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PROCEEDINGS OF THE NUTRITION SOCIETY

ABSTRACTS OF COMMUNICATIONS

A Scientific Meeting was held at Regents College, London on Wednesday and Thursday, 2/3 December 1992 when the following papers were presented.

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Protein synthesis rates in individual tissues of critically-ill patients. By P. ESSÉN[1], M. A. MCNURLAN[3], I. TJÄDER[1], A. SANDGREN[2], B. BLOMQVIST[1], J. WERNERMAN[2], A. G. CALDER[3] and P. J. GARLICK[3], *Departments of Anaesthesiology and Intensive Care,* [1]*Huddinge University Hospital* and [2]*St. Göran's Hospital, Stockholm, Sweden* and [3]*Rowett Research Institute, Aberdeen AB2 9SB*

The critically-ill patient loses body protein as evidenced by substantial negative N balance. Free amino acids from peripheral tissues like muscle are transported to the splanchnic area for oxidation, gluconeogenesis and liver protein synthesis. In this investigation the protein synthesis rate of muscle has been studied quantitatively *in vivo* on the tissue level in nine patients in the intensive care unit. Albumin synthesis (Ballmer *et al.* 1990) as well as protein synthesis in muscle (Garlick *et al.* 1989) and lymphocytes were determined and the results were compared to a 95% confidence interval of a metabolically healthy reference group.

After an intravenous injection of L-[d_5]phenylalanine (45 mg/kg, 7·5 atoms % excess) given during 10 min, blood samples were drawn at intervals for the isolation of secreted albumin. A percutaneous biopsy was taken, 90 min after injection, from the quadriceps femoris muscle for the determination of enrichment in the muscle protein and a blood sample was taken for the preparation of lymphocyte protein. The rate of protein synthesis was calculated from the enrichment of phenylalanine in protein and the enrichment of plasma phenylalanine which was used to indicate the enrichment of the precursor for protein synthesis. Gas chromatography–mass spectrometry was used to determine enrichment. Enrichment at levels as low as 0·005 atoms % was possible by enzymic purification and modification of mass spectrometric techniques (Calder *et al.* 1992).

	Protein synthesis		
	Quadriceps muscle (%/d)	Lymphocytes (%/d)	Albumin (mg/kg per d)
Critically-ill (Mean (SEM))	1·36* (0·20)	11·1 (2·3)	179 (27)
Reference group (95% CI)	1·58 1·76	6·9 9·7	130 147

* Significantly lower than in the reference group ($P>0·05$).

In conclusion, the rates of muscle protein synthesis in critically-ill patients were significantly lower than in the reference group ($P<0·05$), but the protein synthesis rates in lymphocytes and the absolute albumin synthesis rates for several subjects showed values higher than the 95% CI for normal subjects.

Ballmer, P. E., McNurlan, M. A., Milne, E., Heys, S. D., Buchan, V., Calder, G. A. & Garlick, P. J. (1990). *American Journal of Physiology* **259,** E797–E803.

Calder, A. G., Anderson, S. E., Grant, I., McNurlan, M. A. & Garlick, P. J. (1992). *Rapid Communications in Mass Spectrometry* **6,** 421–424.

Garlick, P. J., Wernerman, J., McNurlan, M. A., Essén, P., Lobley, G. E., Milne, E., Calder, G. A. & Vinnars, E. (1989). *Clinical Science* **77,** 29–336.

Short-term parenteral feeding does not mitigate the decrease in albumin synthesis rates induced by interleukin-1β or turpentine injection in the rat. By P. E. BALLMER[1,2], M. A. MCNURLAN[1], I. GRANT[1] and P. J. GARLICK[1], [1]*Rowett Research Institute, Bucksburn, Aberdeen AB2 9SB* and [2]*Department of Internal Medicine, University of Berne, Switzerland*

In recent work we have shown that the recombinant human interleukin-1β (IL-1β) or turpentine-induced increase in the synthesis rate of total liver protein (Ballmer *et al.* 1991*a*) is in part augmented by 2 h of intravenous feeding with glucose and amino acids (Ballmer *et al.* 1991*b*). Albumin comprises about 100 g/kg of total liver protein synthesis and, in contrast, its synthesis rate decreases in an acute-phase reaction induced by IL-1β or turpentine (Ballmer *et al.* 1992). We have, therefore, measured albumin synthesis rates in postabsorptive rats at 9 and 24 h after subcutaneous injection with saline (Controls), IL-1β or turpentine, and infused for 2 h prior to measurements with Ringer's lactate or a mixture of glucose and amino acids (PN:feeding). Liver protein synthesis rates were measured using a 'flooding dose' of [^{3}H]phenylalanine, and albumin was immunoprecipitated from the liver homogenates by a specific anti-rat albumin antibody. Albumin synthesis was then calculated as the fraction of total liver protein synthesis (FT), and also as absolute synthesis rate (ASR) expressed as mg/100 g body-weight per day.

	Control				IL-1β				Turpentine			
	Ringer		PN		Ringer		PN		Ringer		PN	
Time	Mean	SEM	Mean	SEM	Mean	SEM	Mean	SEM	Mean	SEM	Mean	SEM
	Albumin synthesis as fraction of total liver synthesis											
9	11·87**	0·65	12·43	0·93	8·24	0·44	8·13	0·34	8·12	0·17	8·37	0·38
24	13·15**	0·58	13·04**	1·22	6·20	0·47	6·20	0·42	4·42	0·27	3·32	0·19
	Absolute synthesis rates of albumin (mg/100 g body-weight per day)											
9	56·4	4·6	65·6	9·1	51·9	4·1	62·8	3·4	49·5	3·9	59·4	3·9
24	60·6*†	4·6	81·6**	10·6	39·7	3·1	41·3	3·7	36·9	2·8	31·3	0·7

*$P<0·01$ *v.* IL-1β and turpentine; **$P<0·001$ *v.* IL-1β and turpentine; †$P<0·01$ *v.* feeding, by ANOVA.

In Ringer's lactate-infused animals, IL-1β and turpentine induced a consistent decrease in FT at 9 and 24 h, whereas ASR decreased at 24 h only. In control animals feeding stimulated ASR only at 24 h. At both 9 and 24 h, feeding did not affect the decrease in FT and ASR during the acute-phase reaction. In conclusion, IL-1β or turpentine injection have a down-regulatory action on albumin synthesis *in vivo* in this rat model. Moreover, short-term intravenous feeding with a glucose–amino acid solution is not potent enough to prevent this decrease.

Ballmer, P. E., Ballmer-Hofer, K., Repond, F., Kohler, H. & Studer, H. (1992). *Journal of Histochemistry and Cytochemistry* **40**, 201–206.

Ballmer, P. E., McNurlan, M. A., Grant, I. & Garlick, P. J. (1991*b*). *Proceedings of the Nutrition Society* **50**, 170A.

Ballmer, P. E., McNurlan, M. A., Southorn, B. G., Grant, I. & Garlick, P. J. (1991*a*). *Biochemical Journal* **279**, 683–688.

The effect of nutritional status on interleukin-6 response to elective surgery. By G. E. CURTIS[1], C. MCATEAR[2], L. FORMELA[2], A. WALSH[1] and A. SHENKIN[1], *Departments of* [1]*Clinical Chemistry* and [2]*Dietetics and Surgery, Royal Liverpool University Hospital, Prescot Street, Liverpool L7 8XW*

Interleukin-6 (IL-6) is the major inducer of the acute-phase protein response (APPR) (Heinrich *et al.* 1990) which promotes repair and healing following injury and trauma. Malnutrition attenuates the APPR (Cruickshank *et al.* 1989) and may contribute to increased postoperative morbidity. This attenuated C-reactive protein response may be cytokine-mediated. The present study was therefore undertaken to investigate the effect of preoperative nutritional status on the IL-6 response following elective surgery.

Nineteen patients, ten male and nine female, undergoing elective surgery for upper gastrointestinal malignancies were studied. Their preoperative nutritional status was assessed and patients classified as well-nourished or malnourished on the basis of recent weight loss (< or >10%) and by anthropometric measurements, including body mass index (BMI) (> or <18), mid-upper arm circumference and triceps skinfold thickness (above the 10th centile or below the 5th centile). There were ten well-nourished patients of whom two underwent colectomy, four pancreatectomy and four gastrectomy, and nine malnourished patients of whom three underwent colectomy, four pancreatectomy and two gastrectomy.

The serum IL-6 response was measured preoperatively, and then monitored during the first 24 h postoperatively at 0, 0·5, 1, 2, 4, 6, 8, 12 and 24 h, on blood samples taken via an indwelling intravenous cannula. IL-6 was measured by bio-assay of hybridoma growth stimulation using a mouse B-cell hybridoma B9 cell line. The growth of cells was measured by thiazolyl blue dye incorporation and cell numbers estimated on a microplate reader, standardized with an international reference preparation of recombinant human IL-6 (No. 88/514, NIBSC, South Mimms). All samples were analysed at eight doubling dilutions in duplicate to eliminate effects of inhibitors. CRP was measured daily, preoperative to day 5 postoperative, by immunoturbidimetry (Bayer Diagnostics Ltd).

Serum CRP increased post-operation, statistical analysis of the data by Mann-Whitney U test showing a significant difference at $P<0·05$ in the 48 h CRP level between the two groups, 164 (SD 58) mg/l for the malnourished group and 205 (SD 64) mg/l for the well-nourished group. Serum IL-6 increased significantly in both groups reaching a peak value at 4–12 h, similar to previous results (Cruickshank *et al.* 1990). However, there was no significant difference in the peak IL-6 concentration or the IL-6 area under the curve over the first 24 h between the two groups.

In this particular patient population undergoing major abdominal surgery there was, therefore, an attenuated CRP response in the malnourished group, but no effect of preoperative nutritional status on the IL-6 response. This suggests that the APPR to elective surgery is more sensitive to malnutrition than is the IL-6 response.

Cruickshank, A. M., Fraser, W. D., Burns, H. J. G., Van Damme, J. & Shenkin, A. (1990). *Clinical Science* **79,** 161–165.

Cruickshank, A. M., Hansell, D. T., Burns, H. J. G. & Shenkin, A. (1989). *British Journal of Surgery* **79,** 165–168.

Heinrich, P. C., Castell, J. V. & Andus, T. (1990). *Biochemical Journal* **265,** 621–636.

Metabolic features of multiple organ failure. By P. MCCLELLAND[1], M. YAQOOB[1], G. CURTIS[2], I. A. HASHIM[2], G. SMITH[5], J. MCLAUGHLIN[3], H. DAVIES[3], S. M. MOSTAFA[4], J. M. BONE[1] and A. SHENKIN[2], *Departments of* [1]*Renal Medicine,* [2]*Clinical Chemistry,* [3]*Immunology,* [4]*Intensive Care* and [5]*Medical Microbiology, Royal Liverpool University Hospital, Liverpool L69 3BX*

Multiple organ failure (MOF) represents one extreme of a systemic inflammatory response which is commonly initiated by bacteria or bacterial products and mediated by cells of the immune system. The mortality from this condition is very high, partly because of the intractable nature of the underlying problem and partly due to a lack of knowledge of the pathophysiology of this condition.

