Unreviewed reports

Assemble editors of biomedical journals together and it will not be long before they start discussing an old conundrum: what should be done with the anecdotal contribution—the interesting case or event that may be important but may also be coincidence? To print these in a section largely devoted to peer reviewed reports of rigorous scientific research may overinflate their importance and, by association, may devalue the reliability of the research studies; equally, to reject anecdotal reports for publication may deprive the community of important information.

Some editors devote much of the correspondence columns to these contributions; nevertheless, how many of their readers realise that usually these have not been peer reviewed and carry little of the weight of the Letters to the Editor in a journal such as, say, *Nature*? The confusion has been compounded by data bases such as *Index Medicus* which give letters, whatever their provenance, equal ranking with the formal scientific articles.

To make the distinction plain we have largely reserved the correspondence columns of the *BMJ* for comment on published work, creating a separate section of (peer reviewed) Short Reports. Though in theory such an arrangement is tidy, in practice problems remain. When is an event in a patient taking a drug possibly a true side effect, and when should it be printed as a Short Report rather than reported only to the drug manufacturer and regulatory authority? Should journals print negative results of minor importance? Should a small scale follow up study appear in the same journal that printed the original work? To try to solve some of these difficulties we are starting this week a new occasional column, called Unreviewed Reports. Given that the emphasis here will be on brevity and quick publication, the limitations on format will be considerable (p 1028), even though the articles will still be subject to selection by the editorial committee, containing two hospital consultants, which meets weekly. We hope that the new section will help solve some of the difficulties of both editors and authors.

STEPHEN LOCK
Editor, *BMJ*

Regular Review

Artificial nutrition in hospital

A M J WOOLFSON

The nutrition of patients in hospital has only recently become of much interest to the doctors looking after them. As is often the case with subjects newly recognised as important, enthusiasm has (to an extent) taken precedence over evaluation, and treatments have tended to become standard for no very clear reasons. In some ways the pharmaceutical industry has a lot to answer for in its uncritical promotion of nutritional products. Its interest has, on the other hand, also produced technical advances in the presentation of nutrients and administration systems for enteral and intravenous feeding which have at least reduced the dangers of artificial nutrition, even if its value in different clinical settings is still uncertain.

Evidence directly linking malnutrition with increased morbidity and mortality is not difficult to find. Loss of weight and nitrogen may be rapid after injury or during any illness with a combination of increased breakdown of body tissue and insufficient intake of food.¹ A study reported in 1965 showed that in a group of patients with severe complications of abdominal surgery and virtually no intake of nutrients, all those who had lost 30% or more of their original weight died.² The outcome of elective operations may be compromised if the surgery is preceded by weight loss. In 1936 Studley observed that patients with peptic ulceration who had lost more than 20% of their mass in the preoperative period stood a one in three chance of dying postoperatively, whereas only 3.5% of those who had lost less weight succumbed.³ Today patients with peptic ulcer do not normally become so ill before coming to surgery, and smaller degrees of loss of weight may not have quite the same prognostic significance, but the general relation is undeniable. Immune mechanisms

function less effectively and resistance to bacterial infection is impaired in undernourished states,^{4 5} and wounds heal poorly when albumin concentrations are low.⁶

Clear though these associations generally are, they do not prove that artificial nutritional support will be effective in countering the excess morbidity. Possibly poor nutrition and high morbidity might each be associated independently with more severe disease or more extensive surgery. There is, however, some circumstantial evidence of the potential benefit of giving nutrients. Immune competence returns on refeeding,⁵ and higher albumin concentrations lead to better healing of wounds and anastomoses.⁶ Survival from episodes of acute renal failure is greater when patients are given essential amino acids in addition to fulfilling energy requirements,⁷ but this may reflect only the potential dangers of producing something akin to kwashiorkor by administration of glucose with no source of nitrogen.^{7 8} Nevertheless, these observations give some encouragement to the proponents of artificial nutritional support—but firmer and more convincing evidence is needed and can come only from controlled clinical trials.

Evidence from controlled trials is sadly lacking, perhaps because of the practical difficulties of carrying out studies of this type. The degree of benefit (if any) is unlikely to be the same in groups of patients with widely different disease processes. Unless sizeable improvements result from administration of nutrients many patients need to be studied to give a trial enough statistical power to detect any advantage, so that either the study will take a long time or a multicentre investigation—with all its problems—must be set up. These

difficulties explain why the results of many metabolic studies (which need few patients) have been reported but very few have addressed themselves to the outcome in patients.

