1. INTRODUCTION

Food assimilation is the major function of the gastrointestinal tract. Many gastrointestinal diseases have important nutritional effects. Digestion and absorption of nutrients are discussed elsewhere. This chapter reviews physiologic considerations that are essential for planning proper nutritional management. The focus will be on the role of the liver in regulating the supply of carbohydrate and lipid fuels as well as ensuring the availability of essential substrates to peripheral tissues. The clinical features of malnutrition and specific effects of malnutrition on the gastrointestinal tract and liver will be discussed along with diet therapy in gastrointestinal disease. Finally, an approach to clinical nutrition will be presented, including nutritional assessment and the rational use of enteral and parenteral nutritional support.

2. ESSENTIAL PHYSIOLOGIC CONCEPTS IN NUTRITION

To maintain a continuous supply of nutrients in the bloodstream in the face of intermittent dietary intake, a complex set of regulatory mechanisms have evolved. These allow the storage of nutrients during feeding, and their release from storage pools during the interdigestive period so as to maintain nutrient levels in the bloodstream within remarkably narrow limits. Short-term regulation between the fed state and the interdigestive state is mediated principally by (1) the concentration of several key substrates and (2) a set of regulatory hormones, which include insulin, glucagon, catecholamines and corticosteroids (Table 1).

Taken together, the actions of glucagon, catecholamines and corticosteroids work to increase plasma glucose and free fatty acid levels in direct opposition
to insulin. Therefore, the release of these hormones, which occurs in response to low glucose levels and/or stress, leads to insulin resistance.

The fate of glucose in the fed and the fasting states is detailed in Figure 1. Glucose is rapidly absorbed following ingestion as starch, disaccharides or monosaccharides. The glucose is transported via the portal system to the liver, which extracts a considerable fraction of portal venous glucose. The remainder enters the systemic circulation and causes pancreatic secretion of insulin. The high portal vein insulin and glucose concentrations lead to hepatic glucose uptake with conversion to glycogen and fatty acids. The peripheral rise in insulin, which occurs in association with the rise in plasma glucose concentration, causes a large peripheral uptake of glucose, first by muscle cells, and second by adipocytes. Glucose is the essential substrate for brain, renal medulla and red cell metabolism; other organs mainly use fatty acids for energy. The rise in plasma insulin also leads to amino acid uptake by muscle and has an antiproteolytic effect. These effects on muscle protein have led to the designation of insulin as an “anabolic hormone.” In the postabsorptive or interdigestive state, plasma glucose is low, with low plasma insulin levels. The low plasma insulin influences the metabolism of all three macronutrients (i.e., carbohydrates, fat and protein). Glycogenolysis occurs in the liver to maintain plasma glucose levels. The low plasma insulin also allows lipolysis to take place, such that fatty acids can be utilized as the

### TABLE 1. Hormonal regulation of nutrient metabolism

<table>
<thead>
<tr>
<th>Hormone</th>
<th>Principal metabolic actions</th>
</tr>
</thead>
</table>
| Insulin         | Increases glucose uptake in peripheral tissues  
|                 | Stimulates protein synthesis  
|                 | Inhibits lipolysis and glycolysis  
|                 | Increases amino acid uptake into muscle (particularly important post-exercise) |
| Glucagon        | Increases cyclic AMP levels in the liver and adipose tissue, with stimulation of fatty acid mobilization, glycogenolysis, glycolysis and gluconeogenesis, thereby increasing plasma glucose |
| Catecholamines  | Increase cyclic AMP levels in the liver, skeletal muscle and adipose tissue, with release of glucose, free fatty acids and lactate |
| Corticosteroids | Increase gluconeogenesis  
|                 | Increase amino acid mobilization from the periphery (chiefly skeletal muscle)  
|                 | Increase fatty acid release from extremities  
|                 | Decrease glucose utilization by peripheral tissues by increasing post-receptor insulin resistance |
|                 | Increase glucagon release |
FIGURE 1. Carbohydrate, fat and protein metabolism.
Figure 2. Lipoprotein metabolism.
major energy substrate. Finally, the low plasma insulin leads to proteolysis, particularly of muscle protein, which leads to release of alanine and glutamine, which can be used for gluconeogenesis in the liver. This gluconeogenesis occurs in concert with glycogenolysis to ensure an ongoing supply of glucose for the body.

Other hormones, such as glucagon, catecholamines and growth hormone, play less important roles in macronutrient metabolism, but in general have been termed the “stress hormones,” since they are released during times of stress and have anti-insulin effects. In particular, if for any reason there is a low blood sugar, all these hormones are released and will promote an elevation in plasma glucose.

The flux of lipid nutrients in the fed and the interdigestive states is contrasted in Figure 2. In the fed state, fat enters the circulation as chylomicrons, which are large droplets of triglyceride emulsified by a surface monolayer of phospholipid and apolipoproteins. Additional apolipoproteins are transferred onto the chylomicrons from HDL. The artificial fat emulsions used for parenteral nutrition are very similar to chylomicrons in that they contain a core of triglyceride with a surface monolayer of phospholipid. They initially contain no apolipoproteins, but acquire these from HDL very rapidly once they have entered the circulation. One of the apolipoproteins, apolipoprotein C-II, is particularly important in that it is an essential cofactor for the action of lipoprotein lipase. This enzyme is attached to the capillary endothelium in tissues, such as the heart and adipose tissue, that are active in utilizing fatty acids. Chylomicrons bind to the enzyme and the core triglyceride is rapidly hydrolyzed. The released fatty acids are then taken up and utilized in the peripheral tissues. As the chylomicron particle shrinks in size, the excess surface material is transferred back to HDL, and ultimately the remnant particles are cleared via a specific receptor in the liver. The process of lipolysis is extremely efficient, and the half-life of chylomicron triglyceride in the circulation is normally less than 15 minutes. The lower panel of Figure 2 depicts the postabsorptive or interdigestive state. Chylomicrons are absent, but triglyceride fuels are available in the circulation in the form of VLDL, which are secreted by the liver. The substrates for triglyceride assembly include free fatty acids released from adipose tissue through the action of a hormone-sensitive lipase, and fatty acids synthesized in the liver from acetyl-CoA. The newly secreted VLDL acquire apolipoproteins and cholesterol ester from HDL. Lipolysis of VLDL in peripheral tissues is mediated by lipoprotein lipase. As the particle decreases in size, free cholesterol transfers to HDL, where it is esterified through the action of lecithin–cholesterol acyltransferase (LCAT), and the resultant cholesterol ester is then transferred back to the lipolyzed particle, where it forms part of the core. When lipolysis is completed, what is left behind is termed an LDL particle. This is smaller and more dense than VLDL, has lost all apolipoproteins except apolipoprotein B, and has a core of cholesterol.
ester rather than triglyceride. LDL is cleared relatively slowly, with a half-life of several days. The uptake of LDL is mediated by a specific membrane receptor, termed the LDL receptor, whose activity in turn is regulated by intracellular cholesterol levels. The most active tissues (on a weight basis) for LDL clearance are steroidogenic tissues, such as the adrenals, gonads and the liver; because of its size, the liver accounts for over half of total LDL catabolism. As peripheral tissues cannot degrade cholesterol, excess cholesterol is returned to the liver via HDL, where it is used for bile acid synthesis or excreted in the bile.

