## Contents

Foreword ................................................................. viii
Preface ................................................................. ix
Acknowledgements .................................................. xi
Reviewers .............................................................. xii
Abbreviations ......................................................... xiii

### Chapter 1  Basic training requirements .......................... 1

### Chapter 2  The written examination .............................. 8
The examination format ................................................. 8
Approaching multiple-choice questions .......................... 9
Preparation for the written examination ......................... 9

### Chapter 3  The clinical examination ............................. 12
The examination format ............................................... 12
The mini-CEX ............................................................. 16
Preparation for the clinical examination ......................... 16

### Chapter 4  The long case ............................................ 22
The history-taking and physical examination .................. 23
The presentation ......................................................... 26
The long case rationale ............................................... 28
Types of long case ...................................................... 31

### Chapter 5  The cardiovascular long case ......................... 32
Ischaemic heart disease ................................................ 32
Revascularisation ......................................................... 37
Infective endocarditis ................................................. 39
Congestive cardiac failure ............................................ 46
Diastolic heart failure (heart failure with preserved ejection fraction) ......................................................... 53
Hyperlipidaemia .......................................................... 54
Hypertension .............................................................. 59
Heart transplantation ................................................... 64
Cardiac arrhythmias .................................................... 68

### Chapter 6  The respiratory long case ............................ 81
Bronchiectasis .......................................................... 81
Lung carcinoma ........................................................ 85
Chronic obstructive pulmonary disease ...................... 90
Sleep apnoea ............................................................. 96
Interstitial lung disease, including idiopathic pulmonary fibrosis ......................................................... 99
Pulmonary hypertension .............................................. 102
Sarcoidosis ............................................................... 109
Cystic fibrosis .......................................................... 113
# Contents

<table>
<thead>
<tr>
<th>Chapter 7</th>
<th>The gastrointestinal long case</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peptic ulceration</td>
<td>124</td>
<td></td>
</tr>
<tr>
<td>Malabsorption and chronic diarrhoea</td>
<td>127</td>
<td></td>
</tr>
<tr>
<td>Inflammatory bowel disease</td>
<td>132</td>
<td></td>
</tr>
<tr>
<td>Colon cancer</td>
<td>138</td>
<td></td>
</tr>
<tr>
<td>Chronic liver disease</td>
<td>142</td>
<td></td>
</tr>
<tr>
<td>Liver transplantation</td>
<td>155</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Chapter 8</th>
<th>The haematological long case</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Haemolytic anaemia</td>
<td>158</td>
<td></td>
</tr>
<tr>
<td>Thrombophilia</td>
<td>164</td>
<td></td>
</tr>
<tr>
<td>Polycythaemia</td>
<td>168</td>
<td></td>
</tr>
<tr>
<td>Idiopathic myelofibrosis</td>
<td>172</td>
<td></td>
</tr>
<tr>
<td>Essential thrombocythaemia</td>
<td>173</td>
<td></td>
</tr>
<tr>
<td>Chronic myeloid leukaemia</td>
<td>174</td>
<td></td>
</tr>
<tr>
<td>Lymphomas</td>
<td>175</td>
<td></td>
</tr>
<tr>
<td>Multiple myeloma (myeloma)</td>
<td>182</td>
<td></td>
</tr>
<tr>
<td>Bone marrow (haematopoietic cell) transplantation</td>
<td>187</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Chapter 9</th>
<th>The rheumatological long case</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rheumatoid arthritis</td>
<td>191</td>
<td></td>
</tr>
<tr>
<td>Systemic lupus erythematosus</td>
<td>201</td>
<td></td>
</tr>
<tr>
<td>Systemic vasculitis</td>
<td>208</td>
<td></td>
</tr>
<tr>
<td>Antiphospholipid antibody syndrome</td>
<td>213</td>
<td></td>
</tr>
<tr>
<td>Systemic sclerosis (scleroderma)</td>
<td>215</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Chapter 10</th>
<th>The endocrine long case</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Osteoporosis (and osteomalacia)</td>
<td>220</td>
<td></td>
</tr>
<tr>
<td>Hypercalcaemia</td>
<td>220</td>
<td></td>
</tr>
<tr>
<td>Paget’s disease of the bone (osteitis deformans)</td>
<td>228</td>
<td></td>
</tr>
<tr>
<td>Acromegaly</td>
<td>233</td>
<td></td>
</tr>
<tr>
<td>Types 1 and 2 diabetes mellitus</td>
<td>237</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Chapter 11</th>
<th>The renal long case</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chronic kidney disease (chronic renal failure)</td>
<td>248</td>
<td></td>
</tr>
<tr>
<td>Renal transplantation</td>
<td>256</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Chapter 12</th>
<th>The neurological long case</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Multiple sclerosis</td>
<td>260</td>
<td></td>
</tr>
<tr>
<td>Myasthenia gravis</td>
<td>264</td>
<td></td>
</tr>
<tr>
<td>Guillain-Barré syndrome</td>
<td>267</td>
<td></td>
</tr>
<tr>
<td>Transient ischaemic attacks and ‘funny turns’</td>
<td>269</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Chapter 13</th>
<th>The infectious disease long case</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pyrexia of unknown origin</td>
<td>274</td>
<td></td>
</tr>
<tr>
<td>HIV/AIDS</td>
<td>277</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Chapter 14</th>
<th>Think like a physician, think like an examiner – an approach with long case examples</th>
<th>Page</th>
</tr>
</thead>
</table>
## Contents

**Chapter 15**  
*The short case* ........................................ 303

**Chapter 16**  
*Common short cases* ..................................... 308
  - The cardiovascular system .................................. 308  
  - The cardiovascular examination ............................. 308  
  - Notes on valve diseases ..................................... 318  
  - The hypertensive examination ................................ 337  
  - Marfan’s syndrome .......................................... 339  
  - Oedema .................................................... 340  
  - The respiratory system ...................................... 341  
  - The respiratory examination ................................ 341  
  - Chest X-ray films ............................................ 346  
  - The gastrointestinal system .................................. 358  
  - The abdominal examination ................................... 358  
  - The haematological system ................................... 364  
  - The haemopoietic examination ................................. 364  
  - The endocrine system ....................................... 369  
  - The thyroid gland ........................................... 369  
  - Panhypopituitarism .......................................... 374  
  - Cushing’s syndrome ......................................... 376  
  - Acromegaly .................................................. 378  
  - Addison’s disease ........................................... 382  
  - Diabetes mellitus ............................................ 384  
  - Hirsutism .................................................... 387  
  - The rheumatological system .................................. 388  
  - The hands .................................................... 389  
  - The knees .................................................... 399  
  - The feet ..................................................... 401  
  - The back ..................................................... 405  
  - The nervous system ........................................ 408  
    - Cranial nerves ............................................. 408  
    - Eyes ........................................................ 413  
    - One-and-a-half syndrome .................................. 414  
    - Horner’s syndrome ....................................... 415  
    - Notes on the cranial nerves ................................. 415  
  - Higher centres ............................................. 429  
    - Speech .................................................... 432  
    - Upper limbs ............................................... 433  
    - Shoulder girdle examination ............................... 436  
    - Lower limbs ............................................... 437  
    - Notes on the neurological examination of the limbs .... 440  
    - Notes on spinal cord lesions ............................... 448  
    - Dystrophia myotonica ..................................... 455  
    - Gait ....................................................... 456  
    - Cerebellum ................................................ 457  
    - Parkinson’s disease ...................................... 459  
    - Chorea ..................................................... 461  

**Index** ..................................................... 462
Foreword

The business of becoming a specialist physician requires many years of intensive training, but beyond that there is, in Australia and New Zealand, a major hurdle – the examination set by the Royal Australasian College of Physicians. This hurdle is encountered at the end of basic training, and must be passed before the trainee can begin advanced training.

The College of Physicians exam was undoubtedly the most stressful event that many of us practicing physicians had experienced to that point in our lives. Those of us who sat the exam in the years before 1986 (in my case, 1964), when the first edition of Examination Medicine appeared, had no authoritative guidance about how best to approach this ordeal. And an ordeal it certainly was. We can still vividly remember details of the written exam and of our long and short cases. We remember well which examiners were terrifying and which were of a gentler disposition.

Examination Medicine immediately found its niche. It was unapologetically written to help those about to sit the College exam. It was not a textbook of internal medicine, systematically trawling through every known disease of every system. Rather, the knowledge it imparted was particularly directed towards helping the examinee give their best possible performance in the clinical exam, where clinical skills were to be tested, in addition to medical knowledge. One chapter was devoted to requirements for basic training and one to a discussion of the written exam, but the remainder of the book was focused on the approach to the clinical examination, with many examples of the long and short cases likely to be encountered.

Examination Medicine is now, in 2014, in its seventh edition. It has clearly fulfilled a need widely recognized by physician trainees for over 25 years. Not only does it give wise advice about how candidates should prepare themselves, conduct themselves in the exam, use their time to best effect and avoid pitfalls, it also imparts a lot of medical knowledge. One might cavil at the number of long lists encountered, but they can be readily put into context by a trainee physician, if not by a medical student. Overall, trainees will gain a helpful perspective from this volume which will stand them in good stead.

This seventh edition follows the general format of previous editions. It contains many high-quality color illustrations not seen before. There are also newly filmed videos available for both long and short cases to include history-taking and physical examination under the eye of the authors.

This edition of Examination Medicine is both instructive and informative. I have no doubt that it will be welcomed by today’s generation of physician trainees as the preceding editions were by those who went before.

Richard Smallwood
AO MBBS, MD(Melb), Hon DMedSc(Melb), FRACP, FRCP, FACP(Hon), FAMM(Hon), FAMS(Hon)
Emeritus Professor of Medicine, Professorial Fellow at the University of Melbourne
Preface to the 7th edition

This book is written to help candidates sitting for the Royal Australasian College of Physicians (Part One) examination ... It is the masterly application of clinical skills, as well as the breadth of theoretical knowledge that makes a doctor a consultant physician whose advice is sought after by his or her colleagues. We hope this book will help candidates understand what it means to be a physician.

When we wrote this preface to the first edition of Examination Medicine in 1985 neither of us imagined there would be a need to write a preface for a 7th edition nearly 30 years later. Both the FRACP clinical examination and the book have been remarkably enduring. The exam now lasts a whole day instead of half a one, and this book has evolved too (or at least become longer). However, the primary function of the exam, to select people to progress to advanced training and become specialist physicians, has not changed. We still believe strongly that to be successful in the examination, candidates need to understand what it means to be a specialist physician.

FRACP training has an international reputation as one of the most difficult and rigorous in the world. There is no doubt in our view that the exam has become fairer, but it remains very difficult. Up to now attempts to replace the clinical exam with only a written exam or in-training summative assessments have been resisted by the College.

It is the College examiners, a remarkable group of talented and dedicated physicians who have supported the clinical exam with their time and thoughtful approach, who have ensured the exam has academic rigour. There is a genuine feeling among examiners that the exam must be fair, but that standards should remain very high. One question examiners often ask themselves is: ‘Would I want this candidate working as my registrar?’ This means they want candidates to be sensible and safe. Of course, many candidates after being examined must ask themselves, ‘Would I ever want to work as this person’s registrar?’

Preparation is the key to success and to quote Winston Churchill, ‘Never give in. Never. Never. Never.’ When we wrote this book most information for candidates came from stories told to the upcoming cohort by senior registrars who were often given to exaggeration. There is now plenty of information available to candidates. A number of examiners have been concerned by a tendency for candidates to be ‘over-prepared’. By this they mean they hear or see very similar approaches to long and short cases from numerous candidates based on a formula, rather than taking into account the individual case. Practising medicine of the highest standard is both art and science; physicians are meant to think and think deeply. A mature clinical approach requires you to understand each patient’s unique personal and social environment, and complex medical problem-solving must be considered in this context. Use this book as a help for your preparation, not something to be learned by heart.

To quote from the end of the 1985 preface ‘we sincerely hope our contribution will minimise the pain of preparing for the FRACP (Part One) examination’. 1

Nicholas J. Talley
Simon O'Connor
Newcastle and Canberra, 2014

1 There has not been a part two exam for a very long time.
Chapter 5

The cardiovascular long case

A rule of thumb in the matter of medical advice is to take everything any doctor says with a grain of aspirin.

Goodman Ace (1899–1982)

Ischaemic heart disease

Patients with recent acute coronary syndromes, including myocardial infarction, are always available for long cases if required. Many patients with more exotic medical problems will also have ischaemic heart disease. The whims of the long-case examiners may lead to concentrated questioning about the ischaemic heart disease of a patient in hospital for the management of, say, renal transplant rejection. These patients are more likely to present management rather than diagnostic problems once they reach the status of long-case patients.

There have been important changes in the classification of patients with episodes of acute coronary ischaemia. These are based on electrocardiogram (ECG) changes and on the detection of markers of myocardial damage (troponins), which have prognostic as well as diagnostic usefulness for patients with chest pain. Patients with chest pain and raised troponin levels have had a myocardial infarction, even if the creatine kinase level is not elevated. Those who present with chest pain and ECG changes of ST elevation have an ST elevation myocardial infarction (STEMI). Those without ST elevation are said to have a non-ST elevation acute coronary syndrome (NSTEMI), but once abnormal cardiac markers have been detected the diagnosis can be revised to a non-ST elevation myocardial infarction (non-STEMI). The diagnosis unstable angina is no longer part of this classification, but is still often used to describe patients with increasing exertional angina.

Patients with ST elevation benefit from urgent action to re-open the blocked coronary artery (angioplasty or thrombolytic treatment). Those with non-STEMI are usually treated medically in the first instance. The presence of abnormal cardiac markers indicates an adverse prognosis (increased risk of further infarction or death) and these patients benefit from early but not immediate intervention (angioplasty or coronary surgery) and from immediate aggressive anti-platelet treatment and anticoagulation with fractionated or
unfractionated heparin. Non-STEMI patients who have ST depression on the ECG have a worse prognosis than those with T wave inversion or flattening. The concept of risk stratification is based on these factors and determines the urgency and type of treatment.

**The history**

1. Find out whether the patient has been or is in hospital because of a recent myocardial infarction or an acute coronary syndrome or for some other cardiac or non-cardiac reason. The patients with the worst prognosis are those with chest pain and ECG changes at rest (see Table 5.1). Clearly, these may represent different pathophysiological states, varying from occlusion of a coronary artery and inadequate collateral flow to rupture of a lipid-rich plaque with thrombus formation. Ask about obvious precipitating factors, such as a gastrointestinal bleed or the onset of an arrhythmia. Questions need to be asked about the character of the chest pain and what precipitated the admission. Remember that the diagnosis of angina can be suspected from the history, but needs to be established by investigations – an abnormal ECG or exercise test at least. You should be suspicious of the diagnosis unless it has been confirmed by investigations. The most common differential diagnosis is gastro-oesophageal reflux disease (GORD). This can be difficult to prove without endoscopy (and, if normal, oesophageal pH testing), but an excellent response to a trial of a proton pump inhibitor (PPI) is very suggestive. Oesophageal spasm is another cause of central chest pain.

2. Detail the patient’s current treatment. Oral medications will probably include:
   - aspirin with or without an ADP inhibitor (clopidogrel, prasugrel)
   - a beta-blocker or occasionally a calcium antagonist
   - nitrates (intravenous, oral or topical)
   - statin
   - an angiotensin-converting enzyme (ACE) inhibitor or angiotensin II receptor (AR) blocker (ARB).

