METABOLIC EFFECTS OF THREE KETOGENIC DIETS IN THE TREATMENT OF SEVERE EPILEPSY

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Ketogenic diets have been used successfully in the treatment of childhood epilepsy since their use was first suggested by Wilder (1921). Despite their widespread use, little is known about either the metabolic changes induced or their mode of action.

As early as 1926, Talbot and colleagues showed that the 'classical' high-fat ketogenic diet proposed by Wilder produced similar chemical changes to those that occurred during fasting, in that both produced an increase in blood acetone concentration and a reduction in blood sugar concentration. Later workers have examined the effect of the classical diet on acid-base balance (McQuarrie and Keith 1929), water and electrolyte distribution (Bridge and Iob 1931, Millichap *et al.* 1964) and lipid concentration (Dekaban 1966), although most studies have been restricted to small numbers of patients. More recently, Huttenlocher (1976) introduced a ketogenic diet based on medium-chain triglycerides (MCT), but this and the more recent study of Sills *et al.* (1986) are the only studies comparing some of the metabolic changes seen in response to the MCT diet.

In this study we report the results of 24-hour metabolic profiles performed on epileptic children receiving normal diets, the classical (4:1) ketogenic diet, the medium-chain triglyceride (MCT) diet and a modified MCT diet devised at the John Radcliffe Hospital. The study was designed to establish the relative efficacy of the classical, MCT and modified MCT diets, and to document their biochemical effects. Details of the composition of the diets are summarised in Table I. Further details of the diets and their clinical effects are reported in our accompanying paper (Schwartz *et al.* 1989).

Patients and method

Fifty-five children attending the paediatric neurology clinic at the John Radcliffe Hospital, and four adults specially referred for study by adult neurologists, were entered into the study, which received the approval of the Oxford Area Health Authority Ethical Committee. All patients had been referred because conventional management with anti-epileptic drugs had failed, and in each case the patient or parent was willing to undergo a trial of dietary manipulation and metabolic investigation. When they started dietary treatment, 20 of the patients were under five years of age, 25 were between five and 10 years, nine were between 11 and 15 years and five were older than 15. 24 patients suffered predominantly from drop attacks, nine

TABLE I
Composition of diets

	Calculation based on	*MCT oil*	*Long-chain saturated fats*	*Protein*	*Carbohydrate*
Classical (4:1)	75cals/kg bodyweight; 1g protein/ kg bodyweight	36 cals from fat to 4 cals from protein and carbohydrate			
MCT	RDI	60%	11%	10%	19%
Modified MCT	RDI	30%	41%	10%	19%

MCT = medium-chain triglyceride; RDI—recommended daily intake.

had absence attacks (generalised myoclonic absences, complex absences and primary absences), 16 had other forms of generalised seizure (tonic-clonic seizures and infantile spasms) and nine had partial seizures. All but two were on one or more anticonvulsant drugs, including sodium valproate, carbamazepine, phenytoin, nitrazepam and clonazepam.

Before admission to hospital for the metabolic studies, a three-week baseline record of seizure frequency was ascertained. During the trial period the anticonvulsant medication was not altered.

After an overnight fast, an indwelling venous catheter was inserted and left *in situ* for the 24-hour period of the study. Physical activity was not restricted. A free-flowing blood sample was taken without venestasis from each patient immediately before and one hour after they had eaten the three standard hospital meals and before breakfast the next morning to measure the substances listed in Table II. A total of 35ml of blood was taken during the 24-hour period. After this period on the normal hospital diet the patients were fasted for 18 hours and then commenced on one of the three trial diets. The choice of diet was influenced by the dietary habits of the family and was not by random allocation. The patients remained in hospital until the mother was sufficiently confident to administer the diet at home. Patients were readmitted for a further 24-hour metabolic profile three weeks after stabilisation on the trial diet, and further seizure records were kept during that period. Nine children were changed to a second trial diet and were then studied again with a further 24-hour profile three weeks later.

