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PROCEEDINGS OF THE NUTRITION SOCIETY

ABSTRACTS OF COMMUNICATIONS

The Three Hundred and Eighty-fifth Meeting of the Nutrition Society (One Hundred and Fifty-second of the Scottish Group) was held in the Hugh Nesbit Building, Riccarton Campus, Heriot-Watt University, Edinburgh, on Tuesday and Wednesday, 12/13 *April* 1983, *when the following papers were read:*

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Whole-body protein turnover in diabetics. By D. HALLIDAY, K. S. NAIR, G. C. FORD and J. S. GARROW, *Clinical Research Centre, Watford Road, Harrow HA1 3UJ, Middlesex*

We have measured whole-body leucine metabolism in four healthy controls and in four poorly controlled diabetics before and during insulin treatment. Within the same infusion period employing L-[1-^{13}C]leucine as tracer (Matthews *et al.* 1980). Control subject infusions were of 4 h duration when an isotope plateau was achieved. Infusion of leucine was continued in the diabetics after this time with the addition of a primed constant infusion of Actrapid insulin (8 units + 4·8 units/h). A new plasma leucine isotope plateau was obtained at approximately 2–3·5 h following insulin administration. Results were calculated using a two-pool stochastic model (Waterlow *et al.* 1978). Estimates of protein synthesis were calculated assuming that the leucine content of mixed body proteins is 8%.

	Leucine flux (μmol/kg body-wt per h)		Leucine oxidation (μmol/kg body-wt per h)		Protein synthesis (g/kg body-wt per d)	
Subject	Mean	SD	Mean	SD	Mean	SD
Diabetics						
Pre-insulin	114·6	16·4[a]	29·7	5·0[a]	3·5	0·6[a]
Insulin treated	75·5	10·3[b]	24·1	3·0	2·2	0·5[b]
Controls	81·7	2·9	15·3	2·3	2·7	0·2

[a] Higher than controls ($P<0·05$).
[b] Reduced from pre-insulin state ($P<0·01$).

Both the elevated leucine flux and rate of protein synthesis in poorly controlled diabetics (compared with controls) were reduced by insulin treatment. The observed elevation in the rate of protein synthesis may be contributing to the increased energy expenditure we have observed in similar patients and reported earlier (Nair *et al.* 1983).

Matthews, D. R., Motil, K. J., Rohrbaugh, D. K., Burke, J. F., Young, V. R. & Bier, D. M. (1980). *Am. J. Physiol.* **238**, E473.
Nair, K. S., Garrow, J. S., Halliday, D. & Mahler, R. F. (1983). *Clin. Sci.* **64**, 24P.
Waterlow, J. C., Garlick, P. J. & Millward, D. J. (1978). *Protein turnover in Mammalian Tissues and in the Whole Body*. Amsterdam: North Holland Publishing Co.

Effect of total starvation on protein synthesis in obese women. By K. S. NAIR, G. C. FORD, D. HALLIDAY and J. S. GARROW, *Clinical Research Centre, Watford Road, Harrow HA1 3UJ, Middlesex*

Five obese women (mean ± SD; age 33±5 years, body-weight/height^2 (W/H^2) 41±6) had their endogenous thyroid hormone secretion suppressed with 120 μg triiodothyronine (T_3) daily for 1 week before commencement of the study. All subjects had an energy intake of 9·2 MJ/d during the first week of study followed by total starvation for 2 weeks. T_3, 60 μg, was administered daily during the first and third week of the study. A control group of three obese women (age 27±4 years, W/H^2 43±5) followed the same dietary regimen, but received no T_3. Whole-body protein turnover was measured after an overnight fast at weekly intervals on three consecutive occasions by the method of Matthews *et al.* (1980). Results are given in the Table.

		Leucine flux (mmol/h)		Leucine oxidation (mmol/h)		Protein synthesis (g/d)	
Subject	Week	Mean	SD	Mean	SD	Mean	SD
T_3 group	1	7·0	0·8	1·44	0·20	225·3	26·8
	2	6·0	0·6	1·14	0·10	197·2	21·4
	3	5·4	0·8	0·83	0·10	183·6	35·7
Control	1	6·3	0·7	1·16	0·08	209·3	28·1
	2	6·0	0·4	1·30	0·20	186·2	23·2
	3	5·3	0·6	0·86	0·10	180·0	25·3

Total starvation resulted in an average fall of 19% in leucine flux and 15% in protein synthesis rate. Maintenance of physiological levels of T_3 did not alter the change in leucine flux or protein synthesis rate.

The fall in protein synthesis rate with starvation in our subjects was smaller than that reported in obese subjects on a low-energy protein-free diet (Garlick *et al.* 1980). In a previous study on obese subjects on a low-energy diet we reported that a pharmacological dose of T_3 caused an increase in protein synthesis, which was not observed in the present study (Nair *et al.* 1981). This difference in results may reflect differences in the response to starvation or semi-starvation, or indicate errors in the glycine-NH_4 end-product method used in the previous study to measure the rate of protein synthesis.

Garlick, P. J., Glugston, G. A. & Waterlow, J. C. (1980). *Am. J. Physiol.* **238**, E235.
Matthews, D. E., Motil, K. J., Rohrbaugh, D. K., Burke, J. F., Young, V. R. & Bier, D. M. (1980). *Am. J. Physiol.* **238**, E473.
Nair, K. S., Baldwin, I., Halliday, D. & Garrow, J. S. (1981). *Clin. Sci.* **61**, 9P.

