# POSITIVE PREGNANCY OUTCOME IN WOMEN WITH PHENYLKETONURIA IS POSSIBLE!

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## What is Phenylketonuria (PKU)?

A rare autosomal recessive hereditary metabolic disorder

Maternal phenylketonuria were first described by Dent in 1957, and by Mambry in 1963 (1)

The world's first newborn screening test was introduced by Robert Guthrie in early 1960s via *Guthrie's test* for PKU

The epidemiology of phenylketonuria in the UK is estimated as 1 in 14,300 (2)

In 2004, mean prevalence in Wales is approximately 1: 10 700 newborns (3)

In 2016-17, the incidence rate of positive screening tests for phenylketonuria was 0.0137% (107 babies screened positive and 779,688 babies were tested) (4)

## Case Summary

A 37-year-old G3 P1+1 lady with **congenital phenylketonuria**, BMI of 38.8 kg/m$^2$ is presently 27 weeks pregnant

She had a **positive outcome in her last pregnancy** following commendable effort from her clinicians combined with her compliance

Patient had **optimised Phenylalanine (Phe) levels** with **excellent adherence to PKU treatment prior to** and **throughout** her last pregnancy. At 20 weeks gestation, tyrosine supplements were arranged due to low tyrosine levels <50µmol/L (refer to the metabolic pathway below), she also developed hypothyroidism in pregnancy

At 30 weeks, she was referred to Fetal Medicine Unit with **suspected fetal growth restriction** and was delivered by elective caesarean section at 37$^{+5}$ weeks for the same reason

A baby girl was born with **good apgars** weighing **2.3kg** with **no intrapartum or immediate postnatal complication**

Both were discharged home after day 2

## Pathogenesis of Phenylketonuria (PKU)

An inborn error of phenylalanine (Phe) metabolism caused by:

- Deficiency of phenylalanine hydroxylase activity
- Reduced metabolism of BH4

Phe accumulates in the blood and brain

High concentrations of Phe byproducts (phenylpyruvic acid and phenylethylamine) are produced.

They become neurotoxic above a threshold concentration

Therefore, if left untreated, it can lead to irreversible intellectual disability, microcephaly, motor deficits, eczematous rash, autism, seizures, developmental problems, aberrant behaviour and psychiatric symptoms (5)

