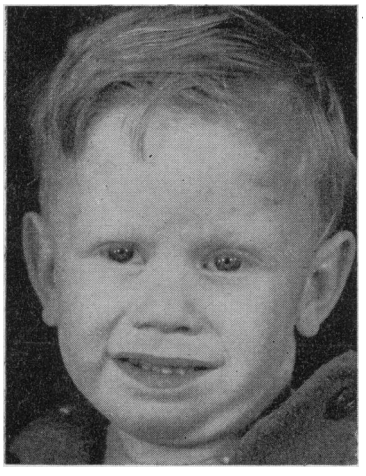

Fig 1 *DA, showing characteristic facies*

vessels, also audible without stethoscope (? through patient's mouth). Carotid thrill present. Blood pressure 100/50. Femoral pulses normal. Behaviour retarded (IQ ? about 60), hyperkinetic and destructive but affectionate and lovable.

Comment

This case corresponds closely to those recently described by Williams *et al.* (1961) and Beuren *et al.* (1962) having a low birth weight at term, failure to thrive physically, mental retardation of moderate degree, supravalvar aortic stenosis and a characteristic facies. No new evidence is provided to support the suggestion by Black & Bonham Carter (1963) that these cases are the survivors of the severe type of infantile hypercalcæmia (Fanconi *et al.* 1952). The two groups bear an undoubted facial resemblance to one another and both have in common the low birth weight, failure to thrive, mental retardation and a systolic murmur. It is perhaps significant that in the present case there is not only supravalvar stenosis but also general hypoplasia of the aorta, narrowing of the retinal arteries, stenosis of some branches of the pulmonary artery and an abnormality of the superficial veins of the head and neck. This would suggest a generalized vascular or perhaps even a connective tissue disorder in some ways analogous to Marfan's syndrome. It is interesting to speculate whether the hypercalcæmic syndrome might be based on a similar hypothesis.

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Leucine-sensitive Hypoglycæmia

C Harmer MB and L Sinclair MRCP DCH
(for H M T Coles MD MRCP)

K C, male, aged 18 months

Perinatal history uncertain. At 3 months began having convulsions two or three times daily. Each lasted four or five minutes, usually with fixed smile on face, staring of eyes and clonic movements of limbs. Pupillary dilatation and excessive perspiration observed on some occasions. Admitted to Queen Mary's Hospital, Carshalton, at 5 months; attacks observed to occur just preceding and just after meals.

Treatment with methylprednisolone 5 mg b.d. commenced in November 1962, reduced to 2 mg b.d. after two months. No convulsions occurred while the child was on steroid therapy but these recurred when steroids were temporarily discontinued in June 1963.

Investigations

Glucose tolerance test: Fasting level of blood sugar 55 mg/100 ml. At 30, 60, 90 and 210 minutes after 10 g glucose, the levels were 120, 70, 55 and 50 mg/100 ml respectively.

Oral L-leucine tolerance test (Fig 1): There was a significant fall of blood sugar after oral administration of leucine associated with excessive rise of plasma insulin and fall in plasma inorganic phosphate.

Intravenous leucine tolerance tests: L-leucine 75 mg/kg was given intravenously (these tests were performed while the patient was having methylprednisolone 2 mg b.d.):

	Blood glucose (mg/100 ml)					
	Fasting		*After 75 mg/kg L-leucine*			
Date	*(1)*	*(2)*	*10 min*	*20 min*	*30 min*	*60 min*
18.4.63	25	21	9	10	13	30
25.4.63	58	63	46	32	25	56

Tolbutamide tolerance test: Fasting blood sugar 75 mg/100 ml. At 15, 30, 45 and 75 minutes after 30 mg/kg tolbutamide i.v., the blood sugar levels were 60, 60, 43 and 47 mg/100 ml respectively.

Discussion

There are three points of interest about the investigations of this case:

(1) We have confirmed the observations of Grumbach & Kaplan (1960) that the ingestion or the injection of L-leucine is associated with an excessive rise of plasma insulin which is released, presumably, from the pancreas. The normal tolbutamide tolerance test (Fajans & Conn 1959) revealed differential sensitivity of the islet tissue

