Pass MRCP Part 2
A Problem-based Approach

edited by
Paul Hamilton BSc(Hons) MD FRCP(Edin)
Specialty Registrar, Chemical Pathology (Metabolic Medicine)
Belfast Health and Social Care Trust
Honorary Lecturer, Queens University Belfast
Locum Consultant Physician in General (Internal) Medicine
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CASE 1

A 38-year-old lady is admitted complaining of a week-long history of chest tightness. She has no risk factors for coronary artery disease and has no past medical history of note other than a bout of an influenza-like illness around four weeks ago. Her ECG is shown in Figure 1.1.

Figure 1.1

Blood testing reveals: High sensitivity troponin T 456 ng/litre, C-reactive protein 31 mg/litre, Full blood picture normal.

There is no evidence of pulmonary oedema on a chest X-ray, but she is noted to have a few beats of non-sustained ventricular tachycardia on monitoring. What is the most likely diagnosis?

A. Unstable angina
B. Acute myocardial infarction
C. Myocarditis
D. Pericarditis
E. Cardiomyopathy
CASE 2

A 73-year-old man is seen in the emergency department having been referred by his GP for assessment of an irregular heartbeat. He has a history of hypertension and type 2 diabetes, but is otherwise in good health. He had attended his GP with symptoms of a chest infection but had not experienced any palpitations. The irregular pulse was detected as part of a routine physical examination.

On examination his heart rate is 100 bpm and a 12-lead ECG shows atrial fibrillation (AF). Blood testing reveals: C-reactive protein 54 mg/litre, white cells $11 \times 10^9$/litre.

A chest X-ray does not show any consolidation or pulmonary oedema. Which of the following is not true?

A. It is appropriate to start anticoagulation
B. It is appropriate to arrange an outpatient cardioversion
C. It is appropriate to perform an urgent inpatient cardioversion
D. It is inappropriate to commence aspirin
E. It is appropriate to commence a rate-controlling agent
A 40-year-old man with no history of cardiac disease has been brought to the emergency department complaining of palpitations which awoke him from his sleep. He is assessed by the triage nurse who records his heart rate as 184 bpm and blood pressure of 126/82 mmHg. A 12-lead ECG is shown in Figure 1.2. Which of these drugs is most likely to result in an adverse outcome for the patient?

Figure 1.2

A. Beta blocker  
B. Digoxin  
C. Calcium channel blocker  
D. Adenosine  
E. Amiodarone
A 31-year-old man develops chest pain while playing football and is brought by ambulance to the emergency department. On arrival he complains of a 3-day history of intermittent chest pain which peaked during the game today and was associated with some shortness of breath. In the department he is still in pain but finds relief in sitting forward and breathing shallowly. He is normotensive with a heart rate of 108 bpm. He denies any illicit drug use and has no personal or family history of cardiac disease. A 12-lead ECG shows widespread ST elevation, as shown in Figure 1.3. Which of the following would be most suggestive of an ischaemic origin to his symptoms?

**Figure 1.3**

A. Concave ST elevation globally  
B. PR depression  
C. PR elevation in AVR  
D. Reciprocal ST depression in the inferior leads  
E. Concave ST elevation in a specific territory
CASE 5

A 73-year-old lady attends a cardiology outpatient clinic for follow-up of aortic stenosis. She is usually in good health but has recently begun to complain of shortness of breath on walking to the shops and has had two episodes of feeling faint. She does not describe any chest pain or palpitations and her GP started her on a diuretic without any real improvement in symptoms. You review her most recent echocardiogram, which had been performed three weeks before this appointment. This shows that the mean gradient across her aortic valve is 30 mmHg while the valve orifice is 0.7 cm². Her last study had shown a mean gradient of 29 mmHg with a valve orifice of 1.3 cm². You also notice that her left ventricular function has deteriorated from an ejection fraction of 60% to 37%. What is the most appropriate course of action for this lady?

