Proceedings of the Nutrition Society

Abstracts of Original Communications

A joint meeting of the Clinical Nutrition and Metabolism Group of the Nutrition Society and the British Association for Parenteral and Enteral Nutrition was held at Harrogate International Centre on 28–30 November 2000, when the following papers were presented.

All abstracts are prepared as camera-ready material.

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Nutritional status of children on admission to a children's hospital. By H. McCARTHY[1] and H.R.M. McIVOR[2], [1]*Manchester Children's Hospitals NHS Trust, Manchester M9 7AA and* [2]*North Stafford City General Hospital, ST4 6QG*

Malnutrition in hospital has been well documented over the past 25 years. The clinical implications of malnutrition include impaired immune response, cardiac and respiratory function, as well as an altered psychological state (Green, 1999). In children, malnutrition also impairs growth.

The majority of these reports have looked at adult populations; few have investigated the extent of malnutrition within the population of a children's hospital (Moy *et al*. 1990; Hendriske *et al.* 1997). One reason may be the difficulty in clearly identifying malnutrition in children, as there is no universally recognized classification.

This study compared the nutritional status of a sample of thirty-one children (who fulfilled certain selection criteria), as defined by a number of methods. Weight for age was compared to UK growth reference charts in terms of centiles and standard deviation scores (SDS) (Freeman *et al.* 1995). Weight for height ratios were calculated for each child (Waterlow, 1972; Hendriske *et al*. 1997). Body mass index (BMI) was also calculated and compared to UK centile reference charts (Cole *et al*. 1995). Mid-upper arm circumference (MUAC) was measured and compared to reference standards (Frisancho, 1981).

Using these criteria, between 13% and 26% of the sample could be defined as being malnourished or at risk of becoming malnourished.

Anthropometric measure	At risk of malnutrition	Malnutrition
Weight for age (centiles)	Defined: 0.4th–2nd centile space $n = 3$	Defined: <0.4th centile line $n = 1$
Weight for age (SDS)	Defined: –1 to –2 SDS $n = 3$	Defined: >–2 SDS $n = 4$
MUAC	Defined: <5th centile $n = 4$	–
BMI (centiles)	Defined: 0.4th–2nd centile space $n = 5$	Defined: <0.4th centile line $n = 0$
% BMI for age	Defined: 80–90% $n = 5$	Defined: <80% $n = 0$
% weight for height (Waterlow)	Defined: 80–90% $n = 4$	Defined: <80% $n = 0$
% weight for height (Hendriske *et al.*)	Defined: 80–90% $n = 5$	Defined: <80% $n = 3$

Nutritional status as assessed from anthropometric measurements. Classifications and number of children falling within these measures.

These results are in keeping with those of a larger survey carried out within the same NHS Trust. A comparison with the other studies of this nature is difficult, as different growth reference charts are used. Hendriske *et al*. (1997) identified 27% of their sample as being malnourished or at risk of developing malnutrition on the basis of percentage weight for height using the Tanner-Whitehouse growth reference charts (Tanner *et al.* 1966). In our sample, 26% were identified using their calculation; however the median values for weight and height in this study were taken from current growth reference data.

This study suggests that malnutrition remains a prevalent feature among children on admission to hospital, and therefore also has implications for community health. Time and resources need to be directed at screening for malnutrition in children. Identifying and treating these at-risk children has the potential for improving clinical outcomes and reducing costs.

Freeman JV, Cole TJ, Chinn S, Jones PRM, White EM & Preece MA (1995) *Archives of Disease in Childhood* **73**, 17–24.
Cole TJ, Freeman JV & Preece MA (1995) *Archives of Disease in Childhood* **73**, 25–29.
Frisancho AR (1981) *American Journal of Clinical Nutrition* **34**, 2540–2545.
Green CJ (1999) *Clinical Nutrition* **18** (suppl. 2), 3–28.
Hendriske WH, Reilly JJ & Weaver LT (1997) *Clinical Nutrition* **16**, 13–18.
Moy RJD, Smallman S & Booth IW (1990) *Journal of Human Nutrition and Dietetics* **3**, 93–100.
Tanner JM, Whitehouse RH & Takaishi M (1966) *Archives of Disease in Childhood* **41**, 454–471.
Waterlow JC (1972) *British Medical Journal* **3**, 566–569.

The effect of nutritional management on the mood of undernourished patients. By J. FIELD[1], Z. STANGA[1], D.N. LOBO[2] and S.P. ALLISON[1], [1]*Clinical Nutrition and Investigation Unit, and* [2]*Section of Surgery, University Hospital, Queen's Medical Centre, Nottingham NG7 2UH*

Starvation and weight loss are almost universal accompaniments of severe illness. Psychological changes with depression, anxiety, irritability, apathy, poor sleep pattern and loss of concentration are also associated with disease-related malnutrition. Most studies on patients receiving nutritional support have concentrated on metabolic, clinical and functional outcomes, but limited attention has been paid to the effects of nutritional management on the psychological state of patients. Studies involving chronic semi-starvation, physical immobilization, and short-term sedation all demonstrate diminished intellectual and psychomotor performances. A rise in anxiety and depression scores followed by slow recovery with refeeding has been shown in normal subjects (Keys *et al*. 1950) and in surgical patients (Windsor & Hill, 1988).

Ten undernourished patients with gastrointestinal disease/failure (six male, four female), with a median age (range) of 61.5 (34–80) years, were studied during the first week following transfer from other hospitals or departments to our clinical nutrition unit for nutritional support (nine parenteral, one enteral) which was begun on Day 2. Psychological assessment was performed using a structured and standardized Profile of Mood States (POMS) questionnaire (McNair *et al*. 1971; Albrecht & Ewing, 1989) administered to all the patients by the same interviewer on Days 1 and 8 after admission to the unit. The POMS questionnaire comprises sixty-five adjectives and assesses various aspects of mood. Each of the sixty-five items is scored from 0 (not at all) to 4 (extremely), to detect changes in tension/anxiety, depression, anger, vigour, fatigue and confusion.

There were striking improvements in mood during the period of study.

	Tension	Depression	Anger	Vigour	Fatigue	Confusion
Pre-treatment score (Day 1)	29.7	44.6	30.2	4.0	27.7	20.0
Mean (95% CI)	(26.5–32.9)	(36.0–53.2)	(21.4–39.0)	(1.8–6.2)	(27.0–28.4)	(17.3–22.6)
Post-treatment score (Day 8)	8.6	4.5	2.3	23.5	11.3	6.6
Mean (95% CI)	(3.3–13.9)	(0.4–8.6)	(0.01–4.6)	(17.7–29.3)	(8.7–13.8)	(1.3–11.9)

The provision of nutritional support to undernourished critically ill patients in the context of a dedicated nutritional unit resulted in significant improvement in all components of the POMS scores. It has not proved possible, in this study, to separate the effects of nutritional support from the other aspects of management in the unit. Further studies are required to control for these factors, but our results confirm those of other studies (Windsor & Hill 1988, Young *et al.* 1993), showing that psychological testing is a useful parameter for monitoring the outcome of treatment.

Albrecht RR & Ewing SJ (1989) *Journal of Personal Assessment* **53**, 31–39.
Keys A, Brozek J, Henschel A, Mickelsen O & Taylor HF (1950) *The Biology of Human Starvation*. Minneapolis: University of Minnesota Press.
McNair DM, Lorr M & Droppleman LF (1971) *Profile Of Mood States Manual*. San Diego: Educational and Industrial Testing Service.
Windsor JA & Hill GA (1988) *Annals of Surgery* **207**, 290–296.
Young LS, Bye R, Scheltinga M, Ziegler TR, Jacobs DO & Wilmore DW (1993) *Journal of Parenteral and Enteral Nutrition* **17**, 422–427.

Hepatic and whole body protein metabolism in hypoalbuminaemic haemodialysis patients. By J.D. LOUDEN[1], R. EDSON[3], C. ALEXANDER[3], D. REAICH[1], K. BARTLETT[2] and T.H.J. GOODSHIP[1], [1]*School of Clinical Medical Sciences and* [2]*Biomedical Mass Spectrometry Unit, University of Newcastle upon Tyne, Newcastle upon Tyne NE2 4HH and* [3]*Department of Nutrition and Dietetics, South Cleveland Hospital, Middlesbrough TS4 3BW*

Malnutrition is an important cause of morbidity and mortality in patients with chronic renal failure treated by haemodialysis (HD). Hypoalbuminaemia is the most powerful predictor of mortality in this group (Lowrie & Lew, 1990) but albumin synthesis has not been directly measured in hypoalbuminaemic patients treated by HD. In the present study, albumin synthesis and whole body protein turnover were measured in hypoalbuminaemic and normoalbuminaemic HD patients and healthy controls using primed constant infusions of L-[1-^{13}C]leucine after an overnight fast and during hourly oral meal feeding (using nutritional supplements based on estimated requirements).

Seven hypoalbuminaemic HD patients (serum albumin < 36 g/l), seven normoalbuminaemic HD patients (serum albumin 40 g/l) and nine age- and sex-matched healthy controls were studied. Body composition was assessed by means of anthropometry (weight, height and skinfold thickness at four sites) and dietary intake by self selected 3-day food diaries.

Body mass index (BMI) and body fat content were significantly lower in the hypoalbuminaemic HD patients (HHD) than in normoalbuminaemic patients (NHD) and controls: BMI, HHD 20.8(1.3), NHD 26.7(1.3), controls 26.2(1.1) kg m^{-2}, P<0.05; fat (% body weight), HHD 23.4(2.0), NHD 33.1(3.2), controls 32.6(1.8) %, P<0.05, ANOVA, mean(SEM). There were no significant differences in fat-free mass index, dietary protein intake and energy intake.

Fasting whole body protein degradation corrected for actual body weight was significantly greater in HHD patients: HHD 170.2(7.4), NHD 150.0(3.8), controls 152.0(6.4) μmol kg^{-1} h^{-1}, P<0.05, but when corrected for fat-free mass there was no significant difference: HHD 223.9(7.2), NHD 226.2(7.9), controls 221.3(5.8) μmol kg^{-1} h^{-1}, mean (SEM). The fasting albumin fractional synthesis rate was not significantly different in the three groups but the HHD group failed to show a significant rise with feeding compared with the other two groups: HHD fasting 13.9(1.4) *v.* fed 16.3(2.7), NS; NHD fasting 11.7(0.9) *v.* fed 15.4 (0.9), P<0.05; controls fasting 11.9(1.0) *v.* fed 15.0(1.1), P 0.05).

This study suggests that there are differences of body composition and albumin metabolism in hypoalbuminaemic haemodialysis patients which may be related to an impaired metabolic response to hourly oral meal feeding.

Lowrie EG & Lew NL (1990) *American Journal of Kidney Disease* **15**, 458–482.

Nutritional status of traumatic and anoxic brain-injured patients on admission to rehabilitation. By M.A. THOMSON, A.D. CARVER and R.L. SLOAN, *Fife Rehabilitation Service, Sir George Sharp Unit, Cameron Hospital, Fife KY8 5RR*

Whilst there is a wealth of literature regarding the nutritional problems of people with traumatic brain injury (TBI) in the acute stage of injury, there is very little about these patients during rehabilitation and even less about the nutritional problems associated with anoxic brain injury (ABI). Early feeding is increasingly advocated for the nutritional support of brain-injured patients but successful use of enteral feeding in critical illness is often limited by the patient's condition, the accessibility of a route for feeding and their tolerance of the enteral formula. Many brain-injured patients present to rehabilitation units with varying degrees of nutritional depletion. This study was a retrospective case-note review of all TBI and ABI patients admitted for rehabilitation between 1996 and 1999. The aim was to collate information on nutritional status and nutritional support on admission, during rehabilitation and at discharge to identify opportunities to improve our practice.

Fife Rehabilitation Service (FRS) provides assessment and rehabilitation for patients with physical disabilities in the 16–64 year age group. Annually there are approximately seventy-five admissions to the twelve-bedded ward. TBI and ABI account for about 20% of all admissions. Forty-three consecutive cases were identified comprising thirty-three (five female, twenty-eight male) with TBI (seventeen falls, eight assaults, eight road traffic accidents) and ten (five female, five male) with ABI (seven ischaemic anoxia, one anoxic anoxia, one anaemic anoxia, one metabolic anoxia). Alcohol was a causative factor in sixteen (48%) of the TBI patients and drugs in four (40%) of the ABI patients. The median time from injury to admission to rehabilitation was 29 (range 7–328) d. Forty (93%) patients were discharged home, one patient died during the rehabilitation period and two anoxic brain-injured patients were transferred to another hospital for continuing care.

The dietitian working in the rehabilitation unit had assessed nutritional status. Body mass index (BMI) in combination with upper arm anthropometrical measurements were used to determine the degree of nutritional depletion using criteria devised by McWhirter & Pennington (1994).

On admission to FRS, twenty-four (56%) patients showed evidence of nutritional depletion (eleven mild, ten moderate, three severe). All patients had lost weight since injury with a mean loss of 9.1 (range 1.7–55.0) kg which equates to a mean loss of 12.6% (range 1.9–52.5) of total body weight. The mean duration of rehabilitation admission was 61 (range 5–366) d. During rehabilitation there was a mean weight gain of 4.9 kg and the mean percentage weight loss from the time of injury had fallen from 12.6% on admission to 5% on discharge from rehabilitation. On discharge, ten (23%) patients remained nutritionally depleted (six mild, two moderate, two severe).

Twenty-three (53%) patients had needed to be enterally tube-fed in the acute period; thirteen (39%) of those with TBI and ten (100%) of those with ABI. On admission to rehabilitation six (14%) patients (four TBI, two ABI) continued with artificial nutritional support (ANS) and a further twenty-eight (65%) patients were started on oral nutritional supplements in an attempt to improve nutritional status. Dysphagia was present on admission in nineteen (44%) patients (thirteen TBI, six ABI).

On discharge, seven (16%) patients remained on nutritional supplements and two (5%) patients with ABI remained on ANS due to persistent vegetative state in one and low awareness state in the other. Five (12%) patients continued to experience dysphagia on discharge.

The prevalence of nutritional depletion in this patient group is higher than reported in acute hospital admissions (McWhirter & Pennington, 1994). In the absence of dietetic input it is likely that malnutrition will go unnoticed. It is our recommendation that all patients with TBI or ABI should be assessed on admission to rehabilitation to determine nutritional status. This should enable the most appropriate dietetic intervention for maximum benefit to be derived from the rehabilitation programme. Unfortunately the working party report of the British Society of Rehabilitation Medicine (1998) did not include dietetic input in their recommendations for staffing of specialised rehabilitation units for head injured patients.

British Society of Rehabilitation Medicine (1998) *Rehabilitation after Traumatic Brain Injury*. London: British Society of Rehabilitation Medicine.
McWhirter J & Pennington C (1994) *British Medical Journal* **308**. 945–949.

Prospective cost-effectiveness analysis of a nutritional support team. By K. WARD[1], N.C MORAN[3], C.E WRIGHT[2], E.R. BRIERLEY[1], K. WATERS[5], M JAMES[4] and A.J. MAKIN[1], [1]*Manchester Royal Infirmary, Oxford Road, Manchester M13 9WL,* [2]*Chester College, Cheyney Rd, Chester CH1 4BJ,* [3]*Northern General Hospital Trust, Herries Rd, Sheffield S5 7AU,* [4]*Centre for Health Planning and Management, Keele University, ST5 5BG and* [5]*University of Manchester, Oxford Road, Manchester M13 9WL*

Nutrition Support Teams (NST) are generally believed to reduce the costs associated with nutritional support by reducing the complications related to parenteral nutrition and decreasing its inappropriate use (Wesley, 1995). However, the perception that the NST are cost effective has largely been based on retrospective analysis (O'Brien, 1986; Lennard-Jones, 1992).

The aim of this prospective study was to assess the costs related to the introduction of a NST. The study was carried out in three phases: baseline data were collected over 20 weeks, followed by an implementation phase of 1 year when the team came into operation, and finally a 17-week re-evaluation phase. In order to assess costs, ingredient costing was carried out whereby all items of care were recorded, including consumables, drugs administered, staff costs to administer care and any time spent on intensive care/high dependency. Costs were collated on eighty patients, forty-five pre- and thirty-five post-NST; there was no significant difference between age (63 *v.* 59 years; independent *t*-test *P* 0.20) and length of stay (22 *v.* 31 d; Mann-Whitney *P* 0.058) in the two groups. However, the total number of days fed was significantly greater post-NST (8 *v.* 11 d; Mann-Whitney *P* 0.007). The cost of the NST was calculated to be £5.43 per day per patient.

All costs of pre- and post-NST	Pre-NST Total costs	Post-NST Total costs
Nutritional support (£)	32 000	37 400
Feeding complications (£)	13 600	1 400
NST (£)	–	4 743
Total costs (£)	45 700	43 543

Mean cost element per day	Pre-NST (*n* 45)	Post-NST (*n* 35)	*P* value
Days fed EN and PN	13	24	0.007[1]
EN and PN feed per day (£)	57	42	
Complication costs per day (£)	22	1.60	0.05[2]
Cost of NST per day (£)	–	5.43	
Total cost per day (£)	79	49	0.05[2]

[1] = Mann-Whitney. [2] = Bootstrap non-parametric.

In conclusion, this prospective cost-effectiveness analysis of the NST indicates that the overall costs associated with nutritional support were reduced by 38% per day. The reduction in the incidence of complications reduced the costs by over 90% per day, and thereby quality of care was improved. The overall increased costs post-NST can be attributed to the increase in the duration of feeding (575 d pre- *v.* 873 d post-NST) and the cost of changing practices.

Lennard-Jones JE (1992) *King's Fund Centre.* London.
O'Brien DD (1986) *Journal of Parenteral and Enteral Nutrition* **10**, 300–302.
Wesley JR (1995) *Nutrition in Clinical Practice* **10**, 219–228.

Home parenteral nutrition in Scotland. By R.F. McKEE[1] on behalf of the SCOTTISH HOME PARENTERAL NUTRITION GROUP (Aberdeen Royal Infirmary, Edinburgh Royal Infirmary, Glasgow Royal Infirmary, Ninewells Hospital Dundee, South Glasgow NHS Trust), [1]*Glasgow Royal Infirmary, 16 Alexandra Parade, Glasgow, G31 2ER*

During the past 2 years, a multidisciplinary group with an interest in home parenteral nutrition (HPN) has developed in Scotland. The aim of this group is to improve the outcome of HPN by establishing common protocols, promoting research in HPN and auditing results. We hope to establish a managed clinical network for HPN in Scotland.

For the year from July 1999 to June 2000, data from forty patients is reported so as to form a baseline for future results. At least ten other patients use HPN in Scotland but either data for these was not supplied or their clinicians have not yet joined the group.

Twenty-seven females and thirteen males (median age 51 years: range 26–75) are on HPN. Three patients started HPN in 1987 and a median of three patients per year have been commenced on HPN since then. Biochemists, dieticians, gastroenterologists, nurses, pharmacists and surgeons from five university trusts are involved in the group and the number of patients treated per trust varies from two to fourteen.

The underlying diagnoses are Crohn's disease (19), ischaemia (5), malignancy (3), motility disorder (6), radiation enteritis (3) and other (4). The proportions of these diagnoses vary between trusts. Thirty-seven patients infuse nutrients while three only require electrolyte infusions. The median number of infusion nights per week is five (range2–7). The total number of HPN days supplied by the group to date is 72 640 with a median per patient of 1298 d (range125–4952 d).

During the year studied, a total of seventy-one lines were used for HPN. Thirty-one lines in twenty patients required removal after a median of 238 d (range 12–2246 d). No correlation was observed between line days and age or length of time on HPN but there was variation between trusts. Fourteen of thirty-one lines were removed due to sepsis. In eighteen episodes of line sepsis, antibiotics were given on nine occasions and preserved line function to allow hospital discharge after eight episodes. However, infection recurred in four patients at 13, 18, 30 and 90 d after discharge and these patients then had their lines replaced. Infection was not associated with the use of either single or double lumen lines, catheters *versus* ports or line site in the groin.

Thirty patients had sixty-nine admissions of a total of 576 d during the year. Eighteen admissions (total 229 d) in eleven patients were due to the underlying disease or other medical problems. Forty-four admissions (total 268 d) in twenty-five patients were due to line problems. Seven admissions in five patients were due to both. Some patients were admitted on one occasion because of disease and on another because of a line problem.

These data form baseline results for HPN in Scotland. The development of common protocols, audit of results and exchange of experience should lead to changes in practice and improvement in outcome. We hope to provide equality of access to a high standard of HPN care throughout Scotland.

Members of the Scottish Home Parenteral Nutrition Group: D. Barbour, J. Broom, A. McKinlay, W. Simpson (Aberdeen Royal Infirmary); S. Bath, J. Baxter, C. Pennington, J. Tait (Ninewells Hospital, Dundee); K. Fearon, C. Muir (Edinburgh Royal Infirmary); A. Cruikshank, L. Davidson, A. McCrimmon, R. Park (South Glasgow NHS Trust); R. Amin, G. Conkey, R. McKee, P. McKeown, D. O'Reilly (Glasgow Royal Infirmary).

The metabolic response to endotoxin in man is augmented by glucose–insulin infusion. By A.O. AGWUNOBI[1], M. SOOP[1], C. CHILDS[2], R.G. COOPER[3], P. MAYCOCK[2], R.A. LITTLE[2] and G.L. CARLSON[1,2], [1]*Department of Surgery,* [2]*MRC Trauma Group and* [3]*Department of Rheumatology, University of Manchester, Hope Hospital, Salford M6 8HD*

Carbohydrate pretreatment is known to reduce endotoxin lethality in animals and postoperative insulin resistance in man. Since endotoxin lethality may be related to the proinflammatory cytokine response to endotoxin, and postoperative insulin resistance to the counter-regulatory hormone response to surgical injury, this study tested the hypothesis that glucose and insulin infusion would reduce the proinflammatory cytokine and counter-regulatory hormone responses to endotoxin in healthy human subjects.

Fourteen apparently healthy adult volunteers (twelve male, two female) were studied on two occasions, 2 weeks apart, in random order, and received either 4 ng/kg IV *E coli* endotoxin (LPS) or an equivalent volume of sterile saline. Approval was obtained from the local ethics committee prior to commencement of the study. Six of the subjects received the LPS or saline after 2 h of an 8 h glucose–insulin clamp (plasma glucose 5 mmol/l, insulin infusion rate 80 mU/m^2/min) and eight of the subjects received the LPS or saline after 2 h of an 8 h infusion of sterile saline. Pulse rate, mean arterial pressure, core temperature, and VO_2 were measured hourly, using an automated monitor (Dinamap), tympanic membrane infrared probe (Genius) and open circuit indirect calorimetry (Deltatrac), respectively. Arterialized venous plasma cortisol, glucose, insulin, growth hormone (GH), noradrenaline (NA), IL-6 and TNF concentrations were measured before administration of LPS and hourly, for 6 h afterwards. Comparison of responses between groups and between each group and their respective saline control arm was made with repeated measures ANOVA and, where treatment-time interactions were significant, with *post hoc* Student's *t*-test employing Bonferroni correction for multiple comparisons.

Glucose–insulin infusion resulted in a significant increase in the magnitude and duration of the IL-6, cortisol and GH responses to LPS (see Table). The NA and TNF responses to LPS were not altered significantly by glucose–insulin infusion. The fever, tachycardia and increase in VO_2 resulting from LPS administration were unaffected by prior glucose–insulin infusion.

Plasma	Clamp/LPS (*n* 6)		Saline/LPS (*n* 8)		*P*
	Peak concentration		Peak concentration		
	Mean	SD	Mean	SD	
IL-6 (pg/ml)	2334.8	1266.0	1227.8	719.4	<0.001
Cortisol nmol/l)	734.8	11.9	566.0	120.6	<0.001
GH (Mu/l)	47.9	11.9	14.8	7.9	<0.001
Insulin (μu/ml)	154.8	33.2	3.8	2.0	<0.001
TNF (pg/ml)	762.8	289.3	607.2	311.0	NS
NA (nmol/l)	1.8	0.8	2.0	0.4	NS

Prior glucose–insulin infusion in man significantly augments the IL-6 and counter-regulatory hormone response to LPS but does not affect the TNF response or the increase in oxygen consumption, fever and tachycardia. This was an unexpected finding given that the insulin and glucose infusion would have been protective. These effects may be of importance when planning nutritional support in patients with sepsis.

Glutamine and glutathione ameliorate the liver dysfunction related to sepsis in neonatal rats. By R. BABU, S. EATON, L. SPITZ, D.P. DRAKE and A. PIERRO, *Institute of Child Health and Great Ormond Street Hospital for Children, London*

Hydrogen peroxide (H_2O_2) and nitric oxide (NO) are important mediators of sepsis which impair neonatal hepatic oxidative metabolism (Romeo *et al*. 1999, 2000). Glutamine has been shown to have beneficial effects on liver metabolism during sepsis (Markley *et al*. 1999).

The aim of the study was (1) to examine whether the effects of glutamine are shared by other amino acids or glutamine dipeptides and (2) to investigate the mode of action of glutamine.

Hepatocytes were isolated from sucking (11–15 d-old) rats and O_2 consumption was measured polarographically (Romeo *et al.* 1999). In Study A, The effects of 10mM amino acids or dipeptides (alanyl glutamine and glycyl glutamine) on cells treated with 1.5mM H_2O_2 or an NO donor (300 μmol/l *S*-nitroso-acetylpenicillamine) were examined. In Study B, the effects of 0.6mM amino-oxyacetate (AOA) or 3.2mM buthionine sulphoximine (BSO) on the ability of glutamine to reverse the effects of H_2O_2 were examined.

The results were as follows: Study A: glutamine reversed the inhibition of O_2 consumption by H_2O_2 and NO whereas other amino acids (arginine, isoleucine, phenylalanine, cystine, glutamate or alanine) were ineffective. The glutamine dipeptides glycyl-glutamine and alanyl-glutamine were also effective (see Fig. 1, *n* 16): Study B: amino-oxyacetate, an inhibitor of glutamine oxidation in the Krebs' cycle, did not block the beneficial effects of glutamine. However, buthionine sulphoximine, which inhibits glutathione synthesis, completely blocked the effects of glutamine, suggesting that the effects of glutamine are exerted by increasing cellular glutathione (see Fig. 2, *n* 16). In support of this, the addition of glutathione reversed the inhibitory effects of H_2O_2 (*n* 13, *P* 0.0001).

Figure 1

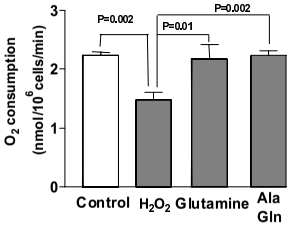
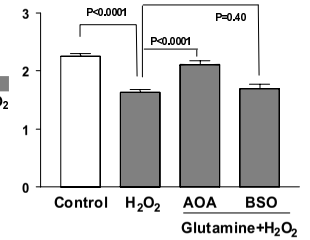


Figure 2



We concluded that glutamine and its dipeptides reverse the effects of septic mediators. These effects are not shared by other amino acids. Glutamine does not seem to exert its effects by providing an alternative fuel but instead appears to increase the synthesis of glutathione, an important cellular antioxidant. Administration of glutamine, its dipeptides, or glutathione may help prevent liver damage in neonatal sepsis.

Romeo C, Eaton S, Quant PA, Spitz L & Pierro A (1999) *Journal of Pediatric Surgery* **34**,1107–1111.
Romeo C, Eaton S, Spitz L & Pierro A (2000) *Journal of Pediatric Surgery* **35**, 44–48.
Markley MA, Eaton S, Spitz L & Pierro A (1999) Hepatocyte mitochondrial metabolism in neonatal sepsis is restored by glutamine. CNMG meeting.

Acute glutamine deprivation facilitates TNF-α-induced bacterial translocation across Caco-2 cell monolayers. By E.C. CLARK[1,2], S.D. PATEL[1], P.R. CHADWICK[4], G. WARHURST[1] and G.L. CARLSON[2,3], *Departments of* [1]*Gastrointestinal Science,* [2]*Surgery and* [3]*MRC Trauma Group, University of Manchester,* [4]*Department of Microbiology, Hope Hospital, Salford M6 8HD*

During periods of critical illness, normally non-pathogenic bacteria resident in the gut are able to translocate across the gut wall. The processes by which this occurs are not yet fully understood, though proinflammatory cytokines such as TNF-α have been implicated. Glutamine has been shown to have beneficial effects on intestinal structure when added to enteral nutrition and may reduce bacterial translocation. This study tested the hypothesis that acute changes in glutamine availability would modulate cytokine-induced bacterial translocation across an intestinal epithelial monolayer.

The human colonic adenocarcinoma cell line Caco-2 was grown (18 d) as polarised monolayers in a bicameral system (Transwell). Monolayers were then either (a) incubated in glutamine-free medium for 6 h, (b) incubated with TNF-α (20 ng/ml) for 6 h or (c) deprived of glutamine and incubated with TNF-α for 6 h. These were compared with control monolayers that had been maintained in normal growth medium (containing 2.0 mmol/l glutamine). Bacterial translocation was then assessed by inoculating the apical well of each chamber with 10^8 colony forming units (CFU)/ml of *E. coli* C25, a strain known to translocate across intestinal epithelia. Bacterial count in the basal chamber was measured 4 h later by quantitative microbiological culture. In a further set of experiments reversibility and specificity of glutamine effects were tested, by replacing glutamine or an iso-nitrogenous mixture of non-essential amino acids in the culture for 2 h before inoculating with bacteria as previously. Each dataset represents the mean ± SD of at least six separate experiments.

Control monolayers exhibited a low level of bacterial translocation which was unaffected by either glutamine deprivation or incubation with TNF-α (see Figure). However, the combination of glutamine deprivation and TNF-α elicited a 50–100-fold increase in *E. coli* translocation across Caco-2 monolayers. Replacement of glutamine for 2 h completely reversed this but the iso-nitrogenous mixture did not.

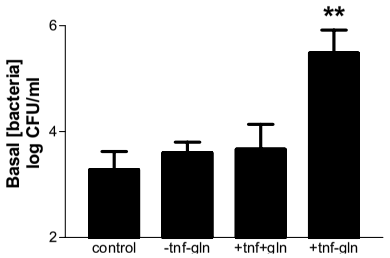


Figure: Effect of 6h glutamine deprivation and TNF incubation on translocation across Caco2 monolayers.

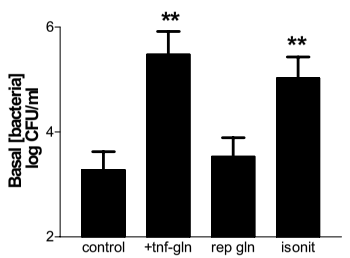


Figure: Reversibility and specificity of glutamine deprivation on translocation.

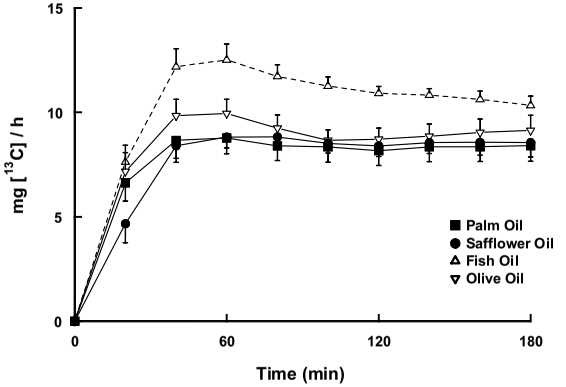
** = P<0.001 vs control ■ = basal bacteria

These data suggest that acute glutamine deprivation has no direct effect on bacterial translocation but sensitizes intestinal epithelial cells to TNF-α, thus facilitating cytokine-mediated translocation. These changes are specifically reversible with glutamine.

These findings suggest that even short periods of glutamine deficiency may have important pathophysiological implications for the intestinal epithelium in critical illness.

Gastric emptying and cholecystokinin response following the ingestion of dietary oils of differing fatty acid composition. By M.D. ROBERTSON[1], K.G. JACKSON[2], B.A. FIELDING[1], C.M. WILLIAMS[2] and K.N. FRAYN[1], [1]*Oxford Centre of Diabetes Endocrinology and Metabolism, Nuffield Department of Clinical Medicine, University of Oxford, Oxford OX2 6HE and* [2]*Hugh Sinclair Unit of Human Nutrition, School of Food Bioscience, University of Reading, Reading RG6 6AP*

Gastric emptying is a limiting factor for the entry of nutrients into the small intestine and hence their subsequent digestion and absorption, and so must be considered as an integral component of postprandial lipid metabolism. Early work (Hunt & Knox, 1968) has suggested that all fatty acids containing >11 carbons empty at a similar rate, although there is an absence of data concerning the effects of naturally occurring dietary fats. Gastric emptying of four dietary oils was assessed using the ^{13}C-octanoate breath test (Ghoos *et al.* 1993). Ten healthy postmenopausal women consumed on four separate occasions a high-fat breakfast containing 40 g of either (i) palm oil (saturated), (ii) safflower oil (*n-6* polyunsaturated (PUFA)), (iii) fish oil (*n-3* PUFA) or (iv) olive oil (monounsaturated), all with the addition of 100 mg 1-[^{13}C]octanoic acid. Postprandial breath and blood samples were taken after 3 and 6 h respectively.



The recovery of ^{13}C in the breath samples after the ingestion of the fish oil was significantly different from the other three test oils (P 0.005) reflecting both a lower half-emptying time and a more rapid gastric emptying rate. There were, however, no differences in the apparent lag phases of emptying between the test oils. The cholecystokinin (CCK) response following fish oil ingestion was significantly delayed (P<0.001) compared with the other oils examined, not peaking until 120 min after the start of the meal. CCK has been strongly implicated in the slowing of gastric emptying by fats and thus more work is needed to examine the mechanisms of CCK production by lipids *in vivo*, especially long chain *n-3* PUFA.

We thank the BBSRC for financial support.

Hunt J & Knox M (1968) *Journal of Physiology* **194**, 327–336.
Ghoos YF, Maes BD, Geypens BJ, Mys G, Hiele MI, Rutgeerts PJ & Vantrappen G. (1993) *Gastroenterology* **104**, 1640–1647.