TABLE II

Biochemical analysis

24 hour profiles	*Fasting*
Total ketone bodies	Electrolytes and calcium
B-hydroxybutyrate	Uric acid
Aceto-acetate	Liver function tests
Glucose	Cholesterol
Pyruvate	Lipoproteins
Lactate	Haemoglobin
Glycerol	
Insulin	
Alanine	
Amino acids*	

*Results limited to nine paired studies on classical and MCT diets.

Blood samples for the measurement of ketone bodies (aceto-acetate and 3-hydroxybutyrate), glucose, pyruvate, lactate, glycerol and alanine were collected into a chilled tube containing perchloric acid, the neutralised supernatant being stored at 4°C until analysed by standard enzymatic assays (Bergmeyer 1974). Plasma amino-acid estimations and blood ammonia by ion-exchange chromatography were carried out on nine paired studies, using a JEOL JLC-6AH autoanalyser. Plasma urea and electrolyte concentrations, bilirubin, aspartate transaminase and alkaline phosphatase concentrations were assayed on heparinized blood, using a Vickers autoanalyser. Plasma lipid concentrations and levels were measured by standard methods.

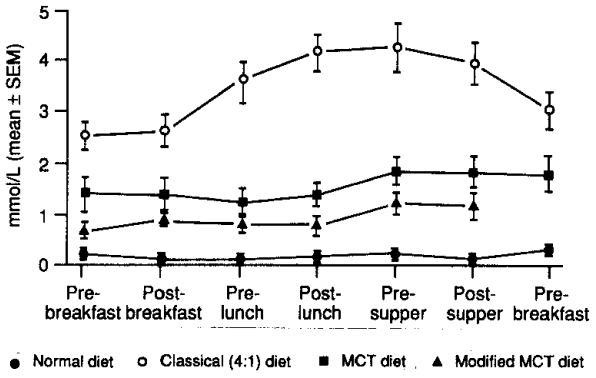

Fig. 1. 24-hour profiles of total ketone body-concentrations.

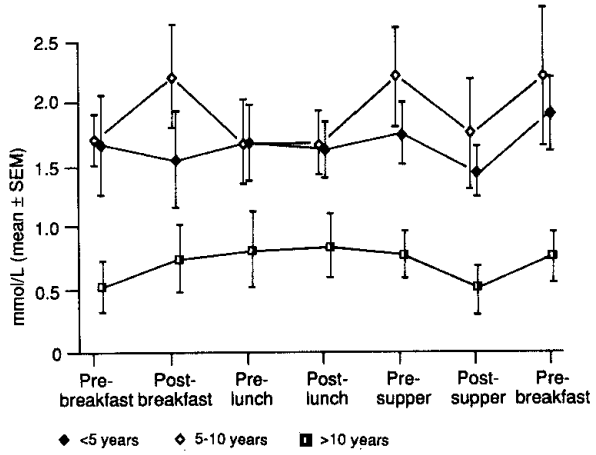

Fig. 2. Influence of age on blood ketone body-changes (MCT diet).

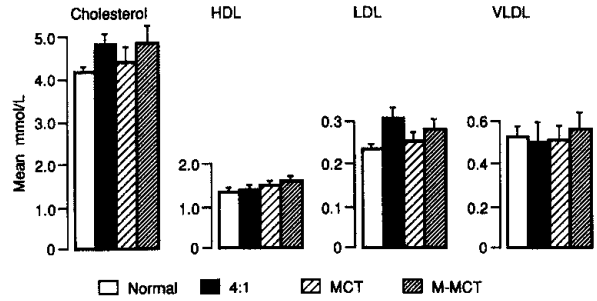

Fig. 3. Mean cholesterol and lipoprotein concentrations. (HDL = high-density, LDL = low-density, VLDL = very low-density lipoproteins. N = normal, 4:1 = classical, MCT = medium-chain triglyceride, and M-MCT = modified MCT diets.)

