Medical complications of anorexia nervosa

Anorexia nervosa is a psychiatric disorder with potential life-threatening medical sequelae. This article reviews the principal medical complications associated with anorexia nervosa, highlights associated diagnostic pitfalls and emphasizes the importance of a multidisciplinary approach to management.

Anorexia nervosa is a psychiatric disorder characterized by preoccupation with maintaining low body weight (a body mass index of <17.5 kg/m^2) through caloric restriction or purging behaviours (induced vomiting, use of laxatives and diuretics) (National Institute for Health and Care Excellence, 2004). For those with anorexia nervosa, positive perception of weight loss is a deep-seated conviction, leading to dismissal of the concerns of others, and development of covert behaviour. Recognizing patients at risk of anorexia nervosa can be challenging and simple screening tools exist, such as the SCOFF questionnaire (see *Table 1*; a score of 2 or above indicates a likely eating disorder) (Morgan et al, 1999). Use should be considered in underweight patients presenting with recurrent vomiting or vague gastrointestinal symptoms of no other overt cause, young patients with poorly controlled type 1 diabetes mellitus and women with menstrual disturbances and low body mass index (National Institute for Health and Care Excellence, 2004).

The average prevalence of anorexia nervosa among young women is ~0.3%, but one tenth this figure in males. Both are probable underestimates because of the secretive nature of anorexia nervosa (Hoek and van Hoeken, 2003). Long-term outcomes of anorexia nervosa are variable, and data are difficult to interpret as a result of the high dropout rate from follow-up (Steinhausen, 2002). Over a period of up to 29 years approximately half of patients diagnosed with anorexia nervosa recovered completely, approximately one-third partially, 20% had a chronic eating disorder and 5% died. Longer follow-up was associated with better rates of recovery (Steinhausen, 2002). Anorexia nervosa can be further classified by the strategy used to achieve and maintain low body mass index. Restrictive type anorexia involves caloric restriction, which may be accompanied by excessive exercising. In purge subtype anorexia weight loss is achieved by self-induced vomiting and/or use of laxatives or diuretics. In binge-purge anorexia purging behaviours are accompanied by binge eating episodes.

Standardized mortality rates vary in the literature, with an overall standardized mortality rate of 6.2% from a large Scandinavian study (Papadopoulos et al, 2009). Rates of alcoholism and other psychiatric disorders such as depression and obsessive compulsive disorder are high in patients with anorexia nervosa (National Institute for Health and Care Excellence, 2004). Although a high suicide rate is seen in patients with anorexia nervosa, circulatory, metabolic and/or electrolyte disturbances resulting from extreme cachexia also play a role in the increased mortality rates observed (Papadopoulos et al, 2009). Furthermore, Papadopoulos et al (2009) reported double the expected number of deaths from cancer and a tenfold increase in death from respiratory and urological causes (of predominantly infective aetiology). Elevated standardized mortality rates from natural and unnatural causes were reported up to 20 years after initial presentation of anorexia nervosa, when many patients will have recovered normal weight.

Table 1. SCOFF questionnaire

SCOFF	Yes/No
Do you make yourself Sick because you feel uncomfortably full?	
Do you worry you have lost Control over how much you eat?	
Have you recently lost more than One stone in a 3-month period?	
Do you believe yourself to be Fat when others say you are too thin?	
Would you say that Food dominates your life?	

**One point for every 'yes'; a score of ≥2 indicates a likely case of anorexia nervosa or bulimia. From Morgan et al (1999)*

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Table 2. Indications for admission for patients with anorexia nervosa (high physical risk)

History of collapse	Present
Heart rate	<40 bpm
Systolic blood pressure	<80 mmHg
Diastolic blood pressure	<50 mmHg
Postural blood pressure drop	>20 mmHg
Corrected QT interval (QTc)	>450 ms
Temperature	<34.5°C
Sit up test	Inability to sit up at all
Squat stand test	Inability to stand without using arms as leverage
Serum potassium	<2.5 mmol/litre
Serum sodium	<130 mmol/litre
Sodium phosphate	<0.5 mmol/litre
Acrocyanosis	Present
Purpuric rash	Present

Adapted from National Institute for Health and Care Excellence (2004) and Royal College of Psychiatrists, Royal College of Physicians (London) and Royal College of Pathologists (2014)

