

# check

Independent learning program for GPs



Unit 532 October 2016

## Men's health



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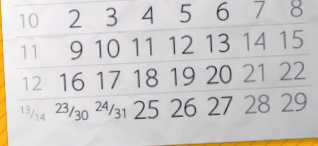
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**Reandron® 1000 (Minimum Product Information) Reandron 1000** (testosterone undecanoate) 1000 mg/4 mL, solution for injection. **Indication:** Testosterone replacement in primary and secondary male hypogonadism. **Dose:** 1 ampoule/vial injected i.m every 10-14 weeks into gluteal muscle. The first injection interval may be reduced to a minimum of 6 weeks to achieve steady-state testosterone levels more rapidly. **Contraindications:** Androgen-dependent prostate/breast carcinoma, hypercalcaemia accompanying malignant tumours, hypersensitivity to testosterone undecanoate or the excipients, past or present liver tumours, use in women. **Precautions:** Regular prostate/breast and haemoglobin/haematocrit monitoring. Patients with diabetes, bleeding or coagulation disorder, predisposed to oedema, hypertension, epilepsy or migraine, severe cardiac/hepatic/renal insufficiency. Potentiation of pre-existing sleep apnoea. Effect on doping tests. Inject strictly i.m and very slowly to avoid pulmonary oily microembolism. **Interactions:** Hypoglycaemic agents, inducers of microsomal enzymes (e.g. barbiturates), oxyphenbutazone, cyclosporin, oral anticoagulants, thyroid laboratory tests. **Adverse Effects:** Polycythaemia, weight increased, acne, PSA increased, prostate examination abnormal, benign prostate hyperplasia, hot flush, various kinds of injection site reactions, suspected anaphylactic reactions. For other events refer to full PI. **Date of most recent amendment:** 29 November 2013. **References:** 1. Reandron Product Information November 2013. 2. Bhasin S et al. Testosterone Therapy in Men with Androgen Deficiency Syndromes: An Endocrine Society Clinical Practice Guideline. J Clin Endocrinol Metab, June 2010, 95(6):2536–2559.

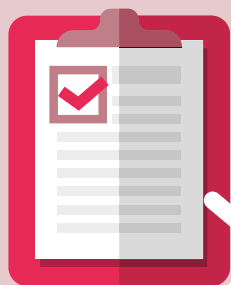
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Unit 532 October 2016

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### 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

### ABOUT THIS ACTIVITY

Australian general practitioners (GPs) are less likely to see male than female patients, as they accounted for only 43.1% of all patient encounters in 2013–14.<sup>1</sup> However, men in Australia are known to be less healthy than women, and have a life expectancy that is five years shorter than their female counterparts.<sup>2</sup> Australian men are also more likely to carry more burden of illness, compared with women.<sup>3</sup>

In 2013, 86.9% of newly diagnosed human immunodeficiency virus (HIV) infections in Australia were in men.<sup>4</sup> It is hoped that the introduction of pre-exposure prophylaxis (PrEP) may decrease this figure.<sup>5</sup> According to Bettering the Evaluation and Care of Health (BEACH) data, three out of every 100 patient encounters in general practice were for pregnancy and family planning issues, and 1.2 for the male genital system.<sup>1</sup>

While screening asymptomatic men for prostate cancer with prostate-specific antigen (PSA) testing is currently not recommended, GPs need to recognise when PSA testing could be considered in those who are at high risk of developing the disease.<sup>6</sup> The rates of sexually transmissible infections (STIs) are rising in Australia, where infectious syphilis has increased from 6.1% in 2008 to 6.7% in 2012 among men.<sup>7</sup>

Aboriginal and Torres Strait Islander men's health is among the worst of any subgroup in Australia, and this can be attributed to complex and multifactorial reasons.

This edition of *check* considers the management and treatment of various conditions specific to men in general practice.

### LEARNING OUTCOMES

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

- outline the assessment of and investigations for male fertility
- summarise the investigations and treatment of patients exposed to human immunodeficiency virus
- describe the diagnosis and management of syphilis
- discuss the health assessment for Aboriginal and Torres Strait Islander men
- list the current recommendations for prostate cancer screening.

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## ACRONYMS

<b>ACCHS</b>	Aboriginal community controlled health service	<b>MSM</b>	men who have sex with men
<b>ART</b>	assisted reproductive technology	<b>MSU</b>	mid-stream urine
<b>ARV</b>	antiretroviral medications	<b>NAAT</b>	nucleic acid amplification test
<b>ASHM</b>	Australasian Society for HIV, Viral Hepatitis and Sexual Health Medicine	<b>NHMRC</b>	National Health and Medical Research Council
<b>AUSDRISK</b>	Australian type 2 diabetes risk assessment tool	<b>PBS</b>	Pharmaceutical Benefits Scheme
<b>BEACH</b>	Bettering the Evaluation and Care of Health	<b>PCR</b>	polymerase chain reaction
<b>BMD</b>	bone mineral density	<b>PEP</b>	post-exposure prophylaxis
<b>BMI</b>	body mass index	<b>PHI</b>	prostate health index
<b>BSL</b>	blood sugar level	<b>PHN</b>	Primary Health Network
<b>CI</b>	confidence interval	<b>PIP</b>	Practice Incentives Program
<b>CLIA</b>	chemiluminescence immunoassay	<b>PrEP</b>	pre-exposure prophylaxis
<b>COPD</b>	chronic obstructive pulmonary disease	<b>PSA</b>	prostate-specific antigen
<b>CROI</b>	Conference on Retrovirus and Opportunistic Infections	<b>RACGP</b>	The Royal Australian College of General Practitioners
<b>DRE</b>	digital rectal examination	<b>RPR</b>	rapid plasma reagin
<b>eGFR</b>	estimated glomerular filtration rate	<b>SMS</b>	short message service
<b>FSH</b>	follicle stimulating hormone	<b>SNAP</b>	smoking, nutrition, alcohol, physical activity
<b>FTC</b>	emtricitabine	<b>STI</b>	sexually transmissible infection
<b>GP</b>	general practitioner	<b>STIGMA</b>	Sexually Transmissible Infections in Gay Men Action Group
<b>HIV</b>	human immunodeficiency virus	<b>T2DM</b>	type 2 diabetes mellitus
<b>IHI</b>	Indigenous Health Incentive	<b>TDF</b>	tenofovir disoproxil fumarate
<b>LGBT</b>	lesbian, gay, bisexual, transgender	<b>TGA</b>	Therapeutic Goods Administration
<b>LH</b>	luteinizing hormone	<b>TPPA</b>	<i>Treponema pallidum</i> passive particle agglutination
<b>MBS</b>	Medicare Benefits Schedule	<b>VDRL</b>	venereal disease research laboratory
<b>MRI</b>	magnetic resonance imaging	<b>WHO</b>	World Health Organization

**CASE 1**

**JEREMY AND CHRISTINA ARE TRYING FOR A CHILD**

Christina, 29 years of age, comes to see you because she and her partner Jeremy, also 29 years of age, have been trying to conceive for eight months. Christina has had regular menstrual cycles since stopping the combined oral contraceptive pill nine months ago. She has been actively monitoring her cycles and believes Jeremy and she are having appropriately timed intercourse. You establish that intercourse has been occurring every second day over the fertile week.

**QUESTION 1** 

How long after a couple had tried unsuccessfully to conceive would you order investigations? What initial assessments would you perform?

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**FURTHER INFORMATION**

Christina agrees to make an appointment for both of them the following week.

Jeremy is a plumber. He does not smoke or drink, and attends the gym regularly. He appears to be in excellent health. There is nothing in his past medical history except a 'groin operation' when very young, but he cannot provide any details.

Jeremy is fit and well, and has a normal body mass index (BMI). A general examination is unremarkable.

**QUESTION 2** 

What further questions would you ask Jeremy?

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**FURTHER INFORMATION**

Your questions do not identify any risk factors for infertility, as Jeremy answers 'no' to all except the question about his operation. He is unsure of the nature of the operation he had when he was a young child.

**QUESTION 3** 

What are your thoughts so far? What examination needs to be performed now?

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**FURTHER INFORMATION**

Jeremy's examination reveals:

- normal body/facial hair distribution and no gynaecomastia
- bilateral inguinal scars are noted
- testes: using an orchidometer, his testes are 10 mL in volume and of normal texture. Testicular volumes of between 15 and 35 mL would be considered normal in adulthood<sup>1</sup>

- epididymides: normal
- vas deferens: normal
- varicoceles: none present
- no penile abnormalities.

Jeremy's testes are reduced in size. He has no symptoms of androgen deficiency but you are aware that he is at increased risk and that Jeremy may not recognise its features because of their chronicity.

Jeremy returns to see you a week later for his semen analysis results (Table 1).

	Jeremy's result	Normal <sup>2</sup>
Volume of semen	3.2 mL	≥1.5 mL
Sperm concentration	1 million/mL	≥15 million per mL
Sperm motility	12%	≥40% motile within 60 minutes of ejaculation
Sperm morphology (shape)	2% normal	≥4% (ie percentage normal)
pH	7.9	≥7.2
White blood cells	Nil	<1 million cells per mL
Sperm antibodies	Immunoglobulin G (IgG) – not detected Immunoglobulin A (IgA) – not detected	<50% motile sperm showing antibody activity

Jeremy tells you that he asked his mother about the surgery he had when he was younger, and she said that it was for undescended testes (cryptorchidism).