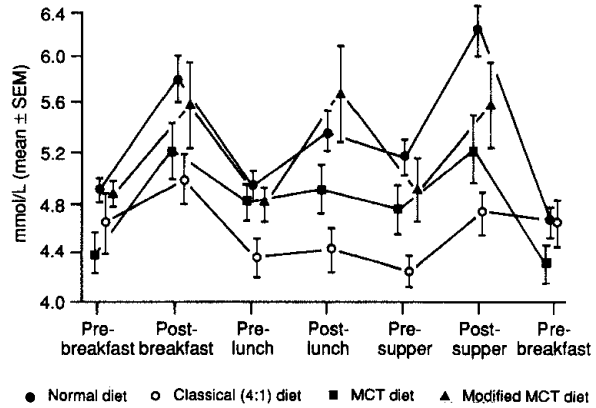

Fig. 4. 24-hour profiles of blood glucose concentrations.

Plasma insulin concentrations were measured by radioimmunoassay with a charcoal separation phase (Albano *et al.* 1972). Statistical analysis was performed with with the Student t test, and the results presented are means ± SEM.

Results

Cumulative results from 56 profiles on the normal diet, 29 on the MCT diet, 24 on the classical (4:1) diet and 12 on the modified MCT diet are reported. (These numbers on special diets are larger than the total number of patients because some children were studied on more than one therapeutic diet.)

The 24-hour profile for total ketone body-concentrations (aceto-acetate and 3-hydroxybutyrate) is shown in Figure 1. All three therapeutic diets produced a significant increase in total and individual ketone body-levels. This was most marked on the classical ketogenic diet. All three ketogenic diets led to a build-up of ketone body-concentrations during the day, reaching maximum levels in the afternoon, in contrast to the normal diet, which, as expected, led to slightly higher levels in the morning fasting samples. Urinary ketone bodies, as detected with Ketostix reagent strips, reflected these changes induced by therapy, showing higher levels in the afternoon and lower levels in the morning samples. The levels of concentrations of blood ketone-bodies measured in patients on the classical ketogenic diet were significantly higher than those of patients on the other diets ($p < 0{\cdot}001$). No significant difference occurred between the levels detected on the MCT and modified MCT diets. The ratio between the two component ketone bodies (hydroxybutyrate:aceto-acetate) was not altered.

The magnitude of the blood ketone body-changes was independent of sex, but was influenced by age, as shown in Figure 2, which refers specifically to the MCT diet, since this was the only therapeutic diet used for the older patients because of the extremely rigid restrictions imposed by the classical diet.

Levels of blood glycerol are shown in Table III. The highest values were obtained while fasting and the levels fell following meals. Higher values were

TABLE III
Glycerol mmol/l (mean ± SEM)

Diet	*Pre-breakfast*	*Post-breakfast*	*Pre-lunch*	*Post-lunch*	*Pre-supper*	*Post-supper*	*Pre-breakfast*
Normal	(N = 52) 0·17 ± 0·01	(N = 50) 0·13 ± 0·10	(N = 53) 0·14 ± 0·01	(N = 53) 0·13 ± 0·01	(N = 50) 0·14 ± 0·01	(N = 49) 0·13 ± 0·01	(N = 43) 0·17 ± 0·01
Classical (4:1)	(N = 24) 0·193 ± 0·02	(N = 24) 0·139 ± 0·02	(N = 24) 0·158 ± 0·01	(N = 24) 0·145 ± 0·01	(N = 23) 0·159 ± 0·01	(N = 23) 0·142 ± 0·01	(N = 23) 0·172 ± 0·02
MCT	(N = 27) 0·166 ± 0·02	(N = 26) 0·14 ± 0·01	(N = 26) 0·13 ± 0·01	(N = 27) 0·104 ± 0·01	(N = 25) 0·134 ± 0·01	(N = 24) 0·019 ± 0·01	(N = 17) 0·169 ± 0·03
Modified MCT	(N = 13) 0·16 ± 0·01	(N = 13) 0·10 ± 0·01	(N = 13) 0·13 ± 0·01	(N = 13) 0·115 ± 0·015	(N = 13) 0·106 ± 0·013	(N = 12) 0·106 ± 0·014	*

*Values not measured (Tables III to V) because of problems in maintaining patency of cannula.

obtained on the classical diet than on the other three diets.

