check

Independent learning program for GPs

Unit 505 May 2014

Gastroenterology

RACGP

www.racgp.org.au/check

Subscriptions

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

Published by

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

ABN 34 000 223 807
ISSN 0812-9630

check

Independent learning program for GPs

Gastroenterology

Unit 505 May 2014

The five domains of general practice

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

RACGP

ABOUT THIS ACTIVITY

Patients present with a range of gastrointestinal disorders in general practice settings. These include functional disorders, such as constipation or irritable bowel syndrome, and structural disorders where there is a bowel abnormality that often requires surgery. Food-borne disease is a common cause of self-limiting gastrointestinal problems. However, consumption of certain foods or components of foods (eg gluten) may lead to other more pressing problems that require medical management, such as allergies or coeliac disease. Alcohol consumption in excessive amounts and certain medications can lead to a number of wide-ranging gastrointestinal problems.

The focus on gastrointestinal problems in general practice also extends to prevention and guidelines, such as the *Guidelines for preventive activities in general practice* 8th edition (the Red Book),[1] which provide guidance for the prevention of common gastrointestinal cancers including oral cancer and colorectal cancer.

This unit of *check* considers gastrointestinal disorders presenting to general practice and discusses current options for management.

LEARNING OUTCOMES

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

- outline current diagnostic and management options for people with suspected coeliac disease
- explain the steps involved in *Helicobacter pylori* eradication for a patient diagnosed with an infection
- describe the pathophysiology, diagnosis and management of ascites
- describe the diagnosis and management of non-alcoholic fatty liver disease
- list considerations when planning travel advice for a patient.

AUTHORS

John Scally MBB,S DObst, RCOG, FRACGP, CTH was an examiner for the RACGP and contributor to *Therapeutic Guidelines: Gastrointestinal*. He has been in general practice for 40 years and has a special interest in travel medicine.

Peter Katelaris MBBS (Hons I), FRACP, FRCP, MD, AGAF is a senior consultant gastroenterologist at Concord Hospital in Sydney and Clinical Associate Professor at The University of Sydney. His main research interests are in acid-peptic disorders and, in particular, gastro-oesophageal reflux disease and *Helicobacter pylori* infection. Peter has conducted international collaborative research in the field and has been an invited speaker at international and regional meetings in many countries in Asia and Europe. He is currently an Australian representative to the Asia Pacific Association of Gastroenterology. He is an experienced clinician, researcher and educator. He has taught at all levels of medical education for many years.

Bambi Ward MBBS, FRACGP, Grad Dip Fam Med, MFam Med is an academic general practitioner with a special interest in coeliac disease. She currently works as a medical educator with Northern Territory General Practice Education (NTGPE) and is part of the NTGPE Medical and Cultural Educator team awarded the RACGP's National Faculty of Aboriginal and Torres Strait Islander Health Standing Strong Together Award in 2013. Bambi is a FRACGP examiner and is currently completing a PhD.

May Wong MBBS is a conjoint associate lecturer at the University of New South Wales and currently also works at Bankstown Lidcombe Hospital.

PEER REVIEWERS

Ashwin Garg BSc (Med) MBBS GradDipBiomedEng (UNSW) FRACGP DCH is a general practitioner working in a private practice in North Strathfield, Sydney.

Peter Bampton MBBS MD FRACP AGAF is Head of Luminal Gastroenterology, Department of Gastroenterology and Hepatology, Flinders Medical Centre, and Associate Professor of Gastroenterology, Flinders University of South Australia. He is a founding member of IBD Australia and Australian Neuro-gastroenterology and Motility Association, past chair of Digestive Health Foundation and member of council, Gastroenterological Society of Australia. Peter's areas of clinical interest include colorectal cancer screening, inflammatory bowel disease, colonic motility and clinical practice improvement.

REFERENCES

1. Britt H, et al. 2001. General practice activity in Australia 2000–01. AIHW Cat. No. GEP 8. Canberra: Australian Institute of Health and Welfare (General Practice Series No. 8).

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

ALT	alanine transaminase	HCC	hepatocellular carcinoma	NSAID	non-steroidal anti-inflammatory drug
AST	aspartate transaminase	IBS	irritable bowel syndrome	PCR	polymerase chain reaction PCR
BMI	body mass index	IgA	immunoglobulin A	SSRI	selective serotonin reuptake inhibitor
CRP	C-reactive protein	LFTs	liver function tests	tTG	transglutaminase antibody
DGP	deamidated gliaden peptide	MCS	microculture and sensitivity	UEC	urea, electrolytes creatinine
FBE	full blood examination	NAFLD	non-alcoholic fatty liver disease		
GGT	gamma glutamyl transpeptidase	NASH	non-alcoholic steatohepatitis		

CASE 1

JOHN IS TRAVELLING OVERSEAS

John, aged 39 years, has to travel to New Delhi, India, in March for 5 nights. The purpose of his trip is business in relation to his employment as a software consultant. He will attend meetings in an office environment during the day and most evenings he will be entertained by his hosts.

He attends for a pre-travel consultation. He is in good health and takes no medications.

QUESTION 1

What issues need to be addressed in such a consultation?

QUESTION 2

What specific advice would you give to John, who is in good health, for a 5-night business stay in New Delhi in March?

FURTHER INFORMATION

John sees you again 4 weeks after his return. The trip was successful but he developed severe diarrhoea on the last evening in New Dehli. John took the medications suggested and was able to fly home on his scheduled flight. He says he is much better but his bowels remain loose, windy and unpredictable.

QUESTION 3

How would you manage this presentation?

FURTHER INFORMATION

John does not have any other symptoms. There is no history of fever, rash, blood or mucus in the stools and systemically he is well. Examination is normal with no abdominal signs and no hepatomegaly.

QUESTION 4

Would you organise any laboratory investigations for John and, if so, what investigations would you request?

FURTHER INFORMATION

John's PCR results confirm the presence of *Giardia* and *Blastocystis*. His FBE, CRP and LFTs are normal.

QUESTION 5

How would you treat John considering these findings and the persistence of his symptoms?

QUESTION 6

Would you treat the *Blastocystis* infection?

FURTHER INFORMATION

You schedule a review in 3 months. John is now well but still has intermittent loose bowel actions associated with cramping abdominal pains.

QUESTION 7

What is John's diagnosis?

QUESTION 8

What do you advise John regarding further management?

CASE 1 ANSWERS

ANSWER 1

Advice needs to incorporate the following considerations[1]:

- destination
- duration of travel
- time of year
- activities to be undertaken
- personal health
- pregnancy, if appropriate
- age of the patient
- visiting friends and relatives
- travelling with children
- previous vaccinations (especially travel vaccinations) and any vaccination and medication allergies.

ANSWER 2

As well as addressing his individual considerations, John's consultation provides an opportunity to provide general information regarding health and travel. It also allows the GP an opportunity to review his current overall vaccination status with Australian guidelines.[2,3]

The provision of printed material is strongly recommended. This allows the GP to have a structure to refer to in the consultation and to be able to highlight the risks that John may encounter.

