check

Independent learning program for GPs

Unit 503 March 2014

Heart health

RACGP

www.racgp.org.au/check

Subscriptions

For subscriptions and enquiries please call 1800 331 626 or email check@racgp.org.au.

Published by

The Royal Australian College of General Practitioners
100 Wellington Parade
East Melbourne, Victoria 3002, Australia
Telephone 03 8699 0414
Facsimile 03 8699 0400
www.racgp.org.au

ABN 34 000 223 807
ISSN 0812-9630

check

Independent learning program for GPs

Heart health

Unit 503 March 2014

The five domains of general practice

- Communication skills and the patient-doctor relationship
- Applied professional knowledge and skills
- Population health and the context of general practice
- Professional and ethical role
- Organisational and legal dimensions

RACGP

Despite the improvements in cardiovascular health, cardiovascular disease (CVD) remains a leading cause of disability, illness and premature death, and is the most expensive disease group in Australia.[1,2] The prevalence of CVD in Australians is predicted to increase in the next decades.[1]

CVD is associated with a number of risk factors, many of which are preventable or modifiable[1] (e.g. lifestyle factors such as smoking, obesity), indicating a role for preventive strategies.[3] General practitioners (GPs) play a critical part in CVD preventive activities[3] and are central to the long-term management of people with CVD by identifying risk factors and navigating patients through the healthcare system for acute care and secondary prevention. However, in 2010 the National Heart Foundation (NHF) reported[2] a significant gap between guideline recommendations for the management of CVD and actual clinical practice.

The NHF has called for the implementation of preventive measures and improved management of people with CVD or at risk of CVD. Of relevance for GPs, one of the NHF's key prevention initiatives is a cardiovascular health check in general practice and use of the CVD risk assessment to identify people at high risk of CVD and commence treatment where necessary.[2]

This unit of *check* will explore the management of common presentations of CVD in general practice.

LEARNING OUTCOMES

At the end of this activity, participants will be able to:

- describe pharmacological and non-pharmacological options for managing the signs and symptoms of heart failure
- compare and contrast the risks and benefits of warfarin versus the newer oral anticoagulant agents
- describe anticoagulant protocols for management of superficial venous thromboembolism, deep vein thrombosis and pulmonary embolism
- describe the benefits of using a cardiovascular risk assessment calculator when making clinical decisions for patients
- outline appropriate management strategies and resources available to family members following sudden cardiac death of a loved one.

AUTHORS

Sam Hayman BSc, MSc, MBBS (Hons) is an Advanced Trainee in Cardiology at the Royal Brisbane and Women's Hospital. He has special interests in heart failure and coronary artery disease.

John Atherton MBBS, PhD, FRACP, FCSANZ is Director of Cardiology at the Royal Brisbane and Women's Hospital and Associate Professor, Department of Medicine, University of Queensland. He has special interests in heart failure, cardiac genetics and cardiac rehabilitation.

Julie McGaughran BSc (Hons), MBChB (Hons), MD, FRCP, FRACP is the Director of Genetic Health Queensland and an Associate Professor at the University of Queensland. She has special interests in dysmorphology, cardiac genetics and legal and ethical issues in clinical genetics.

Louise McCormack BsC, BCom, MBBS is an advance trainee in Cardiology at the Royal Brisbane and Women's Hospital.

Kate Johnston MBBS FRACGP is a general practitioner and GP Liaison Officer for Gold Coast University Hospital and Gold Coast Medicare Local. Her interests are quality use of medicines and optimising integrated care and communication at the hospital-primary care interface.

Deanna Devers BMus, MMus, PhD, BMBS is a general practice registrar working in Hobart. She has a background in teaching and research.

Mark Kennedy MBBS, BMedSc (Hons), Grad Dip Fam Med is a general practitioner in Geelong, Victoria and clinical director of Northern Bay Health, a network of three medical clinics and a community-based diabetes centre. He has special interests in diabetes, chronic disease management and health and medical law. He is involved in the education of medical students, GP registrars and GPs at state, national and international levels, and in primary care research.

PEER REVIEWERS

Mark Beeby MBBS, FRACGP Dip Pal Med, has worked in a group general practice in Lalor for 31 years. He has been an FRACGP examiner for 21 years, a clinical supervisor associated with VMA, and was a member of the Cardiovascular Expert Group for Therapeutic Guidelines Cardiovascular (version 6) in 2012. He is also a board member of Infiniti Health Solutions.

Mark Nelson MBBS (Hons), MFM, PhD, FRACGP, FAFPHM is a Professorial Research Fellow at Menzies Research Institute Tasmania, University of Tasmania.

REFERENCES

1. Australian Institute of Health and Welfare 2011. Cardiovascular disease. Available at www.aihw.gov.au/WorkArea/DownloadAsset.aspx?id=10737418530) [Accessed 14 February 2014].
2. National Heart Foundation of Australia. Improving cardiovascular health outcomes in Australian general practice. Available at www.heartfoundation.org.au/SiteCollectionDocuments/General-Practice-Policy-Paper.pdf [Accessed 14 February 2014].
3. The Royal Australasian College of General Practice. Guidelines for preventive activities in general practice. 8th Edn. East Melbourne 2012. Available at www.racgp.org.au/download/Documents/Guidelines/Redbook8/redbook8.pdf [Accessed 18 February 2014].

GUIDE TO ABBREVIATIONS AND ACRONYMS IN THIS UNIT OF *CHECK*

ACEI	angiotensin-converting enzyme inhibitor	GFR	glomerular filtration rate	NSTEMI	non-ST segment elevation myocardial infarction
AF	atrial fibrillation	HDL	high density lipoprotein	NYHA	New York Heart Association
BNP	B-type natriuretic peptide	HR	heart rate	PBS	Pharmaceutical Benefits Scheme
BP	blood pressure	INR	international normalised range	PE	pulmonary embolism
BPM	beats per minute	JVP	jugular venous pressure	SCD	sudden cardiac death
CAD	coronary artery disease	LBBB	left bundle branch block	TC	total cholesterol
CMI	consumer medicine information	LDL	low density lipoprotein	TG	triglycerides
CrCl	creatinine clearance	LMWH	low molecular weight heparin	TIA	transient ischaemic attack
CT	computerised tomography	LV	left ventricular	TRAGEDY	Trans-Tasman response Against Sudden death in the Young
CVD	cardiovascular disease	LVEF	left ventricular ejection fraction	TSH	thyroid stimulating hormone
DVT	deep vein thrombosis	LVH	left ventricular hypertrophy	TTR	time in therapeutic range
ECG	electrocardiogram	MRA	mineralocorticoid receptor antagonist	uARC	urine albumin-to-creatinine
EEG	electroencephalogram	MRI	magnetic resonance imaging		
FBG	fasting blood glucose				

CASE 1

RUSSELL IS SHORT OF BREATH

Russell is a truck driver aged 68 years and is new to your practice. He describes progressive dyspnoea that he has had for the past three months and is now breathless when showering and dressing. For the past week he has felt more comfortable overnight sleeping on three pillows.

Russell says he had a heart attack 15 years ago, which was treated with a stent, and has had no chest pain since then. He has had problems with high blood pressure and cholesterol. His medications are aspirin 100 mg mane, perindopril 5 mg mane, atenolol 50 mg mane and atorvastatin 40 mg daily.

Russell is married and has two children. He stopped smoking when he had his heart attack and drinks a small amount of alcohol.

On examination his heart rate (HR) is 90 bpm and regular, and blood pressure (BP) is 150/90 mmHg. Jugular venous pressure (JVP) is difficult to measure but you think it is slightly elevated. There is a soft systolic murmur at the apex. The chest is clear. He has mild bipedal pitting oedema.

QUESTION 1

What is your provisional diagnosis? What initial investigations will you order? What initial therapy will you start?

FURTHER INFORMATION

Russell's electrocardiogram (ECG) is shown below. Biochemistry results are: Na 135 mmol/L; K 4.2 mmol/L; urea 8.9 mmol/L; creatinine 98 µmol/L; eGFR (MDRD) 69 mL/min. Full blood count is normal; BNP is 1680 ng/L (normal <50 ng/L). A chest X-ray shows an increased cardiothoracic ratio and clear lung fields. The ECG shows a dilated left ventricle with severe systolic dysfunction (left ventricular ejection fraction (LVEF) 25% with anterior akinesia) and moderate mitral regurgitation. Russell's dyspnoea improves with frusemide.

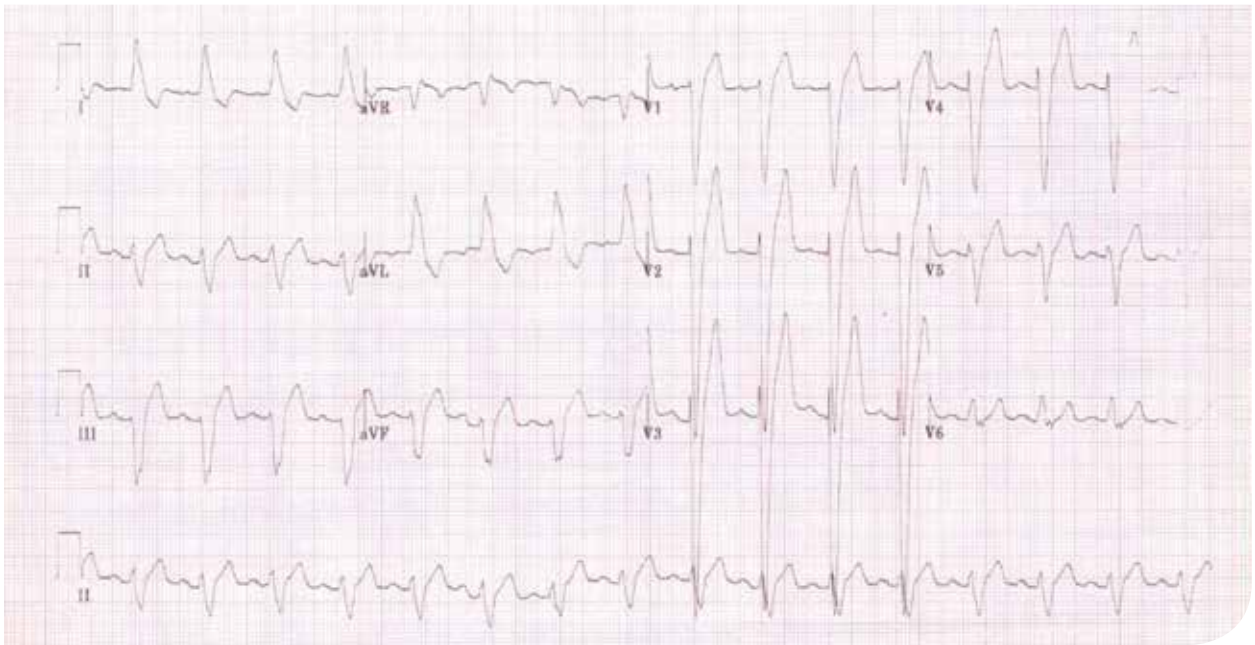

Figure 1. Russell's ECG results

QUESTION 2

What does Russell's ECG show? What is his diagnosis?

QUESTION 3

Which patients should be referred for specialist opinion?

QUESTION 4

What non-pharmacological recommendations, if any, do you make for Russell?

QUESTION 5

Which drugs have been shown to decrease mortality in systolic heart failure? How will you achieve maximum tolerated doses of these medications?

QUESTION 6

How should patients taking mineralocorticoid receptor antagonists (MRA), such as spironolactone, be monitored?

QUESTION 7

What will you tell Russell about driving?

FURTHER INFORMATION

Russell is seen by a cardiologist. A coronary angiogram reveals a patent stent with diffuse distal disease not amenable to revascularisation. His LVEF is 30%. Russell now takes aspirin 100 mg mane, perindopril 10 mg mane, carvedilol 50 mg twice daily, spironolactone 50 mg mane and atorvastatin 40 mg daily. He is in sinus rhythm with a heart rate of 80 bpm, and blood pressure 100/50 mmHg.

QUESTION 8

How important is heart rate reduction in treating heart failure? When should a sinus node inhibitor (i.e. ivabradine) be added?

QUESTION 9

Which patients should be considered for device therapy?

FURTHER INFORMATION

Following discussion with the cardiologist, Russell decides to defer device therapy as there has been some improvement in his LVEF. A repeat echocardiogram 3 months later demonstrates a LVEF of 40%, and Russell remains symptomatically well.

