

1 Cardiology

Questions

BASIC SCIENCE

Answers can be found in the Cardiology Answers section at the end of this chapter.

1. Beta-blockers are recommended as first-line therapy for stable angina by both the American College of Cardiology/American Heart Association (ACC/AHA) and the European Society of Cardiology. Their mechanism of action in this condition is explained by:
 - A. Plaque stabilisation
 - B. Increased coronary blood flow
 - C. Reduction in blood pressure
 - D. Reduction in myocardial oxygen demand
 - E. Reduction in systemic vasodilatation
2. Which one of the following compensatory mechanisms occurs in heart failure?
 - A. Decreased ventricular preload
 - B. Peripheral vasodilatation
 - C. Increased renal sodium and water excretion
 - D. Activation of the adrenergic nervous system
 - E. Myocardial atrophy
3. Which is the most common origin of idiopathic ventricular tachycardia in the absence of structural heart disease?
 - A. Aortic annulus
 - B. Aortic sinuses
 - C. Great cardiac vein
 - D. Epicardium
 - E. Right ventricular outflow tract

4. Which one of the following viral infections is the commonest cause of myocarditis in developed countries?

- A.** Enterovirus
- B.** Cytomegalovirus
- C.** Hepatitis C virus
- D.** Human immunodeficiency virus (HIV)
- E.** Influenza virus

5. Which one of the following statements is correct regarding the electrical conduction and contraction of the heart?

- A.** Electrical conduction is transmitted from the sino-atrial node to the bundle of His to the atrioventricular node to the Purkinje fibres to the myocardium
- B.** Muscle contraction is associated with release of calcium by the sarcoplasmic reticulum
- C.** Repolarisation of cardiac muscle is due to flow of potassium into the myocytes
- D.** On an electrocardiogram the QRS complex corresponds to ventricular repolarisation
- E.** The perfusion of the coronary arteries increases during systole

6. Perhexiline has been used in patients with chronic heart failure and refractory angina. Which one of the following statements about perhexiline is correct?

- A.** It is metabolised by cytochrome P450 3A4
- B.** About 7–10% of Caucasians are slow metabolisers
- C.** The recommended dose for slow metabolisers is 100 mg on alternate days
- D.** It can cause hyperglycaemia in diabetic patients
- E.** It improves 5-year survival

Theme: Beta-blockers (for Questions 7 and 8)

- A.** Propranolol
- B.** Metoprolol
- C.** Nebivolol
- D.** Atenolol
- E.** Pindolol
- F.** Sotalol
- G.** Bisoprolol
- H.** Carvedilol

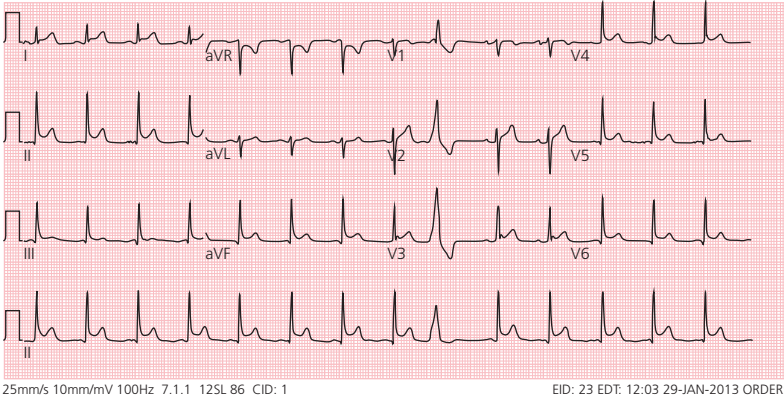
Select the drug that best fits the description in each of the following statements.

7. A non-selective beta-blocker with α_1 -adrenoreceptor blocking activity.

8. A selective β_1 -adrenoreceptor blocker with nitric-oxide potentiating vasodilatory effect.

CLINICAL

9. A 47-year-old man presents with chest pain. He reports moderately severe central chest pain of 24h duration. The pain is worse with inspiration and is alleviated by maintaining an upright position. He also reports having had a fever recently. His medical history and physical examination are unremarkable. His ECG is shown below. What is the most likely diagnosis and the most appropriate treatment approach for this patient?



- A.** Acute pericarditis; perform an echocardiogram in 1 week to confirm diagnosis
- B.** Acute pericarditis; start a non-steroidal anti-inflammatory drug (NSAID)
- C.** Acute pericarditis; start prednisolone
- D.** ST elevation myocardial infarction; start thrombolytics
- E.** Pericardial tamponade; requires pericardiocentesis

10. A 21-year-old Aboriginal woman presents with a sore throat for 2 days. She has fever (38°C) and coryza. On physical examination, the patient appears well but has a markedly infected posterior pharynx and exudates over her tonsils. Streptococcal pharyngitis is suspected. Which one of the following approaches to management is most appropriate?

- A.** A throat swab is adequate to establish diagnosis in Aboriginal patients
- B.** Intravenous benzylpenicillin 1.2g four times a day for 10 days is the treatment of choice in eradicating Group A streptococci from the nasopharynx
- C.** Treatment should be started within 9 days of the onset of symptoms to prevent acute rheumatic fever
- D.** Aspirin can prevent rheumatic chorea
- E.** Asymptomatic family contacts of patients with streptococcal pharyngitis should have throat swabs for streptococcal infection

11. A 50-year-old man presents with a 2-h history of severe chest pain. The pain started suddenly while eating, was constant and radiated to the back and interscapular region. His past medical history includes hypertension and hyperlipidaemia. On examination, his heart rate is 120 beats/min and his blood pressure is 80/40 mmHg. Jugular venous pressure is not visualised. All peripheral pulses are present and equal. While stabilising the patient, which one of the following investigations should be undertaken?

- A. Serum lipase
- B. Computed tomography (CT) angiography of the chest
- C. D-dimer
- D. Lung ventilation–perfusion scan
- E. Upper gastrointestinal endoscopy

12. Which one of the following best describes the use of plasma brain natriuretic peptide (BNP) in the assessment of congestive heart failure (CHF)?

- A. BNP level is more useful in detecting diastolic heart failure than systolic heart failure
- B. Measurement of BNP is recommended as routine in the diagnosis of CHF
- C. BNP offers additional diagnostic information beyond that provided by echocardiogram
- D. BNP levels have been shown to predict all-cause mortality, including sudden death
- E. Plasma BNP or N-terminal pro-BNP measurement is not useful in patients presenting with new-onset breathlessness

13. A 46-year-old woman presents with a 2-week history of shortness of breath and ankle swelling. On examination her jugular venous pressure (JVP) is elevated and there are fine crackles at the bases of both lungs on auscultation. She was diagnosed with breast cancer a year ago and has been treated with surgery, doxorubicin, cyclophosphamide and radiotherapy. She has no cardiac risk factors or family history of cardiac disease. Computed tomography pulmonary angiography (CTPA) is normal and chest X-ray shows interstitial pulmonary oedema. What is the most likely cause for this presentation?

- A. Anthracycline cardiotoxicity
- B. Constrictive pericarditis
- C. Pulmonary fibrosis
- D. Radiation-induced cardiomyopathy
- E. Pulmonary embolism

14. All of the following drugs can be utilised in patients with heart failure. Which one is the most effective in improving systolic function?

- A. Spironolactone
- B. Angiotensin converting enzyme (ACE) inhibitor
- C. Digoxin

- D. Frusemide
- E. Hydralazine

15. A 72-year-old man describes substernal chest pressure while walking for more than 100m and this is relieved by rest. His medical history is remarkable for hypertension and a myocardial infarction 3 years ago. His medications include aspirin 150mg daily; metoprolol 50mg twice daily; atorvastatin 40mg daily; perindopril 5mg daily; and isosorbide mononitrate 120mg daily. He had a cardiac catheterisation 1 month ago that showed a left main coronary artery stenosis of 85%, a proximal left anterior descending artery stenosis of 70% and a 80% stenosis of the first obtuse marginal branch. His left ventricular ejection fraction (LVEF) was estimated at 45%. Which one of the following therapies would be most beneficial for this patient?

- A. Addition of clopidogrel
- B. Regular exercise programme
- C. Percutaneous transluminal angioplasty (PCTA)
- D. Coronary artery bypass grafting (CABG)
- E. Transmyocardial revascularisation procedure (TMR)

16. The use of computed tomography coronary angiography (CTCA) is most appropriate in which one of the following patients?

- A. An asymptomatic patient who has a strong family history of ischaemic heart disease
- B. A patient with coronary stents presenting with chest pain in whom you suspect in-stent restenosis
- C. A patient presenting with severe crushing chest pain and an ECG showing ST-elevation myocardial infarction (STEMI)
- D. A patient presenting with chest pain and palpitations and an ECG showing rapid atrial fibrillation (heart rate: 125 beats/min)
- E. A patient with chest pain with normal serial cardiac enzymes and ECGs who you think has a low-to-intermediate pre-test probability of coronary artery disease

17. An 86-year-old woman with a history of ischaemic heart disease, atrial fibrillation and type 2 diabetes presented to the emergency department with flank pain and symptomatic anaemia with haemoglobin of 69g/L. After abdominal CT imaging, she was found to have a retroperitoneal haemorrhage. Three weeks prior to the presentation she had been changed from warfarin to dabigatran (taking a standard dose of 150mg twice a day) for stroke prevention. Prior to this change, her INR has been within the target range for 6 years. What is the most likely explanation for the significant haemorrhagic complication in this patient after commencing dabigatran?

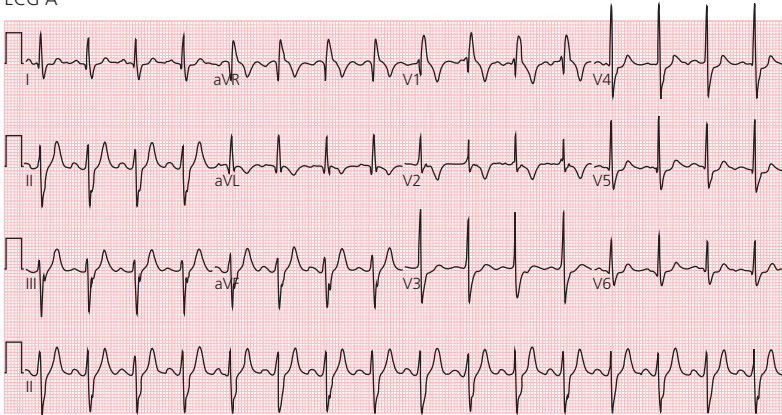
- A. She is also taking phenytoin
- B. She has impaired renal function

- C. Her atrial fibrillation had reverted to sinus rhythm
- D. Her INR has not been checked during the 3 weeks on the new medication
- E. She is also taking digoxin

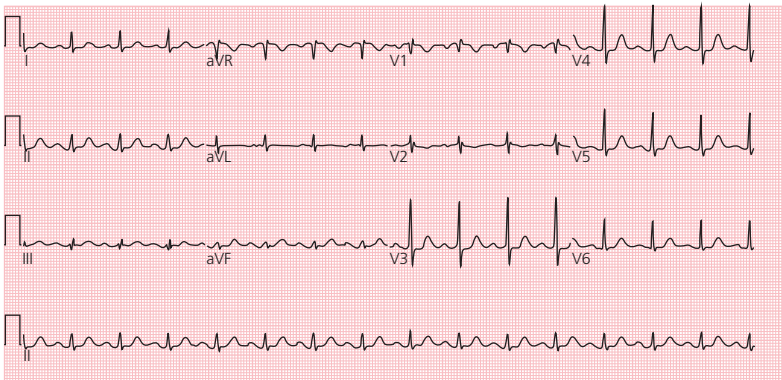
18. A 60-year-old man has had an inferior myocardial infarction 5 days ago. Today he is feeling lightheaded and his pulse rate is 40 beats/min. Blood pressure is 85/65 mmHg. An ECG is done immediately. Which one of the following findings is an indication for temporary pacing?