You explain his sperm concentration is low and that his sperm showed reduced motility and percentage of perfectly shaped sperm. These changes are often associated with a marked decrease in fertility.

You explain to Jeremy that the semen analysis must be repeated in a few weeks at a specialised laboratory (often affiliated with a fertility program).

**QUESTION 4** 

What are the long-term health implications of undescended testes? Why should undescended testes be corrected?

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**FURTHER INFORMATION**

Jeremy's reproductive hormone levels are:

- luteinizing hormone (LH): 12 IU/L (reference range: 1–8 IU/L)
- follicle stimulating hormone (FSH): 13 IU/L (reference range: 1–8 IU/L)
- serum total testosterone levels: 10.5 nmol/L (reference range: 9–29 nmol/L).

**QUESTION 5** 

How do you interpret these hormone results?

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**QUESTION 6** 

What is your management plan?

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**FURTHER INFORMATION**

Jeremy's ultrasound scan came back normal.

**QUESTION 7** 

Is there anything else you can offer Jeremy and Christina? What options are available through an assisted reproductive technology (ART) clinic?

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## CASE 1 ANSWERS

### ANSWER 1

Most healthy couples conceive within 12 months; however, basic investigations of both partners should be performed immediately when risk factors are identified.<sup>3</sup>

For women, history should include menstrual history, previous fertility and use of contraception. Initial assessment would be to perform a Pap test and arrange to check her day 21 progesterone level, check rubella and chickenpox immunity, and ensure she is taking a folate supplement.

You should explain to Christina that Jeremy will also need to be assessed for risk factors. Male infertility is the second biggest factor after maternal age in affecting the chances of conception.<sup>4</sup>

For men, risk factors for infertility include:<sup>3</sup>

- a past history of chemotherapy
- undescended testes
- previous testicular trauma or infection.

Semen analysis should be considered at presentation to avoid frustration of a late diagnosis of severe male infertility.

### ANSWER 2

Specific questions to consider for Jeremy are:

- Has he previously fathered any children?
- Has he ever been diagnosed with swollen testes?
- Has he ever had severe trauma to his testes?
- Has he used anabolic steroids or opioids?
- Has he had any sexually transmissible infections (STIs) or urinary tract infections?
- What was the nature of his groin operation?
- Has he ever used anabolic steroids?
- Does he have any problems with erections or ejaculation?
- Does he have low libido or energy?
- Does he have mood problems?

### ANSWER 3

In the setting of infertility, an examination of Jeremy's genitals and secondary sexual characteristics is mandatory (see 'Resources for doctors and patients'). A reduction in the size of the testes suggests a spermatogenic problem. Identification of inguinal scars would be consistent with the history of a previous groin operation and suggest a past history of undescended testes.

You should also arrange for Jeremy to have semen tests, preferably at a laboratory that provides onsite collection and uses World Health Organization (WHO) guidelines (Table 1).<sup>2</sup> Jeremy should abstain from ejaculation two to five days prior to collection (see 'Resources for doctors and patients').

### ANSWER 4

Jeremy's undescended testes were noted at six months of age and surgically corrected.

Undescended testes are linked to:<sup>3,5</sup>

- testicular cancer
- androgen deficiency
- infertility (see 'Resources for doctors and patients').

Undescended testes are common in premature babies and are seen in about 5% of full-term infants, but often descend spontaneously. If persisting at six months, surgery is recommended. Correction reduces the risk of later cancer but may not enhance fertility prospects.<sup>6,7</sup>

Undescended testes must be distinguished from retractile testes and absent testes.

### ANSWER 5

Jeremy's elevated serum FSH levels points to severely impaired spermatogenesis. There are many congenital and acquired causes but it is commonly seen in men with a past history of cryptorchidism even after corrective surgery.<sup>8,9</sup>

The borderline testosterone and mildly elevated LH levels indicate reduced testosterone secretory ability. Jeremy's results suggest borderline but as yet asymptomatic androgen deficiency, but this may become clinically apparent in the future.

### ANSWER 6

You explain to Jeremy and Christina that Jeremy has had a problem with testicular development leading to undescended testes and now infertility. While his fertility is greatly reduced, couples such as Jeremy and Christina still have about a 30% chance of conceiving naturally over the next two to three years.

You should refer them to a fertility specialist associated with an ART clinic who can explain the different treatment options.

You should arrange for Jeremy to have a testicular ultrasound and explain that while his risk of testicular cancer is low, it is much higher than the general population.<sup>10</sup> Testicular ultrasound is able to detect testicular lesions as small as 1–2 mm in diameter.

You should also educate Jeremy about regular testicular self-examinations and ask him to present early if any lumps appear.

### ANSWER 7

It is important for general practitioners (GPs) to be available for counselling and follow-up of patients going through fertility treatment, and in this case, review Jeremy's androgen status in the long term (see 'Resources for doctors and patients').

Treatment to restore sperm output is not available, but if any motile sperm are found, couples can frequently achieve pregnancy using intracytoplasmic sperm injection.<sup>11</sup>

Finally, even in patients with overt symptomatic testosterone deficiency, testosterone therapy should **not** be considered until fertility aspirations have been exhausted. Exogenous testosterone is contraindicated in men

seeking fertility due to its potent contraceptive effect through the suppression of gonadotrophin secretion.

### RESOURCES FOR DOCTORS AND PATIENTS

- Andrology Australia, Fact sheet – Male infertility, [www.andrologyaustralia.org/wp-content/uploads/Factsheet\\_MaleInfertility.pdf](http://www.andrologyaustralia.org/wp-content/uploads/Factsheet_MaleInfertility.pdf)
- Andrology Australia, Fact sheet – Undescended testes, [www.andrologyaustralia.org/wp-content/uploads/Factsheet\\_UndescendedTestes.pdf](http://www.andrologyaustralia.org/wp-content/uploads/Factsheet_UndescendedTestes.pdf)
- Andrology Australia, Clinical summary guide – No 3: Adulthood. Examination of male genitals and secondary sexual characteristics, [www.andrologyaustralia.org/wp-content/uploads/clinical-summary-guide-03.pdf](http://www.andrologyaustralia.org/wp-content/uploads/clinical-summary-guide-03.pdf)
- Andrology Australia, Clinical summary guide – No 5: Male infertility, [www.andrologyaustralia.org/wp-content/uploads/clinical-summary-guide-05.pdf](http://www.andrologyaustralia.org/wp-content/uploads/clinical-summary-guide-05.pdf)

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CASE 2

ETHAN REQUESTS AN HIV TEST

Ethan, 27 years of age, sees you today to request a rapid human immunodeficiency virus (HIV) test. He seems extremely anxious. He has been sexually active for the past eight years. Ethan is currently single and often frequents male sex-on-premises venues and beats around the city for sex with other men. You have seen him once before for a simple cold but are not fully familiar with his sexual history.

QUESTION 1 

How should you proceed with this consultation?

Horizontal lines for writing the answer to Question 1.

FURTHER INFORMATION

Ethan reveals that he may have been 'stealthed' during an encounter at a gay sauna the previous night. He went on to explain that he was the 'bottom' and discovered towards the end of the sexual encounter that the 'top' may have secretly taken the condom off. There was ejaculation internally and no condom in sight. Ethan insists on getting a rapid HIV test to ensure that he is not infected. He was last tested about two months ago and 'everything was okay'.

QUESTION 2 

What would you do next?

Horizontal lines for writing the answer to Question 2.

FURTHER INFORMATION

Ethan followed your advice and took a course of post-exposure prophylaxis (PEP) with your recommendations, and the subsequent HIV tests came back non-reactive.

Six months later, Ethan presented to you again requesting to go on pre-exposure prophylaxis (PrEP). Recently, he entered into a relationship with John, who is HIV-positive. John is on antiretrovirals (ARVs) and his last viral load four months ago was 'undetectable'. He would like to be able to have sexual intimacy without condoms.

QUESTION 3 

How would you counsel Ethan? What does an undetectable viral load mean for Ethan?

Horizontal lines for writing the answer to Question 3.

**QUESTION 4** 

What is PrEP?

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**FURTHER INFORMATION**

You agree to prescribe PrEP for Ethan.

**QUESTION 5** 

What baseline tests would you do and how would you monitor the safety and efficacy of emtricitabine (FTC)/tenofovir disoproxil fumarate (TDF)?

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**FURTHER INFORMATION**

Ethan is aware of the cost of FTC/TDF and would like to know if there are other ways of acquiring it.

**QUESTION 6** 

What advice can you give Ethan?

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**CASE 2 ANSWERS**

**ANSWER 1**

It is important to obtain a clear sexual history from Ethan to make a proper risk assessment. This requires the general practitioner (GP) to appear genuinely interested, non-judgemental and open-minded. Awkward hesitations, avoidance, accusations or presumptions may be construed as criticism or even homophobia. Using patient-centred language or words that are familiar to the patient will help to diffuse any tension and perhaps create a more trusting doctor–patient relationship. For example, you could ask, ‘Were you the top or bottom?’ and ‘Did he cum inside you?’

You will need to explore Ethan’s reason for wanting an HIV test. Specific information relating to a potential exposure to HIV will include:<sup>1</sup>

- When did the incident(s) happen?
- Were condoms used/removed/broken?
- Was Ethan the insertive or receptive partner? Refer to Table 1.
- Did the sex involve ejaculation?
- Was there more than one sexual partner?
- Were drugs or alcohol involved?
- Is Ethan circumcised? Circumcised males are two to eight times less likely to become infected with HIV.

