens, the development of organs in the baby, including the brain and heart, will be abnormal, leading to severe, possibly fatal consequences. If the blood concentration is just a little too high, there may not be obvious effects on internal organs, but there could be effects on mental function, because of subtle damage to the brain. Problems in mental function can show up as difficulties in reasoning or problem solving, hand-eye coordination, attention, communication ability, and overall IQ.

## **How common is PKU during pregnancy?**

In North America, PKU occurs in approximately 1 person per 100,000. The prevalence of the condition varies greatly around the planet. In Turkey, for example, the prevalence of PKU is very high with 1 case per every 2,600 people. PKU is also fairly common in Ireland.

It is very unlikely that you would have PKU and find out about it as an adult because newborns have been screened for PKU since the 1960s. On the other hand, since management of PKU depends on a special diet, it is not uncommon for the condition to worsen in early adulthood, due to the individual going to live on her own and letting her diet lapse.

## **How is PKU during pregnancy diagnosed?**

Nearly all cases are diagnosed very soon after birth because newborns are screened for the condition. However, if you were diagnosed with PKU as a newborn, the condition will stay with you, if and when you become pregnant. Additionally, since you will pass on an abnormal PAH gene to your child, your doctor will recommend genetic counseling and referral to a medical genetics specialist. This may lead to further tests both for you and the child's father, first to see whether he is a carrier for PKU. Should he be a carrier, the developing baby would then have a 50 percent chance of having PKU and it will be very helpful to know which specific PAH mutations you and the father possess. Testing of the developing baby will also be possible.

## **Does PKU cause problems during pregnancy?**

As with a non-pregnant person who has PKU, if the concentration of phenylalanine in the blood is too high, mental difficulties can develop. These can include problems in concentration, memory, or reasoning. During pregnancy, such effects can interfere with one's ability to take care of herself, which ultimately can harm the pregnancy.

## **Does PKU during pregnancy cause problems for the baby?**

For the proper development of the developing baby, the mother's blood concentration of phenylalanine must be kept within the range of 120-360  $\mu\text{mol/l}$ . The reason for the lower limit of 120  $\mu\text{mol/l}$  is that everybody needs some phenylalanine in order to build proteins. If the level of phenylalanine rises about 360  $\mu\text{mol/l}$ , the developing baby is at high risk of developing what doctors called "maternal PKU (MPKU) syndrome", which can include any or all of the following complications:

- Microcephaly (small head and brain)

- Poor fetal growth
- Congenital heart defects (CHD -- malformation of structures within the heart or the great vessels connected to it). Elevated blood levels of phenylalanine during the first 810 weeks of gestation elevate the CHD risk.
- Fetal growth retardation
- Non-familial facial features (the babys face looks as if the baby were not biologically part of the family)
- Intellectual disability

### **What to consider about taking medications when you are pregnant or breastfeeding:**

- The risks to yourself and your baby if you do not treat the PKU. These can be significant
- The risks and benefits of each medication you use when you are pregnant
- The risks and benefits of each medication you use when you are breastfeeding

### **What should I know about using medication to treat PKU during pregnancy?**

The only medication approved for the treatment of PKU is sapropterin. It is effective in roughly 25-50 percent of mothers who are deficient in the enzyme PAH and it is not harmful to the developing baby. If your PKU is the result of mutations from both of your parents that cause you to make no PAH enzyme at all (null mutations"), then sapropterin probably will not work for you. However, along with the special diet, you will be given a trial of sapropterin to see if it does help. Additionally, there is an experimental treatment being tested in clinical trials called "large neutral amino acids (LNAA)". Although LNAAs appear to be very effective, there is concern that they may harm the fetus, so this particular treatment should be avoided during pregnancy.

### **Who should NOT stop taking medication for PKU during pregnancy?**

If sapropterin works for you, there is no reason to stop taking it during pregnancy. In fact, ceasing to take it would be harmful for both you and your baby.

### **What should I know about choosing a medication for my PKU during pregnancy?**

Sapropterin does not appear to be harmful during pregnancy, but LNAAs may be harmful.

You may find Pregistrys expert reports about the individual medications to treat maternal PKU [here](#). Additional information can also be found in the sources listed at the end of the report.

### **What should I know about taking a medication for my PKU when I am breastfeeding?**

Sapropterin is thought to be safe, whereas allowing the maternal blood concentration of phenylalanine to rise could be dangerous if the baby has PKU. If the baby does not have PKU, the mother nevertheless must continue her treatment to benefit her own health.

### **What alternative therapies besides medications can I use to treat my PKU during pregnancy?**

The main treatment for PKU is not medication, but rather a special diet, consisting of food that is very low in phenylalanine. The medication mentioned above, sapropterin, can be used together with the special diet, but the diet is mandatory. The diet consists of simple foods that are very low in phenylalanine plus medical foods, which are foods that are produced specifically with protein that is free of phenylalanine. There are products that you must specifically avoid, such as certain artificial sweeteners. The treatments depend on routine monitoring of the blood levels of phenylalanine to make sure that they do not get too high, nor, by the way, too low, as you and the baby need some of this amino acid. It is plausible that within several years, gene therapy to cure PKU will become available.

### **What can I do for myself and my baby when I have PKU during pregnancy?**

Work with your doctors to keep your phenylalanine level within the needed range, adjusting your diet as need

### **Resources for PKU in pregnancy:**

For more information about **PKU** during and after pregnancy, contact <http://www.womenshealth.gov/> (800-994-9662 [TDD: 888-220-5446]) or read the following articles:

- New England Consortium for Metabolic Problems: [PKU in Pregnancy](#).
- March of Dimes: [PKU](#).

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## **General information**

It is very common for women to worry about having a miscarriage or giving birth to a child with a birth defect while they are pregnant. Many decisions that women make about their health during pregnancy are made with these concerns in mind.

For many women these concerns are very real. As many as 1 in 5 pregnancies end in a miscarriage, and 1 in 33 babies are born with a birth defect. These rates are considered the background population risk, which means they do not take into consideration anything about the health of the mom, the medications she is taking, or the family history of the mom or the baby's dad. A number of different things can increase these risks, including taking certain medications during pregnancy.

It is known that most medications, including over-the-counter medications, taken during pregnancy do get passed on to the baby. Fortunately, most medicines are not harmful to the baby and can be safely taken during pregnancy. But there are some that are known to be harmful to a baby's normal development and growth, especially when they are taken during certain times of the pregnancy. Because of this, it is important to talk with your doctor or midwife about any medications you are taking, ideally before you even try to get pregnant.

If a doctor other than the one caring for your pregnancy recommends that you start a new medicine while you are pregnant, it is important that you let them know you are pregnant.

If you do need to take a new medication while pregnant, it is important to discuss the possible risks the medicine may pose on your pregnancy with your doctor or midwife. They can help you understand the benefits and the risks of taking the medicine.

Ultimately, the decision to start, stop, or change medications during pregnancy is up to you to make, along with input from your doctor or midwife. If you do take medications during pregnancy, be sure to keep track of all the medications you are taking.