Moderate hypothermia ameliorates liver energy failure during intestinal ischaemia-reperfusion. By P. VEJCHAPIPAT[1,2], S.R. WILLIAMS[2,3], E. PROCTOR[2], L. SPITZ[1] and A. PIERRO[1], [1]*Surgery Unit,* [2]*Biophysics Unit, Institute of Child Health, Great Ormond Street Hospital, London WC1N 1EH* [3]*Imaging Science and Biomedical Engineering, University of Manchester, Manchester M13 9PT*

Intestinal ischaemia-reperfusion (IR) is a serious surgical condition. Diseases leading to this condition include acute mesenteric occlusion, midgut volvulus, necrotizing enterocolitis, haemorrhagic shock with resuscitation and sepsis (Vejchapipat *et al.* 2000). Intestinal IR may cause distant organ failure such as liver failure (Turnage *et al.* 1996). Mild to moderate hypothermia has been reported to have beneficial effects in cerebral ischaemia (Thoresen & Wyatt, 1997) as well as fulminant liver failure (Jalan *et al.* 1999). The aims of this study were to characterize the effects of intestinal IR on liver energy metabolism and to evaluate whether moderate hypothermia offers protection to the liver.

Intestinal IR was produced by clamping (90 min) and unclamping the superior mesenteric artery in adult rats. In the first experiment, animals were slaughtered after 60 min reperfusion and in the second experiment after 240 min reperfusion. Environmental temperature was adjusted to maintain either normothermia (rectal temperature 36–38°) or moderate hypothermia (30–33°) throughout the experiments. Three groups of rats were studied (*n* 12 per group): (A) sham operation at normothermia; (B) intestinal IR at normothermia; (C) intestinal IR at moderate hypothermia. Hepatic inorganic phosphate (P_i) and ATP were continuously monitored using ^{31}phosphorus magnetic resonance spectroscopy. In addition, hepatic P_i, ATP and lactate in extracted liver samples were also measured at the end of the experiment. One-way analysis of variance with multiple *post hoc* comparisons was used. The statistical significance was established at $P<0.05$. Data are expressed as mean and SEM.

During the first 60 min of intestinal reperfusion there was a progressive increase in the hepatic P_i:ATP ratio (liver energy failure) in normothermic but not in hypothermic animals (see Fig. 1). Similarly, analysis of liver extracts at 60 min of intestinal reperfusion revealed that moderate hypothermia preserved hepatic P_i, ATP and lactate (see Fig. 2).

Fig. 1

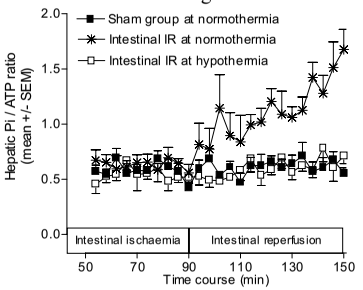
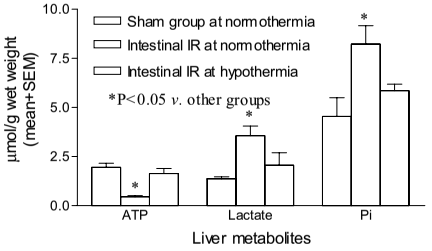


Fig. 2



All hypothermic animals survived until the end of the experiment whereas all normothermic animals died between 70 and 240 min of intestinal reperfusion. Deaths were always preceded by a significant elevation of the hepatic P_i:ATP ratio.

In conclusion, intestinal IR at normothermia was associated with liver energy failure and high mortality. Moderate hypothermia ameliorated liver energy failure and prevented mortality in this model. Induction of moderate hypothermia may prove to be an innovative and fruitful area of investigation in the management of patients with intestinal IR injury in the future.

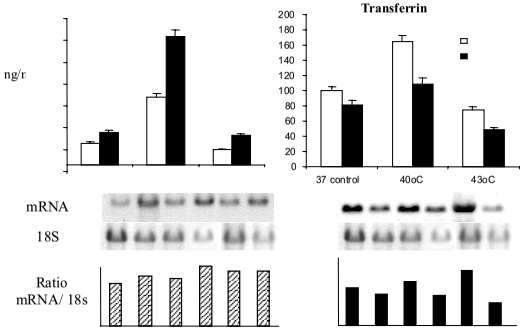
Jalan, R, Damink SWMO, Deutz NEP, Lee A & Hayes PC (1999) *Lancet* **354**, 1164–1168.
Turnage RH, Kadesky, KM, Myers SI, Guice KS & Oldham KT (1996) *Surgery* **119**, 151–160.
Thoresen M & Wyatt J (1997) *Acta Paediatrica* **86**, 1029–1033.
Vejchapipat P, Williams SR, Spitz L & Pierro A (2000) *Journal of Pediatric Surgery* **35**, 759–764.

The hepatocyte metabolic response to thermal stress: implications for acute phase protein production. By S.J. WIGMORE[1], K.C.H. FEARON[1], H.W. HARRIS[2] and W.J. WELCH[2], [1]*Department of Clinical and Surgical Sciences (Surgery), University of Edinburgh, Royal Infirmary, Edinburgh EH3 9YW and* [2]*Surgical Research Laboratory, University of California San Francisco, San Francisco, USA*

Following heat shock, cells adopt a thermotolerant phenotype. This is associated with increased cell survival and augmentation of certain other cellular functions. Enhancement of secretory protein pathways has not previously been described as part of the thermotolerant phenotype. The liver secretes acute-phase proteins (APP) which are important for maintaining oncotic pressure, coagulation and limiting inflammation. This acute-phase protein response (APPR) is also believed to confer a survival advantage. It would make teliological sense for the heat shock (cell survival response) and APPR (systemic survival response) to be linked.

The purpose of this study was to examine the effect of heat shock preconditioning on the subsequent constitutive and interleukin-6 (IL-6)-induced production of acute-phase proteins. Human Hep G2 cells were either heated to febrile range temperature (40°) or heat shocked (43°) for 45 min and were then allowed to recover for 24 h at 37° in the presence or absence of IL-6 (10 ng/ml). Alpha-1 antichymotrypsin (ACT) was studied as an example of a positive APP (concentrations rise in response to IL-6) and transferrin (TRF) was studied as an example of a negative APP (concentrations decrease in response to IL-6). Concentrations of APP were measured in cell supernatants by ELISA. DNA probes were constructed for ACT 806 bp and TRF 536 bp and Northern blot analysis of cytoplasmic RNA was performed.

In cells treated by heat shock for 45 min at 40° and allowed to recover for 24 h (preconditioned), there was increased production of both positive and negative acute-phase reactants (upper Figure). The APPR of heat-shocked cells to IL-6 was qualitatively the same as that of 37° controls but was enhanced. By contrast, heat shock at 43° consistently inhibited production of both positive and negative APPs, both immediately following heat shock and in cells that had been preconditioned and allowed to recover. Changes in mRNA levels were relatively small and were not entirely consistent with the observed pattern of protein production (lower Figure).



Heat shock within the febrile range is associated with increased APP synthesis and augmentation of IL-6-induced synthesis. Changes in mRNA expression were not consistent with the pattern of secreted protein, suggesting a post-transcriptional regulation of APP synthesis. One explanation for these observations is that augmented secretion of acute phase proteins at 40° may require increased expression of heat shock proteins (acting as molecular chaperones).

Intestinal ischaemia-reperfusion injury causes a sustained rise in serum inorganic phosphate concentration. By S.B. WILLIAMS[1,2], S.R. WILLIAMS[3], L. SPITZ[2] AND A. PIERRO[2], [1]*RCS Unit of Biophysics and* [2]*Department of Paediatric Surgery, Institute of Child Health, University College London, London WC1N 1EH and* [3]*Imaging Science and Biomedical Engineering, University of Manchester, Manchester M13 9PT*

Several serious surgical conditions involve intestinal ischaemia-reperfusion injury – for example necrotizing enterocolitis, midgut volvulus and strangulated intestinal hernia. A proportion of these patients suffer liver dysfunction, and some go on to develop multiple organ failure. The link between intestinal ischaemia-reperfusion injury and liver dysfunction has not yet been fully characterized. It has been shown that intestinal ischaemia-reperfusion injury in a rat model is associated with a large rise in hepatic inorganic phosphate (Changani *et al.* 1998). We hypothesized that this excess hepatic inorganic phosphate (P_i) is delivered to the liver *via* the superior mesenteric vein (SMV) from the reperfused, formerly ischaemic, intestine.

Six groups of adult Sprague-Dawley rats (250–300 g) were studied. Four groups of experimental animals were given a general anaesthetic, a laparotomy and the superior mesenteric artery (SMA) was occluded with a clip for 90 min. In experimental group 1, the SMA clip was removed and 0.5 ml blood samples were taken from the SMV and the right atrium (RA) after 2 min of intestinal reperfusion. In experimental groups 2, 3 and 4, blood was taken from the SMV and RA after 10, 30 and 60 min of intestinal reperfusion respectively. Two groups of control animals had laparotomy only under general anaesthetic, and blood samples were taken from the SMV and RA after 100 min (control group 1) and 150 min (control group 2). All blood samples were immediately centrifuged and serum WAS removed for analysis. Serum P_i levels were measured using a Kodak multichannel dryslide analyser. The Figures show mean ± SEM, *n* 5 in each group.

Fig 1: SMV and RA Serum Pi

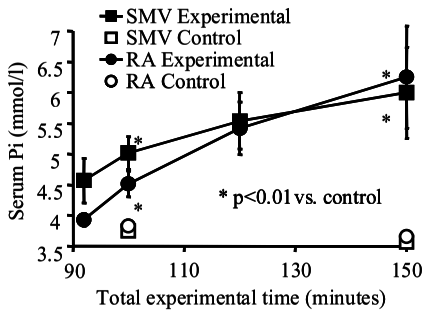
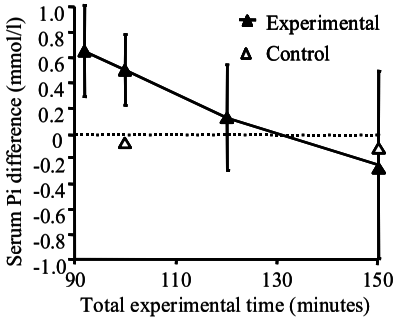


Fig 2: Serum Pi difference (SMV-RA)



Serum P_i increases after intestinal ischaemia-reperfusion injury in the experimental group in both the SMV and (after a lag) in the RA, but not in the control group (Fig. 1). The P_i difference between the SMV and RA during reperfusion falls in the experimental group, but not in the control group (Fig. 2). The decrease in experimental group SMV-RA difference during reperfusion is significantly different from zero change over time (*P* 0.013), and the experimental group SMV-RA difference at projected reperfusion time zero is also significantly greater than zero (*P* 0.0008).

The liver is exposed to an elevated level of P_i in SMV blood during intestinal reperfusion. At first the liver appears to filter out the excess P_i delivered to it and maintains a normal mixed venous (RA) P_i level. However, the capacity of the liver to filter out the excess P_i appears to decline rapidly and is exceeded between 120 and 150 min of experimental time (30–60 min reperfusion time). With prolonged intestinal reperfusion, the liver may actually release P_i into the systemic circulation.

Changani KK, Lauro V, Pierro A & Williams SR (1998) *Proceedings of the International Society of Magnetic Resonance in Medicine* **6**, 201.

Exposure to TNF- , IFN- and LPS reduces insulin-stimulated 2-deoxyglucose uptake in isolated murine soleus muscle. By C.R. BYRNE, R. LITTLE and G.L. CARLSON, *MRC Trauma Group, University of Manchester, Oxford Road, Manchester M13 9PT*

Insulin resistance is commonly associated with injury, sepsis (Carlson & Little, 1994), obesity, Type II diabetes and cancer. Impaired insulin-stimulated glucose uptake in skeletal muscle plays a major role in insulin resistance but the underlying mechanisms are as yet unknown. Although increased gene expression for proinflammatory cytokines such as TNF-α has been associated with insulin resistance, it is still unclear whether proinflammatory cytokines have a direct effect on insulin action at the cellular level (Nolte *et al.* 1998; Del-Aguila *et al.* 1999). We therefore tested the ability of TNF-α to modulate insulin sensitivity, in combination with IFN-γ and lipopolysaccharide (LPS).

Insulin-stimulated uptake of radiolabelled 2-deoxyglucose (2-DG) in oxygenated (95%O_2:5% CO_2) culture medium (supplemented with 1.5 % (w/v) BSA, 1 mM-sodium pyruvate, 10 μU/ml insulin) was employed to determine insulin sensitivity *ex vivo*. After removal from male C57BL/6 mice, intact soleus muscles underwent a pre-incubation phase (1 or 4 h in medium 199, 29°), a rinse phase (10 min, glucose-free DMEM, 29°), and an insulin-stimulation phase (30 min, glucose-free DMEM, 35°) in the presence of 2-DG (1mM), 2-deoxy-D-[2,6-^{3}H]glucose (0.25 μCi/ml) and with [U-^{14}C]sucrose (0.08 μCi/ml) as an extracellular marker. Muscles under test were co-incubated with TNF-α (10 ng/ml), IFN-γ (200 units/ml) and LPS (10 μg/ml) throughout all phases. Muscle samples were digested in 1M NaOH, and specific activity determined by liquid scintillation counting using a dual label protocol.

Insulin at 1000 μU/ml induced a highly significant increase ($P<0.01$ by paired *t* test) in 2-DG uptake over basal after pre-incubation periods of both 1 and 4 h. Co-incubation with TNF-α, IFN-γ and LPS had no effect on 2-DG uptake after 1 h, but caused a significant reduction ($P<0.01$ by paired *t* test) in insulin-stimulated 2-DG uptake after 4 h (Fig. 1).

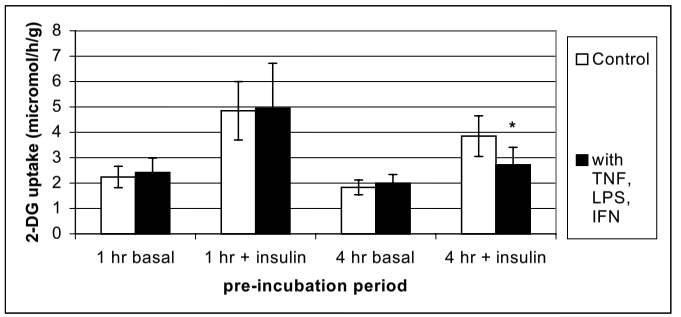


Fig. 1

Basal and insulin-stimulated 2-DG uptake into isolated mouse soleus muscle after pre-exposure (1 or 4 h) to TNF-α (10 ng/ml), IFN-γ (200 units/ml) and LPS (10 μg/ml) *$P<0.01$ for reduction in insulin stimulated uptake at 4 h.

Co-incubation with TNF-α, IFN-γ and LPS for 4 h prior to determination of 2-DG uptake acutely induces insulin resistance in isolated skeletal muscle. This confirms previous findings in a skeletal muscle cell line where chronic exposure to this combination of cytokines and LPS resulted in a loss of insulin sensitivity (Bedard *et al.* 1997).

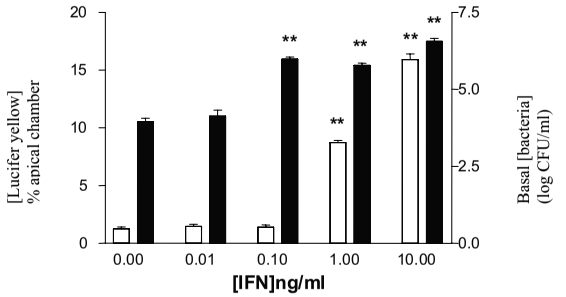
Bedard S, Marcotte B & Marette A (1997) *Biochemical Journal* **325,** 487–493.
Carlson GL & Little RA (1994) In *Organ Metabolism and Nutrition: Ideas for Critical Care,* pp. 49–69 [JM Kinney, editor]. New York: Raven Press.
Del-Aguila LF, Claffey KP & Kirwan JP (1999) *American Journal of Physiology* 1**276**, E849–E855.
Nolte LA, Hansen PA, Chen MM, Schulter JM, Gulve EA & Holloszy JO (1998) *Diabetes* **47,** 721–726.

IFN -induced increases in bacterial translocation are dissociated from increased paracellular permeability in intestinal epithelial monolayers. By E.C. CLARK[1,2], C.J. WATSON[1], P.R. CHADWICK[4], G.L. CARLSON[2,3] and G. WARHURST[1], *Departments of* [1]*Gastrointestinal Sciences,* [2]*Surgery,* [3]*MRC Trauma Group, University of Manchester,* [4]*Department of Microbiology, Hope Hospital, Salford M6 8HD*

Proinflammatory cytokines such as interferon gamma (IFNγ) have been implicated in the passage of bacteria across the intestinal tract induced by injury, shock, sepsis and intestinal inflammation. The mechanism of this bacterial translocation is presently unclear but may reflect movement of bacteria through disrupted intercellular junctions. The aim of this study was to investigate whether there is a direct relationship between IFNγ-induced bacterial translocation and changes in permeability of the paracellular marker, lucifer yellow (LY) in a human intestinal cell line, T84.

T84 cells were grown in a bicameral system to form confluent monolayers. IFN , (0.01–10 ng/ml) or Hank's balanced saline solution (control) were added to the basal chamber of each well and the monolayers were then incubated for 48 h at 37°. Bacterial translocation was then assessed by inoculating the apical well of each chamber with 10^8 colony forming units (CFU)/ml of *E. coli* C25, a translocating bacterial strain. The bacterial count in the basal chamber was measured 4 h later by quantitative microbiological culture. LY (50 μM) was added to the apical chamber and the percentage appearing in the basolateral chamber was monitored at the beginning of the experiment and after 4 h by spectrofluoroscopy. Each data set represents the mean ± SD of at least six separate experiments.

IFN produced a dose-dependent increase in LY permeability with a threshold at 1 ng/ml (see Figure). Bacterial translocation was also increased by more than 100-fold by IFNγ, although in this case the threshold concentration was much lower than for LY permeability (0.1 ng/ml) and there was no clear dose-relationship. Incubation with 0.1 ng/ml had no measurable effect on LY permeability but produced the same increase in bacterial translocation as the highest dose of IFNγ, suggesting that IFNγ-induced bacterial translocation is an all-or-none phenomenon.



Effect of IFN on paracellular permeability, indicated by percentage flux of lucifer yellow and bacterial translocation in T84 monolayers.

***P*<0.01 *v*. Control
□ = Lucifer yellow flux
■ = Bacterial translocation

IFN induces changes in permeability of an intestinal epithelium to both bacteria and the paracellular marker, lucifer yellow. The failure of changes in epithelial paracellular permeability to reflect bacterial translocation suggests that IFNγ-induced bacterial translocation may involve a route other than the paracellular pathway.

Conjugated linoleic acid reduces breast tumour growth. By B. MAJUMDER[1], S. MOIR[1], K. WAHLE[2] and S.D. HEYS[1], [1]*Department of Surgery, University of Aberdeen, Aberdeen AB25 2ZD,* [2]*Rowett Research Institute, Aberdeen AB21 9SB*

Dietary fatty acids play an important role in carcinogenesis. Oleic acid (OA) – present in olive oil (Trichopoulou *et al.* 1995), eicosapentanoic acid (EPA) and docosahexanoic acid (DHA) – both present in fish oil (Minami *et al.* 1996), may have anti-tumour effects. Recently attention has focused on CLA, conjugated linoleic acid (Ip *et al.* 1999), as this appears to be the most potent of all fatty acids. This study evaluates the anti-tumour effects of CLA on breast cancer cells (oestrogen receptor positive and negative).

Breast-cancer cell lines (MCF7, MDA-MBA-231) were grown to subconfluence in supplemented RPMI media and incubated with the above fatty acids containing ethanol and a control containing albumin, in concentrations of 0 to 200 μM. After 24 and 48 h of treatment with fatty acids, culture cell growth was assessed using a standard MTT assay. All experiments were carried out in triplicate.

The MTT assay is a rapid, quantitative test for assessment of viability, proliferation and cytotoxicity. After the fatty acids had been introduced, 50 μl of MTT was added to all 96 well plates and the plates were placed in the incubator for 4 h at 37° and 5% CO_2. The MTT-formazan crystals were then dissolved by addition of 200 μl of DMSO and the absorbance read immediately at 570 nm since the product is unstable.

EPA elicited an inhibitory effect on both cells at high concentrations only (>100 μM, $P<0.01$) but no effect was observed at lower levels. However, exposure to CLA resulted in a dose-dependent reduction in growth in MCF7 cells – a 20% reduction at 6.25 μM, 50% at 100 μM and 65% at 200 μM of CLA ($P<0.01$). Similar results were obtained for the oestrogen receptor-negative MDA-MBA-231 cells (reductions up to 39% at 200 μM of CLA ($P<0.01$).

CLA had the most potent action of the fatty acids assessed in reducing cell growth and its effects were more marked in oestrogen receptor-positive cell lines. Further studies are now indicated to determine whether these effects will occur *in vivo*.

Ip MM, Masso-Welch PA, Shoemaker SF, Shea-Eaton WK & Ip C (1999) *Experimental Cell Research* **255**, 22–34.
Minami M & Noguchi M(1996) *Oncology* **53**, 398–405.
Trichopoulou A, Katsouyanni K, Stuver S, Tzala L, Gnardellis C, Rimm E & Trichopoulos D (1995) *Journal of the National Cancer Institute* **87**, 110–116.

Are the anti-tumour effects of conjugated linoleic acid mediated by increased expression of key genes involved in the apoptotic pathway? By B. MAJUMDER[1], A. FARQUHARSON[2], K. WAHLE[2] and S.D. HEYS[1], [1]*Department of Surgery, University of Aberdeen, Aberdeen AB25 2ZD,* [2]*Rowett Research Institute, Aberdeen AB21 9SB*

Studies have shown that dietary fatty acids play an important role in carcinogenesis (Trichopoulou *et al.* 1995; Rose & Connolly, 1999). Recent interest has focused on the fatty acid, conjugated linoleic acid (CLA) (Clement *et al.* 1994), as it was found to have the most potent anti-tumour effect of all fatty acids. Its anti-tumour effects may be mediated through enhanced apoptosis (Ip *et al.* 1999). However, the effects of CLA on genes involved in apoptosis are unknown and this study examines the effects of CLA on *p53*, p21WAF1 and *bcl-2* expression.

Breast-cancer cells (MCF7, MDA-MBA-231) were grown in RPMI media which were then media was supplemented with CLA (in a minimal volume of ethanol) in different concentrations (0 to 200 μM) for 24 h. At the end of this time, Northern blotting was performed to determine the effects on the expression of *p53*, p21WAF1 and *bcl-2* and to ensure equal loading of RNA all samples were quantified by 18S. High quality RNA was extracted (QIAGEN, UK). Overnight hybridization was done after transferring RNA to a positively charged membrane. We have used oligonucleotides P^{32} labelling. All experiments were carried out in triplicate.

Northern blot analysis showed that after treatment with CLA there was a dose-dependent effect on wild type *p53* expression (MCF7 cells) with a 284% increase at 12.5 μM CLA supplementation, 347% at 100 μM, and 523% at 200 M of CLA ($P<0.01$). CLA also increased the expression of p21WAF1 up to 200% ($P<0.02$). In contrast, there was a non-significant reduction in *bcl-2* expression. CLA did not change the expression of mutant *p53* or p21WAF1 (present in MDA-MBA-231 cells) but it did increase the expression of *bcl-2* by 103% at 12.5 μM, 201% at 50 μM, and 207% at 100 μM of CLA ($P<0.01$) in these cells.

This study is the first demonstration of the effects of CLA on gene expression in breast-cancer cells. These results now indicate a possible mechanism for the anti-tumour activity of a dietary nutrient, CLA, which works by increasing the expression of the wild type *p53* and p21WAF1 genes. However, in cells which express mutant *p53*, CLA presumably acts through a *p53*-independent pathway.

Clement I, Scimeca JA & Thompson HJ (1994) *Cancer* **74**, 1050–1054.
Ip MM, Masso-Welch PA, Shoemaker SF, Shea-Eaton WK & Ip C (1999) *Experimental Cell Research* **255**, 22–34.
Rose DP & Connolly JM (1999) *Pharmacology and Therapeutics* **83**, 217–244.
Trichopoulou A, Katsouyanni K, Stuver S, Tzala L, Gnardellis C, Rimm E & Trichopoulos D (1995) *Journal of the National Cancer Institute* **87**, 110–116.

Changes in body composition in post-menopausal women receiving endocrine therapy for early breast cancer. By M.N. HARVIE[1], I.T. CAMPBELL[1], A. BAILDAM[2], A. HOWELL[3] and N. THATCHER[3], *University Departments of* [1]*Anaesthesia,* [2]*Surgery and* [3]*Medical Oncology, Withington Hospital, Manchester M20 2LR*

Endocrine (anti-oestrogen) therapy is widely used as a treatment, and more recently as a preventative agent against breast cancer. There is a perception that this leads to weight gain but randomized studies have shown only modest weight gains of 1.1–2.2 kg in both study and control patients (Kumar *et al.* 1997), which are similar to those reported in healthy post-menopausal women (Reubinoff *et al*. 1995). The effects of endocrine therapy on body composition, however, have not been determined. A recent cross-sectional study reported greater fat stores in women receiving tamoxifen than in healthy women (Ali *et al*. 1998). We determined changes in body mass and composition throughout the first year of endocrine therapy in post-menopausal women who had recently undergone breast surgery for early breast cancer.

Twenty-three women receiving tamoxifen, Arimidex, or tamoxifen and Arimidex were studied; age mean (SD) 54.7 (3.9) years, weight change in the 3–6 weeks since diagnosis 1.5 (3.0) kg, BMI 27.5 (0.6) kg/m^2. Patients were seen within 2 weeks of commencing endocrine therapy (Time 1), after 6 months of therapy (Time 2) and after 1 year of therapy (Time 3). On each occasion weight, height, skinfolds at the triceps, biceps, subscapular, suprailiac, abdomen, waist and hip circumference, were measured. Waist:hip ratio was calculated. Fat-free mass (FFM), total body fat (kg) and percentage body fat were calculated from skinfolds.

	Time 1	Time 2	Time 3
Weight (kg)	69.8 (15.7)*	70.8 (15.7)	71.9 (15.8) [a]
Total body fat (kg)	27.6 (9.3)	29.4 (10.5)	31.6 (10.5) [a]
% body fat	38.3 (4.9)	40.1 (6.2)	42.1 (5.6) [a]
FFM (kg)	42.3 (6.4)	41.8 (6.0)	40.6 (5.7) [a]
Abdominal skinfold (mm)	45.7 (10.0)	52.1 (10.8)	56.0 (8.3) [a]
Waist (cm)	87.9 (13.0)	90.0 (13.0)	92.0 (15.0) [a]
Hip (cm)	102.4 (11.2)	103.4 (12)	104.3 (12.2) [b]
Waist:hip ratio	0.86 (0.07)	0.87 (0.07)	0.88 (0.07) [b]

* Mean (SD).
[a] Significant change over the year (ANOVA repeated measures $P<0.01$).
[b] Significant change over the year (ANOVA repeated measures $P<0.05$).

Patients receiving endocrine therapy experienced weight gains comparable to those reported in healthy post-menopausal women (Reubinoff *et al.* 1995). Over the year of endocrine therapy there was a 14% increase in total body fat, a 4.0 (2.0) cm increase in waist and 2.2 (0.8) cm increase in hip circumference and a decline in FFM of 1.87 (0.8) kg. This compares with published figures (in healthy women over 1 year) of a 3% increase in body fat, a 2.8 (0.4) cm increase in waist, a 1.1 (0.5) cm increase in hip circumference (Espeland *et al*. 1997) and a decline of only 0.5 kg in FFM (Poelholm *et al*. 1995). Thus endocrine therapy may have a different effect on body composition compared to that seen in normal post-menopausal women.

The propensity for increased fat deposition, particularly central fat, may have adverse metabolic effects and is of major concern to the women themselves. This concern may explain the perception of a greater weight gain in women which is independent of changes in body mass and may decrease compliance with adjuvant endocrine therapy.

Ali PA, Al-Ghorabie FH, Evans CJ, El-Sharkawi AM & Hancock DA (1998) *Applied Radiation Isotopes* **49**, 643–645.
Kumar NB, Allen K, Cantor A, Cox DE, Greenberg H, Shah S & Lyam GH (1997) *Breast Cancer Research and Treatment* **44**, 135–143.
Reubinoff BE, Wurtman J, Rojansky N, Adler D, Stein P, Schenker JG & Brzezinski A (1995) *Fertility and Sterility* **64**, 963–968.
Poelholm ET, Toth MJ & Gardner AW (1995) *Annals of Internal Medicine* **123**, 673–675.
Espeland C, Stefanick ML, Kritz-Silverstein D, Fineberg E, Waclawiw MA, James MK & Greendale LA (1997) *Journal of Clinical Endocrinology and Metabolism* **82**, 1549–1556.

The impact of oral ingestion of free L-glutamine on glutathione blood levels in volunteers. By E. VALENCIA, A. MARIN and G. HARDY, *Pharmaceutical Nutrition Group, School of Biological and Molecular Sciences, Oxford Brookes University, Oxford OX3 OBP*

Physiological rhythms of amino acids and proteins have been the subject of considerable interest since the term, 'circadian rhythm' was first proposed. Glutathione, or L-γ–glutamyl-L-cysteinylglycine (GSH) is the most abundant antioxidant inside the cells. Recent studies have shown that intravenous administration of GSH (70 mg/kg) decreases the peroxidative stress of patients with septic shock (Ortolani *et al*. 2000) and, since glutamine (Gln) is a precursor of glutathione, its supplementation in the diet could be used to maintain high levels of GSH and to minimize oxidative stress damage. The goal of this study was to determine the profile of circadian variations in whole-blood GSH levels over a 24 h period in healthy subjects who consumed a standard oral diet plus free L-Gln over a 10-d period.

Three clinically healthy subjects (two male and one female), mean age 40 years, mean body weight 64.6 kg, mean height 166 cm with mean BMI 23.2 were studied twice over a 2-week period. Subjects were first adapted to the test diet with known contents of protein and total glutamate (Glu) (values include both Glu and Gln) for 3 d. The meals were individually prepared to provide 25 kcal energy/kg per d, with 16.3% of the energy as protein (1 g/kg per d), 60% as carbohydrate, and 23.7% as fat (polyunsaturated:saturated fatty acid ratio = 1). The Glu and Gln contents of each meal were 6.9 g for breakfast, mid-morning and afternoon snacks, 4.98 g for lunch and dinner. Main meals were eaten at 08.00, 12.30 and 19.00 hours and snacks were eaten at 10.00, 15.00 and 21.30 hours. Each subject ate the same diet for the next 10 d but supplemented with GlutaminOx (Oxford Nutrition) 0.3 g/kg/body weight per d (15–20 g L-Gln) at breakfast, lunch and dinner.

On days 3 and 14 of the study, approximately 5 ml of whole blood was taken from a forearm vein by venepuncture at 4-h intervals commencing at 13.00 hours, and placed into a tube containing (25 mg) EDTA for anticoagulation. All preparations were performed at room temperature. Within 30 min the tube was centrifuged at 15 000 rpm for 5 min and immediately deproteinized with 500 µl of TCA (25%), and 40 mM of *N*-ethylmaleimide final concentration. Specimens were stored at –20°, for 24–48 h before analysis. Spectrophotometric measurements at 240 nm were performed using the Glyoxalase-I method.

After 10 d of L-Gln oral ingestion the 24-h GSH levels decreased significantly by 37% (869 (SD 54) *v*. 542 (SD 56), *P* 0.00091). and ANOVA did not show a significant inter-time circadian variability of GSH.

The data from this pilot study show that the concentrations of whole blood GSH do not vary as a function of the time of the day when minimal levels of GSH (or its precursors) are consumed orally. Although Gln could be a precursor of GSH, according to basic biochemistry, we unexpectedly observed a decrease of GSH levels in healthy volunteers, after L-Gln oral ingestion. This decrease in whole blood GSH concentration may be a result of three factors: First, splanchnic bed (enterocytes) take up 53% of Gln from oral ingestion to produce Glu, thus increasing Glu plasma concentrations, as we have also reported (Marin *et al*. 2000). Second, high Glu concentrations could inhibit cysteine production (another likely GSH precursor) in red cells. Third, red cells have limited Gln (20%) and Glu (4%) exchange. We therefore suggest that Gln is not the only precursor required to raise GSH concentrations within the red cells, and different cell types may have a different precursor requirement to increase or maintain GSH levels.

Ortolani O, Conti A, Gudio AR, Moraldi E, Cantini Q & Novelli G (2000).*American Journal of Respiratory Critical Care Medicine* **161**, 1907 – 1911.
Marin A, Valencia E & Hardy G (2000) Clinical Nutrition *(In the Press)*.

Changes in total body potassium in advanced cancer patients receiving chemotherapy. By M.N. HARVIE[1], I.T. CAMPBELL[1], M.A KEEGAN, B. MURBY, A. BAILDOM[2], A. HOWELL[3] and N. THATCHER[3], *University Departments of [1]Anaesthesia, [2] Surgery and [3] Medical Oncology, Withington Hospital, Manchester M20 2LR*

In normal subjects, total body potassium (TBK) is an index of body cell mass (BCM), the metabolically active portion of fat-free mass (FFM) (Moore, 1980). In disease and malnutrition, however, TBK may change independently of changes in FFM due to changes in intracellular potassium concentration. There are few data relating changes of TBK and FFM in cancer patients (Shike *et al.* 1984).

We prospectively determined changes in body mass, TBK and FFM over 3–7 months of chemotherapy in seventeen patients with advanced non-small-cell lung cancer (NSCLC) (twelve male; five female), nine with metastatic melanoma and seven with metastatic breast cancer. Patients were seen pre-chemotherapy (Time 1) and 1 month post-chemotherapy (Time 2). On each occasion, weight, FFM (from skinfolds) and TBK (shadow shield whole body counter) were determined. Changes in these parameters were determined.

	NSCLC				Metastatic melanoma and breast cancer			
	Male (*n* 12) Age 58 (46–66) *years BMI 25.1 (18.2–31.4) kg/m^2		Female (*n* 5) Age 60 (46–71)* years BMI 22.1 (18.7–34.3) kg/m^2		Response/stable (*n* 10) Age 57 (45–62) *years BMI 28.2 (22.5–50.4) kg.m^2 6 melanoma; 4 breast 5M 5F		Progressive (*n* 6) Age 53 (45–68) *years BMI 28.2 (26.1–32.3) kg/m^2 3 melanoma; 3 breast 2M 4F	
	Time 1	Time 2	Time 1	Time 2	Time 1	Time 2	Time 1	Time 2
Weight (kg)	77.9 (61.1–94.8)	79.9 (58.2–92.4)	58.4 (41.8–77.8)	56.0 (41.8–74.3)	84.2 (59.5–123)	83.4 (58.2–109)	71.7 (60–106)	74.3 58.8–110.8)
FFM (kg)	57.8 (47.0–64.8)	52.8 (45.5–63.8)	41 (29.7–46.2)	38.4 (30.9–46.2)	58.4 (39.9–70.7)	55.8 (37.8–73.8)	47.4 (39.8–66.4)	46.0 (36.8–74.9)
TBK (counts)	1232 (902–1330)	1200 (1026–1478)	960 (749-–1261)	673[a] (532–914)	1120 (702–1396)	1196 (702–1396)	1050 (705–1251)	932[a] (687–1037)
Grip strength (kg)	40.5 (20–55)	38.0 (22–53)	22.5 (15–32)	21.0 (15–29)	30.0 (23–49)	30.0 (22–49)	18.0 (16–46)	22.5 (19–41)

*Median (range); a significant difference between Time 1 and Time 2 $P<0.05$ (Wilcoxon).