Plasma cholesterol and high-density lipoproteins (HDL), low-density and very low-density lipoproteins (LDL and VLDL) concentrations are shown in Figure 3. Despite the high fat content of the diets, none of the concentrations was significantly raised in any of the therapeutic diet groups.

Twenty-four hour profiles of blood glucose levels are shown in Figure 4. Marked post-prandial increases are seen on the normal and MCT-based diets, but these were less marked on the classical ketogenic diet. Blood glucose levels were significantly lower after meals on the classical diet, possibly reflecting the smaller carbohydrate intake. Despite the fixed amount of carbohydrate eaten at each meal on this diet, there was a smaller rise in glucose following the midday meal compared with that seen following breakfast and supper. Hypoglycaemia was not documented in any patient at any time.

The profile results for blood lactate and pyruvate concentrations are summarised in Tables IV and V. There was no significant difference in blood lactate changes between any of the ketogenic diets, but blood concentrations of pyruvate were significantly lower on all three ketogenic diets.

The 24-hour profile of blood alanine concentrations is shown in Figure 5. Lower blood levels of alanine occurred on all three diets, the most marked difference being in children receiving the classical diet.

Paired profiles of the remaining plasma amino-acid concentrations were obtained for nine children on normal diets and during treatment with both the classical and MCT diets. There were wide variations in the concentrations of individual amino-acids during the day on all three diets. In general the levels tended to be lowest on the classical diet, probably reflecting lower levels of alanine, but the differences between the mean concentrations of the individual amino-acids on the three diets failed to reach statistical significance, other than for alanine values. Thus the mean concentrations of valine, isoleucine, leucine, tyrosine, phenylalanine, ornithine, lysine, histidine, tryptophan, arginine, taurine, aspartate, glutamate, glutamine, threonine, serine and glycine were similar in all the profiles. Low concentrations of asparagine, proline, citrulline, cystine, methionine and norleucine were detected in the specimens obtained. Blood ammonia levels were also similar on all three diets tested.

Plasma insulin concentrations corresponded to the blood glucose profiles—plasma insulin levels rose after each meal on all four diets, but with significant differences, as illustrated in Figure 6.

Mean plasma concentrations of sodium, potassium, chloride and bicarbonate did not differ significantly between the four diets; plasma urea, creatinine, calcium, phosphate, total protein, albumin and bilirubin levels were also similar. Plasma uric-acid levels were higher on all three ketogenic diets, with

TABLE IV
Lactate mmol/l (mean ± SEM)

Diet	*Pre-breakfast*	*Post-breakfast*	*Pre-lunch*	*Post-lunch*	*Pre-supper*	*Post-supper*	*Pre-breakfast*
Normal	(N = 52) 1·24 ± 0·07	(N = 52) 1·51 ± 0·08	(N = 54) 1·27 ± 0·08	(N = 54) 1·41 ± 0·09	(N = 51) 1·13 ± 0·07	(N = 50) 1·44 ± 0·08	(N = 46) 1·19 ± 0·06
Classical (4:1)	(N = 24) 1·15 ± 0·11	(N = 24) 0·95 ± 0·09	(N = 24) 0·97 ± 0·09	(N = 24) 0·90 ± 0·06	(N = 23) 0·91 ± 0·06	(N = 23) 0·80 ± 0·05	(N = 24) 0·90 ± 0·05
MCT	(N = 29) 1·04 ± 0·10	(N = 28) 1·04 ± 0·10	(N = 28) 1·04 ± 0·13	(N = 28) 1·01 ± 0·12	(N = 27) 0·95 ± 0·13	(N = 27) 0·93 ± 0·13	(N = 22) 1·07 ± 0·13
Modified MCT	(N = 13) 0·97 ± 0·05	(N = 13) 1·08 ± 0·07	(N = 13) 1·12 ± 0·12	(N = 13) 0·98 ± 0·08	(N = 13) 0·93 ± 0·03	(N = 12) 1·05 ± 0·05	