An excellent source for printing this information is wwwnc.cdc.gov/travel/destinations/list

John should be advised his health risks lie broadly in relation to food- and water-borne disease as well as vector-related illness. He should be reminded of the need for insurance, personal health and safety, and respect for cultural considerations. Recommendations for his 5-day business trip urban-based in India are:

- to be vaccinated against hepatitis A and typhoid

- to protect himself against mosquito borne disease, especially Dengue fever
- to be advised about prevention and treatment of traveller's diarrhoea
- to be aware of HIV/AIDS risk
- to avoid animal bites.

John's general vaccination status should be reviewed, especially hepatitis B, tetanus and pertussis. His measles immunity is important to determine for this destination. John may have a record of past illness or vaccination. If not, he should have his measles serology checked.

Medications for the treatment of diarrhoea that John could take with him include rehydration formula, loperamide and azithromycin. Azithromycin 500 mg tablets, 2 tabs stat, is recommended for most of Asia as the first step in the treatment of moderate-to-severe diarrhoea, as the prevalence of quinolone resistance to *Campylobacter* species is high. In Thailand, India and any other country with known high rates of quinolone resistance, azithromycin should be first-line therapy. Azithromycin is also the drug of choice for children and pregnant women.[4–6] Antibiotic prophylaxis for traveller's diarrhoea is not recommended for healthy travellers, including children.[5] Probiotics are not recommended for prevention of traveller's diarrhoea.[4]

Antimotility agents are useful for short-term management of diarrhoea during periods of inconvenience (eg travel, work). John should be provided with instructions on the use of loperamide (4 mg orally for the first dose, followed by 2 mg orally after each unformed stool, up to a maximum dose of 16 mg/day). Antimotility agents are not indicated for use in infants and children.[6,7]

The risk of insect-borne disease is low in the context of John's trip. Dengue fever is the highest risk, whereas malaria risk is low for New Delhi in March as that is the dry season and John is not scheduled to have outdoor exposure.[8–10]

Chikungunya exposure is through mosquito bite but is a lesser risk. This is more prevalent in Southern India and can be day and night exposure related.[11]

John should also be advised of the risk of animal bites (rabies) as well general travel risks of accidents, crime, jet lag, deep venous thrombosis and the need for insurance.[1]

Travellers should be advised to seek medical advice if they have a fever or are suffering from diarrhoea.[1]

John should consider carrying a letter from his GP detailing any prescription and over-the-counter medications he is carrying (such as loperamine, azithromycin, paracetamol) to avoid problems at customs.

ANSWER 3

A thorough history and examination are important. When assessing a person who has returned from an overseas trip, useful information to seek includes a complete travel history, including dates and places visited, potential exposure to disease (eg travel to rural areas, insect bites) as well as symptom onset.[12] John could be asked about possible exposure to or ingestion of contaminated food and water. Specifically, if he ate salads, had ice in drinks and/or consumed any raw food or dairy products. Examine John and note in particular whether he is febrile, jaundiced and whether there are abdominal signs, particularly hepatomegaly.

ANSWER 4

John should have a full blood examination (FBE) and C-reactive protein (CRP) measurement. In addition, liver function tests (LFTs), faeces microculture and sensitivity (MCS) and polymerase chain reaction (PCR) should be performed. LFTs are indicated to exclude underlying hepatitis (hepatitis E is to be considered in India).[1]

Faeces multiplex PCR is a new test to detect 10 pathogens:

- *Salmonella*
- *Campylobacter*
- *Shigella*
- *Yersinia*
- *Aeromonas*
- *Giardia*
- *Entamoeba*
- *Dientomoeba*
- *Blastocystis*
- *Cryptosporidium* species.

The advantage of the test is increased specificity and sensitivity as well as providing rapid (24-hour) results.[13] This is beneficial in deciding treatment and for public health notification in an outbreak setting.

ANSWER 5

Giardia is the most common gastrointestinal protozoan that causes chronic diarrhoea.[14] It is transmitted by the ingestion of food or water contaminated by faeces, by exposure to faecally contaminated surfaces and through person-to-person contact (including sexual contact).[15] Symptoms usually appear 1–2 weeks following infection and resolve within 2–4 weeks. Foul-smelling diarrhoea with greasy stools, abdominal cramps, bloating, flatulence and fatigue may be present, as well as anorexia and nausea. Fever and vomiting are uncommon but weight loss may occur.[15] In Australia, the treatment recommended for adults includes tinidazole 2 g orally as a single dose or metronidazole 2 g orally, daily for 3 days, or metronidazole 400 mg orally, 8-hourly for 5–7 days. Nitazoxanide 500 mg orally, 12-hourly for 3 days, is also an option; however, this drug is not currently registered in Australia and is only available through the Special Access Scheme.[14]

The clinical significance of *Blastocystis hominis* is contentious. Therapeutic guidelines suggest clinicians consider treatment with metronidazole or trimethoprim+sulfamethoxazole for symptomatic patients when other infectious/non-infectious causes have been excluded.[16]

You prescribe tinidazole 2 g stat for John's *Giardia* infection.

ANSWER 6

Treatment is not recommended for asymptomatic patients with *Blastocystis* on stool examination. However, it is recommended for symptomatic patients with *Blastocystis* when other infectious and non-infectious causes have been excluded.[16,17] Following discussion with John, who is symptomatic, you choose to treat John with the recommended dose[16] of metronidazole.

ANSWER 7

Following infection with *Giardia*, people may present with reactive arthritis, irritable bowel syndrome (IBS) or other chronic symptoms.[15] John most likely has post-infective IBS as he fulfils the diagnostic criteria outlined in *Table 1*[18]

Table 1: Rome III diagnostic criteria for IBS[18]

Criteria
Recurrent abdominal pain or discomfort (where discomfort means an uncomfortable sensation not described as pain) at least 3 days per month in the previous months that is associated with 2 of the following variables: • improvement with defecation • onset associated with a change in frequency of stool • onset associated with a change in form (appearance) of stool.
NOTE: Criteria must be fulfilled for the previous 3 months, with symptom onset at least 6 months prior to diagnosis. Adapted with permission from Clinical Infectious Diseases. © 2008 Infectious Diseases Society of America.

ANSWER 8

You advise John that your diagnosis needs to be confirmed by a gastroenterologist and provide him with a referral. He is likely to be symptomatic for months to years. Referral to a dietician would also be valuable for his ongoing management.