**Table 1. Risk of HIV transmission via anal intercourse, per sexual act<sup>2</sup>**

	Per-act probability
Insertive partner’s risk (circumcised)	0.11% (1 in 909)
Insertive partner’s risk (uncircumcised)	0.62% (1 in 161)
Receptive partner’s risk (without ejaculation)	0.65% (1 in 154)
Receptive partner’s risk (with ejaculation)	1.43% (1 in 70)

It may also be relevant to enquire whether the sex was consensual. If the source partner was known to be HIV-positive, it may be worth knowing if he is on HIV ARVs and whether he has an undetectable viral load.

You should take the opportunity to ask about usual risk-taking behaviours, including regularity of condom use, recreational drug use, number of sexual partners over the past six months and the frequency of testing for sexually transmissible infections (STIs). Sexually Transmissible Infections in Gay Men Action Group (STIGMA) guidelines provide recommendations for the frequency of testing in men who have sex with men (MSM).<sup>3,4</sup>

**ANSWER 2**

You will need to explain to Ethan the concept of the ‘window period’ for diagnosing HIV after a known exposure. This refers to the time it takes for an HIV infection to appear reactive on a test. This window period relies not only on the time it takes for the person to produce antibodies against HIV but also on the sensitivity of the available immunoassays. Current fourth-generation serological laboratory tests are able to reduce the window period to around six weeks after exposure.<sup>5</sup> Australia’s Therapeutic

Goods Administration (TGA) first approved the use of rapid HIV testing in 2012.<sup>6</sup> Although this test is convenient and produces results within about 20 minutes, most approved rapid tests have poorer sensitivity and specificity when compared with the fourth-generation HIV serological tests.

Keen et al found that compared with fourth-generation immunoassays, the Uni-Gold rapid test has a sensitivity of 56.8% (95% confidence interval [CI] = 39.5–72.9) in acute infections and 98.2% (95% CI = 90.6–100) in established infections. The specificity of the Uni-Gold is around 99.9% (95% CI = 99.9–100).<sup>7</sup> The window period with most rapid tests extends beyond 8–12 weeks and any reactive tests must be confirmed by serological immunoassays. Hence in this scenario, the use of a rapid test (or any other HIV tests) to rule out an infection would be highly inappropriate.

You should offer Ethan post-exposure prophylaxis, commonly known as PEP. For PEP to be most effective, it should be given within 72 hours of exposure and the course should last 28 days.<sup>8</sup> PEP medications are in fact ARVs commonly used to treat HIV. Most doctors will prescribe dual therapy but high-risk cases may receive triple therapy. Refer to local PEP providers for their protocols or recommendations. All Australian states provide these medications free of charge. Refer to [www.getpep.info](http://www.getpep.info) for clinics and hospitals in each state and territory that dispense PEP medications. GPs may otherwise prescribe PEP medications, but they are not subsidised by PBS.

Large-scale prospective, placebo-controlled trials have never been conducted for PEP; hence, a definitive answer regarding its effectiveness cannot be established. One of the most conclusive studies was conducted in Brazil and reported at the Conference on Retrovirus and Opportunistic Infections (CROI) in 2002. This study concluded that PEP reduced the seroconversion rate by 83%, from 4.1 cases per 100 patients a year to 0.7 cases when men took AZT/3TC PEP.<sup>9</sup>

Before prescribing PEP, it is mandatory to ensure that Ethan is HIV-negative at baseline. PEP should not be delayed while waiting for an HIV result – the test should be done and PEP started immediately. If positive, PEP should be stopped and the result discussed with an experienced HIV clinician.

Ethan should have blood tests for HIV, syphilis, hepatitis C and baseline hepatitis B (surface antigen and antibody, core antibody), if not previously done. The reason for hepatitis B serology is that the medication used for PEP, emtricitabine/tenofovir disoproxil combination (Truvada) or its generic components, has antiviral activity against the hepatitis B virus and abruptly stopping PEP after 28 days may lead to an acute hepatitis flare. Testing for other STIs, including gonorrhoea and chlamydia, should also be considered. You should suggest repeat HIV testing at one to two weeks after PEP completion and again at three months after starting PEP.

Most Australian states have their own guidelines and protocols for prescribing PEP. The Australasian Society for HIV, Viral Hepatitis and Sexual Health Medicine (ASHM) has produced a national guideline for the use of PEP in occupational and non-occupational exposures.<sup>10</sup>

### ANSWER 3

It is not unusual for HIV-serodiscordant men to have sexually fulfilling long-term relationships. The risk of HIV transmission from the person who is HIV-positive is highest in a person with very high viral loads; an undetectable viral load greatly reduces this risk. In 2008, the Swiss

National AIDS Commission released a statement (now popularly known as The Swiss Statement) that if a person is fully adherent to ARVs, has an undetectable viral load and does not have an STI, the risk of transmission is in the region of 1 in 100,000.<sup>11</sup> This was based on epidemiological and biological analyses rather than any robust clinical trial.

The Partner study enrolled 1166 serodiscordant couples between September 2010 and May 2014 from 14 European countries where the partner who is HIV positive had an undetectable viral load on ARV and the couples were not always using condoms. With 1238 couple years of follow-up, the study group found no linked HIV transmissions to the positive partner.<sup>12</sup>

The current lower limit of viral load detected in most Australian laboratories is 20 copies/mL. Hence it is important to explain to patients that 'undetectable' does not mean 'no virus'.

It is not unreasonable for Ethan to commence PrEP to prevent acquiring HIV, but you should continue advocating the use of condoms outside the relationship to reduce the risk of other STIs (eg syphilis, gonorrhoea or chlamydia).

### ANSWER 4

PrEP is the use of antiretroviral medications to prevent acquiring HIV. In Australia, the combined single tablet consisting of FTC, a nucleoside reverse transcriptase inhibitor, and TDF, a nucleotide reverse transcriptase inhibitor, has been approved by the TGA for use as PrEP. However, this is yet to be subsidised on the Pharmaceutical Benefits Scheme (PBS). A private script for Truvada (FTC/TDF) would cost around AU\$900 a month. Refer to Question 6 for other, more affordable ways to obtain FTC/TDF PrEP.

FTC/TDF is generally well tolerated. In the PROUD study, PrEP was interrupted by 30 out of 544 participants because of a medical event; however, this was only considered a side effect of the drug in 13 participants, including two cases of renal disease as measured by raised creatinine, five cases of nausea and/or diarrhoea, two of joint pain and two of headache, some of whom also complained of fatigue and abdominal pain.<sup>13</sup>

The main concerns of PrEP are centred around loss of bone mineral density (BMD) and tubular renal disease.<sup>14,15</sup> BMD loss of 1–5% may be expected, but studies have not shown higher fracture rates in the TDF containing arms.<sup>6</sup> A small percentage of men may experience a drop in their estimated glomerular filtration rate (eGFR), as well as haematuria and/or proteinuria due to renal tubular toxicity. In a recently published US PrEP Demo Project, grade 1 and 2 renal events occurred in about 2.3% of participants.<sup>15</sup> Fanconi syndrome has also been described in men who are HIV-positive taking FTC/TDF.<sup>16</sup>

The efficacy of PrEP in MSM was first demonstrated in the iPrEx trial reported in 2010.<sup>17</sup> In this double-blinded, placebo-controlled trial, HIV infections in the study group decreased by 44% compared with the placebo group. It was discovered that more than 50% of the subjects did not take the pills as prescribed and did not have blood levels of TDF high enough to confer protection against HIV. Correcting for dosing adherence, the efficacy increased to 92%. More recent studies in the UK (PROUD)<sup>13</sup> and France (iPERGAY)<sup>18</sup> found the efficacy to be 86%. In the PROUD study, three participants in the immediate (versus delayed-

starting PrEP) arm acquired HIV. One had an early, undiagnosed HIV infection at baseline. The other two participants appeared to have stopped their PrEP at least one month and 12 months, respectively, prior to diagnoses.

### ANSWER 5

Baseline tests should include HIV serology and screening for other STIs, including syphilis and hepatitis C serology, and throat and anal swabs and first-pass urine for chlamydia and gonorrhoea nucleic acid amplification tests (NAATs). Other recommended baseline tests include baseline renal function tests including eGFR, and midstream specimen of urine to rule out haematuria and proteinuria (ie a midstream urine [MSU] for microscopy, culture and sensitivity, protein-to-creatinine ratio).<sup>19</sup>

Baseline hepatitis B serology should include Hep BsAg, Hep BsAb and Hep BcAb to enable proper interpretation of hepatitis status and vaccinate as needed. A baseline bone densitometry scan is not necessary without other added risk factors. Unless qualifying specific criteria, this test is not rebatable through Medicare. Three-monthly HIV, STI and renal monitoring (eGFR +/- serum phosphate to rule out hypophosphataemia, and MSU for protein-to-creatinine ratio) are recommended if patients are to continue taking FTC/TDF.

Starting dual therapy of FTC/TDF without ensuring that Ethan is HIV-negative will be problematic because taking a suboptimal ARV regimen (usually three ARVs are needed to suppress HIV) in the presence of HIV may cause the development of resistance mutations. Giving Ethan FTC/TDF in the presence of active hepatitis B is also problematic because FTC/TDF may clear the hepatitis B virus from the hepatocytes and upon withdrawal of the ARV cause a hepatic flare.<sup>20</sup>

You should consider arranging a follow-up appointment for Ethan in order to 'close' any window period, if necessary, before starting FTC/TDF. However, in men who are at very high risk of acquiring HIV, the urgency for PrEP may outweigh the necessity to close the window period. In this scenario, some HIV prescribers may consider prescribing a third ARV until the window is closed. This is an evidence-free area.