Table 3. Investigations for patients with severe anorexia nervosa during refeeding

Admission	Full blood count Urea and electrolytes Liver function tests including albumin Calcium, phosphate and magnesium C-reactive protein Glucose (serum or fingerprick) Zinc, copper, selenium Serum iron studies, ferritin, vitamin B_{12} and folate Vitamin A, D, E and carotene Thyroid function tests Post voiding early morning weight Electrocardiogram
Daily	Urea and electrolytes, phosphate, magnesium, calcium (daily for 1 week then twice weekly) Glucose (fingerprick) pre meal, and overnight if daytime readings low
Twice weekly	Full blood count Liver function tests Post voiding early morning weight
Monthly	Copper Zinc Electrocardiogram (if baseline electrocardiogram and electrolytes normal)

Adapted from Royal College of Psychiatrists, Royal College of Physicians (London) and Royal College of Pathologists (2014)

While the mainstay of anorexia nervosa treatment is within the outpatient setting, inpatient treatment is advisable in certain situations. Multiple factors should be considered case by case; limited response to outpatient treatment, very low body mass index, e.g. body mass index <13 kg/m^2, rapid weight loss, or specific physical abnormalities (*Table 2*) may prompt a decision to admit. Admission to a specialist eating disorder unit is preferred, unless the patient requires medical management not available in a specialist eating disorder unit. Specialist eating disorder units provide care by a multidisciplinary team including psychiatrists, dieticians, psychologists and mental health nurses. Many specialist eating disorder units provide nasogastric feeding, electrocardiograms and biochemistry, but do not provide cardiac monitoring or intravenous infusions, and patients require transfer to a medical ward if such interventions are necessary. In this situation, a patient may already be detained under the Mental Health Act, which also gives powers for compulsory feeding and prohibition of exercise. Such concepts are often unfamiliar to the general physician, but it is important to recognize that inappropriate lack of application and enforcement of the Mental Health Act in severely unwell patients with anorexia nervosa has resulted in fatal consequences (Royal College of Psychiatrists, Royal College of Physicians (London) and Royal College of Pathologists, 2014). For patients detained under the Mental Health Act, the psychiatric consultant remains the patient's named consultant after transfer to the medical ward. Hospitals should pre-identify a physician with an interest and experience in clinical nutrition to oversee the care of medical inpatients with anorexia nervosa (Royal College of Psychiatrists, Royal College of Physicians (London) and Royal College of Pathologists, 2014).

As problems may quickly arise on a medical ward without specialist psychiatric input, medical staff may feel ill equipped, through inexperience, nurse:patient staffing ratios and frequent shift changes, to deal with challenging patient behaviours, such as feed tampering and microexercising (constant small amplitude movements), which can be fatal if not dealt with. Equally, there may be uncertainty regarding the recommended rate of feeding and the need for and frequency of biochemical monitoring, which could result in underfeeding or refeeding syndrome, again with potentially fatal consequences (Royal College of Psychiatrists, Royal College of Physicians (London) and Royal College of Pathologists, 2014).

This article reviews the principal medical complications associated with anorexia nervosa, including symptoms, signs or physical findings associated with anorexia nervosa, highlights associated diagnostic pitfalls and emphasizes the importance of a multidisciplinary approach to management. It is divided into systems and concludes with sections on the refeeding syndrome and multidisciplinary care. Regular assessment of patients with anorexia nervosa is vital to protect patients and provide the opportunity to treat complications as they arise. An investigation schedule is outlined in *Table 3* covering admission and ongoing care. Where relevant, the tests covered are detailed in each of the following sections.

Cardiological complications

Patients with anorexia nervosa frequently have abnormal physiological parameters: bradycardia (pulse less than 60 beats per minute) (Galetta et al, 2003), hypotension and impaired orthostatic responses may be the result of increased vagal tone or endocrine changes (see below) and tend to reverse with refeeding (Roche et al, 2005). Hypotension should be treated if below the patient's baseline, with closely monitored administration of small intravenous fluid boluses to avoid precipitating heart failure. Tachycardia – or even a high–normal heart rate – is unusual, and should prompt a thorough search for infection. Cardiac auscultation often reveals a mitral valve prolapse murmur which results from preservation of valve size but reduced myocardial mass (Mascolo et al, 2012).

