Medical aspects of anorexia nervosa and bulimia nervosa

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Abstract

Eating disorders (EDs) have a lifetime prevalence of 8.4% for women and 2.2% for men. Anorexia nervosa (AN) and bulimia nervosa (BN) are commonly encountered in medical practice.

The main medical issue for BN and the binge-purge subtype of AN is electrolyte disturbance associated with purging and vomiting, which untreated can be fatal. This loss of K^+ and Cl^- with associated hypovolaemia may lead to hypokalaemic alkalosis. Treatment is by fluid and electrolyte replacement. Damage to the upper gastrointestinal (GI) tract, including reflux oesophagitis, dental problems, aspiration and, occasionally, oesophageal rupture, can occur.

In patients with the restrictive form of AN, the biggest risks are weight loss and malnutrition, which can have profound effects on the heart, gut, endocrine system and bone. Safe refeeding is essential. The risk to the person should be assessed using comprehensive, graded, multifactorial assessment tools, for example, Medical Emergencies in Eating Disorders (MEED). There is increasing evidence that patients can be safely refed at higher rates than was previously recommended, but it is important to assess the risk of refeeding syndrome and reduce the rate of refeeding if it is high.

Underfeeding syndrome, where patients fail to establish an adequate intake, is equally important. It is critical to manage anorexic behaviour on the ward to prevent it from frustrating the process of refeeding and stabilisation. Using established protocols, communicating effectively with the patient and their family, and being aware of the methods that may be used to avoid weight gain is important, as is an understanding of mental health legislation if the least-restrictive measures fail.

Recognising that the ED drives the behaviour of the patient and externalising the disorder, rather than blaming the patient, is important.

Patients with EDs have high rates of functional GI disorders and bone problems. A multidisciplinary approach to treatment is essential.

Introduction

Eating disorders (EDs) are common and most clinicians will encounter people with them during their careers. In EDs, the physical and psychological consequences are inseparable, and one can directly influence the other. Addressing both the physical and psychiatric aspects of EDs is essential for their management.

Patients with EDs are usually looked after by mental health and primary care teams and, with early diagnosis, attentive monitoring and careful follow-up, their physical problems can often be managed without the need for hospitalisation or the involvement of general medical specialists. In EDs, however, physical complications can arise which may be life-threatening or pose a significant risk to the long-term health of the person. In some cases, admission to a specialist eating disorder unit (SEDU) may be a possibility, but these are not always available and they may not be able to look after patients who require close laboratory monitoring, complex nutritional support or those who have severe malnutrition. Consequently, ED patients may come under the care of acute medical teams, particularly those specialising in gastroenterology or general medicine.

This review is directed towards acute medical specialists, and to guide psychiatrists, mental health teams and general practitioners who have patients whose physical condition is deteriorating. It concentrates principally on the medical problems associated with anorexia nervosa (AN) and bulimia nervosa (BN), but patients with any eating disorder can develop physical complications. People with avoidant/restrictive food intake disorder (ARFID) or autism spectrum disorder may have very disordered eating patterns and significant nutritional problems, but unlike in AN or BN, weight control is not usually the dominant motivation (1).

In AN and BN, concern about potential weight gain drives compensatory behaviours, and the balance between the primary drivers and the compensatory behaviours determines the presentation of the disease (Box 1). In AN, fear of weight gain is obsessive and the compensatory behaviours and calorie restrictions are disproportionate, leading to weight loss and undernutrition. In BN, the binging and compensatory behaviours are in balance, and the patient remains at normal or near-normal weight. In both conditions "the disease drives the behaviour" of the patient, which, in turn, may frustrate the medical treatment of the underlying condition (1). Similarly, the physical condition of the patient affects their mental state, particularly in AN where malnutrition can have a significant effect on the patient's

Box 1. Eating disorder definitions based on ICD-11 classifications (4)

Feeding and eating disorders

Involve abnormal eating or feeding behaviours that are not explained by another health condition and are not developmentally appropriate or culturally sanctioned. Eating disorders involve abnormal eating behaviour and preoccupation with food as well as prominent body weight and shape concerns.

Anorexia nervosa (6B80)

Characterised by significantly low body weight for the individual's height, age and developmental stage that is not due to another health condition or to the unavailability of food. A commonly used threshold is body mass index (BMI) less than 18.5 kg/m^2 in adults and BMI-for-age under the 5th percentile in children and adolescents. Rapid weight loss (e.g., more than 20% of total body weight within 6 months) may replace the low body weight guideline as long as other diagnostic requirements are met.