Starvation leads to a number of adaptive responses. There is a depletion of liver glycogen within 24 to 48 hours, with stimulation of gluconeogenic enzymes to allow the production of glucose from amino acids released through protein breakdown in skeletal muscle. Lipolysis in adipose tissue leads to increased fatty acid levels and activation of enzymes responsible for β-oxidation of fatty acid in the liver (acyl-CoA-carnitine acyltransferase). In addition to acetyl-CoA, fatty acid oxidation generates ketone bodies. One important adaptive response to starvation is the induction of 3-hydroxybutyrate dehydrogenase in the brain, which allows this organ to utilize ketone bodies as a fuel. Decreased dependence on glucose reduces the need for excess gluconeogenesis and spares muscle protein. In a relatively lean 70 kg man with 12% body fat, survival without food can be expected to be about 60 days or longer.

**TABLE 2. Causes of protein-energy malnutrition**

<table>
<thead>
<tr>
<th>Impaired intake</th>
</tr>
</thead>
<tbody>
<tr>
<td>Insufficient quantity or quality</td>
</tr>
<tr>
<td>Impaired intake due to systemic disease (e.g., cerebrovascular accident, chronic infections)</td>
</tr>
<tr>
<td>Impaired intake due to localized gastrointestinal disease (e.g., benign or malignant esophageal stricture)</td>
</tr>
</tbody>
</table>

**Impaired digestion and/or absorption**

| Selective enzyme defect (e.g., enteropeptidase deficiency, trypsinogen deficiency) |
| Generalized enzyme defect (e.g., pancreatic exocrine insufficiency) |
| Impaired small intestinal assimilation (e.g., celiac disease) |

**Excessive enteric protein loss**

| Gastric or intestinal mucosal disease (e.g., Ménétrier’s disease, intestinal lymphangiectasia) |
| Extraintestinal disease with lymphatic blockage (e.g., pericarditis, lymphoma) |

**Disorders with multiple causes**

| Advanced malignancy |
| Chronic renal failure with uremia |
| Other chronic debilitating diseases |
3. CLINICAL AND LABORATORY FEATURES OF PROTEIN-ENERGY MALNUTRITION

Protein-energy malnutrition may result from a number of causes. These are shown in Table 2. Intake or assimilation may be impaired or, alternatively, losses may be increased, as occurs with excessive enteric protein loss in protein-losing enteropathies. In some disorders, multiple causes may be present. Moreover, requirements may be significantly increased in some patients as a result of growth, pregnancy, tissue injury or a superimposed disease process. In some patients with chronic debilitating diseases, multiple factors may be responsible.

Malnutrition has been classically divided into kwashiorkor (protein restricted) and marasmus (protein-calorie restricted). In kwashiorkor, the subject ingests a moderate number of calories, usually as complex carbohydrate (e.g., rice), but very little protein. The carbohydrate is absorbed as glucose, causing rises in plasma glucose and insulin, and leading to decreased lipolysis and proteolysis. The liver is therefore supplied with inadequate amino acids, with little oral intake and little peripheral mobilization from skeletal muscle stores. Transport of triglyceride made from ingested glucose is impaired since there is inadequate production of apoprotein, which is needed for the formation of VLDL. The liver becomes fatty and enlarged. Furthermore, other proteins,
including albumin, are inadequately produced by the liver in kwashiorkor, and serum albumin falls, with resulting peripheral edema. With marasmus the subject takes inadequate amounts of protein and calories. The low caloric intake means that only small amounts of carbohydrate are taken; plasma glucose and insulin are low. Hence, lipolysis and proteolysis occur, with adequate delivery of amino acids from muscle to the liver for protein production. Fatty liver does not occur, and serum albumin levels tend to be normal, with no peripheral edema. Often patients fall between these two extremes of nutritional states, but there are examples of kwashiorkor and marasmus in Western clinical practice. Anorexia nervosa is a classic example of marasmus. Marked muscle wasting and loss of subcutaneous tissue (adipose tissue) occur with normally sized nonfatty livers and no peripheral edema. In contrast, the intensive care unit patient who has received intravenous dextrose (glucose) without amino acids for a prolonged period will often show a fatty liver and marked hypoalbuminemia and edema. Other changes in the liver that may occur in nutritional disorders are listed in Table 3.

Clinical vitamin deficiencies are listed in Table 4. Except for cheilosis and glossitis, which are seen with multiple vitamin B deficiencies, physical findings of vitamin deficiencies are seldom observed in protein-calorie malnourished patients in developed countries. Trace elements are elements that are required in small quantities (milligram amounts or less) for normal growth and/or function. Essential trace elements for humans include iron, iodine, zinc, chromium, copper, selenium, cobalt (as vitamin B₁₂), molybdenum, manganese and possibly vanadium. Except for iron deficiency due to blood loss and/or poor intake, deficiency states of trace elements are rare in subjects with some oral intake, since only minute amounts are required.

4. EFFECTS OF MALNUTRITION ON THE GASTROINTESTINAL TRACT AND PANCREAS

Protein-energy malnutrition may produce major structural and functional changes in the gastrointestinal tract and pancreas, which, in turn, may aggravate the underlying poor nutritional condition. In severe protein-energy malnutrition, for example, acinar cell atrophy occurs and exocrine cells have decreased numbers of zymogen granules. Pancreatic secretion may be reduced following stimulation with cholecystokinin and/or secretin. With malnutrition, the activities of enzymes contained in pancreatic juice (i.e., trypsin, chymotrypsin, lipase, amylase) are reduced. With reversal of malnutrition these can return to normal levels, but this may require several weeks.

In addition to pancreatic exocrine changes, the entire wall and mucosal lining of the stomach and intestine may be reduced in thickness. Microscopi-
### TABLE 4. Vitamin deficiency syndromes

<table>
<thead>
<tr>
<th>Vitamin</th>
<th>Name of deficiency state</th>
<th>Clinical occurrence</th>
<th>Common clinical features</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Water-soluble</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>B&lt;sub&gt;1&lt;/sub&gt; (thiamine)</td>
<td>Beriberi: Dry (neurologic) Wet (cardiac)</td>
<td>Refeeding after starvation</td>
<td>Neurologic: Peripheral neuropathy, Wernicke-Korsakoff Cardiac: Heart failure</td>
</tr>
<tr>
<td></td>
<td>Wernicke-Korsakoff syndrome</td>
<td></td>
<td></td>
</tr>
<tr>
<td>B&lt;sub&gt;2&lt;/sub&gt; (riboflavin)</td>
<td>—</td>
<td>Rare</td>
<td>B-complex deficiency*</td>
</tr>
<tr>
<td>B&lt;sub&gt;6&lt;/sub&gt; (pyridoxine)</td>
<td>—</td>
<td>Only with pyridoxine-antagonist drugs (isoniazid, cycloserine, penicillamine)</td>
<td>Neurologic: Convulsions B-complex deficiency* Anemia</td>
</tr>
<tr>
<td>B&lt;sub&gt;12&lt;/sub&gt; (cyanocobalamin)</td>
<td>Pernicious anemia (when secondary to idiopathic gastric atrophy)</td>
<td>Achlorhydria Terminal ileal disease or resection Bacterial overgrowth Diphyllobothrium latum Pancreatic insufficiency</td>
<td>Hematologic: Pancytopenia Neurologic: Subacute combined degeneration Peripheral neuropathy Glossitis</td>
</tr>
<tr>
<td>Folic acid</td>
<td>—</td>
<td>Pregnancy Poor intake Malabsorption</td>
<td>Hematologic: Pancytopenia Glossitis</td>
</tr>
<tr>
<td>Niacin</td>
<td>Pellagra</td>
<td>Poor diet</td>
<td>Characteristic dermatitis Dementia Diarrhea</td>
</tr>
<tr>
<td>Pantothenic acid</td>
<td>—</td>
<td>Rare</td>
<td>—</td>
</tr>
<tr>
<td>Biotin</td>
<td>—</td>
<td>Excess egg white ingestion ? TPN</td>
<td>Dermatitis Glossitis Anorexia</td>
</tr>
</tbody>
</table>

continued...
TABLE 4. Vitamin deficiency syndromes (cont’d)