Up to one third of sudden deaths in patients with anorexia nervosa may be cardiac in origin (Jauregui-Garrido and Jauregui-Lobera, 2012). Patients with anorexia nervosa frequently have significantly longer QT and rate-corrected QT (QTc) intervals on electrocardiogram than healthy individuals, with a QTc >440 ms found in 30% of women with anorexia nervosa (Olivares et al, 2005). Prolonged QT is associated with ventricular arrhythmias and if QTc is >450 ms patients should be admitted for cardiac monitoring, serum electrolyte measurement and full prescription review (National Institute for Health and Care Excellence, 2004). Commonly prescribed medications, including tricyclics, antipsychotics, macrolides, antihistamines and prokinetic agents, prolong the QTc interval and should be avoided or prescribed cautiously in patients with anorexia nervosa (Royal College of Psychiatrists, Royal College of Physicians (London) and Royal College of Pathologists, 2014).

Typical echocardiogram findings include 'restrictive pattern' diastolic filling of the left ventricle and reduced left ventricular mass which, in addition to bradycardia, results in a lower cardiac output and blood pressure (Casiero and Frishman, 2006).

Chest pain in patients with anorexia nervosa may relate to mitral valve prolapse, but in the presence of ischaemic-type ST changes on electrocardiogram may indicate takotsubo cardiomyopathy. This mimics myocardial infarction in patients without coronary artery disease. It is caused by widespread coronary vasospasm and myocardial stunning, with raised cardiac enzymes, as a result of sympathetic activation. Fortunately rare, it can occur in young females with anorexia nervosa after precipitating hypoglycaemia or emotional stress (Jauregui-Garrido and Jauregui-Lobera, 2012). Early echocardiography reveals apical ballooning that may revert to normal within a few days after the initial event (Volman et al, 2011). Most patients require supportive treatment only, as it is typically self-limiting, but in rare cases patients may develop severe cardiogenic shock requiring urgent treatment including intra-aortic balloon pumping.

Renal and biochemical complications

Electrolyte disturbances are common in patients with anorexia nervosa, with hypokalaemia and hypomagnesaemia occurring frequently (Birmingham et al, 2004). First-line treatment is oral replacement or intravenous if levels are severely low.

Binge-purge anorexia nervosa confers a higher risk of electrolyte disturbance and metabolic alkalosis from laxative and diuretic abuse. Induced vomiting results in loss of hydrogen ions and a shift in blood pH toward alkalosis. Resorption of hydrogen ions in the renal collecting ducts occurs at the expense of potassium loss into the urine. Volume depletion from purging may further enhance potassium losses by activation of the renin–angiotensin–aldosterone system (Bouquegneau et al, 2012). Rapid body fluid shifts increase the risk of both acute kidney injury and chronic kidney disease secondary to hypokalaemia causing tubulointerstitial nephritis (Arimura et al, 1999).

Assessing renal function in patients with anorexia nervosa is challenging: estimated glomerular filtration rate via serum creatinine levels and urinary creatinine clearance may overestimate renal function as a result of very low muscle mass and should be interpreted cautiously. Chronic kidney disease in patients with anorexia nervosa is usually tubular (non-albumin protein loss) so will not be detected on urine dipstick. 24-hour urine collection is the preferred method of assessment (Bouquegneau et al, 2012).

Patients with anorexia nervosa usually have a normal albumin level (Caregaro et al, 2001), challenging the erroneous belief that low albumin levels are a useful marker of nutritional status. Low serum albumin level may signal infection as the body switches from producing albumin to acute phase proteins or may be a result of redistribution in extracellular fluid. Infection can become overwhelming following a muted immune response in patients with anorexia nervosa resulting from alterations in CD4/CD8 ratio, reduced granulocyte adherence and bactericidal capacity, and complement deficiencies (Hutter et al, 2009). Patients may not display clinical signs of a systemic inflammatory response, delaying the diagnosis of sepsis. Increased mortality rates are seen from infection in patients with anorexia nervosa; the typical triad of hypothermia, hypoglycaemia, caused by low muscle mass and impaired glycogen storage, and hypoalbuminaemia should therefore prompt a thorough infection screen and early treatment.

