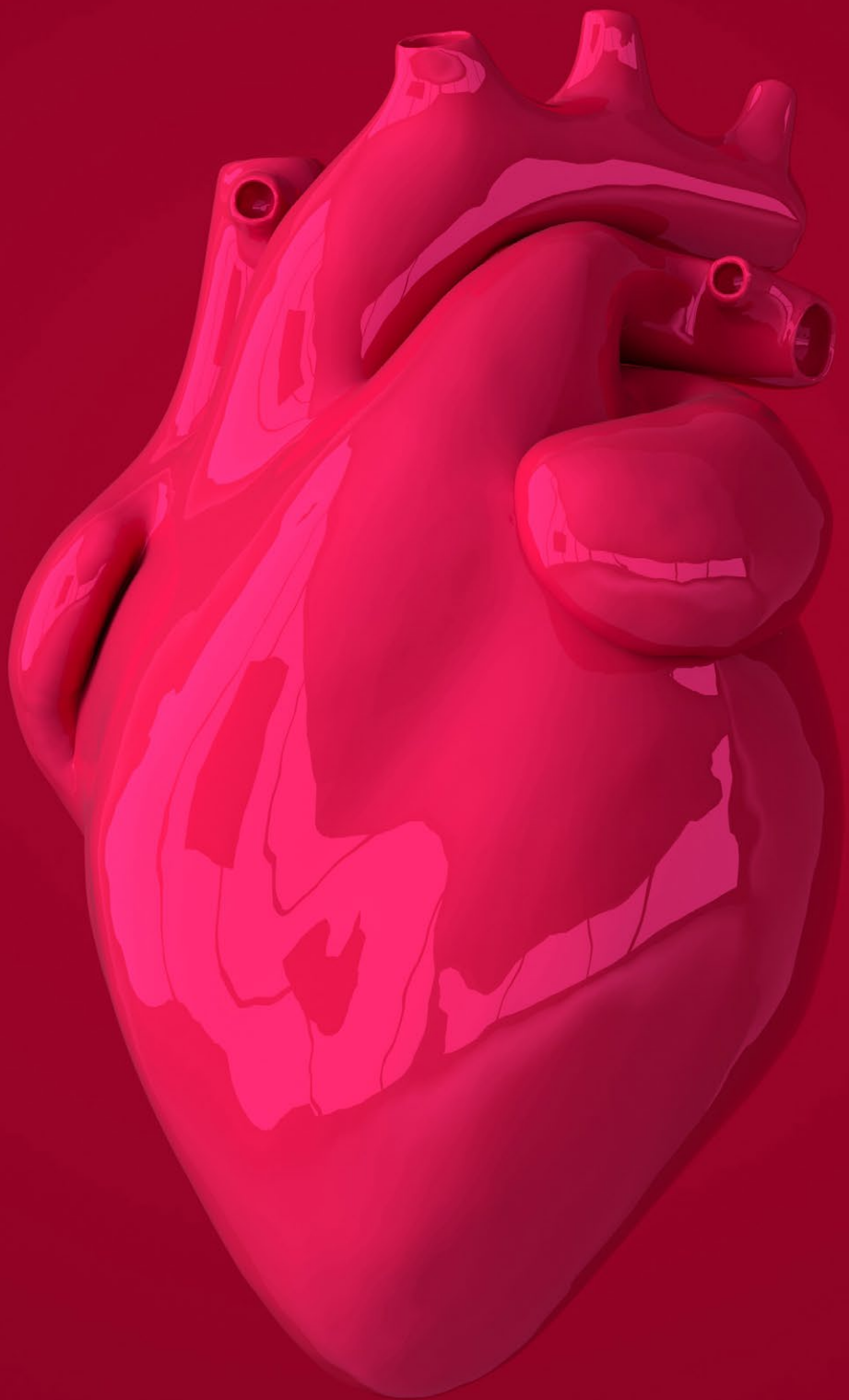
check

Independent learning program for GPs

Unit 584
July 2021

Cardiovascular disease



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We acknowledge the Traditional Custodians of the lands and seas on which we work and live, and pay our respects to Elders, past, present and future.

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Cardiovascular disease

Unit 584 July 2021

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
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Heart Foundation

NPS MEDICINEWISE

About this activity

According to the Australian Bureau of Statistics 2017–18 National Health Survey, approximately 1.2 million Australian adults have one or more conditions related to heart or vascular disease.[1]

Acute coronary syndrome (ACS) results in 75,000 hospitalisations and 10,000 deaths each year in Australia.[2] It is most commonly seen in patients with diabetes or mental illness, women, elderly patients, culturally and linguistically diverse patients and Aboriginal and Torres Strait Islander peoples.[3]

Patients with takotsubo cardiomyopathy present similarly to those with ACS; however, the prognosis of takotsubo cardiomyopathy is generally good, with inpatient mortality rates of 0–8%.[4]

Deep vein thrombosis has an incidence of 160 per 100,000 Australians, with 6500 cases diagnosed per year.[5]

At the end of 2017, there were 4255 Australians with rheumatic heart disease on state and territory registers; 87% of these patients were Aboriginal and Torres Strait Islander peoples.[6]

This edition of *check* considers the investigation and management of cardiovascular disease in general practice.

References

1. Australian Institute of Health and Welfare. Cardiovascular disease. Cat. no: CVD 83. Canberra, ACT: AIHW, 2020. Available at www.aihw.gov.au/reports/heart-stroke-vascular-diseases/cardiovascular-health-compendium/contents/how-many-australians-have-cardiovascular-disease [Accessed 7 June 2021].
2. Nadel J, Hewitt T, Horton D. Acute coronary syndrome in Australia: Where are we now and where are we going? Australas Med J 2014;7(3):149–56. doi: 10.4066/AMJ.2014.1921.
3. Chew DP, Scott IA, Cullen L, et al. National Heart Foundation of Australia & Cardiac Society of Australia and New Zealand: Australian Clinical Guidelines for the Management of Acute Coronary Syndromes 2016. Heart Lung Circ 2016;25(9):895–951. doi: 10.1016/j.hlc.2016.06.789.
4. Rahman A, Liu D. Broken heart syndrome – A case study. Aust Fam Physician 2012;41(1–2):55–58.
5. Goergen S, Tran H, Zallman M, Woinarski N. Suspected lower limb deep vein thrombosis. Education modules for appropriate imaging referrals: Royal Australian and New Zealand College of Radiologists; 2015.
6. Australian Institute of Health and Welfare. Acute rheumatic fever and rheumatic heart disease in Australia, 2013–2017. Cat. no: CVD 86. Canberra, ACT: AIHW, 2020. Available at www.aihw.gov.au/reports/indigenous-australians/acute-rheumatic-fever-rheumatic-heart-disease/contents/summary [Accessed 7 June 2021].

Learning outcomes

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

- outline the management of patients with suspected acute coronary syndrome
- describe the features that would indicate a diagnosis of stress cardiomyopathy
- discuss the investigations that would be performed in a patient presenting with symptoms of deep vein thrombosis
- identify the recommended follow-up of patients with rheumatic heart disease.

Authors

Case 1

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Peer reviewers

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Abbreviations

ACS	acute coronary syndrome
COCP	combined oral contraceptive pill
DOAC	direct-acting oral anticoagulant
DVT	deep vein thrombosis
ECG	electrocardiogram
LMWH	low–molecular weight heparin
NSTEMI	non–ST elevation myocardial infarction
PBS	Pharmaceutical Benefits Scheme
STEMI	ST elevation myocardial infarction
VTE	venous thromboembolism

CASE

1 Maria is feeling tired

Maria, aged 58 years, presents to you reporting intermittent episodes of severe fatigue that limit her ability to perform her usual activities. She reports the fatigue started in the past few days and is associated with nausea and occasional indigestion. She says that she has not done her vacuuming this week and skipped a planned social gathering because of a lack of energy. She is frustrated by these episodes of exhaustion, as she has been sleeping well, eating normally and is usually quite a busy person.

Question 1

How would you approach the assessment of Maria?

Further information

Maria is frustrated by her lack of energy, but she says her mood is otherwise normal and she enjoys the activities she can do. She describes a sensation of breathlessness, especially when taking the stairs, and says that, although she has never had chest pain, her chest did feel 'tight' this morning when she was getting ready to come to her appointment. She has had no infective symptoms and no recent change in diet or medication. Maria does not report feeling faint or ever having palpitations. There has been no melena or other gastrointestinal upset. She lives alone and has never smoked. Her medical history is significant only for hypertension, which is well controlled by perindopril 4 mg once daily.

Maria is of Caucasian ethnicity and has a body mass index of 28.2 kg/m^2. Her cardiorespiratory exam is unremarkable, and she has no clinical features of anaemia or hypothyroidism. Her blood pressure today is 130/90 mmHg, and her pulse rate, respiratory rate and oxygen saturation are all within normal limits.

Question 2

What investigations should be performed in the primary care setting for Maria? What is the most appropriate next step in her management?

Further information

Maria is transported to the emergency department by ambulance, where she undergoes risk stratification, including serial troponin and electrocardiography testing. Her symptoms and vital signs remain stable throughout her time in the department, while she is resting in bed. Maria's initial and repeat electrocardiograms (ECGs) are shown in Figures 1 and 2.

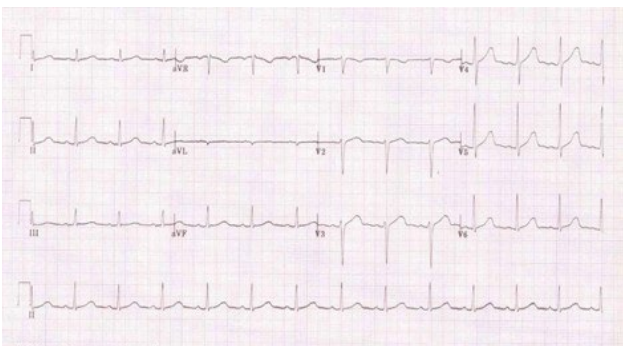

Figure 1. Initial electrocardiogram

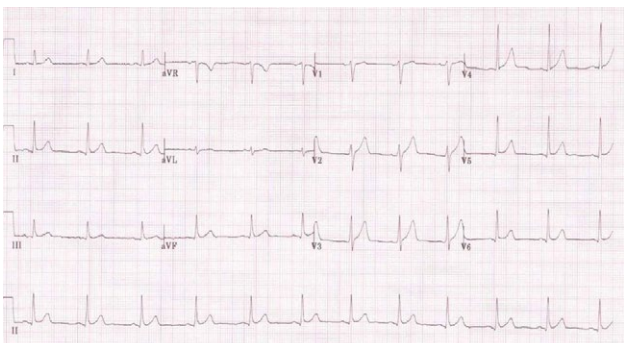

Figure 2. Repeat electrocardiogram

Maria's first troponin is 4 ng/L and the second, at two hours, is 6 ng/L (reference range ≤10 ng/L for women and ≤20 ng/L for men using a high-sensitivity cardiac troponin assay). She has additional investigations, including a full blood examination, chemistry and metabolic screening (CHEM-20) and a chest X-ray, which are all unremarkable.