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<table>
<thead>
<tr>
<th>Table 5.1 Risk stratification in patients with ischaemic chest pain at rest</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>HIGHEST TO LOWEST RISK</strong></td>
</tr>
<tr>
<td>1. ST elevation myocardial infarction</td>
</tr>
<tr>
<td>2. ST depression</td>
</tr>
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<td>3. T wave inversion</td>
</tr>
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<td>4. Non-specific ST–T wave changes</td>
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<tr>
<td>5. Normal ECG</td>
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<tr>
<td>- The risk is higher in each group if cardiac biomarkers (troponins) are elevated.</td>
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<tr>
<td>- The risk is higher in each group for patients with previous ischaemic heart disease or diabetes.</td>
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<tr>
<td>- The higher the risk, the more the benefit of aggressive treatment.</td>
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</tbody>
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**MANAGEMENT HISTORY**

1. Acute coronary syndromes are managed with heparin and aspirin and clopidogrel or prasugrel. Remember that prasugrel should not be used in patients older than 75.

   Thrombolytic treatment is not effective for NSTEACS. This is possibly because acute coronary syndromes are not a single pathological entity and also because a state of increased thrombogenesis may follow initial thrombolysis with these drugs.

   Most patients have early angiography (within 48 hours) with the intention of angioplasty to the culprit lesion if this is practical. Ask whether the patient knows details of what investigations or treatment were performed.
2. If the patient has had an infarct during this or previous admissions find out about the management, which may have included primary angioplasty or thrombolysis, and treatment of complications such as arrhythmias, cardiac failure, further angina and embolic events.

3. In many hospitals a comprehensive cardiac rehabilitation program will have been offered to the patient. Ask whether this has been helpful and ask about the hospital staff’s explanations to the patient about his or her condition and prognosis. Also ask questions about the effect of this illness on the patient’s life and work.

4. Next ask standard questions about risk factors in addition to age and male sex. Remember that risk factors are of vital importance to long-term prognosis, but add little to the likelihood that undiagnosed chest pain is ischaemic. Risk factors include:
   - previous ischaemic heart disease
   - hyperlipidaemia
   - diabetes mellitus (the increased risk in these patients is as high as that in non-diabetics who have already had an ischaemic event)
   - hypertension
   - family history (in particular, first-degree relatives with ischaemic heart disease before the age of 60; 92-year-old great-uncles with heart trouble do not count)
   - smoking
   - use of oral contraceptives or premature onset of menopause
   - obesity and physical inactivity
   - high serum homocysteine levels, which may have been measured if the patient has premature coronary disease and few other risk factors – levels in the top population quintile increase coronary risk twofold; trials of treatment (mostly with folate), however, have been negative and routine treatment is not recommended
   - long-term use, in high doses, of cyclo-oxygenase 2 (COX-2) inhibitors or other non-steroidal anti-inflammatory drugs (NSAIDs) (which should be stopped)
   - erectile dysfunction (which often precedes symptomatic ischaemic heart disease and is a marker of endothelial dysfunction). Remember that the presence of multiple risk factors is more than additive.

5. Then find out whether risk factor control has been successful. Remember the important results of recent secondary prevention trials.
   a. Aggressive cholesterol lowering to below a level of 4 mmol/L of total cholesterol (LDL <1.8) is now considered appropriate for patients with established coronary disease.
   b. There is some evidence that statins have beneficial effects beyond their effect on cholesterol levels (pleotrophic effects).

6. Find out what investigations the patient can remember.
   a. An echocardiogram may have been performed to assess ventricular function and possible complications of infarction, such as a pericardial collection, a left ventricular thrombus, mitral regurgitation or a ventricular septal defect (VSD).
   b. An exercise test, a sestamibi or a stress echocardiogram may have been performed to assess ischaemia or myocardial viability (MRI scan).
   c. Cardiac catheterisation is perhaps the most memorable of the investigations for ischaemic heart disease. The patient may know how many coronaries are abnormal and whether angioplasty was performed. Ask whether a drug-eluting stent (DES) was used and for how long dual anti-platelet treatment was recommended. Remember clopidogrel, and most PPIs, use the same metabolic pathway in the liver and if used together may result in a theoretical loss of anti-platelet benefit. The clinical relevance of this is disputed.
7. Complications such as acute mitral regurgitation or an infarct-related VSD are usually treated surgically but have a relatively poor prognosis. All complications are less common if early coronary patency and normal flow have been achieved.

**The examination**
Examine the cardiovascular system (Ch 16).

1. Note the presence of intravenous treatment. This might include heparin, nitrates, inotropes, vaspressors or antiarrhythmic drugs.
2. Record the blood pressure.
3. Look for signs of valvular heart disease, cardiac failure, rhythm disturbances (e.g. atrial fibrillation, frequent ectopic beats) and murmurs suggesting mitral regurgitation or a VSD caused by an infarct.
4. There may be spectacular bruises at venepuncture or femoral puncture sites if the patient has had thrombolytic treatment. Abdominal wall bruising suggests subcutaneous low-molecular-weight heparin therapy, and a bruise (sometimes very large) over one of the femoral arteries suggests cardiac catheterisation or angioplasty. If radial angiography was performed there may be a bruise over the radial artery at the wrist. Occasionally the radial pulse may be absent. More general complications include a stroke owing to embolism from the heart.

**Management**
It is best to concentrate on discussing the management of the presenting problem. If the patient has only recently been admitted with an infarct, this means a discussion of thrombolysis and primary angioplasty.

1. Candidates should have some knowledge of the major thrombolysis and angioplasty trials.
   a. These have shown that early treatment has improved mortality. Treatment up to 12 hours after the onset of an infarct is worthwhile.
   b. The indications and contraindications to the use of these techniques need to be well understood. The major differences between streptokinase and the fibrin-specific drugs (tPA (alteplase) or reteplase) are important. Streptokinase is much cheaper. Alteplase and reteplase have been shown to produce a small survival advantage, probably because they are more effective in opening occluded vessels, but have a slightly increased risk of causing cerebral haemorrhage. Alteplase is the drug of choice for patients who have had a previous dose of streptokinase more than a few days before. This is because antibodies to streptokinase develop within a few days and may cause an allergic reaction to a second dose, thus reducing its effectiveness.
   c. Alteplase is given as a bolus followed by an infusion, and reteplase is given as a double bolus injection with a 30-minute interval. Even when thrombolysis seems successful (resolution of symptoms and ST depression) patients are now routinely transferred so that angiography can be performed as soon as practical.
2. Urgent coronary (primary) angioplasty, if available, is of proven benefit and has been shown to reduce mortality compared with treatment with thrombolytic drugs.
   a. The advantages, theoretical and real, include definite re-opening of the infarct-related artery in more than 90% of patients (compared with <60% of patients given thrombolitics), normal flow in the infarct-related artery in most cases, dilatation and stenting of the offending (culprit) lesion and often removal of clot, very low risk of stroke and shortening of hospital stay, often to only 3 days.
   b. Patients are treated with potent anti-platelet drugs: aspirin, clopidogrel (or prasugrel or ticagrelor) and sometimes with one of the platelet aggregation inhibitors, abciximab or tirofiban. Prasugrel is more rapidly effective than clopidogrel and in
many protocols is now preferred for primary angioplasty patients. Ticagrelor may improve prognosis compared with the other drugs. Its most common side-effect is dyspnoea, which may develop after 5–10 days.

c. There is now trial evidence that transport of patients to a hospital where this procedure can be performed is preferable to treatment with thrombolytic drugs, if transport time is less than 2–3 hours.

d. Rapid transport to the catheter laboratory is important and the ‘door to balloon’ time should be less than 90 minutes when angioplasty is available in the hospital to which the patient presented.

3. If the history has suggested complications resulting from the infarct, these will have to be discussed. Common complications include:
   • ventricular arrhythmias
   • bradyarrhythmias (especially following an inferior infarct)
   • cardiac failure
   • further ischaemia or reinfarction.

It is important to have planned an approach to the management of these problems.

Investigations
These are aimed at assessment of the infarct size, complications and presence of further ischaemia:
1. left ventricular function – echocardiogram, left ventriculogram
2. complications – echocardiogram for valvular regurgitation, left ventricular thrombus, infarct-related VSD
3. further ischaemia – exercise test, sestamibi stress test, cardiac catheterisation
4. viability – MRI scan, sestamibi scan.

Long-term treatment
1. Early revascularisation is of proven benefit for high-risk patients with acute coronary syndromes (ST elevation, troponin elevation).
2. Prognosis is improved with aspirin, beta-blockers and, for large infarcts (ejection fraction <40%), ACE inhibitors and beta-blockers (e.g. carvedilol, bisoprolol and extended-release metoprolol).
3. Patients with three-vessel disease and significant left ventricular damage or with left main coronary artery stenosis benefit prognostically from coronary artery bypass surgery even if their symptoms have settled on medical treatment. Those with tight proximal (before the first diagonal branch) left anterior descending lesions probably also benefit from surgery or angioplasty.
4. Eplerenone, an aldosterone antagonist, is indicated for patients with cardiac failure following an infarct.

Secondary prevention
1. Control of cardiac risk factors is even more important once the presence of coronary artery disease has been established. It should be a routine part of the management of these patients.
2. Dietary advice for weight and lipid reduction may be indicated. Lipid-lowering drug treatment with a statin should be introduced for all patients who can tolerate it. Total cholesterol should be reduced to less than 4.0 mmol/L (aim for the LDL to be below 1.8 mmol/L).
3. Patients should be encouraged to take part in a cardiac rehabilitation program, if this is available, where advice about safe exercise, weight reduction and changes to dietary and smoking habits can be encouraged.
Revascularisation
For some long-case patients with ischaemic heart disease the emphasis will be on revascularisation (coronary surgery or angioplasty). These procedures are so common that many patients with other presenting problems will have had them.

The history
Similar information to that outlined in the ischaemic heart disease long case is required.
1. Careful questioning about risk factor control, both before and after surgery or angioplasty, is very important. The patient should know whether he or she has ever had an infarct and may know whether there was significant left ventricular damage.
2. Find out what procedure (or procedures) the patient has had and whether there has been complete relief of symptoms.
3. If coronary artery surgery was performed, ask how many grafts were inserted and whether internal mammary or other arterial (e.g. radial artery) conduits were used. It may be possible from the history to work out whether surgery was performed to improve symptoms or prognosis (e.g. three-vessel or left main disease), or both.
4. The patient may know how many vessels were dilated if angioplasty was performed and whether stents were inserted. The patient should know whether bare metal stents (BMS) or drug-eluting stents were used. Ask whether the angioplasty was performed in the setting of a myocardial infarction or acute coronary syndrome. Find out for how long dual anti-platelet treatment was prescribed.

The examination
Examine the patient as for the ischaemic heart disease long case.
1. Note the presence of a median sternotomy scar. Patients who have had a left internal mammary artery (LIMA) graft often have a numb patch to the left of the sternum. This may be permanent.
2. Look at the sternal wound for signs of infection; osteomyelitis of the sternum is a rare but disastrous complication of surgery. Look and feel for sternal instability. Sternal wires are often palpable.
3. Examine the arms for the very large scar that results from radial artery harvesting.
4. Examine the legs for saphenous vein harvesting wounds. Infection and breakdown of these wounds are more common than for the sternal wound.

Management
Surgery
Use of the left internal mammary artery to graft the left anterior descending (LAD) coronary artery has been routine for more than 20 years. Other arterial conduits are used less often, but ‘all arterial revascularisation’ is performed routinely in some centres or where saphenous vein grafts (SVGs) are not possible, e.g. previous coronary artery bypass graft (CABG) or varicose veins in both legs and thighs. In these cases the right internal mammary artery (RIMA) may be used, usually to graft the right coronary, or the radial artery is used as a free arterial graft. The RIMA may also be used as a free graft attached to the aorta, if that is necessary to make it reach. There is excellent evidence that left internal mammary artery (LIMA) grafts have a higher long-term patency rate (>90% at 10 years) than SVGs (50% at 10 years). There is less information about other arterial conduits.

In response to the increasing numbers of angioplasty procedures, surgeons have begun to perform fewer invasive bypass procedures. The most widely used alternative is the ‘off-pump’ LIMA graft to the LAD coronary artery. A median sternotomy incision is still used, but the LIMA is attached to the LAD coronary artery on the beating heart.
A ‘Y’ graft from the LIMA to the circumflex and right coronaries can be performed using the RIMA attached to the LIMA. These operations avoid the need for cardiopulmonary bypass, speed recovery and possibly reduce the risk of intraoperative cerebral events. Minimally invasive bypasses are carried out in some centres. A series of lateral chest incisions are used as ports for surgery using thorascopic equipment. The technique is not easy and the chest wound, although small, is not necessarily less painful than a median sternotomy.

Angina may recur at any time after CABG. Very early angina suggests a technical problem, such as mammary artery spasm, thrombosis of an SVG, grafting of the wrong vessel or grafting of the correct vessel, but proximal to the area of stenosis. Sometimes revascularisation may be ‘incomplete’ because one or more vessels were unsuitable for grafting – usually because of distal disease in the target vessel.

Recurrence of angina is more common if risk factors have not been aggressively controlled. Low-dose aspirin has also been shown to prolong graft survival. When angina recurs the patient usually describes symptoms similar in character to the old ones. Recurrent chest aspirin is less likely to be ischaemic.

ANGIOPLASTY

Angioplasty is now performed more often than surgery in many centres. It has not been shown to improve the prognosis for patients with stable angina (COURAGE trial). A number of studies have shown a similar outcome to surgery in patients with three-vessel disease, but at the expense of a higher number of repeat procedures. Diabetics were a subgroup with a worse outcome from angioplasty than from surgery.

Many angioplasties are performed to provide symptom relief for patients with one- or two-vessel disease. Increasingly, however, patients with acute coronary syndromes, and especially those with raised troponin levels, are treated with early angioplasty. There is now good evidence that this group of patients has an improved prognosis (fewer deaths and fewer large infarcts) and a shortened hospital stay when treated aggressively with angioplasty.

The majority (>90%) of dilated vessels are now stented, which has made a considerable difference to the risk of acute closure of the artery or the need for urgent surgery (now a rare event). It has also reduced the clinical restenosis rate (i.e. recurrence of symptoms and angiographic evidence of >50% loss of luminal diameter) from almost 40% to 10%.

Dual anti-platelet treatment with aspirin and clopidogrel or prasugrel has made subacute stent thrombosis a rare event (<1%). Clopidogrel is ideally given for 48 hours before angioplasty and for at least 4 weeks afterwards; 6 months to a year is often recommended for patients who have had an acute coronary syndrome.

For patients treated for an infarct or acute coronary syndrome, a loading dose of 300–600 mg of clopidogrel is given (60 mg of prasugrel), and 6 months to a year of dual anti-platelet treatment is often recommended.

If a drug-eluting stent is used, 1 year or more of dual-platelet treatment is now recommended because of concerns about delayed healing and a risk of late stent thrombosis (about 1% per year). Patients should continue with aspirin forever.