We have studied the changes in energy expenditure (EE; measured continuously by indirect calorimetry) and nitrogen excretion (Kjeldahl method) in four critically-ill patients with MOF over 9–21 (mean 14·8) d at the same time as monitoring plasma levels of endotoxin, tumour necrosis factor, interleukin-6 (putative mediators of MOF) and the acute-phase protein response (C-reactive protein).

EE ranged from 101–168 kJ/kg per day with a reducing trend in two patients who survived and the reverse pattern in the two non-surviving patients. N excretion ranged from 0·08–0·49 g/kg per day with no obvious pattern in relationship to outcome or clinical events. Plasma endotoxin (by limulus amoebocyte lysate assay) and tumour necrosis factor (by ELISA) could not be detected on any occasion. Plasma interleukin-6 (RIA) was found in high concentration in all patients and ranged from 0·691–23·47 ng/ml. IL-6 appeared to mirror the clinical state of the patient and levels of less than 1 ng/ml were associated with survival. The C-reactive protein response (range 22–420 mg/l) mirrored the IL-6 response but lagged behind by 24–48 h. No correlations were found between the metabolic and the acute-phase responses except, in one patient, a negative correlation between N excretion and IL-6 (r −0·71). One patient who received methyl prednisolone (1g) markedly attenuated his IL-6 and acute-phase protein response with a concurrent rise in N excretion but no apparent effect on EE.

Changes in the metabolic states of patients in MOF do not appear to reflect changes in plasma levels of endotoxin, tumour necrosis factor or IL-6. Changes in IL-6 levels do, however, tend to reflect the clinical condition of the patient and may prove useful in determining prognosis.

Manipulation of glucose utilization in multiple organ failure using somatostatin. By J. ARNOLD[1,2], I. T. CAMPBELL[1,2], L. J. HIPKIN[1,2], S. JENKINS[1,2], E. O'SULLIVAN[1,2], M. KEEGAN[1,2] and S. CHADWICK[1,2], *Intensive Care Units,* [1]*Royal Liverpool Hospital, Liverpool L69 3BX* and [2]*Withington Hospital, Manchester M20 8LR*

Injury and sepsis are generally accompanied by increases in circulating levels of the counterregulatory hormones. Using the hyperglycaemic glucose clamp we have previously demonstrated, in patients suffering multiple organ failure, a failure of glucose utilization to increase over a 3 h 'clamp' (Green *et al.* 1989). The present study was undertaken to determine whether glucose utilization rates could be favourably influenced by infusion of somatostatin and insulin, the latter at 'physiological' rates.

Seven artificially-ventilated patients suffering failure of at least the respiratory system and gastrointestinal tract and being fed intravenously were studied: six male, one female, 49–79 (median 68) years, Acute Physiological and Chronic Health Evaluation Mark II (APACHE II; Knaus *et al.* 1985) scores 14–28 (median 20). Intravenous feeding was stopped at midnight and the study started at 10.00 hours. A primed infusion of glucose (200 g/l) was given over 3 h and the rate adjusted to the algorithm of De Fronzo *et al.* (1979) to maintain plasma glucose at a target concentration of 12 mmol/l. During the first hour glucose alone was infused, and during the second hour glucose and a somatostatin analogue at 100 μg/h were infused. At 2 h a bolus of soluble insulin (5 U) was given followed by an infusion of 2 U/h, the glucose clamp and the somatostatin analogue infusion continuing. Oxygen consumption and respiratory exchange ratio (RER) were measured using the Engstrom Metabolic Computer (Engstrom, Bromma, Sweden) and protein metabolism was assessed from urinary N excretion and plasma urea appearance rates.

Glucose utilization rates at 40–60 min were compared with rates at 100–120 and 160–180 min. Energy expenditure (EE) did not alter, – 126 (SD 29)% of basal EE predicted from the Harris Benedict equation. Insulin increased with the glucose infusion ($P<0{\cdot}01$), decreased to basal levels during the second hour and increased during hour 3 to levels comparable with hour 1. Glucagon was initially 5–6 times higher than the normal range and decreased ($P<0{\cdot}01$) to 56 and 58% of preinfusion values at hours 2 and 3 respectively. Growth hormone concentrations did not alter significantly and remained within the normal range. Cortisol was about twice the normal range and did not alter.

Glucose utilization decreased by 53% ($P<0{\cdot}05$) at 100–200 min. At 160–180 min it is increased threefold above the 100–120 min value ($P<0{\cdot}05$) and was 55% higher than at 40–60 min ($P<0{\cdot}05$). RER increased from 0·81 at 40–60 min to 0·86 at 100–120 and 0·93 at 160–180 min. Net fat oxidation, calculated from indirect calorimetry, was completely abolished by 160–180 min.

It is concluded that utilization rates of infused glucose can be favourably manipulated by infusions of somatostatin and insulin, the latter infused at normal 'physiological' rates.

De Fronzo, R. A., Tobin, J. D. & Andres, R. (1979). *American Journal of Physiology* **237,** E214–E223.

Green, C. J., Regan, C. J., O'Sullivan, E., Underhill, S., Clegg, A. M., Maclaren, D. P. M. & Campbell, I. T. (1989). *Clinical Nutrition* **8,** Suppl. 44.

Knaus, W. A., Draper, E. A., Wagner, D. P. & Zimmerman, J. E. (1985). APACHE II: A severity of disease classification. *Critical Care Medicine* **13,** 818–827.

Metabolic and hormonal effects of hyperglycaemic glucose clamping in multiple organ failure. By C. J. GREEN[1], C. J. REGAN[1], E. O'SULLIVAN[1], S. UNDERHILL[1], A. M. CLEGG[1], D. P. M. MACLAREN[1], L. J. HIPKIN[2], I. A. MACDONALD[3] and I. T. CAMPBELL[1], [1]*Intensive Care Unit, Royal Liverpool Hospital L69 3BX,* [2]*Paediatric Endocrine Pathology, Alder Hey Hospital, Liverpool L12 2AP* and [3]*Department of Physiology and Pharmacology, University of Nottingham NG7 2UH*

It has been reported that hyperglycaemic glucose clamping in multiple organ failure failed to produce the rise in energy expenditure and increase in glucose utilization seen in normal controls (Green *et al.* 1989). We now report the glucose oxidation and hormonal findings of that study.

Fifteen ventilated patients suffering multiple organ failure (seven males, eight females, age 18–76 (median 66) years, Acute Physiological and Chronic Health Evaluation Mark II (APACHE II; Knaus *et al.* 1985) scores 11–32 (median 16)), and seven healthy volunteers were studied. All patients were fed intravenously and this was discontinued at 18.00 hours the night before. Volunteers fasted overnight. All studies were started between 09.00 and 10.00 hours. Following a 30 min rest blood glucose was raised and maintained at 12 mmol/l using a primed infusion of D-glucose (200 g/l) and the algorithm of De Fronzo *et al.* (1979). Oxygen consumption and respiratory exchange ratio (RER) were measured in the patients using an Engstrom Metabolic Computer (Engstrom, Bromma, Sweden) and in the controls with a ventilated hood system. Protein metabolism was assessed from urinary nitrogen excretion and urea appearance rates.

Blood glucose was maintained at 12·1 (SD 0·5) mmol/l in the patients and 12·2 (SD 0·4) mmol/l in the controls. Glucose oxidation and non-oxidative disposal (storage) were calculated from the glucose utilization rate and the indirect calorimetry data (allowing for protein oxidation). In the controls, RER increased from 0·80 (SD 0·6) pre-infusion to 0·92 (SD 0·6) at 160–180 min ($P<0·001$). In the patients, RER increased from 0·78 (SD 0·4) to 0·89 (SD 0·8) ($P<0·001$). Glucose oxidation in the controls increased from 10·4 (SD 2·9) μmol/min per kg at 40–60 min to 15·4 (SD 3·5) μmol/min per kg at 160–180 min ($P<0·001$), and in the patients from 9·5 (SD 5·8) μmol/min per kg to 12·5 (SD 5·0) μmol/kg per min ($P<0·001$). There was no difference between the groups. Non-oxidative disposal in the patients decreased from 28 (SD 14) μmol/kg per min at 40–60 min to 18 (SD 16) μmol/kg per min at 160–180 min ($P<0·01$). In controls non-oxidative disposal was 18 (SD 13) and rose to 45 (SD 24) μmol/kg per min ($P<0·02$). Insulin concentrations rose in both groups ($P<0·001$) but were lower in the patients ($P<0·001$). Adrenaline and cortisol did not change in either group. Noradrenaline tended to increase in both groups ($P=0·09$) and glucagon decreased significantly by 44% in the patients ($P<0·001$) and 32% in the controls ($P<0·001$). Growth hormone did not alter in the controls; seven patients showed a marked elevation ($P<0·001$) and in eight patients there was no change.

It is concluded that in multiple organ failure the lower glucose utilization rate is due to a deficiency in non-oxidative disposal. This could represent an inability to store glucose as glycogen.

De Fronzo, R. A., Tobin, J. D. & Andres, R. (1979). *American Journal of Physiology* **237,** E214–E223.

Green, C. J., Regan, C. J., O'Sullivan, E., Underhill, S., Clegg, A. M., MacLaren, D. P. M. & Campbell, I. T. (1989). *Clinical Nutrition* **8,** Suppl. 44.

Knaus, W. A., Draper, E. A., Wagner, D. P. & Zimmerman, J. E. (1985). APACHE II: A severity of disease classification. *Critical Care Medicine* **13,** 818–827.

Modification of postprandial substrate balance by the addition of fat. By A. J. GRIFFITHS, K. N. FRAYN, S. M. HUMPHREYS and M. L. CLARK, *Oxford Lipid Metabolism Group, Radcliffe Infirmary, Oxford OX2 6HE*

Flatt *et al.* (1985) showed that when fat was added to a low-fat meal there was no effect on carbohydrate balance. We have tested a more extreme situation. Eight fasted normal subjects were given 80 g carbohydrate, 80 g fat and 17 g protein, and on another occasion, 80 g carbohydrate, 17 g protein and <1 g fat. Indirect calorimetry was performed, and arterialized blood samples taken, before and for 6 h after the meal.

	EE (MJ)		RER		Substrate oxidation (g)				Substrate balance (g)			
					Fat		Carbohydrate		Fat		Carbohydrate	
	Mean	SE	Mean	SE	Mean	SE	Mean	SE	Mean	SE	Mean	SE
High-fat	1·90	0·09	0·81	0·01	20·7	2·4	44·4	3·7	59·3	2·4	35·6	3·7
Low-fat	1·85	0·10	0·89*	0·01	10·6*	1·4	63·2*	5·5	−9·6*	1·4	16·8*	5·5

EE, energy expenditure; RER, respiratory exchange ratio.
RER is time averaged, other results are integrated over the 6 h postprandial period.
* Significantly different from high-fat $P<0·01$.