CASE 1 ANSWERS

ANSWER 1

You suspect that Russell's dyspnoea may be due to heart failure, given his history of previous myocardial infarction and hypertension. He currently displays New York Heart Association (NYHA) functional class III symptoms[3] (see *Table 1*).

Table 1. New York Heart Association functional classification of heart failure[3]

Class	Symptoms
Class I (mild)	No limitation of physical activity. Ordinary physical activity does not cause undue fatigue, dyspnoea or palpitations (asymptomatic LV dysfunction).
Class II (mild)	Slight limitation of physical activity. Ordinary physical activity results in fatigue, dyspnoea, angina or palpitations.
Class III (moderate)	Marked limitation of activity. Less than ordinary physical activity leads to symptoms.
Class IV (severe)	Severely limited by symptoms. Symptoms present at rest.

Initial investigations should include ECG, blood tests (biochemistry, full blood count) and chest X-ray.[3,4] Given that he has had longstanding elevated blood pressure, urine albumin-to-creatinine ratio (uACR) should also be measured, but blood pressure control is not the goal of treatment. However, none of these tests allows you to exclude a diagnosis of heart failure, so further investigation is required.

The most useful test to perform in patients with suspected heart failure is an echocardiogram, which provides information on cardiac structure, systolic and diastolic function and valvular function.[3]

Routine measurement of plasma B-type natriuretic peptide (BNP) is not recommended for diagnosis of chronic heart failure; however, if an echocardiogram cannot be arranged in a timely fashion, plasma BNP measurement may be useful.[3] A low BNP level (<100 ng/L) makes the diagnosis of heart failure unlikely, and alternative diagnoses should be considered.[5]

Angiotensin converting enzyme inhibitors (ACEIs) are first-line treatment for heart failure of any class. They should be commenced immediately, at a low dose, with the view to titrating the dose over intervals (e.g. 2–4 weeks) to maximally tolerated maintenance doses as per current guidelines.[2,6]

As Russell is already taking an ACEI, you start frusemide 40 mg mane for control of fluid overload symptoms.[2,4]

ANSWER 2

The ECG shows sinus rhythm of 97 bpm with left bundle branch block (LBBB): QRS >120 ms, positive broad complex in I, aVL, V5 and V6. The ST segment deviation is as expected for LBBB.

The cause of Russell's dyspnoea is heart failure (elevated BNP, symptomatic response to frusemide, LVEF 25%) due to severe left ventricular (LV) systolic dysfunction (systolic heart failure), underlying coronary artery disease (CAD) and previous myocardial infarction.

ANSWER 3

Ideally, a specialist opinion should be sought for all heart failure patients as referral improves patient symptoms, outcomes and reduces hospital admissions.[3] As a minimum this should include: i) when the diagnosis is in question; ii) when there are questions regarding management; iii) when a patient is being considered for revascularisation, a cardiac device or cardiac transplant; and iv) in patients under 65 years of age.[3]

ANSWER 4

Current heart failure guidelines recommend a range of non-pharmacological management strategies for patients.[3,4]

People with heart failure should be provided with information to enable them to monitor and manage their fluid balance. As high salt intake can exacerbate heart failure symptoms, restriction of both sodium (<2 g/day) and fluid (<2 L/day) is recommended. A lower fluid intake (<1.5 L/day) is advised for patients during episodes of fluid retention.[3] Patients can monitor their fluid status by measuring their morning weight before breakfast.

Once heart failure is stabilised, regular physical activity is advised to improve symptoms and functional capacity. Referral to a physical activity specialist could also be considered to enable individual tailoring of an exercise program.[3,7]

All patients should be advised about healthy lifestyle strategies. For example, quitting smoking if smokers, limiting alcohol to less than 1–2 standard drinks per day and limiting caffeinated beverages to 1–2 drinks per day.[2]

Dietary assessment and advice could also be considered as people with heart failure may become nutritionally deficient.[4]

Prevention strategies that could be discussed include vaccination against influenza and pneumococcal disease.[3]

ANSWER 5

ACEIs (or angiotensin receptor blockers in patients intolerant of ACEIs), heart failure beta-blockers (carvedilol, bisoprolol, metroprolol succinate, nebivolol) and MRA (i.e. spironolactone or eplerenone) prolong survival in patients with symptomatic systolic heart failure.[3,8–14] Digoxin has not been shown to reduce mortality; however, it reduces hospitalisations for heart failure, maintains clinical stability and exercise capacity in patients.[6]

Optimisation or the achievement of maximally tolerated doses of medications may take months (especially for beta-blockers), and requires close monitoring of symptoms, fluid status, kidney function and electrolytes.[4] 'Start low and go slow' is the generally accepted mantra. Beta-blockers should be initiated when the patient is stable and euvolaemic.[4] A Heart Failure Service with a titration prescription can facilitate this (www.health.qld.gov.au/heart_failure/pdf/medn_titration.pdf).

You continue frusemide 40 mg mane, increase perindopril to 10 mg mane, change atenolol to carvedilol, starting with a dose of 6.25 mg orally twice daily and aiming to increase the dose to 25–50 mg twice daily[4] and add spironolactone 25 mg mane (and consider uptitration to 50 mg mane). You refer Russell to a cardiologist.

ANSWER 6

Mineralocorticoid receptor antagonists (MRAs) improve survival and reduce hospital admissions in people with heart failure.[4] They can be initiated if the patient's potassium level is normal and there is adequate renal function. The RALES trial[14], which evaluated the benefits of spironolactone in heart failure, excluded patients with creatinine levels >221 µmol/L. In patients with renal failure, the addition of an MRA to an ACEI or an angiotensin-2 receptor antagonist can lead to life-threatening hyperkalaemia.[4]

Note, several contraindications apply for the use of MRAs. Spironolactone and eplerenone are contraindicated if the creatinine clearance (CrCl) is <30 mL/min of if the serum potassium is >5.5 mmol/L.[6]

Monitoring of potassium and renal function closely is mandatory for people on MRAs,[6] e.g. 1 week after commencing or titrating the dose, monthly for 6 months and then 6 monthly thereafter once stable dosing is achieved (see www.health.qld.gov.au/heart_failure/pdf/medn_titration.pdf).

ANSWER 7

The medical standards for driving a private vehicle stipulate that there must be a response to treatment and minimal symptoms associated with driving. Where these conditions are met, a conditional licence subject to periodic review (a specific time frame is not indicated) will be issued.

A commercial driver's licence requires that the patient has a satisfactory response to treatment, adequate exercise tolerance, LVEF ≥40%, have had the underlying cause considered and have minimal symptoms related to driving. Where these conditions are met a conditional licence subject to annual review will be issued (see Resources for Doctors for the Assessing Fitness to Drive guidelines).

ANSWER 8

Elevated resting heart rate is a predictor of death and hospitalisation in heart failure.[15,16]

Ivabradine is a specific sinus node inhibitor, which inhibits the sinoatrial 'pacemaker' current, leading to a reduction in heart rate.[17] It improves outcomes in patients with symptomatic systolic heart failure (LVEF ≤35%) in sinus rhythm with an elevated heart rate (≥70 bpm) despite optimal therapy.[3,8] According to the SHIFT study,[18] the main heart failure trial for ivabradine, its benefits are greater in patients with higher heart rates, with a 19% reduction in mortality seen in patients with heart rates ≥77 bpm. Additionally, significant reductions in hospitalisations were also observed.[18] A number needed to treat of 26 was calculated in the SHIFT trial. That is, 26 patients needed to be treated for one year to prevent one cardiovascular death or one hospitalisation from chronic heart failure.[18]

Ivabradine is available on the Pharmaceutical Benefits Scheme (PBS) with multiple restrictions and requires an authority script. As of December 2013, patients with chronic heart failure with a baseline heart rate ≥77 bpm, LVEF ≤35% and NYHA class II or III, in combination with optimal standard chronic heart failure treatment were eligible for PBS therapy.[17] Therapeutic Guidelines Cardiovascular[4] recommends doses of 2.5 to 7.5 mg (orally) twice daily. Note, that ivabradine may be prescribed by nurse practitioners where treatment has been previously initiated by a medical practitioner.[17]

Ivabradine is contraindicated if the heart rate is <60 bpm in the untreated state, where the sinoatrial node is not the cardiac pacemaker, in unstable angina, in unstable or acute heart failure or if the BP is <90/50 mmHg. Its use is also contraindicated in severe hepatic impairment.[6]

Russell meets the PBS criteria, and it would be appropriate to start ivabradine 5 mg twice daily in addition to his other therapy with a view to titrate up if the heart rate remains elevated.

ANSWER 9

In addition to the reductions in mortality associated with medical therapy, implantable cardioverter defibrillators have been shown to further decrease mortality in symptomatic heart failure patients with a LVEF ≤35%,[19] and in patients with prior myocardial infarction and a LVEF ≤30%.[20]

Cardiac resynchronisation therapy (biventricular pacing) decreases mortality in patients with symptomatic heart failure with a LVEF ≤35% and a broad QRS. Benefit is greatest in LBBB with a QRS ≥150 ms.[21–23]

CONCLUSION

Current evidenced-based guidelines emphasise the benefits of multidisciplinary, guideline-based care for people with heart failure. People receiving multidisciplinary care achieve better outcomes than patients who do not.[1] A number of tools are available to assist GPs managing patients requiring multidisciplinary care, including the GP Management Plan (Item 721) and for review (Item 725) as well as Team Care Arrangements coordinated by the GP (Item 723) and for review (Item 727). As an example, a multidisciplinary team might consist of the GP, an exercise physiologist and a dietician.[2]

Current guidelines highlight important gaps in the management of people with heart failure and suggest that greater attention in certain areas may improve patient outcomes. For example, this includes greater use of echocardiography, which is currently underused at diagnosis and for ongoing assessment of patients. Studies show that both ACEIs and beta-blockers are generally under-prescribed and used at suboptimal doses. Lastly, clinicians need to mindful of not prescribing medications that may exacerbate heart failure, as prescribing of such medications (e.g., corticosteroids, moxonidine) is common.[2]

REFERENCES

1. National Heart Foundation of Australia. A systematic approach to chronic heart failure: a consensus statement August 2013. Available at www.heartfoundation.org.au/SiteCollectionDocuments/HF_CHF_consensus_web_FINAL_SP.pdf [Accessed 3 February 2014].
2. National Heart Foundation of Australia. Quick reference guide for health professionals. Diagnosis and management of chronic heart failure. Updated October 2011. Available at www.heartfoundation.org.au/SiteCollectionDocuments/Chronic-heart-failure-QRG-2011.pdf [Accessed 3 February 2014].
3. National Heart Foundation of Australia. Guidelines for the prevention, detection and management of chronic heart failure in Australia 2011. Available at www.heartfoundation.org.au/SiteCollectionDocuments/Chronic_Heart_Failure_Guidelines_2011.pdf [Accessed 3 February 2014].
4. Cardiovascular Expert Group. Heart Failure. In: eTG [Internet]. Melbourne: Therapeutic Guidelines Ltd; 2012. Available at www.tg.org.au [Accessed 3 February 2014].
5. Maisel AS, Krishnaswamy P, Nowak RM, et al. Rapid measurement of B-type natriuretic peptide in the emergency diagnosis of heart failure. N Engl J Med 2002;347:161–67.
6. Rossi S, editor. Heart failure. Australian Medicines Handbook. In: Australian Medicines Handbook 2013. Adelaide: Australian Medicines Handbook Pty Ltd; 2013.
7. O'Connor CM, Whellan DJ, Lee KL, et al. Efficacy and safety of exercise training in patients with chronic heart failure (HF-ACTION). JAMA 2009;301:1439–50.
8. Krum H, Jelinek MV, Stewart S, et al. 2011 Update to national heart foundation of Australia and cardiac society of Australia and New Zealand guidelines for the prevention, detection and management of chronic heart failure in Australia 2006. MJA 2011;194:405–09.
9. Shibata MC, Flather MD, Wang D, et al. Systematic review of the impact of beta blockers on mortality and hospital admissions in heart failure. Eur J Heart Failure 2001;351–57.
10. McMurray JJV, Adamopoulos S, Anker SD, et al. ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure 2012. Eur Heart J 2012;33:1787–47.
11. Flather MD, Yusuf S, Kober L, et al. Long-term ACE-inhibitor therapy in patients with heart failure or left ventricular dysfunction: A systematic overview of data from individual patients. Lancet 2000;355:1575.
12. Pfeffer MA, Swedberg K, Granger CB, et al. Effects of candesartan on mortality and morbidity in patients with chronic heart failure: the CHARM-Overall programme. Lancet 2003;362:759–66.
13. Zannad F, McMurray JJ, Krum H, et al. Eplerenone in patients with systolic heart failure and mild symptoms (EMPHASIS). N Engl J Med 2011;364:11–21.
14. Pitt B, Zannad F, Remme WJ, et al. The effect of spironolactone on morbidity and mortality in patients with severe heart failure (RALES). N Engl J Med 1999;341:709.
15. Bohm M, Swedberg K, Komajda M, et al. Heart rate as a risk factor in chronic heart failure (SHIFT): the association between heart rate and outcomes in a randomised placebo-controlled trial. Lancet 2010;376:886–94.
16. Pocock SJ, Wang D, Pfeffer MA, et al. Predictors of mortality and morbidity in patients with chronic heart failure. Eur Heart J 2006; 27:65–75.
17. NPS MedicineWise. Ivabadrine (Coralan) for chronic heart failure. Available at www.nps.org.au/publications/health-professional/nps-radar/2013/december-2013/ivabradine [Accessed 3 February 2014].
18. Swedberg K, Komajda M, Bohm M, et al. Ivabradine and outcomes in chronic heart failure (SHIFT): a randomized placebo-controlled study. The Lancet 2010;376:875–85.
19. Bardy GH, Lee KL, Mark DB, et al. Amiodarone or an implantable cardioverter-defibrillator for congestive heart failure (SCD-HeFT). N Engl J Med 2005;352:225–37.
20. Moss AJ, Zareba W, Hall WJ, et al. Prophylactic implantation of a defibrillator in patients with myocardial infarction and reduced ejection fraction (MADITII). N Engl J Med 2002;346:877–83
21. Bristow MR, Saxon LA, Boehmer J, et al. Cardiac-resynchronization therapy with or without an implantable defibrillator in advanced chronic heart failure (COMPANION). N Engl J Med 2004;350:2140–50.
22. Cleland JGF, Daubert JC, Erdmann E, et al. The effect of cardiac resynchronization on morbidity and mortality in heart failure (CARE-HF). N Engl J Med 2005;352:1539–49.
23. Tang ASL, Wells GA, Talajic M, et al. Cardiac-resynchronization therapy with mild-moderate heart failure (RAFT). N Engl J Med 2010;363:2285–95.