<table>
<thead>
<tr>
<th>Vitamin</th>
<th>Name of deficiency state</th>
<th>Clinical occurrence</th>
<th>Common clinical features</th>
</tr>
</thead>
<tbody>
<tr>
<td>C (ascorbic acid)</td>
<td>Scurvy</td>
<td>Infants, the elderly and alcoholics with very poor intake</td>
<td>Purpura, Gum disease (when teeth present)</td>
</tr>
<tr>
<td>2. Fat-soluble</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A</td>
<td>—</td>
<td>Third World children, Severe low intake</td>
<td>Night blindness, corneal changes, xerophthalmia, xeroderma and hyperkeratosis</td>
</tr>
<tr>
<td>D</td>
<td>—</td>
<td>Inadequate sun exposure, Inadequate intake, Renal disease</td>
<td>Osteomalacia (rickets in children), Hypocalcemia</td>
</tr>
<tr>
<td>E</td>
<td>—</td>
<td>Cholestatic liver disease (especially children)</td>
<td>Neurologic: Posterior column degeneration, areflexia</td>
</tr>
<tr>
<td>K</td>
<td>—</td>
<td>Warfarin anticoagulant, Long-term antibiotics (especially with TPN), Newborn infants</td>
<td>Hemorrhage with prolonged prothrombin time</td>
</tr>
</tbody>
</table>

*B-complex deficiency: cheilosis, angular stomatitis, glossitis.*
cally, marked changes may develop, including severe “flattening” of the small intestinal mucosa, similar to celiac disease. In contrast to celiac disease, however, reduced numbers of crypt mitoses are seen. Changes may be present throughout the small intestine in an irregular patchy distribution, although the jejunum appears to be most severely affected. Some brush-border enzymes (e.g., disaccharidases) may be reduced; as a result, malabsorption of a variety of substances (e.g., lactose) may be observed. Altered uptake of glucose and D-xylose has also been reported, and steatorrhea may be present with impaired absorption of fat and some fat-soluble vitamins. In addition, there may be increased protein loss from the gut, leading to increased fecal nitrogen loss. Finally, specific nutrients may be deficient and cause alterations in certain tissues. In particular, folic acid and vitamin $B_12$ deficiencies may lead to subtotal villous atrophy in association with crypt hypoplasia (Table 5).

Restitution of small bowel mucosa occurs after renutrition. There is growing evidence that mucosal atrophy occurs during total parenteral nutrition with associated increased intestinal permeability, especially in stressed metabolic states, and that atrophy is absent or minimal in patients fed enterally. Therefore, whenever possible, intestinal (i.e., enteral) feeding is preferred to parenteral feeding. When refeeding occurs after a period of malnutrition, however, it should be appreciated that gut function may be impaired, with resultant malabsorption and diarrhea, and that total refeeding via the gut may not initially be achieved. In this circumstance, partial enteral refeeding with parenteral supplementation is usually given, provided there are no contraindications to enteral feeding (e.g., bowel obstruction).

There is evidence that the colonic mucosa uses short-chain fatty acids (especially butyrate) as an energy source. In patients who undergo a colostomy, the bowel that is left distally does not have a fecal stream. The mucosa of this bowel may develop inflammation, called “diversion colitis.” Some improvement in the colitis has been reported with administration of short-chain fatty acid enemas or with irrigation of fiber. A major source of the short-chain fatty acids in the colon is fermented dietary fiber, and thus fiber may be considered a “nutrient.”

5. DIETARY THERAPY IN GASTROINTESTINAL DISEASE

5.1 General Principles
A number of specific diets are useful in different gastrointestinal disorders. These may involve diet restriction or supplementation, or alternatively, a change in the consistency or content of specific nutrients. In patients with steatorrhea, for example, luminal fatty acids are present and involved in the pathogenesis of diarrhea. In these patients, reduction in diarrhea can be
accomplished, in part, by a reduction in the oral intake of triglycerides; a low-fat diet may be beneficial. In some patients with steatorrhea, supplementation with medium-chain triglycerides may be useful because these are hydrolyzed more rapidly by pancreatic enzymes, do not require bile acid micelles for absorption, and are primarily directed to the portal rather than the lymphatic circulation. Because medium-chain triglycerides undergo \( \omega \)-oxidation to metabolically nonutilizable dicarboxylic acids, the effective caloric content of medium-chain triglycerides is less than expected. Medium-chain triglycerides in a daily dose of 60 mL will provide approximately 460 calories. Low-fat dietary supplements may be provided in the form of a number of commercially available products prepared as complete nutritional supplements. Fat-soluble vitamins can be replaced using oral water-miscible formulations, if steatorrhea is present. For vitamin K, a water-soluble form is available. Fat-soluble vitamins require bile acid micelles for absorption; thus, if steatorrhea is due to bile acid depletion (as might occur in the short bowel syndrome following surgical resection for extensive Crohn’s disease), increased amounts of vitamins may be required.

Bloating and cramping pain may follow ingestion of lactose-containing foods. This may be due to lactase deficiency (e.g., small bowel disease, “ethnic” lactase deficiency). Dietary lactose restriction may be indicated in patients if there is a history of lactose intolerance or a positive lactose tolerance test (i.e., rise in blood sugar less than 20 mg/dL after 50 g of lactose) accompanied by characteristic symptoms. An alternative test involves measurement of breath hydrogen; a rise of more than 20 ppm is consistent with lactose intolerance.

<table>
<thead>
<tr>
<th>Nutrient</th>
<th>Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Protein-energy malnutrition</td>
<td>Total or subtotal villous atrophy and crypt hypoplasia</td>
</tr>
<tr>
<td>(e.g., especially, kwashiorkor)</td>
<td></td>
</tr>
<tr>
<td>Folic acid deficiency</td>
<td>Total or subtotal villous atrophy and crypt hypoplasia;</td>
</tr>
<tr>
<td></td>
<td>macrocytic and/or “megaloblastic” enterocytes</td>
</tr>
<tr>
<td>Vitamin B(_12) deficiency</td>
<td>Total or subtotal villous atrophy and crypt hypoplasia;</td>
</tr>
<tr>
<td></td>
<td>macrocytic and/or “megaloblastic” enterocytes</td>
</tr>
<tr>
<td>Vitamin E deficiency</td>
<td>(?) Small intestinal ceroidosis (i.e., “brown bowel syndrome”)</td>
</tr>
<tr>
<td>Vitamin A deficiency</td>
<td>Reduced numbers of intestinal goblet cells</td>
</tr>
</tbody>
</table>

TABLE 5.  Effects of depletion of specific nutrients on the intestine

60  FIRST PRINCIPLES OF GASTROENTEROLOGY
Lactose may be found in milk, including buttermilk, even if it has been naturally fermented. Commercial yogurt should also be avoided, since this often has milk or cream added after fermentation to avoid the sour taste produced by fermenting lactose. Ice cream and sherbets have high lactose concentrations and should be avoided. Cheese or desserts made from milk or milk chocolate as well as sauces or stuffings made from milk, cream or cheese should also be avoided. Calcium supplements may be necessary with dairy product restriction, particularly in postmenopausal women. Liquid dairy products may be used to a limited extent by patients who have lactose intolerance; in these patients, an enzyme preparation (prepared from yeast or bacteria) added to milk at 4°C (15 drops/L) can hydrolyze up to 99% of the lactose in 24 hours. Nonliquid dairy products cannot be treated with enzyme preparations, although lactase tablets may be chewed prior to eating solid food.

5.2 Celiac Disease
Celiac disease, also known as gluten-sensitive enteropathy or celiac sprue, is a malabsorption disorder resulting from ingestion of proteins derived from certain cereal grains of the grass family, Gramineae: wheat, rye, barley and possibly oats. It is believed that the alcohol-soluble gliadin fraction of wheat gluten or similar alcohol-soluble proteins from the other grains (termed prolamins) cause the intestinal damage. Consequently, absolute restriction is required for life. Table 6 provides some dietary guidelines for celiac disease patients. Gluten, however, is a particularly ubiquitous substance and can be found in coffee, catsup, dip, frozen TV dinners, ice cream and even in the capsules of medications! Although wheat, rye, barley and possibly oats are

<table>
<thead>
<tr>
<th>Foods to avoid</th>
<th>Acceptable foods</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wheat, rye, barley, oat products</td>
<td>Corn, rice, buckwheat products</td>
</tr>
<tr>
<td>Triticale (wheat–rye hybrid)</td>
<td>Wine and distilled alcoholic beverages</td>
</tr>
<tr>
<td>Millet and sorghum</td>
<td>Fruits and vegetables</td>
</tr>
<tr>
<td>Malt and hydrolyzed vegetable protein</td>
<td>Meat</td>
</tr>
<tr>
<td></td>
<td>Nuts</td>
</tr>
<tr>
<td></td>
<td>Dairy products (unless lactose-intolerant)</td>
</tr>
</tbody>
</table>

TABLE 6. Dietary guidelines for celiac disease patients
important, corn and rice do not appear to activate celiac disease. Data on other grains are not as clear. Buckwheat is not derived from the grass family and is usually permitted. Millet and sorghum are often allowed, but have not been thoroughly evaluated. Triticale, a hybrid of wheat and rye, should be avoided. Rye whiskey, Scotch whiskey and other cereal-derived alcohols can be consumed, since gluten is not present in distilled spirits. Similarly, brandy and wine made from fruit pose no difficulties. Beer and ale are produced from barley; it is not entirely clear if they can activate disease and would best be avoided. Malt made from barley should be avoided, as well as hydrolyzed vegetable proteins used as flavor enhancers in processed foods, since they may be made from soy, wheat and other cereal proteins.

For both symptomatic and asymptomatic patients with celiac disease, a lifelong gluten-free diet is recommended. Multivitamin supplements are frequently required and specific vitamin, mineral and trace element deficiencies should be corrected. Iron and folate supplementation may be needed and poor absorption of oral iron may sometimes necessitate parenteral administration. Supplements of calcium and vitamin D may be required to prevent mobilization of skeletal calcium, and in some patients magnesium may be needed.

5.3 Inflammatory Bowel Disease
Malnutrition in patients with inflammatory bowel disease, especially Crohn’s disease, is a frequent problem. Weight loss may be seen in over 65% of patients and growth retardation may be observed in up to 40% of children. As shown in Table 7, there are multiple causes for malnutrition, especially in patients with Crohn’s disease with small bowel involvement. The goal of nutritional management is to ensure adequate nutrient intake with modifications that reduce symptoms. Although only limited studies are available, evidence suggests that energy expenditure in quiescent Crohn’s disease and ulcerative colitis is no greater than one would predict for a healthy individual. If the disease is quite active, or is accompanied by fever or sepsis, resting energy expenditure increases. Interestingly, patients, even with quiescent Crohn’s disease, have evidence of increased fat oxidation at rest, similar to findings in starved individuals. There may be increased caloric as well as nutrient requirements, particularly if gastrointestinal losses are substantial and malabsorption is significant. Attention should also be placed on micronutrient deficiencies in these patients, particularly if concomitant malabsorption is present. For example, patients with significant ileal disease or resection require regularly administered parenteral vitamin B₁₂.

Lactose intolerance is no more common in patients with ulcerative colitis than in healthy individuals. Furthermore, lactose intolerance is also
probably no more common in patients with Crohn’s disease. However, the effect of lactose intolerance in a patient with impaired colonic obstruction may be much more profound in terms of diarrhea. Owing to the problems with malnutrition in Crohn’s disease, a lactose-restricted diet should not be recommended unless there is clear-cut improvement in diarrhea with lactose restriction.

Specific drugs may also alter nutrient absorption. Cholestyramine is the classic example of an agent that interferes with nutrient (especially cations such as zinc) and drug absorption.

The role of enteral and parenteral nutrition in Crohn’s disease is discussed in Section 7.5.2.

6. DIETARY THERAPY IN LIVER DISEASE

Two important manifestations of chronic liver disease, ascites and portosystemic encephalopathy, have dietary modification as a cornerstone of treatment. The prime dietary objective in the treatment of ascites is sodium restriction. Some authorities have recommended restriction of dietary sodium intake to as little as 10–20 mmol/day for patients with symptomatic, large-volume ascites. However, it is almost impossible to design a palatable diet or provide sufficient protein to maintain nitrogen balance with such stringent restrictions, and therefore these will not be satisfactory for long-term use. Well-motivated patients can often be maintained on a 40 mmol sodium diet (equivalent to about 1 g of sodium or 2.5 g of sodium chloride).

The treatment of portosystemic encephalopathy includes dietary protein restriction. Management will obviously need to be individualized for patients with fulminant hepatic failure or coma, but patients with chronic liver disease and mild to moderate encephalopathy should usually have dietary protein intake restricted to 0.5–0.8 g/kg body weight. Even more rigorous restriction may be necessary to control encephalopathy in the short term, but is difficult to maintain for prolonged periods because of limited patient compliance and negative nitrogen balance. It is believed that vegetable protein may be less ammoniagenic than meat, but part of this may relate to decreased efficiency of absorption of vegetable protein. Disproportionately high levels of aromatic amino acids are found in plasma of patients with decompensated cirrhosis. Hence, nutritional supplements rich in branched-chain amino acids have been advocated; however, unequivocal evidence for their efficacy is lacking.