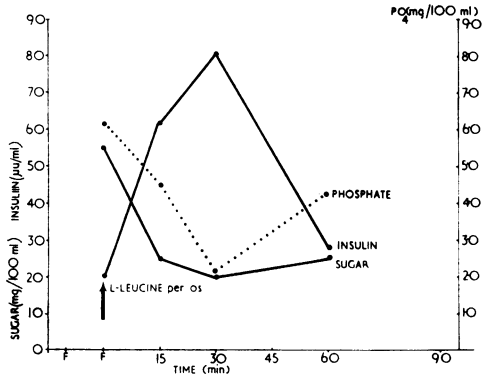

Fig 1 *Demonstrating the effects of the oral administration of* L-*leucine on blood sugar, phosphate and plasma insulin concentrations. (Dose of* L-*leucine 150 mg/kg)*

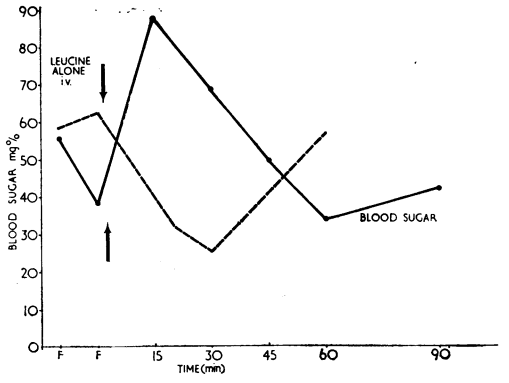

Fig 5 *To show the effects of simultaneous intravenous administration of* L-*leucine and α-keto-isocaproic acid (75 mg/kg). Interrupted lines show result of experiment with intravenous* L-*leucine alone*

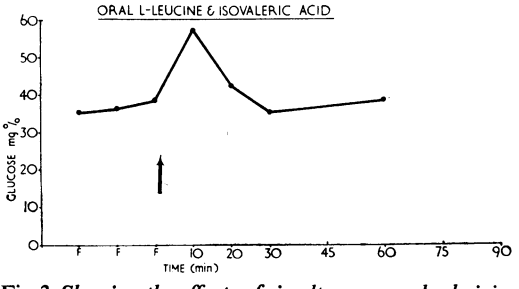

Fig 3 *Showing the effects of simultaneous oral administration of isovaleric acid and* L-*leucine (150 mg/kg) on blood glucose concentration.* F=*fasting level.* L-*leucine given at point marked by arrow*

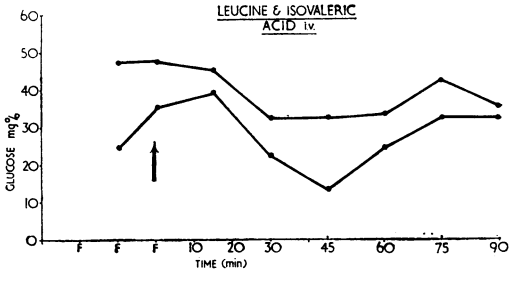

Fig 4 *Demonstrating the effect of simultaneous intravenous administration of both* L-*leucine and isovaleric acid on blood glucose. The results of two separate experiments are shown*

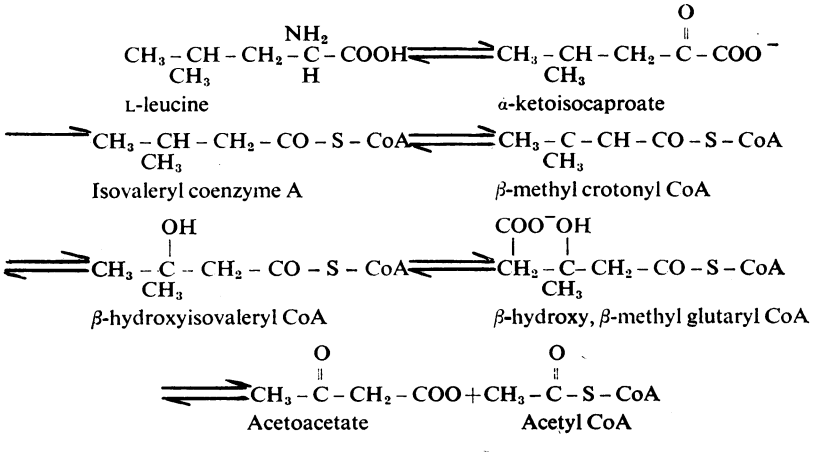

Fig 2 *Catabolic pathway of* L-*leucine.* –S–CoA *stands for coenzyme A*

and indicated that an islet cell tumour was not present, although figures for tolbutamide tolerance tests in this age group are not available, and there may be hyperplasia of the islet cell tissue. (2) While the infant was on steroids, although the blood sugar fell after intravenous leucine administration, he showed no clinical evidence of hypoglycæmia and had no further convulsions.