The plasma glucose concentration remained elevated for a more prolonged period after the high-fat meal but areas under both the glucose and insulin concentration *v.* time curves were similar after the two meals. There was a significantly increased area under the plasma non-esterified fatty acid (NEFA) concentration *v.* time curve after the high-fat meal ($P<0·01$).

The respiratory exchange ratio was lower after the high-fat meal. Energy expenditure was very similar after the two meals. The rate of carbohydrate oxidation was lower, and the rate of fat oxidation higher after the high-fat meal. Carbohydrate balance was greater after the high-fat meal, and fat balance markedly so.

We conclude that during the 6 h period following a meal very high in fat, carbohydrate oxidation is spared, perhaps because of a greater availability of NEFA for oxidation. This may also explain the more prolonged elevation of the plasma glucose concentration after the high-fat meal.

This study was sponsored by Mars Confectionery.

Flatt, J. P., Ravussin, E., Acheson, K. J. & Jéquier, E. (1985). *Journal of Clinical Investigation* **76,** 1019–1024.

Utilization of intravenous fat in the surgical newborn infants. By A. PIERRO[1], M. O. JONES[1], P. HAMMOND[2], A. NUNN[1] and D. A. LLOYD[1], [1]*The Royal Liverpool Children's Hospital Alder Hey L12 2AP* and [2]*The University of Liverpool, Eaton Road, Liverpool L12 2AP*

In spite of the frequent use of intravenous fat emulsions during total parenteral nutrition (TPN) in newborn infants, little is known about their utilization and deposition. Excessive administration of intravenous fat in neonates can cause significant complications. Lipid tolerance is usually monitored by measuring serum triacylglycerol levels. However, clearance from plasma does not necessarily indicate that the fat emulsion is being utilized to meet energy requirements. The aim of the present study was to investigate the characteristics of fat utilization during TPN in stable surgical newborn infants.

Thirty-one 2 d metabolic studies were performed in twelve stable surgical newborn infants receiving fixed TPN diets. Gestational age was 36·2 (SEM 0·8) weeks, weight was 3·4 (SEM 0·2) kg, postnatal age was 33·1 (SEM 5·1) d. All patients received TPN with 2·5 g/kg per d of amino acids and various amounts (0–6 g/kg per d) of intravenous fat. Patients were divided into two groups according to the intake of carbohydrate (CHO) which was 10 g/kg per d (Group A, *n* 18) and 15 g/kg per d (Group B, *n* 13). Both CHO intakes were within the recommended range for TPN in infancy (AAP, 1983). The two groups were comparable for gestational age, weight and postnatal age. On day 3 respiratory gas exchange was measured by computerized indirect calorimetry. Resting energy expenditure (REE) and the rate of substrate utilization were calculated according to the principles of indirect calorimetry (Pierro *et al.* 1989).

No difference was observed between the two groups in REE (Group A, 208 (SEM 5·0); Group B, 214 (SEM 6·0)). Significant correlations between different variables are shown in the figure.

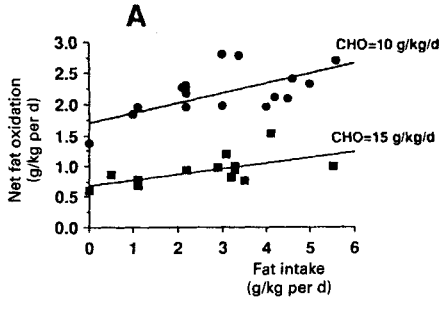

Fig. A: Relationship between net fat oxidation (y) and fat intake (x): group A (CHO = 10 g/kg/d; y = 1·7018+0·1624x; *r* 0·7; *P*=0·002); Group B (CHO = 15 g/kg/d; y = 0·7327+0·0917x; *r* 0·6; *P* = 0·03).

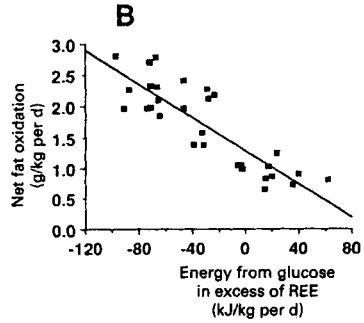

Fig. B: Relationship between net fat oxidation (y) and glucose energy given in excess of REE (x); (y = 1·373−0·243x; *r* 0·9; *P*<0·0001).

Net fat oxidation is significantly influenced by CHO intake. When the intake of glucose energy exceeds the basal energy requirements of the infant, net fat oxidation is minimal regardless of fat intake. In order to use intravenous fat as an energy source, it is necessary to maintain CHO intake below basal energy requirements.

American Academy of Pediatrics (1983). *Pediatrics* **71**, 547–552.
Pierro, A., Carnielli, V., Filler, R. M., Smith, J. & Heim, T. (1989). *Journal of Pediatric Surgery* **24**, 95–102.

The effect of glucose intake on substrate utilization and energy expenditure in the surgical newborn infant. By M. O. JONES[1], A. PIERRO[1], P. HAMMOND[2], A. NUNN[1] and D. A. LLOYD[1], [1]*The Royal Liverpool Children's Hospital Alder Hey L12 2AP* and [2]*University of Liverpool, Eaton Road, Liverpool L12 2AP*

Glucose is the main source of non-protein calories in total parenteral nutrition (TPN). However, its use has been associated with various nutritional, metabolic, and respiratory complications. The aim of the present study was to determine the characteristics of carbohydrate (CHO) metabolism in the stable, surgical newborn infant.

Twenty-one studies were done on eleven infants, weight 2·82 (SEM 0·19) kg, gestational age 34·9 (SEM 0·8) weeks, postnatal age 24·8 (SEM 5·0) d. During the study each infant received 3 d continuous TPN containing constant amounts of amino acids (2·5 g/kg per d) and fat (3·0 g/kg per d), and different amounts of glucose (range 10–25 g/kg per d). Oxygen consumption ($\dot{V}_{O_2}$), Carbon dioxide production ($\dot{V}_{CO_2}$), and resting energy expenditure (REE) were measured by indirect calorimetry. Urinary N excretion rate was measured and substrate utilization calculated from the non-protein respiratory quotient (NPRQ) (Pierro *et al.* 1989). Blood samples were taken for measurement of plasma triacylglycerol levels 4 h after stopping the fat infusion on the last day of the study.

There were correlations between the predictor variable glucose intake and the dependent variables shown in the Table.

Dependent variable (y)	Equation	*r*	*P* values
REE (kJ/kg per d)	$y=165{\cdot}0 + 3{\cdot}213x$	0·650	<0·005
$\dot{V}_{O_2}$ (ml/kg per min)	$y= 5{\cdot}786+0{\cdot}081x$	0·546	<0·05
$\dot{V}_{CO_2}$ (ml/kg per min)	$y= 3{\cdot}849+0{\cdot}183x$	0·825	<0·0001
Respiratory rate	$y= 36{\cdot}93 + 0{\cdot}732x$	0·460	0·06
NPRQ	$y= 0{\cdot}723+0{\cdot}015x$	0·934	<0·0001
CHO utilization (g/kg per d)	$y= -1{\cdot}948+0{\cdot}836x$	0·936	<0·0001
Fat utilization (g/kg per d)	$y= 4{\cdot}547-0{\cdot}254x$	–0·937	<0·0001
Triacylglycerol levels (mmol/l)	$y= -0{\cdot}050+0{\cdot}022x$	0·665	<0·01

x = glucose intake.

When glucose intake exceeded 18 g/kg per d the NPRQ was greater than 1·0, indicating glucose conversion to fat. Above this level of intake the gradient of the correlation between the predictor variable glucose intake and the dependent variables CO_2 production ($y=2{\cdot}62+0{\cdot}244x$; r 0·746; $P<0{\cdot}05$) and REE ($y=128{\cdot}1+5{\cdot}025x$; r 0·634; $P<0{\cdot}05$) increased.

From these results we conclude that glucose intake is the principal determinant of glucose utilization and exerts an influence on the metabolism of exogenous fat. Once the maximum oxidative capacity for glucose (18 g/kg per d) is reached: (a) net fat oxidation ceases and net fat synthesis occurs, (b) the thermogenic effect of glucose increases and the efficiency with which glucose is metabolized decreases, (c) CO_2 production increases, and is associated with an increased respiratory rate, and (d) endogenous triacylglycerols are released into the circulation.

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Dietary compliance and changes in the nutritional status of chronic renal failure patients on conventional low-protein diet. By P. D. HART[1], B. ENGEL[2], A. EDWARDS[1], K. EVANS[1] F. P. MARSH[1] and J. POWELL-TUCK[3], *Departments of* [1]*Nephrology,* [2]*Dietetics* and [3]*Human Nutrition, The Royal London Hospital and Medical College E1 1BB*

There is evidence in experimental animals and man that reduced dietary protein intake ameliorates uraemic symptoms and may slow the rate of progression of chronic renal failure (CRF), but nutritional safety has not been adequately assessed and dietary compliance is a major problem.

First, we identified and investigated seventeen stable adult CRF patients with serum creatinine 350–650 μmol/l who had been previously and routinely prescribed mean (range) protein intake of 0·69 (0·45–0·85) g/kg desirable body-weight per d and unspecified energy intake for a mean (range) period of 22·7 (4–72) months. Intake was estimated by 7 d, semi-weighed food diary (FD), and protein intake verified by urea nitrogen appearance (UNA).

Only six (35·3%) patients were conforming to the recommended 0·6 g/kg per d target protein intake, consuming (mean (SD)) 0·62 (0·08) g/kg per d (FD) and 0·62 (0·18) g/kg per d (UNA); and 90·63 (15·6) kJ/kg per d of energy intake (FD). Eleven (64·7%) patients were consuming a high-protein intake of (mean (SD)) 0·94 (0·15) g/kg per d (FD) and 0·91 (0·13) g/kg per d (UNA) and energy intake of 91·12 (13·6) kJ/kg per d (FD).

These patients, together with nine other similar patients, newly requiring low-protein diet (*n* 26), mean age (range) 45 (20–68) years, were further studied at baseline and after 3 months, to assess the nutritional adequacy of and compliance with an individualized prescription of 0·6 g protein/kg desirable body-weight per d, and energy intake of 147 kJ/kg per d, with monthly reinforcement for 3 months. Using the dual energy X-ray absorptiometry (DEXA) technique we determined the changes in percentage total body fat (% TBF), lean tissue mass (LTM) and whole-body bone mineral content (TBBMC). % TBF and mid-arm muscle circumference (MAMC) were also measured by skinfold anthropometry (SFA). Intake was estimated as previously described.