Patients were weight-stable throughout chemotherapy. There were, however, significant declines in TBK in women, but not men, with NSCLC, and in metastatic melanoma and breast cancer patients with progressive disease. Changes in TBK were independent of changes in FFM. In the NSCLC population, women experienced a 25% decrease in TBK but maintained FFM, while in men FFM declined 8% and TBK was maintained. Similarly TBK declined by 20% in patients with progressive metastatic melanoma and breast cancer while FFM was maintained. It is concluded that TBK is a poor predictor of changes in FFM in these advanced cancer patients receiving chemotherapy. The clinical significance of such large declines in TBK is unclear; it is usually associated with poor functional capacity (Russell *et al.* 1983), but in these patients there was no change in grip strength.

Moore FD (1980) *Journal of Parenteral and Enteral Nutrition* **4**, 228–260.
Russell DM, Prendergast PJ, Darly PL, Garfinkel PE, Whitwell J & Jeyeebhoy KN (1983) *American Journal of Clinical Nutrition* **38**, 229–237.
Shike M, Russell DM, Detsky AS, Harrison JE, McNeith KS, Shepherd FA, Feld R, Evans WK & Jeyeebhoy KN (1984) *Annals of Internal Medicine* **55**, 250–253.

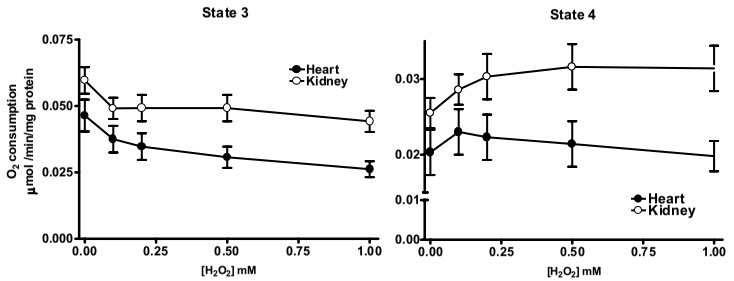
Different response of cardiac and renal mitochondria to sepsis mediators in the neonatal period using a rat model. By K. FUKUMOTO, S. EATON, L. SPITZ and A. PIERRO, *Institute of Child Health and Great Ormond Street Hospital for Children, London*

Overwhelming septicaemia with multiple organ failure is one of the main causes of mortality in neonatal surgery. The liver, kidney and heart are organs for which oxidative metabolism is particularly important. Hydrogen peroxide (H_2O_2), a major mediator of sepsis, has been shown to inhibit liver metabolism (Romeo *et al*. 1999). Our aim was to determine the effects of H_2O_2 on neonatal renal and cardiac oxidative metabolism.

Mitochondria (>95% intact) were isolated from the heart and kidney of 11–15-d-old (peak sucking) rats. O_2 consumption was measured polarographically in mitochondria incubated with 10mM glutamate plus 1mM malate as a respiratory substrate, plus increasing concentrations of H_2O_2. State 3 O_2 consumption, which represents maximum mitochondrial oxidative flux, was measured in the presence of ADP. State 4 O_2 consumption, which represents O_2 consumption that is wasted and not used for ATP generation, was measured after all the ADP had been utilized. Results were compared using paired *t*-tests.

In State 3: H_2O_2 significantly impaired O_2 consumption at all concentrations tested in both cardiac and renal mitochondria ($P<0.01$ *v*. absence of H_2O_2).

In State 4: H_2O_2 had no significant effect on heart mitochondrial O_2 consumption ($P>0.05$) but significantly increased kidney O_2 consumption ($P<0.01$). This probably represents direct membrane damage by H_2O_2. Hence H_2O_2 inhibits maximal rates of ATP generation by both heart and kidney mitochondria (state 3 decrease), but has an even more severe effect on kidney mitochondria because more O_2 is wasted (state 4 increase) and not used for ATP generation.



For heart, n = 17 preparations at each concentration of H_2O_2, and for kidney, n = 20 preparations at each concentration of H_2O_2.

H_2O_2 impairs O_2 consumption and therefore ATP generation in both neonatal cardiac and renal mitochondria, but has a more severe effect on the kidney. The decrease in ATP generation in these organs reduces their efficiency (cardiac work and renal reabsorption) and may be a factor contributing to the failure of these organs in sepsis.

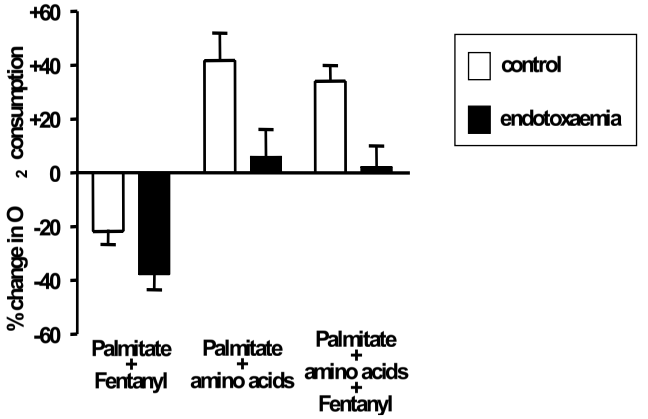
Romeo C, Eaton S, Quant PA, Spitz L & Pierro A (1999) *Journal of Pediatric Surgery* **34**, 1107–1111.

Sepsis enhances the inhibitory effect of fentanyl on neonatal oxidative liver metabolism. By M. ZAMPARELLI[1], S. EATON[1], L. SPITZ[1], G. AMICI[2], A. MARTINO[2] and A. PIERRO[1], [1]*Institute of Child Health and Great Ormond Street Hospital for Children, London and* [2]*Salesi Children's Hospital, Ancona, Italy*

Thermoregulation in neonates is affected by both anaesthesia and sepsis. Non-shivering thermogenesis plays an important role in heat production in neonates, with the liver being a significant contributing organ. In neonates, fentanyl analgesia is associated with postoperative hypothermia and with inhibition of hepatocyte oxidative metabolism (heat production) (Zamparelli *et al*. 1999). However, there are no data on the combined effects of sepsis and general anaesthesia in the neonatal period. We investigated: (1) the effect of fentanyl on hepatocyte metabolism during sepsis; and (2) possible therapeutic approaches.

Sepsis was modelled in neonatal sucking rats (11–13 d old) by intraperitoneal injection of 300 µg/kg lipopolysaccharide. Controls received isovolaemic normal saline. Hepatocytes were isolated after 2 h, when signs of sepsis were apparent. O_2 consumption from palmitate (0.5 mM) was measured polarographically in the presence and absence of fentanyl (2 ng/ml; equivalent to serum analgesic level). Amino acids (AA) were added to hepatocytes from endotoxic and control rats and O_2 consumption measured in the presence and absence of fentanyl (n 10 per study group).

We found that the inhibitory effect of fentanyl was greater in endotoxic hepatocytes compared with controls ($P<0.03$). AA reversed the inhibitory effect of fentanyl during endotoxaemia. However, in contrast to hepatocytes from control rats, AA did not elevate O_2 consumption above baseline level.



We therefore conclude that liver metabolism of septic neonatal rats is more susceptible to inhibition by fentanyl than in controls. This may explain the impaired perioperative thermoregulation observed in septic neonates. Amino acids counteract the combined effect of sepsis and fentanyl and may be useful therapeutically.

Zamparelli M, Eaton S, Quant PA, McEwan A, Spitz L & Pierro A (1999) *Journal of Pediatric Surgery* **34**, 260–263.

The effect of somatostatin and replacement insulin on whole body protein turnover in multiple organ failure. By I.T. CAMPBELL[1,2], M.A. KEEGAN[1,2], M. NIRMALAN[1,2], I. KATSANIKA[1,2], K. SMITH[3], O. ROOYAKERS[3], R.A LITTLE[1], W. TAYLOR[4] and M.J. RENNIE[3], *[1]Intensive Care Unit, Wythenshawe Hospital, Manchester M23 9LT, [2]University Department of Anaesthesia, Withington Hospital, Manchester M20 2LR, [3]Dept of Anatomy and Physiology, University of Dundee, Dundee DD1 4HN, [4]Department of Clinical Chemistry, Royal Liverpool Hospital, Liverpool L69 3BX*

In multiple organ failure (MOF) whole body protein synthesis, breakdown and oxidation are all elevated (Arnold *et al*. 1993). Very large doses of insulin are required to produce positive amino acid balance in skeletal muscles or to maintain normoglycaemia of burn patients (Sakurai *et al*. 1995). We have demonstrated that in patients with MOF, if the gluconeogenic drive is ameliorated by inhibiting glucagon secretion with a somatostatin analogue (Sandostatin, Novartis), and insulin is replaced at 2 IU/h, exogenous glucose utilization can be normalized (Arnold *et al*. 1995). The present study was designed to determine whether Sandostatin infusion aimed at inhibiting glucagon secretion would benefit whole body protein balance by reducing the withdrawal of amino acids from the free body pool (presumably into gluconeogenesis and ureagenesis) and thereby perhaps stimulate protein synthesis or decrease protein breakdown.

Seventeen patients with MOF have so far been studied (twelve male, six female; mean age 61 (SD 12) years, body weight 69.8 (SD 11.9) kg, height 166 (SD 10) cm). Four received Sandostatin (50 µg/h) and replacement insulin (2 iu/h), seven received insulin alone; six received no intervention and acted as controls. Nutritional support was stopped at 00.00 hours on the day of the study. Insulin and Sandostatin infusions were started at 09.00 hours and ran for 6 h. Blood glucose was monitored and normoglycaemia (5–6 mM) was maintained by intravenous infusion of 50% D-glucose; the quantity of glucose infused was noted. After 2 h, whole body protein turnover was measured using a primed constant infusion of L-[^{13}C]leucine (1.5 mg/kg prime, 1.5 mg/kg/h) over 4 h, using [^{13}C]KIC to determine leucine flux and evolution of labelled CO_2 to measure leucine oxidation. The study was approved by the local ethics committee; written informed consent was obtained from next of kin.

	Leucine (µmol/kg/h)						Insulin (mU/litre)		Glucose (mmol/litre)		GUR (mg/kg/min)		Glucagon (pg/ml)	
	$\dot{Q}$		$\dot{S}$		$\dot{O}$									
	Mean	SE	Mean	SE	Mean	SE	Mean	SE	Mean	SE	Mean	SE	Mean	SE
Insulin/ Sandostatin	149*	9.4	111^{+}	3.8	37.4	6.1	28.5	5.5	5.3	0.1	3.9	0.3	173	70
Insulin	174	22.1	128	17.6	46.5	8.0	26.9	3.1	5.2	0.1	2.1	0.6	274	69
Control	176	8.1	132	4.0	44.0	5.1	12.0	5.1	6.1	0.3	0.0	0.0	382	87

$\dot{Q}$: rate of leucine flux (protein breakdown); $\dot{O}$: oxidation; $\dot{S}$: synthesis. GUR: exogenous glucose utilization rate.
*Significant difference from control $P<0.05$, $^{+}P<0.01$.

The Table shows measurements made during the last hour. Glucagon concentrations pre-infusion were comparable in the three groups. It is concluded that whereas insulin at 2 iu/h alone appears to have no effect on protein kinetics in MOF, a combination of Sandostatin at 50 µg/h and insulin at 2 U/h reduces whole body protein breakdown and synthesis and produces a trend towards a reduction in amino acid oxidation.

Arnold Y, Campbell IT, Hipkin LJ, Keegan M, Jenkins S, O'Sullivan E & Chadwick S (1995) *Critical Care Medicine* 23, 71–77.
Arnold J, Campbell IT, Samuels TA, Devlin JC, Green CJ, Hipkin LJ, MacDonald IA, Scrimgeour CM, Smith K & Rennie MJ (1993) *Clinical Science* 84, 655–661.
Sakurai Y, Aarsland A, Herndon DN, Chinkes DL, Pierre E, Nguyen TT, Patterson BW & Wolfe RR (1995) *Annals of Surgery* 222, 283–297.

Oat fibre reduces colitis and stabilizes the gut mucosal barrier in interleukin-10 knockout mice. By R.J. KENNEDY, M. HOPER, P.J. ERWIN, K. DEODHAR, S.J. KIRK and K.R. GARDINER, *The Department of Surgery, Institute of Clinical Science, The Queen's University of Belfast, Grosvenor Road, Belfast BT12 6BJ, Northern Ireland*

Patients with inflammatory bowel disease have different populations of gut bacteria than healthy controls do. There are increased numbers of *Escherichia coli, Bacteroides fragilis* and group D streptococci and a decrease in the potentially protective lactic acid-producing bacteria such as lactobacilli and bifidobacteria (Favier *et al*. 1997). The development of colitis in interleukin-10 knockout mice is also associated with a decrease in the colonic lactobacilli count (Madsen *et al*. 1999). Lactic acid bacteria have a beneficial effect on the health of the host. They have an anti-microbial action within the gut lumen, enhance barrier function by blocking adhesion sites on the colonocytes, produce nutrients beneficial to the mucosa and enhance the immune response (Kennedy *et al*. 2000).

Lactobacilli and bifidobacteria also degrade fibre to short-chain fatty acids (the preferred substrate of colonocytes), which benefit colonic function and morphology (Scheppach, 1994). Increasing the substrate for lactic acid-producing bacteria may reduce colitis and improve gut barrier function. The effect of the addition of oat fibre to the diet of interleukin-10 knockout mice was investigated both as prevention against and treatment of colitis.

Mice were randomized either to receive oat fibre daily by gavage or no therapy (control), from 6 to 12 or 15 weeks of age (prevention) or from 10 to 15 weeks (treatment). Before completion of the experiment, mice received carbon-radiolabelled polyethylene glycol by gavage. Urine was collected for 24 h to assess gut permeability. Systemic antibody response to endotoxaemia (IgM EndoCAb) was assessed; colons underwent histological inflammation scoring (HIS). Permeability and EndoCAb changes were assessed by *t* tests; HIS by the Mann-Whitney *U* test.

Results are expressed as median (inter-quartile range) or mean (standard error of mean).

Study	12 week prevention		15 week prevention		Treatment	
Treatment	Oat fibre	Control	Oat fibre	Control	Oat fibre	Control
HIS (IQR)	5 (3–6)	6.5 (6–10)	3 (2–7)	6 (3–10)	3 (2–4)	6 (3–10)
Permeability % (SEM)	0.36 (0.36)*	0.76 (0.31)	0.91 (0.16)	1.11 (0.38)	1.02 (0.19)	1.11 (0.38)
EndoCAb % (SEM)	69.4 (3.2)†	124.8 (19)	184.3 (29)	168.1 (51)	87.4 (27)	168.1 (51)

*P 0.02 *v.* control, $^{\dagger}P$ 0.03 *v.* control, HIS (all groups) oat fibre 3(2–6) *v.* control 6(3–10), P 0.02.

Oat fibre reduced the severity of colitis in this model. In addition, when used as prevention therapy until 12 weeks, oat fibre improved gut mucosal barrier function as measured by intestinal permeability and IgM EndoCAb.

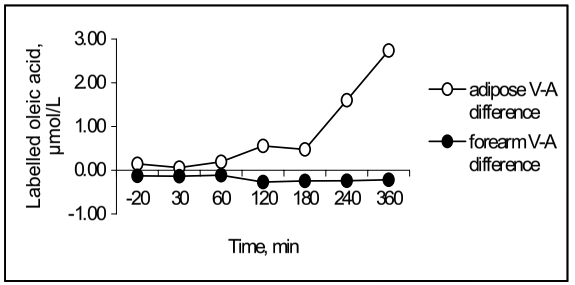
Favier C, Neut C & Mizon C (1997) *Digestive Diseases & Sciences* **42**, 817–822.
Kennedy RJ, Kirk SJ & Gardiner KR (2000) *Jounal of Parenteral and Enteral Nutrition* **24**, 189-195.
Madsen KL, Malfair D, Gray D, Doyle JS, Jewell LD & Fedorak RN (1999) *Inflammatory Bowel Diseases* **5**, 262–270.
Scheppach W (1994) *Gut* Suppl. **1**, S35–S38.

Post-prandial fatty acid release from adipose tissue and skeletal muscle. By K. EVANS[1], G.C. BURDGE[2], M.L. CLARK[3], S.A. WOOTTON[2] and K.N. FRAYN[3], [1]*Department of Clinical Chemistry, Staffordshire General Hospital, Stafford ST16 3SA,* [2]*Institute of Human Nutrition, University of Southampton, Southampton SO16 6YD and* [3]*Oxford Lipid Metabolism Group, Oxford OX2 6HE*

Dietary triacylglycerol (TAG) in chylomicrons is hydrolysed by lipoprotein lipase (LPL) in the capillaries of peripheral tissues, especially adipose tissue and skeletal muscle. Fatty acids liberated by the action of LPL may enter the adjacent tissue, or be released directly into the plasma as non-esterified fatty acids (NEFA). Regulation of this pathway of NEFA release in the post-prandial period has been little studied. We have therefore studied the release of NEFA post-prandially using stable isotopically-labelled fatty acids in combination with venoarterial difference measurements.

Eight healthy volunteers were studied following an overnight fast. Subjects were given a meal containing 37 g fat and 100 g carbohydrate, to which was added 800 mg each of [1-^{13}C]-palmitic acid and [1-^{13}C]-oleic acid in emulsified form. Blood samples were obtained from an arterialized hand vein, a deep forearm vein and a vein draining subcutaneous adipose tissue at baseline and for 6 h following the meal, and venoarterial differences calculated. Portions of the plasma were extracted with chloroform–methanol, and NEFA were separated by thin-layer chromatography and analysed by gas chromatography–isotope ratio mass spectrometry. The study was approved by the Central Oxford Research Ethics Committee and all subjects gave informed consent.

There was clear release of total NEFA across adipose tissue, as expected (not shown). There was clear addition of labelled oleic acid to the NEFA pool from adipose tissue at the later time points (P 0.007). There was no evidence of any release of labelled oleic across the forearm (P 0.8). Similar results were seen for palmitic acid (data not shown).



Previous arteriovenous studies of NEFA balance have been able to measure only net release of NEFA, which may be a result both of intracellular hydrolysis as well as NEFA release into the circulation from LPL action. Using stable isotopically-labelled TAG we have been able to show clearly the release into the circulation of LPL-derived NEFA from adipose tissue in the post-prandial period. The lack of release of labelled fatty acids into the circulation from skeletal muscle implies that all the fatty acids released by LPL in muscle are taken up into the muscle i.e. the action of LPL in skeletal muscle is fundamentally different from that in adipose tissue.

Use of retinyl esters as a marker in test meals of varying fatty acid composition to examine entry into the circulation of previously ingested fat following a second meal. By K.G. JACKSON[1], M.D. ROBERTSON[2], B.A. FIELDING[2], K.N. FRAYN[2] and C.M. WILLIAMS[1], [1]*Hugh Sinclair Unit of Human Nutrition, School of Food Biosciences, University of Reading, Reading RG6 6AP and* [2]*Oxford Lipid Metabolism Group, Nuffield Department of Clinical Medicine, University of Oxford, Oxford OX2 6HE*

Different events have been shown to occur when a second meal is ingested 4–6 h after a first meal (Peel *et al*. 1993; Fielding *et al*. 1996). Compared to the pattern of response seen after a single test meal there is a rapid appearance of chylomicrons, with a peak 1 h after the second meal, with these early chylomicrons carrying fat ingested with the first meal. It has been proposed that a proportion of fat from the first meal is stored in a location from where it is rapidly released on ingesting a second meal. The location of the storage pool and the effects of the type of fat on 'storage' are completely unknown.

The present study was designed to examine whether individual fatty acids have effects on the triacylglycerol (TAG) storage pool as a result of differences in their digestion, absorption and incorporation into chylomicrons. Ten healthy postmenopausal women, mean age 56 (SD 5) years and BMI 25.0 (SD 3.3) kg/m^2, were studied on four separate occasions. Following a 12 h overnight fast, subjects received, in random order, a mixed meal containing 40 g of either (a) palm oil, (b) safflower oil, (c) a 50:50 mixture of fish oil and safflower oil or (d) olive oil. Blood samples were taken before and for 300 min after the meal at which time the subjects consumed a second meal (6 g fat). Blood samples were collected for a further 180 min. Aqueous retinyl palmitate (200 000 IU) was added to the first meal only. A chylomicron (S_f>400) fraction was prepared from plasma by density-gradient ultracentrifugation. TAG was measured using an automated enzymic method and retinyl ester (RE) by normal phase HPLC. Time to reach peak concentration following meal 1 and meal 2 and actual peak concentrations for RE and TAG are shown in the Table.

		Palm oil		Safflower oil		Fish/safflower oil		Olive oil	
		Mean	SE	Mean	SE	Mean	SE	Mean	SE
RE									
TTP (min)	Meal 1	240	19	234	18	216	19	228	16
	Meal 2	18*	3	20*	5	36*	7	19*	4
PC (µg/ml)	Meal 1	3.01	0.75	3.17	1.02	2.54	0.67	4.78	1.21
	Meal 2	2.59	0.71	3.03	0.94	2.35	0.58	4.24	1.32
TAG									
TTP (min)	Meal 1	234	22	246	18	228	25	240	21
	Meal 2	31*	6	31*	7	37*	7	24*	3
PC (µmol/l)	Meal 1	199.8	20.5	209.7	54.0	269.5	68.4	240.6	45.7
	Meal 2	268.6	54.7	322.2	95.8	343.1	76.7	349.6	99.5

Significantly different from meal 1, *P<0.01. TTP: time to peak concentration. PC: peak concentration.

Both the TAG and RE data showed significantly earlier time to reach peak concentrations following the second meal and this was apparent for each of the oils used. The tendency for higher RE concentrations following the olive oil meal may be due to the production of larger TAG-rich chylomicron particles. Further analysis of apo B-48 in this fraction will enable particle number and hence particle composition to be determined. In conclusion, these data suggest that the early RE peak observed after the second meal represents the entry into the blood of dietary fat derived from first meal and the size of chylomicrons after both meals may be influenced by the type of fat in this meal.

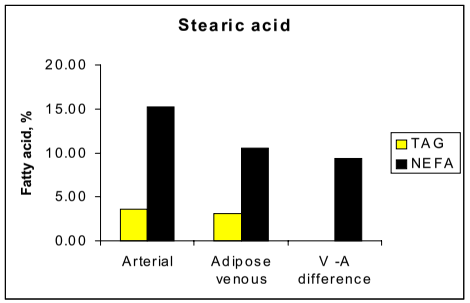
Fielding BA, Callow J, Owen RM, Samra JS, Matthews DR & Frayn KN (1996) *American Journal of Clinical Nutrition* **63**, 36–41.
Peel AS, Zampelas A, Williams CM & Gould BJ (1993) *Clinical Sciences* **85**, 521–524.

Fatty acid composition of triacylglycerol and non-esterified fatty acids in arterial and adipose venous plasma. By K. EVANS[1], G.C. BURDGE[2], M.L. CLARK[3], S.A. WOOTTON[2] and K.N. FRAYN[3], [1]*Department of Clinical Chemistry, Staffordshire General Hospital, Stafford ST16 3SA,* [2]*Institute of Human Nutrition, University of Southampton, Southampton SO16 6YD and* [3]*Oxford Lipid Metabolism Group, Oxford OX2 6HE*

In contrast with other saturated fatty acids, stearic acid is believed to have a minimal effect on raising plasma cholesterol concentrations. Studies have suggested that stearic acid behaves differently from other fatty acids, with arterial concentrations being about twice that predicted from adipose tissue fatty acid release. In the fasting state, most non-esterified fatty acids (NEFA) arise from hydrolysis in adipose tissue, and one possible fate of NEFA is incorporation into very-low-density lipoprotein triacylglycerol (VLDL-TAG) in the liver. We have therefore studied the fatty acid composition of TAG and NEFA in arterial and adipose venous samples.

Eight healthy volunteers were studied following an overnight fast. Paired blood samples were obtained from an arterialized hand vein and a vein draining subcutaneous adipose tissue. Portions of the plasma were extracted with chloroform–methanol, and TAG and NEFA were separated by thin-layer chromatography, and the proportions of specific fatty acids estimated by gas chromatography. The study was approved by the Central Oxford Research Ethics Committee and all subjects gave informed consent.

There were no significant differences in the fatty acid composition of TAG between arterial and adipose venous samples. The relative amount of stearic acid in NEFA differed between sites, with a lower proportion of stearic acid in the adipose venous samples than in the arterial samples (P 0.001). There were significant differences in the fatty acid composition between TAG and NEFA with a significantly greater proportion of stearic acid in arterial and adipose venous NEFA than in TAG (P 0.002 and P 0.02 respectively).



In the fasting state, most circulating TAG is derived from the liver as VLDL. The difference in composition between plasma TAG and its precursor, plasma NEFA suggests selective uptake of individual NEFA into the liver, and/or selective incorporation of individual NEFA into VLDL-TAG. Stearic acid is known to be converted to oleic acid in the liver, and is also preferentially incorporated into phospholipids rather than TAG. While this may partly account for the reduced stearic acid content of TAG, it would not account for the difference in NEFA composition between arterial and adipose venous samples. The results of this study support a reduced extraction of stearic acid by the liver and subsequent reduced incorporation into VLDL.

Nutritional and metabolic aspects of a hill-walk. By P.N. AINSLIE[1], I.T. CAMPBELL[2], K.N. FRAYN[3], S.M. HUMPHREYS[3], D.P.M. MACLAREN[1] and T. REILLY[1], [1]*Research Institute for Sport and Exercise Sciences, Liverpool John Moores University, Liverpool L3 2ET* [2]*University Department of Anaesthesia, University Hospitals of South Manchester, Withington Hospital, Manchester M20 2LR and Oxford Lipid Metabolism Group, Radcliffe Infirmary, Oxford OX2 6HE*

The energetic and metabolic demands of hill-walkers have not been studied systematically despite the potentially deleterious physiological and psychological consequences of activity sustained over a whole day, sometimes in adverse climatic conditions. The aim of the current study was to investigate some energetic and metabolic responses to hill-walking.

Thirteen subjects (eleven male and two female) aged 26 (SE 2) years and peak oxygen consumption ($\dot{V}O_{2\ peak}$) of 59 (SE 2) ml kg^{-1} min^{-1} participated in the study. Each subject completed a 12 km hill-walk, varying in elevation from 100 m to 902 m above sea level, and consisting of a range of gradients and terrain typical of a mountainous hill-walk. Food and fluid intake during breakfast and during the walk was weighed and recorded. During the hill-walk, continuous measurement of respiratory gas exchange using a portable telemetry system (Metamax, Cortex Biophsik GmbH, Brsdorf, Germany) was made to calculate the relative oxidation rates of carbohydrate (CHO) and fat, and the total energy expenditure. Blood samples for the analysis of metabolites, hormones and indices of hydration, were taken before breakfast and lunch, and immediately after the hill-walk. Prior to and immediately following the walk subjects recorded nude body mass and provided a urine sample for the analysis of urine osmolality.

The total energy intake from both breakfast and lunch (6 (SE 1) MJ) was lower than the energy expended (13 (SE 1) MJ; P<0.001) during the 12 km hill-walk. Total CHO and fat oxidized were 432 (SE 16) g) and 162 (SE 6) g), respectively, compared with the CHO and fat intakes of 232 (SE 3) g) and 37 (SE 4) g), respectively. Nude body mass decreased pre-walk to post-walk (72 (SE 2) to 70 (SE 2) kg; P<0.01), along with a subsequent increase in urine osmolality (603 (SE 86) to 744 (SE 71) mosmol; P<0.01). Results of the metabolite and hormonal measurements are shown in the Table.

	Lactate (mmol·l^{-1})		Glucose (mmol·l^{-1})		Glycerol (μmol·l^{-1})		NEFA (μmol·l^{-1})		TAG (μmol·l^{-1})		3-OB (μmol·l^{-1})		Insulin (mU·l^{-1})		Cortisol (mmol·l^{-1})	
	Mean	SE	Mean	SE	Mean	SE	Mean	SE	Mean	SE	Mean	SE	Mean	SE	Mean	SE
Pre-	0.9	0.1	4.8	0.1	93	10	455	83	957	73	65	32	7	1	683	45
Mid-	1.5	0.2$^{\#\#}$	4.7	0.1	262	24***	1757	144***	989	49	332	68	5	1	627	96
Post-	0.8	0.1	5.1	0.2	133	24	868	164•••	1073	110	189	68•••	12	2••	326	50••

Significant differences between pre- to mid-walk: $^{\#\#}P$<0.001; Significant differences mid-, relative to both pre- and post-walk: ***-P<0.001. Significant differences between pre- to post-walk: ••P<0.0.01; •••P<0.001. Abbreviations used: pre-, mid-, post-, blood samples taken before breakfast and lunch, and immediately after the hill-walk; NEFA, non-esterified fatty acid; TAG, triacylglycerol; 3-OB, 3-hydroxybutyrate. n 13 for all measurements.

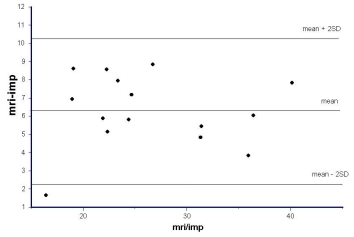
In conclusion, the energy expenditure exceeded the energy intake on the day of the walk. Since food was allowed *ad libitum*, the hill walker is operating at a marked negative energy balance. This negative energy balance may lead to a compromise in physiological function and safety if activity is performed over a prolonged period, indicating the level of energy expenditure could not be sustained in the long term on low energy intakes. However, in spite of the difference in energy intake and expenditure, the blood glucose concentration was maintained. The major source of energy was an enhanced fat oxidation, probably from adipose tissue lipolysis.

This work was supported by Mars Incorporated.

Validation of 'in body' bioelectrical impedance by whole-body MRI. By E.L. THOMAS[1], G. FROST[2], T. HARRINGTON[1] and J.D BELL[1], [1]*The Robert Steiner MR Unit and* [2]*Nutrition and Dietetic Research Group, Imperial College School of Medicine, Hammersmith Hospital, London*

MRI has been shown to be an excellent technique for measuring body fat content, with its ability to separately quantify specific fat compartments giving it a real advantage over other techniques. However, it is not suitable for large population studies. Bioelectrical impedance is widely used as a method for assessing body composition; however, although previous studies have found good correlation between fat measurements by MRI and impedance, agreement between the techniques was poor (Thomas *et al*. 1998). The advent of a new generation of impedance systems for measuring body fat content requires that the relationship between the two techniques be re-examined. The aim of this study was to compare body fat content measured by whole body MRI with that measured by the 'in body' bioelectrical impedance system.

Fifteen volunteers (six male, nine female), aged 24–46 years, BMI 17.7–37.0 kg/m^2 were studied. For whole body MRI, subjects were imaged lying prone in a Picker 1.0T HPQ system with a rapid T_1 weighted spin-echo sequence (TR 36 ms, TE 14 ms). Subjects were scanned from their fingertips to their toes by acquiring 10 mm thick transverse images with a 30 mm gap between slices in the arms and legs and a 10 mm gap in the torso (Thomas *et al*. 1998). Images were analysed using a software program that employs a threshold range and a contour-following algorithm with an interactive image-editing facility (Barnard *et al*. 1997). The 'in body' system is a method of multifrequency segmental bioelectrical impedance. All subjects were measured following a standard methodology, and all measurements made after voiding. The 'in-body' technique uses 8-point tactile electrodes; volunteers stand on a footplate, which has two electrodes per foot and hold a handgrip with two electrodes per hand. The mathematical methodology is presented elsewhere (Cha *et al.* 1996).



The mean percentage body fat from MRI was 23.6 SEM 1.48 and the 'in-body' reading was 23.2 SEM 1.85. The Bland and Altman accuracy plot shows that there is excellent agreement between the two methodologies.

These results of this study demonstrate for the first time good agreement between a 'gold standard' method of body composition analysis, in this case MRI, and multifrequency bioelectrical impedance. Although the multifrequency bioelectrical impedance system cannot be used to assess individual adipose deposits, which is one of the great strengths of MRI, it has the advantage that it is a very simple, cheap technique for estimating body fat, which is quick and has great potential in a large epidemiological study.

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Cha KC, Chertow GM, Gonzalez J, Lazarus JM & Wilmore DW (1996) *Journal of Applied Physiology* **79**, 1316–1319.
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A pilot study to assess the effectiveness of a nasal loop in securing nasogastric feeding tubes in dysphagic stroke patients. By M. O'CONNOR[1], J. WOODWARD[2] and D. O'MAHONY[1], [1]*University Hospital Birmingham Trust (UHBT), Selly Oak, Birmingham B29 6JD and* [2]*University of Birmingham, Edgbaston, Birmingham B15 2TT*

Dysphagia, secondary to stroke, can occur in 27–50% of patients (Odderson *et al*. 1995). It results in malnutrition if the patient's nutritional requirements are not met. Malnutrition increases the risk of complications and prolongs hospital stay, leading to increased costs. Thus, both dysphagia and malnutrition are risk factors for poor outcome after stroke. Enteral rather than parenteral feeding is the preferred route in dysphagic patients. Enteral feeding can be either via a nasogastric (NG) tube or a percutaneous endoscopic gastrostomy (PEG). NG tube insertion is easy, quick and relatively non-invasive and has a negligible mortality rate (O'Mahony & McIntyre, 1995). PEG insertion, in contrast is an invasive procedure which can result in infection of the insertion site, chest infection, peritonitis or abdominal organ perforation (Wanklyn *et al.* 1995). It has a 30-day morbidity and mortality rate of 22% and 10% respectively (Hull *et al.* 1993) and should be avoided in patients with acute illness as they are at a higher risk of serious adverse effects. It has been shown that with a PEG the patient's full nutritional requirements can be provided without any disruption to feeding (Norton *et al.* 1996). In comparison, it is not always possible to achieve this with NG feeding. The primary reason for this is dislodgement of the NG tube by the patient. Dislodgement occurs in 58–100% of patients (Popovich *et al.* 1996). A recent enteral feeding audit at University Hospital Birmingham NHS Trust found the incidence of dislodgement of NG tubes in stroke patients to be 66%. The mean number of times the NG was dislodged during an episode of feeding was five, and the range from three to nine.