- A. (ECG A)
- B. (ECG B)
- C. (ECG C)
- D. (ECG D)
- E. (ECG E)

ECG A

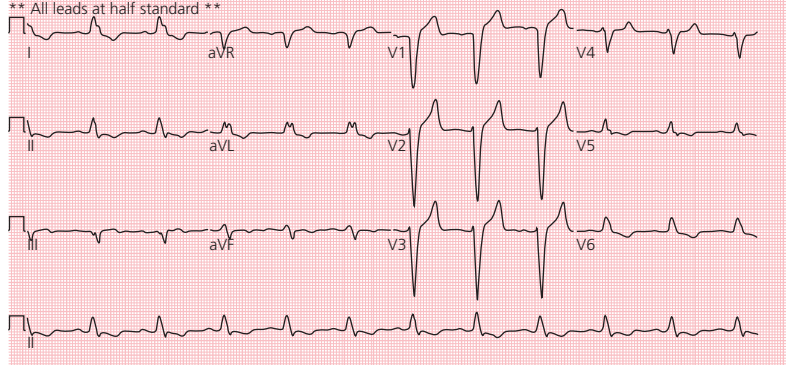


ECG B

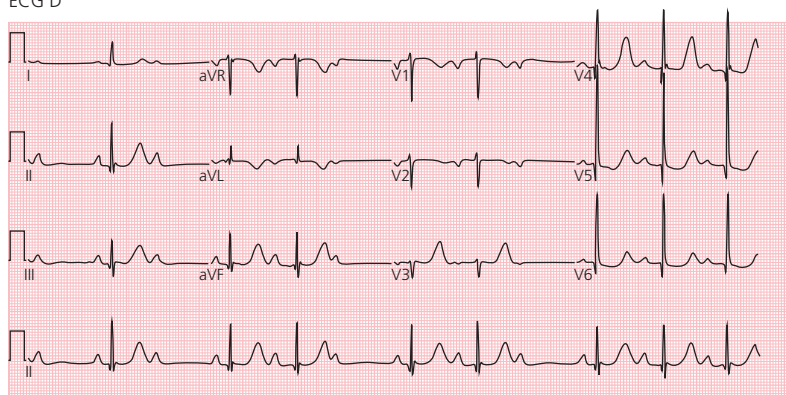


ECG C

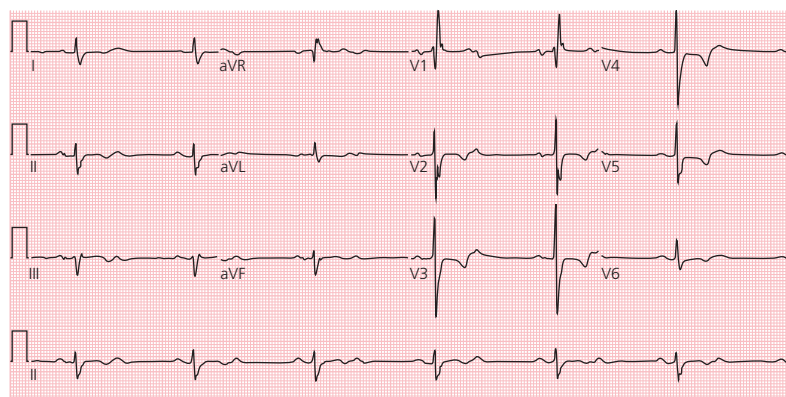
** All leads at half standard **



ECG D



ECG E



19. During pregnancy, which one of the following heart diseases is associated with the highest maternal mortality?

- A. Aortic stenosis
- B. Atrial septal defect
- C. Coarctation of aorta
- D. Eisenmenger syndrome
- E. Mitral stenosis

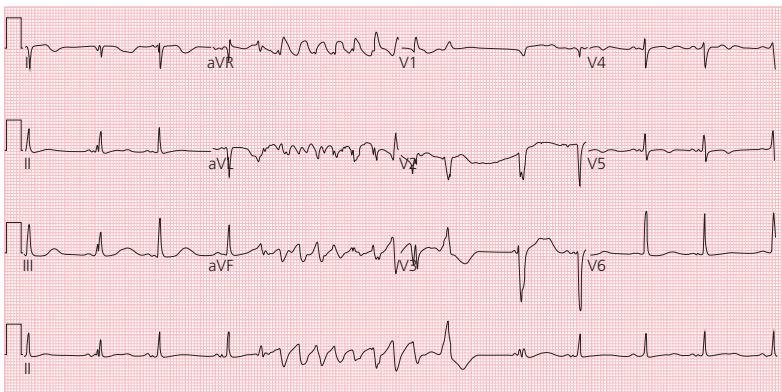
20. A 22-year-old man who is known to have hypertrophic cardiomyopathy undergoes physical and echocardiographic examination. Which one of the following findings is most predictive of this patient's risk of sudden cardiac death?

- A. Hypertension
- B. Double apex beat
- C. Atrial dilatation
- D. Intensity of systolic murmur
- E. Septal wall thickness of 3 cm or greater

21. Which is the commonest organism causing prosthetic valve infective endocarditis?

- A. *Staphylococcus aureus*
- B. Coagulase-negative staphylococcus
- C. *Streptococcus bovis*
- D. *Candida*
- E. *Streptococcus viridans*

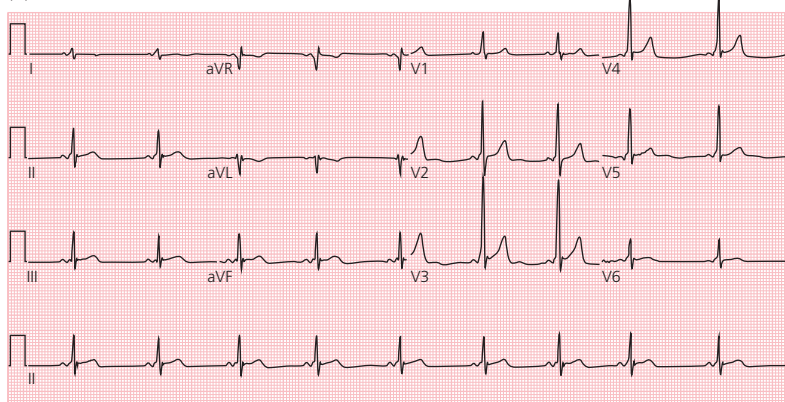
22. A 16-year-old girl has a cardiac arrest while visiting her grandmother in hospital and has the ECG shown below. She revives after DC shock and all the subsequent ECGs show a prolonged QT interval. Blood tests rule out any metabolic derangement. Two of her first-degree relatives died suddenly at a young age. She should be treated with:



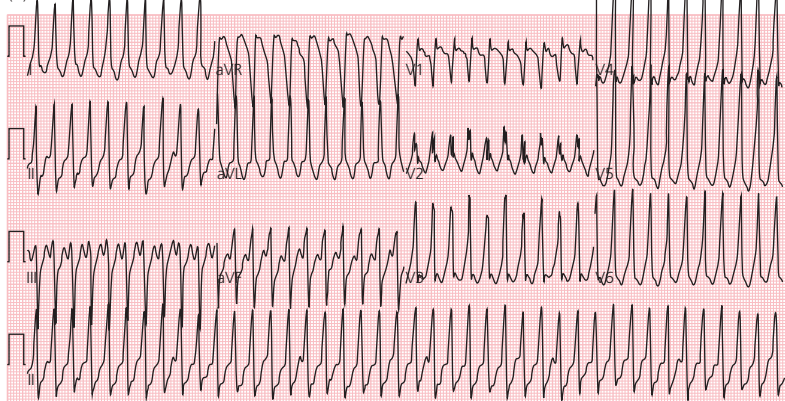
- A. An implantable cardioverter–defibrillator
 - B. Beta-blocker
 - C. Quinidine
 - D. Sotalol
 - E. Verapamil
- 23.** A 35-year-old man who is from an indigenous community in New Zealand has had mitral stenosis due to rheumatic heart disease. He has experienced some exertional dyspnoea recently. He attends a cardiology clinic with his most recent echocardiography results. Which one of the following features should prompt a referral for him to have a percutaneous balloon mitral valvuloplasty (PBMV)?
- A. Mitral orifice area of 1.2 cm^2 with minimal calcification
 - B. The presence of severe mitral regurgitation
 - C. Dyspnoea classified as New York Heart Association functional class I
 - D. Mitral orifice area of 3 cm^2 with fusion of the subvalvular apparatus
 - E. Large left atrial thrombus
- 24.** A 68-year-old male farmer is transferred from a country hospital following a late presentation with acute myocardial infarction. He suffered severe chest pain 2 days ago but did not seek medical treatment. While you are examining the patient you hear a pericardial rub and make a diagnosis of peri-infarction pericarditis. Which one of the following statements is correct?
- A. Aspirin and heparin infusion should be stopped immediately
 - B. The patient should be commenced on ibuprofen
 - C. Reperfusion therapies are associated with a reduced incidence of peri-infarction pericarditis
 - D. The patient should be commenced on high-dose prednisolone
 - E. The echocardiogram is likely to show preserved ejection fraction
- 25.** A 35-year-old man presents to the emergency department with a 1-h history of feeling his heart racing and slight chest discomfort. He has had two similar episodes previously following alcohol binges. An electrocardiography shows a regular narrow complex tachycardia with a rate of 180 beats/min. He otherwise feels well, his blood pressure is 98/68 mmHg and pulse oximetry on air shows oxygen saturation of 97%. What treatment should be administered?
- A. Electrical cardioversion
 - B. Intravenous lignocaine
 - C. Intravenous adenosine
 - D. Intravenous digoxin
 - E. Intravenous verapamil
- 26.** A 45-year-old man presents with a 24-h history of palpitations and chest discomfort. He had one similar episode 5 years ago. He is known to have asthma since childhood and uses a salbutamol inhaler two to three times a week. His initial examination reveals blood pressure of 110/60 mmHg, pulse rate 152 beats/min

and oxygen saturation on room air of 95%. There is a scattered expiratory wheeze but no cardiac murmur. His ECG taken 5 years ago when he was admitted with an acute asthma attack is shown below (A) and his current ECG (B). His biochemistry results are unremarkable and the troponin T level is normal. Which one of the following medications should be administered to achieve rate control?

(A)



(B)



- A. Intravenous adenosine
- B. Intravenous atenolol
- C. Intravenous loading dose of digoxin
- D. Intravenous flecainide
- E. Intravenous verapamil

27. A 75-year old man presents to hospital with a 2-week history of malaise and low-grade fever. He also has had chronic diarrhoea for the past 3 months and a 5-kg weight loss. On examination, his blood pressure is 100/70 mmHg, heart rate 110 beats/min and temperature of 38.4°C. A diastolic murmur (3/6) is heard at the left sternal edge. He is mildly anaemic with mean cell volume (MCV) of 76 fL (normal reference range 80–100 fL). Blood cultures grow *Streptococcus bovis* and transoesophageal echocardiography reveals vegetations on the aortic valve. What additional investigations should be undertaken?

- A. Cardiac magnetic resonance imaging
- B. Computed tomography of the abdomen
- C. Orthopantomogram (OPG)
- D. Colonoscopy
- E. White cell scan

28. Which one of the following disorders does NOT cause high-output heart failure?

- A. Hyperthyroidism
- B. Paget disease
- C. Brachio-cephalic arteriovenous fistula
- D. Cirrhosis
- E. Amyloidosis

29. A 60-year-old woman is diagnosed with *Streptococcus viridians* endocarditis involving the mitral valve. Which one of the following is a poor prognostic factor?