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The sensitivity of protein turnover in different muscle types to fasting. By P. W. EMERY, L. COTELLESSA, M. HOLNESS and M. J. RENNIE, *University College London Medical School, Rayne Institute, University Street, London WC1E 6JJ*

It has been suggested (Jefferson *et al.* 1980) that red skeletal muscles and cardiac muscle lose protein less quickly during fasting than pale muscles with more white fibres, but results are inconsistent (Spence & Hansen-Smith, 1978). We have, therefore, measured the rate of protein synthesis and the efficiency of translation of RNA in cardiac and skeletal muscles in fasted rats, as well as in the smooth muscle of the gastrointestinal tract which may be the source of the increased urinary excretion of 3-methylhistidine in fasted rats (Cotellessa *et al.* 1983).

Male Wistar rats (100 g) were fasted for periods of up to 4 d. Tissue protein synthesis rates were determined using a large intravenous dose of [^{3}H]phenylalanine (Garlick *et al.* 1980); protein and RNA were measured by standard methods.

	Total protein content (mg)				Protein synthetic rate (%/d)				RNA activity (g protein synthesized/g RNA per d)			
Tissue	Day 0	Day 3	% Difference	*P*	Day 0	Day 3	% Difference	*P*	Day 0	Day 3	% Difference	*P*
Carcass	9540	8790	8	<0·01	—	—	—	—	—	—	—	—
Intestinal smooth muscle	490	340	31	<0·01	75	65	13	NS	10·3	10·3	0	NS
Heart	67·8	64·6	5	NS	18·7	10·3	4·5	<0·01	10·2	7·5	26	NS
Soleus	6·69	6·59	2	NS	13·7	6·9	50	<0·01	—	—	—	—
Mixed muscle	13·4	12·6	6	NS	11·4	5·6	51	<0·01	10·3	5·1	50	<0·01

NS, not significant.

During the first 3 d of fasting the gut lost 31% of its protein, while the carcass lost only 8%; none of the individual muscles examined had lost a significant amount of protein at this time. By the fourth day of fasting both soleus (red muscle) and plantaris (pale muscle) had lost 18% of their protein, although heart lost only 9% of its protein. In heart the RNA activity did not change significantly whereas in skeletal muscle it was decreased by 50% on the third day of fasting. In cardiac and skeletal muscles, protein synthesis decreased steadily throughout the period of fasting; protein degradation in skeletal muscle did not rise until the fourth day of fasting. In contrast, in intestinal smooth muscle the rate of protein synthesis and the RNA activity did not change significantly during 3 d of fasting, suggesting that the loss of protein was due to an increase in protein degradation.

This work was supported by The Cancer Research Campaign, The Wellcome Trust, The Medical Research Council and The Nuffield Foundation. L.C. is a Fellow of the advanced training programme of The Italian Labour Department and the EEC.

Cotellessa, L., Emery, P. W. & Rennie, M. J. (1983). *Proc. Nutr. Soc.* **42**, 26A.
Garlick, P. J., McNurlan, M. A. & Preedy, V. R. (1980). *Biochem. J.* **192**, 719.
Jefferson, L. S., Boyd, T. A., Flain, K. E. & Peavy, D. E. (1980). *Biochem. Soc. Trans.* **8**, 282.
Spence, C. A. & Hansen-Smith, F. M. (1978). *Br. J. Nutr.* **39**, 647.

Human placental amino acid transfer and metabolism in oxygenated and anoxic conditions. By PAUL PENFOLD,* NICHOLAS P. ILLSLEY,* PAUL PURKISS† and PATRICIA JENNINGS,† **Division of Perinatal Medicine* and †*Division of Inherited Metabolic Diseases, Clinical Research Centre, Watford Road, Harrow HA1 3UJ, Middlesex*

Materno–foetal amino acid transfer across placental tissue was investigated by the perfusion of an isolated lobular region of the normal term placenta. In each perfusion a dual circulation was used with an 'open' maternal circulation and a 'closed' foetal circulation. The perfusate used in both circulations was a Krebs–Ringer bicarbonate/phosphate buffer containing twenty amino acids at concentrations similar to those found in the maternal plasma at term. Placental amino acid transfer was initially studied in an oxygenated preparation, followed by a second series of perfusions using an oxygen-free perfusate. It was found after 2 h of oxygenated perfusion that there was an average increase in concentration of amino acids of 40% in the foetal circulation, suggesting that active transport had taken place. The specific changes compared well to in vivo results, particularly from premature newborns. In the perfused preparation as in cord plasma, all the essential amino acids increased in concentration, as did a number of the non-essential amino acids, while glutamate and serine concentrations had decreased. Several differences existed between the in vitro and in vivo concentration values, including differences in the uptake of asparagine and alanine. This suggested that transfer control was a complex procedure resulting from interaction between foeto–placental and maternal components. An increase similar to that seen for the oxygenated perfusions in foetal amino acid concentrations was observed in the anoxic perfusions, supporting previous findings that oxidative metabolism is not required for amino acid transport. Further studies revealed that there was a two- to three-fold increase in glucose utilization during the anoxic perfusions, demonstrating that amino acid transfer was powered by glycolysis, and suggesting that as long as the substrate was available to meet energy demands, the mode of production was not critical. The same conclusion was drawn from the protein synthesis results in which [^{14}C]alanine incorporation into protein did not differ significantly between the two conditions of perfusion. The ability of the placenta to transport amino acids from maternal to foetal circulations suggests that chronic foetal hypoxia alone is not a major cause of intra-uterine growth retardation and that other conditions, e.g. restricted substrate supply, are involved.

