Malnutrition in Intestinal Disease

Uptodate: Clinical Nutrition

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<**Opening titles**>

<**Dr Andrew Tomkins to camera**>

One of the most common problems in management of patients with severe gastrointestinal disease is the development of malnutrition in a considerable proportion of cases. Now, this lecture is to deal with the mechanisms of malnutrition in such patients, but before we go any further I think it's worth asking ourselves the question as to whether malnutrition actually matters because there may be considerable difference of opinion, often between surgeons and physicians, as to whether malnutrition of either a mild or severe form makes very much difference in terms of morbidity to the patient.

<**Tomkins over table listing physiological changes that occur with malnutrition**>

And in this first illustration, I'd like to show you some of the changes that are associated with abnormalities of nutrition.

Firstly, there is now well-documented evidence that both humoral and cellular immune responses are decreased in protein energy malnutrition. There is, in addition, poor wound healing which contributes considerably to the post-operative sepsis and failure to thrive. More long-term effects are those of delayed convalescence and apathy, and many patients remain underweight for months after an operation. There are specific changes that are complications of malnutrition. Firstly, paralytic ileus, which is really a problem of hypokalaemia as well as protein malnutrition; oedema which is a problem of hypoalbuminaemia; and anaemia. Now anaemia is a common problem among patients with gastrointestinal disease, particularly due to failure of absorption or intake of iron, vitamin B12 and folic acid and these will be dealt with in greater detail in another lecture in this series. And the final complication of malnutrition that I'd like to consider is malabsorption because it's been recognised increasingly in the last few years that malnutrition itself will produce a gut lesion in terms of the villous atrophy and poor absorption that ensues.

<**Tomkins to camera, then over table listing types of small and large bowel disease, then back to camera**>

The sort of cases that one has in clinical practice are mostly those with small and large bowel disease and we can see in this illustration a sort of grouping of them that are commonly present with nutritional disorders. Crohn's disease, gluten enteropathy (the celiac syndrome) and the blind loop syndrome are particularly at risk for the development of malnutrition. In the large intestine it is the inflammatory bowel diseases such as ulcerative colitis and Crohn's disease that are at risk again. In addition, we have patients who have intestinal resections for tumours or vascular region of both the large and the small intestine.

It may be helpful, in consideration of the sorts of malnutrition that these patients develop, to classify them under 3 main headings. And in this illustration I'll show you these.

<**Tomkins over table listing 3 types of malnutrition, then over diagram of human body showing elements of its constitution, then back to camera**>

Firstly, protein energy malnutrition – this is the one that I'm going to spend most time considering. Secondly, anaemia, and thirdly, electrolyte and trace element deficiencies.

If we then consider the first, protein energy malnutrition, we need to consider what ways in which the body compartment changes and we can look at this schematically in the next diagram. As you can see, the greatest proportion of the body is obviously water with minerals, and fat and carbohydrate occupy perhaps 9% each in the remaining. But the most important part, for our consideration today at least, is that occupied by protein; this occupies 18% of the body and it is responsible for the fat-free skin, skeletal muscle, liver and alimentary system. If we are going to consider changes that occur in this particular compartment, we need to be able to measure these and in the next few illustrations I shall be showing ways in which it is possible to measure them so that we can formulate more effective therapeutic regimes.

Undoubtedly, the most accurate way of measurement of whole-body protein is by determination of the concentration of the stable isotope, or potassium K40. This is because 1 kilogram of lean body mass contains 68 millimoles of potassium and using a whole body scintillation counter, one can accurately and easily estimate whole-body protein. Well, of course most hospitals don't have whole-body counters and therefore we have to use more appropriate methods. In the case of children and adolescents we have one distinct advantage and that is that any abnormality of nutrition is accompanied by severe changes in growth patterns and we can compare the heights and weights per age of our patients with those that have been established among normal children of the same age group. And we've got data for both American children and English children, studied by Professor Tanner, and in the next illustration this just gives us an example of this sort of information.

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<**Tomkins over graphs showing growth/weight charts for normal children and adolescents superimposed with those of a boy with Crohn's disease**>

You can see here that we have the median, M, and the 84th and 16th percentiles of weight for age. If we look at the sort of appearance that occurred in an unfortunate boy who entered his teens with Crohn's disease, you will see the severe impairment of weight gain that occurs in such patients. There is a fluctuation that occurs, but in general terms he has hardly increased at all between the ages of 11 and 17.

This graph demonstrates the normal range of height for age with the median, 84th and 16th centile and when we superimpose the findings in this boy between the ages of 12 and 17, again we find no increase in his height. These measurements can be extremely useful in monitoring changes in nutrition during exacerbations, or monitoring effects of therapy for a variety of gastrointestinal diseases. In adults we can make broad statements about expected weight for height and body frame type and we can measure mid-arm circumference, but the range of these measurements among normals is really quite considerable and we have, therefore, to go back to more direct methods.