To address this problem within the Trust, a pilot study commenced which involved the insertion of a nasogastric feeding tube fixation device called a nasal loop. This was adapted from the technique by Popovich *et al*. (1996). Ethical approval was sought from the Trust Ethics Committee. The nasal loop was inserted in dysphagic stroke patients (*n* 13) who had dislodged their NG tubes on more than two occasions. Those subjects with incomplete data (*n* 3) or who had nasal loop in for less than 2 d (*n* 3) were excluded from the study. The percentage feed received before and after nasal loop insertion was recorded. The nasal loop was tolerated by all subjects, with no reports of any complications.

Subjects (*n*)	Sex		Age (years)		No. days nasal loop in situ		% prescribed feed received pre-nasal loop insertion		% prescribed feed received post-nasal loop insertion	
	Male (*n*)	Female (*n*)	Mean	Range	Mean	Range	Mean	Range	Mean	Range
7	5	2	72	61–83	24	10–41	5	0–90	96	33–100

This pilot study indicates that the nasal loop could provide a safe and effective way of delivering enteral nutrition in patients with dysphagia requiring short-term nutritional support or who those who are unsuitable for a PEG.

Hull MA, Rawlings J, Murray FE, Field J, McIntyre AS, Mahida YR & Hawkey CJ (1993) *Lancet* **341**, 869–872.
Norton B, Homer-Ward M, Donnelly MT, Long RG & Holmes GK (1996) *British Medical Journal* **312**, 13–16.
O'Mahony D & McIntyre AS (1995) *Age and Ageing* **24**, 533–535.
Odderson IR, Keaton JC & McKenna BS (1995) *Archives of Physical Medicine and Rehabilitation* **76**, 1130–1133.
Popovich MJ, Lockrem JD & Zirot JB (1996) *Critical Care Medicine* **24**, 429–431.
Wanklyn P, Cox N & Belfield P (1995) *Age and Ageing* **24**, 510–514.

Outcomes of patients with a percutaneous endoscopic gastrostomy: a two-year interface audit. By J. WATSON[1], B. ABRAHAMS[2], J. WILSON[2], D. SHERMAN[3] and C. CAYLEY[4], [1]*Department of Nutrition and Dietetics, Parkside Health NHS Trust, Wembley Centre for Health and Care, Wembley HA0 4UZ and Departments of* [2]*Nutrition and Dietetics,* [3]*Gastroenterology and Nutrition and* [4]*Care of Elderly, Central Middlesex Hospital, Acton Lane, London NW10 7NS*

The decision to place an enteral feeding tube is most often made in the hospital by hospital clinicians, but a large part of the cost and care of the patient is the responsibility of primary care. Home enteral tube feeding has been increasing at a rate of 23% per year in our Trust and had led to concerns regarding the ability of community resources to meet the additional demands.

The aims of this project were to investigate the selection and preparation of patients for PEG insertion, to assess the long-term care of patients in the community and to collect data on the methods of feeding, including PEG removal, complications and mortality.

All adult patients who had had a PEG inserted in a district general hospital between 1 October 1997 and 31 March 1998 were included. Patients were followed thorough their hospital stay and community care until death or for 2 years post-PEG placement. Data was collected retrospectively from patients' hospital and community records.

A total of forty-one patients had a PEG placed during this time period. Data from thirty-six (87.8%) patients was included. Half of the patients were male. The median (range) age was 79 (38–95) years. Twenty-nine (80.6%) patients were referred for PEG placement by Care of the Elderly. The diagnosis of twenty-seven (75%) patients was cerebrovascular accident while the remainder included Parkinson's Disease, multiple sclerosis, cerebral palsy, cancer of the oesophagus, pressure sores and chronic pancreatitis. The clinical indication for enteral feeding in twenty-nine (80%) patients was swallowing impairment, as assessed by a Speech and Language therapist. The median (range) time from admission to PEG placement was 3 (0–10) weeks. Median (range) time from PEG placement to discharge was 7 (2–140) d.

Nineteen per cent (7 patients) of patients died in hospital. At discharge from hospital the PEG was used to provide the full nutritional requirements for 86% of the patients, 72% (thirteen patients) were bedbound and 94% (seventeen patients) required complete help with the administration of their feed. Nearly half (45%) of the patients were discharged to a local community hospital where they stayed a mean (range) of 18 (0–36) weeks and where 50% died.

In the community, patient contact by the community dietitian occurred seven times in the first 6 months post-discharge. Seventeen patients (71%) experienced at least one PEG-related problem in this time period. The most commonly occurring problems recorded were constipation, nausea and vomiting, tube blockage and feeding pump malfunction. Four patients (17%) were admitted to hospital in the first 6 months, all for reasons not attributed to PEG feeding.

Sixty per cent (21 patients) of patients had died within 1 year of PEG placement and 69% (24 patients) by the end of 2 years. Eleven patients (31%) were able to commence oral feeding during the 2-year period but only as a supplement to PEG feeding. An additional seven patients (20%) were able to have their PEG removed as they were taking sufficient oral intake to meet their nutritional requirements.

Patients discharged into the community are highly dependent on primary care teams and carers. There is a high mortality in the first 6 months post-PEG placement. Patients surviving longer than 6 months continue to require care for over 2 years. Many patients experienced minor problems with PEG feeding but this method of nutrition support proved to be safe in the community setting with regular monitoring by the community dietitian.

A review of services provided for patients who required placement of percutaneous endoscopic gastrostomies (PEG): stage one: patients' experiences. By M. BHINDA[1] and L. PERRY[1,2], [1]*Mayday Healthcare NHS Trust, Thornton Heath, Surrey CR7 7YE and* [2]*Faculty of Health and Social Care Sciences, Kingston University and St George's Hospital Medical School, Kingston Hill, Kingston upon Thames, Surrey KT2 7LB*

The practice of PEG placement is increasing (Elia, 1998) but feeding via PEG may be associated with a range of problems, both physical and/or psycho-social problems (Finocchiaro *et al*. 1997; Rickman, 1998). Structured approaches to management are recommended (Elia, 1994) and have demonstrated benefits (Pattison & Young, 1997). In order to provide information for management reliant upon informal arrangements, a review of services was undertaken in a South London borough (approx. 1/3 million population).

The first stage required establishment of a current list of PEG-fed patients as the list of forty-nine adults held in the hospital dietetic dept. was out-of-date. All seventeen community nursing teams were asked for details of caseload patients with PEGs. Details were eventually produced relating to eight patients, one anonymously. All except the latter were on the original list although two were wrongly believed to have discontinued PEG feeding. Of the original list, three patients had died, two had moved out of area, one was naso-gastric fed, one was an acute-care in-patient, one family was illiterate and one required visiting due to reported problems. Further enquiries were made *via* feed delivery records and other therapy teams.

A questionnaire was developed, piloted with multi-disciplinary team members and sent to forty-two patients/carers. A reminder was sent to non-respondents 2 weeks later. Thirty questionnaires (71%) were returned although not all were fully completed; five patients had died, one was hospitalized, two had moved out of area and four were lost to follow-up. Twelve patients were resident in institutions; of the eighteen living in their own homes, eight completed the questionnaire themselves, two of whom lived alone.

The PEG had been sited in local hospitals in sixteen (53%) respondents, with nine other hospitals cited; ten (36%) patients were admitted specifically for the procedure. PEG feeding duration ranged from 3 to 96 (mean 23.6) months.

In response to questions as to who had discussed PEG pre-placement, seventeen patients (71%) cited hospital and five (22%) community doctors; fourteen (58%) hospital and two (9%) community dieticians; six (26%) hospital and four (17%) community speech therapists; five (21%) hospital and three (13%) community nurses. Commenting on placement preparation, the importance of timing, particularly of placing PEG early enough, and addressing the emotional impact as well as informational needs was repeatedly stressed.

Overall twelve patients (50%) stated that they were very satisfied, ten (42%) that they were satisfied and two (8%) that they were neither satisfied nor dissatisfied with preparation for coping at home. Of those living at home, all respondents reported being taught to attach tubing, tube care, how to control the pump, how much feed was required and how to give extra fluid. However, two cited no instruction in dismantling tubing and a single (different) patient mentioned not knowing where to get supplies, lack of contact numbers and unpreparedness for potential problems. A very varied and inconsistent pattern of follow-up was revealed. The most common problem reported was site infection in fifteen (50%) patients; pump malfunction, supply difficulties and PEG dislodgement were reported by five (19%), leakage by four (15%), tube fracture and blockage for three (11%), stoma overgranulation and difficulties getting help by two (8%) patients. Only six (20%) reported no problems. A variety of strategies were described, occasionally entailing multiple requests for help and repeated hospital admissions.

Overall, whilst the majority expressed themselves as satisfied, there were clear opportunities to improve quality and possibly cost-effectiveness of the service.

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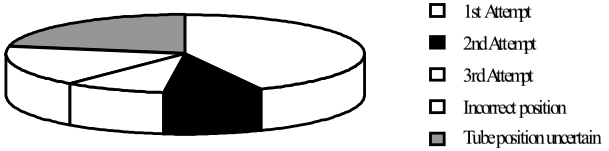
Blind placement of nasojejunal tubes in an intensive care unit. By H.J. PEAKE[1], N.E. JONES[1], G. BALDOCK[2] and G.S. FROST[1], [1]*Department of Nutrition and Dietetics and* [2]*Intensive Care Unit, The Hammersmith Hospitals NHS Trust, London W12 0HS*

Enteral delivery of nutrients is important for the optimal management of critically ill patients. Some patients do not tolerate nasogastric feeds due to impaired gut motility (gastric stasis) (Dive *et al.* 1994). These patients can be successfully fed with post-pyloric enteral nutrition (Tymann, 1997). Our intensive care (ICU) policy advocates the blind bedside placement of nasojejunal (NJ) tubes without imaging guidance (Kallifias *et al.* 1996). This procedure has the advantage of being quick, easy, less invasive and cheaper than alternative methods. This retrospective audit assessed the success rate (correct tube position) of this technique.

In 1999 all ICU patients receiving nasojejunal nutrition were identified using the enteral and parenteral nutrition database, which is compiled by the nutrition and dietetic department. The position of the feeding tubes was confirmed by studying the abdominal X-rays of the patients. Further information regarding the position of NJ tubes and tolerance to feed was obtained by referring to the medical notes and dietetic record cards.

From the information collected, NJ tubes were used to administer feed to twenty patients. Of these patients, fourteen had their tubes inserted using the blind technique. The mean age of these fourteen patients was 62.8 years (SD 12.7). Their diagnosis categories were: cardiac (*n* 7), malignancy (*n* 2), respiratory failure (*n* 2) and other (*n* 3). A total of thirty-one tubes were passed. The results were analysed according to feeding episodes due to the multiple tube insertion in eight patients resulting from tube displacement or incorrect tube position. Twenty-three feeding episodes were initiated, a feeding episode was defined as a patient being fed for 1 day or more. For the twenty-three feeding episodes, ten (43%) NJ tubes were successfully placed on the first attempt, two (9%) on the second attempt, two (9%) on the third attempt. A further nine (39%) were failed placements, five of which were due to inability to confirm tube position on X-ray.



The first attempt success rate was 43% (data expressed per feeding episodes) using the blind placement technique. In four (17%) feeding episodes, parenteral nutrition was commenced due to failed NJ insertion, in these circumstances endoscopic NJ placement should be considered. The ICU enteral feeding protocol is being modified to include this recommendation.

The ICU at Hammersmith Hospital is now prospectively monitoring the success rate of blind NJ tube placement, endoscopic insertion and NJ feed tolerance.

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Endoscopically placed naso-jejunal feeding tubes in ICU patients: a retrospective review. By A.L. JUKES, *Department of Nutrition and Dietetics, University Hospital of Wales, Cardiff and Vale NHS Trust, Cardiff CF14 4XW*

The preferred method of nutritional support in intensive care patients is *via* the enteral feeding route due to its favourable trophic effects on the intestinal mucosa, reduced rate of complications and lower costs compared with parenteral nutrition (Jolliet *et al.* 1999). Impaired gastric emptying can be a limiting factor in providing enteral nutrition, commonly affected by critical illness, drug therapy and feeding formula. Naso-jejunal tube feeding can be useful in patients who fail to tolerate naso-gastric tube feeding. Spontaneous transpyloric passage of enteral tubes is commonly unsuccessful even when gut prokinetics are administered intravenously. Endoscopic placement of naso-jejunal tubes can be performed at the bedside using portable equipment aiming to achieve a final position distal to the Treitz ligament. Endoscopic placement of tubes is highly successful and enteral feeding can start immediately following the procedure (Patrick *et al.* 1997).

The University Hospital of Wales Intensive Care Team and the Nutrition Support Team (established in 1998) both aim to provide appropriate and timely nutritional support. Close links with the endoscopy unit have resulted in an increase in the use of endoscopically placed naso-jejunal feeding tubes since 1998. The aim of this retrospective review was to evaluate the use of feeding tubes placed in ICU patients over a 15-month period (October 1998–January 2000).

Patient details (*n* 27)			Indication		
Male	23	(85%)	Emergency AAA repair	8	(30%)
Female	4	(15%)	Faecal peritonitis	6	(22%)
Surgical	25	(93%)	Acute pancreatitis	5	(18.5%)
Medical	2	(7%)	Multiple organ failure	4	(15%)
			Regurgitation	2	(7.25%)
			Other	2	(7.25%)
Naso-jejunal tubes (*n* 36)					
n 1	20	(74%)	Remained *in situ*	205 d (total)	
n 2	5	(18.5%)	Per patient	1–27 d	(mean 7.6 d)
n 3	2	(7.5%)	Per tube	1–27 d	(mean 5.7 d)
Fate of tube					
Clinical			Tube related		
Patient died	9	(25%)	Blocked	5	(14%)
Tube refluxed	6	(17%)	Fallen out	5	(14%)
Patient pulled out	2	(5.5%)			
Tolerated other route	2	(5.5%)			
Removed for procedure	4	(11%)			
Transferred	1	(2.7%)			
Parenteral nutrition	1	(2.7%)			

A review of these results suggests that the majority of patients would have benefited from placement of an enteral feeding tube during theatre, and that the success of naso-jejunal feeding could be improved by attention to the care of the feeding tubes once placed.

Tube-related complications result from inadequate attention to the care of the feeding tube and are often preventable. Blockages are often a combination of factors including inadequate flushing, administration of concentrated feed and or medication. Proper securing of the tube to the patient should prevent tubes accidentally being removed during procedures such as turning.

Following this review, new standards and guidelines have been produced for the multidisciplinary team members caring for patients who have naso-jejunal feeding tubes.

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Patrick PG, Marulendra S, Kirby DF & DeLegge MH (1997) *Gastrointestinal Endoscopy* **45**, 72–76.

A study of the impact and cost-effectiveness of introducing hospital pharmacist prescribing into neonatal parenteral nutrition. By M. POWELL[1], H. MARTIN[2] , J. PUNTIS[3] and I. GOSS[2], [1]*University of Derby Business School, Derby, DE22 1GB,* [2]*Pharmacy and* [3]*Neonatal Unit, Leeds General Infirmary, LS1 3EX*

There is increasing pressure within the NHS to introduce new clinical roles for nurses and staff in professions allied to medicine. Much recent debate has focused on introducing pharmacist prescribing and more extensive clinical roles for pharmacists in the light of practice in America (Meade, 1993; Cotter & McKee, 1997; Farrell *et al.* 1997). This paper examines the impact and cost-effectiveness of introducing hospital pharmacist prescribing into neonatal parenteral nutrition (PN) at the Leeds General Infirmary (LGI) in the UK.

The original system for prescribing neonatal PN at the LGI was one where junior doctors (SHO) prescribed the PN directly onto a ward-based networked version of Kabi-Pharmacia PN programme. Prescriptions were then checked and processed in the hospital pharmacy. This system was thought to have disadvantages including inflexibility, difficulty in adding new products, error corrections and time required to train SHO to use the system. In the new system, the paediatric PN pharmacist created prescriptions on the ward in consultation with SHO. Pharmacy staff then input prescription data onto the Kabi programme as well as checking and processing the prescription.

Measures of opinions and experience of SHO were collected through questionnaires issued at the start and end of SHO rotations. Measures of time savings and activity changes were collected on the ward and in the pharmacy on selected days. Measures of patient wellbeing were collected from patient blood analyses on relevant days. Data were collected in three phases; a control set using staff in the original system, a comparison set using staff at the changeover with experience of both systems, and an experiment set using staff under the new system.

System	SHO time on ward (min/day)*	No. of interruptions to SHOs per day*	Time to process and check in pharmacy (min/day)*	No. of phone calls to prescriber per day*	Mean use of non-standard ingredients per day*	Mean no. of alterations to prescriptions in pharmacy per day*	Total time spent by pharmacy on TPN (min/d)*
Old	30.9	1.1	21.39	1.38	0.02	0.7	21.39
New	14.46	0.15	15.1	0.70	0.20	0.3	32.32
Time saving	+15	-	+6.3				- 11

* Significant at $P = 0.05$.

The results show that there are significant time-savings for SHO and for pharmacy processing and checking. Total pharmacy time increases but this is outweighed by reductions in SHO time, improvements in pharmacy workflow, consistency of prescribing and improved pharmacist/doctor relationships. There were significantly fewer alterations to prescriptions in the pharmacy and more use of non-standard ingredients in feeds in the new system. SHO preferred increased pharmacist involvement at ward level and place high values on time savings and direct involvement with pharmacists. SHO believed the new system was at least as good in terms of clinical input (82%), understanding of nutrition (75%) and quality of patient care (88%). The monetary value of such improvements is hard to quantify but together with time savings suggests the new system may be cost effective.

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Farrel J, North-Lewis P & Cross M (1997) *Pharmaceutical Journal* **259**, 187–190.
Meade V (1993) *American Pharmacy* **NS33**, 45–47.

Pump alarm pressures and Pall *Lipipor* TNA filters. By E. MAYNARD and A. SEACOMBE, *Scientific and Laboratory Services, Pall Europe Ltd, Walton Road, Portsmouth PO6 1TD*

The Pall *Lipipor* TNA filter (code TNA1E) is an air-eliminating filter with a 1.2 µm modified nylon membrane and phthalate free fluid pathway. This device is indicated for the removal of inadvertent particulate debris, enlarged lipid droplets, microbial contaminants and entrained air, which may be found in nutrient admixtures and lipid emulsions.

In a previous study a returned filter was forwarded to our Scientific and Laboratory Services (SLS) department for evaluation as the pump alarms had been activated while the filter was in clinical use. Scanning electron microscopy (SEM) was performed on the upstream media. The most notable feature was the presence of a large fibre (approximately 1 mm in length) which had calcium chloride particles on its surface. A smaller fibre (approximately 0.2 mm in length) containing magnesium and silicon was also found on the upstream media surface. The origin of these fibres is unclear as they are not representative of any component used in the manufacture of the filters. Unfortunately, in this instance, we could not conclusively identify the cause for the observed blockage.

Therefore, in order to confirm the normal working pressure of the filter and identify appropriate settings of the pump pressure, we tried to reproduce the clinical situation as closely as possible, i.e. similar regimens, pump and flow-rate. This gives us an idea of the 'filterability' of the Clinovia LB17 (with iron chloride) and LB21 (no iron chloride) solutions in combination with the Pall TNA1E.

The solution bags were removed from storage and gently inverted several times to ensure adequate mixing prior to infusion. The TNA1E was primed directly with the regimen, following the instructions for use, the infusion pump was set to deliver at 144 ml/h and the pump pressure readings were recorded at regular timed intervals.

Filter	Regimen	Time (hours:mins)	Flow rate (ml/hr)	Volume infused (ml)	Pump alarm pressure* (mmHg)
TNA1E	LB 17	8:00	144	1160	105
TNA1E	LB 21	7:45	144	1122	73

* The pump did not alarm during testing (nominally set at 500 mmHg).

The filterability tests showed a difference in system pressures between the regimens, but in both cases flow through the filter was maintained. The pressure upstream of the filter rises slowly as the membrane removes droplets >1.2 µm and will eventually trigger the pump alarm, dependent on the pressure at which it is set. The Medical Devices Agency (1995) recommend that pump pressures are set at 500 mmHg or lower, but the exact setting below this figure must be finally a clinical decision. In this case, the pump used clinically was set to alarm at 80 mmHg, but this study suggests that filter blockage had not occurred. In this instance, the equipment functions optimally when the pump alarm is set higher than 80 mmHg.

The US Food and Drug Administration (1994) and the American Society for Parenteral and Enteral Nutrition (ASPEN) (1998) recommend the use of filtration in the administration of parenteral nutrition admixtures. ASPEN's '*Safe Practices for PN Formulations*' (1998) reviews the rationale for use of in-line filters with regard to particulates, phlebitis, microprecipitates, infection and air emboli, and concludes that the use of a filter provides an additional safety check to prevent patient harm.

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US Food and Drug Administration (1994) *American Journal of Hospital Pharmacy* **51**, 1427–1428.
American Society for Parenteral and Enteral Nutrition (ASPEN) (1998) *Journal of Parenteral and Enteral Nutrition* **22**, 49–66.

Analysis of occluded intravenous lipid filter membranes during clinical use. By D. COPE, L. THOMPSON and C. HARTT, *King's College Hospital, Denmark Hill, London SE5 9RS*

A high pump infusion pressure (>150 mmHg) had been noted during administration of a particular feed tailored to one individual. The concern was that when the pump alarmed, the filter and the regimen were discarded, due to infection-control measures, which was inconvenient and expensive. It seemed to occur in spates and often there was no excessive pump pressure.

A number of Pall *Lipipor* TNA filters were returned to Pall Scientific and Laboratory Services (SLS) from the pharmacy at King's Hospital for analysis. At Pall SLS initial visual analysis was performed, followed by scanning electron microscopy (SEM) and x-ray emission spectroscopy (EDS). Media were removed from the filters, sectioned and mounted onto SEM stubs with carbon dag (colloidal graphite). The stubs were sputter gold coated and analysed using SEM and EDS.

Visual examination of all three filters revealed that the media surfaces were covered in lipid material. The analysis of the membrane by SEM and EDS showed that there was amorphous material covering the whole of the upstream filter surface. This substance may have been a result of lipid droplet instability.

Information from one manufacturer, regarding the feed and regimen, advised a slight instability was possible; however, as components were being used from two manufacturers' sources, it was not possible to get conclusive stability data.

Three recommendations were made:

1) Routinely monitor ward refrigerator temperature,
2) Ensure bags are always mixed well prior to infusion,
3) Pre-priming the filters with saline may facilitate throughput and minimize pressure increases.

One further change, which was made after the investigation, was to use TPN components from a single source of manufacturer. This manufacturer gave data predicting that the regimen was stable. There have been no reports of high infusion pressures since the investigation was completed.

Can glutamine and vitamin losses during continuous renal replacement therapy (CRRT) be minimized by supplementation? By A. MARIN and G. HARDY, *Pharmaceutical Nutrition Group, School of Biological and Molecular Sciences, Oxford Brookes University, Oxford OX3 0BP*

Continuous arterial-venous (CAVHD) or veno-venous haemodiafiltration (CAVHD) and continuous veno-venous haemofiltration (CVVH) are reliable methods of CRRT and are particularly suited to critically ill patients in acute renal failure. Fluid and uremic toxin removal by these techniques is normally sufficient to allow unrestricted nutrition support.

To date haemodiafilters cannot discriminate between uremic toxins and nutrients. Therefore, the potential exists for significant losses of vitamins during continuous haemofiltration. It has been reported that critically ill patients requiring CVVH had significantly lower whole blood concentrations of vitamins and trace elements during the first 24 h of CVVH. Certainly losses of folic acid and pyridoxal-5 phosphate, and most likely of other water-soluble vitamins, occur during CRRT (Story *et al*. 1999). In the case of vitamin C, the mean daily loss is 68 mg (528 μM) and for folic acid 290 μg (0.65 μM). The significance of these losses is unclear but they may be clinically important and suggest the need for further investigation concerning vitamin supplementation in CVVH patients. (Fortin *et al.* 1999).

CVVHD induces changes in glutamine (Gln) metabolism and distribution that are reflected by an initial decrease of up to 33% in serum Gln levels at the start of treatment. Subsequently, Gln losses during CRRT may exceed 25–35% (3000 mg/d) Therefore, the need for Gln supplementation in ITU patients may be important in the first days of CVVHD (Novak *et al*. 1997; Kuhlmann, 2000).

We have investigated the stability of a sterile aqueous mixture containing L-Gln (4 g) and multivitamins (MVC 9+3) including: vitamin C 100 mg and folic acid 400 μg.

The 2.5% Gln solution (160 ml) was prepared aseptically as described previously (McElroy & Hardy, 1995) and filled into multilayer Ultrastab bags. The multivitamin preparation (10 ml) was added aseptically to the Gln bags, which were then stored at 4–8° for 72 h. Samples were analysed for Gln and vitamin C (McElroy & Hardy, 1995), at 24-h intervals. Folic acid was not measured.

The assays showed that Gln degradation at 4° was 7.1% at 24 h, 10.3% at 48 h and 13.35% at 72 h. Glu increased from 1.0 mM to 2.5mM. Vitamin C degradation was 8.5% at 24 h, 9.1% at 48 h and 10.5% at 72 h.

Nutritional support for CRRT patients should provide not only optimal dosages of vitamins but also adequate amounts of glutamine, especially if CRRT is applied over prolonged periods. Our preliminary data suggest that the proposed Gln/multivitamin combination is less stable than Gln alone in aqueous solution at 4–8°. The chemical interactions and other potentially destabilizing factors are currently under investigation. In the meantime we recommend that these mixtures should be used immediately after preparation and not stored for longer than 24 h.

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Kuhlmann MK & Kohler H (2000) *Anaesthesist* **49**, 353–358.
McElroy B & Hardy G (1995) *Clinical Nutrition* **14**, 137.
Novak I, Sramek V, Pittrova H, Rusavy Z, Tesinsky P, Lacigova S, Eiselt M Kohoutkova L, Vesela E & Opatrny K Jr (1997) *Artificial Organs* **21**, 359–363.
Story D, Ronco C & Bellomo R (1999) *Critical Care Medicine* **27**, 220–223.

Long-term stability of L-glutamine infusions for clinical administration. By B. MCELROY[1], A. MARIN[2] and G. HARDY[2], [1]*Pharmacy, Royal Shrewsbury Hospital, Shrewsbury SY3 8BR and* [2]*Pharmaceutical Nutrition Group, School of Biological and Molecular Sciences, Oxford Brookes University, Oxford OX3 0BP*

L-Glutamine (Gln) is a conditionally essential amino acid, which is not routinely formulated (as free L-Gln) into amino-acid infusions for inclusion into All-In-One parenteral nutrition admixtures. Free L-Gln is considered unsuitable for heat sterilization and has poor solubility (34.9 g/l at 20°) which has made its formulation and preparation difficult. Earlier studies (McElroy & Hardy, 1995) have reported that 2.5% infusions of L-glutamine were stable for clinical use when stored at between +2° and –20°.

In this study we determined the long-term stability of L-glutamine infusion. Aqueous infusions containing 25 g Gln in 1 litre of water for injections were prepared under aseptic conditions, filter-sterilized (0.2 µm) into oxygen impermeable bags (Evarex Barrier). The bags were stored at 4–8° or frozen at –20°. The concentrations of glutamine and its main degradation product glutamate were determined by standard enzymatic methods (*n* 3) throughout the study period from 1990 to 2000.

Glutamine content (mmol/l; 2.5% Gln = 171.1 mmol/l) stored at 4–8° (*n* 3)

Day 0	Day 30	Year 1	Year 5	Year 6	Year 7	Year 8	Year 9
170	168	142.5	112.6	104.5	99.9	99.9	95.6

Glutamine content (mmol/l; 2.5% Gln = 171.1 mmol/l) stored at –20° (*n* 3)

Day 0	Day 30	Year 1	Year 9	Year 10
170	170	162.7	157.1	143.8

Glutamate content (mmol/l) stored at 4–8° (*n* 3)

Day 0	Day 30	Year 1	Year 5	Year 6	Year 7	Year 8	Year 9
0.74	0.71	28.5	54.04	59.16	64.27	69.38	74.49

Glutamate content (mmol/l) stored at –20° (*n* 3)

Day 0	Day 30	Year 1	Year 9	Year 10
0.74	0.71	2.5	8.1	13.7

The degradation rate for Gln stored at 4–8° was 2.48% per year. When stored at–20° the degradation rate was substantially lower, at 1.62% per year. Glu concentrations increased in accordance with the degradation of Gln. These data further show that infusions of L-Gln can be prepared under suitable pharmaceutical conditions and remain pharmaceutically and clinically acceptable (±5%) after prolonged storage intervals, either under refrigerated conditions or if stored frozen. This stability work has resulted in the use of L-glutamine-supplemented PN for more than 1000 patients in one hospital centre, the Royal Shrewsbury Hospital, with no reports of any adverse effects.

McElroy B & Hardy G (1995) *Clinical Nutrition* **14**, 137.

Stability of fructose-1,6-diphosphate total parenteral nutrition mixtures containing calcium. By W. HICKS[1] and G. HARDY[2], [1]*Department of Biochemistry, University of Liverpool, Liverpool L69 3BX and* [2]*Pharmaceutical Nutrition Group, School of Biological Sciences, Oxford Brookes University, Oxford OX3 OBP*

Calcium phosphate precipitation within total parenteral nutrition (TPN) mixtures represents a problem that needs addressing. Special attention was brought to this fact by a Safety Alert issued by the US Food and Drug Administration (FDA, 1994). The report identified this serious hazard with respect to the safe provision of the recommended intakes of phosphate (P) and calcium (Ca), by means of inorganic phosphate (IP) and Ca salts within 3-in-1 TPN admixtures.

A recent study (Prinzivalli & Ceccarelli, 1999) demonstrated that sodium-D-fructose-1,6-diphosphate (FDP) and calcium chloride are stable over a range of concentrations up to 16.7 mmol Ca and 30 mmol P/litre in Freamine III-based admixtures, dependent on pH, temperature and amino acid (AA) concentration. We have now compared the stability of calcium gluconate with FDP (Esafosfina; Biomedica Foscama) in two adult TPN admixtures, based on Synthamin (or Clinomel; Baxter Healthcare) and one paediatric TPN admixture, based on Vamin (Fresenius Kabi).

Synthamin 14 (8.5% AA) and Vamin 9 (7% AA) were combined in equal volumes with glucose (50%) and electrolytes, then split into three sealed glass containers. Calcium gluconate (10%) and FDP (7.5%) were added to each admixture to provide: 2 mmol Ca: 4 mmol P (S_1, V_1), 10 mmol Ca:20 mmol P (S_2, V_2) or 20 mmol Ca:40 mmol P (S_3, V_3) per litre. The two non-lipid compartments of the multichamber bag containing Clinomel N6-900 (8.5% AA), which already provides 1.8 mmol Ca and 12 mmol IP per litre were combined, thoroughly mixed then split into four sealed glass containers (C_1, C_2, C_3 and C_4). A total of 10 mmol Ca/l was added to C_1, C_2, C_3, C_4 as gluconate. IP was then added to C_1 (22 mmol P) and C_2 (55 mmol P) and FDP was added to C_3 (22 mmol P) and C_4 (55 mmol P). Each combination was thoroughly mixed, inspected, then stored in the dark at RT and submitted to visual inspection after 1 h, 24 h, 48 h, 4 d and 8 d.

No precipitation was observed throughout the study period in any of the FDP-containing regimens. In contrast, admixture C_2 immediately became cloudy on addition of the extra IP and a white precipitate was deposited within 1 h.

Our results confirm that high concentrations of Ca and P precipitate when supplementary IP is added to a 'standard' Ca/P-containing TPN regimen, but not when added as FDP. Moreover, it is possible to prepare a variety of stable TPN admixtures, containing up to 20 mmol Ca:40 mmol P, sufficient to meet most adult or paediatric requirements, by using suitable combinations of FDP with calcium gluconate.

The major pharmaceutical advantage of FDP is that P can be provided in twice the molar ratio compared with other P sources. This increases the scope for specifically tailored TPN regimens, which are otherwise limited to compounds providing Ca and P in a 1:1 ratio. More comprehensive evaluation of FDP within a clinical situation is needed.

FDA (1994) *American Journal of Hospital Pharmacy* **51**, 1427.
Prinzivalli M & Ceccarelli S (1999) *Journal of Parenteral and Enteral Nutrition* **23**, 6.

Parenteral nutrition: treat with respect, handle with care. By J.F. DAVIS[1] and D.L. BOOTH[2], [1]*Department of Nutrition and Dietetics and* [2]*Pharmacy Department, Oxford Radcliffe Hospitals NHS Trust, Radcliffe Infirmary, Woodstock Road, Oxford OX2 6HE*

The Radcliffe Infirmary has a unique mix of specialities requiring specialist nutritional support including neurosciences, head and neck cancer surgery, plastic surgery and gerontology. Until the recent merger with the Oxford Radcliffe Hospitals NHS Trust there was no access to expert parenteral nutrition (PN) support and there were no PN guidelines in use in the hospital.

A multi-professional prospective audit involving dietetics, pharmacy and infection control departments was undertaken between March and December 1999. The aim of the audit was to identify PN practices within the hospital and to develop recommendations.

Data were collected by each discipline during the audit. Information was collected on the indication for the use of PN, who initiated PN, the regimen recommended, nutritional intake prior to PN, refeeding syndrome risk, monitoring, duration of PN, intravenous access and line site observations. A total of twenty-seven patients with an age range of 21–80 years were included in the audit. The majority (70%) had suffered a head injury. Poor gastric emptying was the main reason for instigation of PN.

PN was initiated without the knowledge or support of a dietitian in 25% of cases. PN was not started until 7 or more days of inadequate nutritional intake had elapsed in 22% of patients. Conversely 25% of patients were receiving in excess of 5 KJ/kg/day for the 3 days prior to PN; 50% of the patients were at risk of refeeding syndrome (Dewar & Horvath, 1996). Baseline biochemistry was not available in 26% of patients, which complicates the management of patients at risk of refeeding syndrome. Obtaining daily biochemistry and completed fluid balance also proved problematic. The duration of PN was variable, with an average of 6 days. Generally PN for less than 5 days is considered too short to confer any benefit on the patient (Maurer, 1996). 44% of patients had PN for 0–5 days. PN may not have been necessary in 63% of the patients if post-pyloric feeding had been available. Initial IV access was via peripheral administration in 26% of cases. The incidence of thrombophlebitis (Williams *et al.* 1996) or insertion site inflammation was 71% with peripheral administration and 20% with central venous access.