Haematological complications

Abnormalities of all three lineages (red cells, white cells or platelets) can occur in patients with anorexia nervosa, but is typically the result of malnutrition and reversible on restoration of weight. Anaemia (usually normocytic, normochromic) is seen in a third of patients with anorexia nervosa; plasma volume depletion may mask an anaemia that becomes apparent after rehydration (Caregaro et al, 2005). Serum haematinics are usually normal, although ferritin can be high from circulating volume contraction with subsequent red cell breakdown and ferritin storage

(Kennedy et al, 2004). Neutropenia can develop in patients with anorexia nervosa, which may result in neutropenic sepsis. Treatment response to recombinant granulocyte-colony stimulating factor has been reported (Fukudo et al, 1993; Hutter et al, 2009). Thrombocytopenia is seen in 5–10%, with platelet levels usually 90–130x10^9/litre (Hutter et al, 2009). Spontaneous bleeding or bruising indicate very low levels of platelets and should prompt admission (National Institute for Health and Care Excellence, 2004).

Gastrointestinal complications

Mild transaminitis is common in patients with anorexia nervosa. Causes include starvation-induced autophagy, steatosis (imbalanced triglyceride synthesis and secretion) and hypoxia from reduced cardiac output (Rautou et al, 2008). These abnormalities reverse with refeeding, although initial paradoxical worsening can occur. Continuing feeding while monitoring liver function closely is recommended. In rare cases, a severe transaminitis with elevation of prothrombin time and hypoglycaemia may be seen (Rautou et al, 2008).

Gastric emptying is often delayed in patients with anorexia nervosa, causing bloating, nausea and early satiety. Potentially fatal acute gastric dilatation is a rare refeeding complication (Jauregui-Garrido and Jauregui-Lobera, 2012). Metoclopramide stimulates gastric emptying, but prolongs QT interval and so should be used with caution. Constipation and slow colonic transit are common, causing bloating, which exacerbates body image problems if untreated (Chial et al, 2002).

Endocrine complications

Hypoglycaemia is common and often asymptomatic in patients with anorexia nervosa (Mattingly and Bhanji, 1995). Severe hypoglycaemia may indicate infection or liver dysfunction (Jauregui-Garrido and Jauregui-Lobera, 2012), and can also be induced by excessive exercise, including microexercising, with fatal outcomes (Royal College of Psychiatrists, Royal College of Physicians (London) and Royal College of Pathologists, 2014). Blood glucose levels should be monitored closely after initiating feeding, as the resultant increase in insulin production drives glucose into cells (see below) so blood glucose levels may fluctuate (Ormerod et al, 2010). Patients with pre-existing type 1 diabetes mellitus are likely to be poorly insulin compliant to achieve low weight. They should be intensively monitored and screened for end organ damage (National Institute for Health and Care Excellence, 2004).

Thyroid abnormalities are common with low triiodothyronine, low or normal thyroxine and thyroid-stimulating hormone levels, and with reduced peripheral thyroxine to triiodothyronine conversion (usually stimulated by carbohydrate intake). Reduced triiodothyronine levels can cause hypotension, impaired orthostatic responses and hypothermia, and usually reverse with refeeding (Roche et al, 2005).

Hypercortisolaemia is common, but cushingoid features are rarely seen in patients with anorexia nervosa as a result of peripheral cortisol resistance and reduced adipose tissue (Usdan at al, 2008). Growth hormone release usually results in hepatic production of its intermediary factor, insulin-like growth factor-1. In patients with anorexia nervosa, insulin-like growth factor-1 production is reduced despite growth hormone hypersecretion as a result of growth hormone resistance. Although reversible with refeeding, growth hormone resistance in adolescence may lead to permanent short stature (Usdan et al, 2008).

Primary and secondary amenorrhoea are common in patients with anorexia nervosa. Menstrual abnormalities relate to loss of gonadotropin-releasing hormone pulsatility with increased follicle-stimulating hormone:luteinizing hormone (FSH:LH) ratio. Insufficient gonadotrophin release for ovulation is followed by an insufficient luteal phase for normal menstruation. Furthermore, inadequate adipose tissue reduces the production of oestrogen. Menstruation requires maintenance of normal or near-normal weight, so is an important physiological and psychological milestone in recovery (Usdan et al, 2008).

Metabolic bone disease

Abnormal bone growth and metabolism is a far-reaching consequence of anorexia nervosa. Reduced oestrogen, androgen, triiodothyronine and insulin-like growth factor-1 levels, and raised levels of glucocorticoids and catecholamines reduce bone size and density. Up to 90% of women with anorexia nervosa have reduced bone mineral density; 38% are osteoporotic (Grinspoon et al, 2000). Decreased bone mineral density and increased fracture risk may persist for years after normal weight achievement, because of the slow rate of bone recovery; cortical bone recovery takes longer than trabecular bone. Increasing duration of anorexia nervosa predicts the risk of persisting low bone mineral density (Herzog et al, 1993). Recombinant insulin-like growth factor-1 in combination with oestrogen increases bone mineral density significantly in women with anorexia nervosa and osteopaenia (Grinspoon et al, 2002), but is only advised in specialist settings (National Institute for Health and Care Excellence, 2004). As oestrogen may inhibit insulin-like growth factor-1 release, it is not recommended for monotherapy (Usdan et al, 2008) nor for use in adolescents because of premature epiphyseal fusion (National Institute for Health and Care Excellence, 2004).

Dermatological and dental abnormalities

Dermatological signs are common in patients with anorexia nervosa: xerosis, acne (often excoriated), dermatitis artefacta, alopecia, brittle nails and lanugo hair (a downy, dark hair on trunk, forearms and face). Russell's sign (calluses over the knuckles from contact with the teeth) is pathognomic of binge-purge anorexia nervosa or bulimia, providing a vital clue in undiagnosed cases

(Strumia, 2009). Dental caries provide further evidence of binge-purging as a result of the gastric acid eroding the dental enamel.

Respiratory complications

Generalized muscle weakness also affects the respiratory muscles causing dyspnoea. Aspiration risk is high with purge subtype anorexia nervosa where evidence of infection in dependent parts of the lungs may be seen on chest radiographs. Pneumothorax and pneumomediastinum have been reported as a result of alveolar friability (Hochlehnert et al, 2010).

Refeeding syndrome

The refeeding syndrome occurs after commencing feeding in severely malnourished patients. In prolonged starvation the body switches from carbohydrate as its main energy source, and breaks down fat and protein stores. Intracellular electrolytes become depleted, although serum levels may be normal as a result of cessation of sodium/potassium ATPase membrane pumps, which can consume up to 50% of basal metabolic rate energy expenditure. Subsequent carbohydrate ingestion both stimulates insulin release and reactivates these pumps, causing the intracellular influx of potassium, magnesium and phosphate, resulting in low serum levels.

Phosphate is a source of cellular energy as adenosine triphosphate and is key in many intracellular pathways including nerve conduction and maintenance of the red cell membranes. Hypophosphataemia can result in neuromuscular weakness, haemolysis, confusion, coma and seizures (Ormerod et al, 2010). Hypokalaemia and hypomagnesaemia can lead to life-threatening cardiac arrythmias. Refeeding also stimulates sodium and water retention which, in association with hypophosphataemic-reduced cardiac contractility, can cause oedema and heart failure. Insulin-induced hypoglycaemia can also occur (Ormerod et al, 2010).

To minimize the risk of refeeding in patients with anorexia nervosa, feeding should be gradually increased. Starting to feed at 20 kcal/kg/d, dropping to 5–10 kcal/kg/d in severely underweight patients, is broadly advised, although opinion varies (Royal College of Psychiatrists, Royal College of Physicians (London) and Royal College of Pathologists, 2014). Electrolyte monitoring should be performed pre-feeding and then at least daily if not more frequently, along with close blood glucose monitoring. Electrolyte replacement with oral preparations may suffice, but these are often found to be unpalatable. Oral magnesium and phosphate may induce diarrhoea, such that intravenous replacement may be necessary (National Institute for Health and Care Excellence, 2004; Ormerod et al, 2010).

Wernicke–Korsakoff syndrome, as a result of thiamine deficiency, may develop with refeeding, as thiamine is a key co-factor for carbohydrate metabolism. Thiamine and a vitamin B compound should be given, either orally, or intravenously if the oral route is not possible, before starting intravenous glucose or refeeding in patients with anorexia nervosa.

Multidisciplinary care

Specialist nursing care from mental health nurses overseen by a specialist eating disorder unit nurse is necessary when a patient with anorexia nervosa is admitted to an acute hospital under a medical team. Behaviours such as feed wasting, infusion tampering or covert exercising (including wriggling toes and fingers) may occur and are understandably frustrating to physicians, potentially breaking down the doctor–patient relationship at a high risk period for patient self-harm or suicide exacerbated by the changing care setting (National Institute for Health and Care Excellence, 2004). Care from mental health nurses (including one to one nursing and supervised mealtimes, bathing and toiletting, if appropriate) who are aware of and equipped to manage such behaviours should reduce the chances of treatment failure. Pre-existing arrangements should be in place for such nursing provision (Royal College of Psychiatrists and Royal College of Physicians, 2014).

On decision to admit from a specialist eating disorder unit to a medical ward, representatives from both care facilities, the patient and family, if appropriate, should meet to discuss the aims, practicalities and responsibilities of transfer. Early in the medical admission, a meeting should occur between the medical consultant (ideally a pre-identified physician with a special interest in nutrition) and the psychiatric consultant (who should be experienced in eating disorders) with nursing staff present to discuss treatment aims and means of achievement. The nutrition support team, if available at the hospital, should be involved. These meetings should continue twice weekly throughout the course of admission. Dieticians should contact a specialist eating disorder unit dietician for advice on feeding in this very high risk patient group (Royal College of Psychiatrists, Royal College of Physicians (London) and Royal College of Pathologists, 2014).

Regular, well-documented handover between nursing staff should happen, to avoid staff manipulation by the patient. The team should be aware of potentially complex family dynamics; boundaries for relatives should be clearly set out if needed, and the medical team should meet regularly with key relatives, with patient agreement, to update them and gain information helpful in successfully managing the patient (Royal College of Psychiatrists, Royal College of Physicians (London) and Royal College of Pathologists, 2014).

Once the patient has stabilized and the reason for admission to an acute medical bed has been treated, whether an infection, electrolyte derangement or overcoming refeeding risk, then carefully planned transfer back to specialist eating disorder unit for ongoing management should be prioritized.

KEY POINTS

- Patients with severe anorexia nervosa requiring inpatient admission can often be managed in inpatient specialized eating disorder units, but in certain circumstances (e.g. for cardiac monitoring or intravenous infusions) they will require admission to an acute medical ward.
- Expected physiology in patients with anorexia is very different to that in patients of normal weight and clinicians should be vigilant for subtle changes that can herald the onset of acute pathology such as sepsis.
- Patients with anorexia nervosa admitted to a medical ward should be cared for by a team consisting of a named physician with a specialist interest in nutrition, nurses and dieticians, supported by advice from psychiatrists, psychiatric nurses and dieticians experienced in the care of patients with eating disorders.
- Clinicians should ensure electrolytes are monitored at least daily during early refeeding and corrected promptly to avoid the development of refeeding syndrome in this high-risk group.

The management of patients with anorexia nervosa within the medical inpatient setting will be unfamiliar territory for many physicians. The MARSIPAN (Management of Really Sick Patients with Anorexia Nervosa) guidelines (Royal College of Psychiatrists, Royal College of Physicians (London) and Royal College of Pathologists, 2014) are an invaluable resource in this respect, offering guidance on assessment, feeding and monitoring in this patient group, appropriate multidisciplinary involvement and application of the Mental Health Act.

Conclusions

Anorexia nervosa is characterized by behaviours motivated by overwhelming compulsion to thinness, and management and alteration of these behaviours is best achieved under the care of an expert multidisciplinary team in the outpatient setting. Patients at high physical risk are best managed in specialist eating disorder units, unless treatment that is unavailable on a specialist eating disorder unit is required, at which point admission to a medical ward is needed. Planning is key in transfer to a medical ward and clear medical and nursing handover is vital to identify and address challenging behaviours.