Adherence is paramount. The current recommendation is to take FTC/TDF once daily for at least seven days before being able to rely on PrEP to give adequate protection against HIV. Condoms should be used during this period if engaging in anal or vaginal intercourse. Anderson et al were able to show that patients with blood levels compatible with daily dosing had a 99% reduction in HIV acquisition.<sup>21</sup>

There is some concern that the use of PrEP encourages high-risk behaviours. Risk compensation due to PrEP use (eg an increase in condomless anal sex) is controversial. Previous studies have shown no increase in risk compensation<sup>13,17</sup> (possibly due to an already high-risk group of participants, hence little/no relative increase in measured risk-taking behaviour), although the recent VICPrEP demonstration study did show a decrease in condom use and an association with a higher rate of other STIs (eg syphilis and chlamydia in this study).<sup>22</sup>

### ANSWER 6

The TGA approved the use of FTC/TDF as PrEP in Australia in May 2016. However, the Pharmaceutical Benefits Advisory Committee has yet to

approve its subsidy on the PBS. The cost of FTC/TDF on a private script approaches AU\$900 per month in Australia. However, with a prescription, patients may import generic drugs from trusted websites for personal use and the cost ranges from AU\$165 per three months ([www.prepaccessnow.com](http://www.prepaccessnow.com)) to US\$260 per three months plus shipment ([www.aids-drugs-online.com](http://www.aids-drugs-online.com)).

Ethan may also choose to enrol in state-funded PrEP demonstration studies currently running with limited spaces and time frames across some states (eg Prelude [closed] and EPIC in New South Wales; VicPrEP [closed] and PREPX in Victoria; and QPrEP in Queensland).

### CONCLUSION

Scientists are continuing to look for novel ways to deliver PrEP including vaginal rings<sup>23</sup> and long-acting injectables.<sup>24</sup> Long-acting cabotegravir and rilpivirine reported in CROI this year showed good acceptability among users.<sup>24</sup>

The popularity of PrEP use continues to increase globally, with around 80,000 PrEP users in the US alone at the end of 2015, a 738% increase from 2012 to 2015.<sup>25</sup> Further, the PrEP Health program launched by the San Francisco Foundation in 2014 recorded no HIV infections in almost 1200 patients compared with 82 new infections in the medical clinic.<sup>26</sup>

In Australia, the most common HIV prevention strategy has been the consistent use of condoms; however, only about a third report consistent condom use.<sup>27</sup> The PREPX study in Victoria hopes to discover if 'the provision of generic Tenofovir + Emtricitabine for HIV pre-exposure prophylaxis to 2600 people whose sexual and/or injecting behaviour is associated with a high chance of HIV acquisition, will lead to greater than a 20% decline in new HIV infections across Victoria and a 30% decline in new HIV infections in MSM over the following 12–36 months'.<sup>27</sup>

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**CASE 3**

**ALLAN HAS JUST TURNED 40**

Allan presents to your practice for the first time. He says, 'I've just turned 40, and thought – well, my wife thought – I should get a health check. I've been to three funerals of cousins who were in their 50s recently, which has got me worried about my health, so this is a birthday present to myself'.

Looking at his records, the receptionist has noted that Allan is of Aboriginal descent, but not of Torres Strait Islander descent. He has seen the nurse, who has recorded the following information:

- Smoking status: Smokes 20 cigarettes a day
- Alcohol status: Drinks four light beers a week, never binge drinks
- Height: 168 cm
- Weight: 78 kg
- Body mass index (BMI): 27.6 kg/m<sup>2</sup>
- Waist measurement: 97 cm
- Blood pressure: 138/72 mmHg
- Pulse: 84 beats per minute
- Finger prick glucose: 4.4 mmol/L
- Urine dipstick: Normal, including glucose negative and protein negative

**QUESTION 1** 

What elements need to be included in a health assessment for Allan?

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**FURTHER INFORMATION**

While talking with Allan, and going through the health assessment, you discover that he has not previously been diagnosed with any

medical conditions and is not on any medications. He has not had any immunisations since reaching adulthood. Allan's father had a coronary artery stent inserted for ischaemic heart disease in his 50s. He eats a balanced diet, plays indoor soccer each week and does not gamble. The funerals he attended recently have upset him and made him more conscious of his own health.

Examination is unremarkable apart from the observations made by the nurse. This includes no evidence of hearing loss and visual acuity of 6/6 in both eyes.

**QUESTION 2** 

Given what you now know about Allan's history and examination, what preventive activities do you want to discuss with Allan?

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**FURTHER INFORMATION**

Allan has tried several times without success to stop smoking and you discuss strategies with him. You give him his recommended immunisations and arrange blood testing for renal function, fasting glucose and fasting lipids. You arrange to see him again to discuss these, making a note to yourself to ask him again about his mood.

Allan returns to see you a week later. His blood test results show:

- total cholesterol: 5.4 mmol/L (normal range 3.9–5.2 mmol/L)
- high-density lipoprotein: 1.2 mmol/L (normal range 1.0–2.0 mmol/L)
- estimated glomerular filtration rate (eGFR): >90 mL/min (normal 90–120 mL/min)
- glucose: 4.8 mmol/L (normal 4.0–5.9 mmol/L)

You calculate his absolute cardiovascular disease risk as <5% over the next five years,<sup>1</sup> and discuss this with him, being aware that it does not take into account his family history or that he is Aboriginal. However, on this risk, statins would not be recommended.<sup>2</sup>

You ask him about his mood, and he says, 'I'm doing OK and eating rather too well'. He has no suicidal ideation and has supportive friends. However, Allan has not managed to stop smoking and feels he cannot go very long without feeling the need for a cigarette. 'Is there any medication that can help me?' he asks. He'd also like some help to look at his weight, especially with his diet. After discussion of different options, you advise using varenicline and refer Allan to a smoking

cessation program. You also refer him to a dietitian. He tells you he is worried about the cost of the medication, and thinks he would not be able to afford to see a dietitian, as he works on a casual contract with a security firm.

**QUESTION 3** 

What help is available to Allan with the cost of medications and referrals to allied health professionals?

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**FURTHER INFORMATION**

Allan comes back to see you three weeks later. He has successfully stayed off his cigarettes since his last visit, and is due to have his prescription for continuation of varenicline. He has seen the dietitian twice and is finding this helpful, having made some small changes to his diet at home. Despite this, he tells you he still thinks about his cousins' funerals and worries about death. You discuss this further with him and find out that he still does not have any suicidal ideation, and is eating and sleeping well. Allan still enjoys playing sport, and says he does not think he is depressed, based on people he knows who have depression. You ask 'Is there anything else you think I ought to know?' After an awkward silence, Allan looks at you and says, 'I feel a bit silly telling you this but ... those cousins who died ... they all died in different hospitals. I know they wouldn't have wanted to die there. They'd want to be back on country. There were no Elders. I don't think the proper things were done. You know – culture.'

**QUESTION 4** 

What would be your next steps?

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**CASE 3 ANSWERS**

**ANSWER 1**

The Medicare Benefits Schedule (MBS) requirements for billing an Aboriginal and Torres Strait Islander health assessment (Item 715) for an adult can be found at the MBS website.<sup>3</sup> Informed consent should be obtained before undertaking any screening activities.<sup>2</sup> Reassuring the patient of confidentiality is also advisable.

The main features of a health check are:

- medical history, including assessment of medication use, mood and sexual history
- assessment of risk factors, including physical activity, and family and social history
- appropriate examination and investigations
- an agreed plan for interventions and follow-up.

The Royal Australian College of General Practitioners' (RACGP's) *National guide to a preventive health assessment for Aboriginal and Torres Strait Islander people*<sup>4</sup> sets out the recommendations for preventive activities for Allan. The lifestyle chart<sup>5</sup> outlines the recommendations for a particular age group at a glance.

There are some differences in preventive guidelines for Allan, as an Aboriginal man, compared with those in the RACGP's *Guidelines for preventive activities in general practice* (Red Book).<sup>6</sup> Examples include immunisation and screening for renal disease, and assessment of absolute cardiovascular disease risk. Depending on local epidemiology, it may be important to look for trachoma and rheumatic heart disease.

**ANSWER 2**

There are multiple issues that could be discussed in your consultation with Allan.<sup>4</sup> The issues discussed now and those discussed during later consultations will be determined by a number of factors, including the time available and the urgency of each problem. You could explain to Allan that, because of time constraints, you will focus on the most urgent problems at this consultation, and encourage him to book a subsequent appointment to discuss other issues. If he seems reluctant, it might be an opportunity to explore the reasons for this. He may, for example, feel culturally unsafe or have had an unsettling incident previously. Depending on your setting, it may also be helpful for an Aboriginal health practitioner or a practice nurse to be involved in the discussions.