Isolation, characterization and utilization of carp (*Cyprinus carpio*) enterocytes for the study of intact protein absorption. By S. L. MASON and R. ASH, *School of Applied Biology, University of Bradford, Bradford BD7 1DP, W. Yorks*

Enterocytes were isolated from specific portions of the carp intestine essentially according to the method described by Watford *et al.* (1979), adapted, where necessary, for application to the freshwater teleost.

Populations of isolated cells were characterized with respect to morphological intactness and metabolic viability by reference, where appropriate, to various criteria established with mucosal scrapes. Membrane integrity was assessed by reference to the ability of the isolated cells to exclude the vital dye, Trypan Blue (>90% of cells excluded the dye), and by their capacity to maintain normal levels of various intracellular components. Thus, lactate dehydrogenase (*EC* 1.1.1.27) activity (84·31 units/g wet weight at 20°) and total adenine nucleotide content (16·61 μmol/g dry weight), when compared with values derived from mucosal scrapes, demonstrated that a high proportion (83 and 96% respectively) of the isolated cells retain their integrity throughout the isolation period. During a subsequent 1 h incubation period these percentage values decreased to 80 and 75% respectively. Despite the overall drop in total adenine nucleotide concentration, the relative concentrations (energy charge condition) of the nucleotides within the enterocytes immediately after isolation (0·74), and after 1 h incubation (0·69), compared favourably with the value determined (0·78) for freeze-clamped mucosal scrapes. The intracellular potassium content of isolated enterocytes (303 nmol/mg dry weight), although only 66% of that of mucosal tissue, rose to 83% of this value during the subsequent 1 h incubation.

Oxygen consumption in the presence of selected substrates was found to increase relative to endogenous O_2 consumption (mean ± SE; 1·34±0·57 μmol O_2/min per g dry weight at 20°) in all cases. Percentage increases were: 10 mM-glucose, 32; 5 mM-propionate, 63; 5 mM-butyrate, 71; 5 mM-glutamate, 89; 5 mM-glutamine, 90; 5 mM-alanine, 93; 10 mM-2-oxoglutarate, 126.

A qualitative method was used to investigate the absorption of intact protein (horseradish peroxidase) by isolated enterocytes. Results, in the form of electron micrographs, demonstrated that horseradish peroxidase taken up by pinocytosis was subsequently located in intracellular tubules, vesicles and vacuoles.

Watford, M., Lund, P. & Krebs, H. A. (1979). *Biochem. J.* **178**, 589.

Metabolism of [1-^{14}C]methionine and [1-^{14}C]methionine hydroxy analogue by broiler chicks. By C. LINDA SAUNDERSON, *ARC Poultry Research Centre, Roslin, Midlothian EH25 9PS*

Many studies have shown that methionine hydroxy analogue (MHA) is inferior to added methionine (Met) as a source of dietary methionine for poultry (e.g. van Weerden *et al.* 1982). Two factors may account for this difference (1) MHA is not as well absorbed through the gut wall as Met and (2) the keto acid formed during conversion of MHA to Met is more easily excreted than either the hydroxy or amino acid forms.

To further investigate the metabolism of MHA, broiler chicks (200–500 g) were given [1-^{14}C]Met or [1-^{14}C]MHA (0·5 μg/100 g body-weight) by intubation into the crop or by intraperitoneal (i.p.) injection. Output of $^{14}CO_2$ by the birds was measured over the 6 h following administration of the labelled material, using a sealed glass metabolism chamber. After 6 h the animals were killed, tissue samples rapidly excised and ^{14}C incorporation into proteins measured. ^{14}C in solid excreta was assessed by liquid scintillation counting of acid extracts. The results are shown in the Table.

(Three birds were used in each of the four treatments)

	[1-^{14}C]Met				[1-^{14}C]MHA			
	i.p. Injection		Intubation		i.p. Injection		Intubation	
	Mean	SEM	Mean	SEM	Mean	SEM	Mean	SEM
Excretion (% dose given)								
$^{14}CO_2$	4·5	1·11[a]	4·2	0·18[a]	4·8	0·73[a]	3·4	0·73[a]
Faeces + urine	1·8	0·06[a]	4·3	0·55[a]	20·0	2·49[b]	16·9	1·10[b]
Protein incorporation (counts/min per g wet tissue)								
Liver	9162	1489[a]	11 785	1843[a]	11 897	1701[a]	10 270	231[a]
Breast muscle	4097	499[a]	4567	769[a]	2030	66[b]	2478	464[b]
Heart muscle	6285	707[a]	7837	927[a]	4588	439[b]	3755	365[b]

[a,b]Values in the same line which do not share a common superscript are significantly different ($P<0·01$).

The results show that the route of administration has no effect on oxidation, excretion or protein incorporation of either material. However, by both routes, much more ^{14}C appears in the excreta from [1-^{14}C]MHA than from [1-^{14}C]Met. Incorporation of ^{14}C into protein in liver shows no difference with either material, yet significantly lower incorporation from [1-^{14}C]MHA is evident in peripheral tissues (heart and skeletal muscles).

The results suggest that the increased excretion of MHA and its metabolites lowers the supply of Met to the growing tissues and may well account for the inferiority of MHA as a source of dietary methionine in poultry.

van Weerden, E. J., Bertram, H. L. & Schutte, J. B. (1982). *Poult. Sci.* **61**, 1125.