A. Refer for aortic valve replacement
B. Increase the dose of her diuretic
C. Repeat her echocardiogram in six months
D. Arrange an exercise stress test (EST)
E. Start spironolactone

CASE 6

A 42-year-old lady is referred by her GP for investigation of shortness of breath on exertion. She gives a 6-month history of increasing dyspnoea without chest pain. There are no risk factors for cardiac disease and she is a lifelong non-smoker with no past medical history. A chest X-ray shows some prominence of the pulmonary arteries but no oedema and a 12-lead ECG is normal. A surface echocardiogram later shows moderate tricuspid regurgitation with an estimated pulmonary artery pressure of 54 mmHg with normal biventricular function. Pulmonary function testing is normal apart from a reduction in DLCO to 55% predicted. Right heart catheterisation demonstrates a normal pulmonary capillary wedge pressure and left ventricular end-diastolic pressure with a pulmonary artery pressure of 60 mmHg. What is the most complete diagnosis?

A. Pulmonary venous hypertension
B. Pulmonary arterial hypertension
C. Right ventricular cardiomyopathy
D. COPD
E. Tricuspid regurgitation
A 76-year-old man is seen at the outpatient clinic with progressive dyspnoea. Six months ago he had been able to walk a mile each day, but he has taken to driving this distance recently. He is known to have heart failure on the basis of a myocardial infarction ten years ago. He has never had angina and is a non-smoker. Currently he is short of breath on walking around 30 yards. He sleeps on three pillows and notices that his ankles have become swollen recently. His GP had increased his diuretic without any effect and he is already on maximal doses of an ACE inhibitor, β blocker and spironolactone. His 12-lead ECG is shown in Figure 1.4 and a chest X-ray reveals mild pulmonary congestion. Echocardiography reveals a drop in ejection fraction from 45 to 25% in the last 12 months. Which of the following statements is false?

Figure 1.4

A. He has New York Heart Association class III heart failure
B. His BNP will be elevated
C. He may be considered for cardiac resynchronisation therapy (CRT)
D. His LV function is too low to be considered for CRT
E. He may be considered for an ICD
CASE 8

A 27-year-old man collapses suddenly while playing basketball and dies despite prolonged resuscitation. He had no family history of cardiac disease; however, his grandfather had died while swimming. A post-mortem examination identifies the cause of death as a thoracic aortic dissection and notes his tall habitus with evidence of lens dislocation. The family are keen to know whether there may be an inherited trait and whether his sister should be screened. Which statement is true?

A. There is no need for the sister to be screened
B. The cause of death is most likely sporadic
C. This condition is a result of a fibrillin gene mutation
D. There may be downward dislocation of the lens
E. No other family members will be affected

CASE 9

A 70-year-old man with a history of mitral valve prolapse is admitted with rigors and fever. No source of infection is identified after clinical assessment, but two sets of blood cultures are positive for viridans streptococci. A transthoracic echocardiogram shows mild mitral regurgitation and a trans-oesophageal echo identifies a small mobile mass on the anterior leaflet tip. He is started on intravenous antibiotic therapy and his fever settles within seven days. What is the most appropriate course of treatment?

A. He may require follow-up colonoscopy for possible bowel cancer
B. IV antibiotics are recommended for at least four weeks
C. He should be referred immediately for mitral valve replacement
D. He does not require a prolonged course of antibiotics
E. He can go home with oral antibiotics
CASE 10

A 36-year-old man attends his GP for a routine medical examination for his work insurance. He reports no symptoms and is a keen sportsman; however, his blood pressure is recorded as 152/92 mmHg. Which of the following would be an appropriate next step?

A. Start an ACE inhibitor  
B. Start a thiazide diuretic  
C. Arrange a 24-hour ambulatory BP monitor  
D. Repeat his blood pressure in six months  
E. Start a calcium channel blocker
C: Myocarditis

The diagnosis of myocarditis (inflammation of the myocardium) is often confused with an acute coronary syndrome (ACS) as both can present with chest discomfort together with ECG changes and a rise in troponin levels.

**Learning point**

The clue to the diagnosis of myocarditis rather than an infarct will be in the history. A patient who is younger with no risk factors for coronary artery disease and perhaps a history of a recent coryzal or flu-like illness should raise suspicions of this diagnosis. Myocarditis most commonly is of infectious aetiology, with viral causes being particularly likely. More rarely, cases may be due to autoimmune activity such as in connective tissue diseases and sarcoidosis.

Diagnosis may involve the following:

- echocardiography: to assess ventricular function
- cardiac MRI: typical patterns of enhancement are seen with myocarditis and this modality can be used to guide endomyocardial biopsy
- coronary angiography: to exclude coronary artery disease
- endomyocardial biopsy: provides a tissue diagnosis.