Recommendations from the audit include: all patients receiving PN should be assessed by a dietitian in conjunction with the ward pharmacist. A local protocol on the use of PN should be developed. Regular structured training is required for professional groups who come into contact with PN. Parenteral nutrition should only be administered via a central venous access. Facilities should be developed to allow post-pyloric feeding. All these recommendations have since been enacted or are in the process of being enacted.

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Williams M, Wales S & Irving MH (1996) *British Journal of Surgery* **83**, 114–116.

A clinical audit of a sample of adult patients receiving home enteral nutrition (HEN) in Avon during 1998 and 2000. By L. MARTIN, *Home Management Services, Terrell Street, Bristol BS2 8HW*

In patients who are unable to consume adequate nutrients orally, enteral feeding is the preferred route of nutritional support. The British Artificial Nutrition Survey (BANS) data has reported that the number of patients receiving home enteral nutrition (HEN) has grown by 20% (Elia, 1999). Local data show that the incidence of HEN has increased from 134 patients in August 1997 to 325 patients in July 2000. This is a total increase of 44%, with an annual increase of approximately 20%.

A clinical audit was performed in March 1998 on forty-seven randomly allocated patients and repeated in March 2000 on forty-two patients. Both groups had a similar profile. The individual patient/carer was interviewed using a standard questionnaire. The most common diagnosis was stroke (40% in 1998; 55% in 2000). In both groups 40% of patients had been receiving HEN for a minimum of 12 months.

The product range of solutions has doubled which could be due to the increased number now available or to the presence of a well-established HEN service. In both samples approximately 75% of the adults used a pump either alone or combined with bolus feeding.

Delivery of feed	1998 (*n* 47)	2000 (*n* 42)
Bolus	11 (23%)	6 (14%)
Pump	24 (51%)	29 (69%)
Both	12 (25%)	7 (17%)
Feed timing altered	2 (4%)	2 (5%)
Feed regimen altered	22 (47%)	25 (59%)
Both altered	11 (23%)	10 (24%)
Total no. patients feed altered	35 (74%)	37 (88%)

The energy intake of both samples is shown below.

Calorie range of feeds (MJ)	1998	2000
4.18–6.27	17 (36%)	16 (38%)
6.28–8.36	29 (62%)	21 (50%)
8.32–10.46	1 (2%)	5 (12%)

In both groups, 74% (1998) and 88% (2000) of patients had required a change of regimen since discharge from hospital. The most common reason cited for this discrepancy is changed requirements since last dietetic review. Constipation was the cause of a regimen change in nearly 25% of cases in both samples and was the most commonly reported problem in nearly 40% of the samples, although this was not always feed-related.

Obtaining accurate weights and heights for each individual proved difficult (L'Estrange, 1997) with 25% and 48% of data, respectively, being unavailable at interview. All heights were as reported by the patient/carer. When actual/estimated measurements were compared with the normal BMI ranges, 49% and 69% had reached or were moving towards the normal range.

Percutaneous endoscopic gastrostomy (PEG) was the most common feeding route in both samples. 34% of the patients in 1998 and 45% of the patients in 2000 experienced tube-related problems. Nearly all patients reused syringes and the commonest cleaning method was with soap and water. Two syringes per week were required on average by each adult.

In conclusion, patients who are receiving HEN do have changing requirements and need individualized feeding regimens (McNamara *et al*. 2000) which take into account both their clinical and social needs. Routine monitoring is vital to help achieve optimum nutritional status. Finally, constipation rather than diarrhoea is the commonest complication for most adult long-term feeders.

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McNamara EP, Flood P, Kennedy NP (2000) *Clinical Nutrition* **19**, 15–22.

An audit to evaluate the effectiveness of a nutritional support team at assessing, prescribing and monitoring parenteral nutrition. By S.T. BURDEN[1], K. WARD[1], A. HOLT[1], A. EGAN[1], J. NORMAN[1], F. LESLIE[1], C.E. WRIGHT[2] and A.J. MAKIN[1], [1] *Manchester Royal Infirmary, Oxford Road, Manchester, M13 9WL and* [2]*Chester College, Cheyney Road, Chester CH1 4BJ*

The first 100 patients referred to a recently established Nutritional Support Team (NST) over a 21-month period were audited against standards for assessment, prescription and monitoring of parenteral nutrition (PN). Standards for the suitability of patients for PN prescription and monitoring were devised, based on BAPEN recommendations (Pennington, 1996). Organizational procedures for requesting biochemical tests and assessing patients' suitability for PN were initiated in October 1998. This audit aims to establish the effectiveness of the organizational structures implemented to meet the recommendations for the administration of PN.

Out of the 100 patients, 75% were fed by PN, 7% were referred for enteral feeding and 18% who were referred for PN were fed *via* alternative means following NST assessment. The age range of patients fed by PN was 16–85 (mean 57) years and there were forty-seven males and twenty-eight females. Nutritional requirements derived using standard calculations (Todorovic & Micklewright, 1997) had been assessed and were available in 78% for energy (mean 7.4, range 5–9.6 MJ/d) and 74% for nitrogen (mean 11, range 7–22g/d). The accuracy of prescribing was assessed by comparing these calculated requirements with prescribed PN.

Calculated – Prescribed non-protein calories (Kcal)	Distribution for energy intake % (No.) (*n* 57)	Calculated – Prescribed Amount of nitrogen (g)	Distribution for nitrogen intake % (No.) (*n* 57)
< –400	11 (8)	< –4	11 (8)
< –201	24 (18)	< –2.1	12 (9)
< –200 to > +200	59 (44)	< –2 to > +2	44 (33)
> 201	5 (4)	> 2.1	4 (3)
> 400	2 (1)	> 4	1.3 (1)

Standard for monitoring biochemistry	% of patients (No.)	Standard for nutritional assessment	% of patients (No.)
Electrolytes daily	89 (67)	Weight	75 (56)
Urea daily	81 (60)	BMI (kg/m^2)	42 (32)
Liver function tests thrice weekly	81(61)	Percentage weight loss	25 (19)
Zinc weekly	41 (31)	Oral intake assessed prior to PN	97 (73)
Temperature daily	68 (51)	>50% oral/enteral before PN stopped	46 (29)
Fluid balance daily	72 (52)	Nitrogen balance weekly	43 (32)

The length of time patients were on PN was audited; 69% were fed for more than 7 d, mean 15 (range 1–97, SD 17.7) d. The results indicate that for both energy and nitrogen a larger proportion of patients were underfed when their prescription was compared with their calculated requirements (35% energy/32% nitrogen) than overfed (8% energy/17% nitrogen), Elia (1995) discusses the rationale for this. The basic monitoring which is organized by the NST meets the standards in 80% of patients; however, monitoring, which is reliant on collection of 24-h urine samples, still remains a problem, as does the zinc monitoring, which relies on blood samples being taken on the appropriate day. More than half the sample fed had a documented weight but the availability of other nutritional markers was limited.

The results indicate that the NST was effective in assessing, monitoring and prescribing PN in the majority of areas. A 100% adherence to the guidelines is probably an unrealistic target in a real world clinical arena, although documenting constraints on implementation would aid further assessment of the practical application of the recommendations.

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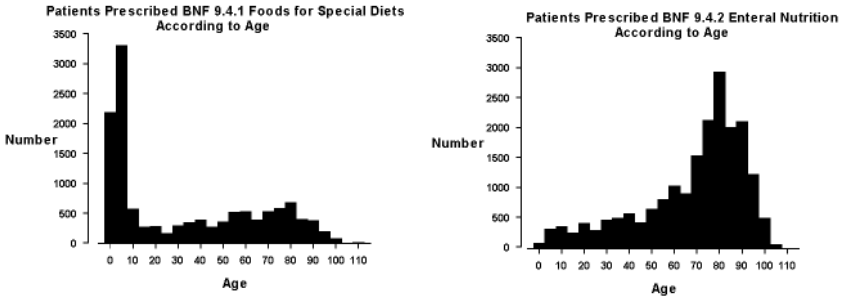
Patterns of prescribing of nutritional supplements in the United Kingdom. By J. EDINGTON[1], S. COLES[1], C.R. GALE[2] and C.N. MARTYN[2], [1]*Abbott Laboratories Ltd, Norden Road, Maidenhead, Berks SL6 4XE and* [2]*MRC Environmental Epidemiology Unit, Southampton General Hospital, Southampton, Hants SO16 6YD*

Records kept by the Prescription Pricing Authority show that nutritional supplements under British National Formulary (BNF) classifications 9.4.1 (foods for special diets) and 9.4.2 (enteral nutrition) accounted for nearly 3 million prescriptions in England in 1997. This represents a substantial cost to the NHS, but little is known about the characteristics of the patients who are prescribed such supplements.

The General Practice Research Database, maintained by the Office for National Statistics, contains information on more than 6 million patients registered with over 500 practices throughout the UK. We searched the database for all patients who had been prescribed nutritional supplements under



BNF classifications 9.4.1 and 9.4.2 during 1996 and 1997.

In total, 28 644 patients received at least one prescription for a nutritional supplement during 1996 and 1997. Among the 27 413 (96%) patients prescribed supplements for oral use rather than for tube feeding, 14 750 received supplements for enteral nutrition alone, 8122 received supplements for special diets alone and 4521 had both types of supplement. Of the patients receiving supplements for special diets, 51% were <18 years old. As the Figure shows, many of these were babies and young children. The commonest diagnoses among such children were milk intolerance (24%) and malnutrition (17%). Among the adults who were prescribed supplements for special diets, the commonest diagnosis was chronic gastrointestinal disease (35%). Of the patients prescribed supplements for enteral nutrition, 94% were adult and many of them were elderly (see Figure); the median age of those who received this type of supplement was 74 years (IQR 55–84); 52% of the adults who were prescribed supplements for enteral nutrition had a diagnosis of cancer or cardiovascular disease.

Height and weight data were available for 13 636 (50%) patients, but only 1165 (4%) had both these measurements recorded in the 3 months before their first prescription of nutritional supplements. The mean BMI of the 886 adults in this group was 21.8 kg/m^2. Before supplementation, 301 (34%) adults had a BMI of <20 kg/m^2, but 170 (19%) had a BMI of ≥25 kg/m^2.

Despite the large number of prescriptions currently issued for nutritional supplements, these data suggest that few doctors record their patients' nutritional status before starting supplementation. If nutritional interventions are to be appropriate, monitoring of weight and height should become a routine part of clinical care.

Monitoring adult enteral nutrition: a national audit carried out on behalf of the Parenteral and Enteral Nutrition Group of the British Dietetic Association. By C. MCATEAR, *Department of Nutrition and Dietetics, Victoria Infirmary, Glasgow G42 9TY*

Several BAPEN reports have addressed the issue of monitoring patients receiving enteral nutrition. Elia (1994) stated that there should be a post-discharge monitoring protocol established by the nutrition team for patients receiving enteral nutrition in the community; Sizer (1996) stated that there should be protocols and procedures relating to enteral feeding to monitor patients status and progress and also in 1996 the British Dietetic Association standards for nutritional support recommended that dietitians monitor all patients receiving enteral nutrition (McAtear & Wright, 1996). None of these documents recommended the parameters that should be monitored or the frequency with which they should be measured. In 1999 McAtear in a BAPEN report suggested that a local policy or standard procedure should be in place for monitoring of enteral nutrition, giving recommendations and reasons for the parameters to monitor, suggested frequency with which the monitoring should occur and whose responsibility it was to ensure that the monitoring occurred.

The aim of this audit was to determine the actual level of monitoring taking place both in hospital and the community. Questionnaires were sent to all 450 members of the Parenteral and Enteral Nutrition Group of the British Dietetic Association, and eighty-eight responses were received. The questions asked related to type of Trust, number of patients receiving enteral feeding, existence of a nutrition support team, types of patients routinely monitored, whose responsibility it was to ensure the monitoring was done and local policies for monitoring enteral nutrition. It also included questions regarding the frequency of monitoring and the parameters that the respondents recommended should be monitored, together with the parameters that actually were monitored and the actual frequency with which they were done. The questions related to adult patients only.

The results showed that only 43% of trusts had a nutrition team (this is only a slight improvement on the number recorded in the survey carried out by Payne-James *et al.* in 1994). Of those who had a nutrition team, 61% had no responsibility for enteral feeding. Of the total, 56% had a policy in place for monitoring of enteral nutrition in hospital and 36% in the community. Most (86%) of these policies originated from the Dietetic Department. In the majority of cases (51%) the respondents considered that the responsibility for ensuring the monitoring takes place lay with the dietitians in hospital, and in the community, 44% of respondents considered that it was the sole responsibility of the dietitian, in most other cases it was the joint responsibility of the dietitian and another health care professional. More hospital patients (89%) were routinely monitored community patients (59%). The actual parameters monitored varied greatly in type and frequency but were consistently less in the community, particularly with regard to biochemical monitoring; fewer than 25% of respondents recommended any biochemical monitoring for patients. There was good correlation between the monitoring recommended and that which actually took place in both the hospital and community.

In conclusion, although only a small number answered the questionnaire, it highlights that, even among individuals who are interested, the level of monitoring is variable and recommended standards are difficult to achieve. The reasons stated for not monitoring related to lack of resources and funding rather than a lack of perceived need. This highlights the need for more dietetic time, particularly in the community where the number of patients being discharged on enteral nutrition continues to grow at an estimated annual rate of 20%, according to the latest unpublished data from the British Artificial Nutrition Survey (BANS).

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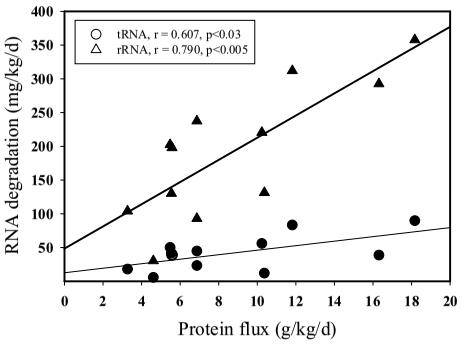
The relationship between whole-body RNA and protein turnover in critically-ill children. By L.F.R. MAIORAL[1], A. PIERRO[2], S.B. MALIK[1], M.R. POWIS[2], J. OPACKA-JUFFRY[1], M.J. RENNIE[3] and, G.K. GRIMBLE[1]. [1]*University of Surrey Roehampton, London SW15 3SN,* [2]*Institute of Child Health, London WC1N 1EH,* [3]*University of Dundee, Dundee DD1 4HN*

A recent study has shown that critical illness suppresses the growth components of energy expenditure and protein turnover in neonates with necrotizing enterocolitis (NEC) (Powis *et al.* 1999). Just as energy and protein metabolism are closely linked, so are rates of tissue protein synthesis and ribosome concentration (Grimble *et al.* 2000). We therefore investigated whole-body RNA turnover in these children, as growth rate correlates closely with urinary excretion of RNA markers (Schöch *et al.* 1982).

Eight premature children (age; median 60 d, range 10 d–33 months: weight; median 4.75 kg, range 1.37–14.2 kg) were studied, comprising four cases of NEC, one of sepsis (meningitis) and four requiring major gastrointestinal surgery. Complete urine collections made during the acute or recovery phases or pre- or postoperatively (Powis *et al.* 1999) were analysed by HPLC for modified nucleosides and nucleobases (7-methylguanine, pseudouridine and *N2,N2*-dimethylguanosine) which are markers of RNA breakdown (Malik *et al.* 1999; Grimble *et al.* 2000). Uric acid, creatinine and neopterin excretion were also measured. Statistical significance was determined by calculating the Pearson correlation coefficient.



rRNA and tRNA breakdown correlated significantly with protein flux (rRNA: r 0.790, P<0.005, tRNA: r 0.607, P<0.05,) and neopterin excretion (r 0.595, P<0.05, r 0.692, P<0.025, respectively). However, mRNA breakdown was unrelated to protein turnover or neopterin excretion. Turnover of tRNA and mRNA was closely related to that of rRNA (r 0.883, P<0.0002 and r 0.656, P<0.02, respectively). Uric acid excretion was unrelated to turnover of any RNA species.

This is the first demonstration in man of a strong relationship between whole-body turnover of the machinery of protein synthesis (i.e. rRNA and tRNA) and of protein itself. The lack of correlation between protein and mRNA turnover can be explained by a neutral effect of simultaneous up- and down-regulation of acute-phase and constitutional genes, respectively. Uric acid excretion (an indicator of *de novo* purine synthesis) did not correlate with RNA turnover. We conclude that measurement of modified nucleoside excretion has use as a sensitive and non-invasive indicator of the way in which clinical situations disturb whole-body metabolism. In addition, *de novo* purine synthesis may be less important in control of RNA metabolism than the salvage pathway which includes dietary nucleotides (Grimble *et al.* 2000).

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Central temperature threshold changes involved in thermoregulation after Lipopolysaccharide (LPS)-induced fever in adult men. By C. CHILDS, A.O. AGWUNOBI and G.L. CARLSON, *MRC Trauma Group, University of Manchester, Oxford Road, Manchester M13 9PT*

The mechanisms for the development of fever in the injured child, in a thermoneutral environment (air temperature approx 30°C) have been described (Childs, 1998). Briefly, fever is preceded by an upward shift in hypothalamic set-point temperature, with a rise in the thresholds for the onset of heat conservation and heat production. The effect is rapid vasoconstriction in acral regions (e.g. toes), brought about by closure of A-V anastomoses and followed by an increase in metabolic heat production.

Because the majority of hospital patients are in an ambient temperature below thermoneutral, the aim of this study was to determine whether the thermoregulatory threshold changes could be identified in the febrile adult studied under these conditions.

Following approval by the local research ethics committee, eight males (aged 24–38 years) were studied in an ambient temperature of 23–24°, before and after i.v. injection of 4 ng/kg *E. coli* lipopolysccharide, LPS. Rectal (T_r) and acral (toe skin) temperatures were measured every 30 min. Air temperature (T_{air}), skin surface temperature (at thirteen different sites), oxygen consumption (VO_2) and arterialized plasma concentrations of pro-inflammatory cytokines, tumour necrosis factor (TNFα) and interleukin-6 (IL-6) were measured every 60 min (see Table) using an EISIA method.

Changes in body temperature, VO_2 and plasma cytokines after LPS - mean values (*n* 8)

	Baseline	Minutes after LPS						
	–60	0	60	120	180	240	300	360
T_{air} (°C)	23.8	24.3	24.4	24.4	24.6	24.6	24.7	24.6
T_r	36.4	36.4	36.5	37.1	37.6	37.8	37.6	37.3
T_{toe}	26.9	27.4	27.1	25.2	26.7	29.2	32.4	32.0
T_{sk}	32.1	32.2	31.5	32.1	32.7	33.0	33.3	33.3
T_b	35.6	35.5	35.5	36.0	36.5	36.8	36.8	36.5
VO_2	3.1	3.0	3.0	3.8	3.8	3.85	3.8	3.7
TNFα	12	13	408	960	519	257	154	113
IL-6	6	7	31	1034	1067	577	144	57

T_{sk}, mean skin temperature, T_b, mean body temperature, VO_2 (ml.min.kg), TNFα, IL-6 (pg/ml).

Changes began about 60 min after LPS, the first being a decrease in thermoregulatory heat loss as shown by closure of the A-V anatomoses in the toes of the four subjects with warm toes at the start of the study. The fall in T_{toe} was 3.9–9.6° (max). This was accompanied in most cases by conjunctival injection, yawning, headache, myalgia and an increase in plasma concentrations of cytokines. The subjects felt cold and started to shiver at T_{sk} above the usual threshold of 26.9 ± 0.5° (Bittel & Curé 1983). These changes were followed by a rise in VO_2. Correction of VO_2 for the rise in T_r (eight subjects) showed that 33–72% of the rise in VO_2 was due to a Q_{10} effect. Peak T_r ranged from 37.5–38.4 (median 37.3°) and was reached after 105–290; median 207 min. At or shortly before this, the A-V anastomoses in the toes opened in all eight subjects at higher skin and body temperatures than normally expected, with increases in T_{toe} of 3.5–12.4, median 10.0°C.

The upward shift in the thresholds for the onset of heat production and loss in adults, accord with the idea that after LPS the body thermoregulates about a higher set-point. These findings are similar to the changes described in the febrile child and should be taken into account in the management of fever.

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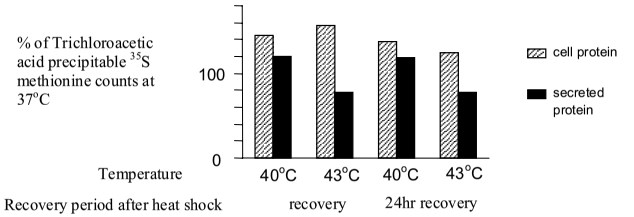
The metabolic cost of thermal stress on human hepatocytes: implications for differentiated cell function. By S.J. WIGMORE[1], K.C.H. FEARON[1] and W.J. WELCH[2], [1]*Department of Clinical and Surgical Sciences (Surgery), University of Edinburgh, Royal Infirmary, Edinburgh EH39YW and* [2]*Surgical Research Laboratory, University of California San Francisco, San Francisco, USA*

Heating cells above normal physiological temperature causes defects in protein folding which initiates a cell survival response *via* production of heat shock proteins (HSP). HSPs are molecular chaperones which facilitate the correct folding and assembly of nascent protein chains. One cost of this cell survival response is a temporary loss of differentiated cell function. The reason for this loss of function is uncertain.

The purpose of this study was to establish the metabolic cost of the heat shock response and the ability of heat-treated hepatocytes to maintain differentiated function measured by production of secreted acute phase proteins. We also compared the effect of heating cells to febrile temperatures (40°) with heat shock at 43° in terms of metabolic cost and differentiated cell function.

Human Hep G2 cells were heated at 40° and 43° for 45 min and then allowed to recover at 37° for variable periods of time. Cells were labelled with ^{35}S methionine and allowed to recover for 12 h following heat treatment. Supernatants and cell lysates were harvested and protein precipitated with trichloroacetic acid (TCA). Precipitable ^{35}S methionine was counted by liquid scintillation and samples were run on SDS-PAGE gels. Other cells treated in identical manner were harvested on ice and ATP concentrations measured using a luciferase assay. Mitochondrial activity of cells was estimated using the Alamar blue reaction.

Heat shock at 43° is associated with decreased secreted and increased intracellular precipitable ^{35}S methionine counts. By contrast a lower heat stress of 40° is associated with increased secreted and intracellular protein compared with 37° control cells. These effects were consistent with increased synthesis of acute phase proteins as demonstrated by immunoprecipitation of acute phase proteins from media of cells labelled with ^{35}S methionine. In addition, ATP depletion occurred at both 40 and 43° compared with 37° controls, the degree of ATP depletion being proportional to the intensity of the heat stimulus. Mitochondrial activity was significantly increased both in cells heated at 40 and at 43°. Inhibition of transcription of proteins by pre-treating cells with actinomycin D limited the ATP depletion associated with heat shock.



Exposure of hepatocytes to heat shock at 43° leads to increased mitochondrial activity and depletion of ATP. This is associated with an increased intracellular protein production and a decreased protein secretion. These results suggest that there is a limited capacity for protein synthesis in the heat-shocked cell possibly due to energy-associated constraints. These results may partly explain the loss of differentiated cell function which is associated with exposure of cells to heat shock but not to febrile range temperatures.

Plasma cytokine concentrations following carotid endarterectomy in patients supplemented pre-operatively with oils rich in *n*-6 or *n*-3 fatty acids. By J.M. GARRY[1], A. CHULAKADABBA[2], F. THIES[1], P. YAQOOB[1], J. WILLIAMS[2], C.P. SHEARMAN[2], R.F. GRIMBLE[1] and P.C. CALDER[1], [1]*Institute of Human Nutrition, University of Southampton, Bassett Crescent East, Southampton SO16 7PX and* [2]*Department of Surgery, Southampton General Hospital, Tremona Road, Southampton SO16 6YD*

The pro-inflammatory cytokines, tumour necrosis factor-α (TNF-α), interleukin (IL)-1β and IL-6 are believed to play a role in post-surgical complications and in sepsis. The effects of these cytokines are antagonized by IL-10. Feeding fish oil (FO), which is rich in long-chain *n*-3 fatty acids, decreases production of pro-inflammatory cytokines by macrophages and monocytes (see Calder, 1997, for references). Compared with vegetable oil, which is rich in *n*-6 fatty acids, FO feeding resulted in lower plasma concentrations of TNF-α, IL-1β and IL-6 following endotoxin administration to mice (Sadeghi *et al.* 1999). These studies suggest that provision of FO to patients undergoing surgery might be a useful approach to diminishing the post-surgery complications caused by the inflammatory response. In this study we examined the effect of pre-operative provision of FO on plasma cytokine concentrations in carotid endarterectomy patients.

Patients destined to undergo carotid endarterectomy were randomly assigned to receive six capsules/d of placebo oil (PO; an 80:20 mix of palm and soyabean oils) (*n* 15), sunflower oil (SO) (*n* 11), or FO (*n* 14) until the day before surgery (range 14–62 d); each capsule contained 1 g oil. Blood samples were collected prior to preparation for the operation, immediately postoperative and at 24 and 48 h after the operation was completed. Plasma concentrations of TNF-α, IL-1β, IL-6 and IL-10 were determined using commercially available ELISA kits. Data were analysed by two-factor ANOVA; data for plasma IL-6 concentration were further analysed by one-factor ANOVA using Bonferroni's correction for multiple comparisons.

The mean time of pre-operative supplementation with the oils did not differ between the groups (mean of 31, 32 and 26 d in the PO, SO and FO groups, respectively). IL-1β was not detectable in any of the plasma samples. There were large variations in the concentrations of the other cytokines among the patients. There were no effects of treatment or time on the plasma concentrations of TNF-α or IL-10, although the concentration of TNF-α tended to be higher in the plasma of patients in the SO group at all time points (see Table), and the concentration of IL-10 tended to be highest 24 h post-operatively in all treatment groups. There was a significant effect of time ($P<0.001$) but not of treatment on plasma IL-6 concentration, and the time × treatment interaction was not significant. Plasma IL-6 concentration was higher 24 h post-operatively than at each of the other time points in all treatment groups (see Table). Plasma IL-6 concentrations did not differ between the treatment groups, although they tended to be lower in the FO group than in the SO group at 48 h post-operation (P 0.084) (see Table).

	Plasma IL-6 (pg/ml)								Plasma TNF-α (pg/ml)			
	Pre-operation		Immediate post-operation		24 h post-operation		48 h post-operation		24 h post-operation		48 h post-operation	
Group	Mean	SE	Mean	SE	Mean	SE	Mean	SE	Mean	SE	Mean	SE
PO	1.2	0.5	10.9	2.9	33.3*	4.8	23.1	4.5	3.3	1.2	5.2	1.2
SO	4.8	2.9	10.5	3.6	43.9*	7.1	29.0	4.2	6.8	3.3	8.9	3.6
FO	3.2	1.8	7.8	3.9	58.9*	17.3	14.3	3.7	2.9	1.0	4.2	1.1

*Indicates significantly different from all other time points ($P<0.001$).

Thus, pre-operative treatment with *n*-6 fatty acids tends to increase post-operative TNF-α concentrations, while pre-operative treatment with FO tends to hasten the return of plasma IL-6 concentrations towards their pre-operative level. Plasma IL-10 concentrations are unaffected by pre-operative *n*-6 and *n*-3 fatty acids, and plasma IL-1β is not detectable following carotid endarterectomy.

This research was funded, in part, by a grant from MAFF (ANO238). J.M.G. holds a MAFF Postgraduate Studentship.

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Xenon washout and microdialysis 'ethanol escape' techniques give discrepant results when monitoring changes in adipose tissue blood flow after oral glucose. By F. KARPE, B.A. FIELDING, V. ILIC, S.M. HUMHREYS and K.N.FRAYN, *Oxford Lipid Metabolism Group, Nuffield Department of Clinical Medicine, Radcliffe Infirmary, Oxford OX2 6HE*

Regulation of adipose tissue blood flow (ATBF) is likely to be important during the postprandial period, when metabolism switches rapidly from energy supply to energy storage. Insulin is thought to be a key regulator of ATBF, which increases in response to a mixed meal but not to an oral fat load. It has been hypothesized that impaired postprandial vasodilatation contributes towards impaired lipid metabolism in insulin-resistant subjects (Summers *et al.* 1999). However, the regulation of ATBF during the postprandial period is not well understood. As an alternative to the 'gold standard' ^{133}Xe washout technique (Larsen *et al.* 1966), microdialysis has been used to measure changes in ATBF (Rosdahl *et al.* 1993). This technique is based on the diffusion of ethanol from the microdialysis perfusate, and allows pharmacological intervention at the site of blood flow measurement without systemic effects. In the present study, we have compared the two techniques after a simple physiological stimulus.

Eight healthy subjects (age 23–39 years, BMI 18.9–29.6 kg/m^2) participated in the study, having fasted overnight. A microdialysis catheter (CMA 60) was perfused overnight with sterile Ringers solution and inserted into the para-umbilical area of the subcutaneous adipose tissue. The probe was then perfused with a Ringers solution containing 30 mmol/l ethanol and allowed to equilibrate for 1 h. Dialysate was collected every 10 min during the experiment. The ratio of the concentration of ethanol in the dialysate to that in the perfusate (the outflow:inflow ratio) was determined. ^{133}Xe in saline (2 MBq) was injected into the contralateral side and left for 30 min before continuous readings were recorded from a probe attached to the exact site of injection. ATBF measurements were calculated in 10-min periods, from 20 min before, and for 180 min after the ingestion of 75 g glucose in water.

Mean ATBF measured by ^{133}Xe washout increased in response to the oral glucose load as expected (RM ANOVA $P<0.001$). There was significant variation between subjects ($P<0.001$) with a range of peak values from 3.1 to 27.0 ml/min per 100 g tissue. The increase in blood flow (peak/mean baseline ATBF) ranged from 1.3 to 5.8. The mean ethanol outflow:inflow ratio at baseline was 0.46 (SE 0.05). There was an unexpected increase in this ratio ($P<0.05$), which is usually taken to signify a decrease in blood flow. The peak value was 0.55 (SE 0.05) at 40 min after glucose ingestion. These unexpected results may have arisen because of metabolic changes in the postprandial period, which have had unexplained consequences on the recovery of ethanol.

The discrepant results obtained in this study, together with the known insensitivity of the ethanol escape technique suggests that ^{133}Xe washout is the preferable method when investigating physiological changes in ATBF in humans.

This work was supported by The Wellcome Trust.

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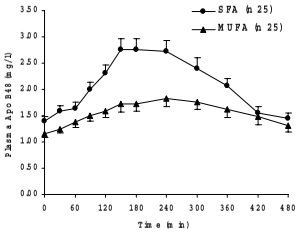
Lower postprandial apolipoprotein B48 and increased chylomicron particle size in subjects on a high monounsaturated fat diet. By K.D.R.R. SILVA[1], A.E. JONES[2], R.D. SMITH[1], C.N.M. KELLY[1], J.A. LOVEGROVE[1], S.A. WOOTTON[2] and C.M. WILLIAMS[1], [1]*Hugh Sinclair Unit of Human Nutrition, School of Food Biosciences, University of Reading, Reading RG6 6AP and* [2]*Institute of Human Nutrition, University of Southampton, Southampton SO16 6YD*

The importance of studying effects of diet on postprandial lipoproteins has been emphasized as a result of a greater recognition of the atherogenic properties of chylomicrons (CM) and their remnants. The lower incidence of coronary heart disease (CHD) in Mediterranean countries despite consumption of a high-fat diet suggests beneficial effects of monounsaturated fatty acids (MUFA). However, little is known about the response of postprandial lipoproteins to background diets rich in monounsaturated fatty acids. The present study compared the effects on postprandial TAG and CM response to a standard test meal, and of substituting background dietary saturated fatty acids (SFA) with MUFA in a controlled dietary trial.

Twenty-five healthy, normolipidaemic students, eleven males and fourteen females, (Age 21 (SE 2) years, BMI 22.3 (SE 2.3) kg/m^2) were recruited from a fully catered student residence, where the fat intakes could be altered through the residence kitchens (Kelly *et al.* 2000). Subjects consumed a SFA-rich diet containing 39% total fat (TF), 15.2% SFA, 13.1% MUFA and 7.2% polyunsaturated fatty acids (PUFA) of total energy (E) for 8 weeks followed by a diet in which SFA were substituted with MUFA (11.2% SFA, 16.3% MUFA and 7.0% PUFA) for 16 weeks. Postprandial responses to a standard test meal were investigated at the end of both dietary periods. Aqueous retinyl palmitate, ^{13}C-palmitic acid (PA) and measurement of apolipoprotein (apo) B48 were used as markers of CM.



	SFA diet		MUFA diet	
	Mean[a]	SE	Mean[a]	SE
Apo B48 AUC (mg.min.l^{-1})	1022	57	760†	61
Apo B48 IAUC (mg.min.l^{-1})	351	44	201‡	30
Apo B48 peak concentration (mg.l^{-1})	3.60	0.22	2.11‡	0.17
Fasting apo B48 (mg.l^{-1})	1.40	0.88	1.16	0.08
RE:apo B48 (mg/mg)[b]	0.59	0.06	0.86*	0.13
^{13}C-PA:apo B48 (μg/mg)[b]	1.99	0.35	2.85*	0.39

[a]*n 25*; [b]Average across 8 h.
Significantly different from SFA diet $^{*}P<0.05$ $^{\dagger}P<0.001$ $^{\ddagger}P<0.0001$.

Postprandial plasma apo B48 responses (see Figure), the area under the response curve (AUC), incremental-AUC (IAUC), peak and fasting concentrations of apo B48 were significantly lower on MUFA diet compared with SFA-rich diet (see Table). However, the postprandial TAG, ^{13}C-PA and retinyl ester (RE) responses were similar for both diets (data not shown). Significantly higher ratios of RE:apo B48 and ^{13}C-PA:apo B48 (see Table) on MUFA diet indicate that CM carry larger amounts of dietary lipids per particle.

Based on recent models of CM synthesis and secretion (Hussain, 2000) we hypothesize that lower levels of plasma apo B48 on the MUFA diet may reflect a reduced requirement for apo B48 molecules arising from a greater capacity to form larger lipid droplets in the enterocyte. We suggest that reduced number of larger CM would lead to more efficient removal of remnants from the circulation, offering beneficial effects on CHD.

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Benchmarking knowledge and understanding of clinical nutrition in an NHS Trust. By H. ROLLINS[1], J. ARNOLD[1], K. BUCKNER[2] and R.A. RICHARDSON[2], [1]*Luton and Dunstable NHS Trust, Luton LU4 0DZ and* [2]*Partnerships in Active Continuous Education, Queen Margaret University College, Edinburgh EH12 8TS*

There is substantial evidence that nutritional status influences morbidity and mortality (Edington *et al.* 2000; Flodin *et al.* 2000) and that nutritional intervention can improve outcome (Delmi *et al.* 1990). However, it is estimated that undernutrition goes unrecognized in 40% of patients who undergo nutritional screening (Pattison *et al.* 1999). It is suggested that one of the reasons for the lack of specificity and reliability of nutritional screening may be related to the depth of understanding of nutritional concepts by staff who perform the screening process (Lyne & Prowse, 1999).

This study sought to use relevant problem-based case studies to determine the level of knowledge and understanding of clinical nutrition among staff (qualified nursing and midwifery) in an acute NHS Trust. Case studies used problem-based scenarios that reflected nutritional issues relevant to the staff's area of work. Eight case studies were developed and focused on cancer, infant feeding, cystic fibrosis, cardiac health, obesity, pancreatitis, obstetrics, generic and explored key nutritional concepts (i.e. energy balance, PEG feeding, local feeding policies). Each case study contained five questions that required a true/false (T/F) response and respondents were asked to provide justification for their response. Questions were designed to test both knowledge (T/F) and understanding (justification of answer). Case studies were carried out under examination conditions and 15 min was allocated for completion.

A total of fifty staff members completed a case study and responses to 153 questions were elicited. Average scores out of five and percentages were derived for knowledge (K) and understanding (U); results are shown by clinical area below.

Case study	Clinical area	*n*	K	U	K%	U%
1	Medicine/surgery (cancer)	5	2.8	1.2	56	24
2	Paediatric (<2 years)	5	3	1.2	60	24
3	Generic nutrition	10	4.1	2.3	60	24
4	Paediatric ≥2 years)	5	2.8	2	82	46
5	Obstetric	5	2.2	1.2	44	24
6	Generic nutrition	10	3.6	1.3	72	26
7	Clinical (pancreatitis)	5	2.8	1	56	20
8	Clinical (obesity/osteoporosis)	5	4.6	1.4	92	28

Knowledge scores ranged from 44% in case study 5 (obstetrics) to 92% in case study 8 (clinical) whereas understanding scores were approximately half that of knowledge and ranged from 20% in case study 7 (clinical) to 46% (generic nutrition).

Whilst knowledge scores may be considered satisfactory, a proportion of these results may be arrived at by chance or may simple reflect the respondents' factual knowledge. The poor performance in understanding score is worrying in that this apparent inability of staff to solve nutritional problems requires further investigation as it may impact on the quality of care. This study has highlighted a requirement for appropriate clinical nutrition education and has permitted identification of core nutrition education needs, thereby facilitating the process of benchmarking by the NHS Trust. After all, the intrinsic link between education and quality will ultimately serve to support the consistent delivery of clinically effective care.

Delmi M, Rapin CH, Bengoa JM, *et al.* (1990) *Lancet* **335**, 1013–1016.
Edington J, Boorman J, Durrant ER, *et al.* (2000) *Clinical Nutrition* **19**, 191–195.
Flodin L, Svensson S & Cederholm T (2000) *Clinical Nutrition* **19**, 75–144.
Lyne PA & Prowse MA (1999) *Journal of Advanced Nursing* **30**, 835–842.
Pattison R, Corr J, Ogilvie M, Farquhar D, Sutherland D, Davidson HIM & Richardson RA (1999) *Journal of Human Nutrition and Dietetics* **12**, 133–140.

Feeding through an open wound? A novel approach when parenteral nutrition fails. By R. BARLOW[1] and B. REES[2], [1]*Nutrition Support Team and* [2]*Department of Surgery, University Hospital of Wales, Heath Park, Cardiff, CF14 4XW*

Patients who develop multiple fistulae of the proximal small bowel are traditionally managed with parenteral nutrition. This is because naso-enteral feeding is usually insufficient to maintain nutritional and fluid status, secondary to reduced gut length for absorption.

A Medline search of the literature identified one case report (Blaylock & Murray, 1992) outlining enteral nutrition management of a patient with one fistula but no evidence of efficacy in multiple bowel fistula was found. We report here the case of a patient admitted.

Mr B was admitted to the University Hospital of Wales for an elective anterior resection for cancer of the rectum. He had no weight loss and was reported not to be malnourished prior to admission. Immediately post-operatively he developed a chest infection and abdominal distension. He then underwent repeated laparotomy for division of small bowel adhesions. Enteral feeding was delayed as Mr B dislodged the naso-jejunal feeding tube. Five days later he developed wound dehiscence and following gastrograffin studies was identified to have four small bowel enterocutaneous fistulae, the most proximal fistula being 20 cm distal to the pyloric sphincter. A normal 100 cm segment of ileum connected the most distal fistula to the end colostomy. Naso-enteral nutrition was contraindicated at this time.

Following several months of parenteral nutrition and pharmaceutical manipulation Mr B developed a line infection, abnormal liver function tests and renal failure, making parenteral nutrition more difficult to deliver: venous access was also very problematic. At this stage it was decided to intubate the distal fistula and semi-elemental enteral feeding was initiated. Following several weeks of difficult nutritional and fluid balance manipulations Mr B was stabilized and his nutritional status improved. He was discharged 4 months post-operatively and is now managing to maintain his nutritional/fluid needs via 100 cm of ileum. This case study/the management and outcome described here begs the question of whether it is time to review our approach to these complex patients?

Blaylock B & Murray M (1992) *Ostomy/Wound Management* **38**, 8–9, 12, 14.

The development of catheter care procedures and protocols by a national clinical network. BY J. TAIT, D. BARBER, L. DAVIDSON, K. KEIRAN, G. MCHATTIE, A MACCRIMMON, T. MCKEOWN, C. MUIR and P. RODGERS *on behalf of the Scottish Home Parenteral Nutrition Managed Clinical Network, Ninewells Hospital, Dundee, Scotland DD1 9SY*

It is widely accepted that the patient referred for home parenteral nutrition (HPN) be supervised in a unit where there is knowledge and experience in the use of HPN (BAPEN, 1996). This can be achieved by establishing one treatment centre. However the management of one centre in Scotland would present difficulties because of the wide dispersion of patients throughout the country. One treatment centre would be unable to provide emergency treatment for all patients, and would cause inconvenience for the patient who may be required to travel long distances for follow-up.

A managed clinical network (MCN) was formally established in November 2000 to discuss standards of care related to the patient on HPN. The group consists of physicians, surgeons, nurse specialists, pharmacists, dietitians and biochemists from the main centres responsible for HPN in Scotland. A MCN ensures the delivery of optimum care *via* local services through access to national expertise. The aim of the network is to ensure that each patient has equal access to optimum treatment, by the adoption of national standards, protocols and procedures. It is therefore intended to develop a network that will allow patient management with respect to both disease and nutrition in their local hospital with access to the network *via* a regional hospital for patient training, advice and guidance.

The nurse within the team has a key role in the prevention of catheter-related complications. This is achieved by the adoption and implementation of optimum catheter care procedures, the provision of advice to the local team, and the establishment of staff and patient training. The nurse specialists within the MCN have developed evidence-based protocols and procedures for the prevention and treatment of catheter-related complications. Best practice was agreed by the group on the basis of current literature, expert opinion and audit data.

The benefits of implementing standardized practice are:

- To promote best practice by influencing practice within each centre,
- To collect data through audit which will be available for meaningful clinical research,
- To facilitate clinical research into improved methods of nutrient delivery,
- To provide a forum to facilitate staff training.

The nursing members of the group will meet 3–4 times a year to discuss current research and clinical issues. The procedures and protocols will be reviewed yearly and refined as new literature becomes available. In the future, issues that have not been resolved in the literature, such as the use of sterile gloves, the dosage of heparin required to lock the catheter, and the most appropriate catheter exit site dressing, can be addressed through the processes of audit and research.

BAPEN (1996) *Standards and Guidelines for Nutritional Support of Patients in Hospitals.* Maidenhead: BAPEN.

Tolerance and non-tolerance in colorectal surgical patients of enteral nutrition administrated from the first postoperative day for 5 days. By L. WILLIAMS, S.A. EL GADDAL and D.J. LEAPER, *Professorial Unit of Surgery, North Tees & Hartlepool NHS Trust, Hardwick Estate, Stockton on Tees TS19 8PE*

Traditionally, colorectal surgery patients have not been fed until the return of bowel sounds, flatus or bowel function, in the belief that early diet would not be tolerated because of gastric ileus, gastric aspiration and the possibility of anastomotic breakdown. However, it has been reported that early enteral diet offers stimulation and protection to the gut, reducing the risk of breakdown, major infections, and overall length of hospital stay. Achieving 50% of target energy intake is reported to maintain gut integrity (McClave *et al.* 1999).

The aim of the present study is to identify how well early enteral diet is tolerated in colorectal surgical patients and additionally to identify the factors which are associated with non-tolerance of enteral nutrition.

This study is a randomized controlled trial of immune-enhanced *v.* isocaloric/isonitrogenous enteral nutrition which examines patients' outcomes following colorectal surgery for cancer. Administration is *via* a naso-gastric feeding tube following an established regimen and tolerance of enteral nutrition is being monitored. Early diet commences on the first postoperative day and continues for 5 d.

Currently sixty-five patients have been recruited. The sample consists of forty-four males and twenty-one females.

Early indications are good: patients are reaching their target feeding rate by day 2 with 55% (*n* 33) achieving >50% of the goal for energy intake and 18% (*n* 11) >90% of this goal. By day 5, 35% (*n* 22) are still receiving >50% target energy and 19% (*n* 12) >90% target energy intake. Early oral diet (day 4) has been commenced in six patients. Interestingly, from the present data, the percentage of female patients tolerating the diet for 5 d is greater than the percentage of male patients (55% female *v.* 38% male). The most common reasons for non-tolerance are: confused patients who repeatedly pull out tubes and patients irritated by the tubes (*n* 11), ileus (*n* 7), nausea and vomiting (*n* 6). In 20% of patients (*n* 14), there were major complications , eight respiratory and six wound/abdominal. The mean length of hospital stay was 11.9 (SD 4.74) d.

With patience, vigilance and re-education of health professionals, the introduction of early enteral nutrition could soon become best practice and improve the quality of the service. Irrational reasons for not commencing or for discontinuing enteral nutrition can be ameliorated.

McClave SA, Sexton LK, Spain DA, Adams JL, Owens NS, Sullins MB, Blandford BS & Snider HL (1999) *Critical Care Medicine* **27**, 1252–1256.

Peripherally inserted central catheter placement for total parenteral nutrition: a six-month survey. J. McGOVERN, L. HINDLE and I.W. FELLOWS, *Nutrition Support Team, Department of Gastroenterology, Norfolk & Norwich Hospital, Norwich NR1 3SR*

A peripherally inserted central catheter (PICC) is an intravenous catheter inserted in the antecubital fossa with the tip in the distal superior vena cava. One of the first reported catheter placements was in 1912 by a German physician using a 4Fr ureteric catheter into the antecubital vein. During the 1960s, 1970s and early 1980s the antecubital approach was used but central placement of catheters was more favoured due to the reported high-risk complications of thrombophlebitis, thrombosis, perforation and malposition with peripherally placed catheters (Ryder, 1993).

PICC placement has gained popularity over recent years as advances in technology have provided safer, less traumatic, insertion methods and catheter materials are better tolerated in the peripheral system. Additionally, nurses have expanded roles, such as PICC placement, whereas historically central venous catheterization was strictly a medical procedure (Gabriel, 1996).

The Nutrition Nurse Specialist with this acute NHS Trust has been placing PICCs since September 1998 for the use of total parenteral nutrition (TPN). A 3Fr, 55 cm polyurethane catheter was used and chest radiography undertaken to confirm catheter tip position. A 6-month retrospective survey, from September 1999 to February 2000, was undertaken to assess the performance of PICCs within the area of nutrition.

PICC Survey Sept. 1998 – Feb. 2000	
No. patients receiving TPN	56
No. patients receiving TPN via PICC	26 (46%)
Successful placement	26 of 28 patients (93%)
No. of attempted insertions	30 in 28 patients
Failed PICC insertion:	4 of 30 (13%)
Oedema	1
Malposition (jugular)	2 (1 successful at second attempt)
Patient anxiety	1 (successful at second attempt)
Duration of TPN:	
Range (d)	4-27
Median	11
Colonization	0
Systemic sepsis	0
Clinical signs of vein thrombosis	0

The results show that only two insertions failed due to malposition and that the earlier high-risk complication of thrombosis did not occur clinically within this patient population. All of the patients received their nutritional therapy uneventfully via the PICC. The other patients (*n* 30) that received TPN during this time already had a central venous catheter *in situ* but a high proportion of these would have been suitable for a PICC which avoids the well-documented risks of centrally placed catheters.

A more active patient assessment has been accepted, leading to a higher placement rate of around 75% at present. Peripherally inserted central catheters are now our line of choice for the delivery of short-term (up to 4 weeks) TPN.

Gabriel J (1996) *Surgical Nurse* **5**(2), 71–74.
Ryder MA (1993) *Nursing Clinics of North America* **28**, 937–971.

Audit of nutritional screening and weight change in patients in an acute hospital trust. By J. ARNOLD[1], L. WYBREW[2], H. ROLLINS[1], A. SMITH[1] and N. SIMMONDS[1], [1]*Luton & Dunstable Hospital NHS Trust, Lewsey Road, Luton LU4 0DZ and* [2]*University of Luton, Park Square, Luton LU1 3JU, UK*

It is recognized that the prevalence of malnutrition in hospitals is between 20 and 50% (Edington *et al.* 2000) and that patients continue to lose weight during their stay (Hill *et al.*1977; McWhirter & Pennington. 1994). Simple anthropometric measurements, such as weight, height and BMI can be useful in identifying patients who are malnourished (Kelly *et al. 2000*). This study reports the incidence of documentation of weight, height, BMI and identifiable weight change during a hospital stay of 7 days or longer. It compares results from immediately after and 1 year after introduction of education and practice initiatives in nutrition. Historical data show that in March 1998, 56% and 6% of patients had weight and height documented respectively.

In 1998 1999, 246 and 232 sets of nursing and medical notes (from patients discharged in November) were audited for the incidence of documented weight, height and BMI within 48 h of admission. Any subsequent documented weights were noted and used to calculate the level of weight change. Adjustments were made to account for individuals with fluid retention/loss and deliberate weight loss. The data was compared for significance using a χ^2 test (0.05 significance level).

	All measurements are % of total								
	Weight			Height			BMI		
	1998	1999	χ^2	1998	1999	χ^2	1998	1999	χ^2
Total documented	86.2	90.5	NS	39.8	61.2	0.001	12.2	33.6	8.27^{-07}
Recorded within 48 h of admission	63.8	58.2	NS	32.1	38.4	NS	8.5	15.5	0.027
Recorded more than once	46.7	56.6	NS	N/A	N/A	-	0.4	-	-
Data available but not calculated	N/A	N/A	-	N/A	N/A	-	28.9	27.1	NS
Could have been calculated more than once (data available)	N/A	N/A	-	N/A	N/A	-	18.7	47.4	4.0^{-8}
Incorrect calculation (±1 BMI)	N/A	N/A	-	N/A	N/A	-	4.5	7.3	NS
Reason given for not recording	6.5	2.5	0.046	-	-	-	-	-	-

	Gained weight					Lost weight					
	Total		BMI <20		BMI <17	Total		BMI <20		BMI <17	
	1998	1999	1998	1999	1999	1998	1999	1998	1999	1998	1999
Number	32	43	7	6	1	48	40	10	4	4	1
Mean weight change (kg)	1.5	1.7	1.6	1.7	1.1	-3.2	-2.3	-3.1	-2.1	-3.7	-2.4
% weight change	2.7	2.7	3.4	3.5	2.6	5.2	3.6	6.3	4.1	7.3	5.2

The results demonstrate that staff are aware of the importance of nutritional screening on admission. The level of documented weight recording remains high and height and BMI recording continues to improve. This suggests the importance of educational initiatives in sustaining improved screening practices. There was a trend towards more patients being weighed more than once. This is essential if weight loss during hospital stay is to be detected. Future education initiatives need to focus on this issue. The results demonstrate a trend towards fewer patients losing less weight however this does not reach statistical significance.

Edington J, Boorman J, Durrant ER, Perkins A, Giffin CV, James R, Thomson JM, Oldroyd JC, Smith JC, Torrance AD, Blackshaw V, Green S, Hill CJ, Berry C, McKenzie C, Vicca N, Ward JE & Coles SJ (2000) *Clinical Nutrition* **19**, 191–195.

Hill GL, Blackett RL, Pickford I, Burkinshaw L, Young GA, Warren JV, Schorah CJ & Morgan DB (1977) *Lancet* **i,** (8013), 689–692.

Kelly IE, Tessier S, Cahill A, Morris SE, Crumley A, McLaughlin D, McKee RF & Lean MEJ (2000) *Quarterly Journal of Medicine* **93**, 93–98.

McWhirter JP & Pennington CR (1994) *British Medical Journal* **308,** 945–948.

Paediatric parenteral nutrition and nutrition support teams in the United Kingdom. By P.M. SACHER, *Dietetic Department, Great Ormond Street Hospital for Children NHS Trust, Great Ormond Street, London WC1N 3JH*

A review of the number of children on parenteral nutrition (PN) and the incidence of nutrition support teams (NSTs) in the UK was undertaken as Great Ormond Street Hospital for Children (GOSH) is in the process of setting up a multidisciplinary NST. Other national surveys have not specifically reviewed paediatric PN and paediatric NSTs. This review was performed by devising a telephone questionnaire and calling paediatric dietitians across the UK. In order to obtain more accurate data, some pharmacists were also contacted. Twenty-three Paediatric and University teaching hospitals were identified and contacted. GOSH was the only hospital with more than twenty children on PN per day, the largest user in the UK.

	No. of children on PN		
	1–10	11–20	>20
No. of hospitals	17	5	1

A comparison of hospitals with children on PN revealed that 56% had a NST. The frequency of NST meetings was variable, with daily, weekly or monthly meetings. Only 30% of the hospitals with children on PN had a home PN team or service; 80% of the NSTs were wholly responsible for hospital PN whilst the remaining 20% were involved with home PN and/or enteral nutrition. The composition of NSTs was varied, although most included a consultant, dietitian and pharmacist:

Profession	Percentage (%)	Profession	Percentage (%)
Consultant	100	Senior House Officer	10
Registrar (two registrars)	50 (20)	Nutrition Nurse	33
Dietitian	92	Other Specialist Nurse	42
Pharmacist	90	No Nurse	25
Biochemist	50	Social worker/Speech therapist	0

The role of the dietitian was found to be quite varied and included prescribing of PN; calculating requirements; liaising between the parenteral and enteral nutrition services; monitoring weight, growth and intake; other anthropometry; nutritional assessment; weaning off PN and deciding on the appropriateness of PN. In hospitals without a NST, professionals undertook the following tasks:

Hospitals with no NST	Doctors	Dietitians	Pharmacists	Mixture of professions	Gastroenterology Team	Standard regimes
Prescribing	50%	10%	20%	20%	–	–
Calculating requirements	0%	40%	10%	20%	10%	20%

It has been reported that patients seen by a NST receive safer and more appropriate nutritional support than patients managed solely by physicians. NSTs have also been shown to reduce the frequency of complications in PN and increase the adequacy of nutritional supplementation (Gales & Gales, 1994). In units with paediatric PN, best practice dictates that a NST should be set up (Milla, 2000). This survey revealed that 44% of hospitals do not conform to this guideline. Where a NST does exist, 92% had a dietitian involved, which is lower than the national average of 97.6% in adult units (Payne-James *et al.* 1995). Since nutrition plays such a vital role in promoting growth and development as well as recovery from illness, all hospitals with a paediatric PN service should be encouraged to examine their provision of nutritional expertise by auditing their own state of affairs and making the results publicly known.

Gales BJ & Gales MJ (1994) *Annals of Pharmacotherapy* **28**, 227–235.

Milla PJ (Editor) (2000) *Current Perspectives on Paediatric Parenteral Nutrition.* Maidenhead: BAPEN.

Payne-James JJ, De Garca CJ, Grimble GK & Silk DBA (1995) *Clinical Nutrition* **14**, 329–335.

Does multidisciplinary nutrition team care in the first 6 months post-PEG have an impact on clinical course? An interim analysis. By H.F.SCOTT[1], F.J. SMEDLEY[1], L. TIMMIS[1], R. BEECH[2], C. ROFFE[1] and T.E. BOWLING[1], [1]*North Staffordshire Hospital NHS Trust, Stoke-on-Trent ST4 6QG and* [2]*Centre for Health Planning and Management, Keele University, Keele, Staffordshire, ST5 5BG*

Complication rates, anthropometric changes, mortality and removal rates in patients fed via percutaneous endoscopic gastrostomy (PEG) are well documented. This study looks at the effect of providing proactive nutrition team care on these outcomes for up to 6 months post-PEG insertion. Any adult patient for whom a PEG was requested was eligible, recruitment was between October 1998 and January 2000. Indications for PEG insertion included dysphagic stroke (62%), oral/pharyngeal cancer (18%) and other neurological disorders (10%). Patients were randomized into two groups, the intervention group A (*n* 38) were visited once a week by the nutrition nurse specialist, with support from other members of the nutrition team as appropriate, during stay in the acute hospital, and monthly once discharged into the community for the 6-month period. There was also telephone advice for primary care professionals and patients/carers. The control group (B) received standard hospital care, which did not involve the nutrition team unless specifically requested.

Data relating to mortality, complications (diarrhoea, vomiting, chest infections and peristomal infections), antibiotic therapy, readmissions and PEG removal were collected throughout the study. In addition weight, anthropometric measurements and grip strength were taken at monthly intervals.

	0–1 month		1–3 months		3–6 months	
	A (*n* 38)	B (*n* 43)	A (*n* 26)	B (*n* 35)	A (*n* 17)	B (*n* 31)
Diarrhoea (no. patients)	10	6	7	6	2	5
Vomiting (no. patients)	4*	14	6	13	2*	13
Chest infection (no. patients)	17	15	12	18	3	10
Peristomal infection (no. patients)	18	17	5	13	4	7
Total complications (no. of patients with one or more complications)	30	31	18	29	7*	23
Antibiotic therapy:						
Number patients treated	22	25	14	17	2	10
Days treatment – mean (SD)	5.2 (5.7)	4.4 (5.1)	5.1 (5.6)	5.8 (7.5)	0.71* (2.0)	5 (11.0)
	0–1 month		0–3 months		0–6 months	
Cumulative mortality (no. of patients (%))	10 (26%)	6 (14%)	17 (45%)	10 (23%)	21 (55%)	21 (49%)

∗$P<0.05$.

Mortality, diarrhoea, chest infections and peristomal infections were all slightly higher in the intervention group during the first month post-PEG, though fewer patients in this group received antibiotics. However, tendencies favouring the intervention group were apparent after the first month post-PEG, with significant differences ($P<0.05$) for the average number of days of antibiotic therapy per patient and number of patients experiencing vomiting. In addition the average numbers of peristomal and chest infections between 1 and 6 months was considerably lower in the intervention group.

No significant differences between the groups were observed for weight, BMI, anthropometrics or grip strength, but PEGs were removed in seven (18%) of the intervention group compared with four (9%) in the control group. The readmission rate was 26% (six patients) in Group A *v.*34.3% (twelve patients) in Group B, with the total number of readmission days 109 and 191, respectively.

Mortality and morbidity in the early post-PEG period are usually associated with the underlying disease process, which may account for the 0–1 month results. However from the clinical course observed in this interim analysis there appears to be a trend towards benefit from intervention by a nutrition team later on post-PEG. More clinical information is being collected, as well as data relating to quality of life and overall costs, which we hope will further clarify the benefits or otherwise of a multidisciplinary approach to care in the long-term follow up of PEG patients.

A study to evaluate the effectiveness of a nutrition support team within a university teaching hospital. By K.WARD[1], S.T. BURDEN[1], C.E.WRIGHT[3], N.C. MORAN[2], E.R BRIERLEY[1], F. LESLIE[1], K. WATERS[4] and A.J. MAKIN[1], [1]*Manchester Royal Infirmary, Oxford Road, Manchester M13 9WL,* [2]*Northern General Hospital Trust, Herries Road, Sheffield S5 7AU,* [3]*Chester College, Cheyney Road, Chester CH1 4BJ and* [4]*University of Manchester, Oxford Road, Manchester M13 9WL*

The benefit of nutrition support teams (NSTs) has been documented previously (Traeger *et al.* 1986), and recommendations state that all patients receiving parenteral nutrition (PN) should be managed by a NST (Lennard-Jones, 1992).

The aim of this prospective study was to evaluate the effectiveness of a NST by comparing the incidence of feeding-related complications and episodes of successful feeding in patients managed both pre- and post-NST. A successful feeding episode was defined as: fed for >5 d enterally; fed for >7 d parenterally; had no major complication; missed <25% of feeding days and feeding was stopped electively. A major complication was defined as any complication caused by feeding that resulted in the suspension of feeding. Data collection periods were 20 weeks and 17 weeks pre- and post-NST, respectively, fifty-two patients pre- and forty-seven post-NST. The NST has an advisory capacity within the Trust.

Complications	Pre NST No/Total (%)	Post NST No/Total (%)	*P* value
Major parenteral	22/30 (73%)	7/33 (21%)	0.001[a]
Major enteral	6/37 (16%)	0/29 (0%)	0.042[a]

[a]χ^2.

Type of episode	Pre NST Total	Number of successes No/%	Post NST Total	Number of successes No/%	*P* value
Enteral	31	13 (42)	21	15 (71)	0.049[a]
Parenteral	23	4 (17)	22	20 (91)	<0.001[a]
Both	5	0 (0)	5	4 (80)	0.048[1]

[a]Fishers exact test.

The results showed that the intervention of a NST significantly decreased complications ($P<0.005$) and increased the successful feeding episodes ($P<0.05$) in patients receiving enteral or parenteral nutrition.

Feeding routes were also compared pre- and post-NST. Pre-NST, twenty-eight central and sixteen peripheral lines were inserted in thirty patients, and thirty-five central and four peripheral lines were inserted in thirty-three patients in the post-NST period. Three-quarters of the lines became infected prior to the NST intervention (75%) this was reduced to 12% post-NST intervention (χ^2 test; $P<0.001$). Jejunal feeding was increased threefold with the NST (χ^2 test, P 0.016).

PN lines	Hazard ratio	95% CI	*P* value
Central	5.55	(2.79, 18.46)	<0.001[a]
Peripheral	6.83	(1.25, 13.64)	0.020[a]

[a]Log rank test.

In conclusion, the NST is effective in decreasing feeding complications, increasing the number of patients fed successfully, and improving the safety of the delivery of artificial nutritional support.

Lennard-Jones JE (Editor) (1992*) King's Fund Centre Report: A Positive Approach to Nutrition as Treatment.* London: King's Fund Centre.

Traeger SM, Williams GB, Milliren G, Young DS, Fisher M & Haug MT (1986) *Journal of Parenteral and Enteral Nutrition* **10**, 418–412.

Are patients on the Avon Home Enteral Feeding Scheme receiving their RNI for vitamins/minerals? By A. JUDD, *Home Management Services, Terrell Street, Bristol BS2 8HW*

It has been shown that patients on home enteral feeding may be at risk of both macronutrient and micronutrient depletion (McWhirter & Pennington, 1994). Micronutrient deficiency not only causes symptoms of overt deficiency, but also more subtle effects on tissue function, including compromised immune function and oxidative damage (Shenkin, 1997).

With over 180 adult patients on the home enteral feeding (HEF) scheme in Avon, and with limited resources in terms of dietetic/nursing time, it is imperative that the scheme can be confident of the nutritional adequacy of 'routine' nutritional prescriptions.

This will enable a standard to be set together with guidelines on supplementation. The case-notes of adult patients on the scheme were used to retrieve relevant information for those on total HEF. The vitamin content of their presented feed was calculated directly and compared with the RNI (DOH, 1991).

All paediatric patients were excluded, together with those who had been on the scheme for <6 weeks. Of 110 patients on total enteral nutrition, 24.7% received their full RNI of vitamins/minerals. Due to the fact that sodium, potassium and chloride levels have always been low in enteral feeds, these have not been included in the results. Carotenoids were also excluded, as these are not present in any feeds. 30% did not meet the RNI for vitamin D alone, 13.6% did not meet the RNI for selenium alone and 19% did not meet the RNI for both selenium and vitamin D. The shortfall in vitamin D may only cause problems in those who are housebound. 12.7% had multiple shortfalls, including calcium, magnesium, manganese, selenium, iodine, vitamin K and folic acid.

The latter group were mostly female and a high percentage were aged over 80 years. The most common diagnosis was stroke and these patients could rarely tolerate more than 1000 ml/d. The greatest deficiencies occurred when 1.5 kcal/ml feeds were prescribed, leading to a reduced total volume.

The study shows that a small number of patients who cannot tolerate large volumes of feed may be at risk of multiple vitamin/mineral deficiencies; and that monitoring of micronutrient status is critical. These data will be further interpreted when results of biochemical analyses (which indicate micronutrient status) currently being collected are available.

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Screening swallowing function of patients with acute stroke: validity of a screening tool used by nurses. By L. PERRY[1,2], S. MCLAREN[1] and M. O'HARA,[2] [1]*Faculty of Health and Social Care Sciences, Kingston University & St George's Hospital Medical School, Kingston Hill, Kingston upon Thames, Surrey KT2 7LB and* [2]*Mayday Healthcare NHS Trust, Thornton Heath, Surrey CR7 7YE*

Stroke affects 4.7% of people aged over 54 years and consumes 5.8% of the NHS and social services budget (1995/96; Bosanquet & Franks, 1998). Dysphagia is a common acute accompaniment, affecting up to 67% in the first 72 h (Hinds & Wiles, 1998). For most, difficulties resolve fairly quickly but whilst only persisting beyond acute stages in the minority, for many nutritional management is a key aspect of rehabilitation. Effects of fasting and malnutrition on areas such as muscle function and mood suggest that nutrition underpins or undermines the rehabilitation process (Jeejeebhoy, 1986; Brozek, 1990).

Dysphagia management is therefore crucial; clinical screening of swallowing function is the essential first step. In this study nurses were identified as best-placed to accomplish screening of all patients with clinical diagnosis of acute stroke within 24 h of admission. The aim of this study was to investigate current screening practice and, in the light of current 'best evidence', to identify, implement and evaluate a screening tool used by ward-based nurses. The Standardized Swallowing Assessment (SSA; Ellul & Barer, 1996) was chosen.

A longitudinal prospective survey was undertaken of multi-professional documentation of 600 consecutive admissions with clinical diagnosis of acute stroke (ICD 10, 160–164) to study wards of Mayday University Hospital, March 1998–December 1999; 200 were surveyed after introduction of the SSA with a training programme. Demographic data, stroke and nutritional information, and details of swallowing function were collected. Reliability of data extraction was independently checked (95% agreement, κ 0.88). For each admission, judgement was made on the basis of all information as to the presence of dysphagia; this summative clinical judgement comprised the 'gold standard' identification of dysphagia.

Training for all eligible nurses was incomplete at study conclusion. SSA was used 173 times for initial and repeat screening, 76 times by nurses who had completed all SSA training. Gag reflex was screened as proxy for swallowing in 157 patients. Compared to summative clinical judgement as to swallowing function:

Was the patient dysphagic?		Yes	No	κ	% agreement
Did the screen detect	Yes	36	3		
a swallowing problem? (*n* 68)	No	1	28	0.88	94.1
Gag function	Impaired	65	14		
(*n* 157 observations)	Intact	33	45	0.4	70.1

In this group SSA demonstrated sensitivity of 0.97 and specificity of 0.9 for dysphagia with positive and negative predictive values (PPV, NPV) of 0.92 and 0.96. Gag reflex as an indicator of swallowing function demonstrated sensitivity of 0.66 and specificity of 0.76, with PPV and NPV of 0.82 and 0.58. Elimination of chance effects by use of κ revealed very good agreement between summative clinical judgement and SSA but only fair concordance with the gag reflex (Landis & Koch, 1977).

Whilst there are methodological limitations to the study, findings support continued development of swallow screening by nurses and abandonment of reliance upon the gag reflex.

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Relationship between fluid administrations and outcome in colorectal surgery. By A. FROST, C.H. WAKEFIELD, F. SENGUPTA and K.C.H. FEARON, *Department of Clinical and Surgical Sciences, Surgery, University of Edinburgh, Royal Infirmary of Edinburgh, Edinburgh EH3 9YW*

Intravenous fluid replacement is fundamental to the resuscitation of critically ill surgical patients. However, fluid administration in the early postoperative period is frequently directed by inappropriate physiological goals, there being controversy over the choice of fluid and the exact requirements of replacement in the early postoperative period. This controversy is exemplified by the National Confidential Enquiry into Perioperative Death (NCEPOD), in which many patients were identified as undergoing surgery from a baseline of significant hypovolaemia, or having received excessive fluid infusions to compensate for hypotension. We have previously reported on 349 consecutive surgical patients admitted to a designated surgical high dependency unit (HDU); 70% of patients studied required physiological goal-directed interventions up until the time of death or discharge from HDU. The most frequent interventions were fluid challenges (43%) for oliguria and interventions for cardiac failure and related problems (22%). Pre-existing cardiac failure and the development of tachyarrhythmias or renal failure were more frequent in non-survivors. Since the development of these conditions may be directly related to inappropriate fluid replacement therapies, this study evaluates the relationship between postoperative fluid replacement and outcome following major surgery.

A subanalysis of a homogeneous group of patients undergoing colorectal resectional surgery was undertaken. The case-notes of these patients were reviewed and the total intravenous fluid prescriptions charted in terms of the volume of crystalloid, colloid and amount of sodium administered in the postoperative period. Outcome measures such as length of hospital stay, in-hospital mortality and morbidity were collected prospectively. Data are expressed as median (and range). Comparison of continuous and discrete variables was by Mann-Whitney *U* test and χ^2 analysis, significance was set at the 5% level.

Over a 7-month period, thirty-nine patients were admitted to HDU having undergone colorectal resections, with a median age of 68 (25–92) years. The in-hospital mortality was 8% (*n* 3) and morbidity 38% (*n* 15). The average daily volume of crystalloid administered was 2189 ml (1370–3310), colloid 929 ml (300–3200) and the average daily sodium administered was 215 mmol (109–676). Fluid administration patterns did not influence mortality. Patients with documented postoperative morbidity received greater total volumes of colloid in the postoperative period; 1000 ml (300–6400) *v.* 3050 (500–9706) (*P* 0.004). Patients in the upper 50th percentile for colloid administration had a longer postoperative stay (*P* 0.02), similar results were noted for those patients in the upper 50th percentile for total intravenous volume administered and total sodium load (*P* 0.006 and *P* 0.03 respectively).

Whilst the expected fluid requirements in the postoperative period have been well described, there appears to be great variation in these administrations in current clinical practice. Excessive fluid loads, particularly colloid fluids, and excessive sodium administration are associated with postoperative morbidity and prolonged hospital stay in this surgical subpopulation. These observations merit further studies into the physiological effects of intravenous fluids in the postoperative period.

Dilutional hypoalbuminaemia: myth or reality? By D.N. LOBO[1], Z. STANGA[2], J.A.D. SIMPSON[1], J.A. ANDERSON[1], B.J. ROWLANDS[1] and S.P. ALLISON[2], [1]*Section of Surgery and* [2]*Clinical Nutrition Unit, University Hospital, Queen's Medical Centre, Nottingham NG7 2UH*

Hypoalbuminaemia is an invariable accompaniment of major trauma, sepsis and surgery, due to the escape of albumin into the interstitial space, consequent upon increased vascular permeability (Fleck *et al*. 1985). This double-blind crossover study was performed on ten healthy male volunteers to determine whether intravenous infusion of a 2-litre bolus of crystalloid results in dilutional hypoalbuminaemia.

Subjects reported at 09.00 hours after a fast from midnight. Height and weight were recorded after voiding of the bladder. Bioelectrical impedance analysis was performed with single (50 kHz) and dual frequency (5 and 200 kHz) devices using tetrapolar distal limb electrodes. Venous blood was sampled for full blood count, serum urea, creatinine, electrolytes, albumin and osmolality.

Two litres of 0.9% saline or 5% dextrose were then infused in random order over 1 h on separate days. Body weight, bioelectrical impedance analysis and blood tests were repeated hourly for 6 h. Subjects voided their bladders as the need arose. The time of each micturition was noted, and urine volume and electrolytes were measured.

The mean (SE) age of the subjects was 22.1 (0.3) years. They had a mean (SE) weight of 73.6 (1.8) kg and height of 1.78 (0.01) m. The changes in serum albumin, haemoglobin, serum osmolality and Na concentration after infusions of 2-litre boluses of saline and dextrose are shown in the Table.

Time (h)	Albumin (g/l)		Haemoglobin (g/dl)		Osmolality (mosm/kg)		Serum Na (mmol/l)	
	Saline	Dextrose	Saline	Dextrose	Saline	Dextrose	Saline	Dextrose
0	43.3 (41.0–45.6)	43.3 (41.0–45.6)	15.1 (14.6–15.6)	15.1 (14.4–15.7)	290 (287–293)	291 (288–293)	141 (140–142)	141 (140–141)
1	34.7 (32.7–36.7)	36.4 (35.0–37.8)	14.0 (13.4–14.5)	14.1 (13.4–14.7)	293 (287–298)	286 (283–288)	141 (140–141)	133 (132–134)
2	35.8 (34.6–37.0)	42.7 (41.1–44.2)	14.1 (13.5–14.6)	15.1 (14.4–15.7)	290 (287–292)	284 (282–287)	140 (139–141)	139 (139–141)
3	36.3 (34.9–38.1)	42.2 (40.9–43.5)	14.1 (13.6–14.7)	15.0 (14.3–15.6)	290 (287–292)	286 (284–287)	140 (139–141)	139 (138–140)
4	36.5 (34.9–38.1)	41.7 (40.1–43.3)	14.1 (13.5–14.7)	14.8 (14.2–15.4)	289 (287–291)	285 (283–287)	140 (139–140)	139 (138–140)
5	37.8 (36.5–39.1)	40.5 (38.9–42.1)	14.3 (13.7–14.8)	14.8 (14.2–15.5)	289 (286–293)	287 (285–298)	140 (139–140)	138 (137–139)
6	37.6 (36.4–38.8)	41.0 (39.2–42.8)	14.2 (13.8–14.7)	14.9 (14.3–15.4)	288 (285–291)	289 (286–292)	140 (139–141)	139 (138–139)

All figures are mean (95% confidence interval).

Subjects developed hyperglycaemia at 1 h and a reactive hypoglycaemia at 2 h after dextrose infusions. Impedance tended to fall and then rise after saline infusions, while the converse was observed after dextrose infusions (data not shown). Mean time to first micturition was significantly shorter after dextrose than after saline infusions (78 min *v.* 212 min, *P* 0.002). Mean (95% CI) urine volume over 6 h was 563 (441–685) ml after saline and 1663 (1512–1813) ml after dextrose. Corresponding figures for urinary Na excretion over 6 h were 95 (75–116) mmol and 26 (15–38) mmol, respectively.

This study shows that crystalloid infusions can cause a substantial fall in serum albumin concentration, even in normal subjects. Dilution was more pronounced and prolonged with saline (mainly distributed in the extracellular compartment), than with dextrose (distributed throughout the total body water). Changes in impedance may be dependent on the electrolyte content of the infused solution. Higher urine output with dextrose may result from hyperglycaemia, reduced osmolality and suppression of antidiuretic hormone.

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Enteral feeding practices on a children's intensive care unit, children's hospital, Leicester Royal Infirmary: a complete audit cycle. S. McDOWELL, *Leicestershire and Rutland Healthcare NHS Trust, George Hine House, Gipsy Lane, Leicester LE5 OTD*

The importance of enteral feeding during critical illness has been well recognized and the benefits include the protection of gastrointestinal function and reduced bacterial translocation, which can prevent further complications at this crucial time. However, there have been reports describing the difficulties of achieving optimal nutrition in this group of patients. For this reason standards of best practice have been laid out in '*Enteral Feeding Guidelines for Patients on a Children's ICU*'. Enteral feeding practices were assessed on the children's ICU and the influence of a dietitian (DT) was established using this document. An initial audit (1) was carried out retrospectively involving 130 patient records over a 1-year period. A re-audit (2) was carried out prospectively over a 4-month period involving thirty-seven patient records. Data were collected from medical and nursing records for admissions whose stay was longer than 24 h up to day 6. Main objectives were to assess (a) time delay before commencing enteral nutrition, (b) average daily intake of energy and protein compared with nutritional requirements and (c) problems encountered initiating enteral feeds.

Enteral nutrition	Number of patients (% not seen by DT)		Time delay for enteral feeds (d)		Volume of feed prescribed (ml/d)		Volume of feed received (ml/d) (% of prescribed)		% Estimated average requirement		% Minimal protein	
	Audit 1	Audit 2	Audit 1	Audit 2	Audit 1	Audit 2	Audit 1	Audit 2	Audit 1	Audit 2	Audit 1	Audit 2
All patients	114	36	0.9	0.7	430	426	259 (71%)	382 (88%)	31	46	89	104
With DT	87	34	0.68	0.65	389	449	346	402	39	49	84	116
Without DT	27 (23%)	2 (6%)	0.71	1.5	470	45	110	34	11	4	20	7

In the first audit the volume of feed actually delivered was significantly lower compared with the volume of feed prescribed by starter regimen or the dietitian using the Paired Samples t Test (P 0.0001). Enteral feeds were initiated earlier and there was a significantly higher level of feed delivery (P 0.008) and consequently nutrition with dietetic involvement. There were few problems encountered establishing enteral nutrition; 92% of the patients were fed nasogastrically. Extubation was the main reason for enteral feed stoppages. Four-hourly gastric aspiration was poorly practiced as only 6% of the sample had this carried out 4-hourly for more than 50% of their stay. Several recommendations were made to the multidisciplinary team at this point to improve feed delivery and hence nutrition. These were: (a) actual feed volume received should be checked every 4 h throughout the day and enteral feed rate adjusted to ensure optimal feed delivery, (b) feed stoppage time pre- and post-extubation was standardized to 4 h, (c) 4-hourly gastric aspiration should be carried out to monitor feed absorption and also to act as a prompt for point (a), (d) the unit should receive full dietetic cover and (e) trans-pylorus feeding should be encouraged to promote a higher level of feed delivery.

In the re-audit, patients were fed 50% more and were fed sooner. The discrepancy between the volume of feed prescribed and the volume of feed delivered decreased from 171 ml to 44 ml. Again, dietetic involvement led to improved nutritional intake. The practice of 4 hourly gastric aspiration had improved as 41% of the sample had this carried out for more than 50% of their stay. Only one patient (3%) was fed trans-pylorus in the re-audit, compared with nine (8%) in the initial audit.

This completed audit cycle has led to better quality patient care since greater nutrition was achieved despite trans-pylorus feeding not being used. However, even though there are starter regimens for enteral feeds, this group of children receive very little nutrition. The dietitian has a role in optimizing nutrient delivery in the volume of fluid available, which is often restricted in these patients.

Nationwide intensive care unit questionnaire to investigate the diversity of nutritional practice. By H.M. DEWAR, *John Radcliffe Hospital, Headley Way, Headington, Oxford OX3 9DU*

Despite the now widespread use of enteral nutrition (EN) on intensive care units (ICU) there is a lack of consensus for the practicalities of establishing nutritional support (Klein *et al.* 1997). Some authors have alluded to the benefits of starting EN early, within 24–48 h of ICU admission, and it is generally accepted that this is more likely to take place if there is an agreed nutrition protocol used within the multidisciplinary team (Heyland *et al.* 1993; Schwartz, 1996; Kennedy, 1997). Controversy exists over the use of immunomodulating agents such as glutamine, arginine and *n*-3 fatty acids. Preliminary clinical data indicate a beneficial effect on immune function, but they are not conclusive and larger randomized controlled studies are needed to look at cost-benefit, target patients and how long immunomodulating agents need to be administered (Jolliet *et al.* 1999).

The aim of this questionnaire was to address some practical issues surrounding enteral feeding in the ICU. With the aid of the clinical audit department, thirty questionnaires were mailed to dietitians covering large ICUs in the UK and Ireland (eight or more adult beds, or more than nine combined paediatric and adult beds). Twenty-three questionnaires were returned, a 77% response rate.

- 87% of units have a protocol which covers how to initiate enteral feeding.
- 39% start feeds within 24 h of admission, 43% between 24 and 48 h.
- 43% give stress ulcer prophylaxis to all patients, 35% to those with a history of peptic ulcer disease, 4% to those who bleed.
- 65% of units accept 200 ml gastric residual volume as a cut-off point when trying to establish an enteral feed.
- 57% enterally feed for over 20 h (range 16–24 h).
- 61% of units start enteral feeds at 10–30 ml/h, 35% start at 30–50 ml/h.
- 57% of units will use nasojejunal/nasoduodenal tube feeding as required.
- 43% of units use novel substrates, of these half use them parenterally and half enterally.

From this questionnaire the commonest novel substrate in use is glutamine (70%) followed by about a third using *n*-3 fatty acid, arginine and nucleotide-enhanced feeds.

The questionnaires returned showed that in some areas there is a general agreement about practice such as in acceptable residual volumes and number of hours over which to enterally feed. However, there is also a diversity of ideas as to when to start feeding the critically ill patient, at what rate, how to manage stress ulcer prophylaxis and the use of novel substrates. This diversity of practice reflects the lack of randomized controlled trials with respect to nutrition in this critically ill patient group. This questionnaire has been a useful exercise in benchmarking our current ICU protocol with that of other units, the next stage is to update our protocol in the light of some of the information gained from this observational study.

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Fluid therapy influences nutrition in intensive care: a prospective evaluation of practice. By P. RAVASCO[1] and M.E. CAMILO[1,2], [1]*Centre for Nutrition and Metabolism, FMUL,* [2]*University Hospital of Santa Maria, Avenida Prof. Egas Moniz, 1949-028 Lisbon, Portugal*

Current standards of practice advise normonutrition; when concurrent therapies are used, the total amount of nutrients provided is seldom accounted for. This prospective study was designed to assess, in an intensive care unit (ICU), whether nutritional support was significantly affected by the concurrent fluid therapy.

Over a period of 24 weeks, forty-four consecutive patients (twenty-five male, nineteen female) who stayed in the ICU for longer than 72 h were evaluated. Mean age was 63 (SD 12, range17–83) years, APACHE II score: 24 (SD 9) points. Basal energy requirements were estimated using the Harris-Benedict formula. Throughout their ICU stay all nutrients provided to the patients by oral, enteral (EN) or parenteral routes were registered daily, as well as intravenous solutions and drugs. The daily volumes and amounts of macro- and micronutrients were the sum of all the components administered. Appropriate software was used for the analysis of oral nutrition.

Early EN (<24 h) was not tolerated in 78% of patients. Throughout the whole hospital stay, the average mean energy provided, including intravenous solutions and propofol, was 8.51 (SD 1.81) MJ/d, which was significantly higher than estimated requirements of 5.74 (SD 1.81) MJ/d (P<0.05). In fact, 54% of patients received an amount of energy which was more than 100% of their caloric requirements. When macronutrients from intravenous solutions and propofol were excluded, the resulting mean energy intake of 5.74 (SD 1.81) MJ/d was similar to estimated needs. On average, intravenous glucose and/or propofol provided at least 17% of the total energy, and more than 20% of the total in 36% of the patients. If glucose and propofol were excluded, the number of patients receiving excessive energy intake would decrease to 42%. Therefore, the administration of glucose resulted an excessive load of carbohydrates (CH) in 43% of patients while 45% received an excessive amount of lipids conveyed by propofol. Conversely, by subtracting the energy provided by both, 93% of the patients received an adequate amount of CH and 48% an adequate amount of lipids. Concerning micronutrients, the major issue was the provision of excessive amounts of sodium in 91% of patients, although 43% of these had overt oedema. Again, this resulted from the huge volumes of normal saline used for resuscitation and/or as a vehicle for a vast array of drug prescriptions.

In conclusion, resuscitation measures often interfere with gastrointestinal motility and early EN may be compromised. In the ICU, the incidence of hypernutrition is probably underestimated, due to concurrent fluid therapy, which is seldom taken into account and affects volume, energy and even micronutrients. Sodium loads are worrying, given the already expanded extravascular space. These are key aspects, which need to be addressed more closely, in order to improve the quality of care.

Effect of enteral glutamine administration on the serum and tissue glutathione levels in an animal model of intestinal obstruction. By H.T. BESLER[1], M.M. ÖZMEN[2], M. ÖZKIRLI[2] and N.A. KAMA[2], *Departments of* [1]*Nutrition and Dietetics, Hacettepe University, 06100 Ankara, Turkey and* [2] *General Surgery, Ankara Numune Teaching and Research Hospital, Ankara, Turkey*

In addition to its traditional role in nutrient digestion and absorption, the gut plays a primary role in immunologic and barrier function. The intestinal tract is the principal organ in utilizing glutamine, which is a source of energy and reduced glutathione (GSH) (Souba *et al*. 1990). Glutathione is the most important antioxidant and scavenger in addition to the number of important functions as in amino acid transport, in protein synthesis and degradation and in cellular redox regulation (Wernerman & Hammarqvist, 1999). It has recently been shown that the depletion of glutathione is associated with states of severe disease so that increase of glutathione may be a very attractive treatment option.

Our aim was to evaluate the effect of supplemental oral glutamine on serum and tissue glutathione production in a stressed rat model.

Forty male Wistar rats weighing 250 (SD 50) g were divided into four groups of ten animals each. All animals underwent midline laparotomy and iliocaecal ligation in order to create an intestinal obstruction. Groups 1 and 2 were controls and 0.5 ml saline was injected subcutaneously. Animals were supplemented with 1 g/kg/d glutamine for 5 d before and after the intestinal obstruction until the second operation in groups 3 and 4. Twenty-four hours (groups 1 and 3) and 48 h (groups 2 and 4) after intestinal obstruction, the rats were killed. Tissue samples were obtained from liver and lungs. GSH levels were measured in blood, liver and lung samples.

	Blood GSH (mg/g Hb)		Liver GSH (mg/g tissue)		Lung (mg/g tissue)	
	Mean	SD	Mean	SD	Mean	SD
Group 1	3.99	0.2	3.09	0.3	2.47	0.1
Group 2	4.09	0.2	3.19	0.4	2.30	0.5
Group 3	4.29*	0.2	3.79*	0.3	2.79*	0.2
Group 4	4.61**	0.3	3.29**	0.2	2.88**	0.2

* Significantly different from the corresponding control group, Group 1; * (P<0.05, Student's t test).
** Significantly different from the corresponding control group, Group 2; ** (P< 0.05, Student's t test).

We conclude that supplemental oral glutamine significantly increases serum, liver and lung glutathione levels in an animal model of intestinal obstruction as compared to controls (P<0.05), which may indicate an easy and safe method to decrease morbidity and mortality associated with intestinal obstruction.

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Identifying needs in nutrition education: a partnership approach. By V.E. TODOROVIC[1], R.A. RICHARDSON[2] and K. BUCKNER[2], [1]*Bassetlaw Hospital and Community NHS Trust, Worksop S81 0BD and* [2]*Partnerships in Active Continuous Education, Queen Margaret University College, Edinburgh EH12 8TS*

The NHS is committed to providing patients with high quality, clinically effective care (Department of Health, 1997). Great emphasis is being placed on a patient-centred approach with an expectation that staff, users and carers should be involved as partners in discussions and evaluations relating to service provision (NHS Executive, 1998; Department of Health, 1999). The government is keen to modernize education and training to ensure that everyone working in the NHS has the skills and knowledge to respond effectively to the individual needs of patients (Department of Health, 2000). Joint training across professions is being encouraged. Nutrition is a subject area that affects nearly all areas of care and the responsibility for providing patients with high quality and consistent nutritional care and information impacts on a diverse range of trained and untrained staff involved in patient care.

In this study an analysis of need was conducted to identify the nutrition education needs of staff (hospital ward staff including managers and health care support workers, community nurses, practice nurses and professions allied to medicine (PAMs)) in a combined acute, community and mental health NHS Trust. The identification of need was undertaken to permit strategic planning of efficient and effective learning programmes acceptable to employee and employer. The views of patients were also sought. A structured questionnaire which included questions relating to generic educational issues and nutrition education issues was used with staff to determine the current level of nutrition knowledge and understanding in nutrition, to identify staff's perceptions of the nutrition education that they required in order to satisfy the needs of their patients, and to identify the preferred mode of delivery for nutrition education. To test knowledge, focus groups were run that used defined clinically based nutritional case studies. Perceived expectations by staff of clients and colleagues of nutritional knowledge was measured using a visual analogue scale.

Fifty-seven (71%) out of the eighty-five staff invited to complete the questionnaire did so and a subgroup of fifty-four staff were involved in the focus groups. Fourteen patients participated in the focus groups. Across staff groups, common areas of nutrition interest included basic nutrition, wound care, nutrition support of vulnerable patients, heart disease and diabetes. Managers supported the need for all staff to participate in basic nutrition education. Three-quarters of the cohort sampled thought that undertaking education and training in nutrition would improve their work performance. In addition, 87% of staff felt that both patients and colleagues had high expectations of their nutritional knowledge. PAMs in particular felt that they had no nutrition knowledge and that raising their awareness would benefit their clients. Provision of nutritional education by contextualization of nutritional problems and concepts in staff's area of work was considered to be the best approach. Staff performed well in focus groups with the case-study scenarios but this approach has the limitation of not considering individuals performances. The patients felt that alongside paper-based materials, other media including specialist videos and cookery demonstrations, would help to increase their knowledge and understanding of the nutritional aspects of their care. The preferred mode of delivery for nutrition education is work-based learning combined with study for hospital-based staff. For community and primary care staff it is short courses and study days. Staff also highlighted the value of cross-discipline training.

The needs analysis has helped to identify nutrition priorities for staff and the preferred mode of delivery for nutrition education. Learning programmes can be introduced in a targeted, staged approach with core nutrition modules being developed for use across staff groups. These core modules could be used to benchmark knowledge and understanding of nutrition. These results show that actively seeking the views of patients is important to ensure that their nutrition education needs continue to be met.

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Effect of increasing intake of *n*-3 PUFAs and co-supplementation with antioxidants on lymphocyte proliferative response in healthy humans. By T. TREBBLE, E.A. MILES, M. STROUD and P.C. CALDER, *Institute of Human Nutrition, Southampton University Hospital Trust, Tremona Road, Southampton SO16 6YD*

High dose *n*-3 polyunsaturated fatty acid (PUFA) supplementation is proposed to induce anti-inflammatory effects (Calder, 1996). *In vitro* studies have demonstrated inhibition of the lymphocyte proliferative response to mitogen stimulation by *n*-3 PUFA in a dose-dependent manner (Calder, 1996). However, *n*-3 PUFA intake may also lead to increased lipid peroxidation and decreased membrane vitamin E concentrations; this may have a pro-inflammatory effect through increased free radical release. Antioxidant supplementation may reduce lipid peroxidation, particularly where vitamin E stores are depleted. The objective of this study was to determine, *ex vivo*, the effect on proliferation of lymphocytes from healthy subjects with increased intake of *n*-3 PUFA with or without antioxidant supplementation.

Sixteen healthy male subjects received of fish oil containing *n*-3 PUFA dietary supplement over 12-weeks. The dose of *n*-3 PUFA increased incrementally every 4 weeks (0.4, 1.2 and 2.4 g/d respectively of *n*-3 PUFA as a triacylglycerol). The subjects were randomized to also receive either a combined antioxidant preparation (containing selenium (200 μg), manganese (3 mg), vitamin A (450 μg), vitamin E (30 mg), vitamin C (90 mg)) or a placebo. Venous blood was collected at 0, 4, 8 and 12 weeks. Mononuclear cells were prepared by standard techniques (Yaqoob *et al*. 2000). The cells were cultured in the presence and absence of the T-cell mitogen concanavalin A and lymphocyte proliferation measured as [^{3}H]thymidine incorporation over the final 18 h of a 66-h culture period (Yaqoob *et al*. 2000). The stimulation index was calculated as thymidine incorporation in the presence of concanavalin A/thymidine incorporation in the absence of concanavalin A.

All sixteen subjects completed the full course of the study. Thymidine incorporation into unstimulated lymphocytes increased with increasing dose of *n*-3 PUFA (Spearman correlation coefficient = 0.32; *P* 0.012). Thymidine incorporation into stimulated lymphocytes was increased in subjects receiving *n*-3 PUFA with the maximal effect occurring at the lowest dose (see Table). Stimulation index tended to increase (non-significantly) at the lowest *n*-3 PUFA dose. There was no effect of antioxidant supplementation.

	Thymidine incorporation (cpm/well)					
n-3 PUFA (g/d)	No Concanavalin A		Concanavalin A		Stimulation index	
	Mean	SE	Mean	SE	Mean	SE
0	368.8	86.8	24358.7	6089.7	104.3	19.6
0.4	449.2	65.7	47417.5*	12672.9	143.0	24.7
1.2	495.6	110.4	41876.5*	10812.5	126.2	21.1
2.4	750.1	154.6	43778.8*	10944.7	97.7	18.2

*Significantly different from no *n*-3 PUFA (P<0.001; one-way ANOVA).

Providing *n*-3 PUFA to healthy subjects resulted in increased thymidine incorporation into both unstimulated and concanavalin A-stimulated lymphocytes which can be interpreted as a pro-inflammatory response; stimulation index was not significantly affected. Thus, the precise effect of *n*-3 PUFA depends upon what is measured. Providing *n*-3 PUFA results in decreased levels of arachidonic acid in immune cell membranes, hence decreasing production of prostaglandin E_2 (Calder, 1996). Prostaglandin E_2 is an inhibitor of lymphocyte proliferation. The effects of *n*-3 PUFA observed in this study are in accordance with an *n*-3 PUFA-induced decrease in prostaglandin E_2 production.

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Anti-inflammatory effects of elemental diet on Crohn`s disease-affected tissue *in vitro*. By D. MEISTER[1], M.C. ALDHOUS[1], A. SHAND[1], J. BODE[1], W. JOHNSON[2], S. GIFFEN[2], N. ANDERSON[1] and S. GHOSH[1], [1]*Gastrointestinal Unit, Department of Medical Science, Western General Hospital, Edinburgh EH4 2XU and* [2]*Scientific Hospital Supplies, Liverpool L7 9PQ*

Elemental diet (ED) is an effective therapy for active Crohn's disease, but the mechanism of action is unknown. It is postulated that low antigen intake, low fat content, alteration of bacterial flora, low residue and nutritional support may all play their roles in improving active Crohn's disease. However, supplemental ED diet has been shown to be effective in maintaining remission in children, suggesting a direct role of elemental diet on inflammatory activity (Wilschanski *et al.* 1996). Using the technique of whole gut lavage, we have shown a decrease in lavage IL-1β concentration after 2 weeks of ED therapy (Ferguson *et al*. 1998).

The aim of this study was to determine any direct anti-inflammatory effect of ED on colonic tissue biopsies by using a 24-h *in vitro* organ culture model, and investigating the ratio of anti-inflammatory cytokines IL-1ra, IL-10 to the proinflammatory cytokine IL-1β.

Colon or ileal biopsies from thirty-nine patients (Crohn`s disease (CD) *n* 16, ulcerative colitis (UC) *n* 12 and non-inflammatory bowel disease (IBD) *n* 11), were incubated for 24 h with ED, ED-casein and ED-whey. Tissues were incubated by adding ED, diluted in modified Waymouth's complete medium, at dilutions of 1:20, 1:10 and 1:5, including a medium control. The tissue viability was assessed by adding bromodeoxyuridine (BrdU) to the culture medium. The *in vitro* BrdU uptake was confirmed by immunohistochemical processing of the tissue and confirmation of BrdU-labelled cells. Non-viable tissue was excluded from further analysis. Interleukin-1β (IL-1β), interleukin-1 receptor antagonist (IL-1ra), and interleukin-10 (IL-10) were measured in the supernatant by immunoassay (ELISA). Student's *t*-test was used for comparison of groups. Ethical approval was gained prior to the study.

Incubation of tissues from CD with ED resulted in an increase in the ratio of IL-1ra:IL-1β *v.* control (45.7 (SEM 9.1)) in dilutions of 1:20, 1:10 and 1:5 (59.7 (SEM 24.0); 89.6 (SEM 17.0) and 93.0 (SEM 38), respectively), which was statistically significant at 1:10 ($P<0.05$). Incubation of CD tissue with ED-casein resulted in a significant increase in IL-1ra:IL-1β ratio at dilutions 1:20 (101.8 (SEM 22.0); *P* 0.05), 1:10 (142.8 (SEM 24.6); $P<0.05$) and 1:5 (109.7 (SEM 25.0); *P* 0.05), respectively, compared with control (45.7 (SEM 9.1)). The ratio of IL-1ra:IL-1β after ED-whey incubation did increase at 1:20, 1:10 and 1:5 concentrations but did not reach statistical significance compared with control. UC tissue incubated with ED-casein and ED-whey resulted in no significant changes in the IL-1ra:IL-1β ratio. In non-IBD tissue a trend towards increase (*P* 0.06) at 1:10 dilution *v.* control (143 (SEM 31); 64.4 (SEM 18)) occurred. At other dilutions of ED, and incubation of ED-casein and ED-whey, no significant change in the ratio was seen. In CD, but not in UC or non-IBD tissue, a trend towards an increase in IL-10:IL-1β ratio *v.* control was seen (ED 1:10 dilution *v.* control 43.1 (SEM 23) *v*. 21.4 (SEM 9.2); NS). In ED-casein an increase in the ratio of IL-10:IL-1β at 1:20 (75.4 (SEM 12); *P* 0.07 *v*. control) and at 1:5 (48.12 (SEM 6.7); *P* 0.07 *v.* control) occurred, but the sample size was small and the results did not reach statistical significance. In ED-whey there was an increase in mean at 1:10 dilution compared with control (165 (SEM 140); 21.4 (SEM 9.2)); however, this was not statistically significant**.**

In *in vitro* incubation of colonoscopy biopsies affected with CD but not with UC, ED alters the anti-inflammatory/proinflammatory cytokine balance. To our knowledge, this is the first *in vitro* study to show any direct anti-inflammatory response to ED in intestinal biopsies of patients with CD. The direct anti-inflammatory effect of ED on intestinal tissue affected by CD is preserved if casein and, to a lesser extent whey, is substituted for amino acids in ED.

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Variability in U.K. vitamin D reference ranges. By P.J. TWOMEY[1] and J.R. PATERSON[2], [1]*Department of Clinical Biochemistry, Royal Infirmary Edinburgh EH3 9YW and* [2]*Area Biochemistry Laboratory, Dumfries & Galloway Royal Infirmary, DG1 4AP*

Vitamin D is essential for skeletal health, and its deficiency is associated with defective mineralization, resulting in rickets or its adult equivalent, osteomalacia. More subtle degrees of insufficiency lead to secondary hyperparathyroidism and increased bone turnover, which play an important part in age-related bone loss and osteoporotic fractures. Over the last decade a wealth of evidence has accumulated documenting vitamin D deficiency in elderly populations (Dawson-Hughes *et al.* 1991; Holick, 1994; Thomas *et al.* 1998). A previous study (O'Shea & Carter, 1998) found significant variation in vitamin D lower reference values (LRVs). We decided to see if there has been any change since then.

In December 1999, we carried out a survey of laboratories in the UK by means of letter, fax, e-mail and telephone calls. The fourteen responding laboratories provided serum 25-OH vitamin D LRVs ranging between 10 and 25 nmol/l. The lowest LRV (10 nmol/l) was provided by a laboratory in the south of England. Cities separated by a distance of less than 50 miles provided LRVs that differed by a factor of 2. Four laboratories provided seasonal information.

Hospital	25-OH vitamin D range (nmol/l)
1	10–100
2	10–100
3	20–150
4	12.5–75
5	25–150
6	15–120
7	25–150
8	20–125
9	15–100
10	15–100
11	15–100
12	> 15
13	23–113
14	20–110

Vitamin D status is most commonly assessed by measuring serum concentrations of 25-hydroxy vitamin D, the major circulating form of the hormone. The LRV quoted by a laboratory is critical in making the diagnosis of deficiency. Despite the fact that levels of serum 25-OH vitamin D below 20 nmol/l are generally regarded as indicating vitamin D deficiency (Compston, 1998), more than half the laboratories in this survey reported lower LRVs. However, circulating concentrations up to 37.5 nmol/l may be associated with adverse skeletal effects (McKenna, 1992) and even higher levels may be required for optimal skeletal health, particularly in elderly people.

In a survey of twelve UK laboratories, a coefficient of variation (CV) of 63% was found at the distribution with the lowest concentration (Carter & Shunt, 1988). In that study inconsistent standard calibration contributed to the poor performance. Some of the differences in vitamin 25-OH D LRVs in our survey may be explained by the analytical methods. However, UK LRVs are generally lower than in other countries, for example, *Tietz Textbook of Clinical Chemistry* (Burtis & Ashwood, 1999) quotes a LRV of 35 nmol/l. Perhaps it is time to set a physiologically relevant LRV for vitamin 25-OH D and to ensure that laboratories meet a minimum intra-assay CV at this level? Otherwise, diagnosis of hypovitaminosis D may be a lottery based on postal code.

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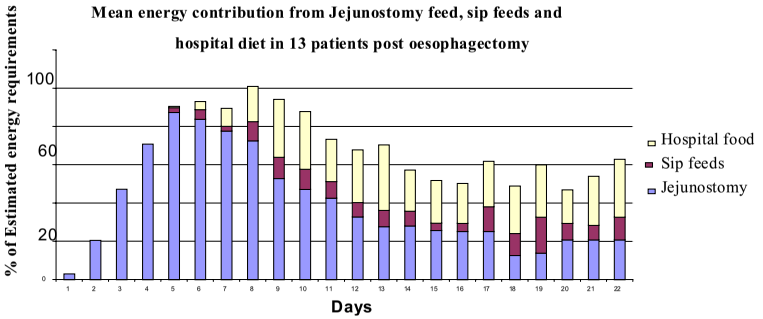
Energy and protein intake in hospital patients after oesophagogastrectomy for oesophageal cancer. By P.M. MURPHY, E.C. CAWDERY and W.G. LEWIS, *Department of Nutrition, Dietetics and Surgery, Royal Gwent Hospital, Newport, South Wales, NP20 2UB*

Patients with oesophageal cancer have been reported to have the highest level of malnutrition (78–79%) when compared with other patients with digestive and extradigestive tumours (Larrea *et al.* 1992). Nausea, early satiety and anorexia are common in these patients, which often results in problems in maintaining an adequate nutritional intake in the postoperative period.

The aim of this study was to audit the energy and protein intake of patients following oesophagogastrectomy. Sixteen consecutive patients (nine males, seven females) with cancer of the oesophagus were studied. The selected group was aged 61 (SD 9) years. Mean body weight on admission was 69.6 (SD 11) kg and BMI was 25.3 (SD 4) kg/m^2. Mean length of hospital stay was 22 (SD 13) d. Days 1–22 are reported. Three people died postoperatively and their data have been excluded from the results.

Each patient received a feeding jejunostomy tube at laparotomy. Jejunostomy feeding was commenced by the second postoperative day in 85% (11/13) of cases. By day 5, jejunostomy feeding had been successfully initiated in all thirteen patients. A standard whole-protein feed (Osmolite) was used. Nutritional supplements were offered to all patients on the introduction of oral fluids and intake of supplements and food was monitored. Total energy and protein intakes were calculated daily from the first postoperative day until discharge.



Energy intake is expressed as a percentage of estimated requirements (Schofield equation with adjustments for stress and activity). Mean energy requirements were met by the eighth postoperative day from a combination of jejunostomy feed, sip feeds and hospital food (73, 10 and 18%, respectively). However, as the jejunostomy feed was reduced and normal hospital diet and sip feeds encouraged, difficulties arose. From the third week onwards, there were only two occasions on which >60% of energy needs were met. Clearly patients failed to increase either their energy intake from sip feeds (9.7 (SD 4.7)%) or from hospital meals (23.7 (SD 3.8)%). This was reflected by a mean weight loss of 3% (SD 4.6%) from the preoperative stage to discharge. Examination of protein intake over the same period revealed a similar trend, with requirements met by day 8 but rarely achieving >60% of requirements (1 g/kg body weight) from day 14 to discharge.