Lactose synthetase (*EC* 2.4.1.22) activity in rats receiving diets of varying protein adequacy. By Y. K. C. MANSARAY and R. GRIMBLE, *Nutrition Department, Southampton University, Southampton SO9 3TU*

Lactose is synthesized in mammary tissue by lactose synthetase (*EC* 2.4.1.22) (LS) which is a complex of two proteins, α-lactalbumin (LA) and glycoprotein β-D-galactosyltransferase (*EC* 2.4.1.38) (GT) (Brew, 1970). Previous studies have shown that protein deficiency in rats causes a greater reduction of α-lactalbumin than of other milk proteins (Grimble, 1981).

The present study examines the effect of diets of varying protein adequacy on LS and GT activities. Pregnant Wistar rats, receiving a standard laboratory ration, were caged separately. After successful parturition, litter size was adjusted to nine and maternal diet changed to contain either 60, 100 or 200 g protein/kg as dried skimmed milk and casein, supplemented with methionine. The diets were fed *ad lib.* for 14 d. Pup growth was monitored as an index of lactational performance. The dams were killed on the 14th day of lactation and abdominal mammary tissue rapidly removed and deep frozen. LS and GT activities were measured in whole-tissue homogenates, as described by Vonderhaar (1977). The effect of added bovine LA (10 mg/g tissue) on LS activity was measured. The results are summarized in the Table.

Dietary protein (g/kg)	*n*	Enzyme activity† LS Mean	LS SE	GT Mean	GT SE	Ratio LS:GT Mean	Ratio LS:GT SE	Stimulation of LS by added LA (%) Mean	Stimulation of LS by added LA (%) SE	Mean pup growth (g/d) Mean	Mean pup growth (g/d) SE
200	9	35·8	3·5	18·1	2·2	2·0	0·1	13·6	6·6	1·81	0·13
100	8	30·4	1·9	17·5	2·0	1·9	0·2	18·7	6·5	1·36*	0·18
60	9	25·9*	2·8	23·8	2·7	1·1***	0·1	48·1**	10·5	0·79***	0·06

Significantly different from 200 g protein/kg diet group: *$P<0.05$, **$P<0.01$, ***$P<0.001$.
†Enzyme activity expressed as nmol product formed/30 min per mg protein at 37°.

The nutritional status of the dams decreased with dietary protein concentration. Weight changes during 14 d lactation were +32, +12 and −45 g for the groups receiving 200, 100 and 60 g protein/kg diet respectively. However, while lactational performance and LS activity fell with decreasing protein intake, GT activity did not and the value for the 60 g protein/kg group was significantly above that of the 100 g protein/kg group ($P<0.05$). Exogenous LA caused a marked stimulation of LS activity in the former group. The reduced LS activities seen in the group receiving the most inadequate diet may be due to a relative deficiency in LA production in mammary tissue, as has been suggested from previous studies in milk composition. It is not known whether decreased lactose production results from the enzyme changes observed.

We are grateful to Nestlé for financial support.

Brew, K. (1970). *Essays Biochem.* **6**, 93.
Grimble, R. (1981). *Ann. Nutr. Metab.* **25**, 221.
Vonderhaar, B. (1977). *Endocrinology* **100**, 1423.

Inhibition of tryptophan metabolism by leucine: an explanation for the pellagragenic effect of excess dietary leucine. By DAVID A. BENDER, *Courtauld Institute of Biochemistry, The Middlesex Hospital Medical School, London W1P 7PN*

Gopalan & Srikantia (1960) suggested that an important factor in the aetiology of pellagra among people whose staple diet was *Sorghum vulgare* was the relative excess of leucine in the proteins of the cereal. Magboul & Bender (1983) have confirmed that feeding rats on diets providing 15 g leucine/kg diet results in depletion of tissue nicotinamide nucleotides—biochemical pellagra. They also showed that in vitro leucine is a competitive inhibitor of the rate-limiting enzyme of the oxidative pathway of tryptophan metabolism, kynureninase. Ghafoorunissa & Narasinga Rao (1973) also suggested that a high-leucine diet increased the activity of picolinate carboxylase, and so reduced the proportion of tryptophan metabolites available for nucleotide synthesis.

The effect of a high-leucine diet (Magboul & Bender, 1983) on the metabolism of tryptophan in vivo in the rat has been assessed by measuring the production of $^{14}CO_2$ from [^{14}C]tryptophan. The metabolism of [methylene-^{14}C]tryptophan was reduced in animals fed on a high-leucine diet, indicating inhibition of kynureninase in vivo, and hence confirming the results of the in vitro studies. The production of $^{14}CO_2$ from [benzene ring-^{14}C]tryptophan was higher in animals fed on a high-leucine diet, indicating increased activity of picolinate carboxylase.

The combined effect of reduced oxidative metabolism of tryptophan, resulting from inhibition of kynureninase, and increased diversion of tryptophan metabolites away from nucleotide synthesis and towards total oxidation, resulting from increased activity of picolinate carboxylase, will be a considerable reduction in the synthesis of nicotinamide nucleotides from tryptophan. When the diet is poor in available niacin and marginal with respect to tryptophan this will precipitate pellagra.

	$^{14}CO_2$ production from:							
	[Methylene-^{14}C]tryptophan				[Benzene ring-U-^{14}C]tryptophan			
Diet ...	Control		High leucine		Control		High leucine	
	Mean	SE	Mean	SE	Mean	SE	Mean	SE
Total (10^3 dpm/4 h)	159	18	91$^{\bullet}$	11	56·9	3·3	82·8$^{\bullet}$	8·6
Peak (10^3 dpm/4 h)	16·1	1·7	8·5$^{\bullet\bullet}$	0·8	5·2	0·3	7·9$^{\bullet\bullet}$	0·7
Half-life (min)	48·6	0·3	63·4$^{\bullet\bullet\bullet}$	0·7	56·8	0·3	53·8$^{\bullet\bullet\bullet}$	0·3

dpm, Disintegrations per minute.