- A. Left ventricular ejection fraction of 50%
- B. Perivalvular extension of infection
- C. Recent dental extraction
- D. Previous adverse drug reaction to penicillin
- E. Previous abdominal aortic aneurysm repair

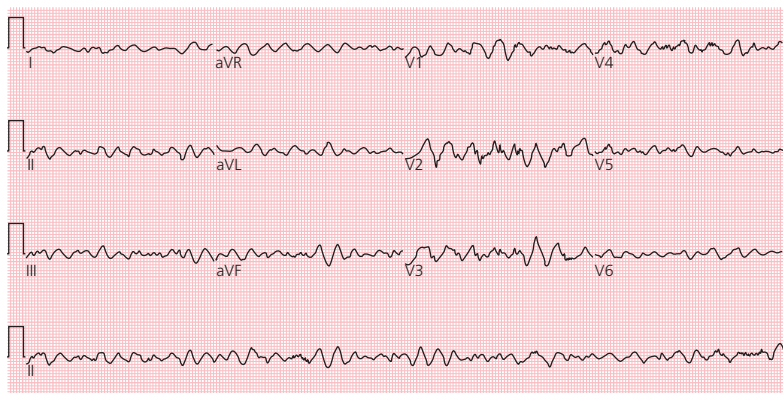
30. A 72-year-old man presents with a 2-day history of pain in his toes. He presented to another hospital with chest pain and received a coronary angiography 7 days ago. His other medical problems include hypertension, type 2 diabetes, chronic kidney disease with a serum creatinine of 156 µmol/L and osteoarthritis. He is taking aspirin, clopidogrel, metformin, atorvastatin and perindopril. On examination, he is afebrile, peripheral pulses are difficult to palpate and toes are painful to touch. His initial blood test results are shown below. Which one of the following diagnoses is most likely?

	Value	Reference range
Haemoglobin	82 g/L	115–155 g/L
White blood cells	13.0×10^9 cells/L	$4.0\text{--}11.0 \times 10^9$ cells/L
Platelet count	593×10^9 cells/L	$150\text{--}400 \times 10^9$ cells/L
Lactate dehydrogenase	344 U/L	110–230 U/L
Creatinine	287 µmol/L	80–120 µmol/L
Urate	0.69 µmol/L	0.21–0.48 µmol/L



- A. Contrast nephropathy
- B. Renal embolus
- C. Cholesterol emboli
- D. Cryoglobulinaemia
- E. Metformin-induced renal failure

31. A 72-year-old man who was admitted with an inferior myocardial infarction has a cardiac arrest on the way to the angiogram suite. After three cycles of cardiopulmonary resuscitation (CPR), two boluses of 1 mg epinephrine (adrenaline) and two defibrillator shocks, his electrocardiography remains unchanged and is shown below. What is the next most appropriate step?



- A. 3 mg of epinephrine (adrenaline)
 - B. 40 units of vasopressin
 - C. 10 ml of 10% calcium chloride
 - D. 10 ml of magnesium sulphate
 - E. 300 mg of amiodarone
- 32.** A 66-year-old woman is admitted for fixation of a left hip fracture. She has a history of osteoporosis and hypertension, but is otherwise in good health. She has no history of chest pain, but she says she experiences dyspnoea after walking about 400 m. She has a 30 pack-year smoking history but stopped 5 years ago. She is currently taking an angiotensin converting-enzyme inhibitor for her hypertension. What is the next most appropriate step in her assessment?
- A. Transthoracic echocardiography
 - B. Dobutamine stress echocardiography
 - C. Coronary angiography
 - D. No further cardiac investigation
 - E. Cardiac magnetic resonance imaging
- 33.** Which one of the following is the modality of choice for diagnosing and monitoring transplant coronary artery disease after orthotopic heart transplantation?
- A. Clinical history
 - B. Coronary angiography
 - C. Exercise electrocardiography (ECG)
 - D. Myocardial contrast echocardiography
 - E. Intravascular ultrasound
- 34.** A 53-year-old woman presents with dyspnoea and ankle oedema for 1 month. Her blood pressure is 110/80 mmHg. On examination, her jugular venous pressure rises with inspiration. She has a soft systolic murmur and a third heart sound. Electrocardiography (ECG) shows poor R-wave progression. An echocardiogram shows no pericardial effusion, increased ratio of early diastolic filling-to-atrial filling and systolic function is mildly impaired. Which one of the following is the most likely diagnosis?
- A. Restrictive cardiomyopathy
 - B. Dilated cardiomyopathy
 - C. Constrictive pericarditis
 - D. Ischaemic cardiomyopathy
 - E. Pulmonary embolus
- 35.** A patient with acute fulminant myocarditis is most likely to present with:
- A. Dyspnoea
 - B. Palpitations
 - C. Hypotension
 - D. Fever
 - E. Chest pain

36. A 63-year-old woman is worried because her elder sister has just had a disabling stroke. Her blood pressure is 148/94 mmHg and her BMI is 30 kg/m². She wishes to reduce her blood pressure by non-pharmacological means. You should recommend which one of the following evidence-based measures?

- A. Weight reduction and a sodium intake of 5 g/day
- B. A diet reduced in sodium intake to less than 1 g/day
- C. Insist on starting an antihypertensive medication
- D. A diet reduced in potassium and sodium intake
- E. Weight reduction and the Dietary Approaches to Stop Hypertension (DASH) diet

Theme: Congenital heart disease (for Questions 37–40)

- A. Ostium secundum atrial septal defect
- B. Ventricular septal defect
- C. Patent ductus arteriosus
- D. Eisenmenger syndrome
- E. Tetralogy of Fallot
- F. Pulmonary stenosis
- G. Bicuspid aortic valve
- H. Coarctation of the aorta

For each of the following patients, select the most likely diagnosis.

37. A 32-year-old man presents to a hospital with fatigue and fever of 2 weeks' duration. He has no chest pain, dyspnoea or orthopnoea. He is known to have a 'heart murmur' since birth. On physical examination the only abnormal findings are a temperature of 38.3°C; a harsh systolic murmur is heard in the left lower sternal border; and the presence of small tender nodules are noted on two fingers. Which cardiac anomaly is most consistent with this patient's clinical presentation?

38. A 21-year-old woman is being evaluated for exertional dyspnoea. She has been having these symptoms for the past 4 months. Her medical history includes one episode of atrial fibrillation 1 month ago. Her physical examination shows fixed splitting of the second heart sound and a systolic murmur in the pulmonic area. An electrocardiogram shows slight right axis deviation and incomplete right bundle-branch block. A chest X-ray reveals an enlarged right atrium and main pulmonary artery. Which cardiac anomaly is the most likely diagnosis for this patient?

39. An 18-year-old man is being evaluated for a murmur and hypertension. He is asymptomatic. On physical examination his blood pressure is 170/100 mmHg in the right arm. The femoral pulses are diminished in amplitude compared to the radial pulses. His cardiac examination reveals a short mid-systolic murmur in the left infrascapular area. Which cardiac anomaly is the most likely diagnosis for this patient?

40. A 19-year-old woman presents with breathlessness on exertion and mild fatigue. She has no significant medical history. She does not smoke and is not on regular medication. Her cardiac examination reveals a systolic murmur at the second left intercostal space, which increases with inspiration. What is the most likely diagnosis for this patient?

Answers

BASIC SCIENCE

1. Answer D

The beneficial effects of beta-blockers in stable angina are secondary to reduction in myocardial oxygen demand. Myocardial oxygen demand varies directly according to the heart rate, contractility and left ventricular wall stress, each of which is decreased by beta-blockers.

Catecholamine activation of the beta-1 receptors, which are primarily found in the heart muscle, leads to increased heart rate, contractility and atrioventricular (AV) conduction, with a decrease in AV node refractoriness. Beta-blockers act by competitively inhibiting catecholamines from binding to these receptors.

No randomised trials have studied the effect of beta-blockers on survival in patients with angina, but survival benefits have been seen in patients with systolic heart failure and following myocardial infarction.

In the treatment of patients with angina, titrating the dose of beta-blocker to achieve a target resting heart rate of 55–60 beats/min is recommended. Adverse side effects can include bradycardia, AV node conduction problems, reduced contractility, bronchoconstriction (notably in patients who are taking a beta-2 adrenergic agonist), worsening of peripheral vascular disease, Raynaud phenomenon, fatigue, nightmares and erectile dysfunction.

2. Answer D

Compensatory mechanisms that are activated in heart failure include:

- Increased ventricular preload with ventricular dilatation and volume expansion
- Peripheral vasoconstriction, which initially maintains perfusion to vital organs
- Myocardial hypertrophy to preserve wall stress as the heart dilates
- Renal sodium and water retention to enhance ventricular preload
- Activation of the adrenergic nervous system, which increases heart rate and contractile function.

These processes are controlled mainly by activation of neurohormonal vasoconstrictor systems, including the renin–angiotensin–aldosterone system, the adrenergic nervous system, and non-osmotic release of arginine–vasopressin. These and other mechanisms contribute to the symptoms, signs and poor natural history of heart failure. In particular, an increase in wall stress along with neurohormonal activation facilitates pathological ventricular remodelling; this process has been closely linked to heart failure disease progression. Management of chronic heart failure targets these mechanisms and, in some instances, results in reverse remodelling of the failing heart (Krum and Abraham, 2009).



Krum, H. and Abraham, W.T. (2009). Heart failure. *Lancet* 373, 941–955.
<http://www.ncbi.nlm.nih.gov/pubmed/19286093>

3. Answer E

Ventricular tachycardia without structural heart disease is often referred to as idiopathic ventricular tachycardia (John et al., 2012). Idiopathic ventricular tachycardia in the absence of structural heart disease most often originates from the right ventricular outflow tract. Diseases such as arrhythmogenic right ventricular cardiomyopathy and sarcoidosis often need to be excluded before a diagnosis is made. Idiopathic ventricular tachycardia must be distinguished from ventricular tachycardia with structural heart disease, because the latter often warrants an implantable cardioverter defibrillator (ICD). Detection of ventricular scar on cardiac imaging can be helpful. Although idiopathic monomorphic ventricular tachycardia can cause syncope, sudden death is rare. Beta-blockers, calcium-channel blockers or catheter ablation are often effective.

Catheter ablation is a reasonable first-line therapy for many patients with symptomatic idiopathic ventricular tachycardias. Success rates approach 80–90% in experienced centres. Success rates are lower for those tachycardias arising in less common locations, such as along the aortic annulus, within the aortic sinuses, within the great cardiac vein or from the epicardium. Failure of ablation is usually due to the inability to induce the arrhythmia for precise localisation, or ventricular tachycardia origin in a location that is inaccessible or in close proximity to a coronary artery, which precludes safe ablation.



John, R.M., Tedrow, U.B., Koplan, B.A., et al. (2012). Ventricular arrhythmias and sudden cardiac death. *Lancet* 380, 1520–1529.
<http://www.ncbi.nlm.nih.gov/pubmed/23101719>

4. Answer A

Myocarditis is most commonly caused by a viral infection in developed countries (Magnani and Dec, 2006). Enteroviruses, including the Coxsackie virus, are the most commonly associated viral species. The Coxsackie virus has a myocardial affinity because of its easy entrance into the myocardial cell through the Coxsackie–adenoviral receptor, which triggers the host immune response.

Cytomegalovirus is commonly associated with post-transplantation myocarditis. Influenza myocarditis is often associated with haemorrhagic pulmonary oedema. HIV has been reported to cause myocarditis. However, it may be difficult to determine the exact cause of cardiac dysfunction because symptoms may be due to the inflammatory response to HIV; the HIV infection itself; or coexisting opportunistic infections, side effects of anti-retroviral treatment, or a combination of these causes.

Hepatitis C, adenovirus, parvovirus B19 and Epstein–Barr virus (EBV) have been reported to cause myocarditis.



Magnani, J.W., and Dec, G.W. (2006). Myocarditis: current trends in diagnosis and treatment. *Circulation* 113, 876–890.
<http://circ.ahajournals.org/content/113/6/876.long>

5. Answer B

Electrical propagation of the cardiac impulse is transmitted from the sino-atrial node to the anterior, middle, and posterior internodal tracts, to the AV node and to the bundle of His (AV bundle), and then via the right and left bundle branches to the Purkinje fibres and thence to the myocardium.

Myocytes have a negative membrane potential when at rest. Stimulation induces the opening of voltage-gated ion channels, leading to flow of cations into the cell. The positively charged ions enter the cell, causing the depolarisation characteristic of an action potential. The action potential spreads through the muscle network of T-tubules, depolarising the inner portion of the muscle fibre. The depolarisation activates L-type voltage-dependent calcium channels (dihydropyridine receptors) in the T-tubule membrane, which are in close proximity to calcium-release channels (ryanodine receptors) in the adjacent sarcoplasmic reticulum. Activated voltage-gated calcium channels physically interact with calcium-release channels to activate them, causing the sarcoplasmic reticulum to release calcium. Calcium release is the main trigger of muscle contraction by causing alterations in the binding of troponin and tropomyosin to actin and leading to the ATP-driven myosin–actin bonding, sliding and releasing interactions that generates contraction. Repolarisation occurs due to a flow of potassium out of the cardiac cells.

In an electrocardiogram the P wave corresponds to the depolarisation of the atria; the QRS complex to right and left ventricular depolarisation; the ST-T wave to ventricular repolarisation; the PR interval is the time from onset of atrial depolarisation (P wave) to onset of ventricular depolarisation (QRS complex); the QRS duration is duration of ventricular muscle depolarisation; and the QT interval is the duration of ventricular depolarisation and repolarisation.

During diastole the pressure within the left ventricle is lower than that in aorta, allowing blood to circulate into the heart itself through the epicardial coronary arteries.

6. Answer B

Perhexiline has been used in the treatment of congestive heart failure and refractory angina. It relieves symptoms of angina, improves exercise tolerance and increases workload needed to induce ischemia. The drug works in part by modifying myocardial substrate utilisation from fatty acids to carbohydrates, which is energetically more efficient for the heart to metabolise, thus reducing myocardial oxygen consumption. Study has demonstrated the effectiveness of perhexiline in relieving symptoms, but there is no evidence that it provides mortality benefit (Phan et al., 2009).

Its major side effects include hepatotoxicity, peripheral neuropathy and hypoglycaemia. To prevent these toxicities, perhexiline plasma levels should be closely monitored and maintained between 0.15 and 0.60 mg/L. Perhexiline is metabolised by cytochrome P450 2D6. Drug level monitoring is essential to identify patients who are slow metabolisers, which occurs in about 7–10% of Caucasians who harbour mutations in *CYP2D6*. In normal metabolisers, perhexiline's half-life

is between 3 and 12 days. In slow metabolisers this half-life can be as long as 30 days. The usual loading dose is 200 mg twice a day for 3 days, then 100 mg/day. Blood is taken 3 days after commencing the drug to determine metaboliser status. If there is no metabolite peak, then the patient is a slow metaboliser, and the dose should be reduced to 100 mg weekly. If the metabolite is present, dose is continued at 100 mg daily. Plasma perhexiline trough concentrations should be monitored monthly until stable, then 3–6 monthly.



Phan, T.T., Shivu, G.N., Choudhury, A., et al. (2009). Multi-centre experience on the use of perhexiline in chronic heart failure and refractory angina: old drug, new hope. *Eur J Heart Failure* 11, 881–886.
<http://eurjhf.oxfordjournals.org/content/11/9/881.long>

7. Answer H

8. Answer C

Commentary for Questions 7 and 8:

Beta-adrenoreceptor blocking agents, commonly known as beta-blockers, are useful in the treatment of angina, myocardial infarction, cardiac failure, hypertension and cardiac arrhythmias. Beta-blockers given long-term have been shown to diminish mortality following acute myocardial infarction.

Some beta-blockers possess beta-agonist activity. Agents with partial agonist activity include pindolol, which causes little or no depression of resting heart rate (partial agonist effect) while blocking the increase in heart rate that occurs in response to exercise or the administration of a beta-agonist such as isoproterenol. The presence of partial agonist activity may be useful when bradycardia limits treatment in patients with slow resting heart rates. Pindolol also produces mild vasodilation. Agents with partial agonist activity cause less change in blood lipid levels than agents without agonist properties.

Non-selective beta-blockers, such as propranolol, sotalol, timolol and carvedilol, induce competitive blockade of both β_1 and β_2 receptors. Metoprolol and atenolol possess relative selectivity for the β_1 receptor. Although β_1 (cardiac)-selective agents have the theoretical advantage of producing less bronchoconstriction and less peripheral vasoconstriction, a clear clinical advantage of cardioselective agents is unestablished. Bronchoconstriction may occur when β_1 -selective agents are administered in therapeutic doses.

Various beta-blockers differ in their water and lipid solubility. The lipophilic agents (e.g. propranolol, metoprolol, bisoprolol and carvedilol) are readily absorbed from the gastrointestinal tract, metabolised by the liver, have large volumes of distribution and penetrate the central nervous system well. The hydrophilic agents (e.g. atenolol) are less readily absorbed, not extensively metabolised and have relatively longer plasma half-lives, resulting in their ability to be administered once per day. Hepatic impairment may prolong the plasma half-life of lipophilic agents whereas renal impairment may prolong the action of hydrophilic agents. Nebivolol is a β_1 -receptor blocker with a nitric-oxide potentiating vasodilatory effect.

Carvedilol has both α_1 -adrenoreceptor blockade and non-selective beta-blockade actions and is devoid of intrinsic sympathomimetic activity (Frishman, 1998). Carvedilol is indicated to slow the clinical progression of heart failure, as evidenced by reductions in hospitalisation rates and mortality. Contraindications to carvedilol therapy in patients with heart failure include severe decompensation requiring inotropic therapy, marked bradycardia, the sick sinus syndrome, and partial or complete atrioventricular block, unless a permanent pacemaker is in place.



Frishman, W.H. (1998). Carvedilol. *N Engl J Med* 339, 1759–1765.
<http://www.ncbi.nlm.nih.gov/pubmed/10328713>

CLINICAL

9. Answer B

The clinical diagnosis of acute pericarditis rests primarily on the findings of chest pain, pericardial friction rub and ECG changes (Imazio et al., 2010). The chest pain of acute pericarditis typically develops suddenly and is severe and constant over the anterior chest. In acute pericarditis, the pain worsens with inspiration – a response that helps to distinguish acute pericarditis from myocardial infarction. Low-grade fever and sinus tachycardia are often present. A pericardial friction rub can be detected in most patients when symptoms are acute. ECG changes are common in most patients with acute pericarditis, particularly in those with an infectious aetiology in which the associated inflammation in the superficial layer of myocardium is prominent. The characteristic change is an elevation in the ST segment in multiple leads. The diffuse distribution and the absence of reciprocal ST segment depression distinguish the characteristic pattern of acute pericarditis from acute myocardial infarction. Depression of the PR segment, which reflects superficial injury of the atrial myocardium, is as frequent and specific as ST segment elevation and is often the earliest ECG manifestation. Analgesic agents or non-steroidal anti-inflammatory drugs (NSAIDs) are often effective in reducing pericardial inflammation. Corticosteroids should be reserved for severe cases that are unresponsive to other therapy, because symptoms may recur after steroid withdrawal.



Imazio, M., Spodick, D.H., Brucato, A., Trincheri, R., and Adler, Y. (2010). Controversial issues in the management of pericardial diseases. *Circulation* 121, 916–928.
<http://circ.ahajournals.org/content/121/7/916.long>

10. Answer C

Acute rheumatic fever (ARF) remains common in the developing world. Indigenous populations in northern Australia have among the highest burden of ARF and rheumatic heart disease in the world, with one in 300 children developing ARF each year and up to 2% of people of all ages having rheumatic heart disease. Similar rates are seen throughout the Western Pacific region, including in Maori and Pacific Islander populations in New Zealand, where some of the most reliable data are available.

Oral penicillin V is the drug of choice in treating streptococcal pharyngitis; twice-daily dosing is as effective as four times a day dosing and may improve compliance. Group A streptococci (GAS) are isolated from throat swabs in less than 10% of ARF cases in New Zealand, and less than 5% of cases in Australian Aboriginal people. Streptococcal antibody titres are therefore crucial in confirming the diagnosis. The most commonly-used tests are the plasma anti-streptolysin O (ASO) and the anti-DNase B titres. Previous data suggest that a rise in the ASO titre occurs in 75–80% of untreated Group A streptococci pharyngeal infections, and that the addition of anti-DNase B titre increases the sensitivity of testing.

Treatment should be started within 9 days of the onset of symptoms to prevent rheumatic fever. Aspirin is recommended as the first-line treatment for arthritis or arthralgia in ARF. Sydenham chorea is self-limiting. Most cases will resolve within weeks and almost all cases within 6 months, although rare cases may last as long as 2–3 years. Because chorea is benign and self-limiting, and anti-chorea medications are potentially toxic, treatment should only be considered if the movements interfere substantially with normal activities. Aspirin does not have a significant effect on rheumatic chorea. Group A streptococci are responsible for only 5% of cases of pharyngitis in adults. Screening asymptomatic family contacts is controversial and probably unnecessary.



RHDAustralia (ARF/RHD writing group), National Heart Foundation of Australia and the Cardiac Society of Australia and New Zealand (2012). *Australian Guideline for Prevention, Diagnosis and Management of Acute Rheumatic Fever and Rheumatic Heart Disease*, 2nd edn. National Heart Foundation of Australia. http://www.rhdaustralia.org.au/sites/default/files/guideline_0.pdf

11. Answer B

The sudden onset of chest pain radiating to the interscapular area and signs of shock suggest a diagnosis of acute aortic dissection, especially in those with risk factors such as hypertension, dyslipidaemia and peripheral vascular disease (Golledge and Eagle, 2008). Computed tomography (CT) angiography or echocardiography is usually needed in patients in whom acute aortic dissection is clinically suspected on the basis of presentation and initial investigations. A systematic review of the diagnostic accuracy of transoesophageal echocardiography, CT angiography and MRI reported a mean sensitivity and specificity of more than 95% for all three investigations. In addition to assisting in the diagnosis of aortic dissection, the results of imaging can help to plan management. Important findings include the extent of the dissection, the size of the true and false lumen, localisation of the intimal tear, the involvement of aortic branches, the presence and extent of aortic regurgitation, and the presence of periaortic haematoma, mediastinal haematoma, or effusion. Guidelines recommend the use of echocardiography or CT angiography, or both, in the initial imaging of patients suspected to have acute aortic dissection, whereas MRI is favoured for the assessment of chronic dissection. Contrast angiography is recommended in patients in whom visceral hypoperfusion is suspected or percutaneous interventions are being considered.

Patients can present with aortic dissection either in the ascending aorta (type A) or in the more distal aorta (type B). The risk factors most probably relate to a combination of inherited and acquired weakening of the aortic media and intimal disease. Marfan syndrome is an important risk factor for aortic dissection, especially in young patients. Other inherited disorders, including Ehlers–Danlos syndrome type IV and Turner syndrome, have been associated with aortic dissection.



Golledge, J. and Eagle, K.A. (2008). Acute aortic dissection. *Lancet* 372, 55–66. <http://www.ncbi.nlm.nih.gov/pubmed/18603160>

12. Answer D

Brain natriuretic peptide (BNP) levels reflect the severity of congestive heart failure (CHF), the risk of hospitalisation and survival. Changes in BNP level in response to medical therapy also predict survival.

Plasma BNP or N-terminal pro-BNP measurement may be helpful in patients presenting with recent-onset dyspnoea; it has been shown to improve diagnostic accuracy with a high negative predictive value. BNP measurement has been demonstrated to be useful for differentiating dyspnoea caused by CHF from dyspnoea due to other causes, especially in the Emergency Department. A cut-off value of 100 pg/mL has a sensitivity of 90% and a specificity of 76%. However, routine use of BNP in the diagnosis of CHF is not recommended. There is no evidence that BNP provides additional diagnostic information to that provided by echocardiogram.

BNP levels appear more useful in detecting systolic heart failure than diastolic heart failure. BNP levels do not discriminate well between elderly female patients with diastolic heart failure (the most common patient group with this condition) and healthy age-matched controls.



National Heart Foundation of Australia and the Cardiac Society of Australia and New Zealand (Chronic Heart Failure Guidelines Expert Writing Panel) (2011). *Guidelines for the Prevention, Detection and Management of Chronic Heart Failure in Australia Update 2011*.

National Heart Foundation of Australia.

http://www.heartfoundation.org.au/sitecollectiondocuments/chronic_heart_failure_guidelines_2011.pdf

13. Answer A

Cardiomyopathy and heart failure are well recognised complications of prolonged anthracycline treatment (Yeh and Bickford, 2009). Anthracycline cardiotoxicity can be divided into acute/sub-acute or late/chronic, with the latter being more common. In adults, chronic anthracycline-related cardiotoxicity typically presents within 1 year after finishing chemotherapy, with the peak time for the appearance of symptoms being about 3 months after the last dose. Late cardiotoxicity is characteristically seen in survivors of childhood malignancy treated with an anthracycline.

A number of risk factors for the development of chronic anthracycline cardiotoxicity have been identified. The strongest predictor is cumulative dose. Studies that have looked at the cumulative probability of doxorubicin-induced heart failure have found that it occurs in 3–5% at 400 mg/m², 7–26% at 550 mg/m² and 18–48% at 700 mg/m². However, intravenous administration, concomitant administration of other cardiotoxic chemotherapeutic agents (particularly paclitaxel, cyclophosphamide and trastuzumab), concurrent or prior chest irradiation, pre-existing cardiovascular disease or risk (including coronary artery disease, hypertension and diabetes mellitus) are also major risk factors.

Dexrazoxane is an EDTA-like chelator that significantly reduces the risk of chronic cardiotoxicity when used with anthracyclines. Dexrazoxane given with either doxorubicin or epirubicin significantly reduced the incidence of clinical

and subclinical cardiotoxicity. It is recommended in patients who are being treated for metastatic disease and are receiving high cumulative doses of anthracyclines.

All patients should have a baseline echocardiogram and serial monitoring of myocardial function during therapy with anthracyclines. Although chest radiotherapy in the past was associated with significant cardiotoxicity, contemporary techniques with minimal exposure to the heart has lessened this complication.



Yeh, E.T. and Bickford, C.L. (2009). Cardiovascular complications of cancer therapy: incidence, pathogenesis, diagnosis, and management. *J Am Coll Cardiol* 53, 2231–2247.
<http://www.ncbi.nlm.nih.gov/pubmed/19520246>

14. Answer B

Pharmacological treatment of systolic heart failure consists of symptom relief with diuretics and disease modification is achieved with ACE inhibitors or angiotensin receptor blockers (ARBs), beta-blockers, spironolactone or a combination of hydralazine and isosorbide dinitrate (McMurray, 2010).

ACE inhibitors are the first-line therapy for patients with systolic heart failure; therapy should be initiated promptly and continued indefinitely. ACE inhibitors reduce ventricular size, increase the ejection fraction modestly and reduce symptoms.

The efficacy of ARBs is similar to ACE inhibitors but they are usually reserved for those who develop cough or other adverse effects with ACE inhibitors (on account of their higher cost). ARBs are sometimes prescribed for those who are symptomatic despite treatment with optimal doses of ACE inhibitors and beta-blockers.

Beta-blockers are essential first-line therapy in patients with heart failure and left ventricular systolic dysfunction. Treatment with beta-blockers improves systolic function, resulting in an increase in ejection fraction of 5–10%, and reduces symptoms. Bisoprolol, carvedilol or metoprolol CR/XL (metoprolol succinate, controlled release or extended release) can reduce the rate of hospital admissions and mortality by up to 34%.

Spironolactone is indicated in severe heart failure, that is NYHA class III or IV despite treatment with a diuretic, an ACE inhibitor (or ARB) and a beta-blocker. Digoxin when added to a diuretic and ACE inhibitor has no effect on mortality but may reduce risk of hospitalisation for heart failure.

Diuretic treatments with loop diuretics should be prescribed to minimise fluid retention and pulmonary oedema.

It is always important to also consider the underlying aetiology of the heart failure, correct this accordingly and address the possible need for anti-platelet agents, rhythm correction, implantable defibrillators, cardiac resynchronisation, coronary bypass surgery and lipid treatment. The presence of other problems such as renal insufficiency, thyroid disease and anaemia should be considered.



McMurray, J.J. (2010). Clinical practice. Systolic heart failure. *N Engl J Med* 362, 228–238.
<http://www.ncbi.nlm.nih.gov/pubmed/20089973>

15. Answer D

Coronary artery bypass graft (CABG) is recommended in patients with any of the following criteria: significant left main coronary artery disease, three-vessel disease [in patients with three-vessel disease, those with left ventricular ejection fraction (LVEF) <50% have the greatest survival benefit] and two-vessel disease with significant left anterior descending coronary artery involvement or abnormal LV function (i.e. LVEF <50%) (Pfisterer et al., 2010). In patients with three-vessel disease and abnormal LVEF, the survival benefit and symptom relief of CABG are superior to those of percutaneous transluminal angioplasty (PCTA) or medical therapy. In transmyocardial revascularisation procedure (TMR), a laser is used to create channels in the myocardium to relieve angina. This procedure has been shown to improve severe refractory angina in patients who could not be treated with conventional revascularisation techniques (PCTA or CABG). For the patient described here, CABG is the preferred procedure.



Pfisterer, M.E., Zellweger, M.J., and Gersh, B.J. (2010). Management of stable coronary artery disease. *Lancet* 375, 763–772.
<http://www.ncbi.nlm.nih.gov/pubmed/20189028>

16. Answer E

Computed tomography coronary angiography (CTCA) is a new imaging test that has been shown in meta-analyses to have excellent sensitivity (98%) and good specificity (88%) for significant coronary artery disease (stenosis >50%). Its high negative predictive value (96–100%) indicates that CTCA is an excellent test for ruling out significant disease in patients with low-to-intermediate pretest probability of coronary artery disease. Current data do not support the use of CTCA in asymptomatic patients. CTCA is not routinely recommended in patients with previous coronary stents since stents are likely to cause artefacts and make the results difficult to interpret. In patients who are likely to require invasive coronary angiograms, such as a patient with ST-elevation myocardial infarction, it is more appropriate to proceed with percutaneous coronary intervention without delay.

To avoid artefacts that may hamper interpretation of the results, the patient should be in sinus rhythm with a heart rate of less than 65 beats/min, able to hold his/her breath for 10s, able to tolerate beta-blockers and nitrates (nitrates are given to dilate the coronary arteries by most centres) and able to hold his/her arms above the head during the scan. Previous contrast allergy and renal impairment should be ruled out prior to CTCA.



Liew, G., Feneley, M., and Worthley, S. (2012). Appropriate indications for computed tomography coronary angiography. *Med J Aust* 196, 246–249. <https://www.mja.com.au/journal/2012/196/4/appropriate-indications-computed-tomography-coronary-angiography>

17. Answer B

Dabigatran is 80% renally cleared (Hankey and Eikelboom, 2011). Therefore, care must be taken when used in patients with impaired renal function. Reduced kidney function in an elderly patient with diabetes is the most likely explanation for the bleeding complication in the patient described. In addition, bleeding rates with dabigatran increase with advanced age. The combination of aspirin and dabigatran is associated with higher bleeding rates.

At present there are no available laboratory tests that have been validated for monitoring of dabigatran. The thrombin clotting time can be used to inform if dabigatran activity is present, but it does not reveal the extent of anti-coagulation. Unlike warfarin, one of the major drawbacks of dabigatran is the lack of an effective antidote for use in the event of a severe bleeding event.

Dabigatran is given as the prodrug dabigatran etexilate, and this prodrug is a substrate for efflux by the p-glycoprotein transporter. Inhibitors of p-glycoprotein, such as ketoconazole (most azoles), protease inhibitors, macrolides, calcineurin inhibitors, amiodarone and verapamil, can increase dabigatran plasma concentrations by decreasing the efflux of the drug into the gastrointestinal lumen. Strong inducers of p-glycoprotein, such as rifampicin, carbamazepine and phenytoin, can reduce plasma concentrations and co-administration should be avoided. No significant interaction was seen with digoxin, also a p-glycoprotein substrate.



Hankey, G.J. and Eikelboom, J.W. (2011). Dabigatran etexilate: a new oral thrombin inhibitor. *Circulation* 123, 1436–1450. <http://circ.ahajournals.org/content/123/13/1436.long>

18. Answer E

The ECGs show:

- A. Bifascicular block
- B. First-degree heart block
- C. Left bundle branch block
- D. Mobitz type I (Wenkebach) heart block
- E. Mobitz type II 2:1 heart block

Temporary transvenous pacing is necessary for patients with severe and symptomatic bradyarrhythmias, but should also be considered for those at high risk of developing complete heart block as a consequence of acute myocardial infarction (AMI). High (second or third)-degree AV block is associated with an increase in mortality in patients with an inferior or anterior AMI (Vardas et al., 2007).

Following an AMI, temporary transvenous pacing should be considered if there is:

- Complete (third-degree) heart block
- New or age-indeterminate bifascicular block (RBBB with LAFB or LPFB or LBBB) with PR prolongation
- Symptomatic bradycardia of any aetiology if hypotension is present and the bradyarrhythmia is not responsive to atropine
- Mobitz type II second-degree AV block
- Bradycardia-induced tachyarrhythmias.

Despite reperfusion treatment, the incidence of intraventricular conduction disturbances post acute myocardial infarction (AMI) has not changed, whereas the incidence of AV block post AMI has decreased but still remains high. AV block occurs in almost 7% of cases of AMI.



Vardas, P.E., Auricchio, A., Blanc, J.J., et al. (2007). Guidelines for cardiac pacing and cardiac resynchronization therapy: The Task Force for Cardiac Pacing and Cardiac Resynchronization Therapy of the European Society of Cardiology. Developed in collaboration with the European Heart Rhythm Association. *Eur Heart J* 28, 2256–2295.
<http://eurheartj.oxfordjournals.org/content/28/18/2256.long>

19. Answer D

Eisenmenger syndrome is pulmonary hypertension due to a left-to-right shunt caused by congenital heart defects such as a ventricular septal defect or a patent ductus arteriosus. Whilst rare in pregnancy (estimated incidence: 1.1 per 100 000 pregnancies), it has been associated with a high maternal mortality, estimated to be between 30% and 56% (Regitz-Zagrosek et al., 2011). Risk for fetal death and premature delivery is also very high. Maternal death occurs in the last trimester of pregnancy and in the first months after delivery because of pulmonary hypertensive crises, pulmonary thrombosis or refractory right heart failure. This occurs even in patients with little or no disability before or during pregnancy. Guidelines from the European Society of Cardiology (ESC) and the American College of Cardiology/American Heart Association (ACC/AHA) strongly discourage pregnancy and suggest consideration of termination should a pregnancy occur.

The importance of early counselling about pregnancy risks and contraception is strongly emphasised. For those who choose to continue pregnancy, obstetric care should be undertaken at a specialist centre, with access to intensive care. Even after successful delivery, maternal risk continues beyond the time of birth; therefore, close monitoring must be maintained in the postpartum period.



Regitz-Zagrosek, V., Blomstrom Lundqvist, C., Borghi, C., et al. (2011). ESC Guidelines on the management of cardiovascular diseases during pregnancy: the Task Force on the Management of Cardiovascular Diseases during Pregnancy of the European Society of Cardiology (ESC). *Eur Heart J* 32: 3147–3197.
<http://eurheartj.oxfordjournals.org/content/32/24/3147.full>

20. Answer E

While it has been recognised for many decades that some patients with hypertrophic cardiomyopathy die suddenly from ventricular arrhythmia, data from contemporary studies suggest that the overall risk is relatively small, with annual

sudden cardiac death (SCD) rates of 1% or less in most series. The challenge for clinicians is to identify the small cohort of patients who are at risk in order to target potentially life-saving therapy with implantable cardioverter defibrillators (ICDs).

Predicting the risk of sudden cardiac death in a patient with hypertrophic cardiomyopathy is notoriously difficult, but a left ventricular wall thickness of greater than 3 cm is associated with a significantly increased risk (Christiaans et al., 2010). One study put the 20-year risk of sudden cardiac death at almost 40% for this population, even in the absence of symptoms such as angina or syncope. The use of the six major risk factors (previous cardiac arrest or sustained ventricular tachycardia, non-sustained ventricular tachycardia, extreme left ventricular hypertrophy, unexplained syncope, abnormal blood pressure response to exercise, and family history of sudden death) in risk stratification for SCD is recommended by international guidelines.



Christiaans, I., van Engelen, K., van Langen, I.M., et al. (2010). Risk stratification for sudden cardiac death in hypertrophic cardiomyopathy: systematic review of clinical risk markers. *Europace* 12, 313–321.
<http://europace.oxfordjournals.org/content/12/3/313.long>

21. Answer A

Staphylococcus aureus is the commonest cause of prosthetic valve endocarditis, followed by coagulase-negative staphylococcus (Wang et al., 2007). Prosthetic valve endocarditis accounts for a significant (20%) and increasing proportion of infective endocarditis cases; this is likely to increase in future years with increasing longevity and prosthetic valve insertion. The causative organisms vary with time since implantation. The most frequently encountered pathogens within 2 months of implantation are *S. aureus* (36%) and coagulase-negative staphylococci (17%); next in frequency are culture-negative (17%) and fungal infections (9%). After 2 months the pathogens involved are coagulase-negative staphylococci and *S. aureus* (18–20% each); next in frequency are no organism identified, enterococci and viridans streptococci (10–13% each).

The majority of infections occur in the first year after valve implantation, there is a strong association with in-hospital care and intravascular devices, and mortality exceeds 20%. Unfavourable features predicting mortality are older age, *S. aureus* infection and complications, including heart failure, stroke, intracardiac abscess and persistent bacteraemia.



Wang, A., Athan, E., Pappas, P.A., et al. (2007). Contemporary clinical profile and outcome of prosthetic valve endocarditis. *JAMA* 297, 1354–1361.
<http://jama.jamanetwork.com/article.aspx?articleid=206241>

22. Answer A

The electrocardiography showing torsades de pointes combined with the family history suggests that the patient has congenital long-QT syndrome (LQT) and the mainstay of therapy for this condition is beta-blockade (Roden, 2008).

A leading cause of sudden death in otherwise healthy young persons, LQT is characterised by abnormal QT-interval prolongation. The two common hereditary variants are Jervell and Lange-Nielsen syndrome and Romano-Ward syndrome, with the former being associated with sensorineural deafness. Based on genetic studies, there are three forms: LQT1 and LQT2 (due to mutations in potassium channels), and LQT3 (due to a sodium channel mutation), with LQT1 being the commonest. Syncope in patients with both the hereditary and acquired forms of LQT is generally attributed to a form of polymorphic ventricular tachycardia called torsades de pointes, which is characterised by twisting of the QRS complex around the isoelectric baseline.

An abnormal ECG obtained while the patient is at rest is the key to diagnosis and a detailed family history should be obtained. All persons with QT-interval prolongation should be screened for acquired causes such as hypocalcaemia, hypokalemia, hypomagnesaemia, hypothyroidism and the use of drugs that can prolong the QT interval; these drugs include anti-arrhythmic agents such as sotalol, quinidine and dofetilide, and non-cardiovascular drugs such as haloperidol, methadone, erythromycin, terfenadine and clarithromycin.

Treatment of LQT in those who have had a syncopal episode begins with a beta-blocker. If the patient has (1) syncope despite full-dose beta-blockade, (2) a successfully resuscitated cardiac arrest, or (3) a contraindication to beta-blockade and high risk of arrhythmia, a cardioverter-defibrillator should be implanted.



Roden, D.M. (2008). Clinical practice. Long-QT syndrome. *N Engl J Med* 358, 169–176.
<http://www.ncbi.nlm.nih.gov/pubmed/18184962>

23. Answer A

The indication for PBMV is progressive exertional dyspnoea (New York Heart Association functional class II, III or IV), associated with documented evidence of moderate or severe mitral stenosis (MS) (mitral orifice area <1.5 cm) (Nobuyoshi et al., 2009). There should be no or only mild associated mitral regurgitation. Asymptomatic patients usually do not need intervention, unless there is a history of thromboembolism, paroxysmal AF or significant pulmonary hypertension (pulmonary artery systolic pressure >50 mmHg). Patients with pliable, mobile, relatively thin valves, with no or minimal calcification, and without significant thickening and fusion of the subvalvular apparatus, are the best candidates. These comprise the majority of symptomatic younger patients. However, experienced operators can obtain acceptable results in older patients with less favourable anatomy.

Patients with pure or dominant MS requiring intervention should be referred for PBMV to a high volume centre with documented low complication rates, regardless of the anatomy of their mitral valve. Early referral is recommended for younger patients, as they have the most favourable valve morphology and the best long-term results.

A large left atrial thrombus is a contraindication to PBMV. However, it can often be performed safely in the presence of a small, stable thrombus in the left atrial

appendage. PBMV is well suited to managing MS in pregnancy, where the risk of surgery and associated fetal loss is high.



Nobuyoshi, M., Arita, T., Shirai, S., et al. (2009). Percutaneous balloon mitral valvuloplasty: a review. *Circulation* 119, e211–219.
<http://circ.ahajournals.org/content/119/8/e211.long>

24. Answer C

Peri-infarction pericarditis usually occurs 1–2 days after an acute myocardial infarction (AMI). The presence of a pericardial friction rub is diagnostic. The incidence of peri-infarction pericarditis has decreased since the widespread use of reperfusion therapy. Peri-infarction pericarditis is associated with larger infarct size, more frequent anterior location of AMI, and lower ejection fraction. The ECG changes seen in other forms of pericarditis are usually overshadowed by the changes due to myocardial infarction.

Peri-infarction pericarditis is usually transient, unlike other viral or idiopathic pericarditis. Treatment with non-steroidal anti-inflammatory drugs is generally avoided because of the associated risks. The use of corticosteroids after AMI has been associated in some, but not all, studies with a greater incidence of ventricular aneurysm formation. Aspirin and anti-coagulation therapy is part of the standard management of AMI. There is great concern that these therapies may promote the development of haemorrhagic pericarditis. However, such concern has not been confirmed and the risk-to-benefit ratio favours the continuation of aspirin and anti-coagulation.

Post-myocardial infarction syndrome, which is also called Dressler syndrome, usually develops weeks to months after AMI. It usually presents with fever, pleuritic chest pain, and pericardial rub. Its pathogenesis involves myocardial injury that releases cardiac antigens and stimulates antibody formation. The immune complexes that are generated then deposit onto the pericardium and lead to an inflammatory response.

25. Answer C

The patient has a supraventricular tachycardia (Link, 2012). Vagal manoeuvres, including a Valsalva manoeuvre, carotid sinus massage, bearing down, and immersion of the face in ice water, can increase vagal tone and block the atrioventricular node and can be attempted. If these manoeuvres are unsuccessful, adenosine should be administered. Adenosine is a very short-acting endogenous nucleotide that blocks atrioventricular nodal conduction and terminates nearly all atrioventricular nodal re-entrant tachycardias and atrioventricular reciprocating tachycardias, as well the majority of atrial tachycardias. Since this drug can also excite atrial and ventricular tissue, rarely causing atrial fibrillation, transient heart block and non-sustained ventricular tachycardia, it should be administered with ECG monitoring and a defibrillator to hand. Adenosine should not be used in patients with asthma. Side effects include chest tightness, flushing and a sense of dread.

Although intravenous verapamil and diltiazem, which also block the atrioventricular node, can be of therapeutic use in narrow-complex tachycardias, they may cause hypotension and are longer lasting and thus are not a first choice in the emergency setting, particularly when blood pressure is already reduced. Electrical DC cardioversion is reserved for patients who are unstable or who do not respond to adenosine or other measures. Although the blood pressure of the patient is 98/68 mmHg, he is alert and has no signs of shock, so his condition is not considered unstable.



Link, M.S. (2012). Evaluation and initial treatment of supraventricular tachycardia. *N Engl J Med* 367, 1438–1448.
<http://www.ncbi.nlm.nih.gov/pubmed/23050527>

26. Answer D

This patient's electrocardiography, while in sinus rhythm 5 years ago, shows a classic pattern of pre-excitation – the Wolff–Parkinson–White (WPW) syndrome. He presents with symptomatic pre-excited atrial fibrillation (AF) with a rapid ventricular response, which now requires urgent treatment.

The goals of acute drug therapy for pre-excited AF are prompt control of the ventricular rate and stabilisation of the haemodynamic status. Treatment of pre-excited AF requires a parenteral drug with rapid onset of action that lengthens antegrade refractoriness and slows conduction in both the AV node/His–Purkinje system and the accessory pathway. The class IC anti-arrhythmic drugs, such as flecainide, are effective in this setting. Intravenous beta-blockers when used alone do not increase accessory pathway refractoriness. Furthermore, inhibition of AV node conduction may enhance the pre-excited ventricular rate response by decreasing the degree of concealed retrograde conduction into the accessory pathway. Intravenous digoxin is contraindicated because blockade of AV nodal conduction can lead to an unpredictable effect on accessory pathway refractoriness. Verapamil is the most dangerous AV nodal blocker to administer during pre-excited AF. Intravenous verapamil lengthens AV node refractoriness, decreases concealed conduction into the accessory pathway and has no direct effect on the accessory pathway. Myocardial contractility and systemic vascular resistance are also reduced; these effects may cause a reflex increase in already elevated sympathetic tone that further shortens accessory pathway refractoriness. Intravenous adenosine is also contraindicated because it causes an effect similar to verapamil and can precipitate ventricular fibrillation. Although not approved for acute therapy of AF, intravenous amiodarone may be effective for reverted AF in WPW or may slow the ventricular rate because of its effect on accessory pathway refractoriness and conduction (Fuster et al., 2006).



Fuster, V., Ryden, L.E., Cannom, D.S., et al. (2006). ACC/AHA/ESC 2006 guidelines for the management of patients with atrial fibrillation. *J Am Coll Cardiol* 48, 854–906.
<http://www.sciencedirect.com/science/article/pii/S073510970601816X>

27. Answer D

Streptococcus bovis, a non-enterococcal group D streptococcus, is a bacterium that is found among the normal flora of the human gastrointestinal tract in 5–16% of adults. In addition, *S. bovis* is commonly detected as a contaminant in packaged meat. If *S. bovis* enters the bloodstream, it can cause bacteraemia and endocarditis; approximately 12% of infective endocarditis is caused by *S. bovis*. Endocarditis caused by *S. bovis* is more common in men and in the elderly. In two studies, patients with endocarditis caused by *S. bovis* type I, recently reclassified as *Streptococcus gallolyticus*, had an increased risk of prevalent colorectal neoplasia. Nearly all patients with *S. bovis* endocarditis are older than 50 years, and there is an association with malignancy of the gastrointestinal tract. Many debate the temporality of this association. One view is that ulcerating colorectal carcinomas allow increased growth of *S. bovis*, invasion of the bloodstream and establishment of infection. Others argue that *S. bovis* is a direct cause of colon carcinogenesis. This patient's clinical picture is suggestive of endocarditis. He also has microcytic anemia and weight loss that may be related to colorectal cancer.



Burnett-Hartman, A.N., Newcomb, P.A., and Potter, J.D. (2008). Infectious agents and colorectal cancer: A review of *Helicobacter pylori*, *Streptococcus bovis*, JC virus, and human papillomavirus. *Cancer Epidemiol Biomarkers Prev* 17, 2970–2979.

<http://cebp.aacrjournals.org/content/17/11/2970.long>

28. Answer E

Most patients with heart failure have a low or normal cardiac output. High-output heart failure is characterised by an elevated resting cardiac index beyond the normal range of 2.5–4.0 L/min/m². Chronic volume overload and chronic activation of the sympathetic nervous and renin–angiotensin–aldosterone systems gradually cause ventricular enlargement, remodelling and heart failure.