REFERENCES

1. Yung A, Ruff T, Torresi J, Leder K, O'Brien D. Manual of Travel Medicine: pre-travel guide for health care practitioners 2nd ed. Melbourne: IP Communications, 2011.
2. Immunise Australia. Available at www.immunise.health.gov.au [Accessed 10 April 2014].
3. Australian Government Department of Health. The Australian Immunisation Handbook 10 ed. Canberra: Commonwealth of Australia 2013. Available at www.immunise.health.gov.au/internet/immunise/publishing.nsf/Content/EE1905BC65D40BCFCA257B26007FC8CA/$File/handbook-Jan2014v2.pdf [Accessed 10 April 2014].
4. Australian Government, Department of Foreign Affairs and Trade. Travel advice: India. Available at www.smartraveller.gov.au/zw-cgi/view/Advice/India [Accessed 19 February 2014].
5. DuPont HL, Steffen R, eds. Textbook of travel medicine and health. Hamilton: BC Decker; 2001.
6. Centers for Disease Control and Prevention. Travellers Health: information for people travelling to India. Available at: wwwnc.cdc.gov/travel [Accessed 19 February 2014].
7. National Institute for Clinical Excellence. Diarrhoea – prevention and advice for travellers. Clinical Knowledge Summaries, 2013. Available at http://cks.nice.org.uk/diarrhoea-prevention-and-advice-for-travellers#!scenario [Accessed 22 April 2014].
8. Expert Group for Gastrointestinal Infections. Traveller's diarrhoea. In: eTG complete [Internet]. Melbourne: Therapeutic Guidelines Ltd, 2014: Available at www.tg.org.au [Accessed 19 February 2014].
9. O'Connor BA. Travelers' Diarrhea. Travelers' Health. Atlanta: Centers for Disease Control and Prevention, 2013; chapter 2. Available at wwwnc.cdc.gov/travel/yellowbook/2014/chapter-2-the-pre-travel-consultation/travelers-diarrhea [Accessed 20 March 2014].
10. Expert Group for Gastrointestinal Infections. Infectious diarrhoea: other supportive agents. In: eTG complete [Internet]. Melbourne: Therapeutic Guidelines Ltd, 2014. Available at www.tg.org.au [Accessed 19 February 2014].
11. Centers for Diseases Control and Prevention. Health information for travellers to India: clinician view. Available at wwwnc.cdc.gov/travel/destinations/clinician/none/india [Accessed 20 March 2014].
12. World Health Organisation. International Travel and Health Interactive. Countries or areas at risk. Available at http://apps.who.int/ithmap [Accessed 25 February 2014].
13. Centers for Disease Control and Prevention. Dengue Map. Available at www.healthmap.org/dengue/en [Accessed 25 February 2014].
14. Centres for Diseases Control and Prevention. Chikungunya fever. Geographic Distribution of Chikungunya virus (as of February 10, 2014). Available at www.cdc.gov/chikungunya/map/index.html [Accessed 19 February 2014].
15. Looke DF, Robson JM. Infections in the returned traveller. Med J Aust 2002;177:212–19.
16. McAuliffe GN, Anderson TP, Stevens M, et al. Systematic application of multiplex PCR enhances the detection of bacteria, parasites, and viruses in stool samples. J Infect 2013;67:122–29.
17. Expert Group for Gastrointestinal Infections. Giardia intestinalis (giardiasis). In: eTG complete [Internet]. Melbourne: Therapeutic Guidelines Ltd, 2014. Available at www.tg.org.au [Accessed 19 February 2014].
18. Gargano JW, Yoder JS. Travelers' Health: giardiasis. Atlanta: Centers for Disease Control and Prevention, 2013; chapter 3. Available at wwwnc.cdc.gov/travel/yellowbook/2014/chapter-3-infectious-diseases-related-to-travel/giardiasis [Accessed 24 February 2014].
19. Expert Group for Gastrointestinal Infections. Blastocystis hominis. In: eTG complete [Internet]. Melbourne: Therapeutic Guidelines Ltd, 2014. Available at www.tg.org.au [Accessed 19 February 2014].
20. Tan KSW. New insights on classification, identification and clinical relevance of *Blastocystis* spp. Clin Micro Revs 2008;21:639–35.
21. Dupont G. Postinfectious irritable bowel syndrome. Clin Infect Dis 2008;46:594–99. Available at http://cid.oxfordjournals.org/content/46/4/594.full [Accessed 20 March 2014].

RESOURCES FOR PATIENTS AND DOCTORS

- Superbug stowaways: multi-drug-resistant bacteria hitch a ride with travellers. NPSMedicineWise: Health News and Evidence 2014, www.nps.org.au/health-professionals/health-news-evidence/2014/superbug-stowaways?utm_source=nps-direct&utm_medium=email%20&utm_campaign=2014-2-iss16&hq_e=el&hq_m=332138&hq_l=14&hq_v=fce54abbbf
- James Cook University School of Public Health, Tropical Medicine and Rehabilitation Sciences. Useful links and databases for travel medicine and links to travel medicine clinics locally and overseas. Links to electronic journals of relevance to travel medicine are also provided, www.jcu.edu.au/phtmrs/abc/JCUPRD_047258.html
- Centre for Disease Control advice for clinicians, wwwnc.cdc.gov/travel
- World Health Organisation. Information regarding international travel and health, www.who.int/ith/en/
- Australian Federal Government, Department of Foreign Affairs and Trade. Travel-smart hints for Australian travellers and travel advice, information and to register travel, http://smartraveller.gov.au/tips/travel-smart.html
- Travel Medicine Alliance. General information and links to Australian government health advisories, general medical information for travellers and links to medical clinics in various countries, information on specific conditions and general information for travellers, www.travelmedicine.com.au/travel-health-information/resources
- Travel Clinics Australia: Fact Sheets. Travel fact sheets to help people plan their travel, www.travelclinic.com.au/fact-sheets-page

CASE 2

SAM HAS WEIGHT GAIN

Sam is a man aged 50 years who has elevated aspartate transaminase (AST) and alanine transaminase (ALT). Tests for viral hepatitis and autoimmune liver disease have been negative. His only symptom is occasional right upper quadrant pain. When asked about his alcohol intake he tells you that he does not consume alcohol. His weight has increased by 15 kg in the last 10 years and his body mass index (BMI) is 34.8 kg/m^2.

He has a medical history of hypertension and high cholesterol. He has a family history of diabetes and ischaemic heart disease but no liver disease. His only medication is rampiril. His physical examination is unremarkable and vital signs are normal. There are no peripheral stigmata of chronic liver disease. His liver span measures 18 cm and there is no splenomegaly.

The results of his initial serum investigations are shown in *Table 1*.

Table 1. Serum investigation results

	Sam's results	Reference values
Bilirubin	0.7 mol/L	2–20 mol/L
AST	68 U/L	10–45 U/L
ALT	120 U/L	5–40 U/L
Alkaline phosphatase	68 U/L	25–100 U/L
International normalised ratio (INR)	1.1	
Platelet count	389 x 10^9/L	150–400 x 10^9/L
Ferritin	285 µg/L	30–300 µg/L
Fasting glucose	9 mmol/L	3.0–6.0 mmol/L
Triglycerides	3.2 mmol/L	<2 mmol/L
HDL	1.2 mmol/L	>1 mmol/L
LDL	3.3 mmol/L	<2.5 mmol/L
Cholesterol	6.2 mmol/L	<5.5 mmol/L

In addition, a liver ultrasound showed a bright, enlarged liver, consistent with fatty infiltration.

QUESTION 1

What is the most likely cause of raised transaminases and fatty liver?