TABLE V
Pyruvate levels mmol/l (mean ± SEM)

Diet	*Pre-breakfast*	*Post-breakfast*	*Pre-lunch*	*Post-lunch*	*Pre-supper*	*Post-supper*	*Pre-breakfast*
Normal	(N = 53) 0·11 ± 0·005	(N = 52) 0·13 ± 0·016	(N = 54) 0·11 ± 0·004	(N = 53) 0·12 ± 0·004	(N = 52) 0·10 ± 0·004	(N = 50) 0·14 ± 0·006	(N = 44) 0·10 ± 0·005
Classical (4:1)	(N = 24) 0·09 ± 0·006	(N = 24) 0·09 ± 0·006	(N = 24) 0·09 ± 0·006	(N = 24) 0·08 ± 0·004	(N = 23) 0·08 ± 0·006	(N = 23) 0·08 ± 0·006	(N = 24) 0·08 ± 0·006
MCT	(N = 29) 0·08 ± 0·004	(N = 28) 0·09 ± 0·006	(N = 28) 0·08 ± 0·006	(N = 28) 0·09 ± 0·006	(N = 27) 0·09 ± 0·01	(N = 27) 0·09 ± 0·08	(N = 22) 0·08 ± 0·004
Modified MCT	(N = 13) 0·09 ± 0·005	(N = 13) 0·10 ± 0·006	(N = 13) 0·10 ± 0·008	(N = 13) 0·11 ± 0·007	(N = 13) 0·10 ± 0·006	(N = 12) 0·10 ± 0·008	

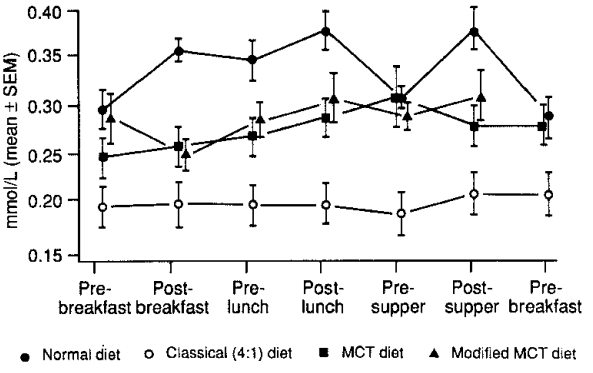

Fig. 5. 24-hour profiles of blood alanine concentrations.

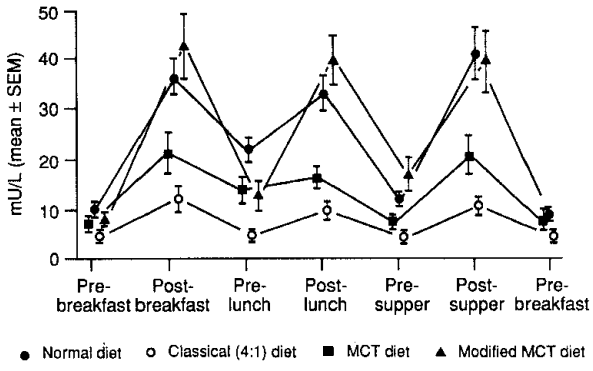

Fig. 6. 24-hour profiles of plasma insulin concentrations.

the highest increase on the MCT diet (normal diet 253 ± 11 μmol/l, *vs.* 334 ± 30 on MCT, 307 ± 15 on modified MCT and 290 ± 17 on classical; $p < 0{\cdot}001$ for each).