Issues to consider include:

- smoking cessation<sup>7</sup> – a brief intervention with more extensive motivational interviewing if Allan is keen to stop
- strategies to lose weight<sup>7</sup> – this is likely to include reducing portion sizes and more frequent physical activity
- immunisations<sup>8</sup> – tetanus booster, influenza vaccine, pneumococcal (as he is an Aboriginal man who smokes)
- calculate absolute cardiovascular disease risk<sup>1</sup> – you need to have Allan's lipid profile

- screen for chronic kidney disease with a urine albumin-to-creatinine ratio and a blood sample giving estimated glomerular filtration rate (eGFR).<sup>4</sup>

A fasting blood sugar could also be considered, as it is more reliable than the finger prick glucose test already done.<sup>4</sup> If the Australian type 2 diabetes risk assessment tool (AUSDRIK) score<sup>9</sup> is used, note that the waist circumference cut-off is different in Aboriginal and Torres Strait Islander peoples. This is because of the higher background risk of developing type 2 diabetes in particular ethnic groups, including Aboriginal and Torres Strait Islander peoples.<sup>10,11</sup>

As Allan does not have any symptoms suggestive of chronic obstructive pulmonary disease (COPD), there is no benefit of screening him with spirometry.<sup>4</sup>

Allan's recent experience of attending many funerals should alert the general practitioner (GP) to ask about symptoms of depression. At this stage, we do not know whether Allan has experiences common to many Aboriginal and Torres Strait Islander peoples, including of overt and covert racism, or experiences resulting from being affected by the Stolen Generations, but knowing that he is Aboriginal should alert the GP to this possibility.

It is important not to overwhelm Allan with information at this stage, and the areas to focus on should be discussed with Allan. Success is much more likely with these lifestyle interventions in the context of a supportive and trusting relationship. It will be important to prioritise what needs to be covered today, and what can be managed in future consultations. This will be determined by clinical priorities and what Allan himself is most motivated to work on.

### ANSWER 3

Allan is an Aboriginal man who is at risk of a chronic disease (because he is a smoker and overweight) and is therefore eligible for the Closing the Gap Pharmaceutical Benefits Scheme (PBS) co-payment program.<sup>12</sup> This will reduce the cost of a medication on the PBS from \$38.30 to the concessional cost of \$6.20 (for patients on a concession card, the cost is reduced to zero). The practice will need to be registered for the Practice Incentives Program – Indigenous Health Incentive (PIP – IHI) to sign the patient up for the Closing the Gap PBS co-payment.

Please note that the practice needs to be registered for the PIP – IHI to register patients for the PBS co-payment program. However, Allan is **not** eligible to be signed up for the PIP – IHI as he does not have a chronic disease, but is eligible for the Closing the Gap PBS co-payment, as he is at risk of a chronic disease. The registration form is the same for both.

As Allan has had an Aboriginal Health Assessment (MBS item 715), he is eligible for five allied health appointments through Medicare. He can be referred to a dietitian using this program. As Allan does not have a chronic disease, he is not eligible for a GP management plan (MBS item 721), or a team care arrangement (MBS item 723) and subsequent referral for allied health.

### ANSWER 4

The reason behind Allan's anxiety is cultural, not medical. It is unlikely that a non-Indigenous practitioner can offer good advice about resolving those

concerns. Having ensured that the risk of suicide is very low and excluded depression, Allan will most likely need to discuss these concerns with someone he trusts from the local Aboriginal community.

Aboriginal (not to mention Torres Strait Islander) communities are different across Australia, and so the most appropriate organisation to contact will vary from place to place. Most commonly, the following services will be able to help Allan or guide the GP as to where help can be found.

- Your local Aboriginal community controlled health service (ACCHS) – these are run by the local Aboriginal community, and employ staff from the community, with excellent links to local Elders and appropriate cultural knowledge. Aboriginal health practitioners are an excellent resource to draw on for help with Allan.
- Your local state-run Aboriginal medical service – in some states, Aboriginal medical services, while not run by the community, have good links into the community.
- Your Primary Health Network (PHN) – PHNs have a Closing the Gap team, which should have good links with the local Aboriginal community.
- Hospital Aboriginal liaison officers – while they focus mainly on hospital in-patients, they are often good guides on who is able to help in the community.
- Cultural educators and cultural mentors – they work for regional training organisations in general practice training, and are a good port of call, especially for training practices.
- Local Aboriginal land council – these organisations represent local Aboriginal communities, especially regarding land rights and protection of sacred sites.
- Local council – most local councils have an Aboriginal officer who will be able to guide GPs around who's who in the local community.
- Cultural centres – some areas have a specific cultural centre or meeting place where people in the local Aboriginal community gather.

It is important that these options are discussed with Allan. He may have already tried contacting them, or the relevant people may be relatives or other people he does not want to discuss this with.

### CONCLUSION

You speak to an Aboriginal health practitioner at an ACCHS, who agrees to see Allan to discuss what happened. You do not see Allan for a few months. However, after three weeks, you see a man called Mitchell. He says, 'I've not seen a doctor for years, but my brother Allan told me I should come. He said you were OK'.

Identifying patients as Aboriginal and/or Torres Strait Islander affects decisions made in GPs' consultations. It allows GPs to tailor their care more effectively, and to use appropriate PBS and MBS programs to allow access to beneficial programs.

The evidence for general health assessments is equivocal at best,<sup>13,14</sup> and there is not yet any evidence for their effectiveness at lowering mortality in Aboriginal and Torres Strait Islander communities. However, their use in the Australian healthcare system has been encouraged as a way of identifying prevalent conditions early. Patients can access five allied health services more easily after a health assessment. For practices, health assessments

generate income, which can be crucial for coordinating complex chronic disease. However, the most crucial role of a health assessment may be to develop trust between doctor and patient, on which good preventive care depends. There are many circumstances where working effectively with the patient will mean involving Aboriginal health practitioners and other members of the local Aboriginal community. When this is done well, not only is that patient helped, but often word will spread to others in the community.

MBS item 715 also includes health assessments for children under the age of 15 years, and adults over the age of 55 years. Refer to 'Resources for doctors' for proformas for the child, adult and older persons health assessment.

### RESOURCES FOR DOCTORS

- The RACGP's National guide to a preventive health assessment for Aboriginal and Torres Strait Islander people, [www.racgp.org.au/yourracgp/faculties/aboriginal/guides/national-guide](http://www.racgp.org.au/yourracgp/faculties/aboriginal/guides/national-guide)
  - The RACGP's Smoking, nutrition, alcohol, physical activity (SNAP): A population health guide to behavioural risk factors in general practice, [www.racgp.org.au/your-practice/guidelines/snap](http://www.racgp.org.au/your-practice/guidelines/snap)
  - Immunisation schedule for Aboriginal and Torres Strait Islander peoples, [www.immunise.health.gov.au/internet/immunise/publishing.nsf/Content/Handbook10-home~handbook10part3~handbook10-3-1](http://www.immunise.health.gov.au/internet/immunise/publishing.nsf/Content/Handbook10-home~handbook10part3~handbook10-3-1)
  - Fact sheet – Medicare health assessment of Aboriginal and Torres Strait Islander people (MBS item 715), [www.health.gov.au/internet/main/publishing.nsf/Content/mbsprimarycare\\_ATSI\\_MBSitem715](http://www.health.gov.au/internet/main/publishing.nsf/Content/mbsprimarycare_ATSI_MBSitem715)
  - Follow-up services after an Aboriginal Health Assessment fact sheet, [www.health.gov.au/internet/main/publishing.nsf/Content/mbsprimarycare\\_mbsitems81300\\_81360](http://www.health.gov.au/internet/main/publishing.nsf/Content/mbsprimarycare_mbsitems81300_81360)
  - Fact sheet – Closing the Gap PBS co-payment, [www.pbs.gov.au/info/publication/factsheets/closing-the-gap-pbs-co-payment-measure](http://www.pbs.gov.au/info/publication/factsheets/closing-the-gap-pbs-co-payment-measure)
  - Practice Incentives Program – Indigenous Health Incentive (PIP – IHI) guidelines, [www.humanservices.gov.au/sites/default/files/documents/indigenous-health-pip-guidelines.docx](http://www.humanservices.gov.au/sites/default/files/documents/indigenous-health-pip-guidelines.docx)
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**CASE 4**

**STEVE HAS A RASH**

Steve, a primary school teacher aged 32 years, is a regular patient at your clinic. In a previous consultation, he disclosed that he has sex with men. He is seeing you today for the management of a persistent rash. One week ago, he saw your colleague for a truncal rash that was mildly itchy (Figure 1). He was told it may be an 'allergic dermatitis' as he had changed his shampoo brand recently. Steve was told to stop using his shampoo and was prescribed hydrocortisone cream and an oral antihistamine. However, the rash has worsened and has now spread to his hands (Figure 2).



**QUESTION 1** 

What are your differential diagnoses?

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**QUESTION 2** 

How will you confirm your diagnosis?

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**FURTHER INFORMATION**

You order syphilis serology. The results, which you receive three days later, show a rapid plasma reagin (RPR) of 1:64 with reactive *Treponema pallidum* passive particle agglutination (TPPA) and chemiluminescence immunoassay (CLIA) total antibody, confirming your suspicion of syphilis. You contact Steve and ask him to see you for review of his results.



**QUESTION 3** 

How would you manage Steve?

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**FURTHER INFORMATION**

On further history, Steve reports that he has a regular male partner but has also had 20 casual male partners over the past six months. He does not use condoms with his regular partner but always uses condoms for anal sex, but not oral sex, with his casual partners.

**QUESTION 4** 

Do you have any further advice for Steve?

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**FURTHER INFORMATION**

Steve agrees to ask his boyfriend to come in for a consultation but feels uncomfortable contacting his previous casual partners.