<**Tomkins to camera**>

Two methods that have been widely used have been firstly, the urinary creatinine/height index, and secondly, the serum albumin. The creatinine/height index was introduced first by Dr Patari for measurement of degree of malnutrition in children. More recently, it has been used in adults with post-operative malnutrition and found to be a useful index of malnutritional status. It is easily measured in a 24 hour urinary excretion and the ratio is expressed quite simply by measurement of the creatinine from your patient compared with the creatinine excreted by a health subject of the same age and sex and obviously, if the patient is well-nourished, the ratio is 1.0. In 11 malnourished patients after abdominal surgery, the ratio was 0.50 or less. The problem with this measurement, however, is that it relies on the assumption that the glomerular filtration rate is normal and, as you know, this just

isn't the case in many ill patients. We may therefore conclude that urinary creatinine is quite helpful but it does take a time to estimate and probably the more useful one is the serum albumin. This is extremely easily determined and has been used for monitoring the patient quite regularly. While it is important to realise that it measures only 1 of the export proteins of liver, it is probably the simplest individual biochemical test.

I'd like now to move on to a consideration of the way in which a patient may develop his malnutrition. And we've obviously got to consider problems of absorption, abnormal utilisation and increase in intestinal protein loss.

<**Tomkins over illustration showing normal food absorption levels in intestinal system, then to camera**>

And if we look at this illustration, you will get some idea of the dynamic aspects of the situation in the intestinal tract. A healthy adult on a very nutritious diet will be ingesting 90 grams of protein, which is contributed to by, perhaps, 30 grams of intestinal secretion, mostly enzymes, together with a further 8 grams of the pancreatic secretions. In addition, because of the rapid turnover of cells in the mucosa of the small intestine, there is an additional 50 grams provided by the mucosal cells. With all this it's perhaps surprising, on first sight, to see that the faecal loss is only 10 grams, however, one must realise that at least 90% or more of the protein is absorbed in patients who are fairly healthy. This degree of absorption is markedly decreased in patients with illness.

It's therefore easy to understand that malnutrition can arise from inadequate intake. This may be inadequate in absolute terms by comparing the amount of food that the patient is presently taking with what they were taking before they were ill. Or it may be inadequate in relative terms, that is, the nutrient requirements of the illness are so high, due to fever, due to, perhaps, sepsis and surgical trauma, that the patient is not taking enough in. It's therefore all the more important to obtain a very full dietary history.

Now, without knocking the undergraduate medical curriculum too much, I think it's safe to say that most doctors are just not capable of taking a full dietary history and therefore it's essential to enlist the help of a skilled dietician.

<**Tomkins over illustration of vegetables**>

One of the things that she should enquire for, specifically, in addition to the protein intake in the diet, is the intake of vitamin-containing foods such as vegetables. There are problems with dietary recall estimations by dieticians but it gives us a very good understanding of what the intake has been in the few weeks or months prior to admission to hospital.

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<**Tomkins to camera, then over graphs comparing amino acid and nitrogen absorption in normal and ill patients, to camera in between**>

So we can see that the intake of these patients is extremely important. In fact, as you will see in the next illustration, a poor intake may even prejudice the absorption of the few nutrients that are being eaten. Here you see the absorption of amino acids in a control subject, compared with the impaired absorption of a subject who's been fasting for 5 days. If we know the dietary intake, we can measure the urinary excretion of nitrogen and we can calculate a nitrogen balance.

This is easily performed on a 24 hour urinary collection and the nitrogen is estimated using a kelldal apparatus. This is a little time-consuming and it's possible to make an estimate of urinary nitrogen excretion by measurement of the urinary urea – this takes the assumption that 80% of the nitrogen excreted is in the form of urea. If we then measure the urinary and faecal nitrogen we can then make some statement which may be of importance to the protein status of our patient. For instance, say, a patient on a 70 gram protein intake will be excreting between 5 and 12 grams of nitrogen; this is mostly in the urine with just 1 or 2 grams in the faeces. However, if a patient eats nothing for 7 days, or very little, he will still excrete 10 grams of nitrogen;

this is mostly derived from muscle protein that has been mobilised for amino acid oxidation as a source of energy. You will see that the nitrogen excretion is higher still if he's had a major operation and only been given 5% dextrose, a sort of figure of 15 grams urinary excretion is common in these sort of patients. If he's unfortunate enough to have had a septic complication, such as peritonitis, it will go higher still and fistulae, such as occur in infectious diseases of the intestine, such as Crohn's disease, will be even higher.