Discussion

Epilepsy is one of the most distressing of medical conditions, with severe and disturbing social consequences for those afflicted. A wide variety of methods of controlling seizures have been recommended, including dietary limitation or excesses of almost every vegetable, animal and mineral substance, frequently without lasting or reproducible results. One of the earliest successful dietary approaches was that of absolute fasting, and many workers were able to confirm the benefit of this treatment (Guelpa and Marie 1911, Geyelin 1921, Conklin 1922). Its obvious limitations led Wilder (1921) to speculate that the anti-epileptic effect of fasting might be the result of ketosis and acidosis, and this concept resulted in the introduction of the classical high-fat, low-protein, low-carbohydrate diet. In

1927 Talbot *et al.* confirmed that the diet produced chemically similar changes with respect to ketosis to those during fasting, while Keith (1931, 1932, 1933) demonstrated in experimentally produced convulsions in rabbits that acetone, ethylacetate, diacetone alcohol and aceto-acetate all possess anticonvulsant properties, with aceto-acetate acid having the most marked effect. Others were less convinced, however, and postulated other mechanisms of action. Thus McQuarrie (1929) thought the beneficial results were due to the accumulation of mildly anaesthetic acetone bodies in tissue, the production of a mild degree of compensated acidosis, with loss of fixed base from the body and a slight lowering of the water content of the body. Bridge and Iob (1931) also believed that the diet was only effective if the extracellular fluid-content of the body was reduced, while Millichap *et al.* (1964) correlated the anticonvulsant action with a negative balance of sodium and potassium, which was independent of acidosis and ketosis. Dekaban (1966) suggested that it was the rise in plasma lipids that occurred and plateaued 10 to 20 days after the introduction of the diet that correlated best, rather than the rise in ketones that occurred earlier after commencing therapy. This theory has not been supported by metabolic data following the use of the alternative ketogenic diets based on medium-chain trigylcerides (Huttenlocher 1976). These substances were shown by Schön *et al.* (1959) to cause a rise in blood and urinary concentrations of acetone and hydroxy-butyric acid when ingested by man, and this observation led Huttenlocher (1976) to introduce the MCT diet, which he found to induce an equivalent level of ketosis to the 3:1 classical diet.

The mechanism whereby MCT produces rapid hyperketonaemia is probably a combination of quick absorption of medium-chain fatty acids by the intestine and prompt delivery to the liver, where rapid degradation to 2-carbon fragments occurs (Schön *et al.* 1959). In addition, MCT may increase hepatic fatty-acid synthesis (Greenberger and Skillman 1969) and reduce ketone clearance (Kritchevsky and Rabinowitz 1966). Huttenlocher (1976), concluded that the mechanism of anticonvulsant action did not appear to be secondary to hyper-lipidaemia, as previously suggested by Dekaban (1966). Chronic extracellular acidosis did not appear to be a factor in the effect and mild hypoglycaemia was an inconsistent finding. He felt that the anticonvulsant effect was most closely related to elevated plasma levels of ketone bodies.

In our study we have confirmed that all three trial diets induce ketosis which is significantly greater than that on a normal diet appropriate for the child's age. The diets were all associated with a marked improvement in seizure control, as reported in our accompanying paper. However, control was not always related directly to ketone levels and complete control of seizures was obtained in our two patients under one year of age, although the level of ketosis induced was lower than that in older children. Moreover, the classical ketogenic diet used in our study induced a significantly greater degree of ketosis than the other two therapeutic diets, but not significantly greater seizure control. We have not confirmed Huttenlocher's observation that the MCT diet is as ketogenic as the classical diet.

On the other hand, like McQuarrie and Keith (1927), a diurnal pattern of ketone body levels was seen on the classical ketogenic diet, which has therapeutic implications for patients in whom the level of ketosis does appear to be important. Several patients in this series experienced a recurrence of seizures at times when the ketone body-levels were lowest (in the early morning) but were fit-free throughout the day. It is unclear whether the actual ketone body-level or the rate of change is of greater importance, and this requires further study.

We have also confirmed the observations of others that it is more difficult to induce ketosis in patients either under the age of one year or over the age of 10 years. The reasons for this remain obscure, though poor compliance in older patients may be a relevant factor.

Like Huttenlocher (1976), we have been unable clinically to correlate the response

with changes in blood lipid levels over the short-term period of the study, so we are unable to confirm Dekaban's theory that the therapeutic effect is related to blood cholesterol levels.