Cardiac amyloidosis is usually dominated by right heart failure and is a cause of low-output heart failure. Hyperthyroidism can cause sympatho-adrenal activation and create a hyperdynamic circulatory state.

There are multiple arteriovenous fistulas in the bony lesions in patients with Paget disease. Extensive Paget disease (>20% of the skeleton) can cause an increase in cardiac output and lead to high-output heart failure.

In dialysis patients with an arteriovenous fistula, blood from a high-pressure artery is shunted to a low-pressure vein, which decreases systemic vascular resistance. A compensatory increase in the heart rate and stroke volume ensues.

In patients with severe cirrhosis, the increased cardiac output is due to splanchnic vasodilation and the development of intrahepatic or mesenteric arteriovenous shunts.

Other causes of high-output heart failure include:

- Severe anaemia
- Vitamin B₁ or thiamine deficiency (beriberi heart disease)
- Psoriasis
- Severe septicaemia

- Congenital fistulas
- Acromegaly
- Pregnancy
- Polycythemia vera.

High-output states can cause or contribute to heart failure, especially in patients with underlying cardiovascular disease. The treating clinician should consider the possibility of high-output cardiac failure in patients with physical signs that suggest an increase in cardiac output, such as warm extremities, wide pulse pressure and systolic flow murmur.



Mehta, P.A. and Dubrey, S.W. (2009). High output heart failure. *QJM* 102, 235–241.
<http://qjmed.oxfordjournals.org/content/102/4/235.long>

29. Answer B

The following features identify high-risk patients with infective endocarditis:

- Heart failure
- Stroke, abnormal mental status
- Recurrent embolic events
- Septic shock
- Fever persisting >7–10 days
- Large or enlarging vegetation
- Perivalvular extension of infection (abscess, pseudoaneurysm, fistula)
- New heart block
- Severe left-sided regurgitation, severe prosthetic dysfunction
- Signs of increased left-cavities' filling pressure, pulmonary hypertension
- Pathogens other than viridans streptococci, especially *Staphylococcus aureus*, fungi and Gram-negative bacilli
- Acute renal failure.



Thuny, F., Grisoli, D., Collart, F., Habib, G., and Raoult, D. (2012). Management of infective endocarditis: challenges and perspectives. *Lancet* 379, 965–975.
<http://www.ncbi.nlm.nih.gov/pubmed/22317840>

30. Answer C

Cholesterol embolisation syndrome refers to embolisation of the contents of an atherosclerotic plaque (primarily cholesterol crystals) from a proximal large-calibre artery to distal small-to-medium arteries, causing end-organ damage by mechanical plugging and an inflammatory response. Cholesterol embolisation syndrome is generally characterised by a multitude of small emboli (showers of microemboli) occurring over time. This is in contrast to arterio-arterial thromboembolism, which is usually characterised by an abrupt release of one or a few large emboli, leading to severe ischaemia of target organs.

Cholesterol embolisation syndrome has a variety of clinical presentations. Cholesterol emboli originating in the descending thoracic and abdominal aorta may lead to renal failure, bowel ischaemia and emboli to the skeletal muscles and skin. Dermatological manifestations (most commonly livedo reticularis and blue toe syndrome) are usually confined to the lower extremities

Cholesterol crystals trigger an inflammatory response after they lodge in the small arteries of the target organ. Constitutional signs and symptoms, such as fever, weight loss, anorexia, fatigue and myalgias, are frequent manifestations of the inflammatory response. Laboratory tests may also show an abnormality in inflammatory markers such as a rise in leucocyte count, erythrocyte sedimentation rate and C-reactive protein, or a decrease in serum complement levels (hypocomplementaemia). The patient may also develop anaemia or thrombocytopenia.

Hypereosinophilia has been reported in up to 80% of the patients with cholesterol embolisation syndrome. The duration and magnitude of hypereosinophilia in cholesterol embolisation syndrome are variable. Hypereosinophilia often occurs only during the first few days, and the proportion of eosinophils may vary from 6% to 18% of the total leucocyte count. The exact mechanism of hypereosinophilia in cholesterol embolisation syndrome is not known; it is believed that cholesterol embolisation syndrome is a form of cytokine-mediated eosinophilic disorder. One of the cytokines may be interleukin 5 derived from vascular endothelium. It is important to emphasise that hypereosinophilia is not pathognomonic for cholesterol embolisation syndrome because it may occur in a variety of other disorders, such as systemic vasculitides, acute interstitial nephritis and radiographic contrast-induced renal injury. Because none of the aforementioned clinical or laboratory findings is specific for cholesterol embolisation syndrome, a high degree of clinical suspicion is required in establishing the diagnosis, particularly if the patient has recently undergone a vascular procedure such as cardiac catheterisation.



Kronzon, I. and Saric, M. (2010). Cholesterol embolization syndrome. *Circulation* 122, 631–641.
<http://circ.ahajournals.org/content/122/6/631.long>

31. Answer E

This patient has ongoing ventricular fibrillation despite defibrillation. The next line of therapy is amiodarone. According to the 2010 American Heart Association (AHA) Guidelines and the Australian Resuscitation Council Guidelines (www.resus.org.au), intravenous anti-arrhythmic therapy should be considered in cases that remain in ventricular fibrillation (VF) or ventricular tachycardia (VT) despite defibrillation or recur promptly after successful defibrillation. Anti-arrhythmic drugs that may be used include amiodarone, lidocaine and magnesium sulphate, with amiodarone being the preferred agent. In the ALIVE trial of 347 patients with out-of-hospital sudden cardiac arrest and persistent or recurrent VF despite three defibrillation shocks and intravenous epinephrine (adrenaline),

survival to hospital admission was significantly higher in the amiodarone group compared to the lignocaine group (23% versus 12%) (Dorian et al., 2002). Magnesium sulphate is indicated *only* in the treatment of VF or pulseless VT arrest due to the drug-induced prolonged QT interval associated with torsades de pointes.

Although the 2010 AHA guidelines concluded that a single dose of vasopressin may be administered in place of the first or second dose of epinephrine (adrenaline) in the treatment of VF or pulseless VT arrest, clear evidence that this is a superior approach is lacking.



Dorian, P., Cass, D., Schwartz, B., Cooper, R., Gelaznikas, R., and Barr, A. (2002). Amiodarone as compared with lidocaine for shock-resistant ventricular fibrillation. *N Engl J Med* 346, 884–890.
<http://www.ncbi.nlm.nih.gov/pubmed/11907287>

32. Answer D

Uncontrolled heart failure is the most important risk factor for cardiac death or complications. A history of functional limitation appears to be the most helpful of all the historical points in this assessment. Patients who can perform activities that require four metabolic equivalents (METs) have a good chance of survival for most surgical procedures; such patients require no further testing. One MET represents metabolic demand at rest, climbing two flights of stairs demands four METs and strenuous sports such as swimming needs more than 10 METs. The use of echocardiography as a predictive tool is controversial. Although many experts advocate echocardiography as a good tool for assessing heart failure control, the procedure may provide little prognostic information beyond that available from a careful history and physical examination. The most important preoperative use of echocardiography is in the differentiation of systolic dysfunction from diastolic dysfunction in patients with new-onset heart failure. The distinction is important, because data clearly show that systolic dysfunction, in a patient with substantial clinical manifestations (i.e. overt congestive failure), adds significantly to the risk of surgery. On the other hand, there are no data showing that echocardiographic evidence of systolic dysfunction in a patient without symptoms or signs of heart failure have any prognostic implications. There are also no good data indicating that diastolic dysfunction increases risk significantly. The preoperative evaluation of the patient with established or probable coronary artery disease (CAD) is of great importance. Recent myocardial infarction is second only to decompensated heart failure as a risk factor for perioperative complications. Decisions regarding the evaluation of chest pain in patients without a history of CAD can be difficult under any circumstance.

The American College of Physicians clinical guidelines on the perioperative assessment and management of risk from CAD state that most patients who do not have an independent clinical need for coronary revascularisation can proceed to surgery without further cardiac investigation. In other words, if there is no prior reason to perform coronary artery bypass surgery, further cardiac investigation

usually does not need to be carried out for the anticipated surgery, unless there is some other overriding consideration.

Cardiac complications after non-cardiac surgery depend not only on specific risk factors but also on the type of surgery and the circumstances under which it takes place. The high-risk group consists of major vascular interventions. Abdominal surgery, head and neck surgery, urological surgery and major orthopaedic surgery, such as hip and spine surgery, belong in an intermediate-risk group.



Fleisher L.A., Beckman J.A., Brown K.A., et al (2007). ACC/AHA 2007 Guidelines on Perioperative Cardiovascular Evaluation and Care for Noncardiac Surgery: A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Revise the 2002 Guidelines on Perioperative Cardiovascular Evaluation for Noncardiac Surgery). *Circulation* 116, e418–e500.
<http://circ.ahajournals.org/content/116/17/e418.full>

33. Answer B

Transplant coronary artery disease (TCAD) remains the most significant cause of morbidity and mortality after orthotopic heart transplantation (OHT) (Zimmer and Lee, 2010). Transplant coronary artery disease is largely an immunological phenomenon, driven by an inflammatory milieu consisting of multiple cell types that contribute to fibromuscular and smooth muscle cell proliferation with subsequent coronary obstruction. Multiple clinical factors contribute to the development of TCAD.

The gold standard for diagnosing and monitoring TCAD is coronary angiography. Although angiography is particularly useful for discerning focal lesions, which are commonly seen in native coronary artery disease, TCAD often presents as diffuse concentric disease without discrete stenosis, making angiography a less sensitive modality for diagnosis in these cases.

Clinical history is generally unreliable in the diagnosis of TCAD, because of the denervation of the allograft, although paediatric patients have indicated that symptoms such as abdominal, chest and/or arm pain are strongly associated with the presence of TCAD.

Intravascular ultrasound (IVUS) can evaluate all layers of the vessel wall as well as the lumen, and an intimal thickness of greater than 0.5 mm in a single transplant coronary artery. IVUS can subsequently confer prognostic information for cardiovascular complications associated with TCAD, as evidenced by findings that severe and rapid increases in intimal thickness, particularly an increase of 0.5 mm or greater within the first year after OHT, are strongly correlated with the future development of angiographic disease up to 5 years after OHT and are also associated with increased mortality, myocardial infarction and the need for repeat revascularisation. Limitations of IVUS include higher cost compared with angiography, lack of general expertise in its use, requirement for concurrent invasive angiography, decreased ability to examine secondary and tertiary vessels because of the larger size of the catheter, and higher risk of complications compared with routine angiography.

Myocardial contrast echocardiography can adequately detect the presence of TCAD but is unable to identify the extent of disease compared with angiography.

Current treatments for TCAD include pharmacotherapy, percutaneous coronary intervention and repeat transplantation; other novel therapies are emerging. Although percutaneous coronary intervention has generally demonstrated high procedural success rates, it has been plagued by a high incidence of in-stent restenosis. Drug-eluting stents reduce in-stent restenosis compared with bare metal stents. Repeat transplantation is the only definitive treatment.



Zimmer, R.J. and Lee, M.S. (2010). Transplant coronary artery disease. *JACC Cardiovasc Interv* 3, 367–377.
<http://www.sciencedirect.com/science/article/pii/S193687981000169X>

34. Answer A

In this scenario, the dyspnoea and peripheral oedema can be caused by any form of cardiomyopathy. The rise in jugular venous pressure (JVP) with inspiration suggests either constrictive or restrictive cardiomyopathy. Echocardiography showing no pericardial effusion and stiffness suggests restrictive rather than constrictive cardiomyopathy. The transmitral Doppler on the echocardiography may show an increased E:A ratio (E: early diastolic filling; A: atrial filling), decreased E-deceleration time (90 ms) and decreased isovolumetric relaxation time (40 ms), which may suggest a restrictive picture.

