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16.5.2 Acute cardiac failure 3397 advances to date for patients presenting acutely to hospital or those with HF-PEF, mean that heart failure still remains a ‘malignant’ condition. FURTHER READING Blecker S, et al. (2013). Heart failure-associated hospitalizations in the United States. J Am Coll Cardiol, 61, 1259–67. Cleland JG, et al. on behalf of the National Heart Failure Audit Team for England and Wales (2011). The national heart failure audit for England and Wales 2008–2009. Heart, 97, 876–86. Cowie MR, et al. (1999). Incidence and aetiology of heart failure: a population-based study. Eur Heart J, 20, 421–8. Davies M, et al. (2001). Prevalence of left-ventricular systolic dysfunc- tion and heart failure in the Echocardiographic Heart of England Screening study: a population based study. Lancet, 358, 439–44. Fonarow GC, et al. (2007). Temporal trends in clinical characteristics, treatments, and outcomes for heart failure hospitalizations in 2002– 2004: findings from the ADHERE registry. Am Heart J, 153, 1021–8. Gerber Y, et al. (2015). A contemporary appraisal of the heart failure epidemic in Olmsted County, Minnesota, 2000 to 2010. JAMA Intern Med, 175, 996–1004. Gottdiener JS, et al. (2000). Predictors of congestive heart failure in the elderly: the Cardiovascular Health Study. J Am Coll Cardiol, 35, 1628–37. Ho KKL, Anderson KM, Kannel WB, Grossman W, Levy D (1993). Survival after the onset of congestive heart failure in Framingham Study subjects. Circulation, 88, 107–15. Hogg K, Swedberg K, McMurray J (2004). Heart failure with preserved left ventricular systolic function: epidemiology, clinical characteris- tics

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 daily electrolytes is essential. Angiotensin-converting enzyme in- hibitors and subsequently β-blockade can be introduced once a satisfactory diuresis has

been achieved. Management of cardiogenic shock is usually determined by the cause. Fluid status should be assessed, and an adequate left ventricular filling pressure ensured by the administration of intra- venous fluids where required (particularly in the case of right ven- tricular infarction). Revascularization is the mainstay of therapy
in acute myocardial infarction. Circulatory support with intra- aortic balloon counterpulsation, inotropic agents, ventricular as- sist devices, and extracorporeal membrane oxygenation should be considered for reversible causes (e.g. ventricular septal rup- ture, papillary muscle rupture, acute myocarditis, and peripartum cardiomyopathy). Prognosis Hospital admission with acute heart failure caries a poor prognosis with an average in-hospital mortality of 10–15% rising to up to 60% at 30 days in cases of cardiogenic shock. Introduction Although the term ‘acute heart failure’ often conjures up an image of a patient with acute pulmonary oedema, in extremis, struggling to breathe and producing pink, frothy sputum, such a dramatic pres- entation is not common. Admissions to hospital for heart failure, on the other hand, are extremely common, and most patients admitted are not breathless at rest, only becoming breathless on mild exer- tion. It is better to think of acute heart failure as being a worsening of symptoms and/or signs leading the patient, carer, or primary care physician to seek urgent expert advice—leading, in turn, to an ur- gent admission to hospital for investigation and/or treatment. Many patients will be able to walk, albeit slowly, from their wheelchair to their hospital bed. Patients admitted with heart failure usually have a problem with oedema (i.e. fluid in the wrong place). The old-fashioned term ‘anasarca’ describes a state of severe generalized oedema. It can be helpful to think of patients as being on a spectrum between pul- monary oedema at one end, in which the fluid is predominantly in the lung, and anasarca on the other, in which patients have an abso- lute excess of fluid, usually manifesting as peripheral oedema. This notion is similar to the classification system used for patients with chronic airways disease and emphysema: patients with pulmonary oedema can be termed ‘puffers’, and those with anasarca as ‘bloaters’ or having dropsy (Table 16.5.2.1). Patients with pulmonary oedema usually present with a short his- tory of deterioration. There is often an obvious acute precipitating factor such as acute coronary syndrome or atrial fibrillation, par- ticularly with a rapid ventricular response. They often have hyper- tension and a high peripheral vascular resistance. The patient has had no time to retain a substantial excess of body fluid. In contrast, patients with dropsy (‘bloaters’) usually have a history of deterior- ation over a period of weeks and no acute precipitating factors (al- though the development of atrial fibrillation with a slow ventricular response, anaemia, and chronic kidney disease (CKD) could be considered chronic precipitants). They have a low blood pressure and have had time to retain many litres (sometimes ≥20 litres) of excess fluid. The distinction is important in interpreting the results of clinical trials: an agent that is designed to improve acute breath- lessness, but given to someone who is already comfortable at rest (perhaps rendered so by standard background therapy) is likely to appear ineffective, even if it is highly effective in the appropriate pa- tient at the appropriate time. There is little evidence from randomized controlled trials in acute heart failure syndromes to guide management. Much of what follows in terms of management advice thus reflects the balance of expert opinion rather than definitive recommendations. The lack of evidence reflects a constellation of difficulties. The reasons for hospital admission may be misunderstood and patients often present at inconvenient hours of the night when it is least likely they will encounter people with the time or inclination to do research (funding nocturnal research can be expensive). Protocol procedures often cause delays which allow standard therapies to be effective before a new intervention can be started. Indeed, the effect- iveness of oxygen, nitrovasodilators, and diuretics for the short-term management of symptoms suggests that the needs for managing acute pulmonary oedema are largely satisfied.

