Malnutrition is a significant problem worldwide and will be faced by all anaesthetists working in developing countries. Anorexia nervosa and malnutrition in Western countries has a high mortality rate. Patients are at increased risk if not identified and managed promptly.

Malnutrition is a whole-body disorder affecting all systems, organs and cells. All patients who are malnourished should be treated as though they have a full stomach. Careful adjustment of drug dosing and an understanding of the pharmacokinetics specific to the malnourished patient are vital.

**AETIOLOGY**

The basic cause of malnourishment is an imbalance between energy intake and energy expenditure. There are a variety of causes, which can broadly be divided into patient factors and environmental factors (Table 2).

**CLASSIFICATION**

Protein–energy malnutrition (PEM) is an umbrella term covering the conditions of kwashiorkor, marasmus and kwashiorkor–marasmus in combination. These are WHO-classified conditions predominantly affecting young children at weaning age.

**Kwashiorkor**

- A term first coined in 1935 translated from the Ga language meaning ‘the sickness the baby gets when the new baby comes’. A syndrome caused by severe protein deficiency despite overall energy intake that is adequate. Characterised by irritability, anorexia, oedema and ulcerating skin lesions. Abdominal distension, fatty liver and immune deficiency also occur (see Table 1).
- Cell membrane dysfunction leads to potassium and water leak from cells, causing oedema and fluid shifts.
• Profound hypokalaemia and hypophosphataemia are of most importance to the anaesthetist. These are due to cellular leakage; whole body sodium is elevated.

• The liver’s inability to process fats is manifested as intracellular fat deposition and fatty liver.

• Xerophthalmia, a severe vitamin A deficiency resulting in conjunctival dryness, corneal dryness, ulceration and ultimately blindness if left untreated, is also recognised.

Marasmus
• Named from the Greek marasmos – decay or wasting.
• Extreme form of malnutrition classified as body weight < 60% of expected.
• Condition caused by overall lack of dietary calorie intake and energy deficit.

PATHOPHYSIOLOGY

Catabolism and the starvation response
The body exhibits an adaptive ‘starvation response’ to prolonged inadequate calorie intake. This is initially focused on mobilising energy stores to provide glucose and later ketones as an energy substrate for the brain and central nervous system. The starvation response can broadly be divided into three main stages, as outlined in Table 3.

When considering the pathological effects of prolonged starvation it is useful to classify the problems using a systems-based approach (Table 4). Starvation is a ‘whole body’ response to inadequate calorie intake that is partly adaptive and partly maladaptive. Cachexia is weight loss as a manifestation of underlying physical disease, cardiac disease, chronic obstructive pulmonary disease (COPD) malignancy and chronic renal failure being the major causes. Inflammatory mediators, especially cytokines, are thought to play a role in the excessive weight loss associated with these conditions.

Refeeding syndrome
Refeeding syndrome describes the metabolic alterations that result from rapid nutrition repletion in severely malnourished patients. It is thought to occur in 6–10% of malnourished patients who are given nutrition in hospital. Severity increases in relation to severity of pre-existing malnourishment status.

Hyperinsulinaemia following commencement of nutrition leads to decreased gluconeogenesis and decreased anaerobic metabolism. Rebound hypoglycaemia can easily occur if blood sugar levels are not checked regularly. Hyperinsulinaemia results in rapid movement of extracellular phosphate, potassium and magnesium into the intracellular compartment, which can cause dangerous spikes in serum electrolyte concentrations (especially potassium). Low extracellular phosphate levels reduce ATP levels intracellularly, and 2,3-diphosphoglycerate (2,3-DPG) levels in erythrocytes are also reduced.

