and urine levels of total biopterin derivative (measured by *Crithidia fasciculata* assay) and an abnormal pattern of pterins on chromatography (Leeming *et al.*, 1976). The results of the *Crithidia* assays carried out by one of us (R.J.L.) in 1975 on the patient of J. Bartholomé (Kaufman *et al.*, 1975; Bartholomé *et al.*, 1977) have not been published and we should like to present them (Table).

Table Levels of total biopterin derivative measured by *Crithidia fasciculata* assay in a patient with phenylketonuria (Bartholomé *et al.*, 1977). Comparison with control values (mean $\pm$ SD)

Subjects	Serum (μ g/l)	Urine (mg/l)	Liver (ng/g wet weight)
Patient	0.2 } 0.7 }	0.09	16.7
Adult liver stored identically	—	—	550
Children with 'classical' PKU on diet	4.86 $\pm$ 3.03	2.46 $\pm$ 1.76	—
Normal children	1.78 $\pm$ 0.79	—	—
Normal adults	1.81 $\pm$ 0.64	2.1 $\pm$ 1.32	—
Adults at abdominal operation	—	—	375 $\pm$ 232

The levels of total biopterin activity in liver are markedly reduced, as are the levels in serum and urine. These results suggest that the patient, like that of Rey *et al.* (1977) and another reported recently by Kaufman *et al.* (1978), is deficient in biopterin. It remains to be explained why other measurements of hepatic co-factor activity failed to demonstrate an abnormality in Dr Bartholomé's case (Kaufman *et al.*, 1975; Bartholomé *et al.*, 1977).

Mr Leeming thanks Dr Bartholomé for allowing investigation of the patient.

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R. J. LEEMING
General Hospital,
Steelhouse Lane, Birmingham B4 6NH
I. SMITH
Institute of Child Health,
30 Guilford Street, London WC1N 1EH

Dr Schaub and co-authors comment:

In our Short Report (Archives, 1978, **53**, 674), it was not our intention to claim the first description of a defect of biopterin synthesis. We only wanted to show that tetrahydrobiopterin (BH₄) can be absorbed from the gut and can be applied to lower the blood phenylalanine level in atypical PKU due to a suspected defect of biopterin synthesis.

Nevertheless, in the meantime we have been able to localise the metabolic block in our patient (Niederwieser *et al.*, 1979). Using high-voltage paper electrophoresis we found large amounts of neopterin in urine but no trace of biopterin or L-erythro-7, 8-dihydrobiopterin (BH₂). A comparable decrease of serum phenylalanine was observed after an oral administration of either BH₄, BH₂, or L-sepiapterin (Curtius *et al.*, 1979). The last is postulated to be an intermediate in the biosynthesis (Eto *et al.*, 1976; Gal *et al.*, 1978) of BH₂ from D-erythro-7,8-dihydroneopterin triphosphate (NH₂-P₃). Therefore, the metabolic block in this child must be between NH₂-P₃ and L-sepiapterin (Figure).

Figure Biopterin biosynthesis from guanosine triphosphate and location of the dihydrobiopterin synthetase defect.

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JÜRGEN SCHAUB
Children's Hospital, University of Munich,
Lindwurmstrasse 4, D-8 München 2, Western Germany
A. NIEDERWIESER AND H. CH. CURTIUS
Department of Pediatrics,
University of Zurich, Switzerland