Question 3

What is your interpretation of the ECG results?

Question 4

What is your interpretation of the troponin results?

Question 5

What is the most likely diagnosis?

Question 6

What additional investigations are required for Maria?

CASE 1 Answers

Answer 1

Fatigue is a common complaint with a very broad differential diagnosis. The abrupt onset of symptoms and marked change in functional capacity raise the suspicion of acute, rather than subacute, pathology. A systems approach can be useful when dealing with non-specific complaints, with questions tailored to help rule in or rule out various differential diagnoses.[1] Maria's symptoms could be explained by infection, anaemia, metabolic change, depression or cardiovascular issues. Further information to clarify the history of the presenting complaint and elicit any features of these disorders is warranted, as well as a careful physical examination.

The combination of fatigue, nausea and reduced exercise tolerance in a female patient raise red flags for the possibility of acute coronary syndrome (ACS).[2] Women, people with diabetes, elderly patients, culturally and linguistically diverse patients, patients with mental illness and Aboriginal and Torres Strait Islander peoples are at greater risk of presenting with atypical symptoms of ACS.[3] Other than chest pain, frequent symptoms of coronary ischaemia include fatigue, dyspnoea, nausea and vomiting, diaphoresis and radiated pain (experienced in the arm/jaw/upper abdomen/back). Unfortunately there is no combination of historical and examination findings that can exclude a diagnosis of ACS; therefore, the index of suspicion needs to remain high.[4]

Answer 2

It is recommended that electrocardiography be performed for any patient aged >50 years who reports dyspnoea or has other symptoms of cardiac ischaemia, to evaluate for signs of ST elevation myocardial infarction (STEMI).[5] In the absence of STEMI, it is important to look for features consistent with non-STEMI (NSTEMI), such as new or presumed new horizontal or down-sloping ST depression ≥0.05 mV (0.5 mm) in two anatomically contiguous leads

and/or T-wave inversion ≥0.1 mV (1 mm) in two anatomically contiguous leads with a prominent R wave or R/S ratio >1.[6]

Even in the absence of ECG findings consistent with STEMI or NSTEMI, ACS cannot be excluded, and the patient should be referred via ambulance to their nearest emergency department for serial ECGs if the clinical suspicion for ACS is high and the patient remains symptomatic.

While awaiting transfer, initial pharmacotherapy can be initiated within the general practice setting. It is recommended that all patients with suspected ACS are given 300 mg aspirin orally if there are no contraindications. Glyceryl trinitrate can be administered if the patient has active chest pain and is not hypotensive. If oxygen saturations are below 93% on room air, supplemental oxygen is recommended.[3]

For patients who have had symptoms suggestive of ACS within the past 24 hours, or who had possible ACS more than 24 hours ago but have persistent high-risk symptoms (heart failure, syncope or an abnormal ECG), outpatient troponin testing is not indicated because of the need to have serial testing in a monitored environment with access to resuscitative and reperfusion therapies. The use of a single troponin is appropriate in community care for patients who have been symptom free for more than 24 hours and have no high-risk features. In this instance, the test should be marked as urgent, and there must be a system in place for the treating physician to be notified of a positive result at any time, to ensure appropriate referral of the patient.[3,4]

Answer 3

The diagnosis of ACS follows a stepwise 'rule-out' approach. The initial ECG is used to assess for STEMI. In its absence, the patient must proceed to have serial ECGs to identify if dynamic change indicating coronary ischaemia is present, as well as serial troponin assays to assess for myocardial injury. If there is a troponin elevation (>99th percentile or upper reference limit), the patient is diagnosed with myocardial injury (Figure 3).[7]

A diagnosis of acute myocardial infarction requires evidence of acute myocardial ischaemia. There are two types of myocardial infarction commonly seen in the acute situation. Type 1 myocardial ischaemia is a diagnosis in association with acute coronary thrombosis, whereas type 2 myocardial ischaemia is seen in conditions with oxygen supply/demand imbalance. In

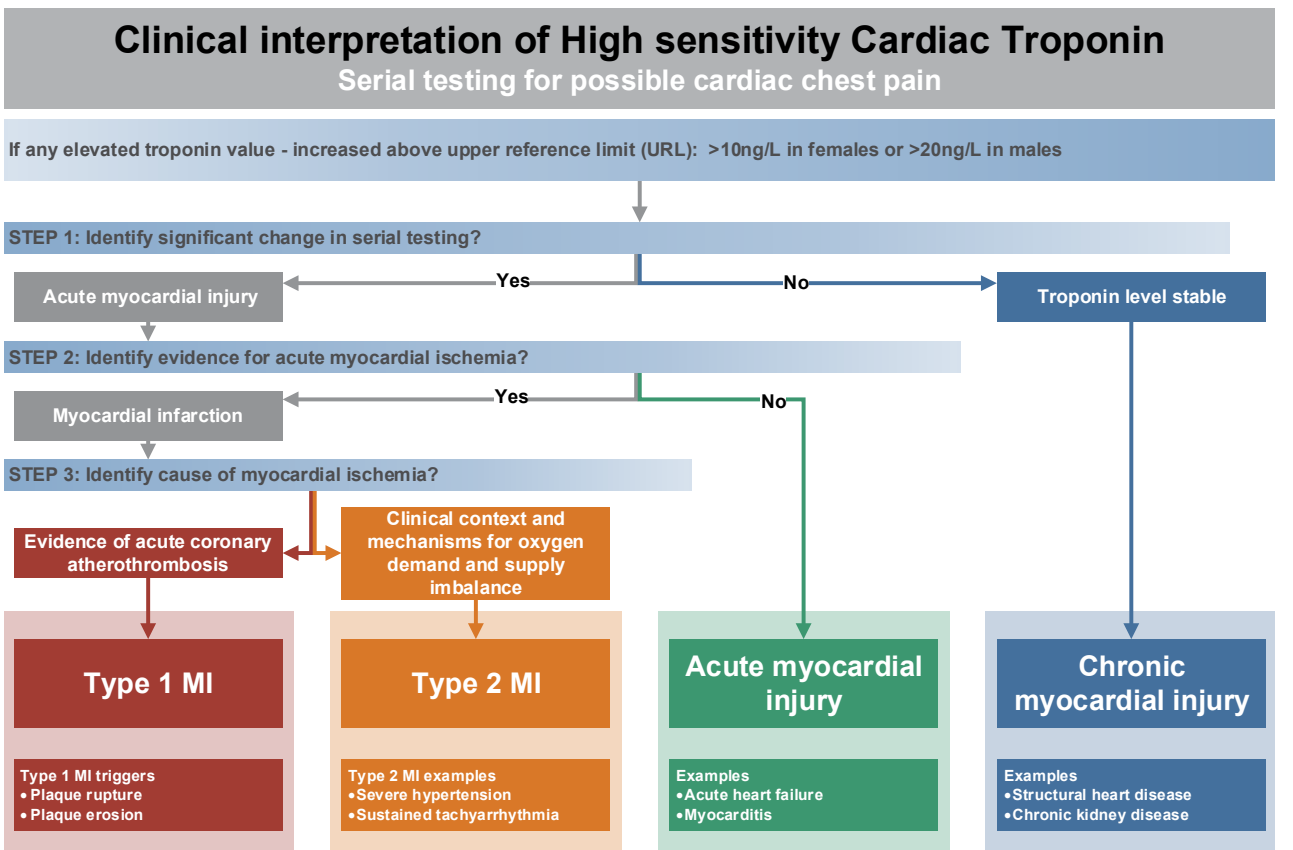

Figure 3. A model for interpreting myocardial injury

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the context of acute ischaemia symptoms but no troponin elevation, the diagnosis is unstable angina.[7,8] Elevated troponin values also occur in many conditions that cause both acute and chronic myocardial injury.

Maria's first ECG excluded STEMI (Figure 1). Her second ECG demonstrated subtle T wave changes, including an upright T wave in lead aVL (Figure 2). These changes are dynamic when compared with her first ECG, and together with her clinical presentation are concerning for myocardial ischaemia.

Answer 4

When interpreting the troponin results, it is important to ensure that both values have been evaluated with the same assay (ie at the same laboratory) so that a meaningful comparison can be made to assess for a change (rise or fall) in the second result. It is not possible to compare results from different assays, which is one of the reasons that pre-hospital or community testing of troponin is rarely done, as the assays available in community laboratories may not be the same as those used in hospital. It is also important to note that each assay will have a specific reference range for its results, and so any troponin result must be interpreted in the context of the reference ranges for that test. Maria has had two high-sensitivity cardiac troponin assays performed in hospital, which have both detected the presence of serum troponin but are both below the cut-off point for an elevated result for this assay. She therefore has 'negative' troponins and does not show evidence of myocardial injury.

Answer 5

With Maria's symptoms suggestive of ischaemia, the working diagnosis is unstable angina.

The introduction of high-sensitivity troponin assays has caused a shift in the incidence of NSTEMI and unstable angina, as serum troponin is now better detected than ever before. Many patients who might previously have been diagnosed with unstable angina are now diagnosed with NSTEMI, with troponin elevations that are only now detectable using the new assays.[9,10] The test is so sensitive that at least 50% of healthy individuals (and ideally more) will have a measurable (but not necessarily elevated) serum troponin level reported.[11] This has led to the introduction of sex-specific reference ranges and research into the need for different cut-off values in other patient populations (eg elderly, those with chronic renal disease) as well.

Answer 6

According to current Australian guidelines,[3] patients with new ischaemic ECG changes are classified as being at high risk for possible cardiac causes of chest pain, necessitating referral for inpatient work-up. This work-up could include primary coronary angiography with coronary revascularisation (percutaneous coronary intervention or coronary artery bypass graft) or an initial provocative test performed to assess for inducible ischaemia to guide further management. This decision will be made after considering the patient's risk factors and symptoms as well as the practicalities and availabilities of the various options.

It is also recommended that Maria have a complete cardiac risk profile work-up with risk modification while in hospital. This includes management of lipids, blood pressure, diabetes and smoking status, which will need the ongoing support and review of her primary care physician.

Conclusion

Maria undergoes primary coronary angiography, which demonstrates three-vessel coronary artery disease, with severe disease in the left anterior descending coronary artery and right coronary artery, moderate disease in the left circumflex coronary artery and moderate left main coronary artery stenosis. She has preserved left ventricular systolic function. Maria is referred for an urgent coronary artery bypass graft, which is undertaken successfully. Her hypertension continues to be medically managed.