Estimated protein intake (g/kg per d, baseline *v.* 3 months; mean (SD)) was 0·87 (0·22) *v.* 0·70 (0·14) (FD) (P=0·001), 0·84 (0·20) *v.* 0·74 (0·19) (UNA) (P<0·05) indicating a significant reduction in protein intake but energy intake was much less than prescribed at 97·90 (23·0) kJ/kg per d *v.* 83·98 (23·6) kJ/kg per d (FD) (P 0·003). At the end of the study compliance to reduced protein intake improved but energy intake was lower than recommended in all subjects.

	Wt (kg)		% TBF (DEXA)		% TBF (SFA)		LTM (kg)		MAMC (cm)		TBBMC (kg)	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Baseline	73·5	13·0	30·93	9·1	27·9	2·7	46·92	11·3	23·8	2·7	2·79	0·59
3 months	72·5	13·3	29·87	8·5	23·7	2·9	47·02	11·5	23·9	2·9	2·75	0·59
P values	0·04		<0·01		NS		NS		NS		<0·001	

Moderate supervised reduction in protein intake may lead to subtle changes in the nutritional status of CRF subjects and DEXA may be useful in measuring the continuing effects of these diets. However, regular individualized dietary reinforcement is mandatory to achieve compliance with target protein intake.

An acute-phase protein response is associated with increased resting energy expenditure in weight-losing patients with either benign or malignant pancreatic disease. By J. S. FALCONER, C. E. PLESTER, L. DOUGLAS, K. C. H. FEARON, J. A. ROSS and D. C. CARTER, *University Department of Surgery, Royal Infirmary, Edinburgh EH3 9YW*

Marked weight loss is a common finding in patients with benign or malignant disease of the pancreas. In such patients anorexia and malabsorption are well recognized phenomena and may contribute to a reduced energy intake and to wasting. Alternatively, an elevated energy expenditure and acute-phase protein response (APPR) have been postulated as factors involved in weight loss in both chronic pancreatitis (CP) and pancreatic carcinoma (PC). It is not clear, however, whether there is any difference in the mechanisms of weight loss in patients with benign (CP) versus malignant (PC) disease, nor what role the APPR plays in the weight loss associated with these conditions.

We have studied a group of twenty-eight weight-losing patients with pancreatic disease (sixteen males, twelve females; mean age 52 years; sixteen PC, twelve CP). Resting energy expenditure (REE) was measured using indirect calorimetry, standard anthropometry and bioelectrical impedance analysis (RJL Systems, Detroit, USA) were used to calculate lean body mass (LBM) and body cell mass (BCM) according to previously validated predictive formulas (Fearon *et al.* 1992). Serum albumin and C-reactive protein (CRP) concentration were also measured and an elevated CRP (i.e. >10 mg/l) was used as an indication of the presence of an APPR. The results are shown in the Table.

	PC (n 16)		CP (n 12)		+ve APPR (n 8)†		−ve APPR (n 20)‡	
	Mean	SEM	Mean	SEM	Mean	SEM	Mean	SEM
REE/kg TBW	26·9	1·4	26·2	1·6	29·7	2·1	25·4	1·1
REE/kg LBM	36·6	2·0	36·0	2·7	41·1	2·8*	34·5	1·9
REE/kg BCM	78·9	7·5	65·3	5·8	94·7	12·0*	64·4	4·0
% wt loss	18·2	2·3**	10·5	1·5	18·1	3·6	13·6	1·7
Albumin (g/l)	37·5	1·3	40·1	1·8	34·0	1·1*	40·2	1·2
CRP (mg/l)					59·0	21·0	<10	

TBW, total body-weight; † Six PC, two CP; ‡ Ten PC, ten CP.
*P<0·03, +ve APPR *v.* −ve APPR; **P<0·02, PC *v.* CP (Mann-Whitney U test).

There was no significant difference in REE between the patients with benign (CP) or malignant (PC) pancreatic disease. However, when patients were grouped according to the presence or absence of an APPR, REE (when expressed in relation to the patient's LBM or BCM) was significantly elevated in those with a positive response. We conclude that in weight-losing patients with pancreatic disease the presence of an inflammatory response rather than the nature of their disease identifies a group who are significantly hypermetabolic. The rate of wasting in such patients might be decreased by agents which dampen the inflammatory response.

This work was supported by the Cancer Research Campaign and the Melville Trust for the Care and Cure of Cancer.

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Small-intestinal absorption of minerals during enteral feeding supplemented with a soya-bean polysaccharide and soya-bean oligosaccharide fibre. By S. A. KAPADIA, ANNA H. RAIMUNDO and D. B. A. SILK, *Department of Gastroenterology and Nutrition, Central Middlesex Hospital, London NW10 7NS*

Fibre-supplemented polymeric enteral diets are currently being prescribed widely in the UK. There is also evidence that mineral absorption may be adversely affected by the addition of fibre to the normal diet. As a result, the present study was carried out to quantitate and compare small-intestinal absorption of the minerals calcium, zinc, magnesium, iron, copper and phosphorus during continuous intragastric infusion of: (1) polymeric enteral diet (PD) (6·3 gN/l; 4·2 kJ/ml); (2) polymeric enteral diet (6·3 gN/l; 4·2 kJ/ml), supplemented with a soya-bean polysaccharide (20 g/l) fibre source (PDSP); or (3) polymeric enteral diet (6·3 gN/l; 1 kcal/ml), supplemented with a soya-bean oligosaccharide (75 g/l) fibre source (PDSO). Nineteen normal subjects (PD *n* 6, PDSP *n* 7, PDSO *n* 6) were intubated with a multilumen tube, the distal end being positioned just proximal to the caecum. A 200 mm segment of ileum was infused at 1 ml/min with normal saline (9 g NaCl/l) containing a non-absorbable marker (0·5 μCi [^{3}H]-PEG/l) in order to quantitate steady-state colonic inflows of minerals during continuous (7 h) intragastric infusion (82 ml/h) of enteral diet. Total small-intestinal absorption values (% of infused load (SEM) measured by colourimetric and flame spectrometry) for PD, PDSP and PDSO were:

	PD (%)		PDSP (%)		PDSO (%)	
	Mean	SEM	Mean	SEM	Mean	SEM
Ca	55·8	4·9	57·9	6·04	54·0	9·5
Mg	24·1†	5·4	52·6	14·4	34·6	13·2
Cu	−5·2	14·5	−15·3	13·7	23·4	15·3
Zn	−5·2†	16·6	47·2	15·3	13·0	18·2
Fe	6·6	14·4	−18·1	18·9	−8·0	25·5
P	78·8	6·2	68·0	8·4	72·5	6·9

Significance of difference of † PD *v.* PDSP, $P<0·05$.

These data show that the addition of 75 g/l soya-bean oligosaccharide to a polymeric enteral diet has no significant adverse effect on the absorption of Ca, Mg, Zn, Fe, Cu or P. The addition of 20 g/l soya-bean polysaccharide significantly increases the absorption of Mg and Zn with no significant deleterious effect on the absorption of Ca, Fe, Cu or P.

How much energy should we prescribe for patients with chronic renal failure? By B. C. N. ANG[1], P. D. HART[2], E. BETTANY[1], B. ENGEL[3], F. P. MARSH[2] and J. POWELL-TUCK[1], *Departments of* [1]*Human Nutrition,* [2]*Nephrology* and [3]*Dietetics, London Hospital Medical College, London E1*

Traditionally chronic renal failure (CRF) patients are prescribed high energy intakes of about 147 kJ/kg per d (Monteon *et al.* 1986) which may lead to poor dietary compliance. We have assessed the energy intake of eight patients with CRF by 7 d semi-weighed dietary analysis. Body weight and composition were assessed by weight and dexascan (dual energy X-ray absorptiometry, DEXA) and repeated after 3 months. Resting energy expenditure (REE) of each patient was measured by ventilated hood indirect calorimetry. Patients were asked to complete a Nottingham Health Profile (NHP; Hunt *et al.*) which enabled physical mobility to be scored.

DEXA wt gain (kg)	BMI	SCr	REE (kJ)	REE/LTM (kJ/kg)	EI/wt (kJ/kg)	EI/REE (%)	NHP_m
−3·0	24·2	568	5531	109	70·1	−9	+
−2·0	23·1	560	5767	105	86·5	−3	0
−0·8	23·5	344	5850	122	107·1	+8	0
−0·6	24·9	444	5103	136	86·5	+15	+
0	28·1	574	6602	101	71·8	+4	+
+0·5	21·3	497	4700	152	107·5	+34	+
+1·0	19·8	556	5086	153	163·8	+78	+
+1·4	20·5	336	6187	198	154·2	+15	0

BMI, body mass index; SCr, serum creatinine (μmol/l); NHP_m, mobility index (+, improved; 0, no change); REE/LTM, REE/kg lean tissue mass; EI/wt, energy intake/kg DEXA weight; EI/REE, percentage energy intake above REE.

Patients were ranked according to the amount of weight lost as estimated by DEXA which correlated well with scales. REE/LTM was negatively correlated with serum creatinine (r 0·62; $P<0·12$). Patients lost weight if they ate less than about 110 kJ/kg body-weight per d or less than 30% above REE. Those who lost weight were above their desirable weight and were encouraged to lose weight by dieting. Over the 3 month study period the degree of weight change did not lead to deterioration of physical mobility. Instead of the very high energy intake previously recommended for CRF patients we suggest that 110 kJ/kg per d are sufficient, less if they are overweight and more if they are underweight. This may lead to better dietary compliance.

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Nutritional assessment in patients on home parenteral nutrition; objective measurements or clinical judgement? By N. G. EGGER, C. WRIGHT, G. L. CARLSON and J. L. SHAFFER, *Nutrition Unit, Hope Hospital, Eccles Old Road, Salford M6 8HD*

The diagnosis of protein-energy malnutrition (PEM) in hospitalized patients is based on measurements including anthropometric, biochemical and immunological variables. However, there are no universally accepted objective criteria by which patients with PEM can be identified and their response to nutritional therapy accurately monitored. Recent reports have suggested clinical judgement (Subjective Global Assessment (SGA)) as an independent variable. SGA related well with the objective measurements but tended to predict outcome more accurately in one study (Baker, 1982) but less so in another (Pettigrew & Hill, 1986). Those studies were performed on preoperative patients. There is no information available on patients on long-term home parenteral nutrition (HPN). We studied thirty-one patients (sixteen female, fifteen male): age, median 49 (range 17–64) years; BMI, median 20 (range 16·4–25·4); HPN, median 34 (range 3–113) months. Diagnoses were: inflammatory bowel disease (61%), other (39%). All patients were clinically stable. Nutritional status was assessed as per cent of ideal weight (Jelliffe, 1966); triceps skinfold thickness (TSF) and mid-arm muscle circumference (MAMC), (Bishop, 1981); serum albumin, transferrin and lymphocyte count. Patients were independently rated SGA class A (well nourished), SGA class B (moderately malnourished) and SGA class C (severely malnourished).