Once a patient is admitted to a medical ward, conditions such as sepsis may present differently in patients with anorexia nervosa; awareness of what constitutes expected physiology in patients with anorexia nervosa, with vigilance for subtle changes, should avoid late diagnosis and poor outcome. Hospitals should consider producing guidelines for medical and nursing staff on managing patients with severe anorexia nervosa, as a result of the complexity of this patient group. With reference to the MARSIPAN guidelines, hospitals should develop local guidance detailing named physicians, dieticians and specialist nurses, ideally comprising a nutrition multidisciplinary team, who will take on the care of medically unstable patients with anorexia nervosa admitted in the acute hospital setting. Agreements should ideally be in place with a local specialist eating disorder unit to offer specialist advice and support for such patients whether known to them or not. Regular consultant-level physician and psychiatrist meetings, involving nursing and dietetic staff, the patient and, if appropriate, the family should continue until discharge. These meetings should be used to define treatment goals and avoid prolonged admission in a setting less suited to ongoing psychological and psychiatric treatment (Royal College of Psychiatrists, Royal College of Physicians (London) and Royal College of Pathologists, 2014). **BJHM**

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Arimura Y, Tanaka H, Yoshida T et al (1999) Anorexia nervosa: an important cause of chronic tubulointerstitial nephropathy. *Nephrol Dial Transplant* **14**(4): 957–9 (doi: 10.1093/ndt/14.4.957)

Birmingham CL, Puddicombe D, Hlynsky J (2004) Hypomagnesemia during refeeding in anorexia nervosa. *Eat Weight Disord* **9**(3): 236–7 (doi: 10.1007/BF03325074)

Bouquegneau A, Dubois BE, Krzesinski JM, Delanaye P (2012) Anorexia nervosa and the kidney. *Am J Kidney Dis* **60**(2): 299–307 (doi: 10.1053/j.ajkd.2012.03.019)

Caregaro L, Favaro A, Santonastaso P et al (2001) Insulin-like growth factor 1 (IGF-1), a nutritional marker in patients with eating disorders. *Clin Nutr* **20**(3): 251–7 (doi: 10.1054/clnu.2001.0397)

Caregaro L, Di Pascoli L, Favaro A, Nardi M, Santonastaso P (2005) Sodium depletion and hemoconcentration: overlooked complications in patients with anorexia nervosa? *Nutrition* **21**(4): 438–45 (doi: 10.1016/j.nut.2004.08.022)

Casiero D, Frishman WH (2006) Cardiovascular complications of eating disorders. *Cardiol Rev* **14**(5): 227–31 (doi: 10.1097/01.crd.0000216745.96062.7c)

Chial HJ, McAlpine DE, Camilleri M (2002) Anorexia nervosa: manifestations and management for the gastroenterologist. *Am J Gastroenterol* **97**(2): 255–69 (doi: 10.1111/j.1572-0241.2002.05452.x)

Fukudo S, Tanaka A, Muranaka M et al (1993) Case report: reversal of severe leukopenia by granulocyte colony-stimulating factor in anorexia nervosa. *Am J Med Sci* **305**(5): 314–17

Galetta F, Franzoni F, Prattichizzo F, Rolla M, Santoro G, Pentimone F (2003) Heart rate variability and left ventricular diastolic function in anorexia nervosa. *J Adolesc Health* **32**(6): 416–21 (doi: 10.1016/S1054-139X(03)00048-X)

Grinspoon S, Thomas E, Pitts S (2000) Prevalence and predictive factors for regional osteopenia in women with anorexia nervosa. *Ann Intern Med* **133**(10): 790–4

Grinspoon S, Thomas L, Miller K, Herzog D, Klibanski A (2002) Effects of recombinant human IGF-I and oral contraceptive administration on bone density in anorexia nervosa. *J Clin Endocrinol Metab* **87**(6): 2883–91 (doi: 10.1210/jcem.87.6.8574)

Herzog W, Minne H, Deter C et al (1993) Outcome of bone mineral density in anorexia nervosa patients 11.7 years after first admission. *J Bone Miner Res* **8**(5): 597–605 (doi: 10.1002/jbmr.5650080511)

Hoek HW, van Hoeken D (2003) Review of the prevalence and incidence of eating disorders. *Int J Eat Disord* **34**(4): 383–96 (doi: 10.1002/eat.10222)