For some primary angioplasties or complicated angioplasties (large dissection or large burden of thrombus), the potent platelet aggregation inhibitor abciximab (a receptor antibody) may be used as a bolus, followed by infusion for some hours. This drug is very effective in preventing closure of the vessel, but is expensive. Abciximab and tirofiban (a small molecule platelet aggregation inhibitor) are very valuable drugs for the management of acute coronary syndromes with angioplasty. Tirofiban has a shorter half-life than abciximab, but should be used for at least 24–48 hours before intervention, unless it is started in the catheter laboratory with a double bolus dose.
Primary angioplasty of the infarct-related artery is the recommended treatment for STEMI if it can be performed in an experienced centre and if there will not be more than 90 minutes additional delay compared with the use of thrombolytic treatment. It results in a lower mortality and shortened hospital stay.

The ‘open artery hypothesis’ suggests that having a patent artery after an infarct is an advantage (possibly because of its effects on remodelling). For this reason occluded arteries may be opened and dilated even late after an infarct, especially if the patient has evidence of persisting ischaemia. However, the Open Artery Trial (OAT) did not show benefit when routine re-opening of the infarct-related artery was performed more than 48 hours after the infarct in the absence of evidence of ischaemia.

Restenosis remains a problem after angioplasty. It is very unusual after 6 months. It is more common in diabetics, in calcified and complex and long lesions, and in dilated vein grafts. A combination of these factors can result in a restenosis rate of more than 60%. Treatment is usually by redilatation and insertion of a drug-eluting stent. Dilatation with a drug coated balloon is a newer option.

Drug-eluting stents have dramatically reduced the incidence of restenosis. The currently available stents have either paclitaxel, everolimus or sirolimus bound via a polymer to the metal surface of the stent. These antineoplastic drugs are eluted for about a month and prevent the migration of smooth muscle cells into the lumen of the vessel that is the cause of restenosis. Very low restenosis rates of a few per cent have been obtained in trials, even when diabetics are included. These stents also seem to be effective in preventing further restenosis when used in a restenosed bare metal stent. Drug-eluting stents are very expensive – about four times the cost of bare metal stents – and the usual indications for their use include long lesions in small vessels, redilatation of restenosis and diabetes. They are not used for patients who may need a surgical procedure within the following 6 months to a year because of the risk of stopping anti-platelet treatment during this period.

Stents do not set off metal detectors and patients can safely have an MRI scan within a month.

**Infecitve endocarditis**

Patients with infective endocarditis stay in hospital for weeks, so they are often available for long cases. The disease presents diagnostic, plus short-term and long-term management problems. Cases combine cardiological, microbiological and immunological problems. The diagnosis is usually known to the patient. An intravenous infusion containing antibiotics is a valuable clue.

**The history**

Ask about:

1. details of presenting symptoms (e.g. malaise, fever, symptoms of anaemia)
2. symptoms suggesting embolic phenomena to large vessels (e.g. brain, viscera) or small vessels (e.g. kidney, with haematuria or loin pain)
3. recent dental, endoscopic or operative procedures – a precipitating event is identified in only about 5% of cases (the time between procedure and diagnosis may be up to 3 months); remember that *Streptococcus bovis* or *Clostridium septicum* endocarditis is associated with colonic cancer and these patients all deserve a colonoscopy!
4. use of antibiotics for prophylaxis, either before an invasive procedure or for rheumatic fever, or both
5. a past history of rheumatic fever
6. a history of other heart disease or heart operations, especially valve replacement
7. a history of intravenous drug abuse, particularly for its association with tricuspid and pulmonary valve infection
8. antibiotic allergies
9. how the diagnosis was made – including the number of blood cultures and the use of transthoracic or transoesophageal echocardiography (TOE)
10. management since admission to hospital, including the names of the antibiotics used, the duration of treatment and whether the possibility of valve replacement has been discussed
11. a history of other major diseases, particularly those associated with immune suppression, such as renal transplantation or steroid use.

The examination
1. Start by examining for the peripheral stigmata of endocarditis.
   a. Hands:
      • clubbing
      • splinter haemorrhages (Fig 5.1)
      • Osler’s nodes on the finger pulp (these are always painful and palpable, are probably an embolic phenomenon and are rare)
      • Janeway lesions (non-tender erythematous maculopapular lesions containing bacteria on the palms or pulps, which are rare).

Figure 5.1 Splinter haemorrhages.

b. **Eyes:** Roth’s spots in the fundus (Fig 5.2), conjunctival petechiae.

c. **Abdomen:** splenomegaly (a late sign).

d. **Urine analysis** for haematuria and proteinuria.

e. **Neurological signs** of embolic disease.

f. **Joints** (occasionally resembles rheumatic fever pattern).

2. Next examine the **heart.** Assess for predisposing cardiac lesions. These are, in order:

   a. acquired:
      - prosthetic valve (mechanical)
      - mitral regurgitation, mitral stenosis
      - aortic stenosis
      - aortic regurgitation
      - prosthetic valve (tissue)
      - repaired mitral valve
      - mitral valve prolapse with mitral regurgitation.

   b. congenital:
      - bicuspid aortic valve
      - patent ductus arteriosus
      - ventricular septal defect
      - coarctation of the aorta.

Remember:

- an atrial septal defect of the secundum type is almost never affected
- 20% of endocarditis patients have no recognised underlying cardiac abnormality
- coronary stents and pacemaker leads do not appear to involve any risk of endocarditis.

3. Examine for the signs of cardiac failure. Look for signs of a prosthetic valve and for scars that may be present from previous valvotomy or repair operations.

4. Look for a source of infection and take the patient’s temperature.

**Investigations**

1. **Three to six blood cultures** (at least) over 24 hours (98% of culture-positive cases will give positive results in the first three bottles).
2. **Full blood count and erythrocyte sedimentation rate (ESR).** Look for anaemia (normochromic, normocytic), neutrophilia, an elevated ESR, which may be >100 mm/h and a raised C-reactive protein (CRP) level. The ESR tends to remain elevated for months, even when treatment has been successful, but the CRP level falls quite quickly and may be useful for assessing the effectiveness of treatment.

3. **Renal function.** A freshly spun urine sample will often show red cell casts but is rarely assessed these days.

4. **Chest X-ray film.** Look for left or right ventricular hypertrophy, increased pulmonary artery markings, Kerley’s B lines, frank cardiac failure and valve calcification (lateral film). The onset of heart failure is a poor prognostic sign.

5. **ECG.** Atrial fibrillation in the elderly (particularly common) and conduction defects may occur, but are not specific.

6. **Echocardiography** (Fig 5.3) *(2-D and Doppler).* Vegetations must be larger than 2 mm to be detected. This procedure cannot distinguish active from inactive lesions. Vegetations are seen in approximately 40% of cases. They tend to occur downstream of the abnormal jet, e.g. on the aortic surface of the aortic valve in cases of aortic stenosis and endocarditis. Colour Doppler examination is a very sensitive means of detecting new valvular regurgitation, which may be an important sign of endocarditis. **Transoesophageal echocardiography** allows better definition of valvular involvement and is more likely to detect vegetations. Perhaps more importantly, it is much more likely to detect such complications as valve abscesses. It is now in routine use for the assessment of endocarditis. Its use is routine in cases of known or suspected endocarditis.

7. **Serological tests.** These include tests for immune complexes and classical pathway activation of complement causing low C3, C4 and CH50 levels. The test for rheumatoid factor gives positive results in 50% of cases and that for antinuclear antibody in 20% of cases.

**Notes**

**ORGANISMS**

Streptococci account for approximately half of these infections.

1. **Streptococcus viridans** *(non-haemolytic)* – usually presents subacutely. The names of the viridans streptococci are subject to frequent revision but current important types for endocarditis include *S. sanguinis, S. gordonii* and *S. mitis.*

2. **Streptococcus faecalis** – traditionally more common in older men with prostatism and younger women with urinary tract infections, but now in intravenous drug users.

3. **Streptococcus bovis** – associated with colon polyps and carcinoma.

4. **Staphylococcus aureus** – particularly in drug addicts; usually presents acutely. Note, though, that only a small minority of *S. aureus* bacteraemias are associated with endocarditis.

5. **Staphylococcus epidermidis** – more common in patients with recent valve replacement but can be a contaminant in blood cultures.

6. Gram-negative coccobicacilli – rarely a cause; more common with prosthetic valves. The responsible organisms are called the HACEK group:
   - **Haemophilus**
   - **Actinobacillus**
   - **Cardiobacterium hominis**
   - **Eikenella** spp.
   - **Kingella kingae**

7. **Fungi** *(e.g. Candida, Aspergillus)* – particularly in drug addicts and immuno-suppressed patients.
Echocardiography Report

**Reason for study:** AR ?, endocarditis

**Study quality:** Good Satisfactory Poor

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**Valves**

- **Mitral:** Mild MR
- **Tricus.** Mild TR
- **Aortic:** Thickened, bicuspid
- **Pulm.** Appears normal

**Doppler – 2D**

The left ventricle is dilated. The fractional shortening is in the normal range. The aortic valve is thickened and probably bicuspid. A mobile mass 2 mm in diameter is visible on the LV side of the valve and represents a probable vegetation.

**Doppler – colour flow mapping**

There is no aortic gradient. A large jet of aortic regurgitation is present, extending three-quarters of the way into the LV cavity. Mild-to-moderate MR is present. Mild TR. RV pressure = 28 mmHg.

**Conclusions**

Severe AR, probable vegetation, bicuspid valve.

**Comment**

The diagnosis of endocarditis cannot really be made on the basis of echocardiography alone. Even what appears to be a vegetation may be sterile. Nevertheless, a mobile mass attached to a valve in a patient with positive blood cultures makes the diagnosis of endocarditis almost certain.

An abnormal echocardiogram adds weight to the diagnosis. It also enables detection of left ventricular enlargement, which suggests haemodynamic compromise. Serial echocardiograms allow assessment of the treatment of endocarditis and help with the decision about the timing of possible surgery.

The underlying valve abnormality may be obvious. Here the aortic valve is congenitally bicuspid.

More detailed analysis of the heart is possible with transoesophageal echocardiography, which is now routine in cases of endocarditis. It enables smaller vegetations to be identified, as well as complications, such as valve ring abscesses.

**Key**

- AR = aortic regurgitation; EF = ejection fraction; FS = fractional shortening; LA = left atrium; LVEDD = left ventricular end-diastolic dimension; LVESD = left ventricular end-systolic dimension; LVPW = left ventricular posterior wall; MR = mitral regurgitation; Pulm. = pulmonary; RV = right ventricle; Sept. = septal thickness; TR = tricuspid regurgitation; Tricus. = tricuspid.

*Figure 5.3* Echocardiography report in a patient with possible infective endocarditis
CAUSES OF CULTURE-NEGATIVE ENDOCARDITIS

Note: This diagnosis should be made with caution. It condemns a patient to prolonged treatment with intravenous antibiotics.

1. Previous use of antibiotics.
2. Exotic organisms (e.g. *Haemophilus parainfluenzae*, histoplasmosis, *Brucella*, *Candida*, Q fever).
3. Right-sided endocarditis (rarely).

POST-VALVE SURGERY ENDOCARDITIS

Early infection is acquired at operation; late infection occurs from another source. This condition has a worse prognosis than native valve endocarditis.

Diagnosis

The diagnosis is usually a clinical one. The Duke criteria are often used to assist. Two major criteria, one major and three minor, or five minor criteria secure the diagnosis.

**MAJOR CRITERIA**

1. Typical organisms in two separate blood cultures.
2. Evidence of endocardial involvement: echocardiogram showing a mobile intracardiac mass on a valve or in the path of a regurgitant jet, or an abscess or new valvular regurgitation.

**MINOR CRITERIA**

1. Predisposing cardiac condition or intravenous drug use.
2. Fever.
3. Vascular phenomena or stigmata.
4. Serological or acute phase abnormalities.
5. Echocardiogram abnormal, but not meeting above criteria.

Treatment

Early involvement in the management by a cardiac surgeon in a cardiac surgical unit is usually indicated, particularly for staphylococcal infection.

1. Intravenous administration of a bactericidal antibiotic. If the organism is a sensitive *S. viridans*, give benzylpenicillin, 6–12 g daily for 4–6 weeks. If it is an enterococcus, at least 4 weeks of intravenous treatment is necessary and the choice of antibiotic depends on the organism's sensitivity. For prosthetic valves, 6–8 weeks of intravenous treatment is necessary.
2. Follow the progress by looking at the temperature chart, serological results and haemoglobin values.
3. The decision to go on to valve replacement is a difficult one; it is best made with the assistance of a cardiac surgeon who has been involved from the start. Indications for surgery include:
   a. resistant organisms (e.g. fungi)
   b. valvular dysfunction causing moderate-to-severe cardiac failure (e.g. acute severe aortic regurgitation)
   c. persistently positive blood cultures in spite of treatment
   d. invasive paravalvular infection causing conduction disturbances, or a paravalvular abscess or fistula (detected by TOE)
   e. recurrent major embolic phenomena, although this is controversial (an isolated vegetation is not in itself an indication for surgery).
Factors suggesting a poorer prognosis
1. Shock.
2. Congestive cardiac failure.
3. Extreme age.
4. Aortic valve or multiple valve involvement.
5. Multiple organisms.
6. Culture-negative endocarditis.
8. Prosthetic valve involvement.

Differential diagnosis
1. Atrial myxoma.
2. Occult malignant neoplasm.
4. Polyarteritis nodosa.
5. Post-streptococcal glomerulonephritis.
6. Pyrexia of unknown origin.
7. Cardiac thrombus.

Prognosis
Prior to antibiotic use, this was an invariably fatal disease. Currently, more than 70% of patients with endogenous infection survive, as do 50% of those with a prosthetic valve infection. Intravenous drug users have a good prognosis.

Prophylaxis
Confusion between rheumatic fever and endocarditis prophylaxis is common. Rheumatic fever prophylaxis consists of long-term, low-dose antibiotic administration. Prophylaxis against endocarditis requires high-dose, short-term treatment only in patients with a very high risk, namely a previous episode of endocarditis, a prosthetic heart valve, a congenital heart malformation (unrepaired cyanotic heart disease, repaired cyanotic heart disease with residual defects or recent surgery within 6 months) or a cardiac transplant with valve disease. According to the latest 2007 American Heart Association guidelines, all other lesions no longer require prophylaxis.

Prophylaxis is also recommended according to the Australian (Heart Foundation) guidelines for:
- complex congenital heart disease, including patients who have had repair operations using shunts or artificial material and have persisting shunts (e.g. VSD repaired with Gortex, but with residual shunt)
- Aboriginal patients with any intermediate or high-risk lesion.

Prophylaxis regimens are as follows (recommendations from Therapeutic Guidelines – Antibiotic):
1. Dental procedures (e.g. gum cleaning) or oral surgery – amoxycillin 2 g, 1 hour before the procedure. For patients unable to take oral antibiotics, use ampicillin IV or IM just before the procedure. If the risk is high, give ampicillin and gentamicin as described below. For those allergic to penicillin, clindamycin 600 mg given orally 1 hour before the procedure is adequate.
2. Gastrointestinal or genitourinary procedures: no prophylaxis is recommended.
Remember that the effectiveness of antibiotic prophylaxis has not been proven. Patients need to be reminded of the need for good dental hygiene and regular dental review.

**Congestive cardiac failure**

This is a common therapeutic problem, but it may be a diagnostic problem. It is uncommonly the only major problem in a long case.

**The history**

1. It is important first to find out what may have precipitated episodes of cardiac failure. Precipitating problems include:
   a. arrhythmias (especially atrial fibrillation)
   b. discontinuation of medications – usually the diuretic (particularly important)
   c. myocardial infarction
   d. anaemia
   e. infection and fever
   f. thyrotoxicosis
   g. anaesthesia and surgery
   h. pulmonary embolism
   i. high salt intake, drugs that cause salt and water retention (e.g. traditional NSAIDs, COX-2 inhibitors) or excessive physical exertion
   j. pregnancy.