	Lower limits of normal	% Patients normal (*n* 31)	SGA class of normals A (%)	B (%)	
% Ideal weight	≥80%	81	48	33	NS
TSF (percentile)	>10th	68	39	29	NS
MAMC (percentile)	>5th	71	39	32	NS
Albumin (g/l)	≥35	100	55	45	NS
Transferrin (g/l)	>2	100	55	45	NS
Lymphocytes (10^9/l)	>1·5	68	33	35	NS

NS, not significant, chi-square test (Fisher's exact test if applicable).

SGA rated 55% as well nourished and 45% as moderately malnourished in the group; no patients were considered severely malnourished. There was no correlation between the SGA class and the objective measurements of malnutrition. Further studies are in progress to assess which technique(s) has the optimal predictive value for monitoring of this group of patients.

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Infusion of the lithium salt of γ-linolenic acid into pancreatic cancer patients increases thymidine uptake and induces tumour necrosis factor release by peripheral blood mononuclear cells. By J. S. FALCONER, J. A. ROSS, K. C. H. FEARON, M. G. O'RIORDAIN and D. C. CARTER, *University Department of Surgery, Royal Infirmary, Edinburgh EH3 9YW*

Polyunsaturated fatty acids such as γ-linolenic acid (GLA) have been shown to modify immune function and reduce tumour growth both in vitro and in animal models. There is, however, little information available as to their effect in human malignancy. As part of a phase II clinical trial we have infused GLA into patients with pancreatic cancer and assessed changes in T-cell function and peripheral blood mononuclear cell (PBMC) cytokine production.

Fifteen patients with pancreatic cancer (seven females, eight males; mean age 57 years) were given a 10 d continuous intravenous infusion of the lithium salt of GLA (gift of Scotia Pharmaceuticals Ltd., Guildford, Surrey). The dose was increased over the first 5 d until the maximum tolerated dose was achieved. The infusion was then continued at this dose for the next 5 d (mean dose of GLA during this period, 7·1 g/d). Immune assessments were carried out at day 0 (pre-treatment), day 5 and day 10. PBMC were isolated and incubated in culture medium supplemented with 100 μl autologous serum/ml. Tumour necrosis factor (TNF) production by unstimulated and LPS (10 μg/ml)-stimulated PBMC was measured at 24 h using the L929 bioassay. T-cell blastogenesis in response to phytohaemagglutinin (PHA) and anti-CD3 antibody stimulation (mimicking an antigen specific response) was assessed after 72 h incubation using tritiated thymidine uptake. The results are shown in the Table.

Day . . .	0		5		10	
	Mean	SEM	Mean	SEM	Mean	SEM
Spontaneous TNF release (pg/ml per 10^5 cells)	750	200	3075*	790	2000**	600
LPS-stimulated TNF release (pg/ml per 10^5 cells)	4750	827	8600*	1212	7475	1310
Spontaneous thymidine uptake (cpm/10^5 cells)	584	29	934*	111	2204*	463
PHA-stimulated thymidine uptake (cpm/10^5 cells)	97 451	8085	103 507	9833	97 195	11 430
Anti-CD3-stimulated thymidine uptake (cpm/10^5 cells)	31 469	9701	29 575	9570	41 540	11 524

Significantly different from day 0 (Wilcoxon signed rank test): *$P<0·01$; **$P<0·05$.

GLA infusion resulted in a significant increase in both spontaneous and LPS-stimulated TNF release. Spontaneous thymidine uptake by PBMC significantly increased during the GLA infusion and was at a maximum at day 10. In contrast, the ability of PBMC to take up thymidine in response to both PHA and anti-CD3 stimulation remained unchanged. We conclude that intravenous GLA infusion in patients with pancreatic cancer results in an activation of the immune system demonstrated by an increase in spontaneous TNF release and thymidine uptake by PBMC; at the same time the ability of these cells to respond to further stimulation by PHA or anti-CD3 is not suppressed and remains unchanged. Whether these changes are associated with an improvement in the patient's clinical condition or duration of survival remains to be determined.

This work was supported by the Cancer Research Campaign and the Melville Trust for the Care and Cure of Cancer.

Antimicrobial activity and long-term use of Taurolin as an additive to parenteral nutrition. By D. A. JOHNSTON[1], G. PHILLIPS[2], J. RICHARDS[3] and C. R. PENNINGTON[1], *Departments of [1]Gastroenterology, [2]Microbiology and [3]Pharmacy, Ninewells Hospital, Dundee DD1 9SY*

Catheter-related sepsis remains a serious complication of parenteral nutrition (PN). The use of aseptic catheter-care techniques virtually eliminates such infection, but there remains a group of patients who develop recurrent sepsis and are at risk of septic complications. The short-term addition of Taurolin (Geistlich-Pharma, Wolhusen, Switzerland) to PN has been advocated for the prevention of infection, although experience of the use of Taurolin is limited. We have examined the stability and the antimicrobial activity of Taurolin in PN and assessed its clinical efficacy over a 12-month period in a patient who had suffered from repeated infections.

Taurolin (20 g/l; 450 ml) was added to a standard lipid nutrient mix (providing 11·5 g N and 8·87 MJ in 2·5 l) to obtain a solution of 3 g Taurolin/l. The Taurolin–nutrient mix was stored at room temperature and observed by inspection and microscopy throughout a 48 h period during which time no evidence of creaming or free oil was noted. It was, therefore, assumed that an expiry of 24 h on the prepared solution would give an adequate safety period for Taurolin stability.

The *in vitro* activity of Taurolin at concentrations of (3–0·1 g/l) in the PN solution was assessed against *Staphylococcus aureus, Staphylococcus epidermidis, Escherichia coli, Pseudomonas aeruginosa* and *Candida pseudotropicalis*. Taurolin to a dilution of 1·6 g/l was cidal to all organisms when compared with a Taurolin-free control of PN after 3 h and 24 h incubation (see Table).

A solution of 3 g Taurolin/l in PN was administered to a 26-year-old male with permanent intestinal failure who had recurrent infection due to an infected intra-atrial thrombus with involvement of the wall of the atrium and inferior vena cava, which was unresponsive to repeated courses of antimicrobial chemotherapy and surgical intervention. Throughout the 12 consecutive months of Taurolin administration there was no evidence of recurrent sepsis or side effects.

The addition of 3 g Taurolin/l as a solution in PN may be a safe and effective method of preventing recurrent sepsis.

Colony counts at 3 and 24 h for organisms grown in standard parenteral nutrition mixture, Taurolin (20 g/l) and Taurolin–PN mixture

(Colony forming units/ml of solution)

	S. aureus		*S. epidermidis*		*E. coli*		*P. aeruginosa*		*C. pseudo-tropicalis*	
	3 h	24 h	3 h	24 h	3 h	24 h	3 h	24 h	3 h	24 h
PN Mix	200	7500	400	6700	1050	7800	2100	2600	115	2400
Taurolin (20 g/l)	—	—	—	—	—	—	—	—	—	—
Taurolin–PN: 3·0 g/l	—	—	—	—	—	—	—	—	—	—
1·6 g/l	—	—	—	—	—	—	—	—	—	—
0·8 g/l	850	—	1050	—	750	—	1350	—	—	—
0·4 g/l	1650	1300	1000	750	850	850	2700	150	50	—
0·2 g/l	1600	1800	955	3600	1600	1700	2700	200	250	2700
0·1 g/l	1650	5600	800	7200	2200	4600	2900	700	150	4200

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Patterns of weight change in stage IV HIV infection. By DEREK C. MACALLAN[1], CAROLE NOBLE[1], CHRISTINE BALDWIN[2] and GEORGE E. GRIFFIN[1], [1]*Division of Communicable Diseases, Departments of Medicine, Cellular, and Molecular Sciences, St George's Hospital Medical School, Cranmer Terrace, London SW17 0RE* and [2]*Department of Genito-Urinary Medicine, King's College Hospital, Caldecot Road, London SE5 9RS*

Weight loss and wasting are major features of infection with Human Immunodeficiency Virus (HIV) and Acquired Immune Deficiency Syndrome (AIDS). Several reports have suggested that weight loss in AIDS is progressive and unremitting and that it is an inevitable consequence of HIV infection. The aim of the present study was to investigate patterns of weight change in stage IV disease and relate them to clinical events.

We performed a prospective analysis of body-weight measured using the same digital electronic scales in thirty male subjects with stage IV HIV infection from the time of AIDS diagnosis, for a period of 9–49 (median 19) months. Contemporaneous clinical events were documented.

Two distinct patterns of weight loss were observed; Type I (acute, severe weight loss episodes) and Type II (chronic, progressive weight loss episodes). An arbitrary cut off of 4 months was taken. Thirty-three acute weight loss episodes (defined as >4 kg in <4 months) were identified in eighteen individuals. The median magnitude of weight loss was 9·3 kg in 1·8 months (5·2 kg/month). Twenty-three chronic weight loss episodes (defined as >4 kg in >4 months) were identified in twenty-one individuals. The median magnitude was 13·2 kg in 9·3 months (1·4 kg/month). Periods of weight stability were observed in thirteen out of thirty (43%) individuals, the duration ranging from 4·5–33 months. Weight gain episodes were common; thirty-five weight gain episodes (defined as >4 kg over any period) were identified in twenty-five individuals. In twenty-one out of thirty-five (60%) such episodes weight gain achieved pre-morbid weight. Median weight gain was 9·1 kg over 3 months (3 kg/month).

Acute weight loss events were clearly associated with non-gastrointestinal infections whilst chronic weight loss events were associated with gastrointestinal disease ($P<0·01$) (see Table). Weight gain episodes were commonly associated with recovery from opportunistic infections, particularly *Pneumocystis carinii* pneumonia.

Pattern of weight change and associated clinical events

	Associated clinical event (%)		
Wt change episode	Non-GI infection	GI disease	Recovery from infection
Acute wt loss	82	30	0
Chronic wt loss	22	65	0
Wt stable	0	0	0
Wt gain	0	3	86

We have demonstrated that weight change in HIV infection follows characteristic patterns despite the multifactorial nature of weight loss. Acute weight loss episodes are commonly associated with opportunistic infections, particularly of the upper respiratory tract, and are often followed by periods of weight gain. Chronic, progressive weight loss seems to be more commonly associated with gastrointestinal disease involving malabsorption. These findings have important implications for our understanding of the pathogenesis of weight loss and emphasize the value of providing aggressive nutritional support during recovery.