The big problems for ‘acute’ heart failure really appear 2–3 days after admission when it is clear that diuretics alone have not solved the immediate problem. For most patients, the problem then is per- ipheral oedema and exertional breathlessness rather than breath- lessness at rest. In the longer term, the big problems are recurrent exacerbations and death. Thankfully, the vast majority of patients who survive to discharge attain a reasonable quality of life in the intervening period. There are guidelines to help guide practice, but those relating to acute heart failure tend to focus most on the patients with acute pulmonary oedema. The European Society of Cardiology’s (ESC) guidelines of 2016 are helpful, but it is noteworthy that the only treatment to receive a class I, level A recommendation was the use of prophylaxis against thromboembolism. The National Institute for Health and Clinical Excellence clinical guideline of 2014 covered both patients with pulmonary oedema and the more common presentation with fluid retention. This placed a great deal of emphasis on the importance of organization of care and the need for patients with acute heart failure to be managed in the appropriate environment, but was notably frank regarding the ab- sence of good trial evidence and gave a series of helpful recom- mendations for future research. Table 16.5.2.1 The spectrum of acute heart failure ranges from patients with acute pulmonary oedema, perhaps 15% of patients presenting to hospital with acute pulmonary oedema, to those with fluid retention. Differences between the two groups are highlighted Pulmonary oedema Anasarca Syndrome Puffers Bloaters Acute precipitant Yes Usually no Oedema In lungs Predominantly peripheral Absolute fluid excess No Yes Time course Minutes to hours Days to weeks

16.5.2 Acute cardiac failure 3399 Cardiogenic pulmonary oedema Pathophysiology In patients with pulmonary oedema, fluid from the lung capillaries collects in the extravascular spaces of the lung. The Starling equa- tion describes the forces acting on fluid in the pulmonary capil- laries (Fig. 16.5.2.1). Hydrostatic pressure tends to force fluid out of the capillaries while the colloid osmotic pressure (largely pro- vided by proteins) tends to maintain the fluid within the capillary. The balance between the forces varies between arteriole and venule; however, there is net filtration along the length of the capillary. Some resistance to fluid movement is provided by the alveolar–capillary membrane and any fluid entering the interstitium is removed by the lymphatics. Problems with any of these components can lead to (or worsen) pulmonary oedema. Pulmonary lymphatic flow may increase substantially in heart failure, reducing the risk of pulmonary oe- dema. However, the lymphatics drain into the venous circulation and so a rise in venous pressure may inhibit lymphatic clearance. Lymphatic occlusion, as occurs in lymphangitis carcinomatosa, and disruption to the alveolar capillary membrane, as happens in adult respiratory distress syndrome, can cause pulmonary oedema. Hypoalbuminaemia causes peripheral oedema and reduces the hydrostatic pressure at which pulmonary oedema occurs. In the normal circulation, the Frank–Starling relation describes the relation between the load on the left ventricle at the end of dia- stole, usually expressed as the end-diastolic pressure, and the work subsequently performed by the ventricle during systole. The end- diastolic pressure is the same as the left atrial and hence pulmonary venous pressure. In patients with heart failure, the curve relating the two is shifted to the right: for any given cardiac output, the filling pressure required is greater in the failing ventricle (see Fig. 16.5.2.2). An acutely failing ventricle needs a higher and higher filling pressure to maintain cardiac output. The rising end-diastolic pressure is re- flected in a rise in left atrial, pulmonary venous, and pulmonary ca- pillary pressure, resulting in faster rates of fluid filtration. Ultimately, fluid is filtered faster than the rate at which the lymphatics can re- move it, and pulmonary oedema results. This sequence cannot be quite the full explanation: a rise in pres- sure (including left ventricular filling pressure) can only arise from an input of energy. In acute