   *Note: Chronic lung disease can be a cause of, or a precipitating factor for, right and left ventricular failure.*

2. Then ask about the symptoms of left ventricular failure (e.g. dyspnoea, orthopnoea, paroxysmal nocturnal dyspnoea) and right ventricular failure (e.g. oedema, ascites, anorexia and nausea). Ask about symptoms of ischaemic heart disease (e.g. angina). These may help distinguish dyspnoea caused by lung disease from that caused by cardiac failure.

3. Enquire about the history of previous heart disease:
   a. hypertension
   b. ischaemic heart disease – infarcts, angina
   c. rheumatic or other valve disease
   d. congenital heart disease
   e. cardiomyopathy
   f. previous cardiac surgery (e.g. coronary artery bypass grafting, valve replacement or resection of an aneurysm)
   g. cardiac transplantation.

4. Find out about coronary risk factors, in addition to age and male sex, including:
   a. hyperlipidaemia
   b. hypertension
   c. smoking
   d. diabetes mellitus
   e. family history of early coronary heart disease
   f. use of oral contraceptives or premature onset of menopause
   g. obesity
   h. physical inactivity.

5. Ascertain the risk factors for dilated cardiomyopathy:
   a. excessive alcohol intake
   b. family history of cardiomyopathy
   c. haemochromatosis.
6. Ask what medications are currently being taken.
7. Ask what investigations have been undertaken – particularly echocardiography, stress ECG testing, nuclear studies and cardiac catheterisation.
8. Find out how the disease affects the patient’s life and ability to cope at home (e.g., climbing stairs, sexual difficulties, etc.). Remember to classify the patient according to the New York Heart Association (NYHA) guidelines.

**NYHA classification**

| I  | No limitation of physical activity. Ordinary physical activity does not cause angina/dyspnoea. |
| II | Angina/dyspnoea on mild activity. |
| III| Angina/dyspnoea on moderate activity. |
| IV | Angina/dyspnoea at rest. |

**The examination**

1. Perform a detailed cardiovascular system examination.
2. Look particularly for signs of cardiac failure, the underlying causes of the problem and any precipitating factors (see Fig 5.4).
3. Look for a pacemaker or defibrillator box.
4. Note wasting as a result of cardiac cachexia.
5. Take the blood pressure lying and standing. Treatment with ACE inhibitors and beta-blockers often results in mild hypotension.

![Figure 5.4 Extremely lateral position of IJV, found with ultrasound.](image-url)

Investigations

1. **Chest X-ray film** (see Fig 5.5). Look for cardiomegaly and chamber size (e.g. left atrium), cardiac aneurysm, valve calcification, sternal wires suggesting previous cardiac surgery, signs of lung disease and pulmonary congestion.

![Chest X-ray](image)

**Figure 5.5** Alveolar pulmonary oedema. When the pulmonary venous pressure reaches 30 mmHg, oedema fluid will pass into the alveoli. This causes shadowing (patchy to confluent depending on the extent) in the lung fields. This usually occurs first around the hila and gives a bat’s wing appearance. These changes are usually superimposed on interstitial oedema. A lamellar pleural effusion (arrow) is seen at the right costophrenic angle where Kerley ‘B’ lines are also evident.

2. **ECG.** Look for arrhythmias, signs of ischaemia or recent or old infarction (Fig 5.6), left ventricular hypertrophy and persisting ST elevation (aneurysm). Left bundle branch block is a common ECG finding in these patients (Fig 5.7). The ECG is rarely entirely normal in a patient with heart failure.

3. **Electrolytes and creatinine levels.** To exclude hypokalaemia (as a cause of arrhythmia), hyponatraemia (which may indicate severe longstanding cardiac failure, a poor prognostic sign) and renal failure.

4. **B-type natriuretic peptide level (BNP; previously called brain natriuretic peptide).** Although there is doubt about the reference range, a definitely elevated level may help distinguish cardiac from non-cardiac dyspnoea. Since BNP falls when heart failure is treated, trials of monitoring BNP are underway as a means of assessing the adequacy of cardiac treatment.

5. **Haemoglobin value.** To exclude anaemia as a precipitating cause.
If the diagnosis is not already obvious, consider dilated cardiomyopathy. Investigations include those outlined below.

1. **Echocardiography** (Fig 5.8). This will show generalised or segmental wall motion abnormalities and reduced fractional shortening. An estimate of the left ventricular ejection fraction can be made. Segmental hypokinesia suggests that ischaemia is the
cause of the cardiac failure. Doppler echocardiography will usually show at least some mitral and tricuspid regurgitation in these patients. The presence of more severe valvular disease suggests a different aetiology for the cardiac failure. Serial echocardiograph measurements of left and right ventricular dimensions can be useful for following the patient’s progress.

2. A gated blood pool scan for the ejection fraction. The right ventricular ejection fraction is normally >45% and the left ventricular ejection fraction is >50%. The scan will also show whether hypokinesis is global or segmental and to what extent the right ventricle is affected.

3. Coronary angiography. This is often necessary to exclude coronary artery disease.

4. Right ventricular biopsy. This may help determine the aetiology in selected patients.

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**Echocardiography Report**

**Reason for study:** Assess left ventricular function, cardiac failure

**Study quality:** Good Satisfactory Poor

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**Valves**

- **Mitral**  Mild-to-moderate MR
- **Tricus.** Mild TR
- **Aortic**  Thickened, not stenosed
- **Pulm.**  Appears normal

**Doppler – 2-D**

The left ventricle is dilated. There is extensive antero-apical hypokinesis. The aortic valve is slightly thickened and there is mitral annular calcification. The mitral valve is not stenosed and there is no mitral valve prolapse.

**Doppler – colour flow mapping**

There is no aortic gradient; mild-to-moderate MR is present. MR jet to two-thirds of LA. Mild TR. RV pressure = 38 mmHg.

**Conclusions**

Severe segmental LV dysfunction; moderate MR.

**Comments**

This echocardiography report demonstrates the typical findings when a patient has cardiac failure caused by previous anterior myocardial infarction. The left ventricular dysfunction is not global (typical of cardiomyopathy) but involves the infarcted area. There is overall LV dilatation with an increase of the LVEDD. The FS is the percentage change in LV size from diastole to systole measured at the base of the heart. It can be in the normal range despite the presence of LV dysfunction, if the base of the heart is not involved.
The ejection fraction can be estimated from the LVEDD and LVESD measurements. There are a number of formulas, which are applied automatically by the calculation software of the echocardiograph machine. It is difficult to obtain an accurate ejection fraction, which is a volume change measurement on the basis of two 2D-image measurements. These calculated ejection fractions tend to have a higher reference range than those obtained by nuclear heart pool scanning. MR is almost always detected when moderate LV dysfunction is present.

Mitral annular calcification is a common finding in elderly patients; it can be associated with MR, but not with mitral stenosis. The presence of left atrial enlargement suggests that the mitral regurgitation is not acute, but can also be associated with hypertension.

TR is commonly found in patients with heart failure, but may also be present in normal people. Interrogation of the regurgitant jet with continuous wave (CW) Doppler allows measurement of its velocity. This can be used to calculate the pressure difference across the valve. Since the pressure in the right atrium is usually close to 5 mmHg, the pressure in the RV can be calculated by adding 5 to the pressure difference. In this case the pressure difference across the valve is about 33 mmHg.

**Key**

EF = ejection fraction; FS = fractional shortening; LA = left atrium; LVEDD = left ventricular end-diastolic dimension; LVESD = left ventricular end-systolic dimension; LVPW = left ventricular posterior wall; MR = mitral regurgitation; Pulm. = pulmonary; RV = right ventricle; Sept. = septal thickness; TR = tricuspid regurgitation; Tricus. = tricuspid.

**Treatment**

1. Remove precipitating causes. Atrial fibrillation and other incessant tachycardias can be a cause of cardiac failure – tachycardia-induced cardiomyopathy. The prognosis is good if normal heart rate can be restored.

2. Correct underlying causes if possible (e.g. thrombolysis for an acute infarct or coronary artery bypass grafting or angioplasty for ischaemia) (see Table 5.2).

3. Control the failure.
   a. Decrease physical activity (e.g. bed rest for the acutely ill patient).
   b. Control fluid retention (e.g. by diuretics, low-salt diet, fluid restriction (1000–1500 mL for severe failure)).
      - Patients should be advised to weigh themselves daily. An increase in weight of 2 kg or more over a few days is usually an indication of significant fluid retention. A temporary increase in the diuretic dose will often prevent a deterioration in symptoms.
   c. Oppose inappropriate activation of the renin–angiotensin system.
      - ACE inhibitors are considered to be the drug class of choice for cardiac failure as they prolong life; symptomatic hypotension is the major side-effect in cardiac failure. ACE inhibitors are indicated for all classes of heart failure, even for asymptomatic patients with left ventricular dysfunction. Every effort should be made to titrate the dose up to the maximum tolerated. The usual limitation is symptomatic hypotension.
      - AR blockers are indicated for patients intolerant (usually because of cough) of ACE inhibitors. The most common reason for the cessation of ACE inhibitors or AR blockers is deterioration in renal function (usually in patients with renovascular disease).
Renal function may improve again if the ACE inhibitor and diuretic doses are reduced and hypovolaemia is corrected. There is little therapeutic difference between the various ACE inhibitors.

Trials have also demonstrated some additional benefit when ACE inhibitors and AR blockers are combined. The treatment of cardiac failure involves polypharmacy. It is probably only the minority of patients who will be prepared to take an AR blocker, as well as all the other drugs usually prescribed. The combination also seems to increase the risk of acute renal failure and is rarely used.

Add spironolactone. This aldosterone antagonist improves survival in class III or IV patients. It may be especially useful for the management of ascites and peripheral oedema. Hyperkalaemia may be a problem for patients with renal impairment. Start with 12.5 mg per day. Epleronone is a newer aldosterone antagonist indicated for heart failure occurring soon after myocardial infarction.

Asking the patient about the difficulties of adherence with a complicated drug regimen may be useful at this point.

---

**Table 5.2 Causes of ventricular failure**

<table>
<thead>
<tr>
<th>LEFT VENTRICULAR FAILURE</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Volume overload</td>
</tr>
<tr>
<td>a. Aortic regurgitation</td>
</tr>
<tr>
<td>b. Mitral regurgitation</td>
</tr>
<tr>
<td>c. Patent ductus arteriosus</td>
</tr>
<tr>
<td>2. Pressure overload</td>
</tr>
<tr>
<td>a. Systemic hypertension</td>
</tr>
<tr>
<td>b. Aortic stenosis</td>
</tr>
<tr>
<td>3. Myocardial disease</td>
</tr>
<tr>
<td>a. Ischaemic heart disease</td>
</tr>
<tr>
<td>b. Dilated cardiomyopathy – causes include:</td>
</tr>
<tr>
<td>i. idiopathic (most common)</td>
</tr>
<tr>
<td>ii. alcohol</td>
</tr>
<tr>
<td>iii. myocarditis</td>
</tr>
<tr>
<td>iv. familial (autosomal dominant)</td>
</tr>
<tr>
<td>v. tachycardia induced (usually AF)</td>
</tr>
<tr>
<td>vi. peripartum</td>
</tr>
<tr>
<td>vii. neuromuscular disease (e.g. dystrophia myotonica)</td>
</tr>
<tr>
<td>viii. connective tissue disease (e.g. scleroderma)</td>
</tr>
<tr>
<td>ix. haemochromatosis</td>
</tr>
<tr>
<td>x. sarcoidosis</td>
</tr>
<tr>
<td>xi. drugs (e.g. doxorubicin)</td>
</tr>
<tr>
<td>xii. radiation</td>
</tr>
</tbody>
</table>

**Note:** Restrictive cardiomyopathy and hypertrophic cardiomyopathy can be causes of heart failure.

<table>
<thead>
<tr>
<th>RIGHT VENTRICULAR FAILURE</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Volume overload</td>
</tr>
<tr>
<td>a. Atrial septal defect</td>
</tr>
<tr>
<td>b. Tricuspid regurgitation</td>
</tr>
<tr>
<td>2. Pressure overload</td>
</tr>
<tr>
<td>a. Pulmonary stenosis</td>
</tr>
<tr>
<td>b. Pulmonary hypertension</td>
</tr>
<tr>
<td>3. Myocardial disease</td>
</tr>
<tr>
<td>a. Cardiomyopathy secondary to left ventricular failure</td>
</tr>
<tr>
<td>b. Right ventricular infarction (rare)</td>
</tr>
</tbody>
</table>
d. Oppose inappropriate increases in catecholamine drive.
   - Give beta-blockers. Trials with carvedilol, bisoprolol and extended-release metoprolol have shown improvements in symptoms and mortality for this drug used in patients with class II–IV heart failure.
   - The drugs must be introduced at a low dose (e.g. 3.125 or 6.25 mg b.d. of carvedilol or 1.25 mg daily of bisoprolol) and titrated upwards as tolerated to 25 mg b.d. of carvedilol or 10 mg daily of bisoprolol.

e. Increase myocardial contractility (e.g. with digoxin).
   *Note:* The use of digoxin in cardiac failure is again controversial. Recent trials have suggested an increase in symptoms if cardiac failure patients who are in sinus rhythm and on treatment with digoxin, diuretics and ACE inhibitors have their digoxin withdrawn. Re-assessment of digoxin mortality trials have suggested a possible increase in mortality. Patients most likely to benefit symptomatically have more severe heart failure, an S3 gallop, impressive cardiomegaly and an ejection fraction <20%.

f. Intravenous inotropes (e.g. dopamine or dobutamine) may have a place in the short-term treatment of severe cardiac failure. Patients may be admitted for a ‘dobutamine holiday’ (a course of treatment with intravenous dobutamine, usually for about 5 days) and have improved symptoms for some months. Levosimendan is an intravenous drug that works as a calcium channel activator. A 24-hour course may improve symptoms and possibly prognosis. No effective oral inotrope is available.

g. Control rhythm. Remember, cardiac failure has a poor prognosis. About 50% of these patients die suddenly of a ventricular arrhythmia. The detection of high-grade ventricular arrhythmias is an indication for an implanted defibrillator, which is associated with a proven improvement in prognosis. Routine use of these devices in patients with a low ejection fraction has been shown to improve survival, even when ventricular arrhythmias have not been recorded.

h. Cardiac transplantation may now be offered to certain patients. The reduced availability of donor hearts and the improvement of many patients who would otherwise be suitable for transplant with beta-blockers have reduced the frequency of this procedure.

i. Biventricular pacing or cardiac resynchronisation therapy (CRT) is helpful for heart failure patients with very wide QRS complexes. The LV pacing wire is placed via the coronary sinus into one of the left ventricular veins. This complicated procedure enables both ventricles to be paced and dyssynchronous contraction of the ventricles associated with a very wide QRS to be corrected. About 70% of patients improve with the treatment. Although echocardiographic measurements of dyssynchrony are available, they have not yet been able to predict a response to resynchronisation treatment and the current guidelines allow their use for symptomatic patients with LBBB.

j. Ventricular assist devices are sometimes used as a bridge to transplant in very ill patients. Survival for weeks or months is possible with these devices. Trials of entirely artificial hearts continue in small numbers of patients.