**QUESTION 5** 

What would you advise him?

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**QUESTION 6** 

How will you follow up Steve?

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**FURTHER INFORMATION**

The next day, Steve brings in his regular partner, Bryan, to see you. Bryan is angry with Steve as he thought they were monogamous. Bryan reports having regular condomless anal sex with Steve over the past 12 months that they have been together. The last time they had sex was one month ago. On further questioning, Bryan reports that he has had a painless ulcer on his penis for the past three days and was planning to see you. He has previously had an anaphylactic reaction to penicillin.

**QUESTION 7** 

How would you manage Bryan?

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**CASE 4 ANSWERS**

**ANSWER 1**

The differential diagnoses for generalised rash are numerous (eg atopic dermatitis, drug eruption, psoriasis, pityriasis rosea, scabies, non-specific viral exanthema, and many more possibilities). However, in men who have sex with men (MSM) who present with a new rash, especially if it is also present on their hands and feet, it is important to exclude secondary syphilis as a cause. Also consider HIV seroconversion illness which can also present with a rash.

Syphilis in Australia occurs primarily among MSM in urban settings, and heterosexual Aboriginal and Torres Strait Islander peoples in remote and outer regional areas.<sup>1-3</sup> There is a rising epidemic of syphilis in Australia and around the world. In Australia, the rate of infectious syphilis among men has increased in the past 10 years from 5.1 per 100,000 in 2005 to 15.9 per 100,000 in 2014.<sup>3</sup> Syphilis is also known to be a risk factor for HIV acquisition, both epidemiologically (risk factors for HIV and syphilis are the same) and clinically (syphilis chancres may facilitate the transmission of HIV). So, all men with a new diagnosis of syphilis should also be tested for HIV.

Syphilis can present in a variety of stages: primary, secondary, latent or tertiary. In this scenario, secondary syphilis is the most likely cause. Secondary syphilis may manifest in a variety of ways. The cutaneous manifestation may occur within six weeks to six months after infection, but may occur more rapidly in people living with HIV.<sup>4</sup> A localised or diffused rash (generally nonpruritic and bilaterally symmetrical) is typical. Other manifestations include patchy alopecia and/or condyloma lata (wart-like lesions in the genital or anal regions). It is also possible for patients to complain of mild constitutional symptoms such as malaise, headache, fatigue and fever.<sup>4</sup>

**ANSWER 2**

To confirm a diagnosis of syphilis, further investigations are necessary. Syphilis serology consists of two types of tests:<sup>5</sup>

- treponemal test (eg fluorescent treponemal antibody absorbed tests, the TPPA assay, enzyme immunoassays, CLIA). A reactive treponemal test may indicate previously treated, untreated or incompletely treated syphilis. The non-treponemal tests (a marker of disease) are useful to distinguish an active infection from previously treated syphilis
- non-treponemal test (eg RPR or venereal disease research laboratory [VDRL] test).

**ANSWER 3**

If Steve is not allergic to penicillin, the recommended treatment<sup>5</sup> is either:

- intramuscular benzathine penicillin, which is long-acting, in a single dose (2.4 million units)
- intramuscular procaine penicillin (600,000 units) daily for 10 days.

Do not give oral penicillin or short-acting formulations (eg benzyl penicillin) as they are not effective for the treatment of syphilis.

If a patient has a significant allergy to penicillin and is not pregnant, an alternative treatment is oral doxycycline 100 mg twice daily for 14 days. This will be the same treatment regime for primary syphilis and early latent syphilis. If a patient has late latent syphilis (ie is asymptomatic with a positive syphilis serology and the last negative test was more than two years ago) or syphilis of unknown duration, give either:

- intramuscular benzathine penicillin (2.4 million units), every week for three weeks
- intramuscular procaine penicillin (600,000 units) daily for 15 days
- doxycycline 100 mg oral twice daily for 28 days.

Warn Steve about the potential for Jarisch-Herxhemier reaction.<sup>5</sup> This follows treatment where dying treponemes cause an inflammatory response that may manifest as myalgia, fever, headache, tachycardia and exacerbation of the rash or chancre. Management of this reaction includes rest, simple analgesics and observation. The reaction usually develops within several hours of treatment and resolves within 24 hours after onset.

It is important to screen for symptoms suggestive of neurosyphilis as this would require admission to hospital for intravenous penicillin and potential lumbar puncture. Involvement of the central nervous system can occur at any stage of syphilis and may present as cognitive dysfunction, motor or sensory deficits, ophthalmic or auditory symptoms, cranial nerve palsies, or symptoms of meningitis or stroke. Neurosyphilis may be more common in people living with HIV, so clinicians should pay particular attention to this in those patients.

Other management points are as follows:

- Encourage the patient not to have sex for the next seven days (until he is non-infectious).
- Patients should not have sex with partners with whom they have had sex over the past six months, until those partners have been tested and treated.
- As syphilis is a notifiable disease, complete the appropriate notification form and return to your health department.

**ANSWER 4**

For secondary syphilis, all sexual partners over the past six months should be contacted and offered testing and treatment. Contact tracing should occur for partners within the past three months for primary syphilis and 12 months for early latent syphilis (see [www.contacttracing.ashm.org.au](http://www.contacttracing.ashm.org.au) for more details). Steve's sexual contacts should be treated with intramuscular benzathine penicillin (2.4 million units) in a single dose regardless of their test results as there can be a fairly long window period for syphilis serology to become positive (up to six weeks).

This is also an opportune time to reinforce condom use and regular sexually transmissible infection (STI) testing. Also check that Steve is aware of his options when there is potential exposure to human immunodeficiency virus (HIV), through use of post-exposure prophylaxis (PEP; [www.ashm.org.au/pep-guidelines](http://www.ashm.org.au/pep-guidelines)) or pre-exposure prophylaxis (PrEP; [www.ashm.org.au/hiv/hivpre](http://www.ashm.org.au/hiv/hivpre)). See Case 2 for further details on PEP and PrEP.

**ANSWER 5**

Other options for contact tracing may be via an anonymous short message service (SMS), letter or email through web resources such as [www.letthemknow.org.au](http://www.letthemknow.org.au). On the same website, there are resources including STI fact sheets and doctor treatment letters. If Steve is willing to give you the contact details of his previous partner(s), you may also support him in contact tracing. If you need further assistance, there are state-specific contact tracing services that can assist you ([www.contacttracing.ashm.org.au/contact-tracing-guidance/ways-of-notifying-contacts](http://www.contacttracing.ashm.org.au/contact-tracing-guidance/ways-of-notifying-contacts)).

**ANSWER 6**

Steve may be at risk of reinfection and should be encouraged to attend every three months for syphilis testing as part of his comprehensive screening for STIs. His RPR titre should generally fall fourfold (eg 1:64 to 1:16) within six months. A fourfold increase signifies a new syphilis infection.<sup>4</sup> Non-treponemal test titres usually become non-reactive with time, but in some, there may be persistently low levels ('serofast'). Interpretation of syphilis serology may be complex and further advice can be sought from your local pathologist, sexual health or infectious disease physicians (or call the Melbourne Sexual Health Centre Hotline at 1800 009 903, Monday–Friday 9.00 am to 5.00 pm).

It is important to note that most patients who have a reactive treponemal test will remain reactive for the remainder of their lives and they **do not** need additional treatment (unless there is a fourfold increase in their non-treponemal titres or they are clinically at high risk for syphilis). A minority (15–25%) of patients who are treated during the primary stage of syphilis may become serologically nonreactive after two to three years.<sup>6</sup>

**ANSWER 7**

As a contact of person with syphilis, Bryan will need treatment with doxycycline 100 mg twice daily for 14 days. The ulcer may be a chancre (ie primary syphilis) and can be swabbed and sent for a syphilis polymerase chain reaction (PCR) test. Bryan will also need syphilis serology at the time of initiating treatment and should be encouraged to have a full STI check in accordance with the Sexually Transmissible Infections in Gay Men Action Group (STIGMA) guidelines.<sup>7</sup> He should not have sex for the next seven days.

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**CASE 5**

**SEBASTIAN ASKS FOR A HEALTH CHECK**

Sebastian is 52 years of age and presents as a new patient to your practice. He is an engineer and has two adult sons. One of his sons is a medical student. His only significant past history is several episodes of major depression in his twenties and thirties, with a recent exacerbation. Sebastian's son has told him that he should see a general practitioner (GP) for a regular health check.

**QUESTION 1** 

What would you include in your initial assessment of Sebastian, including history and examination?

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**FURTHER INFORMATION**

Sebastian is of South Asian descent, has a family history of type 2 diabetes mellitus (T2DM; several relatives on both sides of his family) and his father died from colon cancer. He has never smoked and drinks up to two standard drinks on one or two days each week. He plays tennis and walks regularly with his wife. Their two adult children live away from home. There are no other symptoms apart from low mood and anhedonia, with a K10 score of 31, showing significant abnormality in mood items of the tool.

Sebastian's physical examination is unremarkable and he asks if he should have any routine testing.

**QUESTION 2** 

What investigations would you order, if any, at this time?

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**FURTHER INFORMATION**

Sebastian reports that he completed a faecal occult blood test as part of the National Bowel Cancer Screening Program at 50 years of age, and the results are negative. Sebastian asks if he should also be screened for prostate cancer, because he has read that it is the second most commonly diagnosed cancer in men in Australia.