pulmonary oedema, the energy for the rise in left ventricular pressure can only come from the right heart. When the left ventricle fails, there is a fall in left ventricular stroke volume and consequent mismatch between left and right ventricular stroke volumes. The higher right ventricular stroke volume causes the increase in left ventricular filling pressure and restoration of car- diac output, but an inevitable consequence is some accumulation of fluid in the pulmonary circulation. The greater the fall in stroke volume of the left in relation to the right ventricle, the higher the left ventricular filling pressure will be and the greater the pulmonary fluid volume. Note that the total amount of fluid in the body does not increase and the effect is brought about by fluid moving to the 'wrong' body compartment. The fluid extravasation into the alveoli results in a reduction in blood volume during acute pulmonary oedema, which then increases back to normal levels during successful treatment. The fluid accumulation in the lungs starts with peribronchial swelling/oedema, followed by distension of the alveolar walls; only then does fluid enter the alveoli, initially at the alveolar angles, and eventually flooding the alveoli. The accumulation starts at the lung bases as the hydrostatic pressure is greatest here. Clinical presentation Acute pulmonary oedema is a dramatic medical emergency. The typical patient presents with very severe shortness of breath that has developed abruptly over minutes or hours. He or she has to sit up- right (and might indeed die if forced to lie flat) and may be unable to speak or gasp only a few words. Patients are usually very frightened and often certain that they are dying. Coughing may be prominent and will often produce blood-tinged oedema fluid. There may be some clues in the history as to the precipitant of pulmonary oedema. Sympathetic nervous system activation usually results in a tachy- cardia and a rise in blood pressure; the skin is white, cold, and clammy. The patient usually exhibits central cyanosis. Heart sounds may be inaudible but a gallop rhythm is common. The lung fields Fig. 16.5.2.1 The forces acting on fluid in a pulmonary capillary. Fig. 16.5.2.2 The Frank–Starling relation. As preload increases, so does cardiac output. In the failing ventricle, the relation is shifted to the right so that to deliver any given cardiac output, the ventricle requires a higher filling pressure.

section 16 Cardiovascular disorders 3400 are usually filled with crackles and sometimes wheezes (so-called 'cardiac asthma'). Given how sick the patient with pulmonary oedema is, the initial investigations and management have to be carried out at speed. The ESC guidelines for the management of acute heart failure empha- size the need to investigate and treat simultaneously (Fig. 16.5.2.3). There are three strands: making the diagnosis, identifying the imme- diate precipitant, and initiating treatment. Identifying precipitating factors is particularly important as it will influence subsequent man- agement (see Table 16.5.2.2). Initial investigation A 12-lead electrocardiogram (ECG) will often show grossly ab- normal QRS complexes, including evidence of acute myocardial infarction, or abnormal heart rhythm, including atrial fibrillation with a rapid ventricular response and ventricular tachycardia (see Fig. 16.5.2.4). A chest radiograph gives vital information. At early stages in the development of pulmonary oedema, the patient may have septal (or Kerley B) lines (Fig. 16.5.2.5), fluid in the lung fissures, and pleural effusions. There is peribronchial cuffing and upper lobe blood diver- sion. As oedema worsens, confluent shadows spreading out from the hila develop (Fig. 16.5.2.6). Near-patient testing for cardiac markers is becoming more widely available. Natriuretic peptide measurement can be helpful in making the diagnosis where there is clinical uncertainty: a patient with a normal natriuretic peptide level is extremely unlikely to have heart failure. A raised troponin suggests that there might be an acute Patient with suspected AHF

1. Cardiogenic shock? Urgent phase after first medical contact Immediate phase (initial 60–120 minutes)
2. Respiratory failure? Identification of acute aetiology: acute Coronary syndrome Hypertension emergency C H A M P Arrhythmia No Yes Immediate initiation of specific treatment Diagnostic work-up to confirm AHF Clinical evaluation to select optimal management Follow detailed recommendations in the specific ESC Guidelines acute Mechanical cause' Pulmonary embolism No No Yes Circulatory support Ventilatory support • pharmacological • mechanical • oxygen • noninvasive positive pressure ventilation (CPAP, BiPAP) • mechanical ventilation Immediate stabilization and transfer to ICU/CCU Yes Fig. 16.5.2.3 The treatment algorithm recommended by the European Society of Cardiology. Note that investigations and active management have to be undertaken simultaneously. From Ponikowski P, et al. (2016). 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: The Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC). Eur Heart J, 37(27), 2129–200.