Some reports suggest that the use of intravenous or enteral nutritional support can improve the tolerance of patients to chemotherapy and radiotherapy and that the response of the tumours may be increased, but the evidence is conflicting and would not convince a dispassionate observer that survival or the quality of life is improved. The results are perhaps slightly more hopeful in relation to surgery. Two reasonable well controlled trials of seven to 10 days' preoperative intravenous nutrition in carcinoma of the gastrointestinal tract have shown some benefit, one in a reduction in wound infections⁹ and the other in major complications and mortality.¹⁰ No worthwhile effects have been obtained from shorter treatment times. In the postoperative period, many studies have shown that loss of weight and nitrogen can be much reduced by nutritional support either by the enteral or intravenous routes, and controlled trials in gastrointestinal surgery suggest that complications and duration of hospital stay might be reduced.^{11 12} Results of other studies have been inconclusive, but not a single series has been studied that was large enough to have sufficient statistical power to show that there was *no* improvement.

The benefits of artificial nutrition in inflammatory bowel disease appear to depend primarily on the site of disease. In acute colitis, whether due to ulcerative colitis or Crohn's disease, totally resting the bowel with intravenous feeding does not seem to affect the course of the illness,^{13 14} but there may be some advantage in acute exacerbations of Crohn's disease of the small bowel.¹³ Considerable enthusiasm has been shown for the use of low residue chemically defined ("elemental") feeds in inflammatory bowel disease on various theoretical grounds, including the suggestion that they are hypoallergenic compared with whole protein foods. The evidence that they have any beneficial effect in acute disease is confused, and, though diets of this type may be effective in maintaining the nutritional state in chronic Crohn's disease,¹⁵ they are usually unpalatable, almost always expensive, and supplementation of an ordinary diet with a whole protein liquid feed may produce even better results in terms of activity of the disease and the patient's progress.¹⁶

The outlook in external fistulas of the gastrointestinal tract has changed radically in the past 20 years, and much of this improvement may probably be attributed to the technical feasibility of adequate nutritional support. Early studies reported an overall mortality of about half in gastric and duodenal fistulas. This has now been reduced to about 10%. Depending on which part of the bowel is affected nutrition can be given either enterally or intravenously, and though the output of the fistula may possibly fall more rapidly with intravenous feeding the two methods are probably equally successful in allowing spontaneous closure to occur.^{17 18} This is one of the questions on which evidence is not available from proper controlled trials. Another is the treatment of ill patients with protracted complications after surgery or injury, but the circumstantial evidence strongly suggests that continuing loss of body mass will contribute to their chances of dying. Controlled trials would prove very difficult both for ethical reasons and because of the problems of matching equivalent patients in randomisation.

Attempts have been made to define prognostic factors in surgical practice.^{19 20} Several different measurements have been used, most of which relate to nutritional state, such as weight, triceps skinfold thickness, arm muscle circumference, response to recall antigens, serum concentrations of albumin,

transferrin, retinol binding protein and prealbumin, lymphocyte count, and creatinine height index, but many factors other than nutrition may affect most of these indices, which are best regarded as predictive pointers rather than assessments of nutritional state when used in these circumstances. One group has proposed that the functional test of handgrip dynamometry is the most accurate as a discriminating variable,²¹ but this has yet to be confirmed independently. Though the prognostic value of these indices has been reasonably well validated, they may be no better than simple clinical assessment.²² They do in any case have large intrinsic errors when they are applied to individual patients, and no properly controlled prospective studies have shown that they are of value in selecting patients for early or elective administration of nutrients.

