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*Case Report*

# Coexistence of Cystic Fibrosis and Phenylketonuria

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Phenylketonuria (PKU) and Cystic Fibrosis (CF) have an incidence in Northern Ireland of 1 : 4000 and 1 : 2000 respectively (1994 figures). Management problems are dietary, disease-related and psychological. Search of the literature has revealed no previous report of a child with both conditions.

We present the case of a child in whom both CF and PKU were identified on routine neonatal screening. The case highlights the value of this procedure.

*Case Report* A female infant weighing 3370 g was born by normal delivery at 39 weeks gestation to parents who believed that they were distantly related. They had one other child, a female, aged five years who was alive and well. There were no perinatal problems but an abnormal phenylalanine result from routine neonatal Guthrie card screening was confirmed by a plasma phenylalanine concentration of 934 mcmol/l on the fourteenth day (normal range 64-92 mcmol/l). Urinary phenylalanine was elevated at 45 mcmol/l (normal range 4-17 mcmol/l) and urinary phenylalanine excretion was 163 mcmol/mmol creatinine. Protein, ketoacids and phenylketones were absent from the urine. PKU was diagnosed and she was commenced on XP Analog (Scientific Hospital Supplies) together with 60 ml SMA Gold Cap (Wyeth) for 3 days increasing to 210 ml SMA Gold Cap to provide a small but essential amount of phenylalanine.

By 5 weeks of age concern was expressed about a poor weight gain of 90 g from birth. Neonatal screening had confirmed high immunoreactive trypsin and subsequent sweat tests revealed raised sodium concentration of 104 mmol/l. At 7 weeks she was admitted to hospital for assessment and management of CF. There were no respiratory symptoms but stools were loose and foul-smelling. Serum vitamin A was low at 0.61 mcmol/l (normal range 1.1-3.5 mcmol/l), and serum vitamin E at 5.23 mcmol/l (normal range 16-35 mcmol/l). Nutrizym GR(3) (Merck), flucloxacillin, and vitamin supplements including vitamin E were prescribed and physiotherapy commenced three times daily. There was an increase in height and weight velocity (Figure 1) and phenylalanine tolerance fell (Figure 2) following the commencement of pancreatic enzyme replacement therapy.

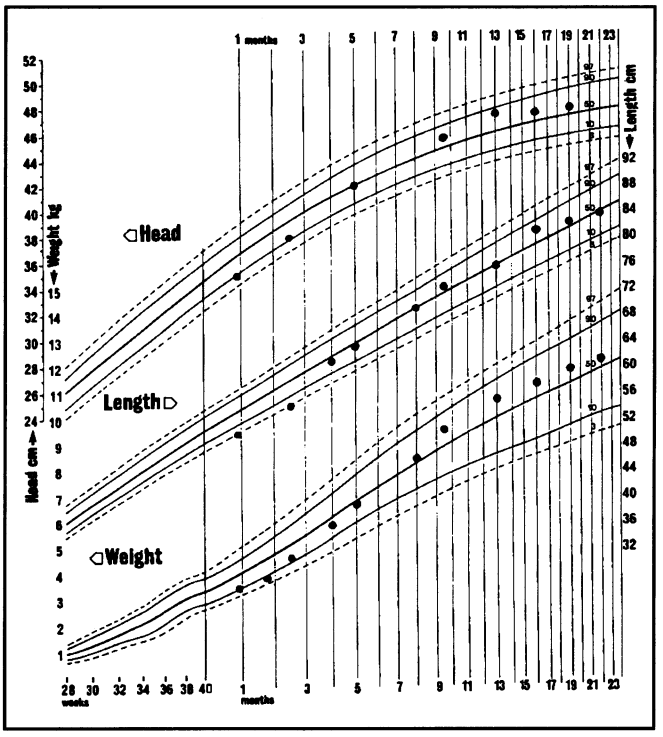


*Fig 1.* Figure 1 shows height, weight and head circumference data. Enzyme treatment commenced at 7 weeks.