Restrictive cardiomyopathy is characterised by increased stiffness of the ventricles leading to compromised diastolic filling with preserved systolic function (Mogensen et al., 2009). These changes may develop in association with inflammatory, infiltrative or storage disease. Infiltrative pathology includes sarcoidosis, amyloidosis, post-irradiation therapy, myeloma, lymphoma or connective tissue disease. Inflammatory disease can be endomyocardial fibrosis or Löffler cardiomyopathy, while storage diseases include haemochromatosis, glycogen storage disease and Fabry disease.

Differentiation of restrictive cardiomyopathy from constrictive pericarditis is important because patients with the latter condition may recover completely following surgical removal of the fibrotic pericardium. However, the distinction between the two may be difficult.



Mogensen, J., Arbustini, E. (2009). Restrictive cardiomyopathy. *Curr Opin Cardiol* 24, 214–220.
<http://qrs.ly/m52zfpa>

35. Answer A

Patients with fulminant myocarditis typically present in acute heart failure up to 2 weeks after a viral prodrome. Many symptomatic cases of myocarditis present with a syndrome of dilated cardiomyopathy and heart failure (Gupta et al., 2008).

Chest pain may be seen if there is concomitant pericarditis. Myocarditis may present with arrhythmias leading to palpitations and hypotension. Troponins are raised in up to one-third of cases and ECG may show changes of myocardial ischaemia, arrhythmias or conduction disturbances.

In the developed world, myocarditis is most commonly associated with viral infections with Coxsackie being the commonest pathogen. Other causes include bacteria, protozoa, spirochaetes, rickettsia, cardiotoxic agents (anthracyclines, cyclophosphamide, cocaine and alcohol), hypersensitivity reactions (penicillins, cephalosporins, sulphonamides, diuretics, lithium, clozapine and methyldopa) and systemic disorders (sarcoidosis, inflammatory bowel disease, celiac disease, Wegener's disease and Kawasaki disease).

Acute myocarditis should always be suspected when a young patient with no significant medical history presents with a new onset cardiac abnormality such as heart failure, myocardial infarction, arrhythmias or conduction defects.



Gupta, S., Markham, D.W., Drazner, M.H., and Mammen, P.P. (2008). Fulminant myocarditis. *Nat Rev Cardiovasc Med* 5, 693–706.
<http://www.nature.com/nrcardio/journal/v5/n11/full/ncpcardio1331.html>

36. Answer E

Weight reduction can achieve important reductions in blood pressure in patients with hypertension and, if combined with a DASH diet, can achieve impressive average reductions in blood pressure, equal or exceeding that seen with single anti-hypertensive agents. The effect of adding weight loss to the DASH diet was evaluated in the Exercise and Nutrition Interventions for Cardiovascular Health (ENCORE) study. Participants were randomised to a control diet, to the DASH diet alone or to a reduced-calorie modification of the DASH diet. At 4 months, blood pressure was reduced by 3.4/3.8 mmHg in the control group, by 11.2/7.5 mmHg in the group given the DASH diet alone and 16.1/9.9 mmHg with the DASH diet plus weight management.

The most carefully studied and established healthy dietary patterns are the DASH diet and variations of the Mediterranean diet. In the original DASH trial, adults whose systolic blood pressure was less than 160 mmHg and whose diastolic blood pressure was 80–95 mmHg, 133 of whom had hypertension, were randomised to a control diet typical of the average US diet, a diet rich in fruits and vegetables, or a combination diet rich in fruits, vegetables and low-fat dairy products and relatively low in saturated and total fat. In hypertensive adults, the diet rich in fruits and vegetables reduced systolic and diastolic blood pressure by 7.2 and 2.8 mmHg more, respectively, than the control diet and the combination diet resulted in even greater reductions (11.4 and 5.5 mmHg). In a subsequent trial, the effect of sodium intake was studied in the context of the DASH diet. Patients were randomised to either the DASH 'combination' diet or a control diet. Participants were then given a diet with high, intermediate and low levels of sodium (3.5, 2.3 and 1.2 g/day, respectively). Reducing sodium intake resulted in

a significant incremental reduction in systolic and diastolic blood pressure in both groups. The DASH diet is characterised by a relatively high potassium content (Sacks and Campos, 2010).



Sacks, F.M. and Campos, H. (2010). Dietary therapy in hypertension. *N Engl J Med* 362, 2102–2112.
<http://www.ncbi.nlm.nih.gov/pubmed/20519681>

37. Answer B

This patient has had an asymptomatic heart murmur for a long time, and he now presents with clinical features consistent with infectious endocarditis. Ventricular septal defects (VSDs) are among the most common congenital cardiac disorders seen at birth, but are less frequently seen as an isolated lesion in adulthood. This is because most VSDs in infants either are large and lead to heart failure, necessitating early surgical closure, or are small and close spontaneously. With the exception of patients who contract infective endocarditis or those with Eisenmenger syndrome, adults with VSD are asymptomatic. The classic physical finding of a VSD is a harsh, pan-systolic murmur heard best at the left lower sternal border and usually accompanied by a palpable thrill. Aortic regurgitation may be present if the VSD undermines the valvular annulus.

With a large defect, there is electrocardiographic evidence of left atrial and ventricular enlargement. If pulmonary hypertension occurs, the QRS axis shifts to the right and right atrial and ventricular enlargement is noted. Echocardiography is the procedure of choice for determining the location, size and haemodynamic significance of a VSD. The physiological consequences of a VSD are determined by the size of the defect.

Eisenmenger syndrome is a serious complication of long-standing left-to-right cardiac shunts in which severe, irreversible pulmonary hypertension develops. The presence of cyanosis is characteristic; symptoms such as dyspnoea and chest discomfort can be seen.

Patients with large VSD defects who survive to adulthood usually have left ventricular failure or pulmonary hypertension with associated right ventricular failure. Surgical closure of the defect is recommended if the magnitude of pulmonary vascular obstructive disease is not prohibitive (i.e. the ratio of pulmonary-to-systemic vascular resistance is <0.7).

38. Answer A

Atrial septal defects (ASDs) occur in three main locations: the region of the fossa ovalis (termed ostium secundum ASDs; 75% of ASDs); the inferior portion of the atrial septum near the tricuspid valve annulus (ostium primum ASDs; 15%); and the superior portion of the atrial septum (sinus venosus ASDs; 10%). The last two are considered to be part of the spectrum of AVSDs. Ostium secundum defects are associated with mitral valve prolapse, ostium primum defects with mitral

regurgitation and sinus venosus defects with partial anomalous drainage of the pulmonary veins.

Most patients with ostium secundum ASDs with small defects are asymptomatic through young adulthood. As the patient reaches middle age, compliance of the left ventricle may decrease, increasing the magnitude of left-to-right shunting. A symptomatic patient with an ASD typically reports fatigue or dyspnoea on exertion. Alternatively, patients may present with complications such as supraventricular arrhythmias, right heart failure, paradoxical embolism or recurrent pulmonary infections.

The hallmark of the physical examination in ASD is the wide and fixed splitting of the second heart sound because phasic changes in systemic venous return to the right atrium during respiration are accompanied by reciprocal changes in the volume of shunted blood from the left atrium to the right atrium, thereby minimising the respiratory changes in right and left ventricular stroke volumes that are normally responsible for physiological splitting. A systolic murmur (from increased pulmonary flow) is common. On electrocardiography, the QRS axis is usually normal in patients with ostium secundum ASD but may have right axis deviation and incomplete right bundle branch block. The chest X-ray reveals an enlarged right atrium, right ventricle and main pulmonary artery. The diagnosis is confirmed by echocardiography. An ASD with a ratio of pulmonary-to-systemic flow of 1.5 or more should be closed surgically to prevent right ventricular dysfunction. Surgical closure is not recommended for patients with irreversible pulmonary vascular disease and pulmonary hypertension. Prophylaxis against infective endocarditis is not recommended for patients with ASD, repaired or unrepaired, unless there is a concomitant valvular abnormality such as mitral valve prolapse.

39. Answer H

In this patient, the findings on physical examination are consistent with coarctation of the aorta. Coarctation is an important cause of secondary hypertension. Although lower-extremity claudication may occur, patients are commonly asymptomatic. Coarctation may occur in conjunction with gonadal dysgenesis, bicuspid aortic valve, ventricular septal defect, patent ductus arteriosus, mitral stenosis or regurgitation or aneurysm of the circle of Willis.

The main feature on physical examination is the differences in pulses and blood pressures above the coarctation as compared to below the coarctation. In coarctation of the aorta, the femoral pulse will occur later than the radial pulse and it is often lower in amplitude. Because of variations in anatomy, blood pressure should be evaluated in both arms and in either leg when evaluating for coarctation of the aorta. When the coarctation is distal to the origin of the left subclavian artery, both arms will be in the high-pressure zone and both legs in the low-pressure zone. However, some coarctations are proximal to the left subclavian. Thus, the left arm and both legs will be in the low-pressure zone, and the diagnosis may be missed if only the left arm is used for measuring blood pressure. In addition to differential blood pressures, physical examination may also reveal a murmur across the coarctation that can be best heard in the left infrascapular area.

ECG usually shows left ventricular hypertrophy. Dilatation of the aorta proximal and distal to the coarctation site may lead to a so-called '3 sign' on chest X-ray. Rib notching is often present; this term refers to apparent effacement or so-called scalloping of the lower edges of ribs because of large, high-flow intercostal collateral vessels that develop as a compensatory mechanism to bypass the narrowing at the coarctation site. Computed tomography or magnetic resonance imaging provides precise anatomical information regarding the location and length of the coarctation.

Complications of aortic coarctation include left ventricular failure, aortic dissection, premature coronary artery disease, infective endocarditis and haemorrhagic stroke from rupture of intracerebral aneurysm. Surgical repair should be considered for patients with a transcoarctation pressure gradient of greater than 30 mmHg. Survival after repair is influenced by the age of patient at the time of surgery.

40. Answer F

This patient presents with a systolic murmur that increases on inspiration. This makes it likely that the aetiology is right sided. Given the location, pulmonary stenosis is more likely than tricuspid regurgitation. These murmurs vary with respiration because filling of the right heart is significantly affected by inspiration (as blood is returning from outside the chest and is therefore influenced by the negative thoracic pressure). In patients with moderate-to-severe pulmonary stenosis, a right ventricular impulse is palpable at the left sternal border and a thrill may also be present at the second left intercostal space.

Obstruction of right ventricular outflow is valvular in 90% of patients and the remainder is either supravulvar or subvalvular. Severe pulmonary stenosis is characterised by a valve area of less than $5 \text{ cm}^2/\text{m}^2$ of body surface area, a transvalvular gradient of greater than 80 mmHg or a right ventricular systolic pressure of greater than 100 mmHg. With moderate-to-severe pulmonary stenosis, the electrocardiogram shows right axis deviation and right ventricular hypertrophy. When the stenosis is severe, dyspnoea on exertion or fatigability may occur. Eventually right ventricular failure may develop and if the foramen ovale is patent, shunting of blood from right to left may occur, resulting in cyanosis and clubbing.

Treatment for this disorder is most commonly by percutaneous balloon valvuloplasty. Valvular replacement is required if the leaflets are dysplastic or calcified or if marked regurgitation is present.



Brickner, M.E., Hillis, L.D., and Lange, R.A. (2000). Congenital heart disease in adults. First of two parts. *N Engl J Med* 342, 256–263.
<http://www.ncbi.nlm.nih.gov/pubmed/10648769>



Brickner, M.E., Hillis, L.D., and Lange, R.A. (2000). Congenital heart disease in adults. Second of two parts. *N Engl J Med* 342, 334–342.
<http://www.ncbi.nlm.nih.gov/pubmed/10655533>



Rouine-Rapp, K., Russell, I.A., and Foster, E. (2012). Congenital heart disease in the adult. *Int Anesthesiol Clin* 50, 16–39.
<http://www.ncbi.nlm.nih.gov/pubmed/22481554>



Therrien, J. and Webb, G. (2003). Clinical update on adults with congenital heart disease. *Lancet* 362, 1305–1313.
<http://www.ncbi.nlm.nih.gov/pubmed/14575977>