<**Tomkins to camera, then over graph showing weight/height chart for a patient with Crohn's disease and complications**>

It's easier to appreciate that nitrogen requirements are high when you're eating very little, or when there's infection. But one thing that's important to remember is that high temperatures themselves have a marked effect on the nitrogen excretion and, in fact, one volunteer recently studied in America, was put in a hot chamber for only 24 hours and he had a negative nitrogen balance for 2 weeks following.

Now if we look at the illustration here, we see the pattern that occurred in the patient that I showed you the weight and the height chart before. This unfortunate chap came in when he was 17 years old and he had an abdominal resection for Crohn's disease. Following this he had a burst abdomen and this was then complicated by further insult – a very severe bilateral bronchopneumonia. This patient was given a low calorific feeding of less than 2,000 calories during this time, and in view of the enormous caloric requirement due to his high metabolic rate, it's perhaps hardly surprising that he failed to put on height or weight as I showed you in the previous charts.

<**Tomkins to camera, then over chart showing absorption deficits in patients with gluten enteropathy, then back to camera**>

Even though the dietary intake may be quite adequate, there may be a problem with absorption as is illustrated by patients with gluten enteropathy.

As you can see here, patients were tested for absorption of glycine and alanine and both these substances were absorbed worse than control subjects. Once these amino acids are absorbed, they're used for protein synthesis and recently, using studies of the stable isotope N15-glycine, it has been possible to measure the rates of protein synthesis. In patients who are in the ages of 25 to 40, 3 grams of protein are synthesised per kilogram per day. That's a whole amount of 200 grams in the 24 hour period. In the elderly, the figure seems to be less, but in children the rate seems to be very much higher, perhaps 5 times as high as the adult rate. It's also been possible to measure the rates of protein synthesis during and after an operation – this is, of course, extremely important if we're looking at the effects of trauma on patients with inflammatory bowel disease requiring resection.

<**Tomkins over graph showing decrease in protein synthesis in patients following laparotomy, then back to camera**>

In this study, 4 patients having laparotomies were studied before and after their operation – before in the light columns, after in the dark columns. As you can see, the synthesis rates in each of these patients fell in the post-operative period. This was accompanied by a decrease of breakdown as well in 3 of these patients. But as you can see, the decrease in breakdown was markedly less than the decrease in synthesis and the so-called negative nitrogen balance of surgery may well be predominantly due to a decrease in synthesis. This would be further supported by the fact that recent studies in Boston have demonstrated a better nitrogen-sparing effect if patients are given amino acids rather than isocaloric carbohydrate in the post-operative period.

So at this stage we've studied absorption, abnormal utilisation, and now we should consider, briefly, excessive loss of protein from abnormal excretion.

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<**Tomkins over graph showing levels of protein loss from abnormal excretion, then to camera**>

We can usually estimate albumin loss using radioactive methods but perhaps, if we're interested in protein loss, we should be measuring the total protein and we can measure faecal nitrogen. In this study a patient was given an oral dose of the stable isotope N15-glycine and this was measured in the faecal samples passed over the next 100 hours. As you can see, the majority of the N15-gylcine came out at 16 to 20 hours, accompanied by the intense red marker – this probably represents unabsorbed glycine. However, there is, in addition, a considerable amount of the N15-glycine still being passed up to 100 hours after the oral dose. And it seems likely that what is happening here is that the N15-glycine has been incorporated into protein, perhaps at the intestinal mucosal endothelial cells, exfoliated and excreted. Therefore whenever one measures faecal loss, one has to differentiate between that due to endogenous loss and that due to exogenous, dietary intake.

I'd now like to finish by turning towards the consideration of those patients with hypoalbuminaemia due to the stagnant loop syndrome. It's now well recognised that a considerable number of people with a stagnant loop syndrome present with severe muscle wasting and low albumin.

<**Tomkins over graph showing serum albumin levels in a patient with stagnant loop syndrome, then to camera**>

As you will see from the first illustration here, this was the serum albumin in just such a patient, a 70 year old subject who presented with severe ankle oedema which had been following diarrhoea for many, many years which was due to jejunal diverticulosis. Bacterial colonisation had occurred and as a result, he had developed this abnormality of albumin. You can see that, after a course of antibiotics, the albumin rose to 3.2, a much more satisfactory level.

However, one of the things that has not been explained until recently has been the precise nature of this abnormality. It's been postulated that bacterial proliferation in the stagnant loop might be producing some form of toxin which would inhibit protein

synthesis. And therefore it's been particularly helpful to have the studies that have been done recently on patients with this syndrome by Dr Tavill.