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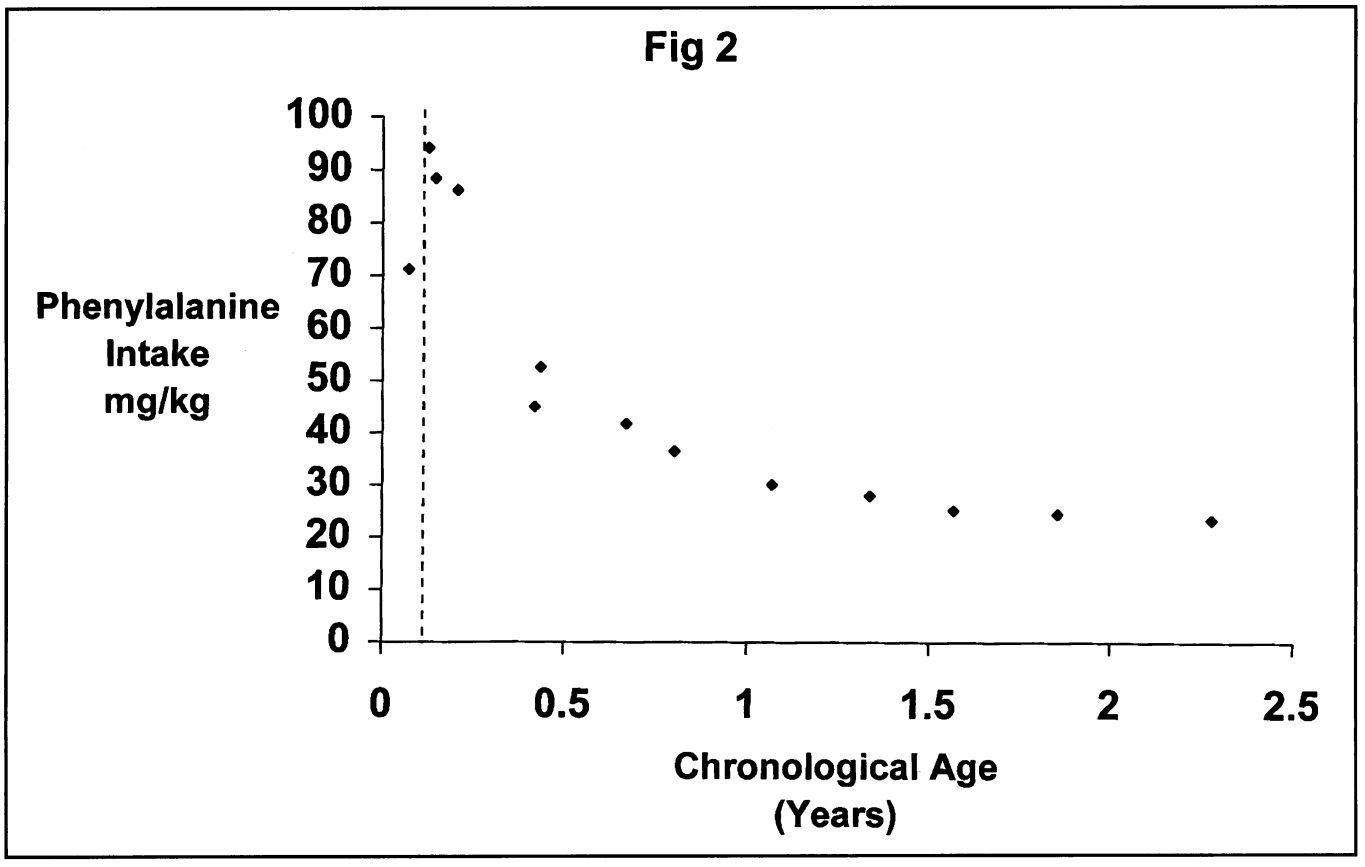


*Fig 2.* Figure 2 shows the variation in phenylalanine intake (mg/kg/day) with chronogical age. Age of commencing enzyme treatment is indicated by the perpendicular dotted line.

At the age of eight months she was admitted with a lower respiratory tract infection for intensive physiotherapy. Prophylaxis with Augmentin suspension, an aspartame-containing antibiotic (7.015 mg phenylalanine/5 ml), was inadvertently prescribed for six weeks although the dosage was low (7.5 ml daily) and unlikely to have affected phenylalanine control significantly.