References

1. Wilson J, Morgan S, Magin PJ, van Driel ML. Fatigue – A rational approach to investigation. Aust Fam Physician 2014;43(7):457–61.
2. DeVon HA, Zerwic JJ. Symptoms of acute coronary syndromes: Are there gender differences? A review of the literature. Heart Lung 2002;31(4):235–45. doi: 10.1067/mhl.2002.126105.
3. Chew DP, Scott IA, Cullen L, et al. National Heart Foundation of Australia & Cardiac Society of Australia and New Zealand: Australian Clinical Guidelines for the Management of Acute Coronary Syndromes 2016. Heart Lung Circ 2016;25(9):895–951. doi: 10.1016/j.hlc.2016.06.789.
4. Aroney CN, Cullen L. Appropriate use of serum troponin testing in general practice: A narrative review. Med J Aust 2016;205(2):91–94. doi: 10.5694/mja16.00263.
5. Glickman SW, Shofer FS, Wu MC, et al. Development and validation of a prioritization rule for obtaining an immediate 12-lead electrocardiogram in the emergency department to identify ST-elevation myocardial infarction. Am Heart J 2012;163(3):372–82. doi: 10.1016/j.ahj.2011.10.021.
6. Reeder GSA, Awtry E, Mahler SA. Initial evaluation and management of suspected acute coronary syndrome (myocardial infarction, unstable angina) in the emergency department. Waltham, MA: UpToDate, 2021. Available at www.uptodate.com/contents/initial-evaluation-and-management-of-suspected-acute-coronary-syndrome-myocardial-infarction-unstable-angina-in-the-emergency-department [Accessed 24 March 2021].
7. Thygesen K, Alpert JS, Jaffe AS, et al. Fourth universal definition of myocardial infarction (2018). Circulation 2018;138(20):e618–51. doi: 10.1161/CIR.0000000000000617.
8. Mendis S, Thygesen K, Kuulasmaa K, et al. World Health Organization definition of myocardial infarction: 2008–09 revision. Int J Epidemiol 2011;40(1):139–46. doi: 10.1093/ije/dyq165.
9. Collet J-P, Thiele H, Barbato E, et al. 2020 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation. Eur Heart J 2020.ePub ahead of print. doi: 10.1093/eurheartj/ehaa575.
10. Sandoval Y, Apple FS, Smith SW. High-sensitivity cardiac troponin assays and unstable angina. Eur Heart J Acute Cardiovasc Care 2018;7(2):120–28. doi: 10.1177/2048872616658591.
11. Andruchow JE, Kavsak PA, McRae AD. Contemporary emergency department management of patients with chest pain: A concise review and guide for the high-sensitivity troponin era. Can J Cardiol 2018;34(2):98–108. doi: 10.1016/j.cjca.2017.11.012.

CASE

2 Arisa has tingling in her leg

Arisa, aged 36 years, presents with a three-day history of tingling sensations in her left leg. She has been working at home during the COVID-19 pandemic. In the past day, she has noticed a bluish discolouration of her toes when standing. She is concerned she may have deep vein thrombosis (DVT). On examination, you note Arisa is well, with pulse rate 80 beats/min, blood pressure 115/75 mmHg and respiratory rate 16 breaths/min. She is afebrile. Her height is 173 cm and weight 75 kg; her body mass index is 25.1 kg/m^2. You note that Arisa is walking cautiously on her left leg. There is no leg tenderness and no obvious swelling, but her left calf is 4 cm larger than the right calf when measured. There are no other signs of DVT.

Question 1

What questions would you ask Arisa?

Further information

Arisa's medical history is unremarkable. She has taken the same low-dose combined oral contraceptive pill (COCP) for the past five years. There are no other recent or previous risk exposures for venous thromboembolism (VTE). There is no family history of venous disease. She does not think she might be pregnant.

Question 2

What investigations would you perform?

Further information

The ultrasound shows an occlusive thrombus in the popliteal vein extending into the calf.

Question 3

In this situation, would you prescribe anticoagulation?

Further information

Arisa has no history to suggest a bleeding disorder. Laboratory investigations are within reference ranges, and β-human chorionic gonadotropin testing indicates she is not pregnant.

Question 4

What anticoagulation therapy would you recommend?

Further information

Arisa is commenced on rivaroxaban at the recommended dose, and you arrange to review her in a few days.

Question 5

How would you assess Arisa's response to anticoagulant therapy?

Question 6

What recommendations about diet and exercise and compression stockings would you give Arisa?

Question 7

Given the unprovoked nature of Arisa's DVT, what other investigations would you perform?

Question 8

What duration of anticoagulant therapy would you advise?

Question 9

Would you cease Arisa's COCP following a VTE diagnosis?

Further information

After two months of anticoagulation therapy, Arisa re-presents to you, as her last menses was extremely heavy with flooding and she was unable to leave the house for two days.

Question 10

What management would you advise?

Further information

You change Arisa's anticoagulation therapy to apixaban 5 mg twice daily. After four months' therapy, Arisa is advised by her dentist that she requires a tooth to be removed.

Question 11

What would you advise her to do with regard to her anticoagulation therapy?

Further information

Arisa wishes to start a family and wonders how her anticoagulation therapy could affect a future pregnancy.

Question 12

What is your advice?

CASE 2 Answers

Answer 1

The symptoms and signs in this case are not specific and do not indicate a diagnosis of DVT.

Further history should include whether there has been any lower back, hip, knee or leg injury that might explain her symptoms. It may be relevant to ask about her recent physical activity now that she is working at home. Is her home office comfortable, or could the symptoms be related to her working position at home?

It would be important to ask about risk factors for DVT. Questions might include the following:

- Does she have any personal history of DVT or superficial venous disease?
- Has there been any recent sudden immobility or extended travel (within four weeks) or exposure to defined risk factors (within three months) for VTE (eg surgery or medical illness)?
- Does she take any medications, including hormonal medications?
- Could she be pregnant?
- Is there a family history of venous disease?

It would also be reasonable to ask about any signs of pulmonary embolism, such as chest pain, shortness of breath (on exertion or rest), cough or haemoptysis and palpitations.

Answer 2

Venous ultrasonography of the left leg would be recommended in this situation.

The symptoms and signs of DVT are not specific, and a clinical diagnosis is not possible. Formal imaging, generally by ultrasonography, is required to determine if DVT is present.

A number of strategies have been validated to provide guidance on whether imaging is indicated. Modified Wells criteria, with or without the use of plasma D-dimer, can help identify a low-risk group of patients for whom imaging need not be performed as the clinical probability of DVT is low (Table 1).[1]
In Arisa's case, the calf swelling and the lack of a suitable alternative diagnosis yield a low clinical probability score. If a rapid plasma D-dimer test were available, this could be performed and, if negative, imaging need not be performed. However, in primary practice and many emergency departments, this test is not readily available.

Answer 3

More information is required before prescribing anticoagulation. It is important to consider the risks (and not just the benefits) of anticoagulant therapy.

A bleeding history should be taken to ensure Arisa does not have active bleeding and/or has not experienced abnormal bleeding in the past. It is also important to assess whether her work/lifestyle is compatible with the safe use of anticoagulant medication. It is recommended to review her medication history for potential interactions with anticoagulant therapies.

Prior to considering anticoagulation, it is essential to check that baseline haemoglobin and platelet count, renal function and liver function and baseline coagulation studies are within reference ranges. It is also essential to confirm the patient is not pregnant prior to commencing anticoagulation. Lung scanning is not indicated in the absence of symptoms to suggest pulmonary embolism.

Table 1. Modified Wells criteria: Clinical evaluation for predicting the probability of a deep vein thrombosis[10]

Clinical characteristics	Score
Active cancer	+1
Paralysis, paresis or recent plaster immobilisation of the lower extremities	+1
Recently bedridden for three days or major surgery within the past 12 weeks	+1
Localised tenderness along the deep venous system	+1
Entire leg swollen	+1
Calf swelling ≥3 cm larger than asymptomatic side	+1
Pitting oedema confined to symptomatic leg	+1
Collateral superficial veins (non-varicose veins)	+1
Previously documented DVT	+1
Alternative diagnosis at least as likely as a DVT	−2
Clinical probability of DVT	**Total score**
Likely	≥2
Unlikely	<2

DVT, deep vein thrombosis

Table adapted from Wells PS, Anderson DR, Rodger M, et al, Evaluation of D-dimer in the diagnosis of suspected deep-vein thrombosis, N Engl J Med 2003;349(13):1227–35, doi: 10.1056/NEJMoa023153. Reprinted with permission from Massachusetts Medical Society.

Answer 4

A direct-acting oral anticoagulant (DOAC) would be the best-suited anticoagulant therapy for Arisa. DOACs are convenient (oral, no injection required), efficacious and safer than warfarin. In the combined analysis of various randomised controlled trials, DOAC therapy was equivalent to low–molecular weight heparin (LMWH) + warfarin in efficacy and was safer, with a 50% reduction in major and fatal bleeding.[2]

There is no need to manage Arisa as an inpatient or treat her initially with intravenous heparin infusion. Patients with severe renal impairment, or who are at high risk of bleeding, may need to be managed as inpatients and given anticoagulant therapy with intravenous heparin.

While efficacious, enoxaparin and warfarin are no longer recommended as first-line therapy in acute DVT for most patients with the ready availability of DOACs in Australia. Three DOACs are available in Australia and are indicated by the Therapeutic Goods Administration for the acute treatment of DVT. Dabigatran is not reimbursed through the Pharmaceutical Benefits Scheme (PBS). Rivaroxaban and apixaban are reimbursed through the PBS, and either medication could be used as initial anticoagulant therapy without the need for initial LMWH treatment. The recommended initial dosing for Arisa would be rivaroxaban 15 mg twice daily for three weeks (followed by 20 mg once daily) or apixaban 10 mg twice daily for one week (followed by 5 mg twice daily).

It is recommended that Arisa's progress be reviewed, at least by telephone, within a few days of her commencing anticoagulation, and that she is offered information to read about her anticoagulant medication (eg consumer medicine information). Arisa should receive counselling regarding symptoms that might indicate progressive thrombosis. These would include increased leg swelling, pain, discolouration and numbness. It is also advised to ensure Arisa is aware of typical symptoms of pulmonary embolism, such as chest pain, shortness of breath, cough and haemoptysis. Bleeding symptoms should be described, and it is recommended that Arisa examines her urine and stool for blood. If any of these symptoms appear, she must contact you or another medical service for advice.

Answer 5

Arisa's response to treatment can be followed clinically; for example, with a telephone call in the first two weeks, then a consultation at 4–6 weeks to check for resolution of symptoms and adverse effects of medication, then at three and six months. At each review it would be important to ask about the progress of her presenting leg symptoms and ensure she has no symptoms to indicate clinical deterioration. It is important to check her medication compliance and to ask about any adverse effects of the medication and any abnormal bruising or overt bleeding. Once again, it is important to emphasise avoidance of aspirin and nonsteroidal anti-inflammatory drugs.

There is no role for measuring medication levels. Progress imaging serves no useful purpose, unless there are concerns of progression of her DVT. It is expected that, even after six months, only 40–50% of patients will experience some resolution of the thrombosis by ultrasonographic criteria. The functional outcome is of much greater importance than the ultrasonic evaluation of the DVT.

Answer 6

There is no advantage to limiting exercise during acute anticoagulation therapy for DVT for most patients, and daily exercise is generally recommended as symptoms permit. Limiting exercise may be recommended for patients with massive ileo-femoral DVT for the first 24–48 hours of anticoagulation therapy to reduce the risk of embolism; however, this patient group is likely to be hospitalised in most situations. The amount of daily exercise should be patient directed on the basis of their physical fitness, leg symptoms (eg pain and swelling) and functional ability. While taking DOACs, patients should avoid contact sports that may cause injury, as they may experience excess bleeding. Compression stockings have not been found to be of benefit in recent studies other than for symptom control.[3] Compression stockings (prescribed class II stockings – usually below the knee) are helpful in mitigating leg swelling when mobile.

Approximately 30% of patients develop post-thrombotic syndrome after DVT. Symptoms can range from mild to significant venous insufficiency with pain, oedema and ulceration. Some studies have shown the use of graduated compression stockings starting approximately one month after the DVT (once the acute symptoms have settled) for at least one year can help reduce this risk of post-thrombotic syndrome. However, compression stockings are contraindicated if there is significant peripheral arterial disease.[4,5]

An exercise program that gradually increases over the first few weeks of acute therapy is recommended. There are no dietary restrictions for patients undergoing DOAC therapy and no requirement to abstain from mild-to-moderate alcohol consumption when undergoing DOAC therapy.

Answer 7

Only routine screening for malignant disease is recommended. A thorough history and examination and sex-specific routine screening is reasonable, as recommended by The Royal Australian College of General Practitioners' *Guidelines for preventive activities in general practice*, 9th edition, (www.racgp.org.au/download/Documents/Guidelines/Redbook9/17048-Red-Book-9th-Edition.pdf). If any unexplained or expected symptoms or signs are detected, they should be investigated.

There is no obvious benefit to the patient to undergo laboratory thrombophilia testing. These investigations should not be undertaken in the acute setting or while the patient is undergoing anticoagulation therapy. Before laboratory thrombophilia testing is undertaken, appropriate counselling of the patient is required. Whether these investigations are undertaken and when they should be collected is a question for a haematologist, who should consult the patient in the future. Detection of laboratory thrombophilia does not change the type of acute anticoagulation therapy. The commonly detected mild laboratory thrombophilias (eg heterozygous factor V Leiden) do not change the duration of anticoagulant therapy. Uncertainty remains regarding the value of laboratory thrombophilia testing for the prediction of recurrent thrombosis if anticoagulation is discontinued. Given the low prevalence of significant laboratory thrombophilia, testing all patients with unprovoked DVT is not worthwhile.

Answer 8

Arisa has unprovoked proximal DVT. Most recommendations would be for long-term anticoagulation.[6] This is increasingly seen in expert guidelines, given the convenience and safety of DOACs when compared with warfarin. Lower-intensity DOAC regimens (rivaroxaban 10 mg daily or apixaban 2.5 mg daily) likely result in lower long-term bleeding complications.

Answer 9

Most guidelines recommend discontinuation of COCP following an acute VTE diagnosis, unless essential to regulate the menstrual cycle. Continuation of a low-dose COCP while undergoing anticoagulation therapy is not associated with an increased risk of therapeutic failure.[7] Continuation or recommencement of the COCP after anticoagulation therapy has been ceased is associated with a significantly increased risk of recurrent thrombosis.

Answer 10

The cessation of the COCP and commencement of anticoagulation therapy is likely to result in heavier menses. Rivaroxaban is more frequently reported to cause menorrhagia than apixaban, so switching anticoagulant medications is a worthwhile strategy. If menses remains heavy, a dose reduction of anticoagulation after three months is reasonable. Hormonal options (eg the progesterone-only pill) or other strategies, such as an intrauterine device, can be explored.[8]

Answer 11

After three months, the risk of recurrence of DVT is relatively low, so Arisa can safely interrupt her anticoagulation therapy briefly without concern for recurrent DVT. Many dentists do not direct interruption to anticoagulation therapy for simple tooth removal; however, some dentists remain uncomfortable with this approach. Apixaban is quickly eliminated, so missing two doses for a low-bleeding risk procedure is sensible. Arisa should be advised to have the tooth socket stitched and recommence anticoagulation therapy 12–24 hours after the procedure.[9]

Answer 12

There are no data to support the safety of DOACs in pregnancy. Apixaban and rivaroxaban are known to cross the placenta and enter the fetal circulation. As with patients who take warfarin, it seems safer for patients to continue their anticoagulation therapy while they try to conceive. On early confirmation of the pregnancy (around four weeks of gestation), the patient should cease oral anticoagulation and immediately switch to enoxaparin.

References

1. Yunyonging P. Ruling out pulmonary embolism in primary care setting. Am Fam Physician 2018;97(11):750–52.
2. Raghavendra CPM, Hoaglin DC, McManus DD, et al. Efficacy and safety of direct oral anticoagulants approved for cardiovascular indications: Systematic review and meta-analysis. PLoS One 2018;13(5):e0197583. doi: 10.1371/journal.pone.0197583.
3. Berntsen CF, Kristiansen A, Akl EA, et al. Compression stockings for preventing the postthrombotic syndrome in patients with deep venous thrombosis. Am J Med 2016;129(4):447. doi: 10.1016/j.amjmed.2015.11.031.
4. Kakkos SK, Daskalopoulou SS, Daskalopoulos ME, Nicolaides AN, Geroulakos G. Review on the value of graduated elastic compression stockings after deep vein thrombosis. Thromb Haemost 2006;96(4):441–45.
5. Brandjes DP, Büller HR, Heijboer H, et al. Randomised trial of effect of compression stockings in patients with symptomatic proximal-vein thrombosis. Lancet 1997;349(9054):759–62. doi: 10.1016/S0140-6736(96)12215-7.

6. Huyen AT, Gibbs, H, Merriman E, et al. New guidelines from the Thrombosis and Haemostasis Society of Australia and New Zealand for the diagnosis and management of venous thromboembolism. Med J Aust 2019;210(5):227–35. doi: 10.5694/mja2.50004.
7. Martinelli I, Lensing AWA, Middeldorp S, et al. Recurrent venous thromboembolism and abnormal uterine bleeding with anticoagulant and hormone therapy use. Blood 2016;127(11):1417–25. doi: 10.1182/blood-2015-08-665927.
8. Bannow BS. Management of heavy menstrual bleeding on anticoagulation. Hematology Am Soc Hematol Educ Program 2020;2020(1):533–37. doi: 10.1182/hematology.2020000138.
9. Clinical Excellence Commission. Non-vitamin K antagonist oral anticoagulant (NOAC) guidelines (updated July 2017). Haymarket, NSW: CEC, 2017. Available at www.cec.health.nsw.gov.au/__data/assets/pdf_file/0007/326419/noac_guidelines.pdf [Accessed 12 April 2021].
10. Wells PS, Anderson DR, Rodger M, et al. Evaluation of D-dimer in the diagnosis of suspected deep-vein thrombosis. N Engl J Med 2003;349(13):1227–35. doi: 10.1056/NEJMoa023153.

CASE

3 Tamara is feeling breathless

Tamara, aged 23 years, presents to your local general practice with shortness of breath and chest tightness. She is 26 weeks pregnant with her first child.

Question 1

What additional information would you ask of Tamara?

Further information

Tamara is an Aboriginal woman. She lives with her partner and his family in urban Western Australia. She tells you that she has been experiencing worsening breathlessness for the past month. Initially this occurred with significant exertion, but she now becomes breathless when walking to the shops at the end of her street. For the past two days she has been breathless when showering and has noticed some associated chest tightness. She has had no presyncope, syncope or palpitations. She has noticed some mild ankle swelling.

Her pregnancy so far has been unremarkable, with a normal anatomy scan at 20 weeks' gestation. Tamara has a history of mild childhood asthma for which she still carries a salbutamol inhaler for use as needed. Tamara has been using her inhaler more frequently without substantial relief during her recent episodes of breathlessness. She has no allergies and is otherwise taking only a pregnancy multivitamin.

Tamara is studying to become a teacher. She previously smoked a few cigarettes per day but quit when she found out about the pregnancy. She grew up in a small town in northern Western Australia and has five siblings. She tells you that one or two of her siblings may have been treated for rheumatic fever, but she cannot remember the details as she was quite young.

You record the following results from your physical examination of Tamara:

- heart rate 130 beats/min, irregular
- blood pressure 105/70 mmHg
- oxygen saturation 98%
- respiratory rate 22 breaths/min.

Cardiorespiratory examination reveals an irregular pulse, a systolic murmur and equal air entry with some crepitations noted. Electrocardiography performed in the practice is shown in Figure 1.

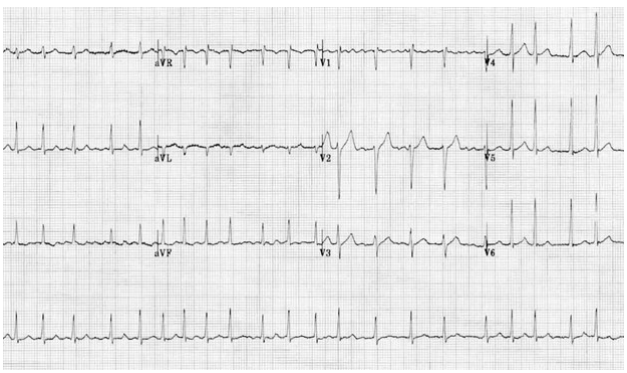

Figure 1. Tamara's electrocardiogram

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Question 2

On the basis of the information you have received from Tamara, what differential diagnoses would you be concerned about?

Question 3

What is the most appropriate next step in the management of Tamara's presentation?