Bulimia nervosa (6B81)

Characterised by frequent, recurrent episodes of binge eating (e.g., once a week or more over a period of at least one month). A binge eating episode is a distinct period of time during which the individual experiences a subjective loss of control over eating, eating notably more or differently than usual, and feels unable to stop eating or limit the type or amount of food eaten. Binge eating is accompanied by repeated inappropriate compensatory behaviours aimed at preventing weight gain (e.g., self-induced vomiting, misuse of laxatives or enemas, strenuous exercise). The individual is preoccupied with body shape or weight, which strongly influences self-evaluation. There is marked distress about the pattern of binge eating and inappropriate compensatory behaviour or significant impairment in personal, family, social, educational, occupational or other important areas of functioning. The individual does not meet the diagnostic requirements of anorexia nervosa.

Avoidant/restrictive food intake disorder (6B83)

Characterised by avoidance or restriction of food intake that results in: (1) the intake of an insufficient quantity or variety of food to meet adequate energy or nutritional requirements that has resulted in significant weight loss, clinically significant nutritional deficiencies, dependence on oral nutritional supplements or tube feeding, or has otherwise negatively affected the physical health of the individual; or (2) significant impairment in personal, family, social, educational, occupational or other important areas of functioning (e.g., due to avoidance or distress related to participating in social experiences involving eating). The pattern of eating behaviour is not motivated by preoccupation with body weight or shape. Restricted food intake and its effects on weight, other aspects of health, or functioning are not due to unavailability of food, not a manifestation of another medical condition (e.g., food allergies, hyperthyroidism) or mental disorder, and are not due to the effect of a substance or medication on the central nervous system, including withdrawal effects.

cognitive abilities (2). Whilst it is difficult to quantify this effect, the classic studies of Ancel Keys in which young, healthy male volunteers who agreed to be starved experienced profound effects on their cognition and mood as their weight fell by 20%, at which point they were all successfully refed (3).

Twin and other genetic studies suggest that both AN and BN have strong genetic predispositions. The female relatives of individuals with AN are 11 times more likely to develop AN than those without. Twin studies suggest a heritability of between 0.28 and 0.744, which is significantly higher than for many purely "physical" conditions. Less is known about the genetics of BN, but the heritability is thought to be 0.6 and there is a strong correlation with AN, at 0.46 to 0.79. EDs are, therefore, very similar to other conditions where a polygenetic predisposition interacts with the environment to produce disease (5, 6).

The lifetime prevalence of EDs has been estimated at 8.4% for women and 2.2% for men. In women, it is estimated that the lifetime risk of AN may be 1.4% and BN 1.9%, with lower rates in men, at 0.2% for AN and 0.6% for BN (7). AN is believed to carry the highest mortality rate of any psychiatric disorder (8).

Basic principles of medical care

Some people, including clinicians, who may not have encountered a person with an ED before, may view the person's food history as being a "lifestyle choice" rather than the consequence of a serious disease. Often, it suits the person with the ED to encourage this and to underplay the intense controlling influence that the condition has on them (1).

Non-psychiatric medical teams (NPMT) with little experience in managing AN and BN can, therefore, underestimate the seriousness of the conditions and the risks they pose to their patients. This may make them less willing to challenge ED behaviours, more inclined to discharge patients early and less familiar with and willing to use mental health legislation.

The most important roles of psychiatric teams and ED specialists are to:

- help NPMTs understand the conditions
- support the medical team whilst ED patients are in the hospital
- advise on mental health legislation
- offer more specific treatment and ongoing psychiatric care.

The complex psycho-pathophysiology of EDs makes them challenging to manage, particularly for medical teams.

The basic principles of medical management (9) are:

- recognise the disease and initiate a multidisciplinary approach, including liaison psychiatry, dietitians and nurses
- assess the risks that the disease poses to the patient
- stabilise the physical condition, initiate safe refeeding and other appropriate treatments
- recognise and manage ED behaviours likely to impact recovery, understanding that they are part of the condition and that "the disease drives the behaviours"
- be prepared to use mental health legislation if required
- manage transitions between care providers, being aware that these are points in the pathway where patients may become lost (10)
- communicate effectively with the patient and their family, whilst recognising that patients still have a right to confidentiality.