Significance of difference from control values by Student's *t* test: $^{\bullet}P<0.05$, $^{\bullet\bullet}P<0.01$, $^{\bullet\bullet\bullet}P<0.001$.

Ghafoorunissa & Narasinga Rao, B. S. (1973). *Biochem. J.* **134**, 425.
Gopalan, C. & Srikantia, S. G. (1960). *Lancet* **i**, 954.
Magboul, B. I. & Bender, D. A. (1983). *Br. J. Nutr.* **49**, 321.

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Inhibition of tryptophan metabolism by oestrogens: implications for the interpretation of the tryptophan load test for vitamin B_6 status in women receiving oestrogens. By DAVID A. BENDER, *Courtauld Institute of Biochemistry, The Middlesex Hospital Medical School, London W1P 7PN*

Bender & Wynick (1981) have suggested that the abnormalities of tryptophan metabolism that have been observed in women receiving oestrogens, which have been interpreted as indicating oestrogen-induced vitamin B_6 deficiency, can be accounted for by competitive inhibition of kynureninase by oestrogen conjugates.

The effect of oestradiol on the metabolism of tryptophan in vivo has been assessed in rats by measuring the production of $^{14}CO_2$ after the administration of [ring-2-^{14}C]tryptophan to estimate tryptophan oxygenase activity and [methylene-^{14}C]tryptophan to estimate kynureninase activity. The administration of 500 μg oestradiol/kg body-weight reduced the production of $^{14}CO_2$ from both positional isomers of [^{14}C]tryptophan. This confirms that oestradiol does not induce tryptophan oxygenase, a finding for which other evidence has also been presented (Bender *et al.* 1983), and that kynureninase is inhibited in vivo as it is in vitro by oestrogens or their metabolites. The effect of oestradiol on the production of $^{14}CO_2$ from [methylene-^{14}C]tryptophan was compatible with competitive inhibition of kynureninase with respect to its substrate—a delay in the time of maximum production of $^{14}CO_2$ and a reduction in the rate constant of the decay phase of the curve, but no change in either the total amount of $^{14}CO_2$ recovered or the peak rate of production. The administration of 10 mg vitamin B_6/kg body-weight did not ameliorate the effects of oestradiol on tryptophan metabolism.

	$^{14}CO_2$ production from:							
	[Ring-2-^{14}C]tryptophan				[Methylene-^{14}C]tryptophan			
	Control		Oestradiol		Control		Oestradiol	
	Mean	SE	Mean	SE	Mean	SE	Mean	SE
Total (dpm/4 h)	28·8	4·1	26·6	3·5	24·6	1·7	27·6	1·6
Peak (dpm/10 min)	3·36	0·63	2·59	0·26	2·18	0·18	2·07	0·67
Time to peak (min)	60	—	60	—	80	—	110	—
Half-life (min)	37·4	1·1	43·6**	2·0	52·4	0·5	57·6***	0·9

dpm, Disintegrations per minute.
Significance of difference from control values by Student's *t* test: **$P<0.01$, ***$P<0.001$.

It is concluded that the abnormalities of tryptophan metabolism that have been observed in women receiving oestrogens are the result of simple inhibition of kynureninase by oestrogen metabolites, and do not reflect oestrogen-induced vitamin B_6 deficiency. The tryptophan load test would seem to be unreliable as an index of vitamin B_6 nutrition in such cases, and the administration of vitamin B_6 supplements may not be appropriate.

Bender, D. A., Laing, A. E., Vale, J. A., Papadaki, L. & Pugh, M. (1983). *Biochem. Pharmacol.* **32**, 843.
Bender, D. A. & Wynick, D. (1981). *Br. J. Nutr.* **45**, 269.

Plasma amino acids in acute fatty liver of pregnancy. By W. M. HAGUE, *Queen Charlotte's Maternity Hospital, Goldhawk Road, London W6* and J. C. ALLEN, *Children's Hospital, Western Bank, Sheffield* (Introduced by J. A. MILNE)

Acute fatty liver of pregnancy is a rare but serious disease of the last trimester of pregnancy with a high maternal and foetal mortality (Hague *et al.* 1983). Following a short prodromal phase, patients develop hepatic failure often associated with renal failure and disseminated intravascular coagulopathy; the aetiology is unknown. Survival is accompanied by complete resolution of liver function and no subsequent recurrence has been recorded. The diagnosis is established by histology of the liver which shows microvesicular fat distributed throughout the liver lobule with periportal sparing, little necrosis and minimal disturbance of hepatic architecture. The only clinical conditions known with similar histology are Reye's syndrome in children, ornithine transcarbamylase deficiency in neonates, and following large doses of intravenous tetracycline.

Serial amino acid levels in plasma have only been reported in three cases. In two, Weber *et al.* (1978) demonstrated a hypoaminoacidaemia which they contrasted with the hyperaminoacidaemia of Reye's syndrome. Burroughs *et al.* (1982) described one patient with initially high levels of amino acids falling, following delivery, to normal levels.

We have documented plasma amino acid levels in a further two patients. These were measured using a Rank Hilger Chromaspek with ninhydrin detection following storage of samples at −20°. Samples from each patient were taken either in the fasting state or during treatment with intravenous saline or dextrose and compared with the normal range in fasting adults.