Hochlehnert A, Löwe B, Bludau HB, Borst M, Zipfel S, Herzog W (2010) Spontaneous pneumomediastinum in anorexia nervosa: a case report and review of the literature on pneumomediastinum and pneumothorax. *Eur Eat Disord Rev* **18**(2): 107–15 (doi: 10.1002/erv.1002)

Hutter G, Ganepola S, Hofmann WK (2009) The hematology of anorexia nervosa. *Int J Eat Disord* **42**(4): 293–300 (doi: 10.1002/eat.20610)

Jauregui-Garrido B, Jauregui-Lobera I (2012) Sudden death in eating disorders. *Vasc Health Risk Manag* **8**: 91–8 (doi: 10.2147/VHRM.S28652)

Kennedy A, Kohn M, Lammi A, Clarke S (2004) Iron status and haematological changes in adolescent female inpatients with anorexia nervosa. *J Paediatr Child Health* **40**(8): 430–2 (doi: 10.1111/j.1440-1754.2004.00432.x)

Mascolo M, Trent S, Colwell C, Mehler PS (2012) What the emergency department needs to know when caring for your patients with eating disorders. *Int J Eat Disord* **45**(8): 977–81 (doi:

10.1002/eat.22035)
Mattingly D, Bhanji S (1995) Hypoglycaemia and anorexia nervosa. *J R Soc Med* **88**(4): 191–5
Morgan J, Reid FF, Lacey JH (1999) The SCOFF questionnaire: assessment of a new screening tool for eating disorders. *BMJ* **319**(7223): 1467–8 (doi: 10.1136/bmj.319.7223.1467)
National Institute for Health and Care Excellence (2004) *Eating Disorders: Core Interventions in the Treatment and Management of Anorexia Nervosa, Bulimia Nervosa and Related Eating Disorders.* Clinical Guideline 9. National Institute for Health and Care Excellence, London
Olivares, JL, Vazquez M, Fleta J, Moreno LA, Perez-Gonzalez JM, Bueno M (2005) Cardiac findings in adolescents with anorexia nervosa at diagnosis and after weight restoration. *Eur J Pediatr* **164**(6): 383–6 (doi: 10.1007/s00431-005-1647-6)
Ormerod C, Farrer K, Harper L, Lal S (2010) Refeeding syndrome: a clinical review. *Br J Hosp Med (Lond)* **71**(12): 686–90 (doi: 10.12968/hmed.2010.71.12.686)
Papadopoulos FC, Ekbom A, Brandt L, Ekselius L (2009) Excess mortality, causes of death and prognostic factors in anorexia nervosa. *Br J Psychiatry* **194**(1): 10–17 (doi: 10.1192/bjp.bp.108.054742)
Rautou PE, Cazals-Hatem D, Moreau R et al (2008) Acute liver cell damage in patients with anorexia nervosa: a possible role of starvation-induced hepatocyte autophagy. *Gastroenterology* **135**(3): 840–8, 848.e1–3 (doi: 10.1053/j.gastro.2008.05.055)
Roche F, Barthelemy JC, Mayaud N et al (2005) Refeeding normalizes the QT rate dependence of female anorexic patients. *Am J Cardiol* **95**(2): 277–80 (doi: 10.1016/j.amjcard.2004.09.018)
Royal College of Psychiatrists, the Royal College of Physicians (London) and Royal College of Pathologists (2014) CR 189. MARSIPAN: Management of Really Sick Patients with Anorexia Nervosa. Royal College of Psychiatrists, London
Steinhausen H (2002) The outcome of anorexia nervosa in the 20th century. *Am J Psychiatry* **159**: 1284–93 (doi: 10.1176/appi.ajp.159.8.1284)
Strumia R (2009) Skin signs in anorexia nervosa. *Dermatoendocrinol* **1**(5): 268–70 (doi: 10.4161/derm.1.5.10193)
Usdan LS, Khaodhiar L, Apovian CM (2008) The endocrinopathies of anorexia nervosa. *Endocr Pract* **14**(8): 1055–63 (doi: 10.4158/EP.14.8.1055)
Volman MN, Ten Kate RW, Tukkie R (2011) Tako Tsubo cardiomyopathy, presenting with cardiogenic shock in a 24-year-old patient with anorexia nervosa. *Neth J Med* **69**(3): 129–31