Assessing risk

Risk is multifactorial in both AN and BN. Deaths occur from many different causes, including suicide, accidents, undernutrition, hypoglycaemia and electrolyte disturbances. Consequently, any risk framework must consider a range of factors, rather than simply concentrating on the psychological or physical danger. In general, patients are in very considerable danger when their disease results in homeostatic failure in any system, if their behaviours are uncontrolled or their mental health is deteriorating.

One of the most comprehensive risk assessments available at present is Medical Emergencies in Eating Disorders (MEED), which has an all-age, graded, risk assessment applicable to all EDs, including ARFID (11).

The risk to life is graded using a traffic-light system into three categories:

- red flags imply "a high risk of impending risk to life"
- amber categories are "an alert for impending risk to life"
- green flags imply a "low impending risk to life"

BMI and weight
Weight loss
Heart rate
Cardiovascular system health
Hydration
Temperature
Muscular weakness
Electrocardiogram
Biochemical
Haematology
Behaviours
Engagement
Activity and exercise
Purging
Self-harm

Table 1. Risk domains in MEED

All the risks are integrated with a comprehensive guide to immediate management. MEED offers a useful framework to discuss patients with an acute medical team and has replaced the previous guidance, the Management of Really Sick People with Anorexia Nervosa, or MARSIPAN, which is now obsolete and should no longer be used (12). MEED has been widely endorsed by expert groups including the UK Academy of Royal Colleges and is, therefore, likely to be cited by legal and disciplinary bodies such as coroners and ombudsmen should a complaint be made (13).

MEED assesses risk across 15 separate fields, which include physical parameters such as weight, BMI, weight loss and cardiovascular parameters but also exercise and self-harm (see Table 1).

The medical management of bulimia nervosa

BN is characterised by recurrent binge eating and loss of control, which triggers compensatory behaviours, particularly self-induced vomiting and purging with laxatives. Over-exercise can occur but is less common than in AN. Although not included in ICD-11 (4), patients with BN are usually of normal or near-normal weight. The most common medical complications relate to plasma electrolyte disturbances due to purging, which can be severe and life-threatening.

Patients with BN do not look malnourished and may have a pseudo-Cushing appearance due to hypertrophy of the parotid glands caused by recurrent purging. BN is frequently associated with feelings of shame and the extent of the purging behaviour can often be understated, meaning the risk to the patient may be underestimated.

Vomiting results in the loss of H^+ and Cl^- ions. It can also be associated with fluid loss and hypovolaemia, which lead to activation of the renin-angiotensin-aldosterone system, with a paradoxical further renal loss of H^+ and K^+ ions. The result is a hypokalaemic metabolic alkalosis sometimes presenting as a Pseudo-Bartter's syndrome (14). If the rise in pH occurs quickly, as a result of massive purging, the plasma $Ca2^+$ may also fall. The net result in severe cases is a complex electrolyte disturbance that cannot be corrected by simply prescribing potassium supplements.

Most K^+ is intracellular, meaning that if plasma levels of K^+ are reduced, the intracellular deficit will be even greater. Failure to correct this adequately, and to address the binge-purge behaviour, can lead to multiple presentations to the emergency department. The symptoms of hypokalaemia may be difficult to pick up and can include muscular weakness, lethargy, fainting and dizziness, cardiac arrhythmias and sudden death.

Correcting a hypokalaemic alkalosis requires recognition of the underlying condition, whether it be BN or the binge-purge subtype of AN.

Key measures include the following.

- A reduction or ideally cessation of the binge-purge activity by addressing the patient's psychological issues and by arranging appropriate follow-up and monitoring.
- Monitoring of plasma urea and electrolytes, including K^+, Ca^{2+}, Mg^{2+} and PO_4^{2-}.
- Correction of hypovolaemia, which may be achieved by reducing the purging and re-establishing a normal oral fluid intake.
- In severe cases with tachycardia and a postural drop in blood pressure, admission will be required for careful monitoring and intravenous fluids.
- Hypokalaemia with a plasma K^+ of less than 3 mmol/L requires expert medical or paediatric assessment and usually admission for oral and intravenous K^+ replacement. This requires access to appropriate nursing, laboratory facilities and ECG monitoring and is usually an indication for admission to a medical ward or a medical high-dependency unit. It is important to continue potassium supplementation after discharge, bearing in mind that if vomiting continues, oral potassium may not be absorbed.
- A proton pump inhibitor, such as lansoprazole or omeprazole, will reduce acid secretion and may help correct the alkalosis but must be combined with the measures above.
- A psychiatric review is essential to start treating the underlying behaviours.