In one patient, delivery of stillborn twins at 34 weeks gestation was followed by a stormy puerperium which the mother eventually survived. She showed an initial hyperaminoacidaemia with a subsequent return to low levels. The other presented at 32 weeks and gradually deteriorated, dying following caesarean section in metabolic failure associated with a severe coagulopathy. Her amino acid levels gradually increased, being maximal immediately prior to her death.

These results compare with the patient of Burroughs *et al.* (1982) and suggest a similar metabolic disturbance to that found in Reye's syndrome.

Burroughs, A. K., Seong, N. K., Dojcinov, D. M., Scheuer, P. J. & Sherlock, S. V. P. (1982). *Q. Jl. Med.* New Series LI, **204**, 481.

Hague, W. M., Fenton, D. W., Duncan, S. L. B. & Slater, D. (1983). *J. Roy. Soc. Med.* (In the Press.)

Weber, F. L., Snodgrass, P. J., Powell, D. E., Rao, P., Huffman, S. L. & Brady, P. G. (1978). *J. Lab. Clin. Med.* **94**, 27.

Copper, zinc and jejuno-ileal bypass surgery. By M. J. FORD and W. SIRCUS, *Western General Hospital, Crewe Road, Edinburgh* and I. FRAZER, S. I. TERRY and J. F. MUNRO, *Eastern General Hospital, Seafield Street, Edinburgh* and N. F. SUTTLE, *Moredun Research Institute, Gilmerton, Edinburgh*

Jejuno-ileal anastomosis has been an accepted treatment for morbid obesity and patients lose up to 40% of their pre-operative weight in the first 24 months after surgery. Clinically significant deficiencies of potassium, magnesium, calcium and iron may occur during this period, requiring oral or parenteral replacement. The present study was stimulated by observations on a patient who developed clinical deficiency of zinc and possibly copper after jejuno-ileal bypass, and was found to have abnormally low serum levels of Cu and Zn. Accordingly, we measured plasma Cu and Zn on forty occasions in eighteen other subjects who had undergone bypass surgery but who had no clinical evidence of Cu or Zn deficiency. Blood was also obtained from sixteen age and sex comparable obese subjects with no history of gastrointestinal surgery or chronic illness (obese control group) and an age and sex comparable normal group. The results are given in the Table.

Plasma copper and zinc concentrations (μg/l) *in obese subjects before and after jejuno-ileal bypass surgery*

	Obese controls			Bypass group: Before surgery			Bypass group: After surgery			Normal subjects
	Mean	SD	*n*	Mean	SD	*n*	Mean	SD	*n*	(range)
Plasma Cu	1185	238	16	1202	170	4	857	137	40	990–1390
Plasma Zn	888	202	16	913	131	4	713	159	40	790–1090

The bypass group had a mean pre-operative weight of 120 kg and a mean maximum post-operative weight loss of 41 kg. Mean plasma Cu and Zn concentrations were significantly lower in the bypass group after surgery than in either the obese control group ($P<0.01$) or the bypass group pre-operatively ($P<0.05$) (Table). There were, however, no significant correlations between plasma Cu and Zn concentrations and the time after bypass or post-operative weight loss at the time of sampling. The plasma Cu and Zn concentrations of two patients who underwent reversal of surgery returned to normal. Plasma Cu and Zn concentrations in the bypass group were invariably greater than those observed in the patient who had developed acrodermatitis, alopecia, fits, a pale waxy skin and a macrocytic anaemia and who had responded to Cu and Zn therapy: her values were 220 μg Cu and 400 μg Zn/l, 14 months after surgery. Nevertheless, we recommend the inclusion of Cu and Zn in the replacement therapy of patients undergoing bypass surgery.

Serum proteins in malnourished patients before and after enteral nutrition. By M. J. HALL,* A. P. MANNING* and J. T. WHICHER,† **University Department of Medicine* and †*Department of Chemical Pathology, Bristol Royal Infirmary, Marlborough Street, Bristol*

A low serum albumin is used to identify patients with malnutrition (Mullen *et al.* 1980) but is unsatisfactory in monitoring nutritional support because of its slow turnover (Shetty *et al.* 1979). Serum transferrin, pre-albumin and retinol-binding protein have shorter half-lives, return to normal more rapidly after surgery than serum albumin (Young *et al.* 1979) and have been proposed as better indicators of nutritional improvement (Shetty *et al.* 1979).

Thirty-seven clinically malnourished patients were assessed by anthropometric measurements and serum protein estimations; twenty-three subsequently received supplementary enteral nutrition via a fine bore nasogastric tube for a mean of 22 (range 9–44) d.

	Albumin (g/l)		Transferrin (g/l)		Pre-albumin (mg/l)		Retinol-binding protein (mg/l)	
Hypoproteinaemic patients†	Mean	SE	Mean	SE	Mean	SE	Mean	SE
Before nutrition	28·6	1·2	1·6	0·1	165·6	20·0	26·6	4·3
After 14 d	28·0	1·4	2·2	0·2	245·6	29·5	50·9	9·2
n	9		6		9		9	
P	NS		NS		<0·01		<0·05	

†Albumin <35 g/l, transferrin <2·0 g/l, pre-albumin <300 mg/l or retinol-binding protein <50 mg/l before enteral nutrition.
NS, not significant.