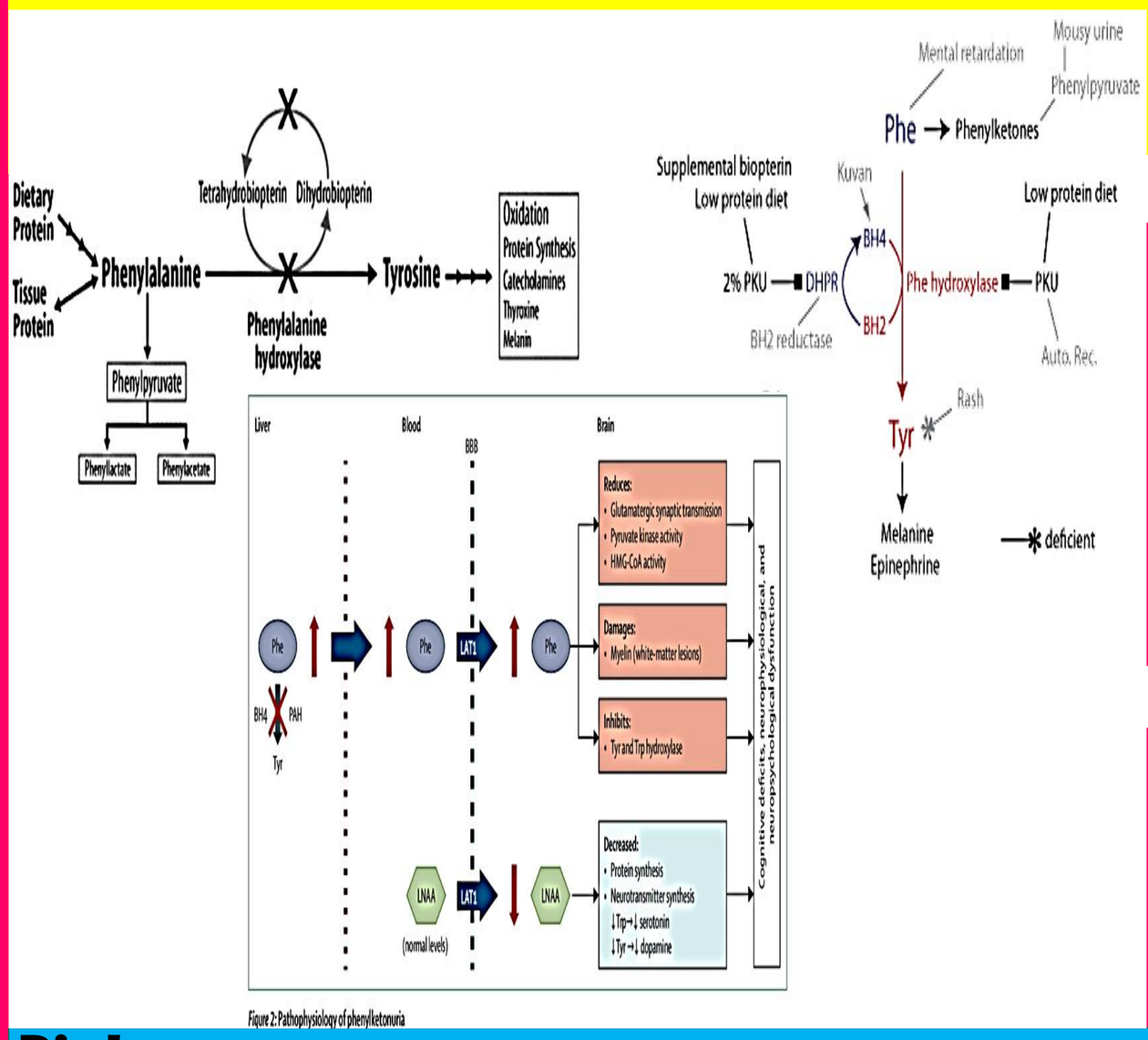


Figure 2: Pathophysiology of phenylketonuria

## PKU Dietary Intervention

Mainstay treatment – lifelong low Phe diet with Phe-free L-amino acid supplements

During pregnancy,

- Achieve total protein intake of 70 g/day by having more Phe free protein supplement
- If nausea and vomiting, energy supplements to prevent weight loss
- If tyrosine levels fall below the normal range, add L-tyrosine supplements
- Monitor Phe levels weekly to ensure levels within the accepted range of 60-240umol/l
- Sapropterin, the only pharmacological option available to PKU patients, is currently commissioned by NHS England to pregnant mothers
- Encourage normal pregnancy weight gain (11-16kg for BMI of 18.5-24.9; 5-9kg for BMI > 30) to reduce microcephaly

Studies on women with PKU have found that up to 65% of them discontinued the special diet because of its unpleasant taste (6)

Matalon et al. have confirmed that the highest occurrence of microcephaly (58%) was found in pregnant women who gained < 70% of recommended weight gain (7)

| Avoid | Include |
|---|---|
| Meat | Most fruit |
| Eggs | Some vegetables |
| Chicken | Sugar |
| Fish | Butter |
| Milk | Boiled sweets |
| Cheese | Some squashes |
| Other dairy products | Low-protein flour |
| Nuts | Low-protein bread |
| Bread | Low-protein pasta |
| Biscuits | Low-protein biscuits |
| Cakes | Low-protein energy bars |
| Pasta | Egg replacer |
| Aspartame (Nutra Sweet®) | |

## PKU in Pregnancy

Prior to 1963, very few women with PKU had successful obstetrics outcome in pregnancy.

Most of them suffered brain damage at childbearing age

Newborn screening has successfully allowed these women to survive past childbearing age

Goal of PKU treatment during pregnancy aims to prevent maternal PKU syndrome

High blood Phe levels during pregnancy is teratogenic

It can result in miscarriage, growth retardation, microcephaly, intellectual disabilities and birth defects, including congenital heart defects (8)

Optimising care of these women preconception and throughout the pregnancy is therefore imperative

## Conclusion

Family planning and preconception counselling are crucial to help support woman with phenylketonuria.

Maintaining normal plasma Phe levels <300µmol/L at least two weeks prior to conception and throughout pregnancy via more frequent monitoring by the pregnant woman herself and dietician is important to help boost chances of favourable obstetric outcomes.

Overall, pregnancy in women with PKU can result in a healthy baby if there is a dedicated multi-disciplinary team which includes the pregnant woman herself who has ultimate control with regards to the food she eats or does not eat while she is pregnant.

## References

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