Other complications of BN and purging

- Recurrent vomiting in ED patients is often effortless and can be carried out quickly and surreptitiously. It can be very difficult to detect. It can quickly lead to oesophagitis and features associated with reflux. Prolonged reflux in predisposed individuals may lead to a Barrett's oesophagus, which is potentially a pre-malignant condition (15).
- Reflux can also cause chronic laryngitis, cough and hoarseness. Recurrent vomiting can also lead to a risk of aspiration pneumonia.
- There can be loss of enamel on teeth and severe dental decay (16).
- Parotid and salivary gland enlargement may mimic a tumour but is almost invariably bilateral. Patients may also have reduced salivary flow and xerostomia (16).
- Calluses on the hands are caused by placing fingers down the throat (Russell's sign) (17).
- Rarely, a severe episode of vomiting may lead to spontaneous disruption of an organ. Rupture of the oesophagus, Boerhaave syndrome, usually occurs in the lower segment of the oesophagus and is associated with pleuritic pain, free gas on x-ray and signs of sepsis (18, 19). A chest x-ray may show free gas, but CT scanning is usually more accurate and helpful. It constitutes a medical emergency and has a high mortality without proper treatment (18).
- Spontaneous gastric rupture is more common in AN where the stomach can become very thin due to starvation. It carries a high mortality even if diagnosed quickly (18, 19). Surgery is extremely hazardous if the patient is malnourished but may be the only option to control peritonitis.

A patient with established purging behaviour who is suddenly unable to vomit as usual, or develops unusual pain, requires urgent assessment and should be suspected of having a perforation until proven otherwise.

Perforation of an organ is one of the few indications for intravenous nutrition in patients with EDs.

Laxative abuse

Laxative abuse can occur in both AN and BN (20) and usually involves stimulant laxatives purchased over the counter, although the increased availability of online pharmacies, where the patient does not have to be present in person or see anyone, has made access to laxatives much easier. Most laxative abuse is surreptitious and may require a urine laxative screen to confirm. It can be a condition in its own right and may result in a lengthy and potentially invasive investigation of the gastrointestinal (GI) tract. Undetected, it can lead to long-term renal damage. Confronting a patient with evidence of laxative abuse requires care and sensitivity, particularly if it has been hidden from family and care staff for long periods.

The medical management of anorexia nervosa

AN has two subtypes, restrictive (AN-R) and binge-purge (AN-BP). Neither is a completely distinct condition and patients may move between types or have aspects of each.

The complications of AN-BP are similar those described for BN but, by definition, with the added complexities of weight loss and malnutrition. In general, the binges are smaller than in BN and the restrictive compensatory behaviours disproportionate.

In AN-R, the complications relate to the acute and chronic effects of malnutrition and the hazards of refeeding.

Malnutrition and starvation

Malnutrition is a sub-acute or chronic state of disordered nutrition in which a combination of varying degrees of over- or undernutrition and inflammatory activity leads to a change in body composition and diminished function (21).

The definition includes both under- and over-nutrition, which emphasises that whilst patients with BN, binge eating disorder or ARFID may have a normal weight, or even be overweight, they can still be malnourished and have for example, significant micronutrient deficiencies.

Patients with AN are, by definition, undernourished but do not typically have an active inflammatory response. Consequently, the C-reactive protein (CRP) and plasma albumin levels are usually normal, sometimes right up to the point of death. There is no universal blood test that either detects or excludes malnutrition. It remains a clinical diagnosis, based on weight, BMI, weight loss, dietary assessment and the overall clinical picture.

Human beings are "heat engines" and obey the first law of thermodynamics. If a person reports an adequate food intake but continues to lose weight, then either their intake is less than reported, or their energy expenditure is greater than has been estimated. In the absence of any food intake, weight loss is linear and progressive, as shown in the Minnesota studies of Ancel Keys (3), and the classic analysis of hunger strikers by Allison, where the loss of 40% of the initial body mass took approximately 70 days with a 30% mortality (22). Any intake of food will slow the rate of loss, whilst exercise and the onset of any illness will increase it, particularly if that illness involves an acute inflammatory response, such as sepsis.