There were significant correlations, before nutritional support, between serum albumin (mean ± SE; 31·6±1·2 g/l), transferrin (2·0±0·1 g/l), pre-albumin (198±23 mg/l) and retinol-binding protein (39±4·6 mg/l) but not between serum proteins and percentage of ideal weight (70·4±1·7), triceps skinfold thickness (41·9±3·1% standard) or arm-muscle circumference (70·9±1·3% standard).

The increases in serum proteins of the fed patients after 7, 14, 21 or >21 d of enteral nutrition were not statistically significant, but there were significant rises in pre-albumin and retinol-binding protein after 14 d in patients who were initially hypoproteinaemic.

In this group, pre-albumin rose in all patients and retinol-binding protein in all except one. Serum albumin significantly decreased after 7 d of enteral nutrition (28·9±1·1 *v.* 26·2±1·3 g/l; $P<0.05$).

We conclude that measurements of serum pre-albumin and retinol-binding protein are useful in the assessment of malnutrition and are superior to transferrin and albumin in monitoring the response to supplemental enteral nutrition in hypoproteinaemic patients.

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Failure of a continuous infusion of naftidrofuryl to modify protein metabolism following elective abdominal surgery. By J. A. INGLIS,* M. B. CLAGUE and I. D. A. JOHNSTON, *Department of Surgery, Royal Victoria Infirmary, Newcastle upon Tyne NE1 4LP*

The catabolic loss of body nitrogen in the fasted post-operative patient may arise in part from inhibition of intracellular metabolic pathways and the need of the body to derive carbohydrate intermediates directly from amino acids to fuel the TCA cycle (Burns *et al.* 1978). Reversal of any inhibition by simple means is an attractive proposition and naftidrofuryl (Praxilene®) is a pharmacological agent believed to stimulate cellular metabolism which has been shown to reduce urinary N losses following elective surgery of moderate severity (Burns *et al.* 1981), although the mechanism involved is not known.

To evaluate this further, a study was planned using eighteen female patients admitted for elective cholecystectomy. Patients were randomly allocated to receive either a continuous infusion of naftidrofuryl (400 mg/d) in dextrose/saline solution, commencing at surgery and continuing for 72 h, or the crystalloid solution alone. Urine was collected throughout this period and urinary N excretion determined using a modified Kjeldahl method. Rates of body protein synthesis and breakdown were also determined in the fed state, pre-operatively, and while patients were still fasted 48 h after surgery, employing a constant rate of infusion of L-[1-^{14}C]leucine (James *et al.* 1974). Appropriate Ethical Committee approval was granted and informed consent obtained from individual patients.

Both groups were matched for age, body-weight, activity of disease, extent of surgical stress at the time of their post-operative study and body protein metabolism prior to surgery. The results of the post-operative studies are shown in the Table.

	Urinary nitrogen excretion (g/kg)						Body protein metabolism (g/kg per d)						
	2nd post-op. day			3-d cumulative			Synthesis (S)		Breakdown (B)		Balance (S − B)		
	Mean	SD	*n*	Mean	SD	*n*	Mean	SD	Mean	SD	Mean	SD	*n*
Naftidrofuryl	0·076	0·020	9	0·233	0·067	9	3·70	1·29	4·32	1·38	−0·62	0·25	8
Controls	0·107	0·057	9	0·284	0·082	9	3·43	0·58	4·05	0·72	−0·63	0·19	8

No significant protein N-sparing effect of naftidrofuryl in fasted post-operative patients could be demonstrated by either of the two independent methods of assessing body protein losses used in this study. This conflicts with previous results (Burns *et al.* 1981) but could arise from the different methods of drug administration (i.e. continuous *v.* bolus injection).

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*Present address: Dryburn Hospital, Durham DH1 5TW.

Post-operative jejunostomy feeding in upper gastrointestinal surgery. By J. GUEST,* C. A. RUSSELL, S. J. EVANS and B. L. DOWLING, *Northampton General Hospital, Cliftonville, Northampton NN1 5BD*

After surgery of the upper gastrointestinal tract, a full oral diet may not be recommenced for 8–10 d, although the small bowel and colon are functioning normally. Twenty-one patients, all suffering from upper gastrointestinal malignancy and with an oesophageal anastomosis, were each fed post-operatively via a Nutricath 'S' catheter (Vygon UK Ltd, Cirencester). The catheter was inserted pre-operatively in the proximal jejunum using a standard serosal tunnel technique (Delaney *et al.* 1973) with the site of insertion into the jejunum stitched to the anterior wall, as described by Page *et al.* (1979). The catheter was designed for tunnelled central venous cannulation and has a removable hub assembly which facilitates needle jejunostomy. The i.d. of 1 mm is satisfactory for most proprietary tube feeds. Jejunal feeding was started on the second post-operative day (day 2) with half-strength Isocal (Mead Johnson, Slough) and by day 5, 120 ml of full strength Isocal was given (12 558 kJ (3000 kcal), 16 g nitrogen in 2880 ml) until an oral diet was established (mean time 9·5 d).

Mean pre-operative serum albumin and transferrin were in the normal range but fell significantly ($P<0.01$) by day 5; albumin was still significantly lower ($P<0.01$) at 1 month (see Table).

	Pre-op.	5 d	1 month
Albumin (g/l)	38	29	32
Transferrin (g/l)	2·8	1·5	2
Pre-albumin (mg/l)	172	71	144
Triceps skinfold thickness (mm)	10·2	11·1	10·6
Mid-arm muscle circumference (mm)	274	280	257
Weight (kg)	64·8	65·3	59·4

Mean pre-operative pre-albumin values were below the normal range and also fell ($P<0.025$) by day 5. The anthropometric measurements were unchanged at day 5 although the mid-arm muscle circumference had fallen significantly ($P<0.01$) at 1 month.