Clinical features include arrhythmias and systolic heart failure. Increased cardiac output, plasma volume and basal metabolic rate can overwhelm the ventricle, leading to congestive cardiac failure. Central nervous system effects include seizures, delirium and coma.
Table 3. Phases of the starvation response

<table>
<thead>
<tr>
<th>Phase</th>
<th>Details</th>
<th>Timing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glycogenolytic</td>
<td>70–100 g of glycogen stored in the liver and a further 400 g stored in the muscles is mobilised as an energy substrate</td>
<td>First 24 hours (early)</td>
</tr>
<tr>
<td>Gluconeogenic (early &lt; 24 hours)</td>
<td>Insulin levels fall in response to low glucose and amino acid levels, glucagon levels rise and lipolysis occurs in the liver. Glucose forms from glycogen due to lower insulin levels.</td>
<td>Up to 24 hours</td>
</tr>
<tr>
<td>Gluconeogenic (late)</td>
<td>After 24 hours all new glucose is derived from: amino acids (alanine being the most important) glycerol (from adipose tissue) lactate (from erythrocytes via the Cori cycle) This coincides with a rise in plasma glucagon concentration and continued insulin suppression Increased catecholamines and cortisol mobilise fat stores, increasing plasma free fatty acids Gluconeogenesis declines after 3–4 days as the body adjusts to mobilise energy from fat stores (fully adjusted by 2 weeks)</td>
<td>Beyond 24 hours (Intermediate)</td>
</tr>
<tr>
<td>Ketogenic</td>
<td>Ketone bodies gradually replace glucose as the fuel source for the brain and nervous system up to a maximum of 50% Ketone body formation by the liver is maintained Other tissues (cardiac and skeletal muscle) obtain energy from free fatty acids In this phase gluconeogenesis is reduced as a protein-sparing mechanism. This occurs at 10 days via reduction in glucagon. Initial protein catabolism = 70 g day⁻¹, reducing to 20 g day⁻¹ by week 3</td>
<td>Up to 2 weeks (and beyond)</td>
</tr>
</tbody>
</table>

To avoid refeeding syndrome, 5 kcal kg⁻¹ day⁻¹ is recommended in a deliberate under-delivery of calories in the early stages of refeeding. This should be coupled with judicious measurement of serum electrolytes on a daily basis with early correction of abnormalities as they occur. Input from a specialist dietitian and early identification of the patient at risk of refeeding syndrome are of the utmost importance.

The WHO recommends a three-phase refeeding protocol for patients at risk of refeeding syndrome:

1. rapid resuscitation phase
2. stabilising phase
3. weight gain and rehabilitation phase.

**PRACTICAL TIPS**

**Preoperative assessment**

**History**

History may be difficult to elicit in some patients, especially those with underlying psychiatric disorders. Aim to quantify overall daily calorie intake, as well as ascertaining whether the diet is balanced or lacking in crucial micronutrients. Specific questions about laxatives, amphetamines and diuretic use as well as menstrual cycle are useful in anorexic patients.

**Examination**

A full examination is essential with particular attention to the following features:

- thin, cachectic or wasted appearance – sunken eyes, prominent clavicles
- oedema and abdominal swelling, which can mask overall malnourished state in kwasiokor patients
- hydration status – dry skin and mucous membranes, dry tongue, decreased skin turgor
- orange tinged palms and soles as evidence of carotenaemia in anorexia nervosa
- lanugo hair
- amenorrhoea in females
- heart murmur
- hypotension.

The European Society for Clinical Nutrition and Metabolism (ESPEN) suggests that severe undernutrition is present if one of the following is present:¹³

- weight loss >10–15% within the past 6 months
- body mass index < 18.5
- subjective global assessment grade C (severely malnourished)
- serum albumin <3 g L⁻¹ (in the absence of hepatic or renal dysfunction).