Further information

Tamara is taken to the local hospital emergency department by ambulance. Following clinical assessment, she undergoes several investigations. Her results are:

- electrocardiogram (ECG)
  - atrial fibrillation
  - ventricular rate 140 beats/min
- chest X-ray
  - bilateral interstitial markings
  - vascular upper lobe diversion
  - prominent fissure markings
- blood examination
  - haemoglobin 105 g/L (reference range 135–175 g/L)
  - white cell count 7 × 10^9/L (reference range 3.5–10.0 × 10^9/L)
  - C-reactive protein 13 mg/L (reference range <5 mg/L)
  - troponin 57 ng/L (reference range <17 ng/L)
  - D-dimer 0.4 mg/L (reference range <0.5 mg/L)
- echocardiogram
  - normal left ventricular size with hyperdynamic left ventricular systolic function, ejection fraction: 75%
  - rheumatic appearance of the mitral valve with severe eccentric regurgitation, and moderate stenosis
  - normal appearance of the aortic valve
  - mild tricuspid regurgitation
  - right ventricular systolic pressure, approximately 45 mmHg
  - normal right ventricular size and systolic function
  - mildly dilated left atrium.

Tamara is admitted to the coronary care unit and commences treatment for pulmonary oedema, including non-invasive ventilation (NIV), intravenous diuretic therapy and unfractionated heparin. On the second day she is stabilised with the cessation of NIV and conversion to oral diuretic therapy, and she commences low-dose β-blocker therapy. After 24 hours she reverts to sinus rhythm. The heparin infusion is converted to low–molecular weight heparin subcutaneous injection.

Following a multidisciplinary meeting with cardiology and obstetric teams, Tamara is discharged with a plan for early follow-up by both teams and a planned induction at 38 weeks' gestation.

Her discharge summary diagnosis states acute pulmonary oedema in the setting of atrial fibrillation and severe rheumatic heart disease (RHD).

Her discharge medications are:

- metoprolol 25 mg twice daily
- frusemide 40 mg twice daily
- enoxaparin 60 mg twice daily subcutaneous injection
- benzathine benzylpenicillin G 1,200,000 units intramuscular injection every four weeks
- oral iron supplementation (elemental iron 100–210 mg daily).

Tamara comes to see you one week following discharge from hospital.

Question 4

What key actions would you take during the consultation?

Further information

Tamara does not recall having acute rheumatic fever (ARF) and is surprised by her diagnosis of RHD.

Question 5

How would you respond?

Question 6

What advice would you offer regarding the prevention of future recurrences of ARF?

Question 7

Are ARF and RHD notifiable diseases in Australia?

Question 8

What treatment is advised for people with severe RHD?

Further information

Tamara's diagnosis of RHD has been classified as 'priority 1'. This provides direction for duration of secondary prophylaxis and necessary follow-up, including specialist care.

Question 9

What would be the appropriate follow-up recommended for Tamara?

Further information

Tamara is managed through her pregnancy with close clinical monitoring by you as her general practitioner, as well as her cardiology and obstetric teams. She undergoes a successful induction at 38 weeks' gestation and delivers a healthy baby boy.

One-month postpartum, she is reviewed by her cardiologist and undergoes transoesophageal echocardiography. This confirms persisting moderate mitral stenosis and severe mitral regurgitation.

It is recommended that Tamara undergoes valve surgery to replace the rheumatic mitral valve.

Question 10

What considerations need to be addressed with Tamara and her care providers prior to undergoing valve surgery?

Further information

Three months following the birth of her son, Tamara undergoes mitral valve surgery, receiving a bioprosthetic mitral valve replacement. Following surgery, she is commenced on warfarin for three months. She remains in sinus rhythm and has had no further documented episodes of atrial fibrillation.

Question 11

What other advice or education would you consider for Tamara?

CASE 3 Answers

Answer 1

Important information to elicit from Tamara would include:

- patient details including ethnicity
- more details regarding the presenting symptoms and any relevant history
- details regarding her pregnancy so far
- previous medical history
- family history
- social history
- allergies
- medications
- observations
- clinical examination.

Answer 2

With the known details of Tamara's presentation, any of the following conditions could be possible:

- pulmonary embolus
- exacerbation of asthma
- cardiac arrhythmia
- myopericarditis
- RHD
- non-rheumatic valvular heart disease
- spontaneous coronary artery dissection.

Answer 3

Given the subacute nature of Tamara's illness, her pregnancy and the concerning observations, the most appropriate next step is to send Tamara to hospital. Tamara has subacute progressive breathlessness as her predominant symptom. The ECG demonstrates atrial fibrillation without definite ischaemic changes. Although spontaneous coronary artery dissection is a differential diagnosis, this is best further investigated in hospital prior to commencing aspirin.

Given the wide differential diagnoses for Tamara's presentation, other reasonable investigations to consider are a blood examination for C-reactive protein, erythrocyte sedimentation rate and D-dimer, and referral for an echocardiogram, chest X-ray and computed tomography pulmonary angiogram. However, given the concerning observations, Tamara is best managed in hospital, rather than in the community.

Answer 4

Key actions to be covered:

- Educate Tamara and her family about ARF and RHD and early treatment of streptococcal infection(s) to prevent recurring ARF and developing RHD.
- Ensure Tamara and her family have access to culture- and language-appropriate RHD education resources and support.
- Ensure that the RHD control program has been notified about Tamara's new RHD diagnosis. More information regarding RHD control programs in Australia can be found at the RHDAustralia website (www.rhdaustralia.org.au/control-programs).
- Continue benzathine benzylpenicillin G 1,200,000 units intramuscular injections every four weeks.
- Discuss the strategy for anticoagulation during pregnancy.
- Ensure appropriate antenatal care is being provided, including checking relevant serologies, such as syphilis, hepatitis B virus and human immunodeficiency virus, and managing anaemia.

Answer 5

It is common for RHD to be diagnosed without a history of recognised ARF, as ARF presentations can be subtle and may be missed by clinicians. Seventy-five per cent of newly diagnosed patients with RHD in northern Australia have no previous history of ARF,[1] and 10% of people have severe RHD at first presentation.[2] ARF results from an abnormal immune response to group A streptococcal (strep A) infection.[3] ARF characterised by carditis (valvular inflammation) can then lead to RHD, and further ARF recurrences lead to progressive valve damage. Mitral valve involvement is common. The diastolic murmur of mitral stenosis is often missed; in Tamara's case, only the mitral regurgitant systolic murmur was noted.

Answer 6

Prevention is important at the household and community level, but also for any individual diagnosed with ARF or RHD, to prevent recurrences and valve disease progression.[4,5] Repeated childhood strep A infections prime the immune system to develop the abnormal autoimmune response that triggers

ARF.[6] Encouragement of healthy living practices, including handwashing and washing of clothing and bedding, are important primordial strategies to reduce strep A infections. Primary prevention comprises early identification and treatment of strep A infections, including strep A–associated sore throats and skin infections. Several educational resources for people with ARF and RHD are available from RHDAustralia (www.rhdaustralia.org.au/resources-search).

Health services need to provide care that is culturally appropriate and welcoming to encourage patient engagement. Responding to individual patient needs – such as involving relevant senior family members in shared decision-making discussions, providing communication in the patient's first language through the use of interpreters, involving an Aboriginal health practitioner in the delivery of care and sharing health literacy resources (eg videos or booklets) designed for the patient's cultural group – can all be important strategies in preventing and managing this serious chronic condition.[7]

Answer 7

ARF and RHD are notifiable diseases in several Australian states and territories, including Western Australia, Northern Territory, Queensland, South Australia and New South Wales. Although the process of notification differs between jurisdictions, notifying the RHD control program or register in the relevant state/territory is a key component of this process. Further information regarding the notification of ARF/RHD is available from RHDAustralia (www.rhdaustralia.org.au/control-programs).

Answer 8

Patients diagnosed with severe RHD should be commenced on benzathine benzylpenicillin G for a minimum of five years following the diagnosis of RHD or until the age of 40 years (whichever is longer).[8] The duration of secondary prophylaxis is determined by a specialist, but guidance can be found within the Australian RHD guidelines.[8]

Anticoagulation is indicated in the setting of moderate or severe mitral stenosis and atrial fibrillation.[9] Direct oral anticoagulants are not indicated because of the exclusion of valvular atrial fibrillation from the relevant trials (the definition of valvular atrial fibrillation is rheumatic mitral stenosis of at least moderate severity or mechanical valve replacement), and warfarin remains the therapy of choice for non-pregnant individuals. In the setting of RHD, anticoagulation may be indicated because of atrial fibrillation, such as in this case, or because of a mechanical valve replacement. The management of anticoagulation during pregnancy requires consideration and discussion with the relevant obstetric and cardiology teams involved in the patient's care.[10,11] Figure 2 provides guidance regarding the choice of anticoagulation during pregnancy. A care pathway and referral algorithm for pregnant women with rheumatic heart disease (RHD) is available from RHDAustralia (www.rhdaustralia.org.au/system/files/fileuploads/a3_referral_algorithm_for_pregnant_women_with_rhd_1.pdf).

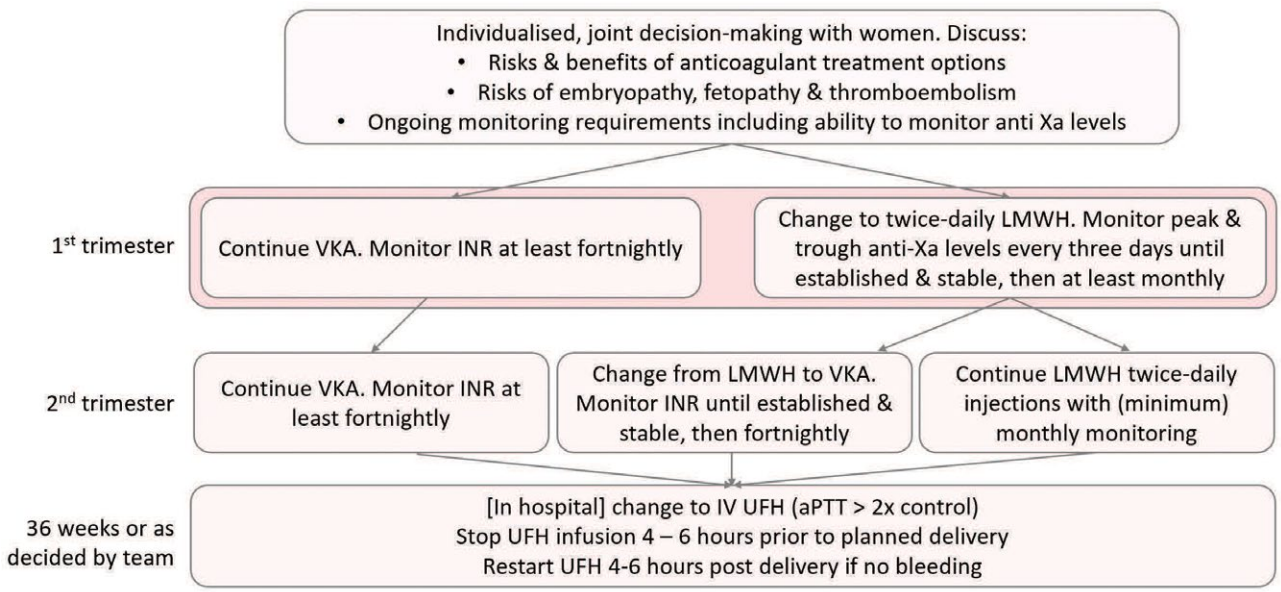

Figure 2. Anticoagulation pathways for pregnant women on vitamin K antagonist (VKA) regimen

Reproduced with permission from RHDAustralia (ARF/RHD writing group), The 2020 Australian guideline for the prevention, diagnosis and management of acute rheumatic fever and rheumatic heart disease, 3rd edition, Darwin, NT: RHDAustralia, 2020.
aPTT, activated partial thromboplastin time; INR, international normalised ratio; IV, intravenous; LMWH, low molecular weight heparin; UFH, unfractionated heparin; VKA, vitamin K agonist

Answer 9

It is recommended that Tamara undergoes specialist review, echocardiography and medical and dental review every six months, and receives an annual influenza vaccination. For further information, refer to the RHD priority classification and recommended follow-up table (www.rhdaustralia.org.au/system/files/fileuploads/a4_priority_classification_and_recommended_follow_0.pdf).

