Definition

Malnutrition – the cellular imbalance between the supply of nutrients and energy and the body’s demand for them to ensure growth, maintenance and specific functions.

Undernourishment – consuming less than the recommended minimum number of calories required for growth whilst performing light exercise. The World Food Programme’s recommended food calorie intake per day is 2100 kcal per person. Additional calories are required when pregnant and if breast feeding.

Starvation – a severe deficiency in calories, vitamins or protein.

Inanition – the symptoms and effects of starvation.

Cachexia – excessive weight loss in the context of on-going disease, usually with disproportionate muscle wasting.

Severe malnutrition – multisystem disorder affecting every cell, organ and system. World Health Organization (WHO) guidelines defined as severe wasting (<70% weight for height or <3 standard deviations) with or without symmetrical oedema (see Table 1).

INTRODUCTION

There are an estimated 923 million undernourished people worldwide according to 2008 estimates. This number is decreasing, but malnutrition remains a major problem, and one frequently encountered in the health care setting of developing countries. Malnutrition is thought to contribute to 5 million of the 10.6 million infant deaths that occur in the world annually. Growth retardation and inability to fight disease cause significant long-term morbidity in survivors.

Children are at particular risk, with an estimated 50.6 million malnourished children < 5 years worldwide. Among hospitalised children, the mortality rate is 30–50% (World Health Organization).

Malnourishment is also a problem for the anaesthetist working in the western world, with 25–40% of hospital inpatients in the USA being malnourished, only half of whom are identified by medical staff. Aside from inadequate dietary calorie intake, a variety of other causes of malnutrition must be considered by the anaesthetist in the preoperative assessment of patients.

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.

Key points

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.

Sean Edwards
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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>
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<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. 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%</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 caloric 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.

Additional tools

- Nutritional Risk Assessment Scale (NRAS).
- Triceps skinfold thickness or mean arm circumference.
- body mass index.

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).
### Table 4. Body systems affected by malnutrition

<table>
<thead>
<tr>
<th>System</th>
<th>Features</th>
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</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  
Mitrval 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$^{14}$ |
| **Respiratory**               | Reduced respiratory muscle strength and function  
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 disturbances**| Vitamin A insufficiency – blindness (xerophthalmia due to corneal ulceration is the leading cause of childhood blindness worldwide), immunosuppression$^{12}$  
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-releaseing hormone levels with blunted response |

*Continued on next page*
System Features

**Haematological** 
Leucopenia. Can be graded using Common Terminology Criteria for Adverse Events:
- $< 1.2$ = grade 3
- $< 2.8$ = grade 2
- $< 3.0$ = 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

Prolonged treatment with non-depolarising muscle relaxants

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

Neostigmine, edrophonium and catecholamines can cause life-threatening arrhythmias

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**Table 5. General principles for routine care of malnourished patients (extracted from WHO nutritional guidelines)**

<table>
<thead>
<tr>
<th>Goal</th>
<th>Description</th>
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<tbody>
<tr>
<td>Prevent hypoglycaemia</td>
<td>50 mL of 10% glucose (one heaped teaspoon of sugar in 70 mL of water) orally or by nasogastric tube If lethargic/fitting/unconscious, 5 mL kg⁻¹ 10% dextrose IV then 50 mL 10% dextrose orally or by nasogastric tube Prevent relapse with 2-hourly feeds</td>
</tr>
<tr>
<td>Prevent hypothermia</td>
<td>If axillary temperature is $&lt; 35$°C or rectal temperature $&lt; 35.5$°C, rewarm until temperature $&gt; 36.5$°C. Consider skin-to-skin, clothing, heaters, wrapping head. Start feeding</td>
</tr>
<tr>
<td>Treat and prevent dehydration</td>
<td><em>Do not treat with IV fluids unless shocked. Low blood volume + oedema can be exacerbated by IV fluids</em> Administer rehydration salts, 5 mL kg⁻¹, orally or by nasogastric tube Assess for tears, fontanelle, skin turgor and mouth moistness Beware of overhydration as evidenced by raised respiratory rate or heart rate</td>
</tr>
<tr>
<td>Correct electrolytes</td>
<td>Use caution $K^+ 3–4$ mmol kg⁻¹ day⁻¹ $\text{Mg}^{2+} 0.4–0.6$ mmol kg⁻¹ day⁻¹</td>
</tr>
<tr>
<td>Identify and treat infection</td>
<td>Normal signs such as raised temperature may be absent in malnourished children Give broad-spectrum antibiotics and metronidazole, which helps heal bowel mucosa</td>
</tr>
<tr>
<td>Correct micronutrient deficiencies</td>
<td>Wait 2 weeks before administering iron Correct vitamin A deficiency immediately, first checking for eye signs (corneal clouding or ulceration) Administer multivitamins and folic acid for 2 weeks Consider zinc if evidence of skin desquamation or ulceration Transfuse if Hb $&lt; 4$ g dL⁻¹ or if compromised and $&lt; 6$ g dL⁻¹</td>
</tr>
<tr>
<td>Cautious refeeding</td>
<td>Homeostatic capabilities will be blunted so feeding should be commenced cautiously Aim for $&gt; 10$ g kg⁻¹ day⁻¹ weight gain Consider refeeding achieved when $&lt; 1$ SD or $&gt; 90%$ weight for length</td>
</tr>
<tr>
<td>Emotional support</td>
<td>Emotional and psychological support should be provided to parents and patient.</td>
</tr>
</tbody>
</table>
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%.14

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.19

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 raise 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