Refeeding patients with AN

Patients with AN face two distinct hazards associated with refeeding. If refeeding is introduced too quickly or in an uncontrolled way, then they can be subject to refeeding syndrome, where sudden changes in electrolytes can be life-threatening. If refeeding is introduced too slowly or attempts to refeed are thwarted by uncontrolled anorexic behaviours, then they may be subject to the underfeeding syndrome, where their nutritional requirements are not met and their nutritional status continues to decline (11).

Refeeding syndrome

A person with little or no intake of nutrients enters a state of adapted starvation, where the body's metabolic processes are progressively shut down to maintain basic homeostatic functions. Very little insulin is secreted, and the body uses any remaining lipid stores to meet energy requirements and tissue protein to maintain gluconeogenesis. Intracellular ions, K^+, Ca^{2+}, Mg^{2+} and PO_4^{2-}, are depleted to maintain the extracellular concentrations.

Introducing calories too quickly, particularly refined carbohydrates, leads to a sudden increase in cellular metabolism. The intra-cellular pool of adenosine triphosphate is rapidly increased, requiring PO_4^{2-}, and K^+, Ca^{2+} and Mg^{2+} ions are taken up by cells resulting in a decrease in their concentration in the extracellular fluid and plasma. This destabilises many systems, but particularly the heart and central nervous system. Sudden death from arrhythmias, seizures and profound muscle weakness may occur (23).

To prevent refeeding syndrome the basic principles are:

- nutrition should be reintroduced slowly
- refeeding ions, Ca^{2+}, K^+, Mg^{2+} and PO_4^{2-}, should be monitored carefully
- micronutrients should be replaced proactively (23).

The controversies in EDs concern the initial levels of protein and calories, and how fast they should be increased.

In 2006, the National Institute for Health and Care Excellence (NICE) published detailed guidance on refeeding syndrome which was necessarily cautious because the evidence base was limited. Advice had to accommodate the needs of the sickest patients, particularly those undergoing artificial nutritional support in acute hospitals (24). Patients who are older or have trauma, burns and sepsis are more at risk of refeeding syndrome than younger patients with EDs without an active inter-current illness. Research in adolescents suggests that higher initial rates of refeeding of 1400 to 2000 kcals per day, increasing by 200 kcals daily, can be used safely in those who are at medium to low risk of refeeding syndrome, providing that they are subject to appropriate monitoring and supervision (25-28). The benefits of more rapid refeeding are faster stabilisation and recovery of weight and shorter times in the hospital. The evidence for refeeding in adults with ED is scarce, however, after a review of the available studies MEED recommended (11):

- Assess the risk for refeeding syndrome (Table 2)
- In patients not at high risk of refeeding syndrome, feeding can commence at 30–35 kcal/kg/day increasing by 200–300 kcal/day every two days, so that weight is starting to increase by the seventh day.
- Patients with other medical conditions such as infections, cardiac disease, liver disease, alcohol misuse or a BMI less than 13 kg/m^2 are at a high risk of refeeding syndrome and need a more cautious approach as outlined in the

NICE guideline (24). Typically, this would be 5–10 kcal/kg/day increased slowly to meet or exceed needs over 4 to 7 days, with frequent monitoring of the biochemical parameters.

- The initial intake should not be less than the patient was taking before admission.
- Food and a properly designed diet plan are the best approach to refeeding, but if the patient cannot manage a sufficient intake then nasogastric feeding may be required. The indications for nasogastric feeding are complex but are detailed in MEED and other references (9, 11).
- Refeeding should be supervised by a registered dietitian. An English coroner's report in 2021 stated that "a failure to follow the basic dietetic input" was a contributing factor in the death of a patient, whilst specifically highlighting that there had been, "no attempt to obtain any advice from a specialist eating disorder dietitian" (29). Obtaining appropriate dietetic advice and implementing it should, therefore, be a high priority.

Underfeeding syndrome

In underfeeding syndrome, the patient fails to achieve an adequate calorie intake and their nutritional status deteriorates. Two main factors lead to underfeeding.

1. An over-cautious approach to refeeding and failure to increase calorie intake. This can be linked to a lack of specialist dietetic input or a failure to follow a refeeding protocol.
2. Failure to control anorexic behaviours.