Patients with advanced cirrhosis often have hepatic glycogen depletion. During fasting, glucagon and catecholamines will be released to maintain blood glucose levels. In the absence of hepatic glycogen stores, this requires gluconeogenesis, and the substrate is provided to a significant extent from
TABLE 7. Malnutrition in inflammatory bowel disease

Reduced oral intake
Disease-induced (e.g., postprandial abdominal pain and diarrhea, sitophobia, anorexia, nausea and vomiting)
Iatrogenic (e.g., restrictive diets, “fad” diets)

Malabsorption
Reduced absorptive surface (e.g., shortened small intestine due to prior resection, diseased segments)
Bacterial overgrowth (e.g., associated with strictures and bypassed loops, stasis)
Bile salt deficiency after ileal resection (e.g., impaired micelle formation and steatorrhea)
Lactase deficiency (e.g., associated with small bowel disease)
Drug-induced malabsorption

Increased nutrient loss
Protein-losing enteropathy
Diarrhea losses of electrolytes, minerals and trace elements (e.g., potassium, zinc)
Gastrointestinal blood loss (e.g., iron loss)

Drug-induced malabsorption
Cholestyramine (e.g., bile acids; fat; fat-soluble vitamins, including vitamins D and K)
Sulfasalazine (e.g., folic deficiency associated with reduced absorption and increased requirement related to hemolysis)
Steroids (e.g., calcium absorption and mobilization)

Increased requirements
Chronic inflammatory disease, fever, superimposed infection

muscle catabolism. Utilization of the amino acids for gluconeogenesis will lead to ammonia production. It is not known whether dietary manipulations designed to provide a continuous supply of glucose, and therefore to reduce gluconeogenesis, would improve the hyperammonemia in these individuals. Cholestatic liver diseases, including primary biliary cirrhosis (PBC), secondary biliary cirrhosis, sclerosing cholangitis and biliary atresia, may be accompanied by malabsorption of fat-soluble vitamins. Vitamin K deficiency can be easily confirmed with the demonstration of a prolonged prothrombin time that corrects with administration of parenteral vitamin K. Assays for vitamins D, A and E are generally available only in specialized laboratories. If confirmatory tests are not available and if there are strong clinical grounds for suspecting a deficiency state, appropriate replacement therapy should be initiated. Table 8 lists a number of hereditary liver diseases for which appropriate therapy includes specific dietary interventions.
7. NUTRITION INTERVENTION

7.1 Introduction
The decision to intervene nutritionally is based on a number of disparate factors, including the current nutritional status of the patient (well-nourished versus malnourished), the duration of the time the patient will be expected to be unable to eat, the underlying medical condition and the prognosis for recovery. Once the decision to intervene has been made, the next decision is the method of intervention: oral, enteral or parenteral.

7.2 Nutritional Assessment
Malnutrition can affect patient morbidity and mortality. It is thus important to detect malnourished patients and improve their nutritional status by providing nutritional support. There are several methods to assess nutritional status; the best method would be the one that predicts clinical outcome. In particular, the best method would predict nutrition-associated complications that increase the risk of morbidity and mortality in the absence of nutritional intervention.

TABLE 8. Diet therapy for hereditary liver diseases

<table>
<thead>
<tr>
<th>Disorder</th>
<th>Dietary intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tyrosinemia</td>
<td>Low-phenylalanine diet</td>
</tr>
<tr>
<td>Hereditary fructose intolerance</td>
<td>Low-fructose, low-sucrose diet</td>
</tr>
<tr>
<td>Galactosemia</td>
<td>Galactose-free diet</td>
</tr>
<tr>
<td>Glycogen storage disease</td>
<td>Continuous glucose feeding</td>
</tr>
<tr>
<td>Cerebrotendinous xanthomatosis</td>
<td>Deoxycholic acid supplementation</td>
</tr>
<tr>
<td>Wilson’s disease</td>
<td>Low-copper diet, zinc supplementation (together with chelating agent)</td>
</tr>
<tr>
<td>Hemochromatosis</td>
<td>Avoidance of excess dietary iron, selection of foods containing phytates or tannins to reduce iron absorption (together with appropriate phlebotomy treatment)</td>
</tr>
<tr>
<td>Cystic fibrosis</td>
<td>Low-fat diet, pancreatic enzyme supplements, fat-soluble vitamin supplements</td>
</tr>
</tbody>
</table>
However, since it is often difficult to dissect out the effect of malnutrition from the effect of disease, nutritional assessment cannot rely on a single parameter or simple model. Furthermore, disease can affect several parameters used for nutritional assessment independently of nutritional status.\(^1\)

### 7.2.1 METHODS OF ASSESSING NUTRITIONAL STATUS (TABLE 9)

#### 7.2.1.1. Body composition
Several methods can be used to measure various body compartments and most are used within a research protocol. The ones most frequently used clinically are based on a two compartment model: body fat and lean body mass (muscle, bones). This can be assessed, for example, by anthropometry, where triceps and subscapular skinfold thicknesses provide an index of body fat, and mid-arm circumference provides a measure of muscle mass. This method is mostly used in population studies and is less reliable in the individual patient because of inter- and intra-observer variability and the effect of hydration status, age and physical activity.

#### 7.2.1.2. Body weight and weight loss
This is a simple measure and is compared to an ideal weight for height, usually by calculating body mass index (BMI). BMI is the weight in kilograms divided by height in meters squared. A normal BMI is 20 to 25 kg/m\(^2\). An ideal weight should give a BMI in that range. On the other hand, a BMI less than 18.5 suggests undernutrition and it is associated with significant morbidity and mortality.\(^2\) A BMI over 25 but below 30 suggests overweight. When BMI reaches 30 or above, the patient is obese and high BMI is also associated with increased risk of morbidity and mortality.\(^2\) A history of weight loss is also important. Studies have shown that unintentional weight loss of > 10% is a good predictor of adverse clinical outcome.

#### 7.2.1.3. Creatinine-height index (CHI)
The excretion of creatinine in the urine is related to muscle mass. Normalized for height, the 24-hour creatinine excretion is an index of muscle mass and can be compared to published tables. However, in a hospital environment, this is not used because of frequent underlying renal disease and use of diuretics.

#### 7.2.1.4. Plasma proteins
Albumin is one of the most studied proteins and several studies have demonstrated that low serum albumin concentration correlates with an increased incidence of medical complications and mortality.\(^1\) However, serum albumin may be inappropriate as a measure of nutritional status because it represents the summation of many events: synthesis, degradation, losses, exchange between intravascular and extra-vascular
compartment and volume of distribution. Therefore, hospitalized patients may have lower albumin levels for several reasons: inflammatory disorders cause a decrease in albumin synthesis, an increase in albumin degradation and transcapillary losses; gastrointestinal, cardiac and renal diseases as well as wound, burns and peritonitis can cause significant albumin losses and during serious illness, vascular permeability increases dramatically (with loss of albumin into the interstitial space). On the other hand, protein-calorie malnutrition causes a decrease in the rate of albumin synthesis, but a short-term reduction in albumin synthesis will have little impact because of albumin’s low turnover rate (half-life: 20 days) and large pool size. Even during chronic malnutrition, plasma albumin concentration is often maintained because of compensatory decrease in albumin degradation and transfer of extra-vascular albumin to the intravascular compartment. Another plasma protein, pre-albumin, is more responsive to nutritional changes because its turnover rate is rapid with a half-life of 2–3 days. However, it is also influenced by underlying diseases such as inflammation, infections, renal and liver failure. Therefore, it is also an unreliable index of nutritional status in patients.

TABLE 9. Methods of nutritional assessment

1. Laboratory determinations
   - albumin, pre-albumin, transferrin, retinol-binding protein
   - lymphocyte count, WBC
   - 24-hour urinary urea nitrogen, nitrogen balance
   - creatinine-height index
   - delayed cutaneous hypersensitivity

2. Anthropometric measurements
   - height, weight, ideal body weight (IBW), usual body weight (UBW), BMI
   - weight as percent IBW or UBW, % weight loss
   - triceps skinfold thickness, mid-arm circumference and others

3. Techniques to assess body composition
   - bio-impedance
   - imaging: DEXA, CT scan
   - dilution radioisotope methods, whole body counting

4. Dietary intake

5. Miscellaneous
   - muscle function
   - indirect caliber of entry
7.2.1.5. **Immune competence** as measured by delayed cutaneous hypersensitivity is affected by severe malnutrition. However, other diseases and drugs may also influence the measurements making it a poor predictor of malnutrition in sick patients.

7.2.1.6. **Global assessment techniques** Several global assessment techniques exist. A prognostic nutritional index depending largely on albumin and transferrin was shown to provide a quantitative estimate of postoperative complication. Subjective global assessment (SGA) is a clinical method that has been validated and is able to identify patients who are at risk of developing complications due to malnutrition. It categorizes the patients as being well nourished (A) or as having moderate or suspected malnutrition (B) or severe malnutrition (C) (Table 10). The use of SGA in evaluating hospitalized patients gives reproducible results and can predict complications in several patient populations such as surgical, dialysis and liver transplant patients.

At present, there is no gold standard for evaluating nutritional status. It is important to recognize the multiple facets of malnutrition to detect the patient at risk of nutrition-related complications. Subjective global assessment combined with selective objective parameters defined above is the best clinical way to detect the patients at risk.

### 7.3 Nutritional Requirements

#### 7.3.1 NITROGEN REQUIREMENTS

In a well-nourished adult in steady state, total nitrogen intake will equal nitrogen output in urine, stool, skin and body fluids. This is termed (zero) “nitrogen balance.” Nitrogen is assimilated almost exclusively as protein, and, on average, 6.25 g protein is equivalent to 1 g nitrogen. The nitrogen is excreted predominantly as urea in the urine, but stool and skin losses account for about 2–3 g daily. In the steady state, ingestion of more nitrogen will merely result in excretion of more nitrogen in the urine, with the excess protein oxidized in the liver and used as an expensive energy source. In growing children or in malnourished adults, the nutritional goal is a positive nitrogen balance, meaning that body tissue is being formed in excess of what is being broken down (i.e., there is net growth). It is less clear that patients with conditions associated with protein loss, such as nephrotic syndrome and protein-losing enteropathy, benefit from extra protein intake. Indeed, there remains concern with nephrotic syndrome that extra protein may contribute to a fall in glomerular filtration rate (GFR), as has been reported in other renal conditions.
If energy requirements are met or exceeded, studies have shown that well-nourished adults can maintain nitrogen balance when given as little as 0.6 g/kg protein intake. In order to allow for biologic variability, the standard recommendation for protein intake is 0.75 g/kg. It is important that the protein supplied be of high quality; it should include all essential amino acids and a balanced mix of nonessential amino acids. Malnourished, septic, injured or burned patients will require more protein, in the order of 1.0 – 1.5 g/kg daily. Pregnant patients should also be given 1.5 g/kg protein daily. It is not clear that patients with conditions associated with protein loss, such as protein-losing enteropathy, benefit from extra protein intake. Indeed, patients with nephrotic syndrome may even benefit from protein restriction, though this is not firmly established.

### 7.3.2 ENERGY REQUIREMENTS

Resting energy requirements in average weight healthy subjects are accurately predicted by the Harris-Benedict equation:

**Males:** \[ \text{Energy (kcal/d)} = 66 + (13.75 \times W) + (5.00 \times H) - (6.78 \times A) \]

**Females:** \[ \text{Energy (kcal/d)} = 655 + (9.56 \times W) + (1.85 \times H) - (4.68 \times A) \]

where \( W \) = weight in kg, \( H \) = height in cm and \( A \) = age in years.
The Harris-Benedict equation may be less accurate in malnourished or obese individuals. Malnourished patients exhibit resting energy requirements about 10% to 20% below predicted. The resting energy requirements of obese patients will also be below predicted since adipose tissue is less metabolically active than other tissues. Unfortunately, there has been no well-validated calculation which will allow prediction of energy requirements in the obese patient, so many clinicians will subtract an arbitrary number of calories from the Harris-Benedict calculation, often in the range of 400 to 1,000 kcal, depending on the overall degree of obesity. (A widely used method to quantify obesity is the “body mass index” or BMI, which is calculated as follows: BMI = weight in kg/(height in m)². A value of BMI from 25 to 29.9 kg/m² is considered overweight, while a BMI > 30 is considered obese.)

Basal energy requirements, as predicted by these equations, increase in the presence of fever (13% per °C), sepsis or injury (up to 20–30%), and burns (up to 100%). Modest physical activity usually requires about 30% above basal requirements.

7.4 Types of Nutritional Intervention
The options for refeeding include oral refeeding, tube feeding and total parenteral nutrition. An assessment by a dietitian regarding current food intake and food preferences is essential. It may well be possible by determining food preferences to provide a well-balanced, nutritionally complete diet. In addition, supplements of high-calorie, high-protein foods such as milkshakes or commercially prepared liquid formula diets may allow for adequate intake. If the patient will not or cannot eat, however, nutritional intervention may be indicated. Examples of patients who will not eat include those with anorexia due to tumor or chemotherapy, and those with anorexia nervosa. Such patients generally have a normal or near-normal nonobstructed bowel, and can be fed enterally. Patients who cannot eat because of severe gastrointestinal illness include those with bowel obstruction or ileus. If nutritional intervention is required in these patients, parenteral (intravenous) nutrition will be necessary.

7.4.1 ENTERAL NUTRITION

7.4.1.1 Methods of delivery
Enteral nutrition generally refers to nutrition provided through a tube that has been inserted into the gastrointestinal tract. Usually the tube is a fine-bore (10 French [3.3 mm] or less) Silastic® or polyurethane tube placed via the nose into the stomach, duodenum or jejunum. When long-term feeding is required, it is often preferable for cosmetic and comfort reasons to perform a gastrostomy.
radiologically or endoscopically, the latter commonly referred to as a PEG (percutaneous endoscopic gastrostomy). These tubes can be placed through the pylorus to feed into the jejunum with only local anesthetic and mild sedation. Despite convincing evidence of efficacy of post-pyloric placement of tubes in reducing pulmonary aspiration, the tube is usually placed in the jejunum if aspiration is a concern.

7.4.1.2 Enteral formulas
A multitude of commercial enteral formulas are available for infusion. The formulas have been traditionally divided into polymeric, oligomeric, monomeric, modular and disease-specific formulas. Polymeric formulas (also called defined formula diets) provide nitrogen as whole protein, often casein, egg white solids or soy protein. Carbohydrate is often provided as corn syrup, maltodextrins or glucose oligosaccharides, with sucrose added for sweetness in oral formulas. Fat is usually provided as soy oil, although corn oil and safflower oil may be used. Medium-chain triglycerides (MCT oil) are rarely used. Protein may be provided as milk (usually dry or skim), with lactose as a major carbohydrate. These formulas are contraindicated in patients with lactose intolerance.

Oligomeric formulas (also called semi-elemental diets) provide nitrogen as peptides from partially hydrolyzed whole protein. Monomeric formulas (also called elemental diets) provide nitrogen as crystalline amino acids. Carbohydrate tends to be provided as glucose oligosaccharides or glucose. Fat is usually present in small quantities, enough to meet the requirement for linoleic acid (an essential fatty acid), which is about 2–4% of total calories. MCT oil is added to some formulas. The oligomeric and monomeric diets were formulated to require minimal digestion by the gastrointestinal tract, with little necessity for bile and pancreatic secretions, and minimal “work” by the enterocyte in terms of brush-border enzyme activity or re-esterification. Hence, these diets have been commercially promoted as ideal for patients with decreased bile output (cholestasis), pancreatic insufficiency and short bowel. However, there is little evidence that these diets are superior to polymeric diets. Furthermore, since the diet is “predigested,” osmolality is high. Finally, the high cost of these diets (often five to 10 times that of polymeric diets) rarely justifies their use.

Most of these formulas provide enough protein, calories, water, electrolytes, minerals, vitamins and trace elements in 2 L/day for most “nonstressed” patients. In other words, these diets are “complete.” Excess requirements may exist in patients with multiple injuries, major infections or burns.

Modular formulas are those that contain or predominantly contain one kind of nutrient. There are commercially available modules for protein, fat, carbohydrates, vitamins, electrolytes and trace elements. These modules are not
required for the majority of patients, and are rarely used. However, they may be used if different nitrogen-to-calorie ratios are indicated for a patient. Examples of this might include burns or protein-losing enteropathy, if more protein is to be given, or liver disease, if less protein is to be given. Modular feeding is time-consuming, since solutions must be mixed by the hospital, and are more expensive than “complete” formulas.

Finally, specialized amino acid solutions have been made for use in special circumstances – for example, liver disease, renal disease and “stress,” such as trauma and sepsis. For liver disease, these solutions are composed mostly or exclusively of branched-chain amino acids, whereas for renal disease the solutions are predominantly essential amino acids. In general, these solutions are expensive and their efficacy is controversial.

Complications of enteral feeding may be divided into aspiration, mechanical, gastrointestinal and metabolic. In general, enteral feeding is well tolerated, and provided the complications are known, preventive and/or corrective measures may be undertaken to minimize patient risk.

7.4.1.3 Complications
Aspiration of the infused formula, with development of pneumonia, is a potentially lethal complication of tube feeding. Proper positioning of the tube requires radiographic verification. Risk factors for aspiration include patients on a ventilator and those with gastroesophageal reflux, poor or absent gag reflex, and impaired mentation. To minimize aspiration, it is suggested that patients, when possible, be fed with the head of the bed elevated 20–30°. Gastric contents should initially be checked by aspirating the tube every four to six hours and if the residual volume is > 150 mL, the infusion should be temporarily stopped. Unfortunately, the small nasoenteric tubes in current use often collapse when aspirated, so small returns do not guarantee that the stomach is not becoming distended with fluid. Hence, examination for epigastric distention and succussion splash should be done. If there is any concern, an upright (if possible) plain film to assess gastric size may be useful. It has also been suggested that the feeding tube be placed into the small bowel well beyond the pylorus to minimize aspiration in those at risk, though studies have failed to confirm this.

The following mechanical problems in patients with nasoenteric tubes include problems in the upper respiratory tract and esophagitis with development of esophageal ulceration, stenosis and even tracheoesophageal fistula. Upper respiratory problems include pharyngeal irritation, nasal erosions and necrosis, sinusitis and otitis media. These mechanical problems can be largely avoided by the use of soft, small-bore nasoenteric tubes.
Gastrointestinal problems related to nasoenteric feeding are common, occurring in 20–30% of patients. The most frequent complaints are nausea, vomiting, abdominal distention and altered bowel habit. Symptoms may be minimized by feeding at a slow rate with dilute solutions, but these symptoms may be just as common as with full-rate, full-strength solutions. Alternatively, a different enteral solution may be tried. If a lactose-containing solution is being used (generally not recommended for tube feeding), changing to a lactose-free solution is indicated. For constipation, fiber-containing solutions may be tried, although they are often unhelpful. Fiber, however, is a potential energy source for the colon, as previously discussed, and may therefore be important for maintenance of the colonic mucosa. At the present time, fiber-containing solutions are not routinely used.

Metabolic complications include overhydration, dehydration, hyperglycemia (including hyperosmolar nonketotic coma) and electrolyte disturbances. Electrolyte problems include hyponatremia, hyper- and hypokalemia, hyper- and hypophosphatemia and hypomagnesemia. In healthy, reasonably nourished individuals with normal cardiac, liver and renal function, these problems are not common. It is recommended that appropriate blood tests be done at intervals over the first few weeks to check for these potential problems.

7.4.2 TOTAL PARENTERAL NUTRITION
Total parenteral nutrition (TPN) involves intravenous administration of all known essential nutrients. This form of therapy is as effective as oral or enteral intake in terms of growth and maintaining body nitrogen. Indications include inability to eat for a minimum of seven to 10 days with a nonfunctional gut. Total parenteral nutrition is also used for “bowel rest,” especially in Crohn’s disease, intestinal fistulas and pancreatitis, even if adequate absorption is possible. Several studies suggest, however, that bowel rest is not helpful in Crohn’s disease. Furthermore, other studies have shown that elemental diets can be used instead of TPN, except when bowel obstruction is present. In general, if the gut is functional, enteral feeding is preferred since it is safer, cheaper and more physiologic.

7.4.2.1 Solutions

_Amino acids_ “Protein” is supplied as synthetic crystalline, L-amino acid solutions; these are commercially available in 7–10% concentrations. Most available amino acid mixtures are devised for patients without special requirements. Solutions with added branched-chain amino acids are available for hepatic failure, and solutions with essential amino acids are available for renal failure.
Fat  There is a human requirement for linoleic acid, which is a precursor of arachidonic acid, which is in turn a precursor of prostaglandins. Linoleic acid, an essential fatty acid, cannot be produced by humans. It has been recommended that this be supplied as 4% or more of total caloric intake. Commercial fat solutions consist of soybean or safflower oil, emulsified with egg phospholipid, and made isotonic at 300 mOsmol/L with added glycerol. Commercially available fat emulsions are available at concentrations of 20%.

Carbohydrate  Glucose is the preferred carbohydrate for intravenous use. Glucose is widely available in concentrations from 5–70%. The osmolality of these solutions may be markedly hyperosmolar up to about 2,500 mOsmol/L.

Nonprotein energy source  Once the initial 100 g of glucose is provided for use in the brain, renal medulla and red blood cells, glucose and fat are equally effective in preserving body nitrogen after an equilibration period of four to five days. Glucose is very inexpensive as an energy source, but requires insulin for uptake into cells, and hyperglycemia can be a problem when large amounts of glucose are utilized. The high osmolality of glucose solutions means that only dilute solutions can be used in peripheral veins, and if glucose is used as a major energy source, a large central vein is necessary to prevent thrombosis. Furthermore, glucose has a respiratory quotient (R.Q. = CO₂ produced/O₂ consumed) of 1.0, meaning that large amounts of carbon dioxide may be produced. Finally, glucose infusion leads to catecholamine release and increased metabolic rate, further increasing carbon dioxide production. These changes may be deleterious for patients being weaned from ventilators, or with borderline respiratory function.

Lipid solutions offer the benefit of being iso-osmolar, containing linoleic acid and having a lower respiratory quotient of 0.7, with less carbon dioxide production. Drawbacks include somewhat higher cost compared to glucose, and poor tolerance in patients with hyperlipidemia.