QUESTION 2

Sam asks you how he can have fatty liver disease despite not drinking any alcohol. How do you explain this to him?

QUESTION 3

Sam's wife is concerned that she may have fatty liver after she finds out about her husband's diagnosis. Would you recommend screening for her, even though she is asymptomatic?

QUESTION 4

What further work-up would you consider?

QUESTION 5

What radiographic finding would you expect with different imaging modalities?

QUESTION 6

What is the role of liver biopsy in the assessment of NAFLD?

FURTHER INFORMATION

A liver biopsy is performed for Sam and the findings are considered to be consistent with steatohepatitis.

QUESTION 7

Sam asks you about the therapeutic options for the management of NASH. What would you tell him?

CASE 2 ANSWERS

ANSWER 1

Non-alcoholic fatty liver disease (NAFLD) is a clinical histopathological entity with evidence of hepatic steatosis, either by imaging or by histology and, by definition, occurs in patients with little or no history of alcohol consumption. The disease ranges from fat accumulation in liver cells to a necro-inflammatory component, known as non-alcoholic steatohepatitis (NASH).

NASH is histologically indistinguishable from alcoholic steatohepatitis[1,2] and may progress to cirrhosis in up to 20% of patients.[3] NAFLD does not correlate with increased short-term morbidity or mortality; however, progression of this condition to NASH markedly increases the risks of cirrhosis, liver failure and hepatocellular carcinoma (HCC). Cirrhosis due to NASH is an increasingly frequent reason for liver transplantation.

The prevalence of NAFLD has doubled in last the 20 years, as have its major risk factors, which include central obesity, type 2 diabetes mellitus, dyslipidaemia and metabolic syndrome[4] (*Table 2*). The median estimate of the worldwide prevalence of NAFLD is 20% in the general population, making it the most common liver disorder in western industrialised countries.[4] The estimated prevalence of NASH is lower, ranging from 3–5%.[5]

Central obesity plus any two of four risk factors listed in *Table 2* constitute a diagnosis of metabolic syndrome. Central obesity is assessed by measuring the waist circumference (halfway between the lower rib cage and iliac crest). According to the International Diabetes Federation, central obesity is defined as a waist circumference >90 cm in males and >80 cm in females; different ethnic groups have different cut-points.

Table 2. Clinical identification of the metabolic syndrome[6]	
Risk factors	**Defining levels**
Elevated fasting triglycerides	≥150 mg/dL (1.7 mmol/L)
Reduced fasting HDL cholesterol	Male <40 mg/dL (1.03 mmol/L) Female <50 mg/dL (1.29 mmol/l)
Blood pressure	Systolic ≥130 mmHg Diastolic ≥85 mmHg
Fasting glucose	≥100 mg/dL (5.6 mmol/L)

Most patients with NAFLD are asymptomatic, although some may complain of fatigue, malaise and vague right upper abdominal discomfort.[7,8] A detailed patient history of alcohol consumption (threshold <20 g/day in women, <30 g/day in men) is critical, as no diagnostic test can reliably distinguish between alcoholic hepatic steatosis and NASH.[4]

Biochemically, patients with NAFLD may have mild-to-moderate elevations in transaminases,[7,8] although normal aminotransferase levels do not exclude NAFLD.[9,10] When elevated, the AST and ALT are typically 2–5 times the upper limit of normal, with an AST to ALT ratio of less than 1. Serum albumin and bilirubin levels are typically normal.

ANSWER 2

The pathogenesis of non-alcoholic fatty liver disease has not been fully elucidated. The most widely supported theory implicates insulin resistance as the key mechanism.[11] Others have proposed the 'multi-hit' hypothesis.[11] A combination of diet, obesity, insulin resistance and genetic predisposition leads to increased free fatty acids known as the 'first hit'. This sensitises the liver to injury from 'second hits' such as oxidative stress, inflammatory cytokines and mitochondrial dysfunction, leading to the necro-inflammatory component steatohepatitis and fibrosis. This results in reduced ability of mature hepatocytes to proliferate (*Figure 1*).

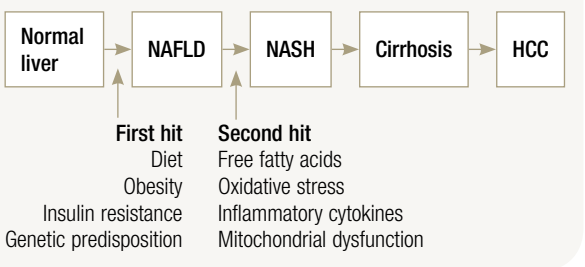

Figure 1. The multi-hit hypothesis (HCC = hepatocellular carcinoma)

Table 3 outlines the diagnostic requirement for a diagnosis of NAFLD.

Table 3. NAFLD diagnostic requirements[13]
Demonstration of hepatic steatosis by imaging or biopsy
Exclusion of significant alcohol consumption
Exclusion of other causes of hepatic steatosis
There are no co-existing causes for chronic liver disease

An alternative theory is that patients with the metabolic syndrome may have an over-accumulation of stored fat in the abdomen and liver (visceral fat), leading to NAFLD, which is the hepatic manifestation of the metabolic syndrome.[12]

ANSWER 3

Currently, the American Association for the Study of Liver Diseases guidelines do not recommend screening for NAFLD because there are uncertainties around which diagnostic test to use, how to treat NAFLD if discovered and whether screening is cost-effective.[13]

ANSWER 4

It is important to test all patients with hepatic steatosis for hepatitis infection to rule out this in patients with elevated aminotransferases and to determine immunity to guide future immunisations.[14] Sam has already tested negative for hepatitis. In addition to NAFLD, other causes of hepatic steatosis include alcoholic liver disease, hepatitis C, Wilson disease and starvation.[14] See *Table 4* for further tests.

Table 4. Tests to consider to exclude other causes of hepatic disease and steatosis[15,16]
Anti-hepatitis C virus antibody
Hepatitis A IgG
Hepatitis B surface antigen
Plasma iron, ferritin, and total iron binding capacity
Serum gamma-globulin level, antinuclear antibody, anti-smooth muscle antibody, and anti-liver/kidney microsomal antibody-1

ANSWER 5

Radiographic findings include a hyperechoic texture or a bright liver because of diffuse fatty infiltration on ultrasound, owing to increased acoustic interfaces because of intracellular accumulation of lipid vesicles. There is decreased hepatic attenuation on computed tomography, and an increased fat signal on magnetic resonance imaging. However, no imaging modality is able to differentiate between the histologic subtypes of NAFLD and NASH.[17] Magnetic resonance spectroscopy has the advantage of being quantitative and may be particularly helpful in patients with small amounts of hepatic steatosis, but it is not widely available.[18]

ANSWER 6

Liver biopsy is the gold standard for diagnosing NAFLD but in many cases a reasonable diagnosis can be made on the basis of the patient's history, laboratory tests and imaging findings, provided other disorders have been excluded.[4] The disadvantages of biopsy are cost, sampling error and procedure-related morbidity and mortality.