Patients with AN have an obsessional fear of weight gain and often go to extraordinary lengths to avoid doing so. It is important to understand that the person's disease drives their behaviour and that their attempts to resist treatment are predictable but can be life-threatening unless managed effectively (1).

Over-exercise

Overactivity and compulsive exercise are extremely common in AN but may also occur in BN. Often, the initial drive is to control body shape and weight. Patients with AN may have higher childhood activity levels and a greater than expected percentage of AN patients have previously been competitive athletes. The ability to exercise obsessively is often preserved, even in the presence of severe undernutrition, and exacerbates weight loss, can lead to severe hypoglycaemia and may make the correction of other complications, such as electrolyte disturbances, more difficult. The physical activity may be "overt", and is often solitary, rigid and obsessive. It may manifest as hours in the gym, running, cycling or swimming long distances. Frequently, however, it is covert, and the true extent is hidden. Even after admission to hospital, patients may use any opportunity to continue to exercise, including running errands for other patients, going up and down stairs and exercising in locked bathrooms. Staff need to be vigilant, particularly whenever patients are out of sight in places such as bathrooms, showers or single rooms. Micro-exercise and fidgeting are common. Patients may wiggle toes and hands, or sit down and stand up, often for hours at a time. It is important to recognise that these are anorexic behaviours, driven by the disease and that they must be controlled if treatment is to be successful. Specialist physiotherapy can be very helpful but may not always be available. Detailed advice is available (30).

Over-exercise may result in falls, which can cause disproportionate injuries because of the high prevalence of osteoporosis in men and women with AN.

Controlling behaviours on the medical ward

NPMTs often have difficulty managing behaviours and may need help and advice from clinicians with experience in EDs. Proactively developing links between acute medical units and SEDUs can be extremely helpful in improving the care of patients with EDs.

Table 2. Factors associated with a high risk of refeeding syndrome in patients with eating disorders, as outlined in MEED (11)

Clinical feature	High risk level	Management
Extremely low weight	%mBMI < 70% or BMI < 13 kg/m^2	Cautious refeeding
Prolonged low intake	Little or no intake for > 4 days	Cautious refeeding
Deranged baseline electrolytes	Low potassium, phosphorous, magnesium, calcium	Measure levels up to twice per day initially and supplement as needed
Low white blood cell count	< 3.8	Monitor
At risk for low thiamine (n.b., the precise requirement for thiamine is not known)	Low thiamine and other vitamins	Pabrinex, oral thiamine and multivitamins
Medical comorbidities and/or complications	Infection (e.g., pneumonia, cardiac disease, liver disease, alcohol misuse or other serious disease)	Should be discussed with an acute medical unit and high-dependency unit/intensive care unit considered if the patient has a serious comorbidity. Refeed cautiously

Useful strategies (1, 9) include the following.

- Develop a ward protocol for ED patients.
- Explain why the ward has adopted certain policies.
- Have established links with liaison psychiatry and with a SEDU.
- Ensure close observation of the patient, particularly at high-risk times such as immediately after meals.
- Avoid locked bathrooms and any area where patients cannot be observed. It may be safer to offer patients the use of a commode.
- Decide as a team what is going to be discussed on a ward round before reaching the patient.
- Have a clear, consistent policy involving all members of the team.
- Avoid splitting, which can be extremely destructive and ultimately endangers the patient's care.
- Limit unobserved time off the ward, such as trips to the hospital shop.
- Patients leaving the ward should be accompanied by an informed, responsible person.
- Patients should wear hospital night clothes because they are less likely to have weights sewn into them.
- Discuss the use of mobile phones and technology. Agree to limits and block harmful websites.
- Manage transitions to other units carefully, noting that these are high-risk points where the patient may be lost to follow-up (10).
- Seek permission to involve friends and family. Communicate with them and involve them in the patient's care if the patient gives permission (31).
- Be prepared to use mental health legislation if all the least-restrictive options have failed (32).
- Seek expert psychiatric advice.
- Document treatment and outcomes carefully.

Other problems

Hypoglycaemia

In the absence of diabetes mellitus, it is important to distinguish symptomatic hypoglycaemia from a slightly lower than normal blood glucose reading in an otherwise asymptomatic patient. The context of the finding is important.