The tendency to lower blood glucose values while on the classical diet probably reflects the low carbohydrate intake. Unlike DeVivo *et al.* (1973) and Livingston (1978), we did not document hypoglycaemia.

A main reason for attempting to develop an alternative diet to the classical 4:1 diet was its reported unpalatability, because of the high content of long-chain triglycerides and low carbohydrate content. One of the advantages of the MCT diet advocated by Huttenlocher is that carbohydrate foods are less stringently restricted, so the diet is more palatable. Carbohydrates are anti-ketogenic, however, and Huttenlocher has shown that low blood ketone body-concentrations and reversal of ketosis occur during an infusion of glucose. This was accompanied by recurrence of seizure activity. This is an important point in practice, since we have also observed recurrence of seizure activity after extra intake of carbohydrate.

Alanine is an important amino-acid which plays a significant rôle in gluconeogenesis. The concentrations recorded in our study were significantly reduced during dietary treatment, but without measurements of glucose and alanine production and consumption rates it is impossible to know whether these changes represent decreased production or increased consumption. A decrease in plasma alanine concentration during an infusion of 3-hydroxybutyrate (Sherwin *et al.* 1975) has led to the speculation that ketone body-concentrations may decrease the alanine efflux from muscle, but this has yet to be proved. Whether ketosis itself plays an important rôle in the regulation of circulating alanine concentrations remains to be elucidated.

During the early stages of starvation there is an increased plasma concentration of branch-chain amino-acids, but these changes were not seen in our children on the ketogenic diets. Therefore the diet-induced ketosis does not entirely mimic the response to starvation. It is also of interest that the ketogenic diets failed to change the blood levels of the precursors of neurotransmitters.

Early workers with the ketogenic diet tried to explain the mode of action in terms of an alteration in body water and electrolyte balance. Like Huttenlocher (1976), we have been unable to document any significant changes in plasma sodium, potassium, chloride or bicarbonate levels, although balance studies would be needed to define whether or not there are changes in whole-body balance. Neither the long-chain triglyceride nor MCT diets produced a significant increase in blood urea or creatinine levels, although there was a significant increase in plasma uric-acid levels, perhaps because of altered renal tubular function. This is important clinically, since the development of renal calculi has been documented in some patients. It is also important that plasma uric-acid levels are monitored regularly, and to ensure that patients have an adequate fluid intake.

One additional area of concern is the potential risk of inducing ischaemic heart-disease. It is generally advocated that a low-cholesterol diet is beneficial for the general population, whereas we are recommending the use of a high-fat diet. Livingston (1972) reported that among his patients followed into adult life, there was no increased evidence of arteriosclerosis, blood-pressure readings were normal and electrocardiographic studies revealed no abnormalities. Blood cholesterol levels, performed on many of these individuals, were also normal. We have been unable to document any significant changes in blood lipid profiles in the short-term, although the long-term effects on lipid metabolism clearly require further study. We feel that the theoretical risks of inducing early changes leading to long-term ischaemic heart-disease are outweighed by the very real benefit of the diets in controlling disabling seizures.

This comprehensive assessment of the biochemical effects of ketogenic diets failed to identify any obvious clue to the mechanism of the beneficial effect. We suspect it may be mediated by changes either in nerve-cell lipid membranes which decrease neuronal excitation, or in the

local production or clearance of neurotransmitters. Further work is needed to clarify the effects of this highly beneficial form of therapy.

Accepted for publication 8th June 1988.

Acknowledgements
The authors thank Dr. B. D. Bower for allowing patients from his paediatric clinical practice to be studied; Dr. D. H. Williamson at the Metabolic Research Laboratory, Radcliffe Infirmary; Mrs. Pat Jenkins and Dr. J. Mann and the staff of the Lipid Laboratory, Radcliffe Infirmary, for assistance in the assays of some of the intermediaries; and the British Epilepsy Association for funding this project.

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SUMMARY
Pre- and post-prandial circulating concentrations of metabolic fuels and plasma insulin are documented in 59 patients with severe epilepsy while receiving either a normal diet, the classical high-fat ketogenic diet, a medium-chain triglyceride (MCT) diet, or a modified MCT diet. All three therapeutic diets improved the control of epilepsy and induced a significant increase in the concentrations of blood aceto-acetate and 3-hydroxybutyrate, the greatest elevation being seen in patients on the classical diet. The classical diet also caused a significant decrease in blood alanine values, which was not observed with the other therapeutic diets. The only consistent change to occur in all patients on therapeutic diets was an increase in plasma uric-acid. The mechanism by which ketogenic diets improve seizure control remains to be elicited.

RÉSUMÉ
Effets métaboliques de trois régimes cétogèniques utilisés dans le traitement d'épilepsies sévères chez l'enfant
Les concentrations circulatoires pré et postprandiales de métabolites énergétiques et d'insuline plasmatique ont été analysées chez 59 patients atteints d'épilepsie grave et recevant un régime normal, un régime cétogénique à haute teneur lipidique, un régime de triglycérides à chaines moyennes (MCT) ou un régime MCT modifié. Les trois régimes thérapeutiques améliorérent le contrôle de l'épilepsie et induisirent une élévation significative de la concentration sanguine des acétoacétates et 3-hydroxybutyrates, l'élévation la plus marquée correspondant au régime le plus hyperlipidique. Ce même régime provoqua également une baisse des taux sanguins d'alanine, non observée avec les autres régimes thérapeutiques. La seule modification consistente apparue chez tous les patients sous régime thérapeutique fut un accroissement du taux plasmatique d'acide urique. La raison pour laquelle les régimes cétogéniques améliorent le contrôle des crises reste à élucider.

ZUSAMMENFASSUNG
Metabolische Wirkungen von drei ketogenen Diäten, die zur Behandlung von Kindern mit schwerer Epilepsie angewendet wurden
Bei 59 Patienten mit schwerer Epilepsie, die entweder eine normale Kost, eine fettreiche, ketogene Diät, eine Diät mit mittelkettigen Triglyceriden (MCT) oder eine modifizierte MCT Diät erhielten, wurden die prä- und postprandialen Konzentrationen verschiedener Metaboliten, sowie die Plasmainsulinwerte gemessen. Alle drei therapeutischen Diäten verbesserten die Epilepsiekontrolle und erhöhten signifikant die Konzentrationen von Azetoazetat und 3-Hydroxybutyrat im Blut, wobei die höchsten Spiegel bei Patienten mit einer fettreichen Diät festgestellt wurden. Die fettreiche Diät bewirkte außerdem einen signifikanten Abfall der Blutalaninwerte, was bei den anderen therapeutischen Diäten nicht beobachtet wurde. Die einzige gemeinsame Veränderung bei allen Patienten mit einer therapeutischen Diät war ein Anstieg der Harnsäure im Plasma. Der Grund für die Verbesserung der Epilepsiekontrolle durch ketogene Diäten muß noch herausgefunden werden.

RESUMEN
Efectos metabólicos de tres dietas cetogénicas usadas en el tratamiento de niños con epilepsia grave
Las concentraciones circulantes pre y postprandiales de substancias energéticas y de insulina plasmática se documentaron en 59 pacientes con epilepsia grave, mientras recibian o una dieta normal, o una dieta altamente cetogénica, o un triglicérido de cadena media (TCM) o una dieta TCM modificada. Las tres dietas cetogénicas mejoraron el control de la epilepsia e indujeron un aumento significativo de la concentratión en sangre de acetoacetato y 3-hidroxibutirato, encontrándose la concentración mayor en los pacientes que recibían una dieta rica en grasa. Esta dieta causó también una disminución de alanina en sangre que no se observó con las otras dietas. El único cambio consistente que ocurrió en todos los pacientes con una dieta terapéutica, fue un aumento en el ácido úrico plasmático. Todavía es obscuro el mecanismo de acción de la dieta cetogénica en la mejoría del control de las convulsiones.

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