Some patients will continue to have an unclear diagnosis following a non-invasive evaluation and in such cases, a liver biopsy is indicated. In addition, liver biopsy is the only method currently available to differentiate between NAFLD and NASH. Furthermore, it can be used to grade the severity of NASH to guide patient care and may also motivate patients to enact lifestyle modifications.[4] For example, those found

to have cirrhosis will require screening for oesophageal varices and hepatocellular carcinoma (HCC), whereas patients with early fibrosis may be motivated to lose weight. Histological findings in NAFLD include steatosis (typically macrovesicular) with or without lobaular and portal inflammation, whereas in NASH there is also hepatocyte injury (typically ballooning degeneration) with or without fibrosis. Situations where a biopsy should be considered are outlined in *Table 5*.

Table 5. Scenarios when a liver biopsy should be considered[19]

Biochemical or clinical findings	Features suggestive of…
Serum ferritin >1.5 times the upper limit of normal >45 years of age with associated obesity or diabetes	NASH and advanced fibrosis
Peripheral stigmata of chronic liver disease Splenomegaly Cytopaenias (suggestive of cirrhosis)	Cirrhosis

Non-invasive methods for assessment of fibrosis rely on two different, but complementary, approaches: serum biomarkers of hepatic inflammation and transient elastography to measure liver stiffness, where an ultrasound pulse wave is transmitted through the liver and the wave velocity correlates with liver stiffness.[20]

The NAFLD Activity Score (NAS) is a new histopathological scoring system for NASH activity that ranges from 0–8 and assesses steatosis, lobular inflammation and hepatocyte ballooning. It is currently used in clinical trials. An NAS >5 indicates definite steatohepatitis.[21]

ANSWER 7

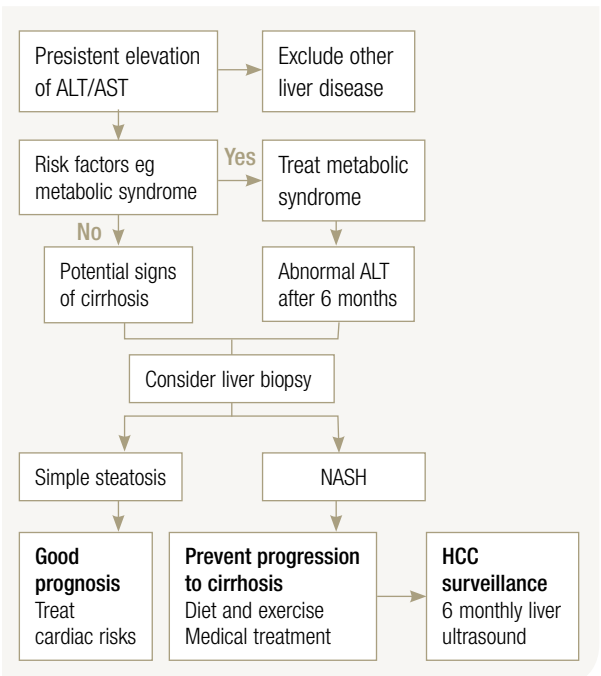

Figure 2. Proposed algorithm for management of NAFLD/NASH

At the present time, there is no evidence-based approved drug therapy.[4] A proposed management algorithim is shown in *Figure 2*. Lifestyle change is critical in any attempt to reverse the course of NASH.[13] NASH should be treated aggressively to prevent progression to cirrhosis, as these patients are frequently not candidates for liver transplantation because of their morbid obesity, cardiovascular disease or other complications of their underlying condition.[13] The goals of treatment for NASH are therefore to reduce the histological features and improve insulin resistance and liver enzyme levels.[13]

Proper control of diabetes, hyperlipidaemia and cardiovascular risks is recommended,[4,14] and referral to a dietician could be considered. Studies with atorvastatin and pravastatin have shown improvement in histology in patients with NASH.[22,23] NAFLD patients with dyslipidaemia should be treated with statins. Patients with underlying liver disease do not seem to have any additional risk of statin toxicity and serious hepatotoxicity from statins is rare.[14]

The overall goal of lifestyle change is to reduce excess weight; even a gradual 5–10% weight loss has been shown to improve liver histology and enzymes.[24] This is usually most successful if combined with a regular exercise program and elimination of a sedentary lifestyle. Drugs targeting insulin resistance, such as thiazolidinediones and metformin, are approved for diabetes but not for NAFLD/NASH, and should be considered experimental/off-label.[13] Foregut bariatric surgery may be beneficial for patients with morbid obesity.

CONCLUSION

A fasting glucose test confirmed a new diagnosis of diabetes mellitus. Sam was referred to an exercise physiologist and dietitian who prescribed a graded exercise program in combination with caloric restriction. This resulted in weight loss of more than 15 kg over 6 months. This weight loss was maintained for a further 6 months. His transaminase, glucose and lipid levels normalised without pharmacological intervention. A repeat liver biopsy 12 months after the initial biopsy demonstrated improved histology.

REFERENCES

1. Ludwig J, Viggiano TR, McGill DB, Oh BJ. Nonalcoholic steatohepatitis: Mayo Clinic experiences with a hitherto unnamed disease. Mayo Clin Proc 1980;55:434–38.
2. Sheth SG, Gordon FD, Chopra S. Nonalcoholic steatohepatitis. Ann Intern Med 1997;126:137–45.
3. Matteoni CA, Younossi ZM, Gramlich T, Boparai N, Liu YC, McCullough AJ. Nonalcoholic fatty liver disease: a spectrum of clinical and pathological severity. Gastroenterology 1999;116:1413–19.
4. Farrell G. Fatty liver disease. Sydney: Digestive Health Foundation, 2007. Available at: www.gesa.org.au/files/editor_upload/File/Professional/Fatty-Liver-1st-Edition.pdf [Accessed 25 February 2014].
5. Amarapurkar D, Kamani P, Patel N, et al. Prevalence of nonalcoholic fatty liver disease: population based study. Ann Hepatolo 2007;6:161–63.
6. Grundy SM, Cleeman JI, Daniels SR, et al. Diagnosis and Management of the Metabolic Syndrome: An American Heart Association/National Heart, Lung and Blood Institute Scientific Statement. Circulation 2005;112:2735–52. Available at http://circ.ahajournals.org/content/112/17/2735.full.pdf+html [Accessed 25 February 2014].