Diastolic heart failure (heart failure with preserved ejection fraction)

Most breathless patients with heart failure have abnormal left ventricular systolic function, which is characterised by dilatation and hypokinesis. Some cases of cardiac
failure, however, may be caused by diastolic dysfunction. In such cases, the myocardium is stiff, often because it is hypertrophied and does not relax normally. The condition seems to be more common in elderly patients. Hypertension is a common cause. The diagnosis is difficult, but an echocardiogram will show preserved or increased systolic contraction without dilatation and there may be left ventricular hypertrophy and left atrial dilatation. Doppler echocardiography may show abnormalities of left ventricular filling caused by the stiffness of the ventricle. However, this is not easy to quantify and is dependent on variations in preload and afterload.

The condition may have a prognosis as bad as that of systolic heart failure. Treatment is similar, but beta-blockers are used early and only small doses of diuretics should be required. At least in theory, digoxin should be avoided if the patient is in sinus rhythm. Every effort should be made to control hypertension. Treatment has not been shown to alter prognosis.

Hyperlipidaemia

Hyperlipidaemia may be present in patients under investigation for vascular disease, pancreatitis, hypothyroidism or diabetes mellitus. It often presents both diagnostic and management problems.

The history

1. The patient should be able to indicate whether the main problem is vascular or not. If the problem is one of premature coronary artery disease, hypercholesterolaemia is the likely lipid problem. The most important inherited cause is familial hypercholesterolaemia, which is caused by a defective or absent low-density lipoprotein (LDL) receptor. The heterozygous form occurs in about one person in 500. As the transmission is autosomal dominant, the patient may know of first-degree relatives who have been affected. There may even be family members with the homozygous form. These people usually present with a tenfold elevation in serum cholesterol levels as a result of an increase in plasma LDL levels and have a myocardial infarction before the age of 20 years. People with the heterozygous form typically have myocardial infarctions in their 30s and 40s and have a two- to threefold elevation in cholesterol level. More than 80% of affected men and nearly 60% of affected women have had myocardial infarcts by the age of 60 years. Find out whether the patient has already had a myocardial infarct and which relatives have been affected.

Familial combined hyperlipidaemia is associated with obesity or glucose intolerance and may be expressed as type IIa, IIb or IV hyperlipidaemia (see Table 5.3). This is also an autosomal dominant trait. Patients develop hypercholesterolaemia and often hypertriglyceridaemia in puberty. Once again, there usually is a strong family history of premature coronary artery disease. There is no doubt that an elevated triglyceride level adds to the risk of hypercholesterolaemia.

Familial dysbetalipoproteinaemia is also associated with coronary artery disease. These patients have elevated cholesterol and triglyceride levels and are usually found to have obesity, hypothyroidism or diabetes mellitus. Find out whether there is any history of these and whether there has been atheromatous disease or vascular disease involving the internal carotid arteries and the abdominal aorta or its branches. Ask about claudication, which occurs in about one-third of patients.
Table 5.3 Hyperlipoproteinaemias

<table>
<thead>
<tr>
<th>TYPE</th>
<th>LIPOPROTEIN ELEVATED</th>
<th>ELECTROPHORETIC MOBILITY</th>
<th>MECHANISM</th>
<th>SECONDARY CAUSES</th>
<th>CLINICAL FEATURES</th>
<th>ASSOCIATIONS</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Chylomicrons</td>
<td>Origin</td>
<td>Deficiency</td>
<td>Extrahepatic lipoprotein lipase or apo C-II deficiency</td>
<td>Rarely SLE, Eruptive xanthomata; lipoaemia retinalis</td>
<td>Pancreatitis</td>
</tr>
<tr>
<td>IIa</td>
<td>LDL</td>
<td>β</td>
<td>Receptor defect</td>
<td>Cushing's; hypothyroidism</td>
<td>Xanthelasma; corneal arcus</td>
<td>CAD, PVD</td>
</tr>
<tr>
<td>IIb</td>
<td>LDL &amp; VLDL</td>
<td>β &amp; pre-β</td>
<td>Cholestasis; nephrotic syndrome</td>
<td>Tendon xanthomata (see Fig 5.9)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>III</td>
<td>IDL</td>
<td>Broad β</td>
<td>Oversynthesis and/or abnormal apo E</td>
<td>Renal and liver disease</td>
<td>Palmar crease and tuberoceptive xanthomata; xanthelasma</td>
<td>CAD, PVD</td>
</tr>
<tr>
<td>IV</td>
<td>VLDL</td>
<td>Pre-β</td>
<td>Oversynthesis and/or under catabolism of VLDL</td>
<td>Diabetes mellitus; alcoholism; chronic renal failure</td>
<td>Usually no xanthomata</td>
<td></td>
</tr>
<tr>
<td>V</td>
<td>VLDL &amp; chylomicrons</td>
<td>Origin and pre-β</td>
<td>Saturation lipoprotein lipase by VLDL</td>
<td>As for IV</td>
<td>As for I</td>
<td>As for I</td>
</tr>
</tbody>
</table>

Notes
- Apo A-1 deficiency is associated with the absence of plasma HDL and severe premature CAD.
- Apo B deficiency is the defect in abetalipoproteinaemia (autosomal recessive), which is characterised by haemolytic anaemia (acanthocytosis), fat malabsorption and neurological defects (proprioceptive loss, retinitis pigmentosa).
- LCAT deficiency results in decreased HDL, cloudy corneas and progressive renal disease.

apo = apolipoprotein; CAD = coronary artery disease; HDL = high-density lipoprotein; IDL = intermediate-density lipoprotein; LCAT = lecithin cholesterol acyltransferase; LDL = low-density lipoprotein; PVD = peripheral vascular disease; SLE = systemic lupus erythematosus; VLDL = very-low-density lipoprotein.

2. The patient may be able to tell you his or her cholesterol and triglyceride levels and what they have been in the past. Some patients even know their LDL and high-density lipoprotein (HDL) levels.
3. If there is no history of coronary artery disease and the patient either knows the triglyceride level to have been very high or has a history of pancreatitis, the likely diagnosis is familial hypertriglyceridaemia. This is also a common autosomal dominant disorder and is associated with obesity, hyperglycaemia, hyperinsulinaemia, hypertension and hyperuricaemia. Although there is a slightly increased incidence of atherosclerosis, this is probably related to diabetes mellitus, obesity and hypertension than to the hypertriglyceridaemia itself.
   Ask about the patient’s alcohol consumption, any history of hypothyroidism or the ingestion of oestrogen-containing oral contraceptives. Any of these can precipitate a rapid rise in the triglyceride level, which may precipitate pancreatitis or the characteristic eruptive xanthomas. Between attacks, patients have moderate elevations of the plasma triglyceride level.
4. Next, find out about treatment. In familial hypercholesterolaemia, this will have been aimed at the cholesterol level itself and at any cardiovascular complications that have
occurred. The patient should be well informed about a low saturated fat diet and may be aware of side-effects from medication usage.

5. The need for drug treatment of hyperlipidaemia depends on the lipid levels and on the patient's other vascular risk factors. Ask about a family history of premature coronary disease (first-degree relatives under the age of 60), previous vascular disease (coronary, cerebral or peripheral), smoking and diabetes mellitus.

6. Ask about any history of cutaneous xanthoma. These may have resolved with treatment or been surgically removed.

The examination

1. Examine the cardiovascular system. There may be evidence of cardiac failure from previous myocardial infarcts or a sternotomy scar from previous coronary surgery. Occasionally one sees the scandalous situation of a patient with untreated hyperlipidaemia presenting with more angina after initially successful coronary surgery.

![Images of cutaneous findings](a) Achilles tendon xanthoma. (b) Xanthelasma. (c) Palmar xanthoma. (d) Eruptive xanthomas.

(a) courtesy A F Lant, J Dequeker, London; (b) M Yanoff, J Duker. *Ophthalmology*. 3rd edn. Fig 12-9-18. Mosby, Elsevier, 2009, with permission; (c) and (d) courtesy R A Marsden, St George's Hospital, London.

2. Look specifically for the interesting skin manifestations of these conditions.

a. Patients with the heterozygous or homozygous form of familial hypercholesterolaemia may have *tendon xanthomas*. These are nodular swellings that tend to involve the tendons of the knee, elbow and dorsum of the hand and the Achilles tendon. They consist of massive deposits of cholesterol, probably derived from the deposition of LDL particles. They contain both amorphous extracellular deposits and vacuoles within macrophages, and sometimes become inflamed and cause tendonitis.

b. Cholesterol deposits in the soft tissue of the eyelid cause *xanthelasma* and those in the cornea produce *arcus cornea* (previously insensitively called *arcus senilis*).
Xanthelasma occur in about 1% of the population and arcus cornea in 30% of people over 50. When corneal arcus is seen in younger people it is more often associated with hyperlipidaemia. Surveys of people with xanthelasma indicate a slightly higher than average cholesterol level. Tendon xanthomas are diagnostic of familial hypercholesterolaemia, but the other signs are not as specific – only 50% of people affected have hyperlipidaemia.

The majority of patients with the homozygous form have even more interesting signs.

• Yellow xanthomas may occur at points of trauma and in the webs of the fingers.
• Cholesterol deposits in the aortic valve may be sufficient to cause aortic stenosis, occasionally mitral stenosis and mitral regurgitation can occur for the same reason.
• Painful swollen joints may also be present. Obesity is uncommon in these patients.

c. These skin manifestations may or may not resolve with treatment of the cholesterol level. Surgical treatment is sometimes indicated.

d. Eruptive xanthomas are a sign of hypertriglyceridaemia (levels often over 20 mmol/L). This is type V hyperlipoproteinemia. Eruptive xanthomas occur on pressure areas, such as the elbows and buttocks, and resolve rapidly with treatment. The association here is with pancreatitis. The problem is often hereditary, but exacerbated with obesity, diabetes and alcohol consumption. It is a less definite risk factor for cardiovascular disease. Palmar xanthomata are a sign of dysbetalipoproteinaemia (type III hyperlipoproteinemia). They also resolve with treatment.

3. If the history suggests combined hyperlipidaemia or hypertriglyceridaemia, obesity is likely to be present. Look also for signs of the complications of diabetes mellitus and for signs of hypothyroidism or the nephrotic syndrome (see Table 11.2).

4. In sick patients with hypertriglyceridaemia, there may be signs of acute pancreatitis.

Investigations

1. A cholesterol level over 8 mmol/L with a normal triglyceride level suggests one of the familial hyperlipidaemias. This diagnosis can be confirmed by an assay of the number of LDL receptors on blood lymphocytes. The diagnosis is more often made from a combination of the lipid pattern, the history and the clinical examination (see Table 5.3). The other necessary investigations are those required for coronary artery disease.

2. Investigation of hypertriglyceridaemia includes tests to exclude possible underlying causes, such as hypothyroidism, diabetes mellitus and excessive alcohol intake. In familial hypertriglyceridaemia the plasma triglyceride level tends to be moderately elevated to 3–6 mmol/L (type IV lipoprotein pattern). The cholesterol level is normal. The triglyceride level may rise to values in excess of 12 mmol/L during exacerbations of the condition.

3. Familial combined hyperlipidaemia produces one of three different lipoprotein patterns – hypercholesterolaemia (type IIa), hypertriglyceridaemia (type IV), or both hypercholesterolaemia and hypertriglyceridaemia (type V).

4. Familial dysbetalipoproteinaemia (type III hyperlipoproteinemia) results in the accumulation of large lipoprotein particles containing triglycerides and cholesterol. These particles resemble the remnants and intermediate-density lipoprotein (IDL) particles normally produced from the catabolism of chylomicrons and very-low-density lipoproteins (VLDL). These patients are homozygous for the apolipoprotein E2 (apo-E2) allele, which is unable to bind to hepatic lipoprotein receptors, thus
preventing the rapid hepatic uptake of IDL and chylomicrons. The condition is usually expressed only in patients with hypothyroidism or diabetes mellitus and tests for these disorders are necessary. Apo-E genotyping may sometimes be useful.

Management

1. A combination of diet and treatment of the underlying condition is usually required. Underlying diabetes mellitus and hypothyroidism must be treated.

2. Some patients with dysbetalipoproteinaemia respond dramatically to the introduction of thyroxine. Effective management of the condition tends to cause disappearance of the skin signs and improves the prognosis as far as vascular disease goes. Effective treatment of familial hyperlipidaemia from early adult life delays the onset of coronary artery disease.

3. Treatment is almost always begun with hydroxymethylglutaryl coenzyme A (HMG-CoA) reductase inhibitors (statins, e.g. pravastatin, lovastatin, atorvastatin, rosuvastatin). Except for atorvastatin, these drugs should be taken at night. They are relatively short acting and most cholesterol is manufactured at night. They work by inhibiting the synthesis of cholesterol in the liver by impeding the activity of the rate-limiting enzyme. Patients need to have their liver function checked after about a month. They are effective drugs; total cholesterol levels may be expected to fall at least 30%.

   a. The Four-S trial in Scandinavia was the first of a number of trials to show a definite survival advantage for patients treated with these drugs for secondary prevention (i.e. those patients who have already had an ischaemic event). Secondary prevention trials for high- and intermediate-risk patients have also been positive. It is now clear that patients with existing coronary artery disease or multiple risk factors benefit most from lipid-lowering treatment. Previous concern about an apparent increase in overall mortality associated with lipid lowering seems to have been allayed.

   b. The current indications for drug treatment of cholesterol allow a statin for patients with established symptomatic coronary artery disease at any total cholesterol level.

   c. The most frequent problem with these drugs is the occurrence of myalgias. These are, however, uncommon. The relatively long experience with the statins suggests they are safe in quite large doses and current starting doses are two to four times those used in the past. Atorvastatin and rosuvastatin are the most potent statins and should be the drugs of choice for severe hypercholesterolaemia. All the statins favourably affect the HDL/LDL ratio.

   d. There is controversy about the need to treat levels that are already below 4 mmol/L. There is evidence that there are pleotropic effects of the statins that reduce coronary risk separately from their effect on cholesterol. This also implies that, for secondary prevention, the use of statins may be beneficial for patients whose total cholesterol is below 4 mmol/L before drug treatment.

4. Ezetimibe reduces cholesterol absorption from the gut and thus interrupts its enterohepatic circulation. It does not seem to interfere with the absorption of fat-soluble vitamins. Its effect on cholesterol levels is substantial, although not as great as that of the statins. It is useful for patients who are intolerant of the statins or, when used in combination with a statin, for patients whose cholesterol level is not controlled on a statin alone.

5. Gemfibrozil increases the activity of lipoprotein lipase and is useful in hypertriglyceridaemia resulting from increased VLDL or IDL levels. Its main use is for patients with elevation of both cholesterol and triglyceride levels. Clofibrate is no longer in common use for lipid control.
6. A few patients may be taking one of the bile-sequestering resins – cholestyramine or colestipol. These are less often used as initial treatment now that the HMG-CoA reductase inhibitors (statins) are generally available. Some patients may use a statin and a resin in combination. Resins bind bile salts in the gut so that cholesterol is withdrawn from the circulation by the liver to make more. They are not absorbed, but can cause constipation and flatulence and can block the absorption of other drugs. Patients may need to take up to two sachets (8 g) three times daily.