<**Tomkins over graph, then table, charting the albumin levels of a patient with stagnant loop syndrome, then over diagram explaining problems of albumin synthesis**>

He looked at albumin synthesis using radioactive iodinated albumin and demonstrated that albumin synthesis was low in the pre-treatment phase and high, going up to 323 milligrams per kilogram per day, in the post-treatment phase. More detailed analyses of this patient is shown in the figures on this chart. As you can see, a control subject has a plasma albumin of 4.5 grams with an intravascular pool of 160 and an absolute catabolic rate of albumin of 150, whereas in our patient, there was a low plasma albumin and a very low intravascular pool which was accompanied by a decrease in the absolute catabolic rate of albumin. Therefore, at this stage it looked as though there was, indeed, some dietary deprivation and on measuring the plasma amino acid levels, the concentrations were so low as to be those found in patients with childhood kwashiorkor.

So, in summary, we can probably diagrammatically explain the situation in this simplified diagram. Usually, dietary protein is directed toward albumin synthesis, however, in the presence of large numbers of bacteria within the upper intestine, there is sufficient deamination of amino acids to produce enormous quantities of ammonia nitrogen. This is then diverted into urea, and on measurement of urea synthesis, it was found that in a patient with very low albumin synthesis, the urea synthesis was extremely high.

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<**Tomkins to camera, then over graph showing results of an experiment on dietary synthesis of a patient with blind loop syndrome**>

Now this has some interest because the ruminant has a large number of bacteria within the small intestine. And it, in fact, is able to utilise the ammonia, provided from the organisms' deaminating dietary nitrogen, for protein synthesis. And therefore, in the final chart, I would like to show you the experiment that was performed, using intravenously administered N15-labelled urea, to see whether such a condition occurred in man. It would, after all, be rather attractive if we could say that man, far from suffering from his bacteria, did, in fact, derive a nutritional advantage.

And in this experiment we see that the enrichment of albumin, after administration of N15-labelled urea, was very much higher in the subject with blind loop syndrome than in the control. But in the analysis of these figures, it seems that the amount of protein that could be possibly provided by the urea was only of the order of 0.18%. So therefore, we can conclude that the enormous amount of ammonia, nitrogen and urea that are synthesised in the patient with blind loop syndrome is not at all useful to him.

<**Tomkins to camera, then over table listing** >

I'd like to finish with a brief consideration of the management of malnutrition in patients with gastrointestinal disease. It is no longer acceptable to think solely in terms of treatment of the established case. Instead, patients with a high risk must be identified at an earlier stage for intensive prophylactic support. This requires a greater attention to treatment of infection, replacement of losses and provision for the extra calorie and protein requirements, particularly in any post-operative period. In the established case, however, nutritional therapy can only be achieved by parenteral feeding and elemental diet. The principles and practice of parenteral feeding will be dealt with by Professor Lee in another lecture in this series, but I'd like to mention some specific indications for elemental diet.

Mortality from gastrointestinal fistulae is still high – between 40 and 70% in some series, despite skilled surgical techniques. This unsatisfactory state probably arises from the diminished rate of wound healing, electrolyte imbalance and the sepsis that accompany malnutrition. Better results have been obtained by Berry, who treated 13

such patients with elemental diet, and 50% of the fistulae in his patients closed. This was accompanied by a positive nitrogen and electrolyte balance and a reduction of mortality to 15%. Small intestinal resection is also complicated by malabsorption of nutrients and elemental diet is of great value in these patients. It's particularly important in view of the studies by Dowling and others showing that luminal nutrition is vital in stimulating adaptive changes of the intestine. Some published cases of severe gluten enteropathy, complicated by marked malnutrition, have also improved on an elemental diet. This has been found particularly useful in cases of celiac crisis where gluten withdrawal, steroids and even parenteral feeding have produced only limited improvement. Russell has shown considerable improvement in patients with cholerheic diarrhoeas – bile acid secretion was reduced during elemental dietary therapy for watery diarrhoea which was the result of ileal resection and Crohn's disease. Finally, Good and others have documented its value in inflammatory bowel disease. They studied 8 patients with Crohn's disease in whom body weight was between 18 and 37% below normal. Using potassium-40 methods, they showed a rapid increase in lean body mass, up to 18% per month, once an elemental diet containing 10 grams of nitrogen per day had been instituted. More recent studies, by Axelson in Scandinavia, suggest that an early remission of inflammatory bowel disease is obtained by a change from conventional to an elemental diet. This improvement occurred without any significant change in haemoglobin, iron, albumin or transferrin levels and suggests that a local mucosal effect might be very important.

<**Tomkins to camera**>

There have been some exciting advances in the diagnosis of gastrointestinal disease in the last few years, but morbidity and mortality from malnutrition remain considerable. Some of the pathophysiological concepts have become clearer and there are now available excellent treatment regimes. It's going to be exciting to see the improvement in patient care as these are used in the next few years.

<**End credits**>