7. Farrell GC, Wong VW, Chitturi S. NAFLD in Asia – as common and important as in the West. Nat Rev Gastroenterol Hepatol 2013;10:307–18.
8. Bacon BR, Farahvash MJ, Janney CG, Neuschwander-Tetri BA. Nonalcoholic steatohepatitis: an expanded clinical entity. Gastroenterology 1994;107:1103–09.
9. Charatcharoenwitthaya P, Lindor KD, Angulo P. The spontaneous course of liver enzymes and its correlation in nonalcoholic fatty liver disease. Dig Dis Sci 2012;57:1925–31.
10. Mofrad P, Contos MJ, Haque M, et al. Clinical and histologic spectrum of nonalcoholic fatty liver disease associated with normal ALT values. Hepatology 2003;37:1286–92.
11. Polyzos SA, Kountouras J, Zavos C. Non-alcoholic fatty liver disease: the pathogenic roles of insulin resistance and adipocytokines. Curr Mol Med 2009:9:299–314.
12. Jeong SK, Kim YK, Park JW, Shin YJ, Kim DS. Impact of visceral fat on the metablic syndrome and nonalcoholic fatty liver disease. J Korean Med Sci 2008;23:789–95. Available at www.ncbi.nlm.nih.gov/pmc/articles/PMC2580019/ [Accessed 16 April 2014].
13. Chalasani N, Younossi Z, Lavine JE, et al. The diagnosis and management of non-alcoholic fatty liver disease: practice guideline by the American Association for the Study of Liver Diseases, American College of Gastroenterology, and the American Gastroenterological Association. Hepatology 2012;55:2005–23.
14. Iser D, Ryan M. Fatty liver disease. Aust Fam Phys 2013:42:444–47
15. Friedman S, Schiano T. Cirrhosis and its sequelae. In: Goldman L, Ausiello D, eds. Cecil Textbook of Medicine. 22nd ed. Philadelphia, Pa.: Saunders, 2004:936–44.
16. Crawford JM. Liver and biliary tract. In: Kumar V, Abbas AK, Fausto N, eds. Robbins and Cotran Pathologic Basis of Disease. 7th ed. Philadelphia, Pa.: Elsevier Saunders, 2005:877–938.
17. Schwenzer NF, Springer F, Schraml C, Stefan N, Machann J, Schick F. Non-invasive assessment and quantification of liver steatosis by ultrasound, computed tomography and magnetic resonance. Hepatology 2009;51:433–35.
18. Szczepaniak LS, Nurenberg P, Leonard D, et al. Magnetic resonance spectroscopy to measure hepatic triglyceride content: prevalence of hepatic steatosis in the general population. Am J Physiol Endocrinol Metab 2005;288:E462–68.
19. Rockey DC, Caldwell SH, Goodman ZD, Nelson RC, Smith AD. AASLD position paper: liver biopsy. Hepatology 2009;49:1017–44.
20. Rockey DC, Bissell DM. Noninvasive measures of liver fibrosis. Hepatology 2006;43(2 Suppl 1):S113–20.
21. Brunt EM, Kleiner DE, Wilson LA, Belt P, Neuschwander-Tetri BA. Nonalcoholic fatty liver disease (NAFLD) activity score and the histopathologic diagnosis in NAFLD: distinct clinicopathologic meanings. Hepatology 2011;53:810–20.
22. Hyogo H, Tazuma S, Arihiro K, et al. Efficacy of atorvastatin for the treatment of nonalcoholic steatohepatitis with dyslipidemia. Metabolism 2008;57:1711–18.
23. Rallidis LS, Drakoulis CK, Parasi AS. Pravastatin in patients with nonalcoholic steatohepatitis: results of a pilot study. Atherosclerosis 2004;174:193–96.
24. Promrat K, Kleiner DE, Niemeier HM, et al. Randomized controlled trial testing the effects of weight loss on nonalcoholic steatohepatitis. Hepatology 2010;51:121–29.

CASE 3

JAMES PRESENTS WITH ABDOMINAL SYMPTOMS

James is 55 years of age. For the past 2 weeks he has been having nausea, vomiting, lower abdominal cramps without diarrhoea, and he has lost weight. His medical history is otherwise non-contributory.

QUESTION 1

While you are taking James's history he mentions that since his wife's death 9 years ago, he drinks everyday. How could you ask James about his alcohol consumption?

FURTHER INFORMATION

You conduct a physical examination, which shows James is cachectic and in moderate respiratory distress, but alert and oriented to time, date and place. He has three spider angiomas on his upper chest. Abdominal examination reveals prominent veins on a very tense abdomen. The liver edge is percussed below the right costal margin and there is no ascites (accumulation of fluid in the peritoneal cavity). The spleen cannot be palpated. Cranial nerves II–XII are grossly intact but there is impaired vibratory sensation of the lower extremities.

QUESTION 2

On the basis of the physical examination, you order a blood test to investigate James's liver function (*Table 1*). How would these results inform your diagnosis?

Table 1. James's blood test results

	James results	Reference ranges
Bilirubin	16	2–17 µmol/L
Albumin	23	35–55 g/L
Aspartate aminotransferase (AST)	37	10–45 U/L
Alanine aminotransferase (ALT)	280	5–40 U/L
Gamma glutamyl transpeptidase (GGT)	137	5–51 U/L
Alkaline phosphatase	954	25–100 U/L

FURTHER INFORMATION

You explain that liver damage resulting from chronic heavy alcohol consumption can manifest as fatty liver, alcoholic hepatitis and cirrhosis. However, you tell James that the assumption that alcoholic liver disease always progresses linearly from alcoholic fatty liver to alcoholic hepatitis and, ultimately, to cirrhosis is not correct.

QUESTION 3

What are the signs and symptoms of alcoholic liver disease and chronic liver disease?

QUESTION 4

How would you manage James's alcoholic liver disease?

QUESTION 5

Are there any specific measures that could be taken to support James' nutrition?

FURTHER INFORMATION

James returns to see you 6 months later with bilateral swelling of his legs, increased distension of his abdomen and yellowing of his skin and the sclera of his eyes.

QUESTION 6

What questions would you ask James to help clarify the cause of his ascites?

QUESTION 7

What investigations would you perform?

FURTHER INFORMATION

James has a liver ultrasound, which confirms a cirrhotic liver.

QUESTION 8

What are the implications for James? What are the long-term management goals for cirrhosis?

CASE 3 ANSWERS

ANSWER 1

Obtaining an accurate history of alcohol use is of prime importance. Questioning the patient's family in private, after receiving permission from the patient to discuss their care with family members, may help extract information about the patient's alcohol use.

Alcohol intake is recorded in standardised units; in Australia, one standard drink contains 10 g of alcohol. The volume of a standard drink varies depending on the alcohol concentration of the beverage. For example, a standard drink of beer (4.8% alcohol) is about 285 ml, whereas a standard drink of wine (11.5% alcohol) is about 100 ml.[7]

Information about alcohol consumption obtained from the patient or their family can be supplemented by use of either the CAGE[8] (*Table 2*) or AUDIT[9–11] (*Table 3*) questionnaires, which may assist in establishing the likelihood of problem alcohol drinking. AUDIT is a 10-item questionnaire that is easy for patients to complete and for health professionals to score. AUDIT-C is a 3-item alcohol screen where a score of 4 or more in men or 3 or more in women is considered positive for identifying hazardous drinking or active alcohol use disorders.[12]

Table 2. Cage questionnaire[8]

C	Have you felt the need to **C**ut down?
A	Have you felt **A**nnoyed at the suggestion that you might have an alcohol problem?
G	Have you felt **G**uilty about excessive drinking?
E	Do you need an **E**ye opener in the morning?
Score 1 for each positive response; scores of 2 or more suggest an alcohol problem	