**Additional tools**

- Nutritional Risk Assessment Scale (NRAS).¹⁶
- Triceps skinfold thickness or mean arm circumference.
- body mass index.
### Table 4. Body systems affected by malnutrition

<table>
<thead>
<tr>
<th>System</th>
<th>Features</th>
</tr>
</thead>
</table>
| Central nervous system | Impaired mental ability  
Mental depression  
Depressed cognitive function  
Fatigue and generalised weakness |
| Musculoskeletal      | Muscle mass and strength reduced  
Histologically confirmed myopathy in severe anorexia nervosa patients  
Reduced bone mass, osteopenia and osteoporosis with secondary fractures  
Impaired thermoregulation  
Impaired wound healing |
| Cardiovascular       | Reduction in cardiac output and blood pressure and bradycardia  
Increased risk of arrhythmia due to vitamin and electrolyte disturbance  
Mitral valve prolapse (poorly understood? due to weak and thin ventricular wall)  
Loss of cardiac muscle mass with associated reduced left ventricular function and ejection fraction (consider echocardiography in anorexic patients)  
Increased vagal tone  
Peripheral vasoconstriction  
Sinus arrest and wandering atrial pacemakers  
ECG changes  
Prolonged QTc  
ST depression and T-wave inversion |
| Respiratory          | Reduced respiratory muscle strength and function  
Spontaneous pneumothorax  
Pneumomediastinum from persistent vomiting  
Decreased respiratory compliance (due to decreased elasticity of lung tissues) |
| Renal                | Reduced glomerular filtration rate  
Total body water proportionally higher  
Proteinuria  
High urea due to dehydration |
| Gastrointestinal     | Decreased enteral feeding leading to gut atrophy, bacterial translocation and impaired immune function (due to larger gaps between enterocytes)  
Oesophagitis and Mallory–Weiss tear from purging  
Gastric dilatation  
Paradoxical decrease in gastric emptying time |
| Micronutrient        | Vitamin A insufficiency – blindness (xerophthalmia due to corneal ulceration is the leading cause of childhood blindness worldwide), immunosuppression  
Reduced iron, ferritin and iron deficiency anaemia  
Folic acid and zinc levels may also be low |
| Electrolyte disturbances | Hypokalaemia (due to repeated purging and vomiting)  
Hypocalcaemia = prolonged non-depolarising muscle relaxation action. Can lead to tetany but low K⁺ prevents this (rapid K⁺ replacement can precipitate it though)  
Hypoglycaemia and hypoglycaemic coma  
Metabolic alkalosis (less common in malnutrition, more likely in patients who purge)  
Increased cortisol and corticotrophin-releasing hormone levels with blunted response |

Continued on next page
Haematological Features

Leucopenia. Can be graded using Common Terminology Criteria for Adverse Events:

- \(< 1.2 = \text{grade 3}\)
- \(< 2.8 = \text{grade 2}\)
- \(< 3.0 = \text{grade 1}\)

Further drop due to stress response can occur due to inability to produce leucocytes.

Often normal immune function until 50% drop in normal expected body weight. Elevated liver transaminases.

Anaemia (often mild, due to bone marrow hypoplasia)

Pancytopenia

Pharmacological Features

Delayed or reduced absorption of drugs.

Hypoalbuminaemia increases free fraction of drugs, decreased protein binding occurs.\(^1\)

Prolonged treatment with non-depolarising muscle relaxants.

Lower total body mass means reduced drug doses required and lowered thresholds for toxicity.

Neostigmine, edrophinium and catecholamines can cause life-threatening arrhythmias.\(^4\)

Table 4. Body systems affected by malnutrition (continued)

<table>
<thead>
<tr>
<th>System</th>
<th>Features</th>
</tr>
</thead>
</table>
| Haematological | Leucopenia. Can be graded using Common Terminology Criteria for Adverse Events:  
- \(< 1.2 = \text{grade 3}\)  
- \(< 2.8 = \text{grade 2}\)  
- \(< 3.0 = \text{grade 1}\)  
  Further drop due to stress response can occur due to inability to produce leucocytes.  
  Often normal immune function until 50% drop in normal expected body weight. Elevated liver transaminases.  
  Anaemia (often mild, due to bone marrow hypoplasia)  
  Pancytopenia |  
| Pharmacological | Delayed or reduced absorption of drugs  
  Hypoalbuminaemia increases free fraction of drugs, decreased protein binding occurs.\(^1\)  
  Prolonged treatment with non-depolarising muscle relaxants.  
  Lower total body mass means reduced drug doses required and lowered thresholds for toxicity.  
  Neostigmine, edrophinium and catecholamines can cause life-threatening arrhythmias.\(^4\) |
Investigations

- Bloods – full blood count (FBC), creatinine and electrolytes, liver function tests, calcium, phosphate, magnesium, glucose, transferrin, albumin.
- Urinalysis for proteinuria and ketonuria.
- ECG for cardiovascular complications or evidence of electrolyte imbalance.
- Where available echocardiography can be considered in selected patients in whom a murmur is heard or who exhibit signs of cardiac failure.

Preoperative optimisation (see Table 5)

- Adequate hydration and correction of electrolyte abnormalities for emergency cases.
- Elective cases with albumin < 34 g·L⁻¹ or lymphocyte count < 1400 should have dietary problems corrected prior to major surgery.
- 7–10 days of preoperative parenteral nutrition has been shown to improve outcomes in malnourished patients.

Perioperative management

Induction

Adequate rehydration prior to induction is essential to avoid cardiovascular collapse. Be wary of IV hydration in oedematous children. Malnourished patients are at increased risk of aspiration due to gastric distension and delayed gastric emptying so consider inserting a nasogastric tube prior to intubation and have a low threshold for rapid sequence induction with cricoid pressure. Consider an antacid and a prokinetic prior to induction.

Intraoperative care

Malnourished patients are at high risk of intraoperative hypothermia. Make efforts to keep the patient warm with warmed IV fluids, patient warmer, heat and moisture exchange (HME) filter and careful monitoring of perioperative core temperature. Careful positioning is paramount to avoid nerve compression as reduced cushioning and muscle mass are common. Pressure-related necrosis or fractures due to careless posturing are also recognised in the underweight population.

Consideration of drug dosing, bearing in mind reduced total body mass, albumin concentration and volume of distribution, can avoid toxicity. Non-depolarising muscle relaxants should be administered with the use of a nerve stimulator to avoid dosing errors and a partial reversal scenario. Smaller initial doses are required as electrolyte abnormalities can potentiate their actions. Avoid reversal of neuromuscular blockade where possible, allowing agents to wear off spontaneously as this increases the risk of arrhythmias.

Hyperventilation should be avoided as this can further lower potassium levels, lowering the threshold for life-threatening arrhythmias. Halothane should be avoided for the same reason given its increased potential to cause arrhythmias. Given the potential for cardiovascular instability and reduced cardiac output state the anaesthetist should have a low threshold for invasive cardiac monitoring. The incidence of intraoperative arrhythmias has been reported to be as high as 16–62%.

Postoperative care

There is a high possibility of difficult extubation due to impaired respiratory muscle function and impaired upper airway reflexes in the severely malnourished patient. Aim to extubate the patient when he or she is fully awake and responding to commands, if feasible.

Early enteral feeding has been shown to be beneficial. Be wary of hypoglycaemia in the immediate postoperative period as the stress response to surgery can deplete glucagon stores. Cautious glucose replacement is required as hyperinsulinaemia following a glucose bolus can result in refractory hypoglycaemia immediately afterwards. The stress response results in catabolism of fat, glycogen and protein, resulting in raised levels of glucose, free fatty acids and amino acids in the serum initially, which in turn raises insulin levels and makes the patient vulnerable to sudden hypoglycaemia.

CONCLUSION

Anaesthetising patients who are malnourished calls for a considered and delicate approach. An in-depth pre-operative assessment looking for the cardinal signs of malnutrition and assessing for severity is crucial, as is with the institution of optimising measures if time allows.

When dealing with malnourished patients, presenting for non-elective surgery, have a low threshold for invasive cardiac monitoring, correct all electrolyte abnormalities promptly and be wary of respiratory compromise on extubation. Treat all malnourished patients as if they have a full stomach as the aspiration risk is high in this cohort, and have a low threshold for post-operative care in an intensive care setting if your institution allows this. Be vigilant for hypoglycaemia in the postoperative period as this is easily treated but can be life-threatening.

REFERENCES


www.wfsahq.org/resources/update-in-anaesthesia


