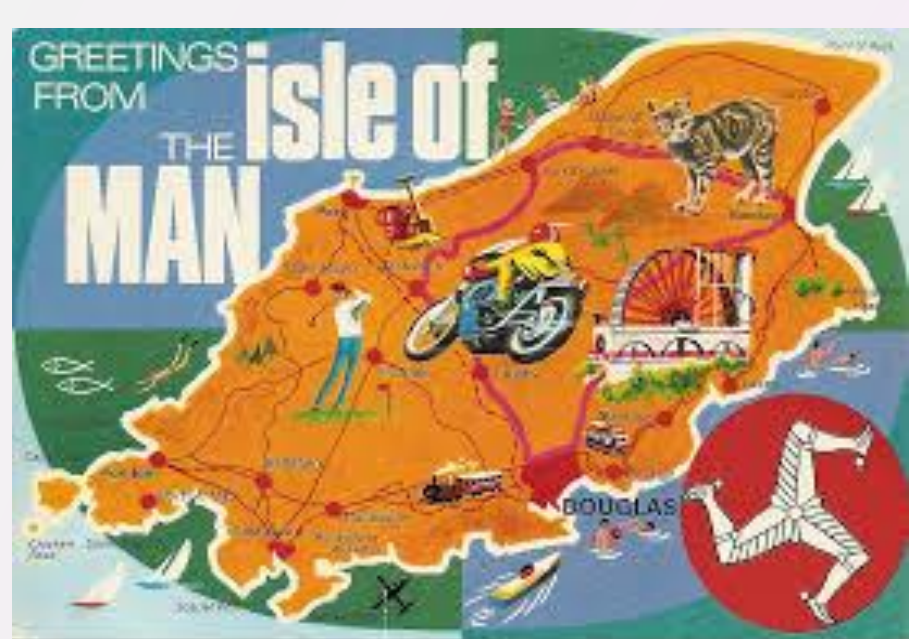




Management of Phenylketonuria in Pregnancy in a Peripheral centre

Saleena Moideenkutty MD FRCOG; Geetha Indira MD FRCOG ; Mr Mohie El Khadem MRCOG; Mrs Michelle Moroney FRCOG
Department of Obstetrics and Gynaecology, Nobles Hospital , Isle of Man

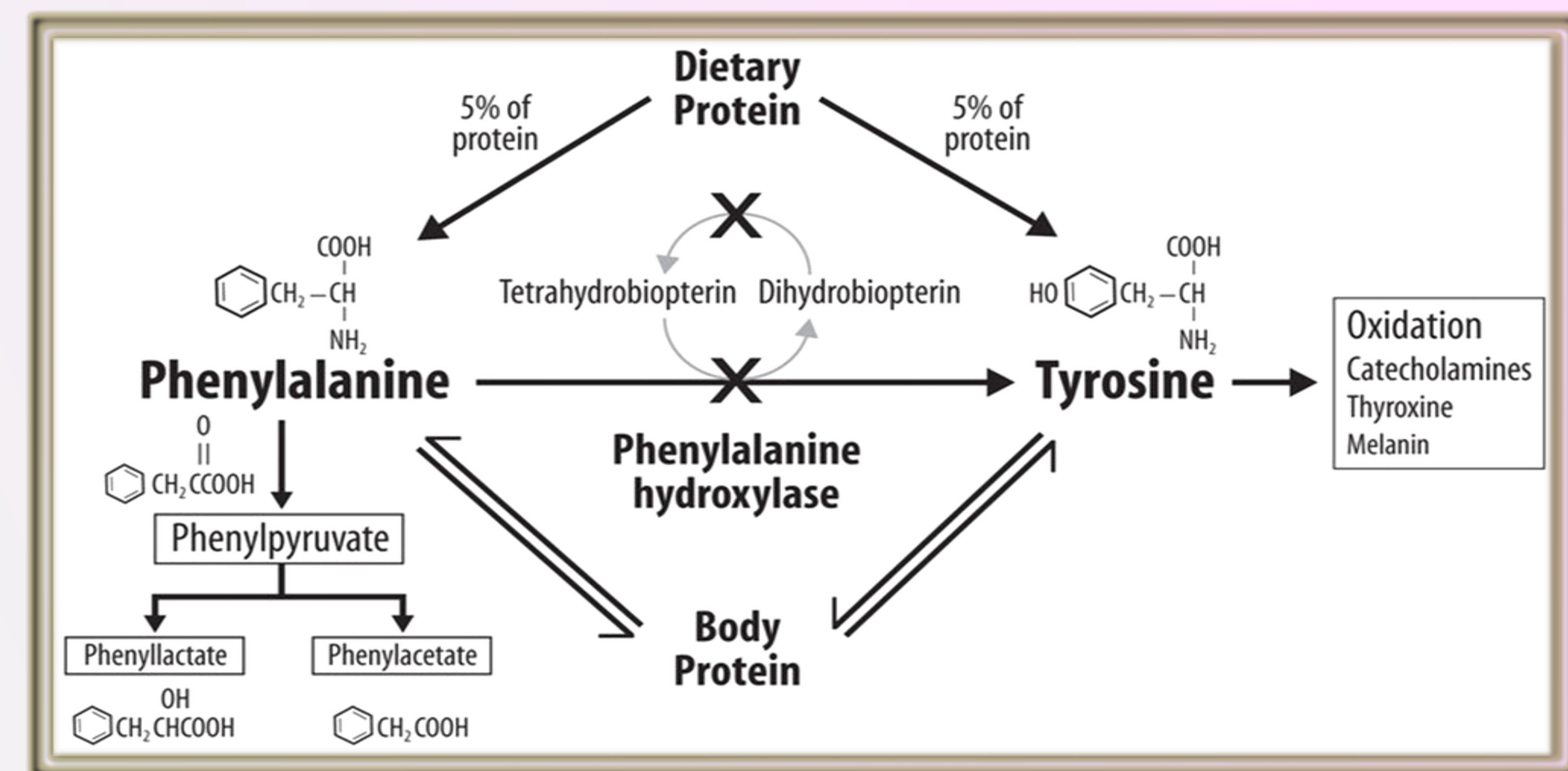


Abstract:

Phenylketonuria (PKU) is a rare autosomal recessive metabolic disorder characterised by inability to utilise the essential amino acid phenylalanine. The prevalence is 1/10000 in European population. In pregnancy if untreated or sub optimally treated it leads to Phenylalanine Embryopathy.

Introduction:

PKU is a disorder affecting the aromatic amino acid phenyl alanine, resulting from a deficiency of the hepatic enzyme Phenylalanine hydroxylase(PAH).This catalyses the conversion of Phenylalanine to Tyrosine.(BH4) is a co factor required for PAH activity. This accounts for the catabolism of 75% of the dietary Phenylalanine with remainder used for protein synthesis. A deficiency results in elevated levels of Phenylalanine (PA), phenyl acetate and phenyl lactate, which affects brain growth, myelination and neurotransmitter synthesis. In pregnancy this results in IUGR, Intellectual disability , microcephaly and cardiac malformations in the fetus. The risk of abnormalities depends upon the maternal blood phenylalanine concentration .Clinical picture is similar to that of Alcohol Embryopathy. Diagnosis is based on an elevated serum phenylalanine concentration followed by molecular testing. Its classified into Classic PKU(>1200micromol/L); Moderate PKU (900 -1200); Mild PKU(600-900); Mild Phenylalninemia(360 - 600); Benign mild phenylalaninaemia (120 - 360). Mainstay of treatment is dietary restriction. Pharmacotherapy is available like, a synthetic formulation of BH4 called Sapropterin and GMP (Glycomacropeptide)

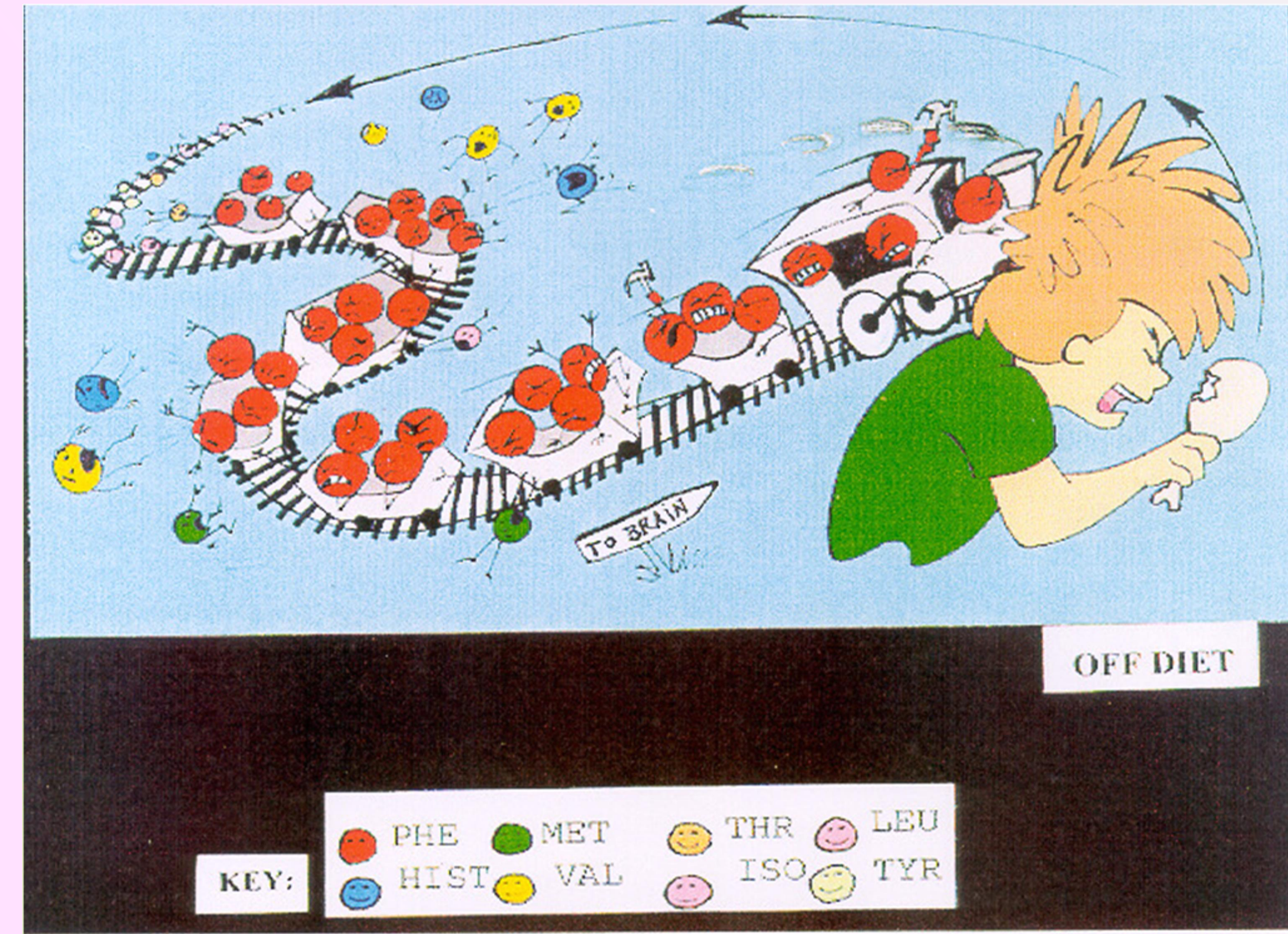


Case Summary:

A forty one year old G2P1 conceived by IVF. She is known to have PKU since birth. Her antenatal care was carried out by the maternity unit at Nobles hospital, Isle of Man, in co-ordination with Mark Holland Metabolic unit at Salford Royal NHS foundation Trust. Her past medical and surgical history includes, Primary parahypothyroidism, Para thyroidectomy; Spastic Para paresis secondary to PKU, worsening spine bone mineral density , scoliosis (Harrington's rods implanted),Osteoporosis, Vit D and B12 deficiency and Cholecystectomy. During the antenatal period , her routine bloods including infection screen were normal. Her aneuploidy screen was of low risk She met the criteria for gestational diabetes screening and required anti coagulation prophylaxis from 28 weeks. She had Covid infection in early pregnancy and had several admissions in this pregnancy with abdominal pain and vomiting. She suffered with renal calculi on the right side and was treated with IV fluids anti emetics and dietary advise. She had serial growth scans from 28 weeks and her baby was small for gestational age, with head circumference on the 5th centile , but normal growth velocity and umbilical artery doppler. She was on strict low protein diet and nutritional supplements. Her phenyl alanine levels were regularly monitored with spot card and maintained within the range (120 -300 micromol/L). In the last trimester she presented on few occasions with decreased fetal movements , but CTG and Fetal Doppler's were normal. Delivery was carried out at Nobles Hospital by caesarean section at 37w+2d and she gave birth to a healthy boy weighing 3.24kg (90th centile)with a HC of 32.5cms(50th centile)for gestational age. A PKU screening was done for the baby and was negative . The postoperative period was uneventful

Discussion:

PKU is one of the most common inborn errors of metabolism. A new born screening program was introduced by NHS in 1969.The screening has been a great success and many women who were treated in their childhood are conceiving and having babies of their own. Elevated serum phenylalanine concentration in a mother with PKU or hyperphenylalaninaemia with consistent PA concentration of >360micromols/L can result in Phenylalanine Embryopathy. Women with PKU should be encouraged to receive family planning and preconception services. Risk results from mothers metabolic control , independent of whether fetus has PKU. The concentration of PA is higher in fetal than in maternal plasma because of the concentration gradient. Even if maternal PA levels are in a reasonable range , fetal level may reach a level that is teratogenic. Outcome is improved substantially with treatment and low maternal levels, before conception or less optimally before ten weeks of gestation. Decreasing IQ was associated with increasing levels of PA exposure. PA Embryopathy can be prevented by dietary restriction of PA intake in women with PKU or HPA before and during pregnancy. The recommendation is to reduce the PA levels to <360micromol/L at least three months before conception and to maintain between 120 - 360 micromol/L during pregnancy. Plasma PA concentration should be monitored twice weekly. Maternal Tyrosine levels should also be maintained between 0.9 and 1.8mgm/dl. Tyrosine supplements may be needed. A multidisciplinary team approach including a nutritionist, a chemical pathologist , a physician with experience in metabolic disorders , an obstetrician , GP and also a social worker and or a clinical psychologist form the core essentials for the management of PKU.



References:

- 1Carol R Munyame;Nirmala vaithilingam; Yousuf Rahman;Roshni Vare; Amanda Freeman - Phenyl Ketonuria in Pregnancy The Obstetrician and Gynaecologist Vol6 2018
- 2.National Society for PKU(UK)- Management of Phenyl ketonuria - a consensus document for diagnosis and management of children , adolescents and adults with phenyl ketonuria 2014
- 3.Waisbren SE;Hanley W; Levy HL,Shifrin I, Alfred E; Azen C et al- Outcome at age 4 ,The Maternal PKU Collaborative study JAMA 2000
- 4.DeogariE; BeasleyM;SmithI;Lloyd I: Timing of strict diet in relation to fetal damage in maternal phenylketonuria- an international collaborative study by the MRC/DHSS PKU register Lancet 1987

Conclusion:

A successful outcome can be achieved with a dedicated multidisciplinary team approach to the management of this rare disorder, with good compliance from the patient , even in a peripheral centre. A co -ordinated team effort between the Salford Hospital and Nobles Hospital helped management of this patient in her home town in familiar surroundings.