Even when a decision is made to give some nutritional support to a patient, problems remain: which route to use, what type of administration equipment, and which products to give. The relations between energy intake, nitrogen intake, and nitrogen balance have been well reviewed recently.²³⁻²⁵ Maintenance requirements for energy are not as high as was previously thought, and very few patients need more than 10.45 MJ (2500 kcal) in each 24 hours. Energy in excess of maintenance requirements when given as glucose results in synthesis of fat (with a respiratory quotient above 1.0) and an increase in energy expenditure.^{26 27} The result is a considerable increase in production of carbon dioxide which may be a problem in patients with compromised respiratory function. Some means is also needed of giving essential fatty acids and fat soluble vitamins, so some fat is now included in most feeding regimens. An additional advantage is that control of blood glucose concentrations becomes easier, though this should not prove a problem even in the sickest of patients if appropriate methods are used.²⁸ Carbohydrate substrates other than glucose (including ethanol) have no advantages over glucose as energy sources and their use is slowly diminishing. Nitrogen requirements are usually provided by giving at least 10 g in 24 hours (equivalent to 62-63 g protein), and for intravenous nutrition most people now use a minimum of about 14 g a day. In truly hypermetabolic patients (those with extensive injuries or large burns) up to 16.72 MJ (4000 kcal) or on occasions even more may be needed in 24 hours, and such patients should receive 25-30 g nitrogen daily. Factors determining requirements for energy and nitrogen are partially independent of one another. It is the absolute amounts of each that are important, and the ratio of energy to nitrogen, so much quoted by nutritional pharmaceutical companies, is of itself irrelevant except where the practical considerations of (say) mixing enteral feeds are concerned.

Water and electrolyte balance is often neglected when nutritional support is used, and gross abnormalities should probably be corrected as the first part of the treatment. Requirements for other nutrients will not be discussed here, but the information is available.²⁹ Similarly, comments on nutritional support in specific disease states are beyond the scope of this article, and the reader is referred to the specialist publications.

If the gastrointestinal tract is not completely out of action, then it should be used, since the metabolic effects of nutrients given by this route are at least as good as, and probably better than, when they are given intravenously.³⁰ Furthermore, enteral feeding is both safer and less expensive than intravenous nutrition. A supplemented normal diet is always the most acceptable method to the patient, and, with the palatability of proprietary liquid feeds having improved appreciably

over the last few years, considerable increases may be achieved in the intake of energy and protein in many ill patients by encouraging the regular sipping of small amounts of the supplement. Many different preparations are marketed both for oral supplementation and tube feeding. Since nitrogen sources are best absorbed from the bowel as peptides,³¹ "elemental" feeds containing the nitrogen component as single amino acids certainly have no advantages over more palatable peptide sources, and at least one "elemental" product has been shown to be inferior in terms of nitrogen retention.³² Whole protein foods should be regarded as standard: they may be easier to administer and provide the best clinical results. Diarrhoea may develop as a complication of supplementation: it is usually associated with rapid or uneven administration of nutrients^{33 34} or the use of antibiotics^{33 35} or other drugs.³⁶ The importance of lactose intolerance has been overstated, and, provided that the feed is given by constant drip most of the day (which also has many advantages in terms of comfort and nursing time,³³ feeds containing lactose do not produce more symptoms or diarrhoea than feeds which are free of lactose, even in patients with proved lactase deficiency.³⁵ None of the standard proprietary preparations has been shown convincingly to be better than the others, but special circumstances may dictate that peptide feeds or those which contain medium chain triglycerides or have other specific qualities should be used. One of the critical issues is convenience of administration, and feeds which require no dilution and can be connected

directly to a compatible administration set are likely to prove more attractive.

Those companies which make and sell intravenous amino acid solutions expend a great deal of effort in extolling the virtues of the particular profile of amino acids that their solutions contain. Their arguments are all based on theoretical grounds which have little relation to the clinical circumstances in which they are used, and, in fact, very little is known about requirements of individual amino acids for optimal progress in different types of patients. As with the enteral feeds, there is no practical evidence that any of the solutions available now is superior to any of the others, and the clinical choice may be made on such criteria as the total concentration of amino acids and the amounts of sodium, potassium, and phosphate included.

The initial phase of investigation in hospital nutrition is now over. The approximate energy and nitrogen requirements are now known for most patients, and nutrition may be given relatively safely by the enteral or the intravenous routes. The next objectives must be to establish whether requirements for specific substrates vary in different types of patients—but of even greater importance is defining more closely the circumstances in which artificial nutrition is likely to have beneficial effects in promoting recovery.

A M J WOOLFSON

Consultant in Clinical Chemistry,
City Hospital,
Nottingham NG5 1PB

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