The recovery of labelled carbon dioxide in pregnant subjects. By B. G. COOPER[1], D. REAICH[1], O. S. OLUFEMI[2] and R. TAYLOR[1] (introduced by D. HALLIDAY[3]), [1]*Human Metabolism Group, University of Newcastle upon Tyne NE2 4HH,* [2]*Princess Mary Maternity Hospital, Newcastle upon Tyne NE2 3BD* and [3]*Nutrition Research Group, CRC, Harrow HA1 3UJ*

Knowledge of the recovery of ^{13}C-labelled carbon dioxide is necessary for calculating protein oxidation in primed continuous infusions of L-[1-^{13}C]leucine. Recent studies have shown that it is inappropriate to use a universal correction factor (usually 0·81) to calculate oxidation and subsequently synthesis in a variety of conditions. The present study was aimed to assess $^{13}CO_2$ recovery in human pregnancy. Previous animal studies have suggested that $^{13}CO_2$ recovery may be higher in the pregnant compared to the non-pregnant state (Whitelaw *et al.* 1972). Six pregnant (30±2 weeks gestation) and four non-pregnant females fasted overnight and received a 4 h continuous infusion (3 μmol/kg per h) of $NaH^{13}CO_3$. Expired breath samples were collected every 15 min in the last hour for $^{13}CO_2$ enrichment by isotope ratio mass spectrometry and total CO_2 production ($\dot{V}_{CO_2}$) was measured by indirect calorimetry (Datex Deltatrac, Helsinki, Finland). CO_2 content of the infusate was measured by blood–gas analyser. The recovery of $^{13}CO_2$ was expressed as per cent recovery of administered dose.

	Age (years)	Wt (kg)	$\dot{V}_{CO_2}$ (l/min)	RER	EE (kcal/d)	APE	Recovery (%)
Pregnant (*n* 6)							
Mean	31·1	73·3	198·2**	0·82	1653**	0·03117	85·6*
SD	3·1	8·7	18·5	0·05	140	0·0029	6·4
Non-pregnant (*n* 4)							
Mean	28·5	56·5	143·3	0·81	1185	0·03023	73·5
SD	3·5	8·7	6·8	0·02	86	0·0030	6·9

Significantly different from non-pregnant subjects $*P<0·02$; $**P<0·001$.
RER, respiratory exchange ratio; EE, energy expenditure; APE, atoms per cent excess.

The $^{13}CO_2$ recovery was higher in the pregnant subjects ($P<0·02$). Absolute $\dot{V}_{CO_2}$ and EE were higher in the pregnant group, although these differences disappeared after correction for body-weight. RER was similar in the two groups. We confirm first that $^{13}CO_2$ recovery is raised in the third trimester of pregnancy compared with the non-pregnant state. This observation may be explained by the relative hyperventilation associated with pregnancy (De Swiet, 1991). Second, the use of universal correction factor to calculate leucine oxidation is inappropriate and if the true recovery value is ignored errors of 10–15% in estimating protein oxidation can occur when comparing pregnant and non-pregnant subjects.

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Estimation of the mass and distribution of body water in surgical patients by multiple-frequency bioelectrical impedance analysis. By K. C. H. FEARON[1], W. J. HANNAN[2], S. J. COWAN[2], C. PLESTER[1], J. S. FALCONER[1], R. A. RICHARDSON[1] and O. J. GARDEN[1], [1]*Department of Surgery, Royal Infirmary, Edinburgh EH3 9YW* and [2]*Department of Medical Physics, Western General Hospital, Edinburgh EH4 2XU*

The distribution of body water between extracellular (EC) and intracellular (IC) compartments has been proposed both as a predictor of survival in critical illness and as a marker of nutritional status and response to feeding. Multiple-frequency bioelectrical impedance analysis (MFBIA) has been suggested as a new method of assessing both total body water (TBW) and its distribution between IC and EC compartments. We have evaluated MFBIA in a heterogeneous surgical population (nineteen males, fifteen females) being considered for nutritional support. Total body resistance and reactance were measured at frequencies of 5, 50, 100, 500 and 1000 kHz using a Xitron 4000 MFBIA (Xitron Technologies, San Diego, CA, USA) operated at a current of 200 μA root mean square. Comparison was made with TBW measured by tritiated water dilution, extracellular water (ECW) measured by bromine dilution space (^{77}Br) and intracellular water (ICW) obtained by subtracting ECW from TBW.

Multiple correlation matrices for TBW, ECW, ICW and ECW/TBW were applied to establish the relationship of each of these to resistance (R_F; Ohm) at frequency F (kHz), reactance (X_F; Ohm) at frequency F (kHz), phase angle (P_F; degree) at frequency F (kHz), height (H; cm), weight (W; kg), age (A; yrs), chest antero-posterior thickness (APT; cm) and plasma albumin and sodium concentration. The parameters H^2/R_F and H^2/X_F were also included. Multiple stepwise regressions were performed using TBW, ECW, ICW and ECW/TBW as the independent variables and the prediction equations with the lowest standard error of the estimate (SEE) are shown in the Table.

TBW (l)	$0{\cdot}4921 \times H^2/R_{50} + 0{\cdot}5066 \times APT + 0{\cdot}334$ (r 0·965, SEE = 2·201)
ECW (l)	$0{\cdot}0131 \times H^2/X_{100} - 0{\cdot}01212 \times R_5 + 0{\cdot}000123 \times H^2/X_5 + 20{\cdot}158$ (r 0·908, SEE = 1·491)
ICW (l)	$0{\cdot}5891 \times H^2/R_{500} - 0{\cdot}4692 \times H^2/R_5 + 5{\cdot}025$ (r 0·913, SEE = 1·781)
ECW/TBW	$-0{\cdot}0271 \times P_{50} - 0{\cdot}00157 \times H + 0{\cdot}941$ (r 0·751, SEE = 0·0293)

These results suggest that MFBIA may provide a rapid and easy to perform method for estimating TBW, ICW, ECW and ECW/TBW on groups of patients within the clinical environment. Moreover, due to the error inherent in isotope dilution methods for TBW and ECW, the error attributable solely to the MFBIA technique may be sufficiently small to allow extension of the technique to investigation of individual patients.

Metabolic effects of 3 h infusion of dopamine at 2 μg and 5 μg/min per kg. By C. J. GREEN[1], R. SARGINSON[1], R. DUCKWORTH[1], I. T. CAMPBELL[1] and P. MAYCOCK[2], [1]*University Department of Anaesthesia, Royal Liverpool Hospital, Liverpool L69 3BX* and [2]*North West Injury Research Centre, University of Manchester, Manchester M13 9PL*

Dopamine is used in critical illness to support renal and cardiac function. Infused at incremental doses of 2, 5 and 10 μg/min per kg, 45 min at each dose, continuously, it increased energy expenditure, plasma-free fatty acids (FFA) and glycerol at 10 μg/min per kg, but not at the lower doses. Noradrenaline increased at 5 and 10 and adrenaline transiently at 2 μg/min per kg (Regan *et al.* 1990). The present study examines the effects of 3 h intravenous (i.v.) infusions of dopamine at 2 and 5 μg/min per kg.

Five healthy male volunteers aged 29–41 (median 31 years) were studied on three occasions and were randomized to receive 2 or 5 μg/min per kg dopamine in a solution of 50 g D-glucose/l or glucose alone (control) at a rate corresponding to the 5 μg infusion into one arm. Oxygen consumption ($(\dot{V}_{O_2})$, and respiratory exchange ratio (RER) were measured for 30 min prior to the infusion, and throughout the 3 h of infusion. Blood was taken via an i.v. cannula in the back of the hand on the other arm (which was held in a 'hot box' at 60°) before the start of the infusion and every 30 min during the infusion. Blood pressure (BP) and heart rate (HR) were measured and the electrocardiogram monitored throughout.

Dopamine at 2 μg/min per kg was associated with an increase in $\dot{V}_{O_2}$ 3·4 (0·8 to 24·5)% above that seen prior to the infusion and significantly higher than that observed during infusion of D-glucose alone ($P<0·05$; ANOVA). The 5 μg infusion was associated with an increase of 11·7 (1·1 to 30·4)% ($P<0·001$; ANOVA). RER was significantly higher between 60 and 180 min of the 5 μg infusion than with D-glucose alone ($P<0·01$). Dopamine, adrenaline and noradrenaline were all significantly higher during dopamine infusion at both doses than during the control infusion ($P<0·05$). Free fatty acids were higher at both 2 and 5 μg/min per kg than during the control infusion ($P<0·01$), but there was no difference in glycerol concentrations at either dose. Dopamine significantly increased Na excretion at both doses but urine volume only at 5 μg ($P<0·05$). Dopamine did not affect BP or HR at 2 μg/min per kg or HR at 5 μg/min per kg, but BP increased transiently at 5 μg/min per kg between 30 and 90 min of the infusion ($P<0·05$).

Dopamine infused over 3 h at both 2 and 5 μg/min per kg has metabolic effects i.e. it increases $\dot{V}_{O_2}$ and stimulates lipolysis. This was not evident in the earlier study, possibly because of the shorter duration of the infusions.

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Non-linear incorporation of tracer into non-albumin plasma protein as a result of a flooding dose of leucine. By K. SMITH, S. DOWNIE, P. W. WATT, C. M. SCRIMGEOUR and M. J. RENNIE, *Department of Anatomy and Physiology, University of Dundee, Dundee DD1 4HN*

Previously we showed an accelerated rate of incorporation of tracer [^{13}C]valine or [^{13}C]leucine or [^{13}C]phenylalanine into muscle and albumin as a result of administration of a flooding dose of leucine or valine (Smith *et al.* 1992*a*,*b*,*c*). We were therefore interested in further investigating the nature of this phenomenon by determining whether the apparent stimulation of tracer incorporation occurred in non-albumin plasma proteins during flooding. Healthy volunteers, studied after an overnight fast, were infused with L-[1-^{13}C]valine (1·5 mg/kg prime, 1·5 mg/kg per h) over a period of 7·5 h; 90 min before the end of the study a flooding dose of L-[1-^{13}C]leucine (50 mg/kg, 20 atoms % excess) was given. Plasma samples were obtained at intervals throughout the study. Plasma proteins were precipitated with 10% trichloroacetic acid and albumin was extracted into absolute ethanol; the remaining protein was solubilized in 0·3 M-NaOH, reprecipitated with perchloric acid then hydrolysed in 6 M-HCl at 110° overnight. Enrichments of non-albumin protein-derived valine and leucine were determined by isotope ratio mass spectrometry after separation by preparative GLC. Tracer valine incorporation was linear during the preflood period but was apparently asymptotic during the flooding period, even though plasma valine labelling was unaltered; incorporation of [^{13}C]leucine was also non-linear. Non-albumin protein synthetic rates were calculated from the tracer valine data as 0·366 (SD 0·022) %/h, preflood and, on average, 0·497 (SD 0·090) %/h, during the flood. These results provide additional evidence of increased tracer incorporation into protein as a result of flooding dose administration and suggest that significant perturbations may occur in the precursor–product relationship.

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The changes in body weight and in body composition, estimated using bioelectrical impedance analysis over 72 h of fasting; comparison with estimates based on energy expenditure measured by indirect calorimetry. By J. WEBBER and I. A. MACDONALD, *Department of Physiology and Pharmacology, Medical School, Queen's Medical Centre, Nottingham NG7 2UH*

Bioelectrical impedance analysis (BIA) is being used increasingly to estimate body composition in man. However, its accuracy in conditions where body composition is changing rapidly, has been questioned (Forbes *et al.* 1992). We examined whether the fat-free mass (FFM) and fat mass (FM) changes as calculated from BIA and weight changes gave similar values to those derived from energy expenditure data over a 72 h fast.