7. If the cholesterol cannot be brought down to normal levels with diet and a resin, nicotinic acid (which blocks VLDL synthesis) can be added. This is an effective drug and may help block the compensating increase in hepatic cholesterol synthesis that occurs with bile-sequestering resins. It is also used to try to raise HDL levels. Side-effects include flushing, pruritus, abnormal liver function tests, hyperglycaemia and aggravation of peptic ulcer disease. The patient will probably have been begun on a small dose and had this gradually increased as tolerance improved. In practice it is a very difficult drug to use because of its side-effects.

8. A patient with one of the combined hyperlipidaemias is likely to need to lose weight, as well as to control the cholesterol and saturated fat intake, and with dysbetalipoproteinaemia may require treatment for hypothyroidism. All these patients need to avoid alcohol and oral contraceptives. Diet is the mainstay of treatment for reducing triglyceride levels; gemfibrozil or one of the newer fibrates may be used if diet fails.

9. The indications for treatment of hyperlipidaemia with drugs on the Pharmaceutical Benefits Scheme (PBS) are complicated. Total cholesterol, HDL, LDL and triglyceride levels, as well as the presence of other risk factors, are all part of the formula. Candidates should be familiar with the latest PBS rules.

10. A patient with familial hypertriglyceridaemia will have been managed in a similar way and may have required treatment for acute pancreatitis.

11. Patients with homozygous familial hypercholesterolaemia are unlikely to live long enough to be present in clinical examinations, but treatment can sometimes involve repeated plasma exchange and even liver transplantation.

12. When patients have muscle pains on statin treatment, reducing the dose or even giving the drug second daily may be worth trying. However, there are no trials showing that second daily treatment is effective.

Hypertension

Many long cases are likely to provide the examiners with an opportunity to ask about the management of hypertension. Although it is an increasingly complicated subject, it is unlikely to be a patient’s major problem. The examiners will want to hear sensible discussion from the candidate about a number of aspects of hypertension, including the diagnosis, appropriate investigations and approaches to treatment.

The history

1. Many patients are well informed about and very interested in their blood pressure. Find out when the diagnosis was made and what sorts of blood pressure readings were obtained before and after treatment. It is common for measurements to be made in a number of ways and in different settings. Apart from clinic measurements, the patient may have taken and continue to take his or her own blood pressure at home. There may have been ambulatory blood pressure (ABP) recordings made. It seems
clear that hypertensive risk is more closely related to non-clinic and ABP results than to those obtained in the outpatient clinic. ABP should, however, be lower than clinic readings to be considered normal. Measurements of <135/85 mmHg during the day and <120/75 mmHg at night are considered normal for ABP recordings. See Table 5.4 for the current classification of clinic blood pressure levels.

<table>
<thead>
<tr>
<th>CATEGORY</th>
<th>SYSTOLIC (MMHG)</th>
<th>DIASTOLIC (MMHG)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Optimal</td>
<td>&lt;120 and</td>
<td>&lt;80</td>
</tr>
<tr>
<td>Normal</td>
<td>120–129 and/or</td>
<td>80–84</td>
</tr>
<tr>
<td>High normal</td>
<td>130–139 and/or</td>
<td>85–89</td>
</tr>
<tr>
<td>Mild hypertension (grade 1)</td>
<td>140–159 and/or</td>
<td>90–99</td>
</tr>
<tr>
<td>Moderate hypertension (grade 2)</td>
<td>160–179 and/or</td>
<td>100–109</td>
</tr>
<tr>
<td>Severe hypertension (grade 3)</td>
<td>≥180 and/or</td>
<td>≥110</td>
</tr>
<tr>
<td>Isolated systolic hypertension</td>
<td>&gt;140 and</td>
<td>&lt;90</td>
</tr>
</tbody>
</table>


2. Ask about current and past antihypertensive treatment and about problems or side-effects caused by treatment. Next find out about possible complications of hypertension. These include stroke, heart failure, peripheral vascular disease and renal failure.

3. Occasionally there may be symptoms that suggest a secondary cause of hypertension: paroxysmal sweating, palpitations and headache (phaeochromocytoma) or daytime sleepiness (sleep apnoea). Rarely, the patient may be aware of a diagnosis of renal artery stenosis, coarctation of the aorta or an adrenal tumour. Primary hyperaldosteronism is now more often recognised.

4. Ask about other risk factors for vascular disease, especially type 2 diabetes, but also hyperlipidaemia, a family history of premature coronary disease or stroke. The presence of any of these conditions, or of existing heart failure, coronary or cerebrovascular disease, is a strong indication for treatment.

5. There are often a number of factors that contribute to the problem. These include obesity, excess alcohol consumption, lack of physical exercise and a high salt intake. Other factors, such as cigarette smoking, add to the patient’s overall risk. Ask what the patient knows about these factors and what efforts (if any) have been made to correct them. Some racial groups have a high risk of premature vascular disease and will benefit more from early and aggressive treatment. These include Aboriginal Australians, Torres Strait Islanders and Pacific Islanders.

The examination

Investigations

1. Test the urine for protein. Measure the serum electrolyte and creatinine, blood sugar, cholesterol and haemoglobin levels.

2. Note the serum potassium. The presence of hypokalaemia in patients who are not on diuretics should prompt investigations for primary aldosteronism. Measurement of plasma renin activity (PRA) and plasma aldosterone (PA) levels may be indicated. A high PA level and a low PRA level leading to a high aldosterone:renin ratio is consistent
with primary hyperaldosteronism. The test is better performed off treatment. Other causes of hypokalaemia and hypertension include renovascular disease (where both aldosterone and renin are elevated), Cushing’s syndrome, chronic liquorice ingestion, Liddle’s syndrome and, in young patients, renin-secreting cancers (rarely).

3. **Ask about snoring.** A history of snoring and obesity should be investigated with sleep studies for sleep apnoea.

4. **Perform a CT angiogram or conventional renal angiogram for patients with intractable hypertension (especially young patients).** These are the most sensitive tests for renal artery stenosis.

5. **Ask about symptoms consistent with a phaeochromocytoma.** These need investigation with 24-hour urinary catecholamines.

6. **Investigate for Cushing’s syndrome if there is any clinical suspicion.**

7. **Perform an ECG to look for evidence of ischaemic heart disease and for voltage changes that suggest left ventricular hypertrophy (LVH)** (Fig 5.10). The presence of LVH on the ECG in hypertensives is associated with an adverse prognosis. Occasionally an echocardiogram is indicated if there is doubt about the presence of LVH.

![Figure 5.10 Sinus rhythm. Left ventricular hypertrophy – the R waves are tall in the lateral leads and the S waves are deep in the septal leads. There are also lateral ST and T wave changes, called a strain pattern.](sample proofs @ Elsevier Australia)

**Treatment**

The decision to begin drug treatment is an important one because it is likely to be lifelong. The current recommendations are that a blood pressure of >140 mmHg systolic or >90 mmHg diastolic, or both, warrants a ‘treatment plan’. It is now very clear that the aggressiveness of intervention depends very much on factors other than the blood pressure level. The whole gamut of cardiovascular risk factors must be taken into account.

Tables have been published by many cardiovascular societies that show the calculated risk of vascular events and the calculated reduction in number of events over time with treatment for patients with different risk factors. The decision to use drug treatment
should be based on information of this kind. Typically, calculators of risk take into account age, sex, smoking status, level of blood pressure, cholesterol, race and existing cardiovascular disease.

Except for very severe hypertension, attempts should be made to bring the blood pressure down by modifying the factors that are known to increase it. Many patients, when faced with the threat of lifelong drug treatment, are amenable to suggestions to change the way they live.

Primary hyperaldosteronism can be treated effectively with spironolactone. Renal artery stenosis may be amenable to balloon angioplasty. This usually makes blood pressure control easier, but does not cure the condition. Treatment of sleep apnoea with an appropriate continuous positive airways pressure (CPAP) mask can also make blood pressure control easier.

Patients with only a mild risk of cardiovascular problems and blood pressure <150/95 mmHg should probably continue with conservative measures and be reassessed. However, at higher levels of blood pressure than this, drug treatment should be considered. Patients with very high risk (e.g. those with target organ disease or of Aboriginal race) should begin drug treatment if the blood pressure remains above 140/90 mmHg. Isolated systolic hypertension in the elderly deserves therapy!

**BLOOD PRESSURE REDUCTION WITHOUT DRUGS**

1. **Weight reduction.** On average, 1 kg of weight loss will reduce systolic blood pressure by 2 mmHg. The goal should be reduction to a body mass index (BMI) of 25 kg/m² and a waist circumference of <94 cm for men and <80 cm for women. Even lower BMIs should be recommended for some racial groups, such as Asians and Aboriginal Australians, whose cardiovascular risk increases at lower BMIs than does Europeans.

2. **Exercise.** Thirty minutes of moderately intense exercise (e.g. brisk walking) at least 5 days a week can lower blood pressure by about 3–5 mmHg.

3. **Alcohol.** Reductions of 4–5 mmHg can be achieved by alcohol restriction to two standard drinks per day for men and one per day for women.

4. **Salt.** Reduction in salt consumption to 90 mmol/day can reduce blood pressure by more than 5 mmHg. Warn patients that prepared and snack foods are usually heavily salted.

The cumulative effect of these measures can be considerable, but repeated encouragement is likely to be required for patients to achieve them.

**DRUG TREATMENT**

Remember that all classes of drugs (see Table 5.5) are fairly similar in their effect on blood pressure. The majority of patients will require more than one drug for effective blood pressure control.

<table>
<thead>
<tr>
<th>Table 5.5 Classes of antihypertensive drugs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thiazide diuretics</td>
</tr>
<tr>
<td>Angiotensin converting enzyme (ACE) inhibitors</td>
</tr>
<tr>
<td>Beta-blockers</td>
</tr>
<tr>
<td>Non-dihydropyridine calcium channel blockers</td>
</tr>
<tr>
<td>Dihydropyridine calcium channel blockers</td>
</tr>
<tr>
<td>Angiotensin II receptor antagonists</td>
</tr>
<tr>
<td>Others: centrally acting (methyldopa), vasodilators (prazosin, hydralazine)</td>
</tr>
</tbody>
</table>
There are many factors to be taken into account when a choice of antihypertensive drug is made (Table 5.6):

- previous intolerance to a class of drugs
- known contraindications to a class of drugs (e.g., renal artery stenosis and ACE inhibitors)
- convenience of drug regimen (e.g., once-daily dosage)
- interaction with other medications (e.g., concerns about bradycardia with beta-blockers and verapamil)
- existing medical problems that favour the use of a class of drugs (e.g., cardiac failure and ACE inhibitors)
- cost
- possible additional protective effects of some antihypertensives (e.g., ACE inhibitors and patients who have had a stroke or have diabetes).

<table>
<thead>
<tr>
<th>CONDITION</th>
<th>DRUG</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asthma or COPD</td>
<td>Beta-blockers</td>
</tr>
<tr>
<td>Bradycardia or heart block</td>
<td>Beta-blockers, non-dihydropyridine calcium channel blockers (verapamil, diltiazem)</td>
</tr>
<tr>
<td>Cardiac failure</td>
<td>Calcium channel blockers</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>Thiazides, beta-blockers (relative contraindication)</td>
</tr>
<tr>
<td>Gout</td>
<td>Diuretics</td>
</tr>
<tr>
<td>Peripheral vascular disease</td>
<td>Beta-blockers</td>
</tr>
<tr>
<td>Pregnancy</td>
<td>Avoid most antihypertensives, especially ACE inhibitors; methyldopa, hydralazine and labetalol are safe</td>
</tr>
<tr>
<td>Renal vascular disease</td>
<td>ACE inhibitors, AR antagonists</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>POSSIBLE INDICATION OR BENEFICIAL EFFECT</th>
<th>DRUG</th>
</tr>
</thead>
<tbody>
<tr>
<td>Angina</td>
<td>Beta-blockers, calcium channel blockers</td>
</tr>
<tr>
<td>Cardiac failure</td>
<td>ACE inhibitors, AR antagonists, diuretics, some beta-blockers</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>ACE inhibitors, beta-blockers</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>ACE inhibitors, AR antagonists</td>
</tr>
</tbody>
</table>

COPD = chronic obstructive pulmonary disease; ACE = angiotensin-converting enzyme; AR = angiotensin receptor.

The current Heart Foundation recommendation is that treatment begin with a small dose of a single drug. Intolerance suggests the need to try a different class. The Foundation recommends that failure to achieve control should be managed with the addition of a small dose of another class of drug. The idea is to minimise side-effects. The disadvantage of this approach is that almost all patients will end up on multiple drugs, which can be a problem for compliance and cost. The other approach is to titrate up the dose of one drug to the maximum recommended, unless side-effects occur. Then a second drug from another class is added. Some drugs are especially effective in combination:

- beta-blocker and dihydropyridine calcium channel antagonist
- ACE inhibitor or AR antagonist and thiazide
• ACE inhibitor or AR antagonist and calcium antagonist
• beta-blocker and alpha-blocker
• beta-blocker and thiazide.

Fixed-dose combinations of two or even three of these are available: ACE inhibitor and thiazide, calcium antagonist and ACEI or ARB + diuretic, beta-blocker and alpha-blocker (labetolol). These combinations are not approved for the initiation of treatment. Candidates should be familiar with the doses of the common antihypertensive drugs and their important side-effects.

**RENAL ARTERY DENERVATION**

Catheter-based denervation of the renal artery can now be performed using radiofrequency energy or drug instillation. Early trials have shown significant — up to 20mmHg — and sustained reduction in blood pressure for the patients not controlled on four or five drugs. The treatment is still experimental.

**Heart transplantation**

Cardiac transplantation is now an accepted form of treatment for intractable cardiac failure. Numbers of patients who have either had a transplant or are on the waiting list for one are available for clinical examinations. Those awaiting transplantation are sick enough to require frequent admissions to hospital, and those who have had a transplant are often re-admitted for various routine investigations. Many patients who would once have required a transplant are now stable on treatment with beta-blockers and ACE inhibitors. Therefore patients on a transplant list tend to have severe heart failure which has not responded to medical treatment or resynchronisation pacing. Patients are usually well informed about their condition and should be able to supply a lot of useful information to the candidate.

Although this fact should not be discussed with our surgical colleagues, heart transplantation is technically not a very difficult operation. Improvements in prognosis have followed medical advances, particularly in the area of the management of rejection. The 5-year survival rate is now slightly more than 75% for patients who have received a transplant since 1981 and the 1-year survival rate is currently about 90%.

As in all transplantation long cases, the examiners will expect the candidate to be familiar with the indications for and contraindications to the procedure. It is also important to know what investigations are required before a patient can be accepted for surgery and to understand the management problems that can occur in patients who have had the operation (Table 5.7).

**The history**

1. Try to establish the cause of the patient’s cardiac failure. In younger patients, cardiomyopathy is more likely to be the problem, but nearly half the patients currently undergoing heart transplantation have ischaemic heart disease. Rheumatic valvular heart disease can also affect younger patients. Combined heart and lung transplantation is occasionally carried out for patients with primary pulmonary hypertension or cystic fibrosis. It may also be the treatment of choice for some forms of congenital heart disease, either in childhood or adult life; if pulmonary hypertension is present, these patients have to be considered for combined heart and lung transplantation.
Ask about previous myocardial infarction or angina and whether the patient knows the results of cardiac catheterisation. All patients undergoing a transplant are required to have cardiac catheterisation. There may have been a preoperative cardiac biopsy performed and the patient may be aware of the results of this test. Also ask about previous thoracotomies.