**QUESTION 3** 

What are the current guidelines for early detection of prostate cancer?

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**FURTHER INFORMATION**

After carefully considering the harms and benefits, Sebastian decides to have the PSA test. His blood tests are all within normal limits, including a PSA of 2.4 ng/mL, which is in the normal range for his age. He is commenced on antidepressant medication and supportive psychotherapy, including lifestyle advice, from you as the GP, and

responds well, but attempts to withdraw the medication after six months, resulting in a relapse into depression.

Twelve months after his initial consultation, Sebastian reports that he has been experiencing reduced libido, moderate erectile dysfunction, and mild to moderate urinary hesitancy with reduced stream.

**QUESTION 4** 

Would you consider repeating the PSA and/or undertaking DRE at this time?

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**FURTHER INFORMATION**

Sebastian's DRE reveals a smooth, regular prostate of moderate size, with no features that would raise a suspicion of malignancy. Repeat PSA (and blood sugar level [BSL] every three years) is unchanged.

Sebastian continues as your patient for the next eight years. His depression remains recalcitrant and his management is shared with a psychiatrist. He takes early retirement at age 60 years because of ongoing mood problems. His physical examination remains largely unchanged, but he develops impaired glucose tolerance and mild hypercholesterolaemia, and is commenced on a statin medication and provided lifestyle advice. PSA testing every two years from 53 years of age reveals a slow but steady rise, and when the level reaches 3.5 ng/mL, you refer Sebastian to a urologist for an opinion as to the need for further investigation. After assessing Sebastian, including prostatic ultrasonography to assess prostate size (noting the low sensitivity of ultrasonography for detecting early prostate cancer), the urologist feels that Sebastian's symptoms are consistent with mild to moderate benign prostatic hyperplasia, and asks you to review him yearly with an annual PSA with free-to-bound ratios.

**QUESTION 5** 

At what point would you consider it appropriate to further investigate Sebastian, and what investigations would be appropriate?

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**FURTHER INFORMATION**

Sebastian underwent ultrasound-guided transrectal prostatic biopsy. High-resolution multiparametric magnetic resonance imaging (MRI), if available, is now considered a more effective tool for identifying areas of the prostate that may be associated with high-grade prostatic cancer, but was not available at the time of Sebastian's assessment. The biopsy samples revealed Gleason score 7 prostate cancer.

**QUESTION 6** 

What management options are available for Sebastian's prostate cancer?

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**QUESTION 7** 

What information should be provided to patients about the risks of active treatment for prostate cancer?

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**CASE 5 ANSWERS**

**ANSWER 1**

The Royal Australian College of General Practitioners' (RACGP's) *Guidelines for preventive activities in general practice*<sup>1</sup> (Red Book) gives clear recommendations for the age-appropriate components of history and examination items to be included in any screening consultation. In addition to these recommended activities, the history (including smoking, nutrition, alcohol and physical activity status) and review of any patient concerns and relevant family history will determine what additional activities may be undertaken in terms of examination or investigations.

As part of your physical examination, you would assess Sebastian's mood through history-taking and a standard screening tool (eg standardised assessment tools for mood and other non-psychotic mental health problems such as anxiety and stress, including the K10 and DASS21 screening instruments, each of which is available in most general practice medical record software programs), to establish whether he is at risk of a significant mood disorder.

**ANSWER 2**

With Sebastian's family history and South Asian heritage, it would be appropriate to assess cardiovascular risk factors, including a full lipid screen and fasting BSL. A full blood count should be done. Depending on the presence or absence of symptoms, such as fatigue or weight change, it may be appropriate to assess Sebastian's thyroid function and iron stores as part of the assessment of his low mood.

Given his family history, it may also be appropriate to refer Sebastian for baseline colonoscopy.

**ANSWER 3**

In Australia, screening for prostate cancer is not recommended and there is no screening program for prostate cancer, but Sebastian can opt to have a prostate-specific antigen (PSA) test included in his blood tests. However, you would need to inform him of the harms and benefits of PSA testing before he chooses to have the test.<sup>1</sup>

The *Clinical practice guidelines for PSA testing and early management of prostate cancer*,<sup>2</sup> approved by the National Health and Medical Research Council (NHMRC) and endorsed by the RACGP, recommend the following:

'For men at average risk of prostate cancer who have been informed of the benefits and harms of testing and who decide to undergo regular testing for prostate cancer, offer PSA testing every two years from age 50–69, and offer further investigation if total PSA is greater than 3.0 ng/mL.'

The relevant factor here is the degree to which men can be offered appropriate information to assist them in making an informed decision. The key issue is the pre-test counselling about the implications of an abnormal result. This necessitates a discussion that includes:

- the likelihood of asymptomatic prostate cancer developing
- the potential outcomes and consequences of untreated prostate cancer
- the potential adverse effects associated with the diagnosis and treatment of prostate cancer
- the limitations in terms of sensitivity and specificity of any test used to screen for prostate cancer
- a recognition that the advice given is based on population studies and cannot be used to predict individual risk or prognosis.

A decision aid could be used to facilitate the discussion of the risks and benefits for prostate cancer screening (refer to 'Resources for patients'). Patients who decide to undertake PSA testing should be informed that they will need to refrain from sexual activity or masturbation for at least two days.

In asymptomatic men interested in undergoing testing for early diagnosis of prostate cancer, DRE is not recommended as a routine addition to PSA testing in the primary care setting.<sup>1</sup>

**ANSWER 4**

The most common cause of lower urinary tract symptoms (LUTS) is benign prostate enlargement. Men with LUTS do not appear to have an increased risk of prostate cancer.<sup>1</sup> Reduced libido, erectile dysfunction and urinary hesitancy/urgency can be associated with many antidepressant medications, and the depression itself may account for some of Sebastian's symptoms. Nonetheless, Sebastian no longer falls into the category of 'asymptomatic men'. It may be prudent to consider undertaking a DRE and a second PSA.<sup>1,2</sup>

**ANSWER 5**

The current recommendations advise against using PSA velocity (ie rate of increase) or the prostate health index (PHI) test as adjuncts to total PSA testing in determining whether or not to offer prostate biopsy, except in the context of research conducted to assess their utility for this purpose.<sup>1</sup>



For men aged 50–69 years with initial total PSA >3.0 ng/mL who have undergone repeat total PSA and free-to-total PSA percentage tests at follow-up one to three months later, offer prostate biopsy:<sup>2</sup>

- if repeat total PSA is >5.5 ng/mL, regardless of free-to-total PSA percentage
- if repeat total PSA is greater than 3.0 ng/mL and ≤5.5 ng/mL and free-to-total PSA is below 25%.

Sebastian does not have other features that increase his relative risk of prostate cancer (family history of first degree relative of prostate cancer), and as someone of South Asian descent, he is at relatively lower risk than other racial groups. However, his free-to-total ratio is 20% and he therefore meets the criteria for considering prostatic biopsy.

### ANSWER 6

The Gleason score (or Gleason sum) represents the sum of the scores of the two most common types of glandular growth patterns seen within the tumour biopsy specimen. For example, if the grade given to the most common growth pattern is 3 and the grade given to the second most common growth pattern is 4, the total Gleason score is 7. Scores of 3 or lower represent normal tissue or well differentiated adenocarcinoma, so a score of 7 or above means that at least one of the common glandular patterns is a potentially more aggressive tumour form. Gleason Scores below 6 are not usually given because it is difficult to determine with certainty that the lowest grade tumours are in fact cancer.

Treatment options for Sebastian fall into three broad categories:<sup>2</sup>

- active surveillance
- watchful waiting
- active treatment.

#### Active surveillance

Patients diagnosed with low-risk prostate cancer receive close follow-up to monitor disease progression. The aim of this approach is to avoid unnecessary treatment of men with indolent cancer, and therefore avoid treatment side effects that may reduce quality of life. Definitive treatment is offered if disease progression is detected and effective treatment is deemed possible.<sup>1</sup>

Monitoring consists of PSA testing, DRE, prostate biopsies and multiparametric MRI, as determined by the treating team. There is uncertainty about what constitutes an optimal protocol for active surveillance, or the optimal frequency of follow-up and triggers for intervention. Many protocols, with varying procedures, have been reported in the literature, but to date these protocols have not been validated in randomised controlled trials. Nor is there information about whether they have led to a reduction in overall or prostate-specific mortality rates. However, the 2016 consensus guidelines<sup>1</sup> recommend that active surveillance should be offered to men with prostate cancer if all the following criteria are met:<sup>1</sup>

- PSA ≤20 ng/mL
- clinical stage T1–2
- Gleason score 6.

While the characteristics of Sebastian's tumour (Gleason score 7) place him outside these criteria, the recommendations state that it would still be appropriate to offer him active surveillance since the following criteria are met:

- PSA ≤10.0 ng/mL
- clinical stage T1–2a
- Gleason score ≤7 (3 + 4) and pattern 4 component <10% after pathological review.

The consensus guidelines<sup>1</sup> further recommend that men with prostate cancer who are managed by an active surveillance protocol should be offered PSA testing every three months, and a physical examination, including a DRE, every six months. A reclassification repeat prostate biopsy should be offered within 6–12 months of starting an active surveillance protocol, and every two to three years thereafter, or earlier as needed to investigate suspected disease progression (ie PSA doubling time is <2–3 years or detection of clinical progression on DRE).