16.5.2 Acute cardiac failure 3401 coronary syndrome (ACS) in progress, but troponin is commonly raised in acute heart failure even in the absence of ACS. A full blood count, biochemical screen, and thyroid function are important investigations. Anaemia is common, often due to iron defi- ciency but exacerbated by plasma volume expansion. Glucose is very commonly raised due to the high sympathetic drive, and does not ne- cessarily mean that diabetes is present. Other appropriate investiga- tions may include CT pulmonary angiography and a septic screen. Echocardiographic assessment early in the course of admission is very useful in confirming the cause of presentation and guiding subsequent therapy. Management Patients with acute pulmonary oedema should be managed in a high-dependency unit. Whether this should be cardiac care or a unit where intubation and ventilation is available will depend upon the degree of respiratory distress. Ventilatory support The lowest dose of oxygen needed to restore normal oxygenation should be used. Care should be taken in patients with chronic air- ways disease who are at risk of developing CO_2 retention (which may be exacerbated by the use of opiates). In a patient who is tiring or whose gas exchange is worsening despite treatment, positive pres- sure ventilation provides immediate relief. Noninvasive ventilation should be tried first: there is good evidence that both continuous positive airway pressure ventilation and bilevel positive airway pres- sure ventilation are safe. Medical treatment Opiates are commonly prescribed to relieve the distress of acute pul- monary oedema, but there is no evidence that they are safe and some data suggest that their use is associated with adverse outcomes. They should be used cautiously, if at all. Table 16.5.2.2 Common precipitants of acute pulmonary oedema, helpful investigations, and possible immediate treatment options. ECG is electrocardiogram; CXR is chest X-ray; (N)STEMI is (non) ST elevation myocardial infarction Precipitant Examples Investigation Immediate management Acute ischaemia STEMI NSTEMI ECG, troponina Immediate cardiology review Arrhythmia Atrial fibrillation Ventricular tachycardia ECG DC cardioversion Mechanical disaster Rupture of: interventricular septum Mitral papillary muscle Sinus of Valsalva Echocardiogram Cardiac surgery Hypertensive crisis Renal artery stenosis Salt load During recovery Vasodilators Intercurrent illness Pneumonia Urinary infection Sepsis CXR, septic screen As appropriate Pulmonary embolus CT pulmonary angiogram Thrombolysis, anticoagulation Environment Lack of compliance with medication/diet High salt intake History Education a often elevated in acute or chronic heart failure in the absence of any other evidence of ACS. An elevated troponin in patients with heart failure is a bad prognostic sign.

Fig. 16.5.2.4 A 12-lead electrocardiogram from a 76-year-old man presenting with acute pulmonary oedema. His ventricular tachycardia had been precipitated by an acute coronary syndrome.

section 16 Cardiovascular disorders 3402 Diuretics Diuretics are almost universally used in patients with acute pul- monary oedema, although trials to prove efficacy are lacking. As patients are usually not fluid overloaded, diuretics may not be the most logical therapy, although by reducing circulating volume, they do reduce filling pressure and relieve oedema. There is a firmly held view that furosemide is a vasodilator, but its haemodynamic effects coincide with the onset of diuresis. Vasodilators Nitrovasodilators are a more logical approach to the treatment of pulmonary oedema. They reduce both preload and afterload, as well as helping to relieve any myocardial ischaemia. Small studies suggest that nitrates may be more helpful than diuretics, but the evidence is not definitive, and clinical surveys suggest that they are used in few patients. The National Institute for Health and Care Excellence (NICE) guideline does not recommend their routine use. Other vasodilators have been tried. Despite early promise (and, indeed, licensing in some countries), nesiritide (human re- combinant B-type natriuretic peptide) had no effect on outcome in a large trial, and no patient subset obtained a striking benefit. Serelaxin (human recombinant relaxin, a vasoactive peptide pro- duced in pregnancy) was again promising, but a definitive trial, RELAX-AHF-2, was again neutral. In TRUE-AHF, patients with acute heart failure were randomized to receive either ularitide (an- other natriuretic hormone) or placebo, and the results were again neutral both for longer term cardiovascular mortality and for short- term symptom relief. Patient selection is part of the reason for the neutral studies of vasodilators. By the time a patient has been through the processes required for study entry, several hours have typically passed since presentation and the worst may by then be over. Severely ill pa- tients may be excluded as not being able to consent, and most studies exclude patients with many of the precipitants of acute pulmonary oedema, such as acute myocardial infarction. Indeed, it can be difficult to tell who, precisely, the criteria for the trials are targeting for inclusion. They usually appear to be trying to recruit patients with pulmonary oedema, who perhaps may have most to gain from a vasodilator, but in are in practice predominantly recruiting those with fluid retention, and if a patient is not breath- less at rest, then a treatment targeting breathlessness is unlikely to be helpful. Inotropes Inotropic support is often used, particularly as a ‘last ditch’ attempt to help very sick patients, more in despair than hope. Such evidence as there is from randomized trials suggests that all positive inotropic drugs working through adrenergic pathways are associated with an adverse outcome. Investigational approaches include cardiac my- osin activators and inhibitors of sarcoplasmic calcium re-uptake. Mechanical support In selected patients, there may be a role for intra-aortic balloon pumping to buy time, particularly when there is a potentially revers- ible cause for the pulmonary oedema. Similarly, a left ventricular assist device and extracorporeal membrane oxygenators may have a role when there is a potential either for recovery or for heart transplantation. Prognosis The clinical course of acute pulmonary oedema is usually very brisk: the patient usually recovers rapidly after treatment, or deteri- orates rapidly and dies. Overall, in-hospital mortality is around 15%, but strongly age-related; it is less than 10% in those aged less than 65 years and much higher in those aged more than 85 years, but these figures do not include those dying before reaching hospital. Fig. 16.5.2.5 A plain postero-anterior chest X-ray in a breathless patient showing Kerley B lines–multiple short horizontal lines visible towards the lung peripheries. There are also small pleural effusions. Fig. 16.5.2.6 More severe pulmonary oedema on supine antero- posterior film showing confluent shadowing spreading out from the hila. Note the relatively small heart shadow suggesting that this is an acute event in a previously normal heart.

16.5.2 Acute cardiac failure 3403 The recovery from pulmonary oedema is in part an active process in which cells take up fluid and return it to the capillary or lymphatic circulation. Novel agents designed to enhance this process are being developed. Cardiogenic anasarca Pathophysiology At the other end of the scale from pulmonary oedema are patients with fluid retention. Two processes result in oedema: the retention of sodium and water, and the transfer of fluid into the tissues. To take the second first: fluid collects in the tissues as a consequence of a rise in intravascular hydrostatic pressure or fall in osmotic pressure. As with the lungs, there is continuous filtration of fluid from the ca- pillaries to the tissues: if extravasation exceeds lymphatic drainage, oedema develops. The effect of gravity means that the hydrostatic pressure is highest in the feet, so ankle swelling is usually the first sign of fluid retention. In a patient confined to bed, though, the fluid will collect around the sacrum. The reasons why the body retains water are less certain. Sodium and water are retained by the kidneys, presumably in response to de- creased renal perfusion or deviation from the kidney's set-point for renal perfusion pressure (i.e. the blood pressure the kidney 'wants'). The consequence is renin production by the juxtaglomerular appar- atus leading to conversion of angiotensinogen to angiotensin I and ultimately to aldosterone production, which in turn causes salt and water retention by the kidney. In addition, antidiuretic hormone (or arginine vasopressin) is released in increased quantities, stimulating fluid retention and, importantly, thirst, and thus greater fluid intake. However, antagonists of each of these systems, even when used in combination, do not seem sufficient to prevent salt and water reten- tion and do not obviate the need for diuretics, although they might reduce the dose required. The stimulus leading to neuroendocrine activation is not clear. A common assumption is that it is a fall in blood pressure due to the failing heart. The body responds in the same way as it would to any other cause of a fall in blood pressure, such as dehydration or haem- orrhage, with avid salt and water retention to maintain blood pres- sure. Although some patients have a normal or high blood pressure compared to healthy people, this blood pressure may be below their individual set-point. If the set-point could be changed, then perhaps salt and water retention would not occur. Clinical presentation The typical picture is of a patient with gradual weight gain, often in the context of previous coronary disease, hypertension, atrial fibril- lation, and CKD. Around 5 litres of fluid (weighing 5 kg) are needed before oedema first appears. As the process is often very gradual, patients will often present only once they have retained many litres of fluid and have pitting oedema affecting the abdominal wall, and sometimes even the thoracic wall. Pleural and pericardial effusions and ascites are common in this situation. In some patients, the oe- dema causes obvious ballooning of the ankles. However, in many patients the oedema does not grossly distort the shape of the leg, and oedema of the trunk may develop and go unobserved by the patient or a careless doctor. Symptoms such as 'I can't get my shoes on' or 'I have had to loosen my belt' or 'I have increased a waist size' in a pa- tient with increasing breathlessness should alert the clinician to the possibility of oedema. The oedema is usually very obvious on examination. Cardiogenic oedema is pitting. The highest level of pitting oedema should be sought. The jugular venous pressure will be raised: however, when it is very high, the top of the column of the blood may not be visible in the neck, even with the patient sitting upright. There is usually a tachycardia and often hypotension. The apex beat is displaced and dyskinetic and there is almost always a third sound or gallop rhythm. Mitral regurgitation is very common. There are commonly signs of ascites and pleural effusions, with basal crackles in some patients who have pulmonary congestion. Differential diagnosis It is important to consider the differential diagnosis of peripheral oedema (Table 16.5.2.3). Once a firm diagnosis of cardiogenic oe- dema is made, the next step is to consider the possible causes of the 'right heart' failure. Although the commonest cause is left heart failure,