RESOURCES FOR DOCTORS

- 2011 Guidelines for the prevention, detection and management of chronic heart failure in Australia. Heart Foundation www.heartfoundation.org.au/SiteCollectionDocuments/Chronic_Heart_Failure_Guidelines_2011.pdf
- Assessing Fitness to Drive. www.austroads.com.au/images/stories/AFTD_reduced_for_web.pdf

RESOURCES FOR PATIENTS

- Heart Foundation Information Booklet – Cardiomyopathy. www.heartfoundation.org.au/SiteCollectionDocuments/Cardiomyopathy.pdf

CASE 2

CHRISTINE PRESENTS WITH FATIGUE

Christine, aged 76 years, presents requesting a repeat prescription of her blood pressure (BP) medication. She was recently widowed and moved to the area to be closer to her daughter. She has no specific concerns but admits she has been a little more tired than usual, which she attributes to her bereavement. She reports general good health. Her BP is 135/80 mmHg with irbesartan 150 mg mane. Examination reveals an irregular heart rate (HR) of 116 bpm and atrial fibrillation (AF) is confirmed on a 12-lead ECG. She had attended her local GP in her previous town regularly for many years but was never aware of this diagnosis.

QUESTION 1

What additional history and investigation is required?

FURTHER INFORMATION

Christine's thyroid stimulating hormone (TSH) level is normal as is her echocardiogram. A diagnosis of non-valvular AF is confirmed. She has monitored her pulse over the past week and it has remained irregular, as is found when reviewed in clinic.

QUESTION 2

How should AF be managed?

QUESTION 3

What anticoagulation options are available to Christine and what considerations should be given to each?

FURTHER INFORMATION

Christine elects to commence warfarin treatment, as her husband tolerated it well for years. She manages well and settles into a monthly pattern of INR monitoring, which is generally stable. After 2 years she leaves the area to live with her son in Central Queensland.

She returns to see you 12 months later, staying with her daughter again, and is scheduled to have neurosurgery in 2 weeks for back pain. While in Central Queensland she was switched to dabigatran owing to the inconvenience of travelling long distances for INR monitoring.

QUESTION 4

How should anticoagulation therapy be managed peri-operatively?

CASE 2 ANSWERS

ANSWER 1

AF may occur in the context of underlying disease (e.g. hypertension, mitral valve disease, hyperthyroidism, ischaemic heart disease, heart failure, sleep apnoea)[1] or in the absence of other diseases. Evidence of underlying disease should be sought through history and investigation. In addition, precipitating factors for an episode of AF should be sought:[1] excess alcohol and/or caffeine consumption, and smoking status (including marijuana).[2]

A number of standard investigations may be considered for the initial evaluation of people presenting with AF, with the aim of evaluating cardiac function at baseline and identifying common comorbid conditions. These include:

- a complete blood count to identify underlying conditions (e.g. anaemia, infection)
- a complete metabolic profile for identification of electrolyte problems that may be causing or exacerbating AF
- echocardiography to assess heart features (e.g. size, shape, chamber pressures, valve structure and function, and systolic/diastolic function)
- electrocardiography to diagnose AF or to identify other arrhythmias and/or cardiac conditions (e.g. ischaemia)
- chest radiography to identify underlying pulmonary disease (e.g. pneumonia)
- additional tests as required on the basis of findings from the above tests.[3]

Appropriate investigations to consider for Christine could include full blood count (FBC), electrolytes and liver function tests (LFTs), measurement of TSH levels to assess thyroid function, and echocardiogram to assess valvular function. It is reasonable to request these tests, given that treatment will probably be necessary.

ANSWER 2

AF has been associated with an increased mortality risk. It has been described as conferring a 5-fold increase in the risk of stroke and a 3-fold increase in the risk of heart failure.[4]

As Christine is well and haemodynamically stable the principles of management for AF are based on:

- rate control and rhythm control to reduce symptoms and morbidity
- consideration of prophylaxis against thromboembolic complications.[1,5]

As this is her first presentation, the clinical pattern (paroxysmal, persistent or permament)[1,5] is not yet established. However, she has tachycardia, has felt tired and has continued to have clinically detectable tachyarrhythmia.

Rate control medication is suitable for minimally symptomatic patients. Rate control was demonstrated in the AFFIRM study, a large randomised trial with 4060 patients, to be at least as effective as rhythm control and had fewer side effects.[5,6] Beta blockers (metoprolol or atenolol) or calcium channel blockers (diltiazem or verapamil) are suitable.[1] Of particular importance is consideration of anticoagulant treatment. An Australian hospital audit in 2011 found that 70% of patients admitted with stroke in AF were not on anticoagulant treatment.[7]

All patients with AF should undergo a systematic assessment of their risk of thromboembolism and bleeding to assist with informed decision-making about anticoagulation therapy. NPS MedicineWise offers a practical solution to this assessment,[8] which outlines three steps:

1. Patient assessment
2. Risk mitigation
3. Anticoagulant selection.

Step 1: Non-valvular AF patient assessment – CHADS $_2$ score calculator[9]

Current guidelines[1,5] recommend treatment of people with non-valvular AF on the basis of their calculated $CHADS_2$ score (*Tables 1 and 2*).

Table 1. $CHADS_2$ tool for estimation of thromboembolic risk in people with non-valvular AF

Risk factor	Score
Congestive heart failure	1
Hypertension (including well controlled hypertension)	1
Age 75 years or older	1
Diabetes mellitus	1
Stroke or history of transient ischaemic attack (TIA)	2

Table 2. Risk of stroke based on $CHADS_2$ score

Stroke risk based on CHADS $_2$ score	Risk of stroke	Adjusted stroke rate
0	Low	1.9%
1	Moderate	2.8%
2	High	4%
3	High	5.9%
4	High	8.5%
5	High	12.5%
6	High	18.2%

Christine is over 75 years of age and has hypertension. Her $CHADS_2$ score is 2 and her risk of stroke is high (4% per 100 patient years without treatment).

Oral anticoagulation treatment is recommended for those determined

to have a moderate-to-high risk of stroke (i.e. $CHADS_2$ score ≥1).[1,5] Current guidelines recommend either asprin or no therapy for a $CHADS_2$ score of 0, whereas for a $CHADS_2$ score of 1 either aspirin or an oral anticoagulant is recommended with a stated preference for the latter.[1,5] The evidence for aspirin (an antiplatelet agent) in stroke prevention in AF is weak, as it is less effective than oral anticoagulants. The risk of major bleeding with aspirin is similar to that of well-controlled warfarin.[1]

Step 2: Risk mitigation

The risk of major bleeding while on an oral anticoagulant treatment has been reported to be in the order of at least 1–1.5% annually; higher rates are reported for those over 80 years of age in the first year (up to 80%) and declines in ensuing years (down to 40%).[1]

The HAS-BLED tool (*Table 3*)[10] can be used to identify correctable risk factors for bleeding and identify patients at high risk of bleeding. It should not be used to exclude patients from anticoagulant treatment. Patients at high risk of bleeding are also at high risk of stroke and increased monitoring may be required.[4] Correctable risk factors for bleeding should be identified and where possible managed.[11]

Table 3. The HAS-BLED tool[10]

H	Hypertension (systolic blood pressure >160 mm Hg)*
A	Abnormal renal or liver function
S	Stroke (history of)
B	Bleeding (history of, or predisposition to bleeding)
L	Labile INRs (<6 in 10 INRs in therapeutic range)*
E	Elderly (e.g. age >65 years)
D	Drugs (antiplatelet agents, NSAIDs, or alcohol ≥ 8 units per week)*

*Correctable risk factors for bleeding

Referring to the HAS-BLED tool,[8] Christine has hypertension, which is controlled, and is over 65 years of age but has no other risk factors that increase her bleeding risk. She is happy to consider anticoagulant treatment to reduce her risk of stroke.

ANSWER 3

Four oral anticoagulant agents are currently available. These include warfarin or the newer oral anticoagulants dabigatran, rivaroxaban and apixaban, which were PBS-listed in 2013 for stroke prevention in non-valvular AF.[12–14] See *Table 4* for a comparison of these agents. It is important to discuss with Christine the risks and benefits of all of these drug options. NPS RADAR has articles available on the role and place of each of these new anticoagulants in therapy.[12–14]

It is worth noting that only a few large trials have assessed the efficacy and safety of the newer oral anticoagulant agents relative to warfarin and there is a paucity of head-to-head data comparing newer agents.[23] In contrast to warfarin, the new oral anticoagulant agents do not require monitoring (*Table 4*). The new agents have not been shown to reduce stroke or systemic embolism to a greater extent than warfarin for patients whose INR is maintained within the therapeutic range (i.e. time in therapeutic range (TTR) ≥66%).[23] Lastly, current Australian guidelines cite both warfarin and dabigatran as first-line options when oral anticoagulation is required in AF.[1]

In comparative trials where warfarin use was well managed, only apixaban (of the new agents) was shown to have a lower incidence of major bleeds, compared with warfarin.[23,24,27,28]

The newer oral anticoagulant agents (dabigatran, rivaroxaban and apixaban)[17,24–26] could be considered as alternatives to warfarin in the absence of significant valvular disease, where there is poor INR control in the presence of good adherence to warfarin and where the CrCl is >30 mL/min.[25] Additionally, the newer agents might be suitable for patients for whom regular blood testing is problematic or who are unable to tolerate warfarin.[12–14]

ANSWER 4

Patient features, such as age and history of bleeding, as well as the nature of the planned surgery, will influence decision making for ceasing and restarting new oral anticoagulant agents.[29] Consideration of bridging anticoagulant pre- and/or post-operatively might be appropriate for some patients (e.g. intravenous heparin or low molecular weight heparin for high-risk patients).[16,29] Decisions about the duration of peri-operative discontinuation of dabigatran depend on renal function as it is cleared predominantly by the kidneys.[30] It has a longer half-life (>24 hours) in people with reduced renal function (CrCl <30ml/min), compared with healthy volunteers (around 13 hours) who are considered to be representative of the target group likely to be using this medication.[31] For those with normal renal function medication can be ceased 24 hours before elective surgery.[30] Some guidelines provide tabulated data suggesting when the last intake of a new oral anticoagulation agent (including dabigatran) should occur, taking into consideration the risk of bleeding (high or low) and renal function.[22,29]