Genotype analysis has shown that she is homozygous for delta F 508, and also shows the PKU mutations R408W, Y414C. At the age of twenty-eight months she is making good progress with normal development. Height and weight are both just above the fiftieth centile.

## DISCUSSION

The case highlights the value of neonatal screening. The chance of an individual having both CF and PKU in our population is very low at approximately 1:8,000,000 and we have been unable to find any previous report of their coexistence. It is possible that CF-related malabsorption may have led to a lower diagnostic plasma phenylalanine concentration than would have otherwise occurred. Most patients with the common CF genetic defect, the delta F508 mutation, have steatorrhoea[1] and there is also known to be a specific defect in the absorption of neutral amino acids in CF[2]. In our experience, however, two other PKU patients with the PKU mutations R408W, Y414C have had similar plasma phenylalanine concentrations at diagnosis suggesting that malabsorption did not affect the result.

Both conditions require skilled nutritional intervention and monitoring by a dietitian. Their coexistence requires a revision of all advice as given for each occurring separately. The management of PKU necessitates a diet with small controlled amounts of natural protein and a daily intake of a protein substitute mixture to meet requirements for normal growth and development. Recommendations suggest a total amino acid intake of 3g/kg/day in children under 2 years of age and 2g/kg/day in children over 2 years.[3] This translates as 3-4g protein/kg/day and 2-3g protein/kg/day for under 2 years and over 2 years respectively. Energy requirements for

individuals with PKU are comparable to those of the general population. Patients who are homozygous for the CF mutation delta F 508 have a significantly higher resting metabolic rate (121% predicted) than those of other genotypes.[2] The estimation of energy and protein requirements used at our centre are 120-150% of requirements for age and a minimum of 2 g/kg/day respectively.[4]

In practical terms the two diets are compatible. From diagnosis our patient was treated dietetically as a PKU patient. At present she is receiving most of her protein requirements from a protein substitute mixture. Low protein products combined with energy supplements play an important role in maintaining her energy intake for appropriate growth and weight gain. Dietary problems can be foreseen. Monotony and taste fatigue are likely to occur because the PKU diet is lifelong and there is a limited number of products available. CF-related chronic respiratory infections will cause an increase in metabolic rate and in energy requirements.[1]

The psychological effects must be recognised. Olsen[5] has described the guilt, marital stress and grief of parents on hearing the diagnosis of CF. The parents of our patient are in the unique position that their child has not one but two chronic inherited diseases both diagnosed on routine neonatal screening. The combined risk of a further child with one or other condition is 1:2. The child herself may suffer from lack of understanding by teachers and peers.[1] Denial of the severity of the illness may lead to non-compliance.[6]

The prognosis of both conditions may be influenced by the coexistence of the other. Poor control of PKU with subsequent intellectual deterioration may lead to non-compliance. Poor control of CF with reduced growth velocity and frequent infections will lead to poor phenylalanine control and its consequences. The frequent use of antibiotics may lead to the child being inadvertently given the aspartame-containing antibiotic, Augmentin, in higher dosage than occurred in our patient. Psychosocial problems associated with CF are likely to be aggravated by those of PKU.

**REFERENCES**

1. Ramsey B W, Farrell P M, Pencharz P, and the Consensus Committee. Nutritional assessment and management in cystic fibrosis: a consensus report. *Am J Clin Nutr* 1992; **55**: 108-16.
2. Dodge J A. Malnutrition and age-specific nutritional management in cystic fibrosis. *Neth J Med* 1992; **41**: 127-9.
3. Report of Medical Research Council Working Party on Phenylketonuria. Recommendations on the dietary management of phenylketonuria. *Arch Dis Child* 1993; **68**: 426-7.
4. Shepherd R W, Cleghorn G, Ward L C, Wall C R, Holt T L. Nutrition in cystic fibrosis. *Nutr Res Rev.* 1991; **4**: 51-67.
5. Olsen D G. Parental adjustment to a child with genetic disease: one parent's reflections. *J O G N N* 1994; **23**: 516-8.
6. Carter B D, Urey J R, Eid N S. The chronically ill child and family stress. family developmental perspectives on cystic fibrosis. *Psychosomatics* 1992; **33**: 397-403.