other cardiac conditions, particularly constrictive pericar- ditis, can result in severe fluid overload and be difficult to diagnose (see Table 16.5.2.4). Pulmonary hypertension leading to right ven- tricular dysfunction appears increasingly common in frail elderly patients with right heart failure, many of whom also have lung and left heart disease. Initial investigations Patients presenting with anasarca should be investigated as patients presenting with chronic heart failure (see Chapter 16.5.3) with the aim of making the diagnosis, unmasking any treatable cause, and identifying any associated comorbidities. • Common ECG abnormalities include previous myocardial in- farction, left bundle branch block, atrial fibrillation. • A chest radiograph will show a large heart shadow and evidence of pulmonary venous congestion. It may also exclude other causes of breathlessness. • Urinary dipstick testing will help pick up infection and gross proteinuria. • Anaemia is common in anasarca due to heart failure. Patients may benefit from an iron infusion should they have iron deficiency. • Renal dysfunction and electrolyte abnormalities are common in patients with heart failure and are major determinants of outcome. Regular testing during treatment (see next) is vital. Table 16.5.2.3 Differential diagnosis of peripheral oedema. Note that anasarca is easily overlooked without careful examination Oedema fluid Cardiogenic Hypoalbuminaemia Fluid overload Pregnancy Lymphatic obstruction Idiopathic Medicines Dihydropyridines/glitazones Venous insufficiency Varicose veins Previous DVT Chronic stasis Fat (Obesity)

 • Natriuretic peptide levels are usually grossly raised. • An echocardiogram is essential (see Fig. 16.5.2.7). The key elem- ents to look at are: ■ Left atrial size—mitral valve disease or chronic elevation in left ventricular filling pressure will cause left atrial dilation. It is probably the best guide to the chronic health of the left heart but may not be enlarged with severe acute-onset disease. ■ Left ventricular size and contractility—the left ventricle is com- monly dilated with reduced systolic function but sometimes small, hypertrophied, and ‘stiff’. Regional wall motion abnor- malities suggest a possible underlying diagnosis of ischaemic heart disease. ■ Valve disease. • More sophisticated investigation may reveal pulmonary hyper- tension, right ventricular disease, and dilated venae cavae. Ultrasound can also be used to identify ‘lung comets’ indicating pulmonary congestion. Management The problem is one of an absolute excess of fluid, and initial man- agement is directed at fluid removal. General care is important: the patient should be managed with bed rest with prophylactic low molecular weight heparin used to reduce the (high) risk of venous thrombosis. The only way to monitor progress accurately is with strict fluid balance monitoring and daily weights. The urea and elec- trolytes should be measured at least daily, and the patient should be reviewed daily by an experienced member of the team. Oedema is due to retention of water, not salt: in 1 litre of oedema fluid, there are 991 g of water and 9 g of salt. There is no good evi- dence that sodium restriction is useful, although restricting a very high intake may be useful in the occasional patient. Salt restric- tion may lead to hyponatraemia. Aquaresis may be greater (and hyponatraemia less likely) when moderate salt intake is allowed. Fluid intake is often restricted to around 1.5 litres per day, but the evidence for this is weak. The aim should be to try and induce a net diuresis of around 2 litres per day. Diuretic management is key. Diuretics work by preventing the re- absorption of some of the filtered sodium from the tubular lumen. • Loop diuretics block the sodium–potassium–chloride cotransporter in the thick ascending loop of Henle. As they reach their site of ac- tion from the lumen of the nephron, they only work if there is at least some glomerular function. Once their effects are over, the kidney goes into overdrive to restore the lost salt and water. • Thiazide diuretics work at the distal convoluted tubule. They in- duce a small but persistent diuresis; over a 24-hour period loop and thiazide

diuretics may have the same natriuretic effect. • Mineralocorticoid receptor antagonists block the effects of aldos- terone at the sodium–potassium exchanger in the distal convo- luted tubule, resulting in potassium retention. A typical approach is to use intravenous loop diuretic. Oral ab- sorption is very erratic in patients with cardiogenic oedema because of bowel oedema. An infusion of 10 mg per hour of furosemide is Table 16.5.2.4 Differential diagnosis of cardiogenic peripheral oedema Possible cause Examples Raised left atrial pressure (left heart failure) Impaired left ventricular Contraction Ischaemic heart disease (IHD) Dilated cardiomyopathy Relaxation Left ventricular hypertrophy (hypertension) Hypertrophic cardiomyopathy Amyloid Mitral valve disease Raised right atrial pressure (right heart failure) Chronic left atrial hypertension Pulmonary hypertension IHD Tricuspid valve disease (often tricuspid regurgitation due to dilated right ventricle) Right ventricular cardiomyopathy Congenital heart disease Left-to-right shunts Right ventricle in systemic position Pulmonary hypertension Chronic left atrial hypertension Lung disease (cor pulmonale) Thromboembolic disease Pericardial disease Constrictive pericarditis Fig. 16.5.2.7 Echocardiogram of a patient presenting with anasarca. Long axis parasternal view. The left ventricular internal diameter is approximately 8 cm, and there is little difference between systolic and diastolic frames.