2. Ask about the patient’s symptoms before surgery. Obtain an idea of the exercise tolerance and the severity of angina, if present. The patient may know the results of investigations of cardiac function, such as exercise tests and gated blood pool scans, before and after surgery.

3. Ask what treatment the patient was receiving before transplantation, particularly the doses of diuretics, ACE inhibitors and beta-blockers (e.g. carvedilol). Find out whether frequent admissions to hospital have been necessary and whether intravenous inotropes were required. There may have been recurrent ventricular arrhythmias before surgery. Treatment may have been with drugs, especially amiodarone or an implanted defibrillator and antitachycardia pacemaker and resynchronisation device. Some patients have undergone previous surgery for arrhythmias. This may include resection of an aneurysm or myocardial resection following ventricular mapping. Occasionally, transplantation is used to treat intractable ventricular arrhythmias.

4. Find out how long it is since the transplant was performed. Ask whether there were any problems with the surgery – either technical or involving acute rejection. Find out how long the patient was in hospital and what further admissions to hospital have occurred since the operation. Ask whether a permanent pacemaker was inserted. Some patients awaiting transplant may have been given a ventricular assist device as a bridge to transplant: ask whether that was necessary.
5. Endomyocardial biopsies are fairly memorable events and the patient should be able to tell you how often these have been performed and when the last one was obtained. It is now routine to perform them at weekly intervals for the first 3 weeks after operation, every 2 weeks for the following month and every 6 months after that for patients whose condition is stable.

6. Find out what drugs the patient is taking currently. Transplant patients should not require antifailure treatment, but will, of course, be taking immunosuppressive drugs. Almost all patients are now maintained on cyclosporin; the dose is determined by its serum level. Cyclosporin and tacrolimus are nephrotoxic and cause hypertension and hyperlipidaemia. Newer immunosuppressive drugs include mycophenolate and rapamycin. Diltiazem is often used as a cyclosporin-sparing agent. It dramatically reduces cyclosporin metabolism and therefore the cost of treating patients. Often azathioprine is also prescribed and the dose is adjusted according to the white cell count.

7. Patients are often well informed about symptoms suggesting rejection – often these resemble an attack of pericarditis. The patient may know of boosts of prednisone that have been given for rejection episodes. Early episodes of rejection are often treated with 1 g of methylprednisolone IV for 3 days. Later rejection tends to be milder and may respond to an increase in oral steroids. Severe rejection is often treated with antithymocyte globulin or the murine monoclonal muromonab-CD3. Repetitive rejection may be treated with total lymphoid irradiation or methotrexate.

8. Enquire about complications of immunosuppression (Table 5.8). Many patients are also taking regular antibiotics to prevent *Pneumocystis jirovecii* (formerly *carinii*) infection. Cotrimoxazole twice daily 3 days a week is a common regimen.

### Table 5.8 Commonly used immunosuppressants for heart transplant patients

<table>
<thead>
<tr>
<th>DRUG</th>
<th>SIDE-EFFECTS</th>
<th>MONITORING/AVOIDANCE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Steroids</td>
<td>Cushingoid, diabetes, osteoporosis</td>
<td>Minimal dose</td>
</tr>
<tr>
<td>Cyclosporin</td>
<td>Renal impairment, hypertension, neurotoxicity</td>
<td>Blood levels, drug interactions</td>
</tr>
<tr>
<td>Mycophenolate</td>
<td>Mild marrow suppression, gastrointestinal upset</td>
<td>Reduce dose, check FBC</td>
</tr>
<tr>
<td>Methotrexate</td>
<td>Hepato- and marrow toxicity</td>
<td>FBC, liver function tests</td>
</tr>
<tr>
<td>Azathioprine</td>
<td>Hepato- and marrow toxicity, pancreatitis</td>
<td>FBC, liver function tests, TPMT</td>
</tr>
</tbody>
</table>

FBC = full blood count. TPMT = thiopurine methyltransferase

9. Some general questions about the transplant patient’s current life are very relevant. Find out how much difference has occurred in the patient’s exercise tolerance and whether he or she has been able to go back to work. If the patient is currently an inpatient, find out why he or she has been admitted to hospital on this occasion. Ask about the patient’s family and how they have coped with the illness and the transplant itself. Make some discreet enquiries about the patient’s finances and whether there have been any problems returning to the transplant hospital for the various investigations required.

10. Ask about routine cardiac catheterisation. This is typically performed biannually in patients who have had transplants. Coronary artery intimal proliferation can cause ischaemic heart disease in the transplanted heart. Because the heart has been denervated there is not usually any pain. However, there are now patients in whom re-innervation seems to have occurred and led to symptoms of angina. This allograft
The cardiovascular long case

Arteriopathy is one of the most important problems after transplant. It represents a rejection phenomenon. The condition is usually diffuse, but once lesions causing 40% coronary stenosis have occurred, the prognosis is quite poor: the 2-year survival rate is only about 50%. The condition is present in 10% of recipients at 1-year post-transplant and in 50% at 5 years. Once myocardial infarction has occurred, the 2-year survival rate is only 10–20%. Although the disease is a form of rejection, it is still considered important that the patient’s cholesterol level be kept as low as possible. Find out whether the patient knows what his or her cholesterol level is and what treatment is being used to keep it low. Intravascular ultrasound is used increasingly to detect subclinical vasculopathy and to study the benefits of various antirejection regimens.

11. Hypertension is another important post-transplant problem. It is associated with the use of cyclosporin. Ask about blood pressure control and treatment.

12. Transplant patients have an increased risk of malignancy. Skin cancers (basal cell and squamous cell carcinomas) are common. There is also a higher incidence of lymphoproliferative disorders. Post-transplant lymphoproliferative disease (PTLD) is an increasingly recognised complication of the immunosuppression required for organ transplants. The incidence in heart transplant patients is less than that for those with liver transplants, but more than that for those with renal transplants. Primary or reactivated Epstein-Barr virus infection is thought to be the cause. The lesions tend to occur in unusual extranodal sites. Reduction in the amount of immunosuppression will sometimes help, but antiviral treatment with acyclovir or interferon may be necessary.

The examination

1. If the transplant has been successful, there should not be many signs. A median sternotomy scar will be present.
2. Look for signs of cardiac failure and pericarditis. Pericarditis can be an indication of rejection.
3. Note the small scars in the neck at the point of introduction of the endomyocardial biopsy forceps.
4. Look for any evidence of Cushing’s syndrome from steroid therapy.
5. Examine the chest carefully for signs of infection, examine the mouth for candidiasis, look for infection at intravenous access sites and look at the temperature chart.

Investigations

These depend somewhat on the reason the patient has been admitted to hospital on this occasion.

1. Endomyocardial biopsies are performed routinely and at any suggestion of rejection. Ask about the results of these biopsies.
2. A full blood count (FBC) may be indicated because of possible infection and to monitor the azathioprine dose.
3. Chest X-ray may show signs of cardiac enlargement, although this is a late sign of rejection. Changes of rejection on the ECG include a reduction in voltage caused by myocardial oedema or atrial arrhythmias. Sometimes the patient’s ECG shows two sets of P waves: one comes from the transplanted heart and one arises from the residual atrium.
4. Recent assessments of myocardial function, including gated blood pool scans and resting or stress echocardiograms, may be available.
5. Routine coronary angiography may have been performed.
6. If there have been problems with possible infection, results of blood, urine and other cultures should be sought.
Management
The discussion should revolve around the patient’s current problem or reason for admission. However, there is likely to be time to discuss the management of rejection, infection, cardiac failure or social problems.

1. Rejection may have been suspected because of pleuritic chest pain, deterioration in left ventricular function or ECG changes. It is diagnosed on the basis of a routine biopsy. The usual approach is to give the patient a boost of methylprednisolone – usually 1 g intravenously daily for 3 days, followed by a repeat biopsy.

2. Infections occurring as a result of immunosuppression are a major cause of death. Possible episodes of infection should be investigated thoroughly and treated aggressively with appropriate therapy. Opportunistic infections are relatively common as a late complication. Cytomegalovirus, herpes, Pneumocystis jirovecii, fungal infection, and Nocardia and Toxoplasma are all more common than in non-immunosuppressed people.

3. Further cardiac failure may be an indication of rejection, which should be treated. Cardiac failure may also be an indication of silent myocardial infarction.

4. Hyperlipidaemia should be sought routinely and treated most vigorously with drugs and diet.

There may be discussion about the patient’s prognosis. The 1-year survival rate after transplant is about 90% and the 5-year survival rate is about 75%. The 10-year survival rate approaches 50%.

The discussion of a patient awaiting cardiac transplantation will probably run along similar lines. However, it is important to know how well informed the patient is about what is likely to happen, whether he or she appears to fulfil the criteria for transplantation (see Table 5.7) and whether there appear to be any contraindications. Some patients awaiting transplantation are sick enough to require intravenous inotropes. There may even have been talk about the use of external circulatory assistance devices for use as a bridge to transplant.

Cardiac arrhythmias
The management of some cardiac rhythm disturbances is complicated. These patients may be in hospital while waiting for diagnostic tests or, in cases of serious arrhythmias, for treatment to become effective.

They sometimes represent diagnostic, but more often management, problems. Ventricular arrhythmias are a more common reason for admission than supraventricular arrhythmias, but patients with the latter may be awaiting diagnostic or therapeutic procedures. Atrial fibrillation, the most common of the significant cardiac arrhythmias, is unlikely to be the patient’s only problem if it appears in a long case.

The history
Ask why the patient is in hospital – all may be revealed without much further effort. Otherwise, the patient may know the name of the arrhythmia or be able to describe symptoms that make the diagnosis likely. If the rhythm problem is a serious and continuing one, the candidate may be fortunate enough to find the patient on an ECG monitor.

Possible presenting symptoms include:

1. rapid and irregular palpitations – suggest atrial fibrillation (AF) (Fig 5.11)
2. rapid and regular palpitations, with or without dizziness and perhaps terminated by Valsalva manoeuvres – suggest supraventricular tachycardia (SVT) (Fig 5.12)
3. rapid and regular palpitations with dizziness, syncope or near syncope – suggest ventricular tachycardia (VT), particularly if there is a history of ischaemic heart disease
4. syncope with bradycardia or no palpitations – suggests heart block (Fig 5.13)
5. symptoms of AF and episodes of syncope – suggest sick sinus syndrome

Figure 5.11 Atrial fibrillation. The ventricular response rate is rapid – between 95 and 160 beats/minute.

Figure 5.12 Supraventricular tachycardia. The complexes are narrow. The heart rate is about 200 beats/minute and the rhythm is regular.
6. a family history of sudden death – suggests the possibility of congenital long or short QT interval (Fig 5.14), Brugada syndrome (ionopathy) or a structural cardiac problem such as hypertrophic cardiomyopathy.

7. the occurrence of syncope in association with antiarrhythmic drug treatment suggests the possibility of proarrhythmia; ask about class 1C drugs and sotalol, perhaps prescribed because of paroxysmal AF, as these drugs may also worsen bradyarrhythmias in patients with sick sinus syndrome.

Ask about previous known heart disease (e.g. ischaemic heart disease and VT, aortic stenosis and heart block) and recent cardiac, thoracic or abdominal surgery.

- Cardiac surgery may be complicated by heart block and all of the above may precipitate AF.
- The "grown-up" congenital heart disease patient may have persisting problems with atrial or ventricular arrhythmias following cardiac surgery in childhood.
- Atrial septal defects are often complicated by atrial arrhythmias even after they have been repaired.

- Consider the common causes and associations of AF:
  1. advancing age (3% of 65-year-olds, >6% of people in their 80s)
  2. hypertension
  3. mitral valve disease
  4. ischaemic heart disease and myocardial infarction
  5. recent thoracic or abdominal surgery
  6. atrial septal defect
  7. Wolff-Parkinson-White (WPW) syndrome (see Figs 5.15 and 5.16)
  8. recent alcoholic binge
  9. pulmonary embolism
  10. thyrotoxicosis.
Figure 5.14 (a) Sinus rhythm. The QT interval is prolonged (423 ms) and the corrected QT (QTc) is 460 ms (normal <440 ms). These patients are at risk of syncope or sudden death as a result of the development of polymorphic VT. (b) Polymorphic VT or torsade de pointes. This apparent twisting of the QRS complexes is named after the gold braid on French military uniforms.

Ask whether the rhythm has been paroxysmal and self-limiting, persistent and requiring cardioversion, or permanent.

Find out about treatment.

1. Has the patient required intravenous drugs to control the heart? Have these been by infusion or bolus injection? Intravenous adenosine is now the drug treatment of first choice for SVT. Patients may well remember its use. It causes a brief but distressing sensation of impending death.
2. Have physical manoeuvres been tried?
3. What oral drugs have been used in the past and during this admission? Make enquiries about the known side-effects of these drugs.
4. The investigations the patient has undergone or may be about to undergo can help sort out the diagnosis.
   a. Certain tests, such as electrophysiological studies (EPS), are more memorable than others. An EPS with induction of VT may mean that direct current (DC) cardioversion was required; despite sedation and reduced cardiac output, some memory of this may remain.
   b. A cardiac biopsy may have been performed to look for right ventricular cardiomyopathy (RV dysplasia), a cause of VT.
   c. Cardiac MRI and CT scans are commonly used to look for the patchy changes of cardiac sarcoid or right ventricular (RV) cardiomyopathy (RV dysplasia).
   d. Other procedures may have been entirely therapeutic: for example, DC cardioversion performed electively under general anaesthesia suggests AF or atrial flutter; catheter ablation, often a fairly prolonged procedure, suggests SVT or VT; pacemaker insertion suggests bradycardia; antiarrhythmia surgery suggests VT or, less often now, SVT.

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**Figure 5.15** Sinus rhythm. Wolff-Parkinson-White conduction. The PR interval is short and delta waves are visible. There are positive delta waves in lead I – seen as a slurred upstroke at the start of the R wave – and negative delta waves in lead III – seen as a slurred Q wave. These patients’ ECGs are usually abnormal between their attacks of tachycardia but the pre-excitation (delta wave) may occur only intermittently. They are at risk of sudden death or syncope if atrial fibrillation or flutter occurs (they are often at increased risk of this arrhythmia) because very rapid ventricular rates may occur if the accessory pathway can conduct at high rates. Treat acute atrial fibrillation or flutter in this setting if unstable using electrical cardioversion (never use verapamil, adenosine or digoxin).
Catheter ablation is now a routine treatment for SVT that does not respond to simple drug treatment. Rarely there may be failure to suppress the arrhythmia, or a complication such as complete heart block or cardiac rupture can occur. Ablation is also very effective for some forms of VT. These include right, and the less common left, ventricular outflow tract tachycardias. These benign forms of VT can cause frequent recurrent episodes of self-limiting VT with a left or right bundle branch block morphology, respectively. They may respond to treatment with verapamil but are otherwise managed with catheter ablation.

Patients with automatic implantable cardioverter-defibrillators (AICDs) can often provide vast amounts of useful information about their devices and about their arrhythmia.

The examination
Examine the cardiovascular system. Is the patient in sinus rhythm clinically? Look for thoracotomy scars, pacemakers and implanted defibrillators. Look for signs of cardiac failure, valvular heart disease and evidence of recent abdominal surgery or thyrotoxicosis.

Investigations
These depend on the actual rhythm problem.