Gomez *et al.* (1961) showed that the convulsive effects of leucine-induced hypoglycæmia could be counteracted by intravenous glutamic acid; this may be due to the fact that glutamate is used as an

alternative source of energy by the brain cells. It has also been shown that both corticotrophin and corticosteroids enhance glutamic acid utilization (preferentially to glucose) in the central nervous system and it may be that this mechanism is at work in this infant.

(3) The third point of interest is a series of experiments with derivatives of L-leucine. The suggested catabolic pathway for L-leucine is shown in Fig 2. The immediate breakdown products are α-keto-isocaproic acid and isovalerate. Cochrane *et al.* (1956), who first described this syndrome, showed that isovaleric acid was not hypoglycæmic in their patients. Fig 3 shows an experiment in which the latter substance was given simultaneously with L-leucine by oral administration and Fig 4 shows the effect of simultaneous intravenous administration. There was a rise in blood glucose over three fasting levels (Fig 3). After intravenous administration there was a fall, but this appears to be delayed (Fig 4).

Mabry *et al.* (1960) demonstrated varying changes of blood sugar concentrations after the intravenous administration of α-keto-isocaproic acid. When this was given intravenously simultaneously with L-leucine to our patient there was in fact a rise of blood sugar over fasting levels (Fig 5), indicating that this substance, like isovaleric acid, might be blocking whatever mechanism was causing the release of insulin after L-leucine administration. The test was, however, repeated and the blood glucose fell from fasting levels of 13 and 20 mg/100 ml to 9 mg/100 ml at 15 minutes and 12 mg/100 ml at 30 minutes after the injection. This illustrates the variability of results to be expected with α-keto-isocaproic acid (Mabry *et al.* 1960) but the fasting concentrations were rather low and the significance of the fall of blood glucose at this level might be questioned. It is felt, nevertheless, that this type of investigation is useful in the study of patients with leucine-induced hypoglycæmia because of the light it may yet throw on the mechanism of release of insulin from the islets of Langerhans.

Acknowledgments: We wish to thank Dr J H Wilkinson and his staff for the biochemical investigations, Miss D Gray for help in preparing the intravenous solutions, Dr Ellis Samols for estimation of the plasma insulins and Sister M Parker and the nursing staff of the Westminster Children's Hospital.

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Trichobezoar

J S Cobb MB (for B D R Wilson FRCP)

C G, female, aged 12

History: She complained of a progressively worsening burning pain under her left ribs on exercise and after meals for six weeks. She had lost her appetite and 7 lb in weight. Her bowels had been normal and there was no history of vomiting.

After operation the parents admitted that between the ages of 2 and 6 she had had the habit of sucking her hair and between these ages they had noticed hair in her stools.

On examination: She was not obviously ill, but was anæmic. There was a large hard mass across her upper abdomen.

Investigations: Hb 49%; PCV 28%; MCHC 28%; WBC 9,050; ESR 26 mm in one hour (Westergren). Barium meal showed filling defects throughout the stomach with an ulcer crater on the greater curve (Fig 1).

Laparotomy (Mr Malcolm Gough): A gastrostomy was performed and an unsuspected trichobezoar removed.

Discussion

The diagnosis was missed because she presented as a short-haired girl who appeared entirely normal mentally and a history of trichophagia was not obtained. The mass was thought to be neoplastic. Her anæmia supported this diagnosis and, because of the large ulcer, the appearances

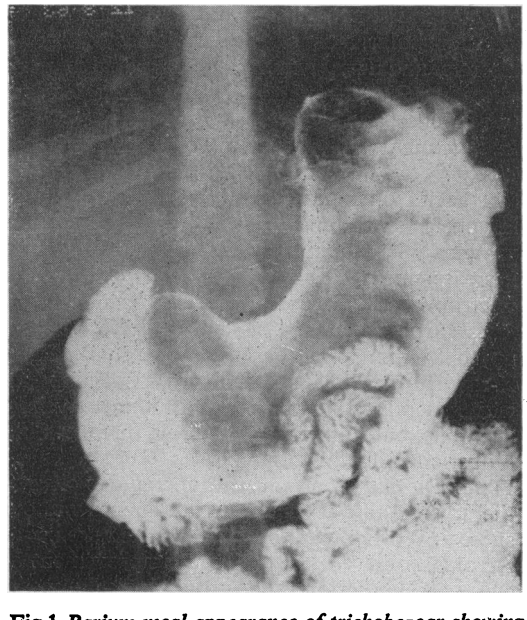

Fig 1 *Barium meal appearance of trichobezoar showing ulcer crater on greater curve*