While the above more complex considerations might be relevant for some patients, it has been suggested that, ideally, dabigatran should be ceased at least 24 hours before invasive surgery and at least 48 hours before procedures associated with a high risk of bleeding.[30] As general guidance, the Therapeutic Guidelines 2012 suggest continuation of all regular antithrombotic medications in patients having a procedure or surgery with a low risk of bleeding.[1] The guidelines stipulate that for procedures or surgery with a high risk of bleeding, anticoagulants usually need to be discontinued for a period of time to reduce the risk of bleeding. The Australian Medicines Handbook recommends cessation of dabigatran treatment 1–3 days before surgery if CrCL is >50mL/min.[16] For patients with impaired renal function (CrCl 30–50 mL/min) it should be ceased 3–5 days before surgery. Consideration could be given to increasing these times where complete haemostasis is needed.[16]

Where there is immediate and complete haemostasis, dabigatran can be restarted post-operatively within 6–8 hours.[29]

Table 4. Comparison of warfarin with newer oral anticoagulants for non-valvular AF

	Warfarin[15]	Dabigatran[16]	Rivaroxaban[17]	Apixaban[19]
Mode of action	Vitamin K antagonist	Direct thrombin inhibitor	Factor Xa inhibitor	Factor Xa inhibitor
Dose	Follow local dosing protocols and adjust dose according to INR (target 2–3)	150 mg orally twice daily Dose reduction to 110 mg twice daily for patients aged ≥75 years or for those with a (potentially) higher risk of bleeding;[1] and those with CrCl <30–50 mL/min[1,16]	20 mg once daily[#]	5 mg twice daily
PBS status	No restrictions	Authority required (streamlined)[19]	Authority required (streamlined)[20]	Authority required (streamlined)[21]
Antidote (for overcoagulation)	Available (vitamin K)	Not available	Not available	Not available
Renal considerations	Dose adjustments based on renal function per se are not required (use with care in severe renal impairment due to increased risk of bleeding)	Contraindicated if CrCl <30 mL/min Reduce dose in renal impairment (CrCl 30–50 mL/min)	Contraindicated if CrCl <29 mL/min Use with caution if CrCl 30–49 mL/min and using drugs that may increase rivaroxaban concentration	Contraindicated if CrCl <15 mL/min Use with caution when CrCl 15–29 mL/min (apixaban concentrations may increase)
Monitoring	Routine INR monitoring is required to maintain INR within target levels	Routine testing is generally not conducted[22] Measuring activated partial thromboplastin time determines if a dabigatran effect is present but does not provide data on the extent of anticoagulant activity[1] INR monitoring not recommended[22]	Routine laboratory monitoring is not recommended as there are no methods to guide dose adjustment	Routine laboratory monitoring not recommended as there are no methods to guide dose adjustment
Adverse events	Common: bleeding Rare: skin necrosis, purple discolouration of toes, alopecia, fever, rash, nausea, vomiting, diarrhoea, hepatic dysfunction, allergic reactions	Common: bleeding from puncture sites and wounds, signs of bleeding (e.g. anaemia) gastritis, dyspepsia, gastrointestinal bleeding Infrequent: increased liver enzymes and bilirubin Rare: severe bleeding	Common: bleeding, signs of bleeding (e.g. anaemia), peripheral oedema, itch, skin blisters, muscle spasm	Common: bleeding, signs of bleeding (e.g. anaemia), nausea Infrequent: thrombocytopaenia, abnormal liver function tests Rare: allergic reactions

[#]Reduce dose to 15 mg once daily if CrCl is 30–49 mL/min[17]

REFERENCES

1. Cardiovascular Expert Group. Therapeutic guidelines: cardiovascular. Version 6. In: eTG [Internet]. Melbourne: Therapeutic Guidelines Ltd; 2012. Available at www.tg.org.au [Accessed 3 February 2014].
2. Crawford MH. Current Diagnosis and Treatment Cardiology 3rd ed. McGraw-Hill Global Education Holdings, 2009. Chapter 21, Atrial fibrillation. Available at www.accessmedicine.com/content.aspx?aID=3648801 [Accessed 4 January 2014].
3. Gutierrez C, Blanchard DG. Atrial fibrillation: diagnosis and treatment. Am Fam Physician 2011;83:61–68.
4. 2012 Focused update of the ESC guidelines for the management of atrial fibrillation: an update of the 2010 ESC Guidelines for the management of atrial fibrillation. Eur Heart J 2012;33:2719–47.
5. Rossi S, editor. Tachyarrythmias. In: Australian Medicines Handbook 2013. Adelaide: Australian Medicines Handbook Pty Ltd; 2013.
6. Wyse DG, Waldo AL, DiMarco JP, et al. A comparison of rate control and rhythm control in patients with atrial fibrillation. N Engl J Med 2002;347:1825–33.
7. Stroke Foundation. National stroke audit acute services. Clinical audit report 2011. Available at strokefoundation.com.au/site/media/National_stroke_audit_acute_services_clinical_audit_report_2011.pdf [Accessed 4 January 2014].
8. NPSMedicinewise. A guide to starting oral anticoagulants in atrial fibrillation. Available at www.nps.org.au/health-professionals/resources-and-tools/decision-and-management-tools/decision-tools/starting-oral-anticoagulants [Accessed 4 January 2014].
9. Gage BF, Waterman AD, Shannon W, et al. Validation of clinical classification schemes for predicting stroke: results from the National Registry of Atrial Fibrillation. JAMA 2001;285:2864–70.
10. Pisters R, Lane DA, Nieuwlaat R, et al. A novel user-friendly score (HAS-BLED) to assess 1-year risk of major bleeding in patients with atrial

fibrillation: the Euro Heart Survey. Chest 2010;138:1093–100.

11. NPS MedicineWise. Evidence summary on oral anticoagulants and stroke prevention in atrial fibrillation. Available at www.nps.org.au/medicines/heart-blood-and-blood-vessels/anti-clotting-medicines/for-individuals/anticoagulant-medicines/for-health-professionals/evidence-summary/atrial-fibrillation [Accessed 14 January 2014].
12. NPS MedicineWise. Dabigatran (Pradaxa) for stroke prevention in patients with non-valvular atrial fibrillation. Available at www.nps.org.au/publications/health-professional/nps-radar/2011/august-2011/dabigatran-af [Accessed 4 January 2014].
13. NPS MedicineWise. Rivaroxaban (Xarelto) for stroke prevention in non-valvular atrial fibrillation. Available at www.nps.org.au/publications/health-professional/nps-radar/2012/december-2012/rivaroxaban-nvaf [Accessed 4 January 2014].
14. NPS MedicineWise. Apixaban (Eliquis) for stroke prevention in non-valvular atrial fibrillation. Available at www.nps.org.au/publications/health-professional/nps-radar/2013/august-2013/apixaban [Accessed 4 January 2014].
15. Rossi S, editor. Warfarin. In: Australian Medicines Handbook 2013. Adelaide: Australian Medicines Handbook Pty Ltd; 2013. Available at www.amh.net.au/online [Accessed 3 February 2014].
16. Rossi S, editor. Dabagitran. In: Australian Medicines Handbook 2013. Adelaide: Australian Medicines Handbook Pty Ltd; 2013. Available at www.amh.net.au/online [Accessed 3 February 2014].
17. Rossi S, editor. Rivaroxaban. In: Australian Medicines Handbook 2013. Adelaide: Australian Medicines Handbook Pty Ltd; 2013. Available at www.amh.net.au/online [Accessed 3 February 2014].
18. Rossi S, editor. Apixaban. In: Australian Medicines Handbook 2013. Adelaide: Australian Medicines Handbook Pty Ltd; 2013.Australian Medicines Handbook: 2013 [Accessed 3 February 2014].
19. Australian Government Department of Health. PBS: Blood and blood forming organs: Antithrombotic Agents. Dabigatran. Available at www.pbs.gov.au/medicine/item/5054B [Accessed online 15 January 2014].
20. Australian Government Department of Health. PBS: Blood and blood forming organs: Antithrombotic Agents. Rivaroxaban. Available at www.pbs.gov.au/medicine/item/5054B [Accessed online 15 January 2014].
21. Australian Government Department of Health. PBS: Blood and blood forming organs: Antithrombotic Agents. Abixaban. Available at www.pbs.gov.au/medicine/item/5054B [Accessed online 15 January 2014].
22. Queensland Health. Guideline for managing patients on Dabagatran (Pradaxa) Statewide. Version No.: 2.0 Effective from 21/052013. Available at http://www.health.qld.gov.au/qhcss/mapsu/documents/dabigatran_info.pdf [Accessed 15 January 2014].
23. Canadian Agency for Drugs and Technologies in Health. Safety, effectiveness, and cost-effectiveness of new oral anticoagulants compared with warfarin in preventing stroke and other cardiovascular events in patients with atrial fibrillation 2012. Available at www.cadth.ca/media/pdf/NOAC_Therapeutic_Review_final_report.pdf [Accessed 15 January 2014].
24. Connolly SJ, Ezekowitz MD, Yusuf S, et al. Dabigatran versus warfarin in patients with atrial fibrillation. N Engl J Med 2009;361:1139–51.
25. Rossi S, editor. Ischaemic stroke and transient ischaemic attacks. In: Australian Medicines Handbook 2013. Adelaide: Australian Medicines Handbook Pty Ltd; 2013. Available at www.amh.net.au/online [Accessed 3 February 2014].
26. Granger CB, Alexander JH, MacMurray JJV, et al. Apixaban versus warfarin in patients with atrial fibrillation. N Engl J Med 2011;365:981–92.
27. Wallentin L, Lopes RD, Hanna M, et al. Efficacy and safety of apixaban compared with warfarin at different levels of predicted INR control for stroke prevention in atrial fibrillation. Circulation 2013;127:2166–76.
28. Patel MR, Mahaffey KW, Garg J, et al. Rivaroxaban versus warfarin in nonvalvular atrial fibrillation. N Engl J Med 2011;365:883–91.
29. Heidelbuchel H, Verhamme P, Alings M, et al. EHRA practical guide for use of the new oral anticoagulants in patients with non-valvular atrial fibrillation: executive summary 2013. Eur Heart J. 2013;34:2094–2106.
30. Hankey GJ and Eikelboom JW. Dabigatran etexilate: a new oral thrombin Inhibitor. Circulation 2011;123:1436–50.
31. Stangier J, Rathgen K, Stähle H, Mazur D. Influence of renal impairment on the pharmacokinetics and pharmacodynamics of oral dabigatran etexilate: an open label, parallel group, single-centre study. Clin Pharmacokinet 2010:49:259–268.

CASE 3

ALISON IS SUDDENLY SHORT OF BREATH

Alison, aged 37 years, developed shortness of breath and chest pain this morning. Her past medical history includes only exercise-induced asthma. She has no known medication allergies and takes only the combined oral contraceptive pill and salbutamol as needed. She is married, has two teenage children and works 4 days a week in a garden centre.

QUESTION 1

What questions should you ask about the presenting complaint?

FURTHER INFORMATION

On examination, Alison is obese and can talk in full sentences. Her heart rate is 104 bpm and regular, respiratory rate is 24 breaths per minute, blood pressure 144/90 mmHg, temperature 37.4°C and oxygen saturation 94%. There is no peripheral cyanosis or chest wall tenderness. Chest expansion, percussion, auscultation and groin/leg pulses are all normal. Her legs and ankles seem normal with the exception of varicose veins, of which one on her left calf shows some tracking nodular inflammation. She says she was prescribed antibiotics for it last week but it has become worse.

QUESTION 2

What is Alison's problem most likely to be? Describe the key features, complications and management of this condition.

QUESTION 3

What is the most likely cause of Alison's chest pain and shortness of breath? What tests/investigations would you perform immediately?

QUESTION 4

Would you perform a D-dimer test?

FURTHER INFORMATION

A discharge summary arrives a week later confirming a pulmonary embolism secondary to an occult DVT in the superficial femoral vein and informs you of Alison's commencement on warfarin.

QUESTION 5

What is significant about the term 'superficial' femoral vein?

QUESTION 6

How does anticoagulation treatment differ for DVT and superficial venous thrombosis?

FURTHER INFORMATION

Alison returns to you with a series of questions.

QUESTION 7

Alison asks, 'What caused it? Can I do anything to stop it happening again?' What would you advise her?

QUESTION 8

Alison asks, 'This warfarin testing and dose changing is a bit much. Can't I just take aspirin?' How would you respond?

QUESTION 9

Alison asks what you think about a 'new' drug. What would you tell her?

QUESTION 10

Alison wants to know why she has to wear a stocking and for how long. How do you answer these questions?

CASE 3 ANSWERS

ANSWER 1

Alison should be asked about any precipitating events that she believes may have led to her current situation. She should be asked to clarify what she means by shortness of breath. You should also ask questions about any associated pain that she may be experiencing and about any other cardiac and/or respiratory symptoms (palpitations, syncope, orthopnoea, claudication, wheeze, haemoptysis or cough) and enquire about symptoms, risk factors and family history of serious conditions, including:

- infection (fever, contact with others, birds, moulds, recent travel, etc.)
- malignancy (weight loss, night sweats, smoking, industrial exposure)
- cardiac disease (hypertension, cholesterol, diabetes, smoking)
- pulmonary embolus (recent stasis/surgery, malignancy, prior deep venous thrombosis (DVT) irritable bowel disease, pregnancy, smoking, oestrogen-based medication).[1]

Alison confirms no precipitating event. The shortness of breath is constant, consisting of short breaths accompanied by right lateral, pleuritic pain that worsens with exercise and is not alleviated by anything. She denies any other symptoms, any contact with others with the same symptoms and any injury, surgery, travel or immobility. There is no significant family history. She works with potting mixes. She ceased smoking 2 years ago. Her blood pressure is usually normal and she has never had her cholesterol or blood sugar tested.

ANSWER 2

Alison's problem is most likely superficial venous thrombosis (thrombophlebitis), which is thrombus formation in the superficial venous system. It is often associated with varicose veins and presents with tracking inflammation (e.g. redness, swelling, heat) that can be confused with cellulitis. It is not infective, so unless there has been some recent instrumentation or injection, antibiotics are not indicated. Intravenous cannulation, pregnancy, malignancy and other causes of venous stasis or trauma have been associated with presentations of superficial venous thrombophlebitis.[2]

Superficial venous thrombophlebitis is usually a self-limiting condition.[2] The main complication is a 10% chance of the thrombus extending, about half of which will 'grow' into the deep vein system. Additionally, up to 25% of patients may present with occult DVT.[3]

Management of spontaneous superficial thrombophlebitis requires low molecular weight heparin (LMWH) (e.g. enoxaparin 40 mg subcutaneous daily) for 4 weeks, unless the bleeding risk is high, in which case surveillance is recommended; 2–3 duplex ultrasounds over several weeks.[2,3] Seek occult DVT with duplex ultrasound.[3]

Use of LMWH does not require any laboratory monitoring and LMWHs should be used cautiously in those with renal impairment.[4]

Baseline haemoglobin, platelets, APTT, INR and creatinine should be checked before starting treatment.[4]

ANSWER 3

Pulmonary embolism seems most likely. Confirm the probability with a Well's score for pulmonary embolism and exclude ischaemia with an ECG (which could also suggest pulmonary embolism: S1 Q3 T3 ±right heart strain).

A Wells score is a validated scoring system of seven criteria and was developed in the late 1990s to clinically predict the likelihood of PE (*Table 1*). Using the table below, you can calculate Alison's Wells score.

Table 1. Wells score for clinically predicting the probability of pulmonary embolism[5]

Variable	Score
Previous pulmonary embolism or DVT	1.5
Tachycardia: >100 bpm	1.5
Recent surgery or immobilisation (within previous 4 weeks)	1.5
Clinical symptoms of DVT	3
Alternative diagnosis is less likely than pulmonary embolism	3
Haemoptysis	1
Cancer: palliative, current treatment or such in last 6 months	1
Risk stratification: low 0–1; intermediate: 2–6; high: 7 or more	
Her Wells score is 4.5 (tachycardia, alternative diagnosis less likely).	

ANSWER 4

A D-dimer test is not required in this instance. A D-dimer test is needed if the diagnosis is doubtful, in which case a negative test plus a Wells score of ≤4 excludes pulmonary embolism.[6]

High clinical suspicion of pulmonary embolism requires immediate inpatient evaluation and guidelines recommend starting appropriate treatment while awaiting test results.[4]

ANSWER 5

Despite its name, it is not a superficial vein. It is a deep vein and acute thrombosis of this vessel is potentially life threatening. Any thrombus therein should be treated with an anticoagulant as per DVT.[3,7]

ANSWER 6

Management of spontaneous superficial thrombophlebitis requires short-term anticoagulation as discussed earlier, whereas DVT requires longer anticoagulation treatment. Three months of anticoagulation is required for an unprovoked distal DVT (below the popliteal vein) or for DVT provoked by a major transient risk factor (e.g. surgery, trauma, immobilisation for more than 3 days, pregnancy or postpartum management, oral contraceptive or hormone replacement therapy). Six months is required after any

first unprovoked proximal DVT or pulmonary embolism. Indefinite anticoagulant treatment is needed for any unprovoked recurrence or any unprovoked DVT with active risk factors: cancer, thrombophilia or antiphospholipid antibody syndrome.[2]

ANSWER 7

You explain that her varicose veins together with her use of the oral contraceptive pill have most likely contributed to her current problems. She can minimise the chance of recurrence by avoiding provoking factors as listed above. Also, because the risk of recurrent superficial thrombosis is high, and varicose veins have been a contributing factor, she should consider treatment.[3]

ANSWER 8

The guidelines do not recommend aspirin for prophylaxis of venous thromboembolism, as a range of more effective therapies are available.[4]

Aspirin prevents platelet aggregation, which is how clots form in arteries. However, in veins, clots are formed by clotting factors, not by platelet aggregation. Aspirin, therefore, is ineffective and warfarin is required.[8]

ANSWER 9

Rivaroxaban has recently been listed on the PBS as a streamlined authority for confirmed acute pulmonary embolism (for use in the initial treatment phase) at a dosage of 15 mg twice daily for 3 weeks, then 20 mg daily thereafter.[9,10]

You explain that, unlike for warfarin, there is no validated test for measuring coagulation levels and no antidote for acute bleeding for rivaroxaban. You download a flyer for patients (rivaroxaban) consumer medicine information (CMI) leaflet. She says she'll think about it.

ANSWER 10

You discuss post-thrombotic syndrome, which may include pain, swelling, varicose eczema, skin thickening and staining, which occurs after 60% of DVTs. The incidence of these problems can be halved by wearing a graduated compression stocking.[8] Wearing a knee high stocking with 30–40 mm Hg pressure at the ankle for 18 months is recommended. Stockings should be fitted by an experienced professional, because of the pressure differences.[2]

REFERENCES

1. Murtagh J. General Practice 5th ed. North Ryde: McGraw-Hill; 2011.
2. Treatment of deep vein thrombosis and pulmonary embolism. In: eTG [Internet]. Melbourne. Therapeutic Guidelines Limited; January 2014 [Accessed Jan13 2014].
3. Robinsons, D. Calf vein thrombosis and superficial venous thrombosis: Advice on management. Medicine Today 2013;14:18–24.
4. Rossi S, editor. Treatment of venous thromboembolism. In: Australian Medicines Handbook 2013. Adelaide: Australian Medicines Handbook Pty Ltd; 2013.Australian Medicines Handbook. Available at www.amh.net.au [Accessed 20 January 2014].
5. Wells P, Andersons M, Rodger M, et al. Derivation of a simple clinical model to categorise patients' probability of pulmonary embolism: increasing the model's utility with the simpliRED D-Dimer. Thromb Haem 2000;83:358–19.
6. Geersing GJ, Erkens PM, Lucassen WA, et al. Safe exclusion of pulmonary embolism using the Wells rule and qualitative D-dimer testing in primary care: prospective cohort study. BMJ 2012;345:e6564.
7. Bundens WP, Bergan JJ, Halasz NA, Murray J, Drehobl M. The superficial femoral vein. A potentially lethal misnomer. JAMA 1995;274:1296–98.
8. Flecknoe-Brown S. How to treat: clotting conditions. In: How to Treat Yearbook 2010 pp295–30.
9. Australian Government Department of Health. Pharmaceutical Benefits Scheme. Available at www.pbs.gov.au/medicine/item/2160Q [Accessed 20 January 2014].
10. National Prescribing Service: Anticoagulant listings 2013. Available at www.nps.org.au/medicines/heart-blood-and-blood-vessels/anti-clotting-medicines/for-individuals/anticoagulant-medicines/for-health-professionals/decision-tools/anticoagulants-listings [Accessed 31 January 2014].

RESOURCES FOR PATIENTS

- Xarelto: Consumer medicine information. Available at www.nps.org.au/__data/cmi_pdfs/CMR09333.pdf [Accessed 20 January 2014].

CASE 4

JOHN HAS HIGH CHOLESTEROL

John is a secondary school vice principal aged 45 years and attends your practice after a health check at work. He says that he was told to see his doctor because his cholesterol was too high and that his blood pressure was borderline. He was advised that he would need treatment.

His health check showed the following:

- Total cholesterol (TC) 6.8 mmol/l,
- Low density lipoprotein (LDL) 5.0 mmol/L
- High density lipoprotein (HDL) 1.0 mmol/L
- Triglycerides (TG) 2.1 mmol/L
- BMI 26 m^2/kg
- Blood pressure (BP) 145/85 mmHg.

He is a non-smoker. He says that he won't take any tablets because he feels perfectly well.

QUESTION 1

How would you assess John's current cardiovascular risk?

FURTHER INFORMATION

John's current cardiovascular risk using the Australian Absolute Cardiovascular Risk Calculator is assessed as being low (6%) for a cardiovascular event in the next 5 years. John accepts that his lipid levels are too high but says he wants to 'fix' them naturally. He has been told that he can achieve the same benefit as those achievable with medication by eating more fish, adopting a Mediterranean diet and exercising more.

QUESTION 2

What advice would you give John about his proposed approach? What further advice and/or medication would you give him in view of his stated intentions and current risk profile?

FURTHER INFORMATION

John returns for a check up after working at a country school for 5 years. He is now 50 years old, overweight (BMI 29) and his BP is 155/95 mmHg. His recent total cholesterol was 6.7 mmol/L, LDL 4.8 mmol/L, HDL 0.9 mmol/L, TGs 2.5 mmol/L.

QUESTION 3

How would you assess, advise and manage John at this point?

FURTHER INFORMATION

John returns after 6 months to get his latest blood test results. His TC is 6.6 mmol/L, LDL 4.9 mmol/, HDL 0.9 mmol/L, TG 2.3 mmol/L. His BP is 160/95 mmHg and home readings have ranged between 145/85 and 180/100 mmHg.

QUESTION 4

What options would you consider in managing John's cardiovascular risk at this time?

FURTHER INFORMATION

John returns for a repeat script for his blood pressure medication 6 months after the last visit and explains that he is no longer taking his statin after having watched a TV show suggesting these tablets are potentially harmful and are not necessary.

QUESTION 5

What advice would you give John at this point? How would you discuss the message described in the TV show?

FURTHER INFORMATION

Despite listening to your explanation and acknowledging that there needs to be a trade-off between benefit and risk, he explains that he prefers to stop taking statin tablets for the time being. John continues to see you for BP medication every 6–7 months but comes to see you 2 years later following discharge from hospital after a non-ST segment elevation myocardial infarction (NSTEMI). He is annoyed that his hospital cardiologist insisted that he has no option now but to take a statin and that he did not seem interested in John's point of view, that statins were more dangerous than helpful in his case.

QUESTION 6

What advice would you give John? How would you advise John in relation to his current cardiovascular risk and need, if any, for medication?

CASE 4 ANSWERS

ANSWER 1

Current guidelines support assessment and management of people like John (i.e. without known history of CVD; primary prevention) on the basis of their calculated absolute cardiovascular risk. The person's calculated risk informs management decisions and clarifies the role of pharmacotherapy.[1]

Dyslipidaemia is only one of several risk factors for CVD. Although there is good evidence to support the use of statins to reduce cardiovascular risk, it is essential to assess absolute cardiovascular risk to appropriately determine overall risk for individual patients[2,3] before making management decisions. Assessment of risk, taking into account multiple risk factors (absolute cardiovascular risk), is more accurate than consideration of single risk factors (e.g. lipid levels), as the cumulative effect of multiple risk factors is believed to be additive or synergistic.[2] More than 90% of adult Australians have one modifiable risk factor for cardiovascular disease and 64% have three or more.[4] When it comes to reducing overall cardiovascular risk, a moderate reduction in several risk factors is more effective than a major reduction in just one risk factor.[1]

In patients not clearly at high risk, it is recommended that their absolute cardiovascular risk is calculated using an appropriate tool such as Australian cardiovascular risk charts provided in the Australian National Vascular Guidelines.[5–7] Pharmacotherapy is not required by all patients. A person's calculated level of risk determines whether pharmacotherapy is needed or not. For those at high risk, guidelines recommend simultaneous treatment with lipid-lowering and BP-lowering medications, unless contraindicated or clinically not appropriate. For those at moderate or low cardiovascular risk, medication (e.g. statins) is not routinely recommended.[8] Lifestyle advice, including support on diet, physical activity and smoking

cessation, should be offered to all patients irrespective of their level of cardiovascular risk.[8] In summary all management decisions should be based on absolute cardiovascular risk.[5].

The Australian cardiovascular risk charts are based on the Framingham Risk Equation and take into account gender, age, BP, smoking status, TC and HDL, diabetes status and left ventricular hypertrophy (LVH) on ECG. The calculator gives a measure of estimated numerical risk of a cardiovascular event within the next 5 years as high (>16%), moderate (10–15%) and low (<10%).

While a risk calculation can help with management decisions, it is still necessary to undertake a full cardiovascular assessment taking into account additional modifiable and non-modifiable risk factors and other related conditions. Fasting blood glucose (FBG) should also be measured to exclude diabetes. Other factors to consider in this assessment include central obesity, waist circumference and BMI, poor nutrition, sedentary lifestyle and excessive alcohol intake, social history (including cultural identity and ethnicity e.g. Aboriginal and Torres Strait Islander, Maori and Pacific Islander, South Asian, Middle Eastern peoples and those of lower socioeconomic status). Related conditions, such as chronic kidney disease (albuminuria with or without proteinuria and/or reduced eGFR), familial hypercholesterolaemia, evidence of AF and mental health issues such as stress, also need to be considered.[1]

It is important to remember that certain groups can have their risk underestimated with a risk calculator and in these patients a calculation should be seen as minimum risk (e.g. predictive value has not been assessed in overweight/obese adults), while others do not do not need their risk calculated as they are known to be at high risk of cardiovascular disease (e.g. people with diabetes over 60 years).[1]

ANSWER 2

Lifestyle changes involving diet and increasing physical activity have been shown to effectively lower disease burden, especially in relation to obesity and future heart disease and diabetes.[1] It is, however, difficult to undertake randomised controlled trials of lifestyle factors when many are related to each other (e.g. diet and exercise or smoking status), without introducing inherent bias. Randomised controlled trials addressing such complex interrelated factors are more difficult to undertake than those investigating pharmacological interventions. Hence, most of the data relating to the effect of lifestyle interventions is from cohort or observational studies.

A 2013 Cochrane review[9] reported that giving people dietary advice, such as reducing consumption of fat, saturated fatty acids, cholesterol and salt, and increasing the consumption of fruit, vegetables, polyunsaturated and monosaturated fatty acids, reduced total and LDL cholesterol and BP, without any statistical significant changes to HDL or TGs.

There is conflicting evidence about the benefits of regularly consuming fish or fish oil (omega-3 fatty acid) supplements. Omega-3 fatty acid supplements reduce TGs by 20–30% and are recommended for treating hypertriglyceridaemia.[5] Lower rates of coronary events, sudden death and total mortality have been reported to be associated with higher fish intake[10–12] but a systematic review of 48 randomised controlled trials showed no benefit in patients with existing CHD.[13] Current guidelines based on population studies recommend fish consumption 2–3 times per week as part of an appropriate balanced diet.[2,5]

The Mediterranean diet involves consumption of high levels of olive oil, legumes, unrefined cereals, fruits, vegetables, moderate-to-high consumption of fish, moderate consumption of dairy products and wine and low consumption of meat and meat products.[14] A 2008 systematic review of 12 observational studies found adherence to a Mediterranean diet is associated with reduced cardiovascular risk and total mortality.[15].

Several meta-analyses have shown an inverse relationship between physical activity and the risk of a cardiovascular event and all-cause mortality.[16–19] Two and a half hours of moderate intense activity per week is associated with a 19% reduction in mortality risk, compared to no activity[20]. Dose–response relationships between exercise duration over a week or exercise intensity on the one hand and mortality risk, have been demonstrated and the greatest benefits are seen in those moving from no activity to low activity.[16,17,20,21] Benefits from increasing physical activity levels can be attained for those starting with minimal activity levels, as well as those increasing from mild or moderate existing activity levels.[6]

A number of randomised controlled trials and meta-analyses show significant benefits of physical activity on a number of cardiovascular risk factors,[22–26] including reducing LDL and TGs, increasing HDL[24] and insulin sensitivity,[26] reducing body fat[23,25] and lowering BP.[22–24]ßß

It is appropriate to recommend that all patients with high LDL undertake lifestyle modifications such as aerobic exercise, a healthy diet and weight loss for overweight patients.

ANSWER 3

John's risk should be recalculated and his calculated risk should inform the development of a management plan for him if required.[1] An ECG should be done to exclude CAD and ILVH. FBG should also be reassessed.

Using the risk calculator, John is now at medium risk (11%) of a cardiovascular event over the next 5 years. Lipid-lowering or BP-lowering therapy is not routinely recommended for patients at moderate cardiovascular risk; however, medication may be appropriate in some circumstances.[1]

Initial recommendations to John should be to reinforce the importance of an appropriate diet and increasing physical activity.

BP-lowering or lipid-lowering medication might be considered if 3–6 months of appropriate behavioural risk factor modification does not reduce his absolute cardiovascular risk or if his BP remains persistently above 160/100 mmHg, he has a family history of premature CVD or he is in a specific population group in which the Framingham Risk Equation underestimates his risk. These groups include Aboriginal and Torres Strait Islander people, certain ethnic groups, younger people with diabetes, overweight or obese people and people of lower socioeconomic status. In these situations, the calculated risk should be treated as a minimum estimate that is then adjusted according to clinical judgement.[1]

ANSWER 4

John is still at moderate cardiovascular risk but now qualifies for PBS-reimbursed statin therapy on the basis of his low HDL and high TC.[1] He is significantly overweight, which is known to underestimate absolute cardiovascular risk[1] and his BP is now consistently elevated despite appropriate lifestyle intervention. The case for commencing low dose statin therapy is now a stronger one. However, ultimately the decision to commence a statin should be made by the patient after appropriate discussion of the risks and benefits of statin therapy.

Statins reduce the risk of cardiovascular events and death in people with increased cardiovascular risk regardless of initial lipid levels. However, the benefits of statin therapy are greatest for those at highest risk.[27,28] The addition of statin therapy for primary prevention (of cardiovascular disease) at this time would be based on the 20–30% expected reduction in CVD events seen in most clinical trials of statin therapy rather than aiming at a specific LDL level.[27,28] Although statins differ in potency, no one statin has been shown to have a clear proven advantage on the basis of outcomes data.[29] The choice of statin, starting and maximum doses and target lipid levels should be individualised on the basis of whether use is for primary or secondary prevention and the degree of patient cardiovascular risk.

The use of non-statin lipid lowering therapy for primary prevention in a case such as this is not generally recommended given the lack of supporting trial data and the concern about increased non-cardiovascular mortality shown in several trials looking at non-statin lipid lowering therapy in primary prevention.[30-33]

Regardless of the decision about lipid-lowering therapy, John should be commenced on BP-lowering therapy at this time given his persistently elevated BP readings despite his best efforts at lifestyle modification.

John's absolute cardiovascular risk should be reassessed in 6–12 months time.

ANSWER 5

It is important to review the risks and benefits of statin therapy with John, in particular, discussing the side effects that were highlighted in the TV program. However, if after appropriate discussion, John is still not willing to resume statin therapy, and given that his cardiovascular risk is only moderate, it would certainly be appropriate to accept his decision as a reasonable one.

It would be important to emphasise again that cardiovascular risk is multifactorial and to remind him of the benefits of lifestyle modification and of the importance of continuing to take his BP medication. It would be appropriate to review his cardiovascular risk again in 6–12 months time.

ANSWER 6

Absolute cardiovascular risk assessment identifies those at risk without overt disease. It is not necessary for certain groups already known to be at high risk of CVD.[1] Such groups are those with diabetes over 60 years of age or with microalbuminuria; moderate or severe chronic kidney disease (CKD); previous diagnosis of familial hypercholesterolaemia, systolic BP ≥180 mmHg, or diastolic ≥110 mmHg; serum TC >7.5 mmol/L or Aboriginal and Torres Strait Islander peoples over 74 years old.

Now that John has had a cardiovascular event, he is and will always remain at high risk with at least a >15% 5-year risk of a further cardiovascular event. Patients, like John who have had a cardiovascular event, have existing CVD and need to managed according to secondary prevention guidelines.[8] The optimal management of John's cardiovascular risk now includes aggressive lipid-lowering and BP-lowering treatment, aspirin therapy and appropriate lifestyle modification.[34] It is important to carefully explain the evidence supporting such treatment as well as the potential side effects of treatment. If after adequate explanation of the appropriate evidence John still decides to refuse statin treatment, discussing alternative lipid-lowering medication as secondary prevention would be worth trying. If John then made an informed decision to refuse any lipid-lowering medication, a summary of the discussion and a note that John understands the risks of not taking such treatment should be recorded in his medical record. John should continue to be seen every 3–6 monthly to ensure his BP is managed at target levels, and he should continue to receive advice as to the importance of appropriate diet and activity levels for controlling his risk.

REFERENCES

1. National Vascular Disease Prevention Alliance. Guidelines for the management of absolute cardiovascular disease risk. 2012. Available at strokefoundation.com.au/site/media/AbsoluteCVD_GL_webready.pdf [Accessed 19 January 2014].
2. Tonkin A, Barter P, Best J, et al. National Heart Foundation of Australia and the Cardiac Society of Australia and New Zealand. Position statement on lipid management 2005. Heart Lung Circ 2005;14:275–91.
3. Cooper A, Nherera L, Calvert N, et al. Clinical Guidelines and Evidence Review for Lipid Modification: cardiovascular risk assessment and the primary and secondary prevention of cardiovascular disease (revised March 2010). London: National Collaborating Centre for Primary Care and Royal College of General Practitioners, 2008.
4. Australian Institute of Health and Welfare 2011. Health determinants, the key to preventing chronic disease. Cat No. PHE 157. Canberra: AIHW.
5. eTG complete [online]. Therapeutic Guidelines: Cardiovascular. Melbourne: 2012. Available at online.tg.org.au/complete/desktop/index.htm [Accessed 19 January 2014].
6. National Vascular Disease Prevention Alliance (NVDPA) absolute CVD risk calculator: Available at www.cvdcheck.org.au [Accessed 19 January 2014].
7. National Vascular Disease Prevention Alliance (NVDPA) absolute CVD risk charts: Available at www.heartfoundation.org.au/SiteCollectionDocuments/aust-cardiovascular-risk-charts.pdf [Accessed 19 January 2014].
8. National Heart Foundation. Absolute cardiovascular disease risk assessment. Available at www.heartfoundation.org.au/SiteCollectionDocuments/absolute-risk-assessement.pdf [Accessed 31 January 2014].
9. Rees K, Dyakova M, Wilson N, Ward K, Thorogood M, Brunner E. Dietary advice for reducing cardiovascular risk. Cochrane Database Syst Rev 2013 12:CD002128. Epub 2013 Dec 6. Available at www.ncbi.nlm.nih.gov/pubmed/23543514 [Accessed 19 January 2014].
10. Bouzan C, Cohen JT, Connor WE, Kris-Etherton PM, Gray GM, Konig A, et al. A quantitative analysis of fish consumption and stroke risk. Am J Prev Med 2005 Nov;29:347–52.

11. He K, Song Y, Daviglus ML, et al. Accumulated evidence on fish consumption and coronary heart disease mortality: a meta-analysis of cohort studies. Circulation. 2004;109:2705–11.
12. Wang C, Harris WS, Chung M, et al. n-3 Fatty acids from fish or fish-oil supplements, but not alpha-linolenic acid, benefit cardiovascular disease outcomes in primary- and secondary-prevention studies: a systematic review. Am J Clin Nutr 2006;84:5–17.
13. Hooper L, Thompson RL, Harrison RA, et al. Risks and benefits of omega 3 fats for mortality, cardiovascular disease, and cancer: systematic review. BMJ 2006;332:752–60.
14. de Lorgeril M, Salen P, Martin JL, et al. Mediterranean diet, traditional risk factors, and the rate of cardiovascular complications after myocardial infarction: final report of the Lyon Diet Heart Study. Circulation 1999;99:779–85.
15. Sofi F, Cesari F, Abbate R, Gensini GF, Casini A. Adherence to Mediterranean diet and health status: meta-analysis. BMJ 2008;337:a1344.
16. Hamer M, Chida Y. Walking and primary prevention: a meta-analysis of prospective cohort studies. Br J Sports Med 2008;42:238–43.
17. Lollgen H, Bockenhoff A, Knapp G. Physical activity and all-cause mortality: an updated meta-analysis with different intensity categories. Int J Sports Med 2009;30:213–24.
18. Nocon M, Hiemann T, Muller-Riemenschneider F, Thalau F, Roll S, Willich SN. Association of physical activity with all-cause and cardiovascular mortality: a systematic review and meta-analysis. Eur J Cardiovasc Prev Rehabil 2008;15:239–46.
19. Shiroma EJ, Lee IM. Physical activity and cardiovascular health: lessons learned from epidemiological studies across age, gender, and race/ethnicity. Circulation 2010;122:743–52.
20. Woodcock J, Franco OH, Orsini N, Roberts I. Non-vigorous physical activity and all-cause mortality: systematic review and meta-analysis of cohort studies. Int J Epidemiol 2011;40:121–38.
21. Hu G, Tuomilehto J, Silventoinen K, Barengo N, Jousilahti P. Joint effects of physical activity, body mass index, waist circumference and waist-to-hip ratio with the risk of cardiovascular disease among middle-aged Finnish men and women. Eur Heart J 2004;25:2212–19.
22. Pal S, Cheng C, Egger G, Binns C, Donovan R. Using pedometers to increase physical activity in overweight and obese women: a pilot study. BMC Public Health 2009;9:309.
23. Pedersen MT, Blangsted AK, Andersen LL, Jorgensen MB, Hansen EA, Sjogaard G. The effect of worksite physical activity intervention on physical capacity, health, and productivity: a 1-year randomized controlled trial. J Occup Environ Med 2009;51:759–70.
24. Carroll S, Dudfield M. What is the relationship between exercise and metabolic abnormalities? A review of the metabolic syndrome. Sports Med 2004;34:371–418.
25. Orozco LJ, Buchleitner AM, Gimenez-Perez G, Roque IFM, Richter B, Mauricio D. Exercise or exercise and diet for preventing type 2 diabetes mellitus. Cochrane Database Syst Rev 2008;3:CD003054.
26. Thomas DE, Elliott EJ, Naughton GA. Exercise for type 2 diabetes mellitus. Cochrane Database Syst Rev 2006;3:CD002968.
27. Baigent C, Keech A, Kearney PM, et al. Efficacy and safety of cholesterol-lowering treatment: prospective meta-analysis of data from 90,056 participants in 14 randomised trials of statins. Lancet 2005;366:1267–78.
28. Heart Protection Study Collaborative Group. MRC/BHF Heart Protection Study of cholesterol lowering with simvastatin in 20,536 high-risk individuals: a randomised placebo-controlled trial. Lancet 2002;360:7–22.
29. NPS News. Managing lipids – reducing cardiovascular disease risk. Feb 2011 (Modified March 2011). Available at www.nps.org.au/publications/health-professional/nps-news/2011/lipids [Accessed 21 January 2014].
30. A cooperative trial in the primary prevention of ischaemic heart disease using clofibrate. Report from the Committee of Principal Investigators. Br Heart J 1978;40:1069.
31. WHO cooperative trial on primary prevention of ischaemic heart disease using clofibrate to lower serum cholesterol: mortality follow-up. Report of the Committee of Principal Investigators. Lancet 1980;2:379.
32. The Lipid Research Clinics Coronary Primary Prevention Trial results. II. The relationship of reduction in incidence of coronary heart disease to cholesterol lowering. JAMA 1984;251:365.
33. Frick MH, Elo O, Haapa K, et al. Helsinki Heart Study: primary-prevention trial with gemfibrozil in middle-aged men with dyslipidemia. Safety of treatment, changes in risk factors, and incidence of coronary heart disease. N Engl J Med 1987;317:1237.
34. National Heart Foundation of Australia and the Cardiac Society of Australia and New Zealand. Reducing risk in heart disease: an expert guide to clinical practice for secondary prevention of coronary heart disease. Melbourne: National Heart Foundation of Australia, 2012. Available at www.heartfoundation.org.au/SiteCollectionDocuments/Reducing-risk-in-heart-disease.pdf [Accessed online 22 January 2014].

CASE 5

SUSAN'S HUSBAND DIED SUDDENLY AFTER EXERCISE

A hospital doctor contacts you to notify you of the sudden death of one of your patients, Graham, aged 30 years, whom you had previously seen intermittently. His last visit was 2 months ago, when you prescribed oral antibiotics for bronchitis. You also treat his wife, Susan, aged 28 years, and their two children aged 2 and 4 years.

You review Graham's notes, which document that he was a non-smoker, on no regular medications and had normal blood pressure. He had no heart murmurs.

You notice that Susan has booked an appointment to see you later that day.

QUESTION 1

What resources are available to families of sudden cardiac death (SCD)?

FURTHER INFORMATION

Susan presents for her appointment and tells you that Graham had been well in the days leading up to his usual weekend touch football match but he collapsed after the game. His teammates called an ambulance and commenced cardiopulmonary resuscitation; however, he was unable to be resuscitated. Susan was told that an autopsy would be done on Graham and that she would be notified of the results.

QUESTION 2

What further history could be relevant?

QUESTION 3

What are the causes of SCD in the young?

FURTHER INFORMATION

Guidelines endorsed by the Royal Australasian College of Pathologists have been developed for autopsies performed on individuals who have died suddenly at a young age. These guidelines recommend a toxicology screen, tests to exclude non-cardiac causes of death (e.g. aortic aneurysm, cerebral haemorrhage and pulmonary thromboembolism), and macroscopic/microscopic examination of the heart. If an inherited cause of death is identified or if the post-mortem is negative (no cause of death identified), tissue or blood should be collected for DNA extraction.[1]

QUESTION 4

What advice should you give to family members?

FURTHER INFORMATION

Subsequently, Susan receives the autopsy report, which indicates that the cause of death was hypertrophic cardiomyopathy. Susan tells you that she was informed that blood was stored for potential genetic testing.

QUESTION 5

How long should clinical screening in relatives be continued?

QUESTION 6

What is the role of genetic testing?

CASE 5 ANSWERS

ANSWER 1

There are many resources available to assist families with SCD. The Australian Genetic Heart Disease Registry has a link dedicated to SCD where comprehensive patient information sheets are available, and links to various support groups are provided (see Resources for Patients below).

ANSWER 2

This is clearly a difficult time for Susan and her children. Your approach will be dependent on their reaction to the recent, sudden, unexpected loss of their husband/father. Susan will want to know why this has happened and whether other family members are at risk.

The Trans-Tasman response Against Sudden death in the Young (TRAGEDY) initiative emphasises the importance of obtaining detailed medical histories in cases of sudden death in young people.[1] At some point, therefore, it is important to take a further history, given that inherited heart disease is a prominent cause of SCD in the young. This will include asking further questions about the circumstances surrounding the event, the amount of exercise that Graham undertook, and whether Graham had any previous history of syncope, palpitations, chest pain or exercise intolerance. A family history of SCD, drownings, epilepsy, recurrent syncope or premature vascular disease is also relevant. You should ask whether Graham was taking any medications, including over-the-counter drugs. You should also ascertain whether any prior cardiac or neurological investigations had been performed for Graham e.g. 12-lead ECG, echocardiogram, stress test, electroencephalogram (EEG), computerised tomography (CT) or magnetic resonance imaging (MRI) of the brain, fasting lipids.

ANSWER 3

In the general population, the most common cause of SCD is CAD; however, it accounts for a smaller proportion of sudden deaths in younger individuals (aged <40 years).[2]

The causes of sudden death can be broadly categorised into structural heart diseases or non-structural diseases (also referred to as primary arrhythmogenic disorders).[8] Structural diseases include CAD, cardiomyopathies (e.g. hypertrophic cardiomyopathy, dilated cardiomyopathy, arrhythmogenic right ventricular cardiomyopathy), myocarditis and congenital heart disease. Primary arrhythmogenic diseases include long QT syndrome, catecholaminergic polymorphic ventricular tachycardia and Brugada syndrome.

The post-mortem has a high probability of identifying structural causes of SCD.[3,4] Hypertrophic cardiomyopathy is one of the most common causes of SCD in the young, especially when related to exercise.[5] However, in 30% of SCD cases occurring in people aged 35 years or younger, no cause of death is identified at postmortem;[3,4] at least 40% of these cases are attributable

to inherited primary arrhythmogenic disorders that cannot be diagnosed at autopsy.[6–8]

ANSWER 4

Many of the causes of SCD in the young (including hypertrophic cardiomyopathy) are inherited, usually as an autosomal dominant condition.[3] Therefore, first-degree relatives (i.e. children, siblings and parents) have a 50% risk of carrying the gene mutation and should be referred to a cardiologist for clinical evaluation. This should occur if the post-mortem either identifies an inherited cardiac disease (e.g. hypertrophic cardiomyopathy) or if the post-mortem is negative (i.e. no cause of death is identified). First-degree relatives should also be referred for clinical assessment if no autopsy was performed. One should consider referring families where no cause of death has been identified at autopsy to specialised centres that run multidisciplinary clinics that coordinate both the cardiological and genetic investigation of families.[6,7]

Clinical screening of family members generally involves,[7] as a minimum:

- ECG
- Transthoracic echocardiogram.

A diagnosis of inherited heart disease in a relative may allow early lifestyle modification, avoidance of specific drugs that may precipitate arrhythmias, and prophylactic treatment to reduce their future risk of SCD.[6,7] It may also identify other at-risk relatives who should undergo clinical evaluation.

You advise Susan that Graham's parents and siblings should undergo clinical screening by a cardiologist. You refer Susan's children to a paediatric cardiologist.

ANSWER 5

Inherited heart diseases are not expressed at a particular age; therefore, depending on the age of the relative, ongoing clinical screening should be performed every 1–5 years. This should be guided by the cardiologist. Guidelines are available on the Cardiac Society of Australia and New Zealand website (see Resources for Doctors below).

ANSWER 6

Genetic testing may have an important role in the investigation of SCD families.[2,7] For a number of inherited cardiac diseases, including hypertrophic cardiomyopathy, genetic testing is now part of standard clinical practice.[2] In approximately 50–60% of hypertrophic cardiomyopathy patients, a causative mutation can be identified.[2] This allows predictive genetic testing in at-risk relatives to determine whether or not they carry the mutation. Carriers require ongoing follow-up;[6,7] however, non-carriers can be discharged from long-term clinical screening and reassured that they are not at increased risk of developing hypertrophic cardiomyopathy.

Genetic evaluation may also be considered in families where no cause of death is identified at autopsy,[2,6–8] depending on the circumstances of the SCD, the number of SCDs occurring in that family, and the outcome of clinical screening performed in relatives. A combined approach to clinical screening in relatives and genetic testing can identify an inherited cardiac disease in up to 30–40% of families.[6–9]

There are a number of genetic testing services available in Australia, including centres that have a special interest in cardiac genetics (see Resources for Doctors below). They are composed of multidisciplinary teams (including cardiologists, clinical geneticists and genetic counsellors) and provide genetic counselling regarding the risk of other family members developing inherited cardiac disease and the potential impact of genetic testing on future employment, recreation, insurance and reproduction.

You refer Susan to a clinical genetics service to consider whether genetic testing for hypertrophic cardiomyopathy could be considered for her family. Blood had been collected from Graham at post-mortem and DNA was extracted and stored. As next of kin, Susan can authorise genetic testing of the DNA samples. This testing has a 50–60% chance of finding the causative mutation. Identification of a mutation could warrant predictive genetic testing of other family members to determine whether or not they are carriers.

REFERENCES

1. Skinner JR, Duflou JA, et al. Reducing sudden death in young people in Australia and New Zealand: the TRAGADY initiative. Med J Aust 2008;189:539–40.
2. Ackerman MJ, Priori SG, Willems S, et al. HRS/EHRA expert consensus statement on the state of genetic testing for the channelopathies and cardiomyopathies this document was developed as a partnership between the Heart Rhythm Society (HRS) and the European Heart Rhythm Association (EHRA). Heart Rhythm 2011;8:1308–39.
3. Doolan A, Langlois N, Semsarian C. Causes of sudden cardiac death in young Australians. Med J Aust 2004;180:110–12.
4. Puranik R, Chow CK, Duflou JA, Kilborn MJ, McGuire MA. Sudden death in the young. Heart Rhythm 2005;2:1277–82.
5. Maron BJ. Sudden death in young athletes. N Engl J Med 2003;349:1064–75.
6. Nunn LM, Lambiase PD. Genetics and cardiovascular disease – causes and prevention of unexpected sudden adult death: the role of the SADS clinic. Heart 2011;97:1122–27.
7. Vohra J, Skinner J, Semsarian C. Cardiac genetic investigation of young sudden unexplained death and resuscitated out of hospital cardiac arrest. Heart Lung Circ 2011;20:746–50.
8. Semsarian C, Hamilton RM. Key role of the molecular autopsy in sudden unexpected death. Heart Rhythm 2012;9:145–50.
9. Skinner JR, Crawford J, Smith W, et al. Prospective, population-based long QT molecular autopsy study of postmortem negative sudden death in 1 to 40 year olds. Heart Rhythm 2011;8:412–19.

RESOURCES FOR DOCTORS

- SCD clinical screening guidelines are available on the Cardiac Society of Australia and New Zealand website (www.csanz.edu.au/documents/guidelines/clinical_practice/Hyertrophic_Cardiomyopathy.pdf).
- Genetic testing services available in Australia including centres with a special interest in cardiac genetics (www.heartregistry.org.au/patients-families/cardiac-genetic-services/).

RESOURCES FOR PATIENTS

- The Australian Genetic Heart Disease Registry has a link dedicated to SCD. Comprehensive patient information sheets are available at www.heartregistry.org.au
- Sudden Arrhythmic Death Syndromes Australia (SADS), www.sads.org.au
- NALAG Centre for Loss and Grief (Australia), www.nalag.org.au
- Lifeline Australia, www.lifeline.org.au

Heart health

In order to qualify for 6 Category 2 points for the QI&CPD activity associated with this unit:

- read and complete the unit of *check* in hard copy or online at the *gplearning* website at http://gplearning.racgp.org.au
- log into the *gplearning* website at http://gplearning.racgp.org.au and answer the following 10 multiple choice questions (MCQs) online
- complete the online evaluation.

If you are not an RACGP member, please contact the *gplearning* helpdesk on 1800 284 789 to register in the first instance. You will be provided with a username and password that will enable you access to the test.

The expected time to complete this activity is 3 hours.

Do not send answers to the MCQs into the *check* office. This activity can only be completed online at http://gplearning.racgp.org.au

If you have any queries or technical issues accessing the test online, please contact the *gplearning* helpdesk on 1800 284 789.

FOR A FULL LIST OF ABBREVIATIONS AND ACRONYMS USED IN THESE QUESTIONS PLEASE GO TO PAGE 3.
FOR EACH QUESTION BELOW SELECT ONE OPTION ONLY.

QUESTION 1

You have been notified that Jackson, a student aged 16 years, died suddenly over the weekend while playing football for his local team. Jackson's family has been seeing you for more than 20 years and Jackson has been your patient for the whole of his life. Jackson was not taking any medications and had no significant medical history. You do not recall any family history of cardiovascular disease. Which of the following statements is NOT true?

A. The causes of sudden cardiac death in young people like Jackson are inherited and are mainly due to rare autosomal recessive conditions.

B. The causes of sudden cardiac death can be categorised as being underpinned by structural diseases of the heart or non-structural diseases.

C. Hypertrophic cardiomyopathy is one of the most common findings at autopsy in young people following sudden cardiac death.

D. First-degree relatives of people dying from sudden death have a 50% chance of carrying a gene mutation and should be referred to a cardiologist for clinical evaluation.

E. Underlying or undiagnosed cardiomyopathy, myocarditis and/or congenital heart disease may account for Jackson's sudden death.

QUESTION 2

Penelope, aged 49 years, presents complaining of calf muscle tenderness and pain of several days duration. She was recently started on hormone replacement therapy (HRT) to manage hot flushes and night sweats, and takes no other medications. There is no family history of thrombophilia. Examination of her calf reveals an area of skin with significant signs of inflammation, including redness, swelling and heat. There are no varicose veins. Which of the following statements is NOT true?

A. Calf vein thrombosis should not be ignored as it carries a degree of risk for pulmonary embolism.

B. Penelope's use of HRT may have precipitated her current problem.

C. Either an antiplatelet agent like aspirin or an anticoagulant such as warfarin could be used to manage Penelope's problem; in the absence of varicose veins she would not benefit from wearing compression stockings.

D. Superficial venous thrombus has a risk of extension of the thrombus, to involve the deep vein system.

E. As Penelope does not have varicose veins, superficial thrombophlebitis can be ruled out.

QUESTION 3

Non-pharmacological management of patients with heart failure is an important part of the overall management plan. All patients should be provided with information about non-pharmacological management strategies that may be of benefit to them. Which of the following statements regarding the non-pharmacological management of patients with heart failure is NOT true?

A. People with heart failure should be provided with information to help them monitor and manage their fluid balance.

B. People with heart failure should be encouraged to weigh themselves before breakfast on a daily basis.

C. Exercise is recommended in those with stable heart failure as this may improve symptoms and functional capacity.

D. Vaccination against influenza and pneumococcal disease should be recommended to all patients.

E. Restriction of both sodium (<2 g/day) and fluid intake (<1.5 L/day) is routinely recommended for all people with heart failure.

QUESTION 4

David, aged 79 years, is a retired soldier who presents complaining of recent tiredness, dizziness and a funny fluttering feeling in his heart, even at rest. He takes a low dose thiazide and an ACEI for his hypertension, and artovostatin for his dyslipidaemia. Occasionally, he uses paracetamol to manage joint pain. Examination reveals a blood pressure of blood pressure of 134/76 mmHg and an irregular heart rate of 136 bpm. Which of the following is the NOT correct?

A. David may have atrial fibrillation (AF) and should be referred for standard investigations, including a 12-lead ECG and an echocardiogram.

B. If David was diagnosed with AF, his CHADS2 score would be 2 and he would be classified as having a high risk of stroke (4% per 100 years without treatment).

C. If David was diagnosed with AF and he developed renal impairment while using an anticoagulant agent, the dose of his anticoagulant agent would need to be reduced.

D. In contrast to warfarin, the newer anticoagulant agents require no routine monitoring.

E. If David has AF confirmed and he had a previous history of TIA, his CHADS2 score would be 4 and he would be classified as having a high risk of stroke (8.5% per 100 years without treatment).

QUESTION 5

In primary prevention of CVD, assessment of an individual's cardiovascular risk on the basis of consideration of multiple risk factors (absolute risk) is more accurate than use of a single risk factor (e.g. cholesterol, blood pressure) for determining risk and for making treatment decisions. Absolute cardiovascular disease guidelines recommend calculating the numerical probability of an event for each patient using the Australian cardiovascular risk charts. Which of the following statements is NOT correct?

A. Lifestyle recommendations to reduce cardiovascular risk should be offered to all patients regardless of their calculated level of risk.

B. The person's calculated level of risk will determine whether they require pharmacotherapy or not.

C. For those calculated to have a low or moderate cardiovascular risk, medication is not routinely recommended.

D. People in primary prevention settings known to have a high baseline risk of cardiovascular disease do not need to have their risk calculated, as they can be assumed to be at high risk.

E. In primary prevention, low dose aspirin is routinely recommended for those at high risk of cardiovascular disease.

QUESTION 6

Christine, aged 20 years, was an only child and an Olympic athlete who died suddenly while training interstate. Her body has been flown back to your hometown for post-mortem examination. Her distraught parents have made an appointment to talk to you. Her mother is extremely distressed as she lost her younger brother suddenly under similar circumstances 50 years ago. Which of the following statements is NOT correct?

A. A family history of sudden death, albeit 50 years ago, is suggestive of a familial propensity for sudden cardiac death.

B. Guidelines for autopsies performed on people who have died suddenly at a young age, like Christine, recommend a toxicology screen, exclusion of non-cardiac causses of death, examination of the heart and under certain circumstances collection of tissue or blood for DNA extraction.

C. If no cause of death is found at autopsy, members of Christine's family do not need to be referred for clinical assessment or genetic investigation.

D. Christine's family might benefit from referral to resources and services available to help families where there has been a sudden cardiac death in the family.

E. Christine's parents and siblings should be referred to, and encouraged to attend, a cardiologist for initial and possibly ongoing clinical screening.

QUESTION 7

Marla, aged 68 years, is a recently retired music teacher. She arrived at your clinic before opening hours and without an appointment, asking to urgently see you. She looks distressed and complains of sudden-onset shortness of breath and sharp chest pain, which feels worse when taking deep breaths. She feels anxious and light-headed. Her symptoms commenced around midnight last night, as she was preparing for bed. She also reports that she did not sleep well last night. Significant medical history includes recent knee surgery and invasive breast cancer diagnosed 5 months ago, for which she is still being treated. Which of the following statements is/are correct?

A. Marla should be reviewed immediately, as her signs and symptoms are consistent with possible pulmonary embolism (PE) or another more serious problem.

B. Marla's medical history, particularly her history of cancer and recent knee surgery, confers an increased risk for deep vein thrombosis (DVT) and/or PE.

C. Warfarin or rivaroxaban would be appropriate anticoagulants to prescribe for Marla if she was diagnosed with PE.

D. All of the above are correct.

E. All of the above are incorrect.

QUESTION 8

Josie is 73 years old and is an active retiree but recently diagnosed with Class II heart failure. Significant medical history includes hypertension, diagnosed 16 years ago, and dyslipidaemia, diagnosed 11 years ago. She had a basal cell carcinoma removed recently from her forearm. Which of the following statements is NOT correct?

A. If Josie was being treated with a beta-blocker (e.g. atenolol) for her hypertension at the time of diagnosis of her heart failure, that treatment should have been stopped and an ACEI commenced immediately.

B. If Josie was being treating with ramipril for her hypertension at the time of diagnosis of her heart failure, that treatment should have been stopped and a heart-failure-specific ACEI commenced at maximal total daily doses, immediately.

C. ACEIs (or angiotensin receptor blockers in patients intolerant of ACEIs), heart failure beta-blockers and mineralocorticoid receptor antagonists prolong survival in patients with symptomatic systolic heart failure.

D. If Josie was being treated with a mid-level dose of ramipril for her hypertension at the time of diagnosis of her heart failure,

she should have the dose slowly titrated to the highest tolerable maintenance dose or dose recommended for use in heart failure.

E. If Josie was being treating with the highest dose of ramipril for her hypertension at the time of diagnosis of her heart failure, she should continue being treated on that dose.

QUESTION 9

With the recent registration and PBS listing of a number of new oral anticoagulant agents, patients diagnosed with non-valvular AF have a range of options to choose from, including warfarin, dabigatran, rivaroxaban and apixaban, depending on whether they meet current PBS criteria for the newer agents. Which of the following statements is NOT correct regarding the currently available oral anticoagulant agents?

A. Patients need to meet strict PBS criteria to qualify for an authority script for all new oral anticoagulant agents.

B. A defining feature of the new oral anticoagulant agents is the lack of antidote to manage over-coagulation and/or uncontrollable bleeding

C. The new oral anticoagulant agents have a different mechanism of action, compared with warfarin.

D. The new oral anticoagulant agents can be monitored to manage over- and undercoagulation.

E. Use of an oral anticoagulant agent may need to be ceased before surgery, depending on the type of surgery/procedure and the associated risk of bleeding.

QUESTION 10

Andrea, a sales assistant aged 46 years, presents to discuss the results of her recent health assessment for people aged 45–49 years. You previously explained the need to collect baseline data to assess her absolute risk of CVD. Andrea has a strong family history of CVD (her father had a non-fatal heart attack at the age of 59 years; her grandfather had a fatal heart attack at the age of 63 years). She smokes but is trying to cut down (currently she smokes half a pack but had previously smoked one pack/day) and she is overweight (BMI is 31.2 m^2/kg). Using the results of her recent lipid profile and today's BP result, her absolute risk of cardiovascular risk is calculated to be 15% using an online calculator. Which of the answers below is CORRECT in terms of describing the implications of her calculated cardiovascular risk?

A. Andrea should be provided with lifestyle information especially about diet and exercise, and smoking cessation.

B. Andrea is at a very high risk of a cardiovascular event over the next 5 years and should be treated aggressively with lipid-lowering therapy, a BP-lowering medication and low dose aspirin.

C. She is at a high risk of a cardiovascular event over the next 5 years and should be treated aggressively with lipid-lowering therapy, a BP-lowering medication but not low dose aspirin.

D. She is at moderate risk of a cardiovascular event over the next 5 years and pharmacotherapy is routinely recommended by current guidelines.

E. Her calculated risk is a true reflection of her cardiovascular risk and is neither an overestimate nor underestimate of risk.

NOTES

NOTES