Answer 10

Key considerations include:

- type of valve disease (mixed disease [regurgitation and stenosis], multiple valves involved)
- choice of valve prosthesis type (mechanical or bioprosthetic) with implications for anticoagulation requirements, and durability of the surgery
- planning of future pregnancies.

A mechanical valve replacement requires lifelong warfarin therapy, whereas bioprosthetic valve replacements require only a short period of anticoagulation post-surgery (1–3 months). Consideration of any contraindications to anticoagulation and access to both monitoring of International Normalised Ratio (INR) and medication itself, as well as adherence to medical therapy, is important. Mechanical prostheses are associated with longer durability when compared with bioprosthetic valves. Acceptability or contraindication to redo surgery later in life, patient preference and age at first operation (ie childhood versus adulthood) all require discussion. Furthermore, access to primary care and specialist follow-up may have an impact on the decision-making process.

Answer 11

It is recommended that contraception and future pregnancy planning are discussed with Tamara and her partner. An important component of future pregnancy counselling needs to include the contraindication of pregnancy while on warfarin. Recommended contraceptives for women with RHD include long-acting reversible contraceptives (intra-uterine contraceptive device or etonogestrel implant).[12] Oestrogen-containing contraceptives are associated with an elevated risk of thrombosis and should be avoided.[13]

Anticoagulation is needed for life for all people with mechanical prosthetic valves, and for 1–3 months for those with bioprosthetic valves to prevent acute valve dysfunction, stroke and other thromboembolic events.[14]

Tamara will require prophylactic antibiotics prior to any procedure with a moderate-to-high incidence of bacteraemia (eg dental or ear, nose and throat procedures, invasive endoscopic procedures in the setting of infection or non-sterile suturing).[15] She should carry an 'advice to prevent infective endocarditis' card to present if undergoing any dental work or invasive or non-sterile procedures (Table 1).

Table 1. Cardiac conditions and procedures for which infective endocarditis prophylaxis is recommended

Endocarditis prophylaxis is recommended only for patients with the following cardiac conditions who are undergoing a procedure listed below*,†

Cardiac conditions	Procedures
Prosthetic cardiac valve, including transcatheter-implanted prosthesis or homograph. Prosthetic material used for cardiac valve repair, such as annuloplasty rings and chords. Previous infective endocarditis. Congenital heart disease, but only if it involves: • unrepaired cyanotic defects, including palliative shunts and conduits • repaired defects with residual defects at or adjacent to the site of a prosthetic patch or device (which inhibit endothelialisation). Rheumatic heart disease in all populations.	**Dental procedures**. Only those involving manipulation of the gingival or periapical tissue or perforation of the oral mucosa (eg extraction, implant placement, biopsy, removal of soft tissue or bone, subgingival scaling and root planning, replanting avulsed teeth). **Dermatological and musculoskeletal procedures**. Only those involving infected skin, skin structures or musculoskeletal tissues. **Respiratory tract or ear, nose and throat procedures**. Only for tonsillectomy or adenoidectomy, or invasive respiratory tract or ear, nose and throat procedures to treat an established infection (eg drainage of abscess). **Genitourinary and gastrointestinal tract procedures**. Only if surgical antibiotic prophylaxis is required or for patients with an established infection.

**Endocarditis prophylaxis is not recommended for patients with forms of valvular or structural heart disease not listed in this table, including patients with mitral valve prolapse, septal defects or cardiac implantable electronic devices.*

†Patients with a heart transplant who have developed cardiac valvulopathy may also be at high risk of adverse outcomes from endocarditis. Consult with the patient's cardiologist for specific recommendations.

Endocarditis prophylaxis is not recommended for procedures other than those listed above. However, surgical prophylaxis may be indicated if endocarditis prophylaxis is not.

Given shared environmental risk factors and a slight familial (genetic) risk of RHD, Tamara's siblings should be offered clinical review, and possibly echocardiographic screening, especially siblings with a possible history of ARF.

Resources for doctors

- RHDAustralia – Resources, www.rhdaustralia.org.au/resources

References

1. Hardie K, Ralph AP, de Dassel JL. RHD elimination: Action needed beyond secondary prophylaxis. Aust N Z J Public Health 2020;44(5):427. doi: 10.1111/1753-6405.13002.
2. He VYF, Condon JR, Ralph AP, et al. Long-term outcomes from acute rheumatic fever and rheumatic heart disease: A data-linkage and survival analysis approach. Circulation 2016;134(3):222–32. doi: 10.1161/CIRCULATIONAHA.115.020966.
3. Carapetis JR, Steer AC, Mulholland EK, Weber M. The global burden of group A streptococcal diseases. Lancet Infect Dis 2005;5(11):685–94. doi: 10.1016/S1473-3099(05)70267-X.
4. Coffey PM, Ralph AP, Krause VL. The role of social determinants of health in the risk and prevention of group A streptococcal infection, acute rheumatic fever and rheumatic heart disease: A systematic review. PLoS Negl Trop Dis 2018;12(6):e0006577. doi: 10.1371/journal.pntd.0006577.
5. Watkins DA, Johnson CO, Colquhoun SM, Karthikeyan G, Beaton A, Bukhman G, et al. Global, regional, and national burden of rheumatic heart disease, 1990–2015. N Engl J Med 2017;377(8):713–22. doi: 10.1056/NEJMoa1603693.
6. Bright PD, Mayosi BM, Martin WJ. An immunological perspective on rheumatic heart disease pathogenesis: More questions than answers. Heart Br Card Soc 2016;102(19):1527–32. doi: 10.1136/heartjnl-2015-309188.
7. Australian Government. Cultural Respect Framework 2016–2026 for Aboriginal and Torres Strait Islander health. A national approach to building a culturally respectful health system. Canberra, ACT: Australian Health Ministers' Advisory Council, 2016.
8. RHDAustralia (ARF/RHD writing group). The 2020 Australian guideline for the prevention, diagnosis and management of acute rheumatic fever and rheumatic heart disease. 3rd edn. Darwin, NT: RHDAustralia, 2020.
9. Brieger D, Amerena J, Attia JR, et al. National Heart Foundation of Australia and Cardiac Society of Australia and New Zealand: Australian clinical guidelines for the diagnosis and management of atrial fibrillation 2018. Med J Aust 2018;209(8):356–62. doi: 10.5694/mja18.00646.
10. D'Souza R, Silversides CK, McLintock C. Optimal anticoagulation for pregnant women with mechanical heart valves. Semin Thromb Hemost 2016;42(7):798–804. doi: 10.1055/s-0036-1593418.
11. Steinberg ZL, Dominguez-Islas CP, Otto CM, Stout KK, Krieger EV. Maternal and fetal outcomes of anticoagulation in pregnant women with mechanical heart valves. J Am Coll Cardiol 2017;69(22):2681–91. doi: 10.1016/j.jacc.2017.03.605.
12. Roos-Hesselink JW, Cornette J, Sliwa K, Pieper PG, Veldtman GR, Johnson MR. Contraception and cardiovascular disease. Eur Heart J 2015;36(27):1728–34, 1734a–1734b. doi: 10.1093/eurheartj/ehv141.
13. Lidegaard Ø, Løkkegaard E, Jensen A, Skovlund CW, Keiding N. Thrombotic stroke and myocardial infarction with hormonal contraception. N Engl J Med 2012;366(24):2257–66. doi: 10.1056/NEJMoa1111840.
14. Baumgartner H, Falk V, Bax JJ, et al. 2017 ESC/EACTS Guidelines for the management of valvular heart disease. Rev Espanola Cardiol Engl Ed 2018;71(2):110. doi: 10.1016/j.rec.2017.12.013.
15. Expert Group for Cardiovascular. Prevention of infective endocarditis. In eTG complete [Internet]. West Melbourne, Vic: Therapeutic Guidelines Ltd, 2019.

CASE

4 Maurice has chest pain

Maurice, aged 57 years, presents with sudden-onset chest pain and shortness of breath since this morning. He reports that he was well when he went to bed last night, and he went to work this morning as usual. Once at work, he received a telephone call from the local hospital advising that his son had been involved in a motor vehicle accident. Maurice has a background of hypertension and hypercholesterolaemia, which he has been managing with diet and exercise. He takes an over-the-counter multivitamin but no other regular medications. He is a non-smoker and drinks approximately 1–2 standard drinks of alcohol on the weekends only.

Question 1

What further history would you seek from Maurice?

Further information

You take Maurice to the treatment room and ask him for further details about his chest pain while you undertake basic observations and prepare him for electrocardiography. Maurice informs you of pressure-like pain that is centrally located and occasionally radiates to his shoulder. He has difficulty breathing and is feeling very anxious. He does not report any palpitations, syncope, back pain, leg swelling or pain. He tells you this has never happened before and he does not have any family history of cardiovascular disease (CVD) or venous thromboembolism (VTE).

On examination, Maurice is alert but looks anxious. He is slightly dyspnoeic when speaking.

Your examination results are:

- temperature: 37.2°C
- blood pressure: 145/82 mmHg
- heart rate: 116 beats/min
- respiratory rate: 26 breaths/min
- oxygen saturation: 96% on room air.

Maurice is well perfused and has no radio-radial delay. His heart sounds are dual with no murmurs, and there are no signs of cardiac failure. His calves are soft and non-tender, and there is no peripheral oedema.

Question 2

What conditions would you include in your differential diagnosis?

Further information

You perform 12-lead electrocardiography, which shows ST segment elevation in anterior leads.

You suspect Maurice is having an acute coronary syndrome (ACS) and call an ambulance. You administer 300 mg aspirin and 400 µg glyceryl trinitrate sublingually. You call the local emergency department and provide handover information to the emergency admitting officer. The ambulance arrives and Maurice is transferred to hospital.

Question 3

What investigations would you expect the hospital to perform on Maurice?

Further information

Maurice undergoes several investigations. Results of his full blood examination and cardiac investigations are shown in Tables 1 and 2.

Table 1. Full blood examination results

Full blood examination, electrolytes, urea and creatinine, liver function tests, coagulation profile	Within normal limits
Troponin	1800 ng/L (reference range <17 ng/L)
Random blood sugar level	5.9 mmol/L (reference range 3.6–7.7 mmol/L)

Table 2. Cardiac investigations

Electrocardiogram	ST segment elevation in anterior precordial leads.
Chest X-ray	The lungs are clear. There is no evidence of pulmonary oedema or a pneumothorax. The cardiomediastinal silhouette is normal.
Transthoracic echocardiogram	Left ventricular systolic dysfunction. The mid and apical segments of the left ventricle are hypokinetic, and the basal segments are hyperkinetic.
Coronary angiography and left ventriculography	The coronary arteries are normal. The mid and apical segments of the left ventricle are hypokinetic, and the basal segments are hyperkinetic.

Question 4

What is your working diagnosis for Maurice, given his investigation results?

Question 5

What are the causes of stress cardiomyopathy?

Question 6

How is stress cardiomyopathy typically managed?

Question 7

What is the prognosis for patients with stress cardiomyopathy?

CASE 4 Answers

Answer 1

As Maurice's symptoms are potentially life-threatening, a brief history should be obtained, as well as conducting an examination and initial investigations. Relevant features of the history that should be elicited include:

- details about his chest pain, including the site, severity, quality, duration, radiation and any exacerbating or relieving factors
- associated symptoms, such as dyspnoea, orthopnoea, palpitations, leg swelling or haemoptysis
- exercise tolerance and any symptoms and signs of peripheral vascular disease (eg claudication)
- risk factors for VTE, such as recent major surgery or prolonged immobilisation, as well as oestrogen therapy in female patients
- family history (in particular, ischaemic heart disease and VTE)
- recreational drug use (in particular, cocaine).

Answer 2

Differential diagnoses for Maurice's presentation include:

- ACS – ST elevation myocardial infarction, non–ST elevation myocardial infarction and unstable angina
- pulmonary embolism
- pneumothorax (including tension type)
- aortic dissection
- coronary artery vasospasm or dissection
- pericarditis
- myocarditis
- pheochromocytoma
- anxiety attack.

Answer 3

Investigations that would typically be performed include:

- a full blood examination and basic blood tests to check renal and liver function
- coagulation profile
- cardiac biomarkers, including serial troponin levels
- electrocardiography
- chest X-ray
- specialised cardiac investigations, such as a transthoracic echocardiogram (TTE) and a coronary angiogram (often undertaken depending on preliminary results and the capacity of the hospital).

A computed tomography (CT) pulmonary angiography or CT aortography could be considered if the clinical suspicion of VTE or aortic dissection is high.

Answer 4

Given Maurice has normal coronary arteries with evidence of left ventricular systolic dysfunction, the most likely diagnosis is stress cardiomyopathy. Stress cardiomyopathy occurs when there is transient regional systolic dysfunction of the left ventricle;[1–5] however, unlike in myocardial infarction, there is no obstructive coronary artery disease or acute plaque rupture.[1–3] It occurs in approximately 1% of patients with suspected ACS and is more common in postmenopausal women.[1,2] Stress cardiomyopathy is also known as apical ballooning syndrome, broken heart syndrome and takotsubo cardiomyopathy; the latter name arising from the ballooning appearance of the left ventricle during systole and its resemblance to the Japanese octopus trap known as 'takotsubo' (Figure 2).[1–6]

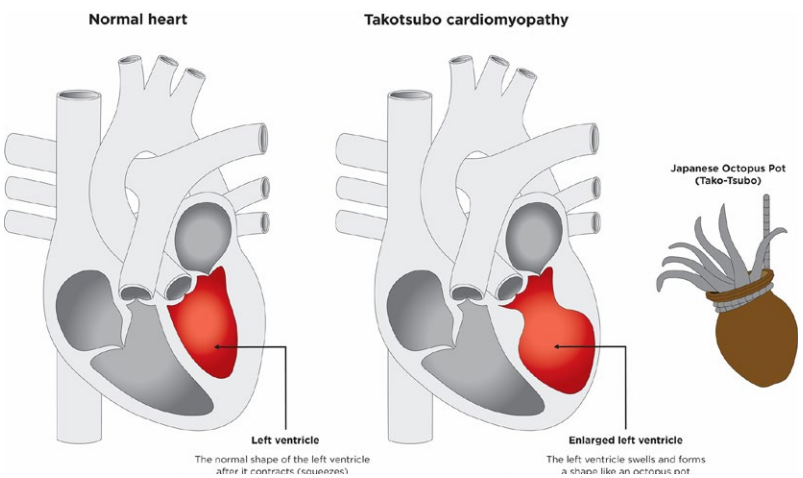

Figure 2. Appearance of the left ventricle in a normal heart (left) and in stress cardiomyopathy (right)
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A diagnosis of stress cardiomyopathy requires all four of the following Mayo Clinic diagnostic criteria to be met:[1,5]

- transient left ventricular systolic dysfunction (hypokinesis, akinesis or dyskinesis)
- absence of obstructive coronary disease or angiographic evidence of acute plaque rupture
- new electrocardiographic abnormalities (either ST segment elevation and/or T-wave inversion) or modest elevation in cardiac troponin (electrocardiogram changes are often out of proportion to the rise in troponin levels)[1–5]
- absence of pheochromocytoma or myocarditis.

A diagnosis of stress cardiomyopathy can still be made if coronary disease is found if the wall motion changes do not correlate with the distribution of obstructive disease.[1,3] However, it is recommended that patients with ST segment elevation be treated as having an ACS until proven otherwise, as most patients with ST segment elevation will have a critical coronary lesion, and some patients with stress cardiomyopathy will have co-existing coronary artery disease.[1,2,5]

Answer 5

The exact pathogenesis of stress cardiomyopathy is not known but is thought to be related to catecholamine excess, coronary artery spasm and microvascular dysfunction.[1,2] It is often associated with an intense physical or emotional trigger, such as:[6]

- acute illness
- surgery
- motor vehicle accident
- natural disaster
- assault
- receiving bad news (eg catastrophic medical diagnosis)
- bereavement
- relationship breakup
- job or financial loss.

In Maurice's case, receiving the news that his son was involved in a motor vehicle accident earlier that morning is likely to have triggered the stress cardiomyopathy. However, it would be important not to dismiss ACS in Maurice, given the typical history and his significant vascular risk factors (hypercholesterolaemia and hypertension).

Answer 6

Treatment of stress cardiomyopathy is usually supportive.[1,2,7] Medical therapy includes β-blockers and angiotensin converting enzyme inhibitors (in the absence of left ventricular outflow tract obstruction) until recovery of systolic function (typically one month).[7] Complications include heart failure, cardiogenic shock, intraventricular thrombus and death.[7] Beta-blockers may be continued indefinitely because of the risk of relapse. Antiplatelets should only be initiated if there is co-existing coronary atherosclerosis, and anticoagulation with warfarin is recommended if there is an intraventricular thrombus.[7]

It is advisable to address Maurice's vascular risk factors with lifestyle modifications, blood pressure–lowering medications and statins, if appropriate. It is recommended to encourage him to participate in regular aerobic exercise and to keep his alcohol usage at safe limits (no more than two standard drinks per day).

It would also be important to screen Maurice for depression or anxiety, as a result of both his and his son's hospitalisation, and arrange referral to a psychologist, if appropriate.

Answer 7

Most patients typically recover within one month; however, the rate of complications is comparable to patients with ACS. There is approximately a 2% per year risk of recurrence.[7]

Conclusion

Maurice is discharged from hospital and is progressing well when you see him in one week's time. He attends his cardiologist in one month for a repeat TTE, and his systolic function has recovered close to normal.

References

1. Reeder G, Prasad A. Clinical manifestations and diagnosis of stress (takotsubo) cardiomyopathy. In: McKenna WJ, Yeon SB, editors. Waltham, MA: UpToDate Inc, 2019. Available at www.uptodate.com.acs.hcn.com.au/contents/clinical-manifestations-and-diagnosis-of-stress-takotsubo-cardiomyopathy?search=stress%20cardiomyopathy&source=search_result&selectedTitle=1~108&usage_type=default&display_rank=1#H16 [Accessed 5 March 2021].
2. Kumar P, Clark M. Kumar and Clark's Clinical Medicine. 8th edn. Edinburgh, UK: Elsevier, 2012.
3. Rahman A. Broken heart syndrome. Aust Fam Physician 2012;41(1):55–56.
4. Rivers R, Ihle J. COVID-19 social isolation-induced takotsubo cardiomyopathy. Med J Aust 2020;213(7):336–336.e1. doi: 10.5694/mja2.50770.
5. Burns E. Takotsubo cardiomyopathy. Sydney, Australia: Life in the Fast Lane, 2021. Available at https://litfl.com/tako-tsubo-cardiomyopathy-ecg-library/ [Accessed 5 March 2021].
6. The National Heart Foundation of New Zealand. Takotsubo cardiomyopathy. Auckland, NZ: NHFNZ, 2021. Available at www.heartfoundation.org.nz/your-heart/heart-conditions/takotsubo-cardiomyopathy [Accessed 5 March 2021].
7. Reeder G, Prasad A. Management and prognosis of stress (takotsubo) cardiomyopathy. In: McKenna WJ, Yeon SB, editors. Waltham, MA: UpToDate Inc, 2020. Available at www.uptodate.com.acs.hcn.com.au/contents/management-and-prognosis-of-stress-takotsubo-cardiomyopathy?search=stress%20cardiomyopathy&source=search_result&selectedTitle=2~108&usage_type=default&display_rank=2#H607854819 [Accessed 5 March 2021].

ACTIVITY ID **269736**

Cardiovascular disease

This unit of *check* is approved for six CPD Activity points in the RACGP CPD Program. The expected time to complete this activity is three hours and consists of:

- reading and completing the questions for each case study
  - you can do this on hard copy or by logging on to the RACGP website (www.racgp.org.au), clicking on the My Account button and selecting the *gplearning* link from the drop-down
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Case 1 – Bhavneet

Bhavneet, aged 64 years, is from a non–English speaking background and has been brought to see you by his son. Bhavneet has had nausea, breathlessness on exertion, epigastric pain and lethargy for the past two days. Last night he had difficulty lying flat to sleep due to breathlessness. He has tried over-the-counter antacids with no effect. He has known hypertension, high cholesterol and type 2 diabetes.

Bhavneet is alert and has normal vital signs except for hypertension (150/90 mmHg). He can speak in sentences without respiratory distress. There are crackles bibasally on auscultation of his chest, but no pedal oedema and normal heart sounds. You are concerned about acute coronary syndrome (ACS) given his symptoms and signs, and risk factors for atypical presentation.

Question 1

Which one of the following is the most appropriate management of Bhavneet?

A. Administer 300 mg aspirin orally if there are no contraindications and ask his son to take him directly to the nearest emergency department.

B. Perform electrocardiography; if ST elevation myocardial infarction (STEMI) is excluded, refer Bhavneet for a chest X-ray and blood tests including a full blood examination (FBE), chemistry and metabolic screening (CHEM-20) and troponin with a plan to review him that afternoon.

C. Administer 300 mg aspirin orally if there are no contraindications, give oxygen via nasal prongs, perform electrocardiography to assess for STEMI, and refer Bhavneet to the nearest emergency department via ambulance.

D. Administer 300 mg aspirin orally if there are no contraindications, perform electrocardiography to assess for STEMI, and refer Bhavneet to the nearest emergency department via ambulance.

Further information

You perform electrocardiography in your clinic, which shows no evidence of ST segment elevation in keeping with an STEMI. Bhavneet's son asks what will happen when they get to hospital, as his father does not speak English well and is nervous about going.

Question 2

Which one of the following describes how Bhaveet will be managed at the hospital?

A. Bhavneet will be taken directly to the catheterisation laboratory for emergency percutaneous coronary angiography +/– stenting.

B. Bhavneet will undergo electrocardiography and a troponin blood test to determine if he has had a myocardial infarction, and will be discharged if these tests are negative.

C. Bhavneet will undergo serial electrocardiography and blood tests and potentially other testing performed to assess for cardiac causes of his symptoms.

D. If it is determined that Bhavneet's symptoms are caused by a heart problem, he will have surgery.

Case 2 – Hanan

Hanan, aged 59 years, presents to you with sudden-onset chest pain and breathlessness. You undertake a thorough history and conduct a physical examination, including electrocardiography. As part of your differential diagnosis, you consider the possibility Hanan is experiencing stress cardiomyopathy.

Question 3

Which of the following statements is true about stress cardiomyopathy?

A. It is rarely triggered by an extreme physical or emotional event.

B. There is typically an absence of obstructive coronary disease on angiography.

C. It is clinically distinguishable from ACS based on troponin levels and electrocardiography.

D. Standard treatment involves anticoagulation.

Question 4

Which of the following is **not** another name for stress cardiomyopathy?

A. Apical ballooning syndrome

B. Dilated cardiomyopathy

C. Takotsubo cardiomyopathy

D. Broken heart syndrome

Case 3 – Myra

Myra, aged 29 years, is a pregnant Aboriginal woman who presents to see you and reports a three-week history of breathlessness, which is worsening. She is having trouble showering and caring for her son, aged two years, as a result of feeling short of breath. You are aware that Myra had acute rheumatic fever as a child and consider rheumatic heart disease (RHD) as part of your differential diagnosis. Her observations demonstrate heart rate 125 beats per minute, blood pressure 105/75 mmHg, respiratory rate 19 breaths per minute and oxygen saturation 98%. Her cardiorespiratory examination demonstrates dual heart sounds with no murmur noted and reduced air entry at the lung bases with scattered crepitations. An electrocardiogram demonstrates atrial fibrillation with no ST changes.

Question 5

What is the most appropriate next step in the management of Myra's presentation?

A. Administer 300 mg aspirin and sublingual glyceryl trinitrate.

B. Request blood tests for C-reactive protein and erythrocyte sedimentation rate.

C. Call an ambulance and send Myra to hospital.

D. Refer Myra for echocardiography and a chest X-ray.

Further information

Myra's is diagnosed with RHD, which has been classified as 'priority 1'.

Question 6

Which one of the following would be the recommended follow up for Myra?

A. Specialist review 1–3-yearly, echocardiography every 1–2 years, dental review every year

B. Specialist review at least six-monthly, echocardiography at least six-monthly, medical and dental review six-monthly, annual influenza vaccination

C. Specialist review 1–3-yearly, echocardiography at least six-monthly, medical and dental review yearly

D. Specialist review if needed, echocardiography 1–2-yearly, medical review six-monthly, dental review if needed, annual influenza vaccination

Case 4 – Marsden

Marsden, aged 45 years, has come to see you reporting tenderness in his right calf, which is 3 cm larger than the left when measured. He is an interstate truck driver and reports sitting for long periods of time every day. Further history and examination indicate that Marsden has deep vein thrombosis (DVT). You consider the management options available.

Question 7

Which one of the following investigations is **not** recommended before commencing anticoagulant medication?

A. Full blood examination/film

B. Liver function tests

C. Coagulation profile

D. Computed tomography pulmonary angiogram (CTPA) or a lung ventilation–perfusion (V/Q) scan

Question 8

Which one of the following anticoagulation management strategies would you recommend?

A. Clexane 1 mg/kg twice daily (eg 80 mg twice daily) initially until haematology review

B. Dabigatran 150 mg twice daily

C. Apixaban 5 mg twice daily

D. Rivaroxaban 15 mg twice daily for three weeks, then 20 mg once daily thereafter

Question 9

How would you assess Marsden's response to anticoagulant treatment?

A. Absence of clinical deterioration

B. Measure rivaroxaban medication levels

C. Progress venous ultrasonography of the left leg within the first month of commencing anticoagulant treatment

D. None of the above

Question 10

Which one of the following recommendations about diet and exercise and compression stockings would you give Marsden?

A. Rest the leg with elevation for at least two weeks.

B. Exercise daily as symptoms permit.

C. Avoid green vegetables and salads as they contain vitamin K.

D. Wear a class II (prescription) stocking for 24 hours daily as it reduces risk of progression or recurrence of thrombosis and formation of leg ulcers.

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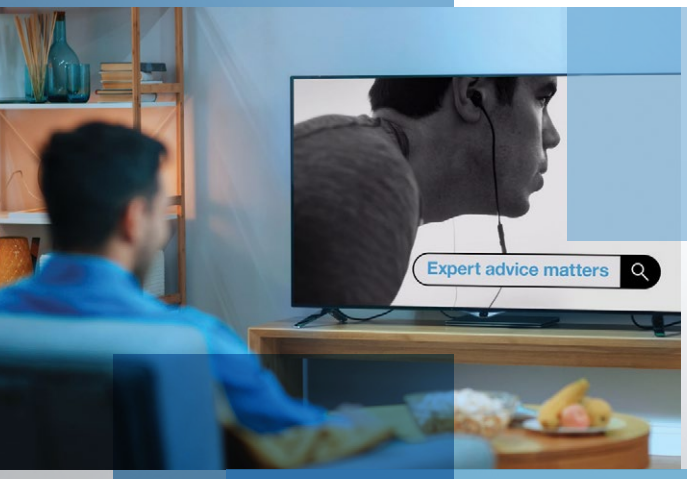

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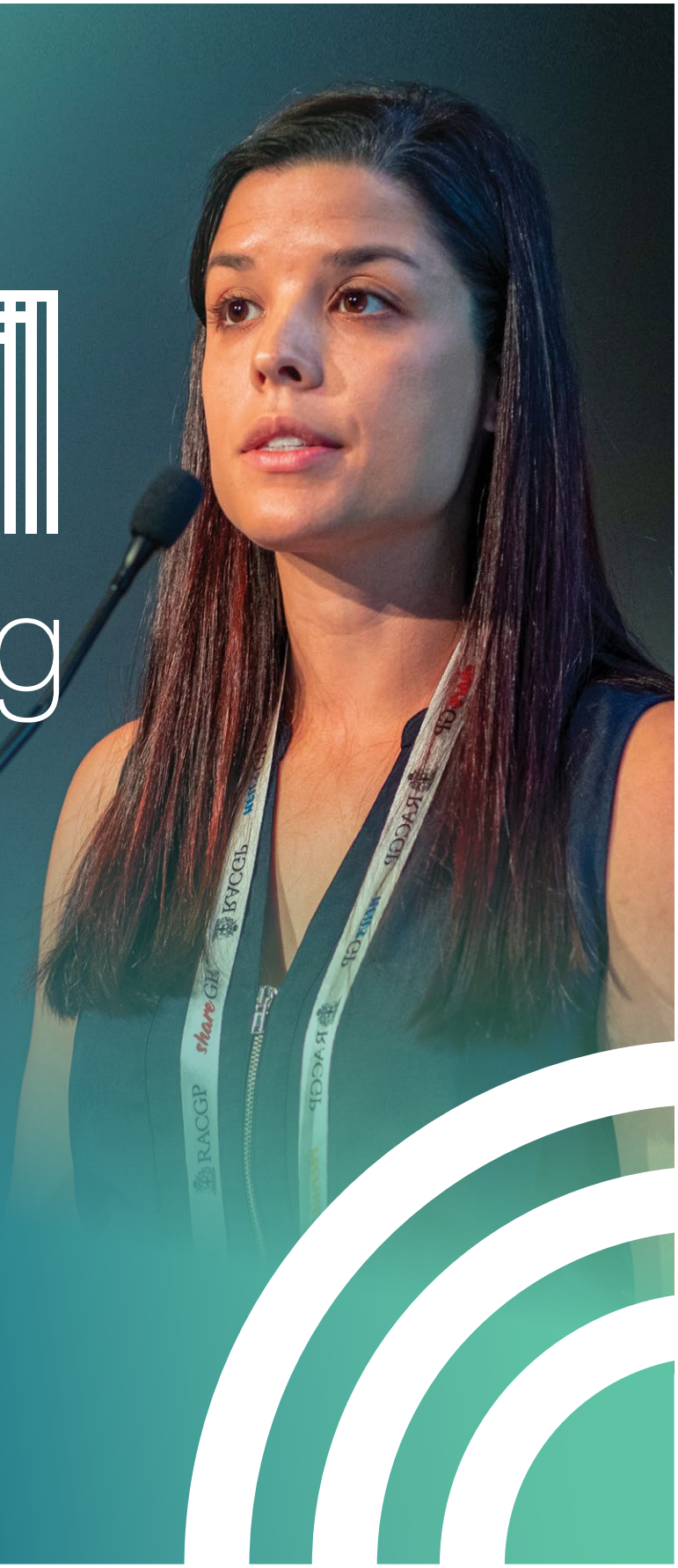

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