7.4.2.2 Routes of delivery

Central  The most flexible way to deliver total parenteral nutrition is through a large central vein, usually the superior vena cava, via either the internal jugular or subclavian approach. With the large flow through the superior vena cava, solution osmolality is not of great concern, and thrombosis of this vessel is uncommon.
Peripheral  While TPN can be provided through a peripheral catheter using a 10% dextrose solution in combination with a 5-8% amino acid solution, the rate of thrombophlebitis is sufficiently high that this method of providing nutrition cannot be recommended.

7.4.2.3 Complications
Complications of total parenteral nutrition may be divided into local and systemic. Local problems relate to the catheter site, and in the case of central lines involve all the complications of central catheters, including inadvertent arterial catheterization with bleeding, pneumothorax, hemothorax and inadvertent infusion of solutions into the pleural cavity. The complication of pneumothorax is much more common with subclavian insertion than with internal jugular insertion, meaning that internal jugular insertion is a safer technique, overall. In general, patients are more comfortable with a subclavian line once the catheter is in place. Air embolism may occur at the time of insertion or any time thereafter with a central line. Catheter embolization may occur, and as mentioned, thrombosis has been reported, particularly with the use of stiff catheters. It is essential that catheter placement be done by persons with considerable experience to minimize these complications.

Systemic complications include sepsis, metabolic problems and bone disease. Bacteremia or fungemia occurs in 3–7% of patients given total parenteral nutrition, and this appears to arise predominantly from the hub where the catheter joins the intravenous tubing. Catheters are always inserted in a strictly aseptic manner, with personnel fully gowned and gloved. Metabolic problems include hyperglycemia, which can be treated by reducing the amount of glucose given in the solutions, hypertriglyceridemia when excess calories and/or excess lipid is given, and alterations in electrolytes. In particular, total parenteral nutrition causes anabolism with increased intracellular water, so that potassium and phosphate are driven into cells, leading to possible hypokalemia and hypophosphatemia. These complications are very uncommon if adequate amounts of these electrolytes are provided and careful monitoring is performed. Liver disease remains a frustrating complication of total parenteral nutrition, but in most cases the changes are restricted to enzyme elevations. In general, mild elevations in AST and alkaline phosphatase occur in the second week, with occasional elevations in bilirubin occurring later. Liver biopsy may show mild cholestasis. Some of these changes may be due to overfeeding or by providing lipid in excess of 1 g/kg; this can be treated by reducing total calories and by ensuring excess lipid is not given. Rarely, long-term TPN (extending over years) may result in cirrhosis without a well-defined cause.
7.4.3 HOME ENTERAL AND PARENTERAL NUTRITION

7.4.3.1 Home enteral nutrition
Enteral nutrition may be provided on a long-term basis at home using any of the standard enteral formulas. While highly motivated individuals may do this using nasogastric tubes placed nightly with nocturnal feedings, most patients will need a gastrostomy or jejunostomy tube for long-term feeding. Intermittent bloodwork and physician follow-up visits, similar to home parenteral nutrition, will need to be done to ensure that the formula is appropriate and that the nutritional goals are being met. The patient or caregiver must be adequately versed in the management of the gastrostomy and jejunostomy tubes as well as in the potential complications of enteral feeding using such tubes. Intermittent replacement of these tubes is generally on an as-needed basis although some nutrition programs provide replacement on a predefined timetable, for example every 12 to 18 months.

7.4.3.2 Home parenteral nutrition
Home parenteral nutrition is used in patients who require long-term parenteral nutrition but who do not need hospital admission for any other medical reason. These patients have gut failure due to short bowel syndrome (e.g., Crohn’s disease, ischemic bowel disease), severe motility disturbances (scleroderma, idiopathic pseudo-obstruction), hyperemesis gravidarum and other miscellaneous problems. In the United States, cancer and AIDS account for a large number of home parenteral nutrition cases.

Home parenteral nutrition patients and/or their caregivers need to undergo appropriate training in aseptic techniques as well as training in management of catheter and pump care. This training may be done in a hospital setting or in an outpatient setting depending on the underlying condition of the patient. Regular bloodwork and follow-up visits with the physician, home care nurse and dietitian are essential.

Long-term complications of home parenteral nutrition include the usual complications of parenteral nutrition. However, line sepsis, venous thrombosis, metabolic bone disease and liver disease represent profound challenges in the long-term setting.

7.5 Nutrition Support in Specific Conditions

7.5.1 THE MALNOURISHED PATIENT
The malnourished patient represents a special challenge in nutrition. Malnourished patients have energy requirements which are 10% to 20% below predicted by the Harris-Benedict equation, as discussed above. Furthermore, such patients
are at particular risk for “refeeding syndrome,” consisting of a variety of problems occurring when nutrition is initiated. Fluid retention with marked edema and even congestive heart failure may occur. As the intracellular compartment is regenerated with refeeding, there may be shifts of extracellular substances into the cell including phosphorous, potassium and magnesium. These shifts are facilitated by insulin which is released in response to glucose given as part of the nutrition. It is very important to provide adequate amounts of phosphorous, potassium and magnesium. Other problems include glucose intolerance and thiamine deficiency.

With the above problems in mind, the malnourished patient who is being re-fed requires careful clinical monitoring of fluid status and daily measurement of serum phosphorous, potassium, magnesium and glucose until normal, stable levels are obtained. Vitamins, especially thiamine, should be administered at the onset of nutritional repletion and continued for several days.

7.5.2 CROHN’S DISEASE
Crohn’s disease represents a special situation for nutrition due to potential problems with strictures, short bowel and sepsis. There was early enthusiasm for the use of parenteral nutrition and elemental enteral nutrition as a mode of both primary and secondary treatment of Crohn’s disease under the guise of “bowel rest.” While many studies have reported clinical remission in patients receiving both enteral and parenteral nutrition, there are no randomized controlled trials demonstrating the efficacy of these treatments. Indeed, corticosteroid therapy has been shown in meta-analyses to be more effective than enteral nutrition. There is clearly a role for enteral nutrition in the pediatric population, where this modality provides for linear growth in growth-retarded patients. It should be noted that monomeric (elemental) diets have not been shown to be more effective than polymeric diets when these formulas have been compared.

7.5.3 PANCREATITIS
Pancreatitis offers a unique challenge in nutrition. First, infusion of nutrients into the duodenum stimulates pancreatic secretion, which may be theoretically harmful in patients with pancreatitis. Second, patients with pancreatitis frequently have vomiting and ileus as a manifestation of their condition. Finally, the pancreas secretes both exocrine and endocrine products important in nutrition, namely pancreatic enzymes and insulin. Despite these considerations, the preferred method of providing nutrition in acute pancreatitis is elemental jejunal feeding which has been found to be safer than parenteral nutrition with fewer septic complications. Uncommonly, parenteral nutrition may be necessary if enteral feeding is not tolerated.
REFERENCES


SUGGESTED READING LIST


OBJECTIVES

1. Know the biochemical pathways important to the understanding of carbohydrate, fat and protein metabolism both in the fasting and fed state.
2. Be able to describe the clinical changes important in malnourished states.
3. Understand the role of diet and nutrition in important gastrointestinal diseases, specifically inflammatory bowel disease, celiac disease and liver disease.
4. Be able to undertake a nutritional assessment.
5. Appreciate the indications for instituting nutritional support.
6. Be able to give an overview of the types of nutritional intervention currently available.