1. **Resting ECG.** Look for:
   a. the current rhythm
   b. evidence of pre-excitation (Wolff-Parkinson-White conduction – see Fig 5.16; Lown-Ganong-Levine syndrome)
   c. heart block
   d. old infarct
   e. paced rhythm (ventricular-ventricular inhibited (VVI) or dual chamber atrial sensing and ventricular pacing or dual-chamber pacing)
   f. long QT interval (increased risk of polymorphic VT – *torsade de pointes*).

![Figure 5.16 Sinus rhythm in WPW conduction. The delta waves and overall QRS are directed anteriorly in V1, superficially resembling RBBB. This is type A WPW where the bundle of Kent inserts into the left ventricular myocardium. Where the delta wave is initially isoelectric, the PR interval appears normal. Note also the close resemblance to an inferoposterior infarction.](image)
2. The examiners may produce previous ECGs or parts of 24-hour Holter monitors. Remember that a broad, complex tachycardia should be considered VT unless there is good reason to consider otherwise. There are a number of ECG criteria for distinguishing VT from SVT with aberrant conduction.

Findings suggestive of VT include:

- a QRS >0.14 seconds (if a RBBB pattern) or >0.16 seconds (if a LBBB pattern)
- left-axis deviation (between –90° and –180°)
- atrioventricular (AV) dissociation (with P waves ‘marching through’ the QRS complexes)
- changes from the pre-existing QRS morphology in pre-existing bundle branch block (but note, these rules do not apply in SVT with aberration caused by WPW conduction).

The presence of known ischaemic heart disease, or cardiac failure, is particularly useful. Broad complex tachycardia in a patient with ischaemic heart disease is usually VT (95%).

3. EPS may be used to assess inducibility of atrial and ventricular arrhythmias before and after treatment. It is now used in conjunction with catheter ablation as curative treatment for SVT caused by accessory pathways and for some types of VT. It can also be performed to ablate the AV node or the regions around the four pulmonary veins for patients with intractable and disabling AF. Ablation treatment has an increasing role for the management of ischaemic and non-ischaemic VT, usually in conjunction with an implanted cardioverter defibrillator.

4. Routine investigations for patients with AF include echocardiography, thyroid function testing and sometimes exercise testing. Echocardiography may reveal an underlying pathology that is responsible for the AF (e.g. mitral stenosis). It is important in helping quantify embolic risk. Look at the echo for:

- valve abnormalities
- cardiomyopathy
- diastolic dysfunction of the left ventricle (especially important in hypertensive patients)
- left ventricular hypertrophy
- atrial size (consider atrial septal defect)
- mitral valve disease
- segmental wall abnormalities consistent with ischaemic heart disease.

Tests may be needed because of actual or potential drug side-effects (e.g. liver function or thyroid function tests for patients on amiodarone).

5. Cardiac catheterisation is often indicated for patients with ventricular arrhythmias, as they may have an ischaemic substrate. Patients whose VT has been stable but becomes unstable (often leading to more activity on the part of their cardioverter defibrillator) may have developed new ischaemia and should have this possibility investigated and treated.

Management

Much depends on the rhythm abnormality.

1. Arrhythmias that are not life-threatening are usually managed, at least at first, with drugs. Candidates will be expected to have a thorough working knowledge of the common antiarrhythmic drugs, their methods of action, indications and side-effects. Remember that many antiarrhythmic drugs have a potentially dangerous proarrhythmic effect.

2. The indications for permanent pacing (Table 5.9) and different uses for VVI, VVIR (rate-responsive) and DDD (dual-chamber) pacers (Figs 5.17 and 5.18) should be well understood. A basic understanding of antitachycardia devices and indications for their use (see Table 5.10) is also important.
Automatic implanted cardioverter-defibrillators (AICDs) are increasingly used to manage recurrent VT. They are often used in combination with antiarrhythmic drugs of some sort. They are becoming smaller, cheaper (between $25,000 and $40,000) and more complicated. It is now established that they improve mortality rates in selected patients.

They are usually the treatment of choice for hypotensive VT or missed sudden death from VF. Drug treatment of these conditions is not very effective.

### Table 5.9 Indications for permanent pacemaker insertion in adults

**GENERALLY AGREED INDICATIONS**
1. Intermittent or permanent complete heart block, with:
   a. symptomatic bradycardia
   b. cardiac failure
   c. arrhythmias that require treatment with drugs that slow conduction
   d. documented asystole of more than 3 seconds or escape rhythm with a rate <40 beats/minute
   e. confusional states that improve with temporary pacing
2. Intermittent permanent second-degree AV block with symptomatic bradycardia
3. Sinus node dysfunction with symptomatic bradycardia

**LESS CERTAIN INDICATIONS**
4. Asymptomatic complete heart block; heart rate ≥40 beats/minute
5. Symptomatic type 2 second-degree heart block
6. Bifascicular or trifascicular block with syncope of unknown aetiology

**NOT INDICATED**
1. First-degree heart block
2. Asymptomatic type 1 second-degree heart block

### Figure 5.17 Atrial sensing and ventricular pacing.
This is the ECG of a patient with a dual-chamber pacemaker. Normal P waves are followed by an atrioventricular (PR) interval and then a pacing spike, which precedes a wide QRS complex with a LBBB pattern (pacing is from the right ventricular apex).
The current models have leads that can be placed intravenously into the vena cava and for pacing purposes into the right ventricle.

They are small enough to be implanted like pacemakers in the chest wall, but are still noticeably larger than pacemakers (Fig 5.19). Implantation takes place under local anaesthetic in the electrophysiology laboratory.

The periprocedural mortality rate is less than 1%, compared with over 5% when surgical implantation was required.

**Table 5.10 Indications for implanted cardioverter-defibrillators (ICDs)**

| GENERALLY AGREED INDICATIONS | | |
|-----------------------------|------------------|
| 1. Confirmed VF or hypotensive VT not related to acute infarct or severe electrolyte abnormality, but VF/VT not inducible at EPS – this means drug treatment cannot be tested by EPS | |
| 2. VF/VT with contraindications to drug treatment (intolerance) | |
| 3. Persistently inducible VT/VF despite drug treatment, ablation or surgery | |
| 4. Persistent spontaneous VT/VF despite drug treatment | |
| 5. Symptomatic long QT syndrome despite drug treatment | |

| LESS CERTAIN INDICATIONS | | |
|--------------------------|------------------|
| 1. Inducible but not spontaneous VT despite other treatment in high-risk patients | |
| 2. VT/VF apparently controlled but in a high-risk patient | |
| 3. Serial drug testing possible but defibrillator preferred | |

| NOT GENERALLY INDICATED | | |
|-------------------------|------------------|
| 1. Very frequent or incessant VT | |
| 2. Reversible cause | |
| 3. Recurrent syncpe, VT/VF not inducible | |
| 4. Poor life expectancy (e.g. class IV cardiac failure but not a transplant candidate) | |

Note: Increasingly proven VT or VF in a patient with poor LV function is considered an indication regardless of EPS findings.

VF = ventricular fibrillation; VT = ventricular tachycardia; EPS = electrophysiological study.
Figure 5.19 (a) PA chest X-ray showing implanted cardioverter defibrillator and biventricular pacemaker. (b) Lateral view: the large defibrillation electrode (which also serves as an RV pacing electrode) (arrow) and the right atrial and left ventricular pacing leads are visible.

Figures reproduced courtesy of The Canberra Hospital.
The programming of these machines is complicated, but candidates should know that they are usually set to attempt reversion of VT by overdrive pacing (antitachycardia pacing, ATP) before administering a DC shock. Patients are usually, but not always, aware of the onset of ATP and almost always aware of DC shock administration. Ask how the device has affected the patient's life and confidence, including how often it goes off and whether the box itself causes problems because of its size. Although AICDs can prevent sudden death, their presence is often associated with a feeling of insecurity. Patients may have clear memories of events leading up to activation of the device. They may avoid places where arrhythmias and activations have occurred. They often require repeated explanation and reassurance.

**The particular management problems of atrial fibrillation**

Examiners require candidates to have a sensible approach to the management of AF and the opportunity for examiners to ask about this common condition will often arise. The principles of management are to:

- maintain sinus rhythm
- control the heart rate (if maintaining sinus rhythm proves difficult)
- protect from embolic events.

1. There is good evidence from recent trials that control of heart rate is at least as satisfactory an approach as that of trying aggressively to maintain sinus rhythm. Nevertheless, patients with paroxysmal AF often find the arrhythmia very disturbing. They should be told at the outset that it may not be possible to keep them in sinus rhythm, but that rate control and freedom from embolic episodes can be achieved. The prophylactic drug treatment of paroxysmal AF involves the use of a class III drug (sotalol or amiodarone) in most cases, but occasionally the class 1C drug flecainide can be used if the heart is known to be structurally normal.

2. Rate control of persistent or paroxysmal AF can be achieved with less-toxic drugs. Digoxin is a common first-line treatment and is usually well tolerated. It is not very effective on its own at controlling the heart rate during exercise. Many patients with chronic AF have persistent dyspnoea during exercise because of inadequate rate control. They benefit from the use of a beta-blocker or one of the non-dihydropyridine calcium channel blockers (diltiazem or verapamil). These can be used with or without digoxin. Control of the heart rate can prevent or reverse the impairment of left ventricular function that is associated with tachycardias (tachycardia-induced cardiomyopathy).

3. When patients remain unhappy with their symptoms despite rate control, further intervention should be considered. AV nodal ablation is a relatively simple procedure that prevents fibrillation waves from reaching the ventricles. The patient then requires an artificial pacemaker. Although atrial systole is lost, the regularisation of the heart rate is usually enough to dramatically improve symptoms. If the patient's AF has been paroxysmal, a dual-chamber pacemaker with a 'mode switch' may be used. When the patient is in sinus rhythm, atrial sensing occurs and the ventricles are paced after an appropriate AV interval. When episodes of AF occur, the pacemaker mode switches and paces the ventricle at a steady rate.

4. DC cardioversion of AF can be a reasonable treatment for the first episode or for patients with infrequent episodes. DC cardioversion is safe in the absence of digoxin toxicity or hypokalaemia, but is associated with a risk of embolism if the patient's AF has been present for more than 48 hours. In this case, 1 month's therapeutic anticoagulation should be instituted before the procedure and continued for 4 weeks afterwards. An alternative is to perform a transoesophageal echocardiogram to look for left atrial
appendage thrombus or spontaneous echocardiograph contrast (a sign of slow blood flow). The absence of these means that DC cardioversion is safe, but that warfarin must be given for 4 weeks afterwards because there is a persisting risk over this period.

5. Reversion of AF with drug treatment is difficult. Many episodes terminate spontaneously but drug treatment is given the credit. It is known that digoxin does not increase the reversion rate, but the class III drugs and flecainide do improve the chances somewhat. Sometimes control of the heart rate and awaiting spontaneous reversion can be an option. A decision to go on to DC cardioversion, however, should be made before 48 hours has passed.

6. Over many years attempts have been made to prevent AF by surgical or catheter ablation techniques. Pulmonary vein isolation is now commonly performed for intractable symptomatic AF. Radiofrequency energy is used to isolate the two pairs of pulmonary veins in the left atrium. The rationale for this approach is that almost all AF seems to be initiated by electrical activity arising from this part of the heart. Isolation of this area from the rest of the heart prevents the initiation of AF. The procedure is complicated and time-consuming (4–6 hours per case). It is not a practical solution for most cases of AF. Success rates of about 60% are usually quoted. Until recently, an uncommon but severe complication involved the late occurrence of pulmonary vein stenosis. Newer techniques have made this a rare problem. Other complications include heart block and cardiac perforation. Successful treatment possibly spares a patient the need for anticoagulation.

7. Protecting patients from embolic events is perhaps the most important aspect of the management of AF. Cerebral embolus is the most feared complication, but life-threatening peripheral embolisation (e.g. to the mesenteric bed) can occur. Patients should have this aspect of AF explained to them early on. The risk of embolism is low in people under the age of 60 and without any risk factors: <0.5% a year. It can be as high as 30% for patients with mitral stenosis. The most recent advice has been to anticoagulate unless a patient seems at really low risk.

Use the CHADS2 or CHA2DS2-VASc scoring system to help you decide whom to anticoagulate with AF:

<table>
<thead>
<tr>
<th>CHADS2 scoring system</th>
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<tbody>
<tr>
<td>Congestive heart failure: 1 point</td>
</tr>
<tr>
<td>Hypertension: 1 point</td>
</tr>
<tr>
<td>Age 75 and over: 1 point</td>
</tr>
<tr>
<td>Diabetes mellitus: 1 point</td>
</tr>
<tr>
<td>Stroke or TIA: 2 points</td>
</tr>
</tbody>
</table>

CHADS2 score = 0 no treatment
CHADS2 score = 1 anticoagulant or aspirin
CHADS2 score = 2 or more anticoagulant

Some patients with CHADS2 score of 0 are not truly at low risk. The CHA2DS2-VASc score adds female sex, age 65–75 and peripheral vascular disease to the risk factors. A man with a CHA2DS2-VASc score of 0 is at truly low risk and a woman with a score of 1 is also truly low risk.

Anticoagulant options include warfarin (monitor INR) or a direct thrombin inhibitor or a factor Xa inhibitor (avoid in chronic kidney disease).

Remember that episodes of AF, for example, on a Holter monitor or at pacemaker interrogation, must last longer than 30 seconds to be considered significant.
8. Patients with risk factors remain at risk of stroke even if sinus rhythm has been restored. Those with self-limiting paroxysmal AF are also at risk if episodes are more than a rare event. Aspirin gives some protection to those unwilling or unable to take warfarin. The combination anti-platelet treatment (e.g. with aspirin and clopidogrel) is somewhat more effective than aspirin alone, but is inferior to warfarin (and dual anti-platelet drugs increase the risk of gut bleeds).

9. An assessment of the patient’s ability to manage regular blood tests and dosage adjustments is necessary before treatment can begin. Patients are often reluctant to undertake the complexities of treatment but should not be allowed to decline treatment until all the risks of this approach have been carefully explained.

10. The availability of home international normalised ratio (INR) testing machines that use a capillary blood sample has made the use of warfarin more acceptable to some patients (e.g. those who travel frequently). A number of studies have shown that this approach is safe for selected patients. The safe therapeutic range is an INR of between 2 and 2.5.

11. Find out from the patient how the warfarin is managed and whether he or she knows the last few readings and dosage. Patients should be encouraged to keep a record of their INR results and warfarin doses. The examiners will expect considerable detail about the patient’s warfarin management.

12. Novel oral anti thrombotic agents are available. The first of these, dabigatran, is an oral anti-thrombin drug with similar efficacy to warfarin. The drug is effective within a few hours of the first dose but has to be taken twice a day. The larger dose (150 mg) is recommended for people under the age of 70 unless they have chronic kidney disease. Bleeding (especially gastrointestinal bleeding) has been a problem for patients especially on the larger dose over age 70 or if they have chronic kidney disease. It is associated with a higher risk of myocardial infarction. Gastrointestinal side-effects are common. The drug does not need monitoring. It is not indicated for valvular AF or for patients with mechanical valve replacements.

There are also the anti-factor Xa agents, e.g. rivaroxiban and apixaban. Rivaroxiban is taken once a day. The usual dose is 20 mg. Some authorities recommend 15 mg for patients with moderate renal impairment. Apixaban is taken as a 5 mg dose twice a day or 2.5 mg twice a day for patients over 80 or with moderate renal impairment. None of these drugs is indicated for patients with severe kidney failure. None is easily reversed, although dabigatran can be dialysed.