Complications can arise from myocarditis and are largely due to the development of an acute cardiomyopathy. Some patients develop severe left ventricular systolic dysfunction, ventricular arrhythmias and high degrees of atrioventricular block. In some cases the cardiomyopathy does not recover.

Treatment of myocarditis is dependent on the presence or absence of left ventricular (LV) dysfunction. Those who escape without LV impairment can be managed with simple pain relief while the acute phase settles. Those with LV impairment require standard heart failure therapy, similar to any patient presenting with heart failure. This would typically include a diuretic, β blocker, angiotensin-converting enzyme (ACE) inhibitor and aldosterone antagonist.
CASE 2

C: It is appropriate to perform an urgent inpatient cardioversion

Atrial fibrillation is one of the most common problems encountered in cardiology. It affects 1.5–2% of adults and those over the age of 40 have a 25% lifetime risk of developing the condition. Causes of AF are multiple: alcohol, ischaemic heart disease, hypertension, valvular heart disease (especially mitral valve disease, which frequently causes the left atrium to dilate, so predisposing to AF) and hyperthyroidism.

The mechanism of stroke risk in AF is sometimes not well appreciated. Fibrillation of the atria (in contrast to their coordinated contraction) increases blood stasis within these chambers, most specifically within the left atrial appendage (LAA). It is this structure which is the main source of clot formation in AF. Hence a trans-oesophageal echo may be carried out to identify the LAA and any evidence of clot within it before cardioversion is performed in patients who have not been adequately anticoagulated.

Learning point

Cardioversion should be considered for all patients with newly diagnosed AF. Novel oral anticoagulant drugs are now being used routinely in this setting as an alternative to warfarin. While warfarin compliance can be checked using the International Normalised Ratio (INR), there is no such comparable test for NOACs and patients must be informed of the increased risk of stroke during cardioversion if compliance has been lacking in the weeks leading up to the procedure. Current guidelines recommend three weeks of anticoagulation before conversion in order to reduce the risk of embolisation from a pre-existing clot in the heart. Four weeks of therapy is needed post-cardioversion even if the procedure has been successful.

Much confusion surrounds rate-controlling agents in AF. In a person with paroxysmal or persistent AF, an anti-arrhythmic agent may be used to prevent episodes of AF. Such agents include amiodarone, sotalol, flecainide and propafenone. Flecainide and propafenone are not used in patients with left ventricular impairment, a history of coronary artery disease or for those over the age of 65 years as they may be detrimental and ironically pro-arrhythmic in such circumstances. For those already in permanent AF there is no point in prescribing an anti-arrhythmic agent as the patient is already permanently in the arrhythmia. In these patients a simple rate-controlling agent is appropriate; β blockers are the most commonly used drug class for this purpose.
Catheter ablation of AF is currently only recommended for those who remain symptomatic of their AF despite medical therapy. Although highly publicised, the success rates are around 80% after two procedures. There is no role for this procedure at present in asymptomatic patients.

CASE 3

D: Adenosine

This man has presented with a broad complex tachycardia which may cause confusion as to whether the diagnosis is that of ventricular tachycardia (VT) or supraventricular VT (SVT) with aberrant conduction. In this case the diagnosis is atrial fibrillation (AF) with Wolff–Parkinson–White (WPW) pattern, or in other terms, AF conducted via an accessory pathway.

Learning point

There are certain features on the ECG that distinguish this from VT. First, the rhythm is irregular with no consistency between complexes. Second, the bundle branch pattern in lead V1 (in this case right bundle branch) is not seen in VT. The patient’s history is also important in determining the cause of the tachycardia. A young man with no history of ischaemic heart disease (IHD) is more likely to present with SVT with aberrant conduction. In those with a history of IHD, 95% of broad complex tachycardias will be ventricular in origin due to previous scar formation from an old myocardial infarction (MI) or an impaired and dilated ventricle.

Administering adenosine in this case in an attempt to distinguish SVT from VT will result in blocking of the atrioventricular (AV) node and subsequent 1:1 conduction of the AF from the atria to the ventricles via the accessory pathway. As the actual atrial rate of AF is commonly 200–300 bpm, this 1:1 conduction caused by blocking of the AV node quickly results in a ventricular rate of 200–300 bpm, which may result in ventricular fibrillation.
CASE 4

D: Reciprocal ST depression in the inferior leads

The diagnosis is pericarditis rather than ST elevation MI (STEMI). This is a young man with no antecedent cardiac disease who describes the typical features of pericardial rather than ischaemic chest pain, ie positional pain that is often pleuritic in nature. The ECG is classic of pericarditis with two very specific features relating to the PR interval.

Learning point

PR segment elevation in AVR is very specific for pericarditis, while PR depression in the other leads is considered pathognomonic of pericarditis. In this instance you should not see reciprocal ST depression as you may see in a STEMI, a feature which suggests ischaemia in a specific coronary artery territory. The changes associated with pericarditis tend not to be confined to such territorial parts of the pericardium, meaning ST elevation is frequently present in all leads.

The importance for management is that the incorrect diagnosis of a STEMI in this situation may lead to the administration of thrombolysis, which would almost certainly result in a pericardial effusion. Given the classic presentation, and features of this man’s presentation he should have an echocardiogram, which may show an echo bright pericardium in keeping with pericarditis. Colchicine has been shown to reduce the risk of recurrent episodes and patients should generally receive up to six weeks of therapy. Less than 1% of patients with acute pericarditis go on to develop constrictive pericarditis. Echo features in keeping with constrictive pericarditis rather than a restrictive cardiomyopathy include a septal bounce indicative of ventricular interdependence, higher mitral annular tissue Doppler velocity and diastolic flow reversal in the hepatic veins.
Aortic stenosis (AS) is increasing in prevalence as the population ages. It is a degenerative disease of the aortic valve resulting in calcium deposition on the valve leaflets which then restricts leaflet mobility. It is graded as mild, moderate and severe depending on the area of the valve orifice and the mean gradient across the valve. Severe stenosis is classified as a valve area of < 1 cm$^2$ and a mean gradient of > 40 mmHg.

Learning point

In this case, the valve area of 0.7 cm$^2$ is in keeping with severe stenosis; however, the mean gradient is lower than would be expected for a severe stenosis. This is a case of low-flow aortic stenosis where the new impairment of left ventricular (LV) function means that the now failing ventricle cannot generate sufficient force to expel blood up the outflow tract and through the aortic valve with as much vigour as when the ventricular function was preserved. This is a common cause of confusion and often leads to erroneous labelling of aortic stenosis as moderate. One should always check LV function when assessing aortic stenosis and, if the ventricle is impaired, then the valve area is a more reliable indicator of the severity of stenosis. In these circumstances, a stress test such as a dobutamine stress echo can reveal the true gradient by increasing LV work.

The natural course of AS is for the valve to progressively tighten. Nearly all patients with severe AS develop symptoms within five years. The annual rate of sudden cardiac death in this asymptomatic group is around 1%.

Class 1 indications for valve replacement are:

✦ severe AS with symptoms
✦ severe AS in those undergoing coronary artery bypass grafting (CABG). (There is little point in opening the patient’s chest for CABG to then have to re-open the same wound when the valve needs to be replaced.)
✦ severe AS in those undergoing surgery on the aorta or other heart valves
✦ severe AS and evidence of LV systolic dysfunction (EF < 50%).

Other indications are as outlined in Table 1.1.
### Indications for aortic valve replacement in aortic stenosis

<table>
<thead>
<tr>
<th>Indication</th>
<th>Class of evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>AVR is indicated in patients with severe AS and any symptoms related to AS.</td>
<td>I</td>
</tr>
<tr>
<td>AVR is indicated in patients with severe AS and any symptoms related to AS.</td>
<td>I</td>
</tr>
<tr>
<td>AVR is indicated in asymptomatic patients with severe AS and systolic LV dysfunction (LVEF &lt; 50%) not due to another cause.</td>
<td>I</td>
</tr>
<tr>
<td>AVR is indicated in asymptomatic patients with severe AS and an abnormal exercise test showing symptoms on exercise clearly related to AS.</td>
<td>I</td>
</tr>
<tr>
<td>AVR should be considered in high-risk patients with severe symptomatic AS who are suitable for TAVI, but in whom surgery is favoured by a 'heart team' based on the individual risk profile and anatomic suitability.</td>
<td>IIA</td>
</tr>
<tr>
<td>AVR should be considered in asymptomatic patients with severe AS and an abnormal exercise test showing fall in blood pressure below baseline.</td>
<td>IIA</td>
</tr>
<tr>
<td>AVR should be considered in patients with moderate AS undergoing CABG surgery of the ascending aorta of another valve.</td>
<td>IIA</td>
</tr>
<tr>
<td>AVR should be considered in symptomatic patients with low-flow, low-gradient (&lt; 40 mmHg) AS with normal EF only after careful confirmation of severe AS.</td>
<td>IIA</td>
</tr>
<tr>
<td>AVR should be considered in asymptomatic patients with severe AS, low flow, low gradient with reduced EF and evidence of flow reserve.</td>
<td>IIA</td>
</tr>
</tbody>
</table>
| AVR should be considered in asymptomatic patients with normal EF and none of the above-mentioned exercise test abnormalities, if the surgical risk is low, and one or more of the following findings is present:  
  - very severe AS defined by a peak transvalvular velocity > 5.5 m/s, or  
  - severe valve calcification and a rate of peak transvalvular velocity progression ≥ 0.3 m/s per year. | IIA               |
| AVR may be considered in symptomatic patients with severe AS low-flow, low-gradient and LV dysfunction without flow reserve. | IIb               |
| AVR may be considered in asymptomatic patients with severe AS, normal EF and none of the above-mentioned exercise test abnormalities, if surgical risk is low, and one or more of the following findings is present  
  - markedly elevated natriuretic peptide levels confirmed by repeated measurements and without other explanations  
  - increase of mean pressure gradient with exercise by > 20 mmHg  
  - excessive LV hypertrophy in the absence of hypertension. | IIb               |

Table 1.1: Indications for aortic valve replacement in aortic stenosis\(^{(1)}\)
Note the use of ‘classes of recommendations’ in this table and throughout this chapter. Class I recommendations relate to situations where there is evidence and/or general agreement that a given treatment or procedure is beneficial, useful or effective. Class II recommendations are when there is conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of a given treatment or procedure (class IIa – the weight of evidence/opinion is in favour of usefulness/efficacy; class IIb – less well established). Class III recommendations relate to when there is evidence or general agreement that a measure is not useful/effective and which, in some cases, may be harmful.

In clinical practice the decision is heavily influenced by patient co-morbidity and patient choice. Transcatheter aortic valve implantation (TAVI) is now considered a viable alternative in patients who are deemed at high operative risk. The procedure involves placing a valve via a catheter into position across the existing valve, and then inflating a balloon to crush the native valve and expand the new percutaneous valve into its position. Thirty-day mortality is in the region of 5–7\% and many patients require insertion of a permanent pacemaker after the procedure due to trauma to the conduction system caused during positioning of the new valve. These figures are felt to be favourable considering the inevitable mortality in those who do not receive a replacement.

**CASE 6**

**B: Pulmonary arterial hypertension**

This is a classic presentation of pulmonary arterial hypertension (PAH), which affects women more than men. Chest X-ray findings are non-specific but may show enlargement of the pulmonary arteries. The ECG tends not to reveal anything abnormal, other than perhaps right bundle branch block if the right ventricle has started to fail or dilate.

**Learning point**

An easily performed test that can point to the diagnosis is pulmonary function testing, which classically shows a reduction in transfer factor without significant restriction or obstruction. A normal DLCO makes pulmonary hypertension unlikely while a DLCO of <50\% predicted is a very high mortality indicator. Right heart catheterisation can be very informative in determining if left-sided heart disease is a likely cause of the pulmonary hypertension. The pulmonary capillary wedge pressure is used as a surrogate of left atrial pressure (the left atrium is not accessible from the venous circulation) and if normal, indicates absence of significant mitral valve disease or LV dysfunction, which are a cause of pulmonary venous hypertension.
The Dana-Point classification of pulmonary hypertension divides causes into groups (see Table 1.2).

<table>
<thead>
<tr>
<th>Group 1: Pulmonary arterial hypertension (PAH)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Causes: Idiopathic, inherited, drug-induced, connective tissue disease, HIV, portal hypertension, congenital heart disease, persistent pulmonary hypertension of the newborn, pulmonary veno-occlusive disease</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Group 2: Pulmonary hypertension due to left heart disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Causes: Systolic dysfunction, diastolic dysfunction, valve disease</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Group 3: Pulmonary hypertension due to lung disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Causes: COPD, interstitial lung disease, sleep-disordered breathing</td>
</tr>
</tbody>
</table>

| Group 4: Chronic thromboembolic pulmonary hypertension |

| Group 5: Pulmonary hypertension with unclear multi-factorial mechanisms |

### Table 1.2: Dana-Point classification of pulmonary hypertension

**Learning point**

The importance of identifying the cause is in order to guide treatment. Familial pulmonary hypertension has an autosomal dominant inheritance pattern and a grave mortality in the young with an untreated median survival of under three years. Group 1 patients are most likely to respond to vasodilator therapy while group 2 patients (those with left-sided heart disease) will be made worse by this therapy. Therefore, vasodilators are offered to group 1 patients only. Therapy may include an endothelin receptor blocker and a phosphodiesterase inhibitor.

Response to therapy can be followed by a functional assessment such as a 6-minute walk test and a pulmonary arterial pressure assessment such as an echocardiogram. The PA pressure should fall as therapy takes effect. Beware the patient whose PA pressure is falling but who feels no better. The onset of right ventricular dysfunction can lower the pressure owing to inability of the failing right ventricle to generate significant pressure into the pulmonary artery.

For those with chronic thromboembolic pulmonary hypertension, pulmonary thrombectomy is associated with a good outcome if they survive surgery (operative mortality is 3–5%).
CASE 7

D: His LV function is too low to be considered for CRT

Heart failure symptoms are classified according to the New York Heart Association (NYHA) scoring system (see Table 1.3).

<table>
<thead>
<tr>
<th>Class</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>no limitation of ordinary activity</td>
</tr>
<tr>
<td>II</td>
<td>symptoms during ordinary activity</td>
</tr>
<tr>
<td>III</td>
<td>symptoms during less than ordinary/minimal activity</td>
</tr>
<tr>
<td>IV</td>
<td>symptoms at rest</td>
</tr>
</tbody>
</table>

Table 1.3: New York Heart Association (NYHA) scoring system for heart failure symptoms

This man has NYHA class III symptoms. Brain natriuretic peptide (BNP) is a marker of LV dysfunction and will be elevated in this case. Caveats in its use include the fact that it may be elevated in those with renal impairment, obesity, sepsis, cirrhosis and pulmonary hypertension. Large randomised trials have consistently demonstrated the mortality benefit of ACE inhibitors, angiotension receptor blockers, diuretics, β blockers and aldosterone antagonists in heart failure and these should be combined in maximal doses in all patients, as tolerated by blood pressure.

Learning point

In CRT, the aim is to place pacemaker leads in the right ventricle and epicardially, via the coronary sinus, to the lateral wall of the left ventricle and thereby resynchronise the dysynchronous ventricular contractions which characterise wide left bundle branch block (LBBB) morphology heart failure. A third lead is placed in the right atrium as with any dual chamber pacemaker. CRT has been shown to improve symptoms and survival in carefully selected patients who meet the criteria described in Table 1.4.
Indication for cardiac resynchronisation therapy | Level of evidence
---|---
CRT is indicated in patients with heart failure whose EF is < 35%, with LBBB and a QRS duration > 150 ms, who exhibit NYHA class II–IV symptoms and who are on adequate medical therapy | Ia
CRT should be considered in patients with heart failure whose EF is < 35%, with LBBB and a QRS duration > 120 ms, who exhibit NYHA class II–IV symptoms and who are on adequate medical therapy | Ib
CRT should be considered in patients with heart failure whose EF is < 35%, with non-LBBB and a QRS duration > 150 ms, who exhibit NYHA class II–IV symptoms and who are on adequate medical therapy | IIa
CRT should be considered in patients with heart failure whose EF is < 35%, with non-LBBB and a QRS duration > 120 ms, who exhibit NYHA class II–IV symptoms and who are on adequate medical therapy | IIb
CRT is not recommended in heart failure patients with a QRS duration of < 120 ms | III

Table 1.4: Indications for cardiac resynchronisation therapy"
CASE 8

C: This condition is a result of a fibrillin gene mutation

This man died as a result of an undiagnosed aortic aneurysm which subsequently ruptured.