16.5.2 Acute cardiac failure 3405 often used. Data from small studies suggests that an infusion causes a greater natriuresis than repeated boluses to the same dose, but the biggest study of infusion versus bolus dosing showed no difference between the two strategies. Particularly after chronic loop diuretic usage, the cells of the distal convoluted tubule hypertrophy and increase their capacity to reabsorb sodium. The addition of a thiazide will block the distal convoluted tubule (so-called ‘progressive nephron blockade’) which may lead to a profound diuresis. Metolazone is often used for this purpose although there is no convincing evidence that it is more potent than other thiazides. Combination therapy can be very helpful, but patients having the two diuretics must be monitored very closely. Potentially nephrotoxic drugs, such as nonsteroidal anti- inflammatory drugs (including aspirin) should be stopped. It is not certain whether pre-existing β-blocker (or angiotensin-converting enzyme inhibitor or ACE) therapy should be stopped: the evidence available suggests that those patients whose pre-existing therapy is not stopped are less likely to be discharged without these life-saving treatments. Towards the end of intravenous therapy, ACE inhibitors and β-blockers should be started simultaneously at low doses. If not al- ready being used, a mineralocorticoid (aldosterone) receptor antag- onist (MRA) should also be started (see Fig. 16.5.2.8). The dose of ACE inhibitor should be titrated rapidly to target with careful moni- toring of blood pressure and renal function. β-Blockers are titrated more slowly and often only after discharge. Intravenous diuretic therapy should be continued until the oe- dema has resolved unless an oral diuretic regimen is clearly having the desired results. It is not uncommon for renal function to im- prove following diuresis and diuretic therapy should not be with- held or reduced in patients with impaired renal function at the time of presentation where there is clear evidence of fluid overload. For some patients, however, complete resolution of oedema cannot be achieved due to worsening renal impairment and a balance has to be struck between some peripheral oedema and a raised creatinine. Ideally, a patient finishing intravenous therapy will be moni- tored for 48 h to make sure that the fluid does not re-accumulate immediately. Some patients may fail to respond adequately to intravenous di- uretics. It is important to reconsider the diagnosis: has constrictive pericarditis been missed? Is there some correctable cause of renal dysfunction, such as renal artery stenosis? Other therapeutic options include the use of digoxin, which has a diuretic effect, although the evidence base for its use in acute heart failure is poor. Positive inotropic drugs, particularly in

hypotensive patients, are sometimes used. There is no evidence to support the practice, and no evidence that ‘renal dose dopamine’ has anything to offer. Ultrafiltration can be used to remove fluid rapidly from patients with anasarca (see Table 16.5.2.5). Veno-venous filtration is possible in a cardiac care unit setting with small devices. There is conflicting evidence as to its value: in one study, its use was associated with a reduction in the need for subsequent emergency care, but in pa- tients with worsening renal function, a second study suggested that ultrafiltration was associated with a higher creatinine, although this finding may simply have reflected haemoconcentration. The most recent study was terminated early by the sponsoring company: al- though the primary endpoint was not met, several of the secondary endpoints suggested a benefit for ultrafiltration. The role of ultra- filtration in routine practice is still uncertain, but there is no doubt that as much as 5 litres can safely be removed from a patient in 24 h, and it is useful in selected patients who are unresponsive to com- bined diuretic therapy or when diuresis is limited by renal dysfunc- tion (Fig. 16.5.2.9). Fig. 16.5.2.8 Time course of diuresis for a patient presenting with approximately 25 litres of anasarca. Note the brisk response once the furosemide infusion was started, and the timing of introduction of long- term medication. ACEi is angiotensin-converting enzyme inhibitor and βB is beta adrenoceptor antagonist. Table 16.5.2.5 Diuretics commonly used in the management of anasarca. DCT is distal, and PCT, proximal, convoluted tubule. MRA is mineralocorticoid antagonist Class Example Route Site of action Comments Loop Furosemide, bumetanide Intravenously Na+/K+/Cl–cotransporter in thick ascending loop of Henle High ceiling; short duration of action Shorter half-life than thiazides Thiazide Bendroflumethiazide By mouth DCT Low ceiling; longer period of action Combined with loop may cause profound diuresis ‘Thiazide-like’ Metolazone By mouth DCT (and PCT) Combined with loop may cause profound diuresis MRA Spironolactone, eplerenone By mouth DCT–Mineralocorticoid receptor antagonists Essential component of
long-term management

 Cardiogenic shock Shock occurs when there is tissue hypoperfusion despite adequate ventricular filling. There is no blood pressure level that can be used to define shock, with the consequence that the incidence and prog- nosis quoted varies from study to study. Pathophysiology Cardiogenic shock most commonly arises from an acute myocar- dial insult which results in sufficient reduction in cardiac output that the perfusion to vital organs is insufficient to maintain organ function. By far the commonest cause is acute myocardial infarc- tion, although patients with acute presentation of cardiomyopathy, including peripartum cardiomyopathy, may develop shock. The result is massive sympathetic nervous system activation as the body tries to restore blood pressure. The consequent increase in afterload cannot be met by the failing left ventricle. Reduced cor- onary artery perfusion results in worsening myocardial function, perpetuating the problem. Clinical presentation The patient is hypotensive, usually tachycardic, pale, and sweaty. Reduced cerebral perfusion results in confusion and agitation, and the patient becomes oliguric or anuric. Except for those patients with predominant right ventricular infarction, some degree of pul- monary oedema is invariably present. Differential diagnosis and investigations Making the correct diagnosis is fundamental: investigations should be directed at finding any reversible cause for the patient’s state. Making certain that the left ventricle is adequately filled is essential to make the diagnosis of shock: if the left ventricle is underfilled, then fluid replacement should result in rapid reso- lution of symptoms. If there is doubt, then fluid challenges with rapid infusion of 100–200 ml fluid can be helpful. In some cases, pulmonary artery catheterization is used to determine the pulmonary capillary wedge pressure and hence confirm adequate filling. There is no evidence that using the catheter to guide fur- ther management is

helpful. An ECG with right-sided leads will help make the diagnosis of a predominantly right-sided myocardial infarct. An echocardiogram to confirm the extent of left and right ventricular damage and to exclude a mechanical problem (free wall rupture, papillary muscle rupture, ventricular septal rupture) is a vital early investigation. Bladder catheterization will confirm that the patient is genu- inely oliguric rather than confused due to retention of urine. Sepsis should be excluded. Management Dealing with any treatable cause of shock is the most important step. Revascularization in patients presenting with acute myocardial in- farction may relieve shock, although if shock develops following or despite a successful procedure, the outlook is particularly poor. Patients with mechanical problems tend to have smaller and more localized infarctions than those without: although it is very high risk, early surgery may be life-saving. For those patients with right ventricular infarction as the cause, fluid loading may improve the patient's condition, but at a cost of high central venous pressure. Trying to sustain the circulation in patients with no readily revers- ible cause is rarely successful. • Positive inotropic drugs, such as catecholamines and phospho- diesterase inhibitors, may improve cardiac output and blood pres- sure: however, their use has not been shown to improve prognosis. Indeed, dobutamine in randomized trials is associated with a worse outcome. • Intra-aortic balloon counterpulsation (IABP) can improve the situation, at least temporarily. Trial evidence suggests that the IABP does not improve prognosis in patients with cardiogenic shock due to acute infarction, but it can certainly help patients with acute mechanical causes such as septal rupture and mitral regurgitation. In some patients with potentially reversible causes, such as peripartum cardiomyopathy, IABP has been used success- fully to sustain the circulation for many weeks. • Advanced therapies with ventricular assist devices (VADs), extra- corporeal membrane oxygenation (ECMO), and even heart trans- plantation have been successful in selected patients. VADs and ECMO are only available in the United Kingdom in transplant centres, but there is a move to make them more widely available as a temporizing measure before patients are transferred to the centres. The prognosis of cardiogenic shock is bleak. Unless there is a readily correctable cause, the mortality rate approaches 60% at 30 days. Once treatable causes of shock have been excluded, conser- vative management and an easy death may be preferred rather than transfer to the intensive care unit for valiant, desperate, protracted, but ultimately futile, intervention. FURTHER READING Chen HH, et al. for the NHLBI Heart Failure Clinical Research Network (2013). Low-dose dopamine or low-dose nesiritide in acute heart failure with renal dysfunction: the ROSE acute heart failure randomized trial. JAMA, 310, 2533–43. Clark AL, Cleland JG (2013). Causes and treatment of oedema in pa- tients with heart failure. Nat Rev Cardiol, 10, 156–70. Fig. 16.5.2.9 A patient receiving ultrafiltration. There is a two-lumen right internal jugular venous line from which blood is continuously removed, pumped through a filter (black arrow) and then returned to the body. Filtrate is seen collecting in the bag (white arrow).

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