#### Watchful waiting

Watchful waiting is used for men with asymptomatic cancer or for those who decline treatment after the available options and their benefits and harms have been discussed.<sup>1</sup> The aim is to delay intervention until deemed necessary.

In men with early-stage prostate cancer of any grade, watchful waiting is associated with higher rates of metastatic disease and death, but lower rates of erectile dysfunction, urinary incontinence and distress, compared with radical prostatectomy.<sup>2</sup> However, studies have shown that rates of anxiety and depression, and wellbeing and patient-assessed quality of life, are similar for men who receive watchful waiting and those who undergo radical prostatectomy.<sup>3–6</sup>

#### Active treatment

Active treatment includes a range of surgical, radiotherapy, hormonal and chemotherapy options.

### ANSWER 7

Prostatectomy is associated with urinary dysfunction and 30–50% of men report an increase in symptoms. The use of a nerve-sparing surgery reduces these effects. The main urinary side effect of prostatectomy is incontinence, including a lack of control, frequent leakage and the need to use absorbent pads. These affects have been reported by 25% of men at six months post-surgery and <10% by three years post-surgery.<sup>7</sup>

Bowel dysfunction may occur, usually in the first few weeks after surgery and is thought to be due to the increased space created by the loss of the prostate. Rectal damage can occur during surgery, but this is rare (<2–3%). Radiation therapy can cause significant damage to the rectum, resulting in any and all of the urinary symptoms listed above as well as faecal incontinence.

Most men experience erectile dysfunction in the first few months after surgery, including nerve-sparing surgery. This improves substantially within one year in men who have had nerve-sparing surgery; erectile function returns to normal in 40–50% of men within the first year in this group.<sup>7</sup>

A lower percentage of men experience erectile dysfunction after radiation therapy (25–50% after brachytherapy and 50% after standard external beam radiation), but there is little improvement over time.<sup>7</sup>

Hormonal therapy and chemotherapy have well-documented side effects. These include loss of libido, negative metabolic effects, loss of muscle mass and bone density for anti-androgen therapies and the usual range

of agent-specific effects from chemotherapeutic agents. These should be discussed with the patient prior to making a decision about the optimal form of therapy, a decision that will primarily involve the patient and the urologist or oncologist, but in which the GP should be prepared to act as an advisor to the patient.

## CONCLUSION

Following discussion of treatment options with his urologist, Sebastian opted for radical prostatectomy with an intention of achieving full cure. Unfortunately, he had a number of acute and longer term complications, including a postoperative pelvic haematoma, which required surgical drainage, and significant urinary incontinence and erectile dysfunction.

Men with prostate health problems rarely experience this condition in isolation. Associated comorbidities can cloud the clinical picture and need to be considered when making treatment decisions.

Each patient has an individual disease trajectory, and there is a lack of high-quality evidence that supports one specific diagnostic or treatment regimen. Nevertheless, consensus-based treatment guidelines are an invaluable tool for informing patients about treatment options and potential risks and outcomes.

## RESOURCES FOR PATIENTS

- Royal Australian College of General Practitioners. Should I have prostate cancer screening, [www.racgp.org.au/download/Documents/Guidelines/prostate-cancer-screening-infosheetpdf.pdf](http://www.racgp.org.au/download/Documents/Guidelines/prostate-cancer-screening-infosheetpdf.pdf)

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ACTIVITY ID: 60402

### MEN'S HEALTH

This unit of *check* is approved for six Category 2 points in the RACGP QI&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 *gplearning* website, <http://gplearning.racgp.org.au>
- answering the following multiple choice questions (MCQs) by logging on to the *gplearning* website, <http://gplearning.racgp.org.au>
  - you must score  $\geq 80\%$  before you can mark the activity as 'Complete'
- completing the online evaluation form.

You can only qualify for QI&CPD points by completing the MCQs online; we cannot process hard copy answers.

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

If you are not an RACGP member and would like to access the *check* program, please contact the *gplearning* helpdesk on 1800 284 789 to purchase access to the program.

#### CASE 1 – HARRY

Harry and his wife, both 31 years of age, have been trying unsuccessfully to conceive for the past 12 months. You have seen Harry's wife and assessed her for any possible problems with fertility, but have found none. On your advice, Harry presents for assessment of any risk factors or conditions that might affect his fertility. Physical examination shows that Harry's testes are 20 mL in volume. You arrange for Harry to have semen tests.

#### QUESTION 1

Which of the following results of Harry's semen analysis might be associated with reduced fertility?

- A. Semen volume 1.5 mL
- B. Sperm concentration 1.5 million/mL
- C. Sperm morphology 4% normal
- D. Semen pH 8.3

#### FURTHER INFORMATION

You order blood tests to further investigate if there are any factors that might affect Harry's fertility.

#### QUESTION 2

Which of the following results might explain his semen test results?

- A. Follicle stimulating hormone (FSH) 15 IU/L
- B. Luteinizing hormone (LH) 7 IU/L
- C. Testosterone 12 IU/L
- D. All of the above

#### CASE 2 – LIAM

Liam, 30 years of age, presents on Monday morning to be tested for human immunodeficiency virus (HIV) because he had unprotected sex with a man he met at a party at the weekend. He discovered the next day that the man from the party is HIV-positive. Liam tells you that he usually uses condoms and this is the first time he has had risky sex. He has never been tested for HIV before. You explain to him the concept of the window period for diagnosing HIV after a known exposure.

#### QUESTION 3

Which of the following is the best advice to give Liam?

- A. Liam could have a rapid test for HIV, which produces a result within 20 minutes.
- B. Liam should have a fourth generation HIV serological test, which has a shorter window period than other HIV tests.
- C. Liam has missed recommended timeframe for post-exposure prophylaxis (PEP) treatment and will need to wait for at least 28 days before being tested.
- D. Liam should have a test for HIV and PEP treatment started immediately.

#### FURTHER INFORMATION

You organise for Liam to have an HIV test and prescribe a course of PEP. The HIV test is negative. Liam sees you again after completion of PEP treatment for a follow-up.

#### QUESTION 4

In Liam's case, the recommended timing for follow-up HIV testing is:

- A. two months after exposure
- B. one to two weeks and two months after completion of PEP
- C. three months after completion of PEP
- D. three and six months after completion of PEP.

#### CASE 3 – TYRONE

Tyrone is 45 years of age and presents with a rash that he first noticed on his back, but that has now spread to his hands and feet. He has also been feeling tired and generally unwell. During the history-taking, Tyrone discloses that he is currently single but has casual sex with men on a regular basis. He does not always use a condom. Tyrone has no past medical history or allergies. Further investigation and testing confirms a diagnosis of secondary syphilis.

**QUESTION 5**

Which of the following options is the recommended treatment for Tyrone?

- A. Intramuscular benzathine penicillin (2.4 million units) every week for three weeks
- B. Intramuscular procaine penicillin (600,000 units) daily for 15 days
- C. Single intramuscular dose of benzathine penicillin (2.4 million units)
- D. Doxycycline 100 mg oral twice daily for 28 days

**QUESTION 6**

Which of the following is the recommended time frame for contact tracing, testing and treatment of Tyrone's sexual partners?

- A. Three months
- B. Six months
- C. Nine months
- D. 12 months

**CASE 4 – ARTHUR**

Arthur, an Aboriginal man aged 41 years, is a new patient at your clinic who presents for a health check. Arthur tells you that he has been generally well, but his brother Ashley, aged 46 years, had a heart attack a few months ago and Arthur thought it would be a good idea to have a check-up. Arthur does not smoke and drinks alcoholic beverages only occasionally.

**QUESTION 7**

Which of the following preventive activities or assessments would you do as a priority at this consultation?

- A. Arrange for Arthur to have urine and blood tests to check lipid levels and screen for chronic kidney disease.
- B. Calculate Arthur's absolute cardiovascular disease risk.
- C. Do spirometry tests to screen for lung disease.
- D. Give Arthur a pneumococcal vaccination.

**FURTHER INFORMATION**

Arthur has no chronic illnesses but your assessment reveals that he is at high risk of developing type 2 diabetes.

**QUESTION 8**

Your assessment indicates that Arthur is eligible for:

- A. the Closing the Gap Pharmaceutical Benefits Scheme (PBS) co-payment
- B. the Practice Incentives Program – Indigenous Health Incentive (PIP – IHI)
- C. a GP management plan
- D. all of the above.

**CASE 5 – CON**

Con, 55 years of age, presents for a health check and, in particular, to ask about screening for prostate cancer. After a discussion about the benefits and harms of testing, Con decides to have a prostate-specific antigen (PSA) test. The results reveal a PSA level of >3.0ng/L. You refer Con to a urologist who, after further investigation, advises that at this stage, Con should see you for annual monitoring.

**QUESTION 9**

Which of the following tests should be done as an adjunct to PSA testing to determine whether Con should have a prostate biopsy?

- A. PSA velocity
- B. Digital rectal examination (DRE)
- C. Prostate health index (PHI) test
- D. Free-to-total PSA percentage

**QUESTION 10**

Current guidelines recommend that prostate biopsy should be offered if:

- A. repeat total PSA is >3.5 ng/mL, regardless of free-to-total PSA percentage
- B. repeat total PSA is 3.0–5.5 ng/mL and free-to-total PSA is <30%
- C. repeat total PSA is >5.5 ng/mL, regardless of free-to-total PSA percentage
- D. repeat total PSA is >5.5 ng/mL and free-to-total PSA is <25%.

# check

Independent learning program for GPs