Learning point

The diagnosis is likely to be Marfan syndrome, which results from a defect in the fibrillin-1 (FBN-1) gene. Marfan syndrome is an autosomal dominant condition affecting connective tissue. It occurs in approximately 1 in 4000 individuals in Western populations. Prognosis is largely dependent on the development of cardiovascular complications such as aortic pathology and valvular heart disease. An ascending aortic diameter of ≥ 45 mm is an indication for surgical treatment of the aorta in Marfan syndrome.

The 2010 Revised Ghent Nosology for Marfan syndrome suggests seven rules in the diagnosis of Marfan syndrome (see Table 1.5).

<table>
<thead>
<tr>
<th>In the absence of family history:</th>
<th>In the presence of family history:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aortic root dilatation Z score ≥ 2 AND ectopia lentis</td>
<td>Ectopia lentis AND family history of Marfan syndrome</td>
</tr>
<tr>
<td>Aortic root dilatation Z score ≥ 2 AND FBN-1</td>
<td>A systemic score ≥ 7 points AND family history of Marfan syndrome</td>
</tr>
<tr>
<td>Aortic root dilatation Z score ≥ 2 AND systemic score ≥ 7 points</td>
<td>Aortic root dilatation Z score ≥ 2 AND family history of Marfan syndrome</td>
</tr>
<tr>
<td>Ectopia lentis AND FBN-1 mutation with known aortic pathology</td>
<td></td>
</tr>
</tbody>
</table>

Table 1.5: The 2010 Revised Ghent Nosology for Marfan syndrome
In each of the scenarios shown in Table 1.5, features suggestive of Shprintzen–Goldberg syndrome, Loeys–Dietz syndrome, or Ehlers–Danlos syndrome must be excluded and genetic testing (eg TGFBR1/2, collagen biochemistry, COL3A1) should be performed.

Systemic features to look for are listed below:

- Wrist sign
- Thumb sign
- Pectus carinatum
- Pectus excavatum
- Chest asymmetry
- Hind-foot deformity
- Flat foot
- Spontaneous pneumothorax
- Dural ectasia
- Protucio acetabulae
- Scoliosis or thoracolumbar kyphosis
- Reduced elbow extension
- Facial features
- Skin striae
- Severe myopia
- Mitral valve prolapse
- Reduced upper segment/lower segment
- Increased arm span/height
B: IV antibiotics are recommended for at least four weeks

This is a case of infective endocarditis (IE) of a native mitral valve and current guidelines recommend four weeks of IV antibiotics in such cases. In prosthetic valves six weeks of IV antibiotics is recommended. The Duke criteria are the most widely used in the diagnosis of infective endocarditis:

<table>
<thead>
<tr>
<th>Definite endocarditis:</th>
<th>Possible endocarditis:</th>
<th>Not endocarditis:</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 major criteria</td>
<td>1 major + 1 minor criteria</td>
<td>Alternative source of sepsis</td>
</tr>
<tr>
<td>OR</td>
<td>OR</td>
<td>Resolution of symptoms and signs with &lt; 4 days of antibiotics</td>
</tr>
<tr>
<td>1 major + 3 minor criteria</td>
<td>3 minor criteria</td>
<td>No evidence of endocarditis at surgery</td>
</tr>
<tr>
<td>OR</td>
<td></td>
<td>Does not meet criteria for possible IE</td>
</tr>
<tr>
<td>5 minor criteria</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Major criteria:**
- Blood culture positive for IE
- Typical micro-organism consistent with IE from two separate blood cultures: viridans streptococci, *Streptococcus bovis*, HACEK group, *Staphylococcus aureus*, or community-acquired enterococci in the absence of a primary focus
- Micro-organisms consistent with IE from persistently positive blood cultures defined as follows: at least two positive cultures of blood samples drawn > 12 h apart; or all of three or a majority of > 4 separate cultures of blood (with first and last sample drawn at least 1 h apart)
- Single positive blood culture for *Coxiella burnetii* or anti-phase 1 IgG antibody titre > 1 : 800
- Evidence of endocardial involvement
- Echocardiogram positive for IE (TOE recommended for patients with prosthetic valves, with ‘possible IE’ by clinical criteria or complicated IE [paravalvular abscess]; TTE as first test in other patients)

**Minor criteria:**
- Predisposition, predisposing heart condition, or IV recreational drug use
- Fever
- Vascular phenomena: major arterial emboli, septic pulmonary infarcts, mycotic aneurysm, intracranial hemorrhage, conjunctival hemorrhages, and Janeway lesions
- Immunologic phenomena: glomerulonephritis, Osler’s nodes, Roth’s spots, and rheumatoid factor
- Microbiological evidence: positive blood culture but does not meet a major criterion or evidence of active infection with organism consistent with IE

Table 1.6: Duke criteria for diagnosing infective endocarditis(6)
Staphylococcus aureus followed by viridans streptococci and coagulase negative staphylococci are the three most common causal organisms in IE. *S. aureus* has a particularly poor prognosis. Some organisms are notoriously difficult to grow from culture samples including *Aspergillus*, *Brucella*, *Coxiella burnetii*, *Chlamydia* and HACEK (*Haemophilus*, *Aggregatibacter*, *Cardiobacterium*, *Eikenella* and *Kingella*) bacteria. *Streptococcus bovis* infection can be associated with underlying bowel malignancy. Surgery for IE is usually only indicated in the presence of consequent heart failure, valve destruction, overwhelming sepsis or to prevent recurrent systemic embolisation.

A recent update to the National Institute for Health and Clinical Excellence (NICE) guidance for endocarditis prophylaxis has removed the recommendation to administer antibiotics before routine dental work in those with predisposing conditions to infective endocarditis (see Table 1.7). The caveat to this is that antibiotics should be administered if active infection is seen in the mouth or gums.

Table 1.7: Antibiotic prophylaxis for those at risk of endocarditis(7)
C: Arrange a 24-hour ambulatory blood pressure monitor

Hypertension is an abnormal elevation of the BP within the arterial system, the vast majority (90–95%) of which is related to no identifiable cause and is therefore termed essential hypertension. In the UK, one quarter of the adult population has hypertension, rising to half of those over the age of 60 years. Globally, almost one third of the population in developed countries is known to have hypertension. A direct correlation exists between the magnitude of hypertension and cardiovascular risk, and for patients aged 40–70 years, each increase of 20 mmHg in systolic BP or 10 mmHg in diastolic BP results in a doubling of risk. Conversely, a 2 mmHg reduction in systolic pressure would translate into a 10% lower stroke mortality and 7% reduction in ischaemic heart disease or other vascular mortality. Current grades of hypertension as defined by the European Society of Cardiology (ESC) are listed in Table 1.8.

<table>
<thead>
<tr>
<th>Grade of hypertension</th>
<th>Clinic systolic pressure (mmHg)</th>
<th>Clinic diastolic pressure (mmHg)</th>
<th>Ambulatory pressure average daytime reading (mmHg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>High–normal</td>
<td>130–139</td>
<td>85–89</td>
<td>–</td>
</tr>
<tr>
<td>1</td>
<td>140</td>
<td>90</td>
<td>135/85</td>
</tr>
<tr>
<td>2</td>
<td>160</td>
<td>100</td>
<td>150/95</td>
</tr>
<tr>
<td>3</td>
<td>180</td>
<td>110</td>
<td>–</td>
</tr>
</tbody>
</table>

Table 1.8: ESC definitions of hypertension. The diagnosis of grade 1 or 2 hypertension requires both a clinic measurement and ambulatory monitoring.
Learning point

The 2011 NICE guidelines for the management of hypertension advise therapy for BP reduction if clinic readings are ≥ 140/90 mmHg together with ambulatory readings of greater than 135/85 mmHg. This represents a lowering of the threshold for therapeutic intervention from the 2006 guidelines, which had advocated treatment in those with readings ≥ 140/90 mmHg together with a calculated ten-year CVD risk of ≥ 10%, existing CVD or evidence of target organ damage.

In a change to NICE’s previous guidance from 2006, the 2011 guideline includes a recommendation that hypertension should be confirmed by 24-hour ambulatory blood pressure monitoring (ABPM) rather than relying on measurements taken exclusively in a clinic setting.

According to the 2013 ESC guidelines, the recommended first agent can be any of an ACE inhibitor (or an angiotensin receptor blocker if the former is poorly tolerated or contraindicated), a calcium channel blocking agent, a thiazide type diuretic or a β blocker. The 2011 NICE guidelines still advocate ACE inhibitor or angiotensin receptor blocker in Caucasians < 55 years and a calcium channel blocker or diuretic in Black patients and those > 55 years.