Table 3. Audit-C questionnaire

1. How often do you have a drink containing alcohol?				
Never	Monthly or less	2–4 times a month	2–3 times a week	4 or more times a week
0	1	2	3	4
2. How many drinks containing alcohol do you have on a typical day when you are drinking?				
1 or 2	3 or 4	5 or 6	7–9	10 or more
0	1	2	3	4
3. How often do you have six or more drinks on one occasion?				
Never	Less than monthly	Monthly	Weekly	Daily or almost daily
0	1	2	3	4

ANSWER 2

Aminotransferase abnormalities, generally <300 IU/L, are common in alcoholic liver disease. Although not seen in James's blood test results, a disproportionate increase in serum AST, compared with ALT, is highly suggestive of alcoholic liver injury, especially if the ratio of AST:ALT is >2.0. GGT is involved in the uptake of amino acids and is raised in chronic alcohol users.[2] Thrombocytopaenia may result from primary bone marrow hypoplasia and/or splenic sequestration due to portal hypertension and an enlarged spleen. Macrocytosis (determined by an elevated mean corpuscular volume) suggests longstanding disease and may reflect poor nutritional status, vitamin B12 or folate deficiency, alcohol toxicity and/or increased lipid deposition in red cell membranes.[3]

Patients may have low serum albumin levels caused by malnutrition and decreased synthesis in the setting of hepatic dysfunction. Iron absorption, synthesis, and uptake through liver receptors and mediators are diminished because of liver impairment. Ferritin synthesis, which occurs in the liver, is decreased in people with liver cirrhosis.[4]

If alcoholic hepatitis is suspected, it is important to check for leukocytosis as the magnitude of the white blood cell elevation correlates closely with the severity of the hepatic injury.[5] Furthermore, elevated bilirubin, hypoalbuminaemia and prolonged prothrombin levels are important indicators of severity.[6]

ANSWER 3

Early alcoholic liver disease may present with few signs and symptoms.[13] Patients may present with non-specific digestive tract symptoms such as nausea, dry retching, diarrhoea, anorexia and abdominal pain.[14] Patients may also seek medical attention because of the consequences of alcoholism, which may include accidents, violent behavior, depression, tremors, poor work performance or social disruptions. Late signs specific for alcoholic liver disease include Dupuytren contracture, parotidomegaly and proximal myopathy. Exocrine pancreatic failure from alcohol-induced chronic pancreatitis may result in pale, fatty motions that are difficult to flush.[15]

Complications of chronic liver disease may present with signs of portal hypertension, including splenomegaly, collateral veins and ascites. As the liver is responsible for the production of coagulation factors, the patient may bruise easily.[15] Patients are often malnourished, which manifests as proximal muscle wasting and decreased grip strength. Palmar erythema, spider naevi, gynecomastia, decreased body hair and testicular atrophy are thought to result from decreased hepatic metabolism and clearance of androstenedione, allowing increased peripheral conversion to estrogen.[16] Oedema, ascites and hepatic encephalopathy result from hepatocellular insufficiency and portal hypertension. In a patient with ascites, physical examination findings may include abdominal distention, bulging flanks, shifting dullness and a fluid wave. If the liver is not palpable, remember that it can be small, so continue percussing for the lower border of the liver above the costal margin.

ANSWER 4

Abstinence from alcohol and good nutrition are pivotal in the management of alcoholic liver disease as continued use of alcohol is associated with progression of disease.[17,18] Other important aspects of management include care when prescribing medications,

ensuring immunisations are up to date (eg pneumococcal, meningococcal, influenza, hepatitis A and B) and early referral for complications. It is particularly important to counsel individuals who are hepatitis C positive about avoiding alcohol because alcohol adds to the risk of developing hepatocellular cancer.[18]

In patients who have not yet progressed to cirrhosis, abstinence may allow for reversal of the alcohol-induced changes in the liver.[19] Simple, uncomplicated fatty liver is usually asymptomatic and self-limiting. It is estimated that 8–20% of patients with alcoholic fatty liver will develop alcoholic cirrhosis.[20] In patients with cirrhosis, alcohol abstinence decreases the risk of hepatic decompensation and improves survival. There is histological improvement, decreased rates of progression of cirrhosis, reductions in portal pressure, decreased rebleeding from varices and improved survival.[21,22]

Patients should be referred for treatment for alcohol abuse or dependence to increase the likelihood of successful abstinence.[10] Pharmacological therapy with agents such as baclofen may aid with abstinence.[23,24] Since many people with alcoholic liver disease have a long history of heavy alcohol use, they are at risk for alcohol withdrawal.[10]

ANSWER 5

All patients with alcoholic liver disease should undergo a nutritional assessment[17] because protein, carbohydrate and lipid metabolism are all affected by liver disease. Patients with alcoholic fatty liver who are not malnourished and do not have evidence of vitamin or mineral deficiencies should be encouraged to eat a healthy, balanced diet.

Nutritional support includes providing adequate calories and protein, as well as vitamins (eg thiamine, folate, and pyridoxine) and minerals (eg phosphate, magnesium) repletion.[25] Vitamin K is often ineffective because the coagulopathy is more a reflection of underlying liver failure than vitamin K deficiency.[26]

The American Association for the Study of Liver Diseases and the American College of Gastroenterology recommend that patients with alcoholic cirrhosis should eat several times per day, including breakfast and a night-time snack, which helps prevent the breakdown of muscle stores overnight.[17] To prevent Wernicke-Korsakoff syndrome, thiamine supplementation should be offered to people with alcoholic liver disease who cannot stop drinking).[9] Patients who develop ascites should be advised to avoid salt, including foods with a high salt content and the addition of salt to meals.[18]

ANSWER 6

Questions regarding the onset of symptoms may be useful for distinguishing between obesity and ascites. Patients generally seek medical advice early, within a few weeks of ascites presenting, as fluid usually accumulates rapidly and patients are intolerant of the distension and associated early satiety and shortness of breath. Conversely, the thickening abdominal wall and other signs associated with obesity develop over a longer period of time (months or years).

ANSWER 7

Physical examination and abdominal imaging, most often ultrasonography, will confirm the diagnosis of ascites. The overall accuracy of physical examination (and its findings) is dependent on a number of variables, including the amount of fluid present and examination technique. An important finding on physical examination that helps confirm ascites is detection of flank dullness. Shifting dullness with rotation of the patient may also be observed. The absence of flank dullness on physical examination is consistent with no ascites being present, with an accuracy of over 90%.[27]

Ascites suspected on the basis of history and physical examination should be confirmed with radiographical imaging.[28] Ultrasonography can detect fat in the liver, increased echogenicity of liver cirrhosis, splenomegaly and varices when portal hypertension develops, and the less common complication of hepatocellular carcinoma. It can also confirm the presence of ascites and show any fluid that might be located in discrete areas of the peritoneal cavity. It is an important investigation and may obviate the need for liver biopsy. Calcification of the pancreas can occur in alcohol-induced chronic pancreatitis. In patients with cirrhosis and portal hypertension, an ultrasound may show dilatation of veins, including the portal vein, to ≥13 mm, dilation of the splenic and superior mesenteric veins to ≥11 mm, as well as reduction in portal venous blood flow velocity, splenomegaly (diameter >12 cm) and recanalisation of the umbilical vein.[29] An ultrasound may also reveal evidence of hepatocellular carcinoma, which can be further evaluated with computed tomography (CT) or magnetic resonance imaging (MRI).