Nineteen healthy (eight male), non-obese subjects aged 20–31 years were recruited. They attended on two occasions having fasted for 12 or 72 h, and were allowed water *ad lib.* and consumed 80 mmol sodium chloride and 50 mmol potassium chloride per 24 h. They were weighed and whilst lying supine bioimpedance (resistance) was measured (EZ Comp 1500; Fitness Concepts Inc, Utah, USA). FFM was calculated using the equations derived from Segal *et al.* 1988. Resting metabolic rate (RMR) and respiratory exchange ratio (RER) were measured using indirect calorimetry. In the calculations of energy expenditure (EE), daily EE was assumed to equal 1·4 × RMR, and the energy equivalent of the FFM to be 4·2 kJ/g and that of the FM to be 38 kJ/g.

Changes in body weight, body composition and metabolic rate during a 72 h fast

	Fasting wt (kg)		Resistance (Ohms)		FFM (kg)		FM (kg)		RMR (kJ/min)		NPRER	
(h)	Mean	SEM	Mean	SEM	Mean	SEM	Mean	SEM	Mean	SEM	Mean	SEM
12	65·88	1·92	621	16	48·18	1·50	17·70	1·45	4·48	0·16	0·79	0·01
72	63·82**	1·89	644*	15	46·83**	1·33	16·99	1·42	4·63	0·15	0·71**	0·01

Significantly different from value at 12 h *$P<0·05$, **$P<0·01$.
NPRER, non-protein respiratory exchange ratio.

Using the data in the above Table the three-day EE is 25·9 MJ, whilst the 1·35 kg FFM represents 5·67 MJ. Thus, fat must provide 20·28 MJ which is equivalent to 586 g, and is comparable with the value of 710 g obtained from body composition analysis. Provided subjects are kept well hydrated during a period of starvation BIA appears able to give a reasonable estimate of changes in body composition for groups of subjects but not in individuals.

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Long-chain triacylglycerol malabsorption and pancreatic function in children with protein–energy malnutrition complicating severe liver disease. By S. BEATH[1], I. HOOLEY[2], K. WILLIS[2], S. JOHNSON[2], D. KELLY[1] and I. BOOTH[2], [1]*The Liver Unit, The Children's Hospital, Birmingham B16 8ET* and [2]*Institute of Child Health, Birmingham B16 8ET*

Steatorrhea is common in children with chronic liver disease and probably contributes to their protein energy malnutrition (PEM). Although pancreatic exocrine dysfunction (PED) is common in children with primary PEM (Barbezat & Hansen, 1968), a potential role for PED in the pathogenesis of steatorrhea in malnourished children with liver disease has not been previously investigated. We have therefore studied the contribution of PED to the malabsorption of dietary lipid in ten children with PEM and liver disease (biliary atresia (*n* 8), neonatal hepatitis (*n* 2)). Growth and fat balance were monitored over a period of 8–18 weeks, during which time high calorie modular feeds containing different amounts of long-chain triacylglycerol (LCT) (17–77% fat intake as LCT) were administered. Intraduodenal pancreatic enzyme activity following a test meal (McCollum *et al.* 1977) was studied sixteen times in ten infants.

	Pancreatic exocrine function (*n* 16)			Reference values
	Median	Range	SD	
Subject details:				
Age (months)	11·96	5·4 to 24·5	5·9	
Weight-for-age Z score	−1·85	−3·1 to −0·78	0·75	0
Height-for-age Z score	−2·46	−3·9 to 0·25	1·26	0
Plasma:				
Bilirubin μmol/l	165	5 to 444	107	<20
Coefficient LCT absorption (%)	67	46 to 89	13	>95
Enzyme in duodenal aspirate:				
Lipase units/ml	161	10 to 437	108	200–1900*
Trypsin μg/ml	120	154 to 289	70	29–80*

* Reference values (McCollum *et al.* 1977).

Only one child had impaired pancreatic enzyme activity which may have been due to abdominal sepsis. The coefficient of LCT absorption was grossly abnormal, but there was no correlation with pancreatic lipase activity. Pancreatic function in six children who had a repeat test was unchanged. In contrast to children with primary malnutrition, there was no association between severity of PEM and PED.

In this study pancreatic function was well preserved despite evidence of severe liver disease and PEM. Therefore, reduced intraluminal bile and impaired lipid solubilization are probably more important than lipolysis in the pathogenesis of fat malabsorption in chronic liver disease. Our data do not support the statement (Chong *et al.* 1989) that pancreatic enzyme supplements are helpful in this disorder.

We thank the Children's Liver Disease Foundation for their support.

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Superior absorption of medium-chain triacylglycerols compared with conventional dietary long-chain fats in children with chronic liver disease. By S. BEATH, T. JOHNSON, K. WILLIS, I. HOOLEY, G. BROWN, I. BOOTH and D. KELLY, *The Liver Unit, The Children's Hospital, Birmingham B16 8ET* and *The Institute of Child Health, Birmingham B16 8ET*

Protein energy malnutrition (PEM) in children with cholestatic liver disease has several interacting aetiologies, but fat malabsorption is a fundamental problem. We have tested the hypothesis that intestinal absorption of medium-chain triacylglycerol (MCT) is superior to long-chain triacylglycerol (LCT) and therefore has a role in the treatment of PEM in liver disease.

Nine children (five females, four males) under the age of 2 years who were cholestatic secondary to biliary atresia (*n* 6), neonatal hepatitis (*n* 2) and Alagille's syndrome (*n* 1) were given dietary supplements of MCT (Liquigen; Scientific Hospital Supplies, Liverpool) under the supervision of a paediatric dietitian.

Jaundiced infants produce numerous small volume stools which are impossible to collect by conventional means. Therefore a novel method for measuring faecal fat based on solvent extraction (Bligh & Dyer, 1959) of lipids from a 3 d collection of soiled nappies was developed and validated. Faecal fat excretion was determined gravimetrically from a portion of solvent extract and the profile of individual fatty acids contained in faeces was determined by gas–liquid chromatography. The coefficient of absorption of individual fatty acids was calculated by subtracting the observed excretion from the fatty acid intake.

MCT intake (g/kg body wt)	Fatty acid absorption coefficient				
	C8/10	C18:1	C18:2	C18:3	*P* (paired *t* test)
1–2 g/kg	100	70	73	36	0·001
2–3 g/kg	99	82	78	43	0·001
3–5 g/kg	98	74	58	46	0·001

Despite the high intake of MCT (2–5 g/kg), none of the infants excreted more than 2% fat as medium-chain fatty acids (C8/10).

These data support the view that the absorption coefficient of MCT is superior to LCT in cholestatic liver disease.

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Metabolic and inflammatory changes following laparoscopic cholecystectomy. By M. S. R. JAKEWAYS[1], V. MITCHELL[2], I. A. HASHIM[3], S. J. D. CHADWICK[4], J. ANDERSON[2], F. CARLI[2] and A. SHENKIN[3], [1]*Department of Surgical Research, Clinical Research Centre, Watford Road, Harrow HA1 3UJ, Departments of* [2]*Anaesthesia and* [4]*Surgery, Northwick Park Hospital, Watford Road, Harrow HA1 3UJ* and [3]*Department of Clinical Chemistry, Royal Liverpool University Hospital, Liverpool L7 8XW*

Laparoscopic cholecystectomy is rapidly becoming the operation of choice in the treatment of uncomplicated gall stones. Possible advantages include reduction in surgical trauma, rapid patient recovery and early hospital discharge. Whilst the metabolic and inflammatory responses following open cholecystectomy have been described they have not been investigated following laparoscopic cholecystectomy.

Hormonal, metabolic and inflammatory changes and alteration in subjective fatigue sensation, at intervals up to 48 h after surgery, have been studied in patients undergoing laparoscopic (*n* 14) and open (*n* 11) cholecystectomy. Patient groups were comparable in height, weight and sex.

			Time (h from the end of surgery)					
		Pre-surgery	0	4	8	12	SEM*	*P*†
Cortisol (nmol/l)	lap	342	895	752	624	383	81	0·15
	open	424	966	951	744	515	91	
Glucose (nmol/l)	lap	5·54	7·46	6·37	6·45	5·75	0·51	0·011
	open	6·16	8·46	8·38	7·84	7·95	0·58	
Albumin (g/l)	lap	38·9	35·2	34·7	33·3	31·7	0·85	0·67
	open	38·5	34·6	36·0	34·3	31·9	0·96	
IL-6‡ (pg/ml)	lap	17·5	48·2	57·2	43·7	41·3		0·007
			37·5–61·9	44·6–73·4	34·1–56·0	32·2–52·9		
	open	16·9	66·6	99·3	76·3	62·6		
			48·8–90·8	72·8–135·4	55·9–104·1	45·9–85·4		

* Pooled SEM 0–12 h; † comparing laparoscopic with open cholecystectomy (ANOVA); ‡ mean and 95% confidence limits.

At the end of surgery (time 0), plasma cortisol, glucose and IL-6 concentrations were significantly increased from their preoperative values in both groups ($P = 0{\cdot}001$). There was no difference in cortisol concentration between the two groups. In the initial 12 h following surgery, plasma glucose concentration remained significantly greater in the open, compared with the laparoscopic group ($P = 0{\cdot}011$). Plasma albumin concentration was significantly reduced, to an equivalent extent, in each group after surgery ($P<0{\cdot}01$). Interleukin 6 (IL-6) levels peaked at 4 h after operation and were significantly greater in the open compared with the laparoscopic group ($P = 0{\cdot}007$). C-reactive protein (CRP) levels increased from 8 h after surgery. Mean CRP levels at 24 h were 49 and 17 mg/l and at 48 h were 70 and 28 mg/l in the open and laparoscopic groups respectively, the difference between the two groups being significant ($P = 0{\cdot}003$). Fatigue scores were increased following both procedures and recovered more rapidly after laparoscopic surgery. Hand-grip strength was reduced only after open cholecystectomy.

These results demonstrate that laparoscopic cholecystectomy stimulates a significant stress response. The cortisol response is similar to that which follows open cholecystectomy. However, aspects of the metabolic and the acute-phase responses appear to be attenuated, consistent with a reduction in tissue trauma in laparoscopic cholecystectomy.

Human growth hormone improves body-weight but not disease activity in a chronic model of colitis. By C. D. WEIR[1], N. H. ANDERSON[2], M. MCCAIGUE[1], M. I. HALLIDAY[1] and B. J. ROWLANDS[1], *Departments of [1]Surgery and [2]Pathology, The Queen's University of Belfast, Grosvenor Road, Belfast BT12 6BJ*

Systemic endotoxaemia and malnutrition are common features of severe inflammatory bowel disease (IBD). Recombinant human growth hormone (HGH) improves nitrogen balance, immune function and wound healing in catabolic illness (Saito *et al.* 1990). We investigated the effects of HGH on disease activity, systemic endotoxaemia, weight change and N balance in animals with established colitis.

Male Wistar rats weighing 250–350 g (*n* 36) were studied in four groups. Groups 1 and 2 had colitis induced by the colonic administration of trinitrobenzesulphonic acid in ethanol (500 ml/l; v/v) via a fine silastic cannula. Groups 3 and 4 received saline as control. After 7 d all animals were transferred to individual metabolism cages. Groups 1 and 3 received daily injections of 0·2 U/kg HGH and groups 2 and 4 received saline vehicle control. Urine was collected for N measurement by chemiluminescence. At sacrifice on day 14 blood was sampled aseptically from the aorta for plasma endotoxin. Endotoxin was assayed using a chromogenic limulus lysate assay. The colon was excised and a colon macroscopic score (CMS) assigned (0–10 scale).

Treatment group	CMS		Systemic endotoxin (pg/ml)		N balance (gN/7 d)		Weight change (g)	
	Mean	SE	Mean	SE	Mean	SE	Mean	SE
Colitis + HGH	4·00	0·44†	37·8	9·5	+4·11	0·06†	+28·1	2·84†
Colitis + Saline	4·44	0·60†	46·1	15·3*	+3·56	0·16	+18·3	3·17
Control + HGH	1·25	0·41	14·3	7·07	+3·48	0·09	+22·5	2·53
Control + Saline	1·11	0·35	16·35	6·37	+3·29	0·12	+19·7	1·08

*$P<0·05$, ANOVA; †$P<0·01$, ANOVA.

Administration of HGH to colitic animals did not influence either CMS or systemic endotoxaemia. The highest mean endotoxin concentration was found in saline treated colitics. Despite this HGH improved both N balance and weight gain in colitics. Treatment of chronic large bowel inflammation in rats with HGH improves body-weight and N balance with no effect on colonic damage.

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Changes in short-chain fatty acids in experimental colitis. By C. D. WEIR[1], L. T. MCGRATH[2], N. H. ANDERSON[3] and B. J. ROWLANDS[1], *Departments of [1]Surgery, [2]Therapeutics and [3]Pathology, The Queen's University of Belfast, Institute of Clinical Science, Grosvenor Road, Belfast BT12 6BJ*

The normal colonic mucosa utilizes short-chain fatty acids (SCFA) in the preferential sequence: *n*-butyrate>acetate>propionate (Roediger, 1982). Chronic inflammatory bowel disease (IBD) may result from deficient production or defective utilization and uptake of SCFA. Assumptions about the role of SCFA in IBD have been based on their measurement in stool samples (Vernia *et al.* 1988). To investigate this we measured SCFA in faecal samples from three colonic sites in an animal model of chronic colitis.

Male Wistar rats (*n* 16) were studied in two groups: group 1 had colitis induced by the colonic administration of trinitrobenzesulphonic acid in ethanol (500 ml/l; v/v). Group 2 had colonic administration of saline as control. Animals were fed a normal laboratory chow containing 14·1 g digestible crude fibre/kg. Seven days later, animals were sacrificed. Faecal material was rapidly extruded from the proximal, distal, and mid-colon (8 cm from rectum). Colonic damage was scored by an independent pathologist using a 0–10 scale. Faeces were stored at −80° until analysis. SCFA were extracted in alcohol and dichloromethane, then esterified in bromopentafluorotoluene prior to analysis by gas–liquid chromatography.

Colitic animals lost significantly more weight (−8·4 g *v.* +50·2 g, $P<0·001$) SCFA profiles are shown in the Table.

	Mean SCFA (μmol/g faeces)								
	Acetate			Propionate			*n*-Butyrate		
Sample site . . .	Proximal	Mid-	Distal	Proximal	Mid-	Distal	Proximal	Mid-	Distal
Colitis	40·92	20·97	20·07	19·32	12·25	13·92	7·62	4·07	3·34
Control	33·63	22·07	19·77	15·06	12·13	13·16	13·25*	4·1	5·83†

*$P<0·05$ (*t* test); †$P<0·05$ (Mann-Whitney U test).

n-Butyrate fell significantly in the proximal and distal colon in colitis compared to controls. There was no significant difference in acetate or propionate. Changes in *n*-butyrate occur after the development of colitis and are seen in the proximal and distal colon. This implies a reduced production of *n*-butyrate. This may not be the cause of colitis but an indirect effect.

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The correction of metabolic acidosis in chronic renal failure reduces whole-body protein breakdown and amino acid oxidation. By D. REAICH, T. H. J. GOODSHIP and S. CHANNON, *Department of Medicine, University of Newcastle upon Tyne NE1 7RU*

Whole-body protein breakdown (PD) and amino acid oxidation (O) is increased in acidotic rats. Correction of acidosis in chronic renal failure (CRF) rats decreases PD and O in patients with CRF the correction of acidosis improves nitrogen balance (Papadoyannakis *et al.* 1984). The mechanism for this has not been studied.

Nine CRF patients were studied on three occasions; acidotic, after 4 weeks treatment with $NaHCO_3$ and after 4 weeks treatment with equimolar NaCl. Primed constant infusions of L-[1-^{13}C]leucine were used to measure PD and O in the postabsorptive state.

There was a significant increase in pH ($P<0{\cdot}01$) during treatment with $NaHCO_3$ compared with the other two studies. PD and O (μmol/kg per h) were significantly reduced ($P<0{\cdot}05$) during treatment with $NaHCO_3$.

	Acidotic		$NaHCO_3$		NaCl	
	Mean	SD	Mean	SD	Mean	SD
pH	7·31	0·01	7·38*	0·01	7·30	0·01
PD (μmol/kg per h)	122·4	1	88·3*	6·9	116·2	9·1
O (μmol/kg per h)	13·0	1·2	9·2*	0·9	14·9	1·9

* Significantly different from acidotic and NaCl.

This suggests that correction of acidosis in CRF patients improved N balance by decreasing protein degradation and amino acid oxidation.

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Collagen synthesis in human bone measured using stable isotope-labelled alanine and proline. By C. M. SCRIMGEOUR, S. DOWNIE, P. K. RICKUSS and M. J. RENNIE, *Department of Anatomy and Physiology, University of Dundee, Dundee DD1 4HN*

Although collagen is the most abundant bodily protein little is known about human collagen synthesis. We have developed methods using stable isotope-labelled amino acids, and applied them to measure collagen synthesis in bone obtained during knee replacement surgery. Three patients (all female aged 75–83 years, 66–78 kg) were studied. A primed constant intravenous infusion of [1-^{13}C,^{15}N]alanine (2 mg prime, 2 mg/kg per h) was started approximately 8 h before surgery. After 6 h, a flooding dose of [^{15}N]proline (20 atoms %, 60 mg/kg) was given intravenously. Blood was taken throughout at 0·5–1 h intervals, more frequently during the early part of the proline flood. Healthy cortical and cancellous bone were obtained during surgery. Enrichments of plasma alanine (both ^{13}C and ^{15}N) and [^{15}N]proline were determined using gas chromatography–mass spectrometry. Collagen, extracted from bone samples using hot-water extraction after HCl demineralization, was incubated with NaOH and precipitated with perchloric acid before hydrolysis with 6 M HCl at 110° overnight; alanine and proline were isolated using preparative gas chromatography and their enrichment determined by combustion-isotope ratio mass spectrometry. Rates of incorporation of ^{15}N and ^{13}C alanine were identical, suggesting an apparent rate of collagen protein synthesis (mean (SD)) 0·061 (0·008)%/h in cancellous bone; in cortical bone the rate was less (0·034 (0·001) %/h). These rates will be underestimates being calculated using the plasma alanine enrichment rather than the labelling of the true collagen precursor pool; the use of the proline flood should, theoretically, avoid this problem. The rates of proline incorporation showed the same pattern of incorporation as for alanine, but the absolute rates were apparently sevenfold higher (cancellous 0·43 (0·20), cortical 0·24 (0·11) %/h).

These results demonstrate that human collagen synthesis proceeds at a rate at least as high as previously observed in, e.g. muscle and possibly higher. Whether the surprisingly large discrepancy between the rates determined by the constant infusion and flooding dose methods is real or an artefact remains to be determined. The methods offer the possibility of investigating changes in collagen synthesis as a result of modulation by hormones, nutrition and disease processes.

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The effect of enteral glutamine deprivation on rat gut mucosa during a systemic injury response. By MONICA WUSTEMAN, NICOLA JORDAN, HELEN TATE, LAWRENCE WEAVER, STEVE AUSTIN and MARINOS ELIA, *Dunn Nutrition Unit, Downham's Lane, Milton Road, Cambridge CB4 1XJ*

Systemic injury has been shown, both clinically (Souba *et al.* 1990) and experimentally (Ardawi *et al.* 1990; Souba *et al.* 1990), to be associated with alterations in gut glutamine metabolism. It has been suggested that glutamine plays an important role in the maintenance of gut mucosal structure and function, particularly since glutamine enriched enteral diets increase gut glutaminase activity (Dudrick *et al.* 1992). However, little data exist to show whether systemic injury leads to any alteration in gut morphology and function. This study was therefore undertaken to assess (1) whether or not a systemic injury, which reproduces the depletion of muscle and plasma glutamine concentrations found in many forms of clinical injury, results in alterations of the mucosal structure in the small intestine and (2) whether or not supplementing with, or excluding glutamine from the diet could have a modifying effect.

Young male rats (43–44 d) were fed *ad lib.* with elemental diets (200 g amino acid/kg) in which glutamine was either absent (OG) or present as 50% of the non-essential amino nitrogen (GLNS). On day 4 of feeding, a systemic injury response (Wusteman & Elia, 1992) was generated over 6 d with three serial subcutaneous injections (each 0·2 ml/100 g body weight) of turpentine (delivered at 48 h intervals) in seven OG and six GLNS rats. Six *ad lib.* and seven pair-fed (70% *ad lib.*) controls from both dietary groups were also included in the study. All rats were killed 48 h after the last turpentine injection and the small intestine (1st tercile) was removed for analysis. Mucosal weights were recorded, N content was measured and histological assessments (villus (V) height, crypt (C) depth) made on standard haematoxylin and eosin stained sections using an eyepiece micrometer.

The injury induced reductions in plasma glutamine concentration in both dietary groups (μmol/l, mean (SEM). OG: abscessed, 494 (12); pair-fed, 767 (25). GLNS: abscessed, 577 (17); pair-fed, 698 (38)). There was no measurable effect of the injury on mucosal mass and N content (mg N/cm, mean (SEM). OG: abscessed, 0·408 (0·04); pair-fed, 0·377 (0·052). GLNS: abscessed, 0·397 (0·042); pair-fed, 0·398 (0·025)). Preliminary assessment of mucosal histology also showed no significant differences between the groups studied.

In conclusion, this study provides no evidence to indicate that this type of systemic injury, in the presence or absence of dietary glutamine, alters the mucosal mass, N content or histological appearance of the upper small intestine.

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