A patient in whom the catheter became dislodged had a laparotomy and a second catheter inserted; subsequently non-absorbable material has been used.

Abdominal distension occurred in five patients and was usually controlled by the reduction of feed volume. Diarrhoea (seven cases) was controlled by codeine phosphate given via the jejunostomy. No patient required total parenteral nutrition (TPN) in 159 d of patient feeding.

The simplicity of insertion and management, the lack of serious complications and the financial savings (cost per day of £7·20 compared with £60·00 for TPN) should encourage the use of this technique.

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*Present address: Hammersmith Hospital, Du Cane Road, London W12.

The effect of supplemental enteral nutrition on anthropometric measurements, nitrogen balance and pre-existing oral intake. By M. J. HALL,* A. P. MANNING* and C. SYMES,† **University Department of Medicine* and *†Department of Dietetics, Bristol Royal Infirmary, Marlborough Street, Bristol*

Enteral nutrition is widely used to restore nutritional status in malnourished patients but few studies have shown significant improvement in anthropometric and other nutritional measurements (Woolfson *et al.* 1976; Smith *et al.* 1982; Jones *et al.* 1983). Continuous infusion of nutrients through a fine bore nasogastric tube facilitates continued oral intake provided there is patient compliance.

Twenty-three malnourished medical patients received supplemental enteral nutrition which provided 9·8 g nitrogen and 8550 kJ (2040 kcal)/d for a mean of 22 (range 9–44) d. Anthropometric measurements, N balance calculated from 24 h urinary urea excretion and approximate oral intake of N and energy were determined before feeding and weekly during nutritional support.

The Table summarizes the anthropometric measurements after 7 d of enteral nutrition.

	% Ideal weight (I)		% Previous weight (P)		Triceps skinfold thickness (TSF) (% standard)		Arm-muscle circumference (AMC) (% standard)	
	Mean	SE	Mean	SE	Mean	SE	Mean	SE
Before enteral nutrition	70·4	2·0	76·2	1·6	44·2	3·2	71·8	1·5
After 7 d	76·3	1·8	82·5	1·2	48·2	3·1	74·9	1·6
n	22		20		21		21	
P	<0·001		<0·001		<0·01		<0·001	

Further significant increments occurred after 14 d (I, P, TSF, AMC), 21 d (TSF) and >21 d (I, P, TSF).

No significant decrease occurred in oral N (mean ± SE; 8·6±0·9 g/d) and non-protein energy (4690±586 kJ (1120±140 kcal)/d) intakes throughout the period of the study. N balance increased from 0·7±1·1 to 6·1±1·1 g/d ($P<0·001$) after 7 d and remained at this level.

We conclude that supplemental enteral nutrition is an effective method of providing nutritional support and does not suppress existing oral intake when given as a continuous infusion via a fine bore nasogastric tube.

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Can nutritional measurements at the start of total parenteral nutrition predict catheter-related sepsis? By S. YOUNG, O. J. GARDEN, J. E. A. SQUIRES, A. S. MCLELLAND and A. SHENKIN, *Surgical Nutritional Advisory Group and Departments of Surgery and Biochemistry, Royal Infirmary, Castle Street, Glasgow*

Catheter-related sepsis remains the most serious complication of total parenteral nutrition (TPN) (Blackett *et al.* 1978). Since nutritional assessment in the pre-operative period has been used to predict post-operative septic complications (Simms *et al.* 1982), we have studied the use of similar measurements as possible predictors of catheter-related sepsis.

Ninety-five surgical patients, requiring TPN, had a total of 115 silicone elastomer catheters inserted by the tunnelled deltocephalic route under aseptic conditions. The following measurements were made within 3 d of catheter insertion: serum albumin (ALB), transferrin (TF), total body-weight (TBW), triceps skinfold thickness (TSF) and mid-arm muscle circumference (MAMC). A prognostic index (PI) was calculated using the method modified by Simms *et al.* (1982). Catheter-related sepsis was defined as a pyrexia returning to normal after catheter removal with at least two positive cultures from the catheter tip, central venous blood or peripheral blood.

There were ninety-eight catheters in the non-infected group (NI), and seventeen in the infected group (I). The mean age and the sex distribution were similar in both groups. There was no significant difference in the duration of TPN between the two groups (mean ± SD; NI, 16·8±11·5 d; I, 16·2±8·5 d).

Nutritional measurements and prognostic index for both groups are shown in the Table.

	% Ideal weight		TSF (% standard*)		MAMC (% standard*)		ALB (g/l)		TF (g/l)		PI	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Infected	91·6	17·2	76·2	23·9	83·7	9·3	28·7	5·4	1·7	0·5	58·7	19
Non-infected	89·9	17·4	78·2	30·5	84·7	13·8	28·7	5·3	1·8	0·8	57·2	23·2

*Jelliffe, 1966.

There was no significant difference in any single measurement or in the PI between the two groups (Mann-Whitney U test).

Eight of the seventeen infected catheters, and thirty-six of the ninety-eight non-infected catheters were inserted in the presence of an intra-abdominal fistula or abscess (not significant, X^2 test). The white-cell count at the outset of feeding (NI, $13·3\pm3·7\times10^9$/l; I, $13·3\pm7·0\times10^9$/l; not significant) in each group confirms that the presence of a septic focus is unlikely to affect catheter-related sepsis.

This study therefore demonstrates that it is not possible to predict catheter-related sepsis using nutritional measurements at the start of TPN.

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