The ascitic fluid should be sent for analysis of appearance, cell count and differential diagnosis, as well as culture. Cirrhotic ascites has the characteristics of a transudate with a gap of more than 11 g/L between the serum and ascitic concentrations of albumin. The presence of an exudate (<11 g/L) can indicate complications such as spontaneous bacterial peritonitis or hepatocellular carcinoma, or that another disease process (eg malignancy, pancreatitis or tuberculosis) may be causing the ascites.[30]

Alpha fetoprotein could be considered as an adjunct to ultrasonography for hepatocellular carcinoma screening in patients with alcoholic cirrhosis.

ANSWER 8

Alcoholic cirrhosis represents a late stage of progressive liver damage whereby the hepatic architecture is distorted by fibrosis, which replaces hepatocytes, and the formation of regenerative nodules. It is usually irreversible in its advanced stages at which point the only option may be liver transplantation. Complications that are best treated by early referral to specialist care include variceal haemorrhage, ascites, neuropsychiatric complications and unexplained deterioration.[31] Unexplained deterioration may indicate the development of complications such as spontaneous bacterial peritonitis or hepatocellular carcinoma. Once these complications develop, patients are considered to have decompensated cirrhosis.

Portal hypertension is a major complication of cirrhosis. It arises when there is resistance to portal blood flow within in the liver due to

structural changes (eg fibrosis) and dynamic changes (eg increased vascular tone).[32] It leads to fluid retention and, ultimately, ascites in patients with cirrhosis. Ascites is problematic on many levels: directly, by causing symptoms of abdominal discomfort and early satiation; and indirectly, by facilitating complications of infections and multi-organ dysfunction such as spontaneous bacterial peritonitis and hepatorenal syndrome.[33]

The treatment approach in patients with ascites includes restricting dietary sodium intake, avoiding sodium-retaining drugs and performing large-volume paracentesis.[33] However, paracentesis should be reserved for patients with tense or refractory ascites and diuretic therapy should be initiated immediately after the procedure. Most patients are started on a combination diuretic regimen with frusemide and spironolactone, titrated to achieve a maximal weight loss of 0.5 kg/day, but this should be done in consultation with a gastroenterologist.[30]

REFERENCES

1. Australian Government Department of Health and Ageing. New national guidelines for alcohol consumption. Canberra: Commonwealth of Australia, 2013. Available at www.alcohol.gov.au/internet/alcohol/publishing.nsf/Content/36E6FEE732C8DF1BCA25767200769CD8/$File/adult.pdf [Accessed 25 March 2014].
2. Nishimura N, Teschke R. Alcohol and gamma-glutamyltransferase. Klin Wochenschr 1983;61:265–75.
3. Marayama S, Hirayama C, Yamamoto S, et al. Red blood cell status in alcoholic and non-alcoholic liver disease. J Lab Clin Med 2001;138:332–37.
4. Büyükaşik NS, Nadire I, Akin FE, et al. Serum iron parameters in cirrhosis and chronic hepatitis: detailed description. Turk J Gastroenterol 2011;22:606–11.
5. Amini M, Runyon BA. Alcoholic hepatitis 2010: a clinician's guide to diagnosis and therapy. World J Gastroenterol 2010;16:4905–12.
6. Udell JA, Wang CS, Tinmouth J, et al. Does this patient with liver disease have cirrhosis? JAMA 2012;307:832–42.
7. Australian Government Department of Health. The Australian standard drink. Available at www.alcohol.gov.au/internet/alcohol/publishing.nsf/Content/standard [Accessed 25 March 2014].
8. Ewing JA. Detecting alcoholism. The CAGE questionnaire. JAMA 1984;252:1905–07.
9. National Institute of Health and Clinical Excellence. Alcohol use disorders: preventing harmful drinking: quick reference guide. London: NICE Public Health Guidance 24, 2010. Available at www.nice.org.uk/nicemedia/live/13001/49024/49024.pdf [Accessed 4 March 2014].
10. Australian Government Department of Health and Ageing. Quick reference guide to the treatment of alcohol problems. Canberra: Commonwealth of Australia, 2009. Available at www.alcohol.gov.au/internet/alcohol/publishing.nsf/Content/864FDC6AD475CB2CCA257693007CDE3A/$File/treatqui.pdf [Accessed 25 March 2014].
11. Saunders JB, Aasland OG, Babor TF, et al. Development of the alcohol use disorders identification test (AUDIT): WHO Collaborative Project on Early Detection of Persons with Harmful Alcohol Consumption–II. Addiction 1993;88:791–804.
12. Babor TF, Higgins-Biddle JC, Saunders, JB, Monteiro MG. Audit: the Alcohol Use Disorders Identification Test : guidelines for use in primary health care, 2nd edition. Geneva: World Health Organization, 2001.
13. Better Health Channel. Know the facts: alcohol and the liver. State Government Victoria, 2012. Available at: www2.betterhealth.vic.gov.au/saywhen/know-the-facts/consequences-of-drinking-alcohol-and-the-liver [Accessed 25 March 2014].
14. Diehl AM. Liver disease in alcohol abusers: a clinical perspective. Alcohol 2002;27:7–11.
15. Talley N. O'Conner S. Clinical Examination. A systematic guide to physical diagnoses. 6th edn. Sydney: Churchill Livingstone; 2009.
16. Gordon GG. Conversion of androgens to estrogens in cirrhosis of the liver. Clin Endocrinol Metab 1975;40:1018–26.
17. O'Shea RS, Darasathy S, McCullough AJ. Alcoholic Liver Disease. Hepatology 51:307–28.
18. Duggan AE, Duggan JM. Alcoholic liver disease: assessment and management. Aust Fam Physician 2011:590–03.
19. Pessione F, Ramond MJ, Peters L, et al. Five-year survival predictive factors in patients with excessive alcohol intake and cirrhosis. Effect of alcoholic hepatitis, smoking and abstinence. Liver Int 2003;23:45–53.
20. Borowsky SA, Strome S, Lott E. Continued heavy drinking and survival in alcoholic cirrhotics. Gastroenterology 1981;80:1405–09.
21. Cuthbert JA, Arslanlar S, Yepuri J, Montrose M, Ahn CW, Shah JP. Predicting Short-Term Mortality and Long-Term Survival for Hospitalized US Patients with Alcoholic Hepatitis. Dig Dis Sci 2014; (epub ahead of print).
22. Raynard B, Balian A, Fallik D, et al. Risk factors of fibrosis in alcohol-induced liver disease. Hepatology 2002;35:635–38.
23. Addolorato G, