based on a *proportionate* change in total calcium with protein rather than an *absolute* change. A slightly improved nomogram would be based on the plasma albumin rather than the total protein and would be derived from the known calcium-albumin association constant. Such a nomogram can be prepared by any physical chemist and will be included by us in a forthcoming publication.—We are, etc.,

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Ketotic Hypoglycaemia

SIR,—Ketotic hypoglycaemia occurs in undergrown infants and children, many of whom were small at birth. The hypoglycaemia is intermittent, occurring after a short period of calorie deprivation. It is sometimes associated with periods of increased calorie requirements such as anorexia associated with a minor infection. The biochemical hallmarks are found only during the hypoglycaemia; they include ketonuria and the failure of intramuscular glucagon to increase the blood glucose, while hypoalaninaemia may also occur. The basic defect is not known, though an error of metabolism has been extensively sought. Hepatic gluconeogenesis from glycerol, fructose, and alanine is intact, ketone metabolism is normal, and hormone responses appear to be appropriate with the possible exception of reduced catecholamine excretion in some children. The hypoglycaemia gradually disappears during childhood and is successfully treated with corticosteroids. The unique identity of this disorder is questioned by some authors¹ since similar ketonuria and lowering of blood glucose are seen in normal children during a prolonged ketogenic diet or starvation.

Most of these children have a normal forehead size. Glucose requirements cerebral metabolism are therefore high relative to the small body size, either during normal feeding or during starvation. I have never seen this condition in a robust and well-nourished child and I am led to consider whether the problem is not purely one of nutrition rather than an inborn error of metabolism.

In a 2-year-old child weighing 12 kg the normal energy requirement would be around 50 kcal/hr. In the face of total glycogen depletion about 50% of this would come from alanine (5.7 g/hr) derived from pyruvate and amino-acids in the muscle. These patients are carbohydrate-depleted, as shown by the exhaustion of the hepatic glycogen reserves. In view of their small size and muscle mass it seems reasonable to postulate a deficiency in total available muscle amino-acids which could result in the hypoalaninaemia and consequently in hypoglycaemia.

Hypoglycaemia may occur in overt malnutrition and Schutt-Aine has reported it in maternally deprived children.² We have occasionally observed ketotic hypoglycaemia in neglected children. Sizonenko *et al.*³ have also shown that after a period of unrestricted feeding children with previous ketotic hypoglycaemia respond to fasting and glucagon administration in a normal fashion. These findings seem to indicate that ketotic hypoglycaemia is yet another facet of nutritional

deprivation rather than an inherent defect in glucose homeostasis.—I am, etc.,

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Deep Venous Thrombosis: a Hypothesis

SIR,—I wonder whether a case which happened some years ago in my own experience fits the hypothesis put forward by Mr. J. Charnley (1 June, p. 499).

A woman aged 58 had an emergency operation for a ruptured cystic ovarian granulosa cell tumour on 2 July 1963. She had a mild degree of rheumatoid arthritis and was taking phenylbutazone at the time of admission to hospital. Her recovery following the operation was quite uneventful and she was discharged from hospital on 16 July. On 17 August she was readmitted with severe pain in her chest, worse on deep breathing. We did not tumble to the diagnosis until five days later, when we discovered in the morning that she had a very swollen, painful, blue leg, undoubtedly due to a left iliac vein thrombosis. We immediately concluded that the preceding chest pain must have been due to an embolism. Treatment with anticoagulants caused all the symptoms and signs in the leg and the chest to disappear within four weeks.

The interesting point is the chronological sequence—the obvious embolism preceding the obvious thrombosis. What I thought was that she must have had a symptomless thrombosis in the deep veins of either the pelvis or the lower limb. I imagined a long, snake-like clot floating in the blood, part of it becoming detached or else growing long enough to reach the point where the vein joined one of the major veins of the lower limb. There perhaps it coiled up or flapped over the point of confluence with the larger vein suddenly blocking it.—I am, etc.,

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Hypoglycaemia Action of Onion on Rabbits

SIR,—We found¹ that onion and garlic juice fed to rabbits resulted in a better utilization of glucose. We report here the results of a further investigation to see what effects various extracts of onion had on blood glucose levels in rabbits with alloxan-induced diabetes.

Fresh onions were cut into pieces, dried for 24 hours in a hot-air oven at a temperature of 60–80°C, and then powdered. The powder was extracted in a Soxhlet apparatus successively with ethyl alcohol 95%, petroleum ether (B.P. 40–60°C), chloroform, and acetone, each extraction lasting for a period of 18 hours. The powder was dried in between each extraction. The extracts were concentrated under vacuum and the residue of each was tested for hypoglycaemic effect.

Test Substance	Mean Blood Glucose Levels (mg/100 ml) in 6 Rabbits					Maximum % Fall in Fasting Blood Glucose (± S.E.M.)
	Fasting	1 hr	2 hr	3 hr	4 hr	
Ethyl alcohol extract	210.5	204.5	170.8	182.4	190.5	18.57 ± 2.4
Petroleum ether extract	218.4	207.5	200.2	207.5	210.4	8.25 ± 1.1
Chloroform extract	200.0	196.0	205.2	200.5	194.4	3.00 ± 0.9
Acetone extract	196.0	190.4	184.5	180.0	192.7	3.20 ± 1.0
Distilled water (control)	205.0	207.0	203.0	200.6	208.6	2.30 ± 0.6

Diabetes was induced in 30 rabbits by the method of Duffy.² Alloxan monohydrate 150 mg/kg was infused as a 5% aqueous solution into the marginal vein of an ear. The rabbits developed diabetes in seven days. The 30 rabbits were then divided into five groups of six. After 18 hours' fasting each of four out of the five groups was given one of the test substances at a dose of 250 mg/kg. Distilled water was given to the fifth group as a control. Blood glucose concentrations were then measured at hourly intervals by the Folin-Wu method as described by King and Wootton.³ The results (see table) showed that all the onion extracts had antidiabetic-like activity. Their potency was expressed as maximum fall percentage on the blood glucose level.

It seems that the mode of action of onion extracts differs from that of tolbutamide. The principal action of tolbutamide is to stimulate release of insulin by the beta cells of the islets of Langerhans. Thus it is ineffective in alloxan-induced diabetes in rabbits. Onion extracts, however, have hypoglycaemic activity when insulin secretion by the pancreas is almost stopped. The hypoglycaemic action of onion may be to enable cells better to utilize glucose. The findings so far are encouraging and further work on the isolation and purification of the hypoglycaemic principles is warranted. We are grateful to B.D.H. Chemicals, London, for the supply of alloxan.—We are, etc.,

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Encroachments on the Patient's Responsibility

SIR.—Writing about doctor/patient responsibilities, Mr. R. F. N. Duke (8 June, p. 557) paints his moral blacks too black and his whites too white. He ignores several lines of relevant argument.

Firstly, the legal position is not clear. If, after careful exposition of the risks by the doctor, the patient chooses to ignore the proffered advice, the surgeon agrees to carry out non-essential surgery nevertheless, and a greater or lesser tragedy results the surgeon's legal position may be in doubt and much more so in some other countries than in Britain. This is especially so in the case of the 10-day rule, where it might well be argued that the woman cannot waive her child's rights.

Secondly, the patient bears responsibility to the surgeon as well as the other way round. If a grossly obese patient fails even to attempt weight loss before undergoing planned major surgery it is at least arguable that the surgeon is within his rights and acting in everybody's best interests (including his own) in insisting on further delay