This audit has highlighted the difficulty of meeting nutritional requirements in these patients. Despite an early proactive approach to feeding, difficulties arise during the third week postoperatively as patients become dependent on hospital diet and sip feeds to meet requirements. Continuation of jejunostomy feeding after discharge from hospital, together with the provision of fortified meals may improve energy and protein intakes.

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Nutritional status of elective gastrointestinal surgical patients pre- and post-operatively. By S.B. FETTES[1], R.A. RICHARDSON[2], R. CHEN[3] and C.R. PENNINGTON[1], [1]*Departments of General Medicine and* [2]*Cardiovascular Epidemiology, Ninewells Hospital, Dundee DD1 9SY and* [3]*Queen Margaret University College, Edinburgh EH12 8TS, UK*

Studies have indicated that malnutrition is common on admission to hospital and furthermore, that nutritional status often deteriorates during the hospital stay. The aims of this study were to assess the nutritional status of patients admitted for elective gastrointestinal surgery and to determine any change in nutritional status during the acute hospital stay.

Patients aged between 18 and 80 years admitted for elective moderate/major gastrointestinal surgery had their nutritional status assessed on admission and once oral diet had been recommenced, generally 2–3 d before discharge home. Data were collected on height, weight, BMI, triceps skinfold thickness (TSF), mid-arm muscle circumference (MAMC) and hand grip dynamometry. Patients who received artificial nutritional support were excluded from the second set of measurements.

On admission 150 patients were assessed, who constituted approximately 60% of admissions during the study period and 113 of these could be reassessed. On admission BMI >25, 20–24.9 and <20 respectively were found in 62%, 32% and 6% males and 42%, 45% and 13% females. There was a mean of 7 d between surgery and recommencing oral diet. Weight loss was significantly more common (90% *v.* 59%, $P<0.001$) and greater (4.1% *v.* 1.6%, $P<0.01$) in males than females. Of patients 34% lost more than 5% body weight. Anthropometric measurements are shown in the table as a percentage of standard values (Jelliffe, 1966). TSF, MAMC and hand grip dynamometry decreased significantly in both males and females but the percentage decrease in MAMC was significantly greater in males ($P<0.05$) while that in hand grip dynamometry was significantly greater in females ($P<0.05$).

		Pre-operative			Post-operative		
		TSF	MAMC	Hand grip	TSF	MAMC	Hand grip
Males (*n* 52)	Mean	108	105	83	102**	102***	79**
	SD	47	10	16	44	10	16
Females (*n* 61)	Mean	120	97	80	111***	95*	71***
	SD	47	12	20	45	12	18

*$P<0.05$, **$P<0.01$, ***$P<0.001$, compared with pre-operative values.

The incidence of malnutrition in the current study (9%) is considerably lower than that found in an earlier study of elective and emergency surgical admissions in this hospital (McWhirter & Pennington, 1994) but similar to that found in more recent studies of surgical patients (Harrison, 1997; Corish *et al.* 2000). Weight loss during the hospital stay has been reported to occur in approximately two thirds of medical and surgical patients (McWhirter & Pennington, 1994; Corish *et al.* 1998). In the current study 72% patients lost weight and 34% experienced a clinically significant weight loss. In conclusion, the prevalence of malnutrition on admission to hospital appears to be lower than previous work had suggested. However, weight loss during the hospital stay is common and additionally, there may be gender differences in the changes in nutritional status experienced by surgical patients. This data may have implications for the nutritional management of surgical patients in relation to the suggested benefits of oral supplementation in mildly malnourished post-operative patients (Beattie *et al.* 2000).

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Hydrochloric acid in the treatment of central venous catheter-related sepsis: a retrospective analysis of safety and efficacy. By A.J. FOWELL, C. HAYWARD, C. CHADWICK, S. GABE and A. FORBES, *St Mark's Hospital and Academic Institute, Watford Road, Harrow, Middlesex, HA1 3UJ*

Line infection is a relatively common and potentially serious complication in patients receiving intravenous nutrition. Failure of antibiotic therapy necessitates line extraction and hence the risks of subsequent replacement. Hydrochloric acid (HCl) has potential antimicrobial and mechanical benefits and has been used in specialist intestinal failure units in the treatment of antibiotic-resistant line-related sepsis. However, we have been unable to find published data on its safety or efficacy in this role.

We performed a retrospective analysis of protocol-driven use of HCl on ten occasions in nine patients over a 1 year period in a specialist intestinal failure unit. Patients receiving intravenous nutrition with clinically evident and culture-proven line infections, not responding to appropriate antibiotics, were to be given a single dose of 3 ml 0.1 M HCl in addition to ongoing antibiotics *via* the line. Non-responders were defined as those patients who had ongoing fevers or rigors despite at least 3 d microbiologically appropriate treatment, or had completed a1 week course of antibiotics and then had shortly afterwards developed a recurrent infection with the same organism. HCl was locked in the line for 4 h before being flushed with 0.9% saline (not aspirated). Patient demographics, the type of infecting organism, presence or absence of intercurrent sepsis, reported adverse events and clinical outcome at 1 month were all assessed.

The patient demographics were in keeping with those receiving home parenteral nutrition. Seven of the nine patients were female; their median age was 53 years (range 19–68). Four patients had underlying Crohn's disease, and one each had mesenteric infarction, scleroderma, autoimmune enteropathy, visceral myopathy, and fistulating complications of ulcerative colitis surgery; five patients had intestinal stomas. Two patients had implanted ports (VitalPort) and eight had Broviac-type tunnelled lines. Three episodes of infection were due to *Staphylococcus epidermidis*, six due to various Gram-negative organisms and one was attributable to methicillin-resistant *Staph. aureus*. In one case both *E. coli* and *Candida albicans* were isolated.

No clinical or biochemical adverse events attributable to HCl were identified. Eight patients responded to treatment and remained infection-free at one or more month's follow up. One patient failed to respond and had immediate line extraction. Another had recurrent line infection with the same *Staph. epidermidis* within 1 week of acid therapy. There was therefore no apparent association between outcome and the infecting bacterial organism, even MRSA responding unexpectedly in one patient, but the patient co-infected with *Candida* predictably failed to respond. Infection was eradicated in both patients with implanted ports.

Hydrochloric acid appears to be safe in the treatment of line infection associated with intravenous nutrition. These data suggest useful advantage from a single dose of acid in resistant cases, where line removal would be the only alternative. Randomized double-blind studies are now justified to confirm the present safety data and to test the apparent therapeutic benefit.

Argon plasma coagulation for the treatment of PEG site hypergranulation. By R.C. EVANS, R. NICHOLSON and P.A. O'TOOLE, *Gastroenterology Department, University Hospital Aintree, Lower Lane Liverpool L9 7AL*

Percutaneous endoscopic gastronomy (PEG) site hypergranulation is a common problem. It causes distress to patients if it is painful or bleeds and, by interfering with effective cleaning of the stoma, it may contribute to PEG site infection. Several approaches to treatment have been described. Sofradex ointment is advocated by some, although this is not a licensed indication. Topical corticosteroids in other formulations are also used. Semipermeable polyurethane dressings (e.g. Lyofoam T) have been shown to reduce wound granulation in other situations, and avoidance of friction at the PEG site by taping the tubing to the skin may prevent the problem from getting worse. If a large amount of granulation tissue has built up, however, these approaches are unlikely to make a major impact and some form of destructive therapy is required. Silver nitrate cautery often keeps the problem at bay but requires repeated application and can be painful. An alternative method of delivering cautery, which is increasingly available in endoscopy units, is argon plasma coagulation (APC). We report *in vitro* work using this technique and our early experience in treating patients.

In vitro experiments were undertaken to determine whether APC would damage PEG tubing. Tubes of three different designs were used: Freka (Fresenius), Corflo (Merck) and Compat (Novartis). The first two are polyurethane, the other silicone. The tubes were pulled through the intercostal spaces on a section of animal carcass which was placed on a diathermy electrode pad. The area immediately surrounding the PEG was then treated with APC using an ERBE ICC 200/APC 300 unit. Standard endoscopic probes 2.3 mm in diameter were used, held free-hand 2-5 mm above the tissue. A flow rate of 2 litres/min was used throughout but power settings varied between 50 and 99 W. Despite application times exceeding 30 s, resulting in considerable tissue destruction, no damage to any of the PEG tubes was seen even at the highest power setting. Direct application to the tube itself caused the argon beam to arc around the tube leaving it unscathed.

We have used APC to treat PEG site hypergranulation in four patients to date. All had more than 8 mm of granulation tissue around the PEG that had failed to be controlled by other means. The treatment site was infiltrated with up to 5 ml 2% lignocaine. Despite local anaesthesia, considerable discomfort was experienced by the first subject during treatment. This is probably due to heating of the surrounding or deeper tissues. Subsequent treatments were performed under conscious sedation with midazolam and were well tolerated. A power setting of 65 W was used. After treatment the surface tissue is black and charred. This eschar separates after a few days to reveal pink healthy granulation tissue underneath. Excellent results were obtained in all cases with almost complete destruction of excess granulation in 1–3 sessions.

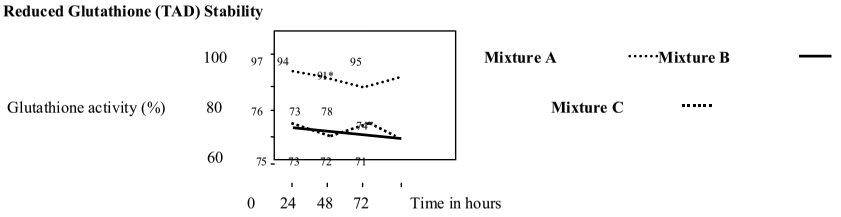
APC lends itself well to the treatment of PEG site hypergranulation. It is widely available in endoscopy units, easy to use, very effective and carries no risk of damage to the PEG tubing.

Stability of reduced glutathione in parenteral nutrition mixtures with or without glutamine. By E. VALENCIA, A. MARIN and G. HARDY,* *Pharmaceutical Nutrition Group, School of Biological and Molecular Sciences, Oxford Brookes University, Oxford OX3 OBP, UK*

The tri-peptide, L-γ-glutamyl-cysteinyl-glycine, or reduced glutathione (GSH), has been assigned an important role in cellular defence against free radical oxidative injuries and detoxification processes in sepsis, burns, trauma, cancer and other critical illness (Ortolani *et al*. 2000). Previous studies have shown that intravenous GSH could have a beneficial effect of restoring GSH levels inside natural killer cells and organs such as gut, liver and muscle. The purpose of this study was to investigate the stability of GSH in total parenteral nutrition (TPN) mixtures with or without glutamine (Gln).

Two TPN mixtures (without lipid) were prepared from different 10% Amino Acid solutions (50 ml), either without Glutamine (Gln) (mixture A), or with Gln (30% total amino acids) (mixture B), and including 5% glucose (40 ml) and water (10 ml). 5% glucose infusion (mixture C) was used as a control. All mixtures were prepared aseptically in 250ml Mixieva bags. The resultant mixtures were isonitrogenous and isoenergetic providing 8 g N and 4200 KJ (1000 Kcal)/l. A 3 ml aliquot of reconstituted GSH sodium salt (TAD^R Biomedica, Foscama, Italy) providing 300 mg GSH (10.68 mM) was aseptically added to each mixture, thoroughly shaken, then stored at 4–8° for 72 h. Samples were taken immediately (T_0) then at T_{24}, T_{48} and T_{72} and frozen at –20°. They were subsequently analysed for GSH activity, by the glyoxalase enzymatic method. Mixture pH was determined at 72 h by standard method.

The results (see Fig.) show that in mixture A (pH 6.3) GSH levels exhibited a mean degradation of 5.4% over 72 h (or 1.8 %/d) (P = 0.98 compared with T_0). In contrast GSH was dramatically lower at T_0 in mixture B (pH 7.2) and mixture C (pH 7.1) by over 20%. Thereafter mean degradation was 6.3% over 72 h (or 2.1%/d) (P = 0.74 compared with T_0) and 0.1 %/d respectively. (Student t test).



GSH as the lyophilized sodium salt was stable in a 'standard' lipid-free TPN mixture for 72 h at 4–8°. However, it was less stable in the Gln enriched mixture and the Glucose control. Both TPN mixtures contained the same total amount of different amino acids but the more stable mixture A, contained *N*-acetyl cysteine (NAC) and taurine (Tau). These two amino acids were not present in mixture B or the control. It is possible that the presence of Gln in the less stable TPN mixture affected GSH activity, but more likely that NAC and/or Tau and the lower pH of the stable mixture provide some protection against GSH oxidation. The nature and significance of these interactions are currently under investigation.

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Pall *Lipipor* TNA filterability studies with Baxter Clinomel. E. MAYNARD and G. BARNES, *Scientific and Laboratory Services, Pall Europe Ltd, Walton Road, Portsmouth PO6 1TD*

The Pall *Lipipor* TNA filter (code TNA1E) is an air-eliminating filter with a 1.2 µm modified nylon membrane and phthalate free fluid pathway. This device is indicated for the removal of inadvertent particulate debris, enlarged lipid droplets, microbial contaminants and entrained air.

In order to assess the filterability of a widely used Clinomel admixture with the Pall TNA1E, we tried to reproduce a challenging filtration situation and measure working pressures within the infusion system.

Clinomel N5-800 (2000 ml) triple-chamber bags were removed from storage and were first mixed as stated in the Clinomel instructions for use supplied with the bag. Sterile water (5 ml) was used to reconstitute one vial of Cernevit with the help of a Pall PharmAssure Dispensing Pin (0.2 µm PTFE vent membrane). The resulting solution was added aseptically to each mixed Clinomel bag; this process was repeated three times. The Clinomel bags with Cernevit multivitamins were then stored in the fridge at 4° for 7 d before testing.

The TNA1E was primed with the prepared Clinomel admixture following the filter priming instructions and data-logger pressure readings were recorded throughout the test period.

TNA1E Filter No.	Regimen	Time (h:mins)	Flow rate (ml/h)	Volume infused (ml)	Maximum pressure(mmHg)*
1	N5-800	25:16	84.0	2126	107
2	N5-800	24:52	84.1	2088	115
3	N5-800	24:38	84.1	2068	115

*The pump did not alarm during testing (nominally set at 500 mmHg).

The filterability tests showed that there were increases in system pressures, but flow through the filter was maintained. The rise in differential pressure is due in part to the removal of lipid droplets larger than 1.2 µm, which had formed as a result of the challenging conditions. Further work would need to be performed to determine the actual cause. The pressure upstream of the filter rises slowly as the membrane removes particles larger than 1.2 µm and becomes partially occluded. The pump alarm may trigger if it is set too low. The Medical Devices Agency (MDA, 1995) recommend pump pressures are set at 500 mmHg or lower, but the exact setting below this figure must ultimately be a clinical decision. In-house tests have previously demonstrated that priming the TNA1E filter with saline, or other aqueous solution compatible with the admixture, results in reduced initial differential pressure across the membrane and thereby increases tolerance to pressure build-up within the system.

We have demonstrated the filterability of this Clinomel admixture with the Pall *Lipipor* TNA, even in conditions that would not normally be seen in clinical practice.

The US Food and Drug Administration (FDA, 1994) and the American Society for Parenteral and Enteral Nutrition (ASPEN) (1998) recommend the use of filtration in the administration of parenteral nutrition admixtures. ASPEN's '*Safe Practices for PN Formulations*' (1998) reviews the rationale for use of in-line filters with regard to particulates, phlebitis, microprecipitates, infection and air emboli and concludes that the use of a filter provides an additional safety check to prevent patient harm.

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Audit of biochemical monitoring of total parenteral nutrition. By N. POLANSKA[1], A. MICKLEWRIGHT, I. FELLOWS and C. NWOKOLO on behalf of the BAPEN REGIONAL REPRESENTATIVES GROUP, [1]*Chemical Pathology, South Tyneside District Hospital, Harton Lane, South Shields NE34 0PL*

Members of the BAPEN Regional Representatives Group carried out a planned retrospective audit on the biochemical monitoring of total parenteral nutrition (TPN) in hospitals in nine regions in England and Northern Ireland.

Although recommendations are made in the BAPEN publications by Sizer (1996) and Pennington (1996), not all hospitals may have drawn up their own detailed guidelines for patients on TPN.

A simple questionnaire was designed and distributed by the BAPEN regional representatives to NHS hospitals in their region. Responses were collated and analysed by N.P. The questionnaire sought to answer the following questions:

1. Are current BAPEN standards achieved?
2. What biochemical monitoring is carried out in patients on TPN?
3. How good is communication between nutrition teams and other members of the health care group?
4. Is there awareness of potential problems, such as hypophosphataemia, which may be encountered when refeeding severely malnourished patients? And how is it managed?

There were sixty-seven usable responses from the 120 questionnaires sent out (55%). Thirty-three (48%) respondents had intravenous nutrition guidelines and protocols; seven were updating, two were for ITU only and three for neonatal and paediatric units. Thirty-eight (57%) had a nutrition team, most of whom were involved in TPN monitoring to a high standard. Pharmacy departments in fifty-one (75%) hospitals had access to biochemistry reports, twenty-three (34%) of these by computer look-up.

Replies on management of hypophosphataemia could be classified into three groups: (1) sixteen with details of treatment and action limits for I/V replacement; a few hospitals used the PENG guidelines or the Oxford refeeding guidelines; (2) thirty-one referred to a specialist, some had protocols on the ITU; (3) twenty did not know whether procedures were in place.

All hospitals provided biochemical monitoring. The commonest pattern of testing (thirty-five hospitals; 52%) was daily electrolytes (El), with liver function tests (LFT) calcium (Ca) phosphate (PO_4), magnesium (Mg) on alternate days. Daily monitoring of these tests was practised by twenty-four (36%) and three were ITUs. Eight hospitals caused concern: four monitored El, Ca and PO_4 once per week, two were unsure what the frequency was for any test, and two provided minimal testing of electrolytes only. Other tests were done less frequently by most responders: thirty-seven (55%) provided urea nitrogen results, most often weekly; zinc, haematinics and trace elements for long-term patients only. Twenty out of thirty-five did El, LFT, Ca, PO_4, proteins daily at the start of TPN. Sixteen sent in copies of their protocols.

Some conclusions can be drawn from this analysis:

1. Less than 50% of hospitals responding to this survey worked to TPN guidelines.
2. Communication across health care groups was deficient in 25% of hospitals, with inadequate involvement of pharmacy staff.
3. This survey confirms that there are controversies about the treatment regimen for hypophosphataemia refeeding syndrome.

BAPEN as an organization has the expertise to produce consensus guidelines in relation to provision of TPN and refeeding syndrome. Wide promotion of such new guidelines would be needed.

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Food choice of adults with intestinal failure on home parenteral nutrition. By C.A. WRIGHT and J.L. SHAFFER, *Intestinal Failure Unit, Hope Hospital, Stott Lane, Salford M6 8HD*

There have been no previous reports detailing the dietary intake of patients with intestinal failure on home parenteral nutrition (HPN). HPN patients' requirements for parenteral nutrition vary from electrolytes only to provision of some or all nutrients, depending on bowel anatomy and function. For most, HPN supplements, rather than replaces, enteral nutrient absorption. Diet is important for psychosocial reasons as well as for the promotion of bowel adaptation following major bowel resection (Bristol & Williamson, 1988), and the maintenance of gut barrier function.

During the period from February to July 2000, eighty-six adults attending the HPN clinic at Hope Hospital were given a questionnaire about how they cope with eating, and a 3-d food diary for completion. Patients who had been on HPN for less than 6 months were excluded. Forty-six records were returned, of which four were incomplete. The remaining forty-two records were analysed using Microdiet software and a database set up on Microsoft Access.

Of the forty-two HPN patients in this group, fourteen were male and twenty-eight female, with an age range from 19 to 72 years. The commonest reason for requiring HPN was short bowel syndrome (*n* 29). Twenty-seven patients had a stoma. Of the group, twenty-one had been on HPN for between 1 and 5 years, and nine for longer than 10 years. Four patients had intravenous electrolytes only.

When asked if their normal eating pattern had been affected by HPN, twenty-two (52%) answered yes, with twelve commenting that HPN suppresses their appetite and two commenting that it makes them feel sick. However, eight rated their appetite as 'excellent', seventeen as 'good', eight as 'fair' and eleven as 'poor'.

Five patients reported a completely unrestricted dietary intake. The remainder cited one or more factors restricting their dietary intake. Common factors were poor appetite (*n* 11), abdominal pain (*n* 10), bloating/wind (*n* 13), a high output stoma (*n* 15), nausea (*n* 9), vomiting (*n* 7) and anxieties about stoma blockage or stoma bag leakage (*n* 8), especially on journeys.

Of the thirty-seven patients whose dietary intake was limited in quantity and/or range, twenty-eight (67% of the total) identified specific foods or drinks avoided or restricted. Two patients ate and drank nothing, or virtually nothing, despite a good appetite, because of severe pain following enteral intake. The main dietary items avoided or restricted were alcohol (*n* 14), fizzy drinks (*n* 17), fried/fatty foods (*n* 8) and spicy foods/curry (*n* 6). Twenty-one patients (50%) avoided some type(s) of vegetable or salad and seven (17%) avoided some type(s) of fruit, the commonest being cabbage (*n* 3), salad (*n* 3), fruit juice (*n* 3), fruit skins (*n* 3) and nuts (*n* 3). Three patients claimed to avoid all vegetables. Among the wide range of other foods restricted were fish (*n* 3), milk (*n* 3), brown bread (*n* 2), tomatoes (*n* 2) and all fruit (*n* 2).

The commonest reasons for avoidance or restriction of foods or drinks were (in order of frequency) stoma blockage or fear of blockage, pain, wind or bloating, diarrhoea, increased stoma output, stoma bag problems (leakage, odour and blowing out) and foods 'going straight through'.

Analysis of the food diaries showed a wide variation in enteral intake, ranging from nil to 15.3 mJ/3665 kcal per day (median 6.82 mJ/1630 kcal) and from nil to 137 g protein/day (median 62 g). The analysis suggests that nutrient intake fell below the lower reference nutrient intake for magnesium (*n* 13), potassium (*n* 11), selenium (*n* 25), iodine (*n* 13), calcium (*n* 9), folate (*n* 8) and zinc (*n* 8), reflecting perhaps the food avoidances or diets low in nutrient density.

These results demonstrate considerable variability in eating patterns in patients on HPN. Being on intravenous nutrition at home (i.e. long term), causes considerable disruption to normal daily activities including food intake. Considerable care and attention is required in designing and monitoring oral intakes for these patients to ensure appropriate nutrient intake.

Bristol JS & Williamson RCN (1988) *Journal of Parenteral and Enteral Nutrition* **12**, 299–309.

Comparison of basic parenteral nutrition solutions for neonates: is standardization possible?

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Commercial complete parenteral nutrition solutions are not available for neonates. Therefore, nutritional solutions have to be compounded in hospital pharmacies. In order to increase safety and reduce cost, hospitals may introduce standard feeding regimens (Digel, 1998). The literature has been searched, using EMBASE, The Web of Science and Medline, for publications about standardized nutrition for the neonatal patient group. Data has been retrieved from England, Spain, and Germany. Discussions with collegues have revealed that several other centres use standardized parenteral nutrition for neonates, but have not published their results.

Standardization of parenteral nutrition for neonates may involve the preparation of a single formula where the volume infused is altered according to the patient's weight. This is only applicable for stable patients without special requirements since if a different quantity of any one volume is required, then the amount of all the others is also altered. In a recent article, it has been estimated that up to two-thirds of neonates could be given a range of pre-compounded standard solutions (Beecroft *et al*. 1999).

The most recent data available on standardized regimens is listed below. In San Sebastian, Spain, a concentrate is manufactured which can be diluted according to the patient's needs (Aldamiz-Echevarria *et al.* 1995). The table shows standard solutions from eight different European hospitals (A-H).

In 150 ml	A	B	C	D	E	F	G	H
Glucose	14	15	15	18.8	15	16.5	23.9	15
Nitrogen	2.9	3.2	2.5	2.5	2.25	1.8	4	2.7
Sodium	-	4.5	4.5	3.8	4.5	2.4	4.7	4
Potassium	-	2	3	2.6	3	1.9	3.4	2.5
Calcium	-	1.5	1.5	1	1.5	1.8	1.2	1.2
Magnesium	-	0.2	0.17	0.15	0.17	0.18	0.54	0.28
Phosphate	-	1.5	1.5	1.1	1.5	0.9	1.8	1

Standardizing parenteral nutrition and producing the solutions in batches makes more extensive quality assurance possible and commercial manufacture practicable, and therefore increases the safety of this treatment. A high quality and safe parenteral nutrition regimen is especially important in these most vulnerable patients. The reviewed data supports suggestions that a wide-ranging standardization of neonatal parenteral nutrition is feasible.

Future directions of this study include a questionnaire directed at key European centres aiming to evaluate the practice of supplying parenteral nutrition to paediatric patients, the development of standard regimens, and stability studies on a standardized regimen, including peroxide formation.

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Beecroft C, Martin H & Puntis JWL (1999) *Clinical Nutrition* **18**, 83–85.

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A two-year audit on percutaneous endoscopic gastrostomy: is the nutrition support team generating more work?

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Percutaneous endoscopic gastrostomy (PEG) is increasingly being used as a means of providing nutritional support. One of the many roles of a nutrition support team (NST) is to assess patient suitability for PEG placement. There has been no publication in the literature reporting the impact of the NST on patient outcome following PEG or in cases where requests for PEG were rejected. We therefore undertook a prospective study examining patient selection and outcomes following PEG, comparing the results with those obtained retrospectively when the hospital did not have a NST. We also examined the outcomes of those patients where the requests for PEG were turned down.

The NST was established at the end of April 1997 and all patients referred for PEG over a 12-month period were included in this audit prospectively. Their suitability for PEG was assessed by the NST. Details of the referral, decision made on patient suitability, reasons for rejection and patient outcomes were recorded. A retrospective study was also conducted, examining the indication and patient outcomes of all the PEG placed in the 12-month period immediately prior to the formation of NST when all requests for PEG were accepted without prior assessment. The table summarizes the results of patient outcomes after PEG placement.

Patient group	Mean age and range	Number of requests	Number of PEG placed	Mortality at (% of patients)		Alive at 6 months (% of patients)	
				30 d	6 months	Eating and PEG removed	Using PEG
Pre-NST	66.2 (17–93)	104	104	17.3	10.6	30.8	41.3
Post-NST	65.3 (17–92)	204	130	20.0	20.0	23.1	36.9

In the 12 months after NST formation, seventy-four out of 204 requests (36%) were rejected. The mean age for the rejected group was 73.9 (range 22–96). In total, 67.5% of those rejected died, with 40.5% dying within 7 d of being assessed; 25.7% of patients in this group were able to eat.

The demand for PEG has increased, which corresponds to the growing number of enterally fed patients (BANS, 1997). However, it would appear that the introduction of NST has not improved patient outcomes. Several explanations for these observations are possible. An increase in awareness of clinical nutrition could have led to more patients being referred even though they were more ill. These results could also reflect a general change in clinical practice whereby a more aggressive approach was adopted. The increase in pressure on acute hospital beds could also push up the demand for PEG, facilitating discharge to nursing homes and rehabilitation units. There were also a large number of inappropriate referrals, not apparent in the pre-NST era, possibly suggesting that clinicians might be using the NST as a convenient way of 'off-loading' their responsibility when it comes to assessing patient suitability for PEG, thus generating a huge workload for the NST.

In conclusion, our results confirmed that the demand for PEG increased after the establishment of NST and although the NST did not appear to impact upon patient outcomes, it remains an important gatekeeper to inappropriate PEG placement. The role of NST extends beyond quantitative measures, which this paper did not set out to address, and serves to improve the quality of the entire PEG service from patient counselling and support to post-procedural care (Brown *et al.* 1987; Elia, 1993).

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Evaluation of the validity and reliability of a computerized nutritional screening tool. By J. SIM, *Department of Nutrition and Dietetics, Arrowe Park Hospital, Arrowe Park Road, Upton, Wirral, Merseyside, L49 5PE*

The publication of The Kings Fund Report (Lennard-Jones, 1992) highlighted the extent of malnutrition in hospitals. The report recommended a multi-disciplinary approach to nutritional support and stated that simple nutritional assessment must form part of the standard patient assessment procedure. One generic screening tool that could be interchangeable between hospitals has yet to be developed. It may be possible for acute hospital settings to use a validated tool from another acute hospital with similar case mixes but further work is required to check for regional variations (BDA Briefing Paper, 1999). The aims of the study were; to evaluate the reliability of the computerized Wirral Hospital Nutritional Screening Tool (WHNST) and to determine its sensitivity and specificity. The WHNST was initially developed in 1992 and updated in 1997, and forms part of the Patient Care Information System (PCIS). The tool was updated with input from dietitians and ward nursing staff. The WHNST is divided into five sections and each section is further divided into four categories. Each category is scored from 0 to 3 and the computer format generates the overall nutritional screening score. This score determines the nutritional risk of patients: low, moderate and high risk.

In the validity study, 103 patients were recruited on admission, forty-six males and fifty-seven females, the mean age was 72.5 years (range 24–94 years, SD 14.1). In the reliability study twenty-nine patients were recruited, twelve males and seventeen females, mean age was 69.4 years (range 18–91 years, SD 20.9). Patients were recruited to both studies across two hospital sites within 24 h of admission to thirteen study wards: medical, surgical, care of the elderly and orthopaedics. Training was provided to all study wards on the use of the WHNST. The nursing staff and the research dietitian completed the WHNST independently and screening scores were derived. The research dietitian then completed a nutritional assessment tool (NAT). The format of the NAT was designed by a group of dietitians and was regarded as the 'gold standard' to determine nutritional status. The NAT included: percentage weight loss over the preceding 3 months, body mass index, mid-arm circumference, triceps skinfold thickness, mid-arm muscle circumference, 24-h dietary recall, estimation of energy requirements, gastrointestinal symptoms, type of diet and mobility. Data from the NAT were assigned a score and a cumulative score was derived. Those patients scoring more than 10 were considered nutritionally at risk. The level of inter-rater agreement between the NAT score and the WHNST score was assessed using kappa statistics. For the inter-observer reliability study two nurses completed the WHNST independently within 24 h of patient admission.

The results of this study revealed that, according to the NAT score, 53% (*n* 55) of the patient sample were nutritionally at risk on admission to hospital. Overall, nursing staff correctly identified 63% (*n* 65) of patients in terms of their nutritional risk classification. Of these patients 42% (*n* 27) were found to be at risk of malnutrition by the nursing staff when compared with the NAT score.

Nurses' WHNST score	NAT score *n* (%)	
	At risk	Not at risk
At risk	27 (26%)	10 (10%)
Not at risk	28 (27%)	38 (37%)

There was poor agreement between the nurses' screening score and the NAT score (kappa 0.3). The nursing staff correctly identified twenty-seven patients as nutritionally at risk with a sensitivity level of 49%. The specificity level was 79%. In the reliability study there was fair to good agreement between two nursing staff completing the WHNST (kappa 0.58) and there was 90% (*n* 26) agreement between the nursing staff regarding nutritional risk classification. The WHNST is not yet sufficiently sensitive for use by nursing staff to categorize patients nutritionally at risk. It is anticipated that sensitivity will improve with further training and hospital-wide implementation of the WHNST.

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The efficacy of dietary advice and oral nutritional supplements in the management of illness-related malnutrition: a systematic review. By C. BALDWIN[1] and T.J. PARSONS[2], [1]*Chelsea & Westminster Hospital, Fulham Road, London SW10 9NH and* [2]*Systematic Reviews Training Unit, Institute of Child Health, 30 Guilford Street, London WC1N 1EH*

It has been suggested that dietary counselling to increase the intake of energy and protein-rich foods is preferable to and should precede the use of oral nutritional supplements in the management of illness-related malnutrition (Stratton & Elia, 1999). This review aimed (1) to determine whether dietary advice (to improve nutritional intake) in adults with illness-related malnutrition can improve survival, weight and anthropometry, and (2) to estimate the size of any additional effect of whole protein enteral food supplements when given in combination with dietary advice. A systematic review of all randomized controlled trials comparing dietary advice with (i) no advice (ii) supplements and (iii) dietary advice plus supplements, has been undertaken, on which this review is based (Baldwin *et al.* 2000). Six electronic databases were searched and unpublished studies have been sought. Studies were assessed independently by two reviewers and data were combined where appropriate. Fifteen trials were identified which met the inclusion criteria (812 participants, from a variety of clinical backgrounds). Duration of follow-up was from 6 weeks to 6 months. Only three trials reported method of randomization and clearly concealed allocation. No trial reported blinded assessment of outcomes. Five trials reported outcomes in a format unusable for meta-analysis.

Comparison and outcome	RR (95% CI)	WMD (95% CI)	[1]No. patients	[2]No. studies	Outcome favours which group?
Dietary advice versus no advice			279 (total)	4 (total)	
Mortality	5.31 (0.28, 102.38)		31	1	No advice
Dietary advice versus supplement			173 (total)	4 (total)	
Mortality	0.33 (0.40, 2.99)		105	3	Advice
Δ weight (kg)		–1.27 (–2.19, -0.27)	74	3	Supplement
Δ energy intake (kcal)		–88 (–157, –19)	112	3	Supplement
Δ grip strength (kg)		0.16 (–1.54, 1.86)	46	1	Advice
Dietary advice versus dietary advice + supplement			351 (total)	8 (total)	
Mortality	0.12 (0.01, 2.25)		190	4	Advice
Δ weight (kg)		–0.99 (–1.53, -0.44)	262	4	Advice + supplement
Δ energy intake (kcal)		–256 (–2920, 2408)	16	1	Advice + supplement
Δ grip strength (kg)		0.14 (–0.62, 0.88)	201	2	Advice

Δ = change in RR = Relative Risk WMD = Weighted mean difference.
[1]*n* = total number of patients on whom result based [2]*n* = total number of studies on which result based.

Gain in weight was significantly higher for groups consuming supplements (with or without advice) compared with advice alone ($P<0.05$). Energy intake was significantly improved in those consuming supplements compared with those receiving advice, but no difference was observed between those consuming supplements and receiving advice compared with those receiving advice alone. These results suggest that supplements have a greater role than dietary advice in the improvement of body weight. Group differences in mortality and change in grip strength were not significant. This review highlights the lack of data addressing the role of dietary advice in the management of illness-related malnutrition and, as such, these results should be treated with caution. There is clearly a need for well-designed, larger scale, randomized controlled trials.

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