A person who meets the high-risk criteria in MEED, who is of very low weight (BMI <13 kg/m^2) or is losing weight rapidly, or who is at a high risk of refeeding syndrome, is likely to have very low reserves of glycogen and may have difficulty maintaining their blood glucose. If they consume too large a calorie intake rapidly, particularly if it is a refined carbohydrate and easily absorbed, they may develop reactive hypoglycaemia in response to the rapid secretion of insulin. In extremely malnourished patients, there is a risk that sudden, severe hypoglycaemia may lead to sudden death.

Symptomatic hypoglycaemia should be treated with food, oral dextrose or, in extreme cases, with intravenous dextrose. This should be followed by more complex carbohydrates that will release glucose more slowly. The most important treatment is controlled refeeding, as described, to prevent refeeding syndrome.

Asymptomatic low-normal or near-normal plasma glucose readings in a patient gaining weight and adhering to a meal plan do not require treatment but may need to be monitored, particularly if the question of fitness to drive is raised.

The combination of type 1 (insulin-dependent) diabetes and EDs is complex and beyond the scope of this review, but detailed advice is available (MEED annex 3) (11).

Disorders of gut–brain interaction

Disorders of gut–brain interaction (DGBIs), previously and more commonly known as functional GI disorders, including functional dyspepsia and irritable bowel syndrome, define a spectrum of GI disorders associated with chronic or fluctuating GI symptoms, such as abdominal pain, diarrhoea, constipation, bloating and nausea, without harbouring an apparent organic structural or biochemical explanation for these symptoms (33).

DGBIs are common in patients with EDs, with some reviews suggesting that over 88% to 98% of patients with AN may have features of a least one DGBI and 35% to 49% will meet criteria for three or more (34). The commonest symptoms are post-prandial bloating and abdominal distension, but features of any functional disorder of the gut can occur. This may be due to ED patients having increased visceral awareness, but severe weight loss also leads to loss of muscle in the gut which may also contribute. The current and past use of laxatives and other drugs can also be relevant.

More detailed discussions of DGBIs are available (15, 34).

Coeliac disease, which affects over 1% of Western populations, may present with functional symptoms and should

be excluded with an IgA anti-tissue transglutaminase antibody test and total IgA. A normal faecal calprotectin and CRP do not completely exclude inflammatory bowel disease but are reassuring in the absence of a strong clinical suspicion. Invasive GI investigation should be undertaken with caution in very low weight patients (15, 34).

DGBIs are important, because symptoms often emerge during refeeding, creating discomfort and anxiety which can complicate management of weight gain. An expert gastroenterology opinion may be necessary.

Liver abnormalities

Abnormal liver function tests are common in AN and are usually mild increases in the transaminases AST and ALT, and do not generally indicate liver failure. Most will resolve over weeks or months as refeeding progresses (19). High transaminase levels, particularly if associated with deranged clotting tests, such as the standardised prothrombin time ratio or low plasma albumin, can be a sign of liver failure, which is more common in very low weight patients (15, 18) and requires an urgent hepatology opinion. Exclusion of other causes of liver disease is essential and patients may be best managed in a medical high-dependency unit.

Bone disease

Reduced bone mass, osteopenia and osteoporosis are common in AN, in both men and women. The causes are complex and centre on the effects of starvation on the hypothalamic-pituitary axis, with loss of pulsatile gonadotrophin-releasing hormone, reduced gonadotrophins, testosterone and growth hormone resistance. Thirty percent of cases may also have raised cortisol levels, whilst sick euthyroid syndrome may also occur (35).

The combination of factors leads to loss of bone mass and delayed bone growth, which is particularly serious during adolescence when maximum bone growth and mineralisation occur. The best test is dual x-ray absorptiometry scanning.

Restoration to normal weight is the safest and most effective treatment. Bisphosphonates should be used with caution in young women as they can have potential teratogenic effects and remain in the body for long periods. The use of hormone replacement therapy may have a role in some cases but is less effective in underweight people. Expert advice should be sought (36).

Conclusions

The medical consequences of EDs are multiple and reflect the complex psycho-pathophysiology of the diseases. NPMTs can find the care of patients with EDs very challenging. Care can be improved with a better understanding of the conditions, particularly the realisation that they are serious illnesses that drive the behaviour of the patient. Externalising the disorder, by moving the blame from the patient to the illness, can be a very helpful approach for both the patient and their family. Psychiatrists and specialist ED teams have a vital role to play in supporting medical teams by acting as sources of expert advice, including for legal issues, and by ensuring that patients go on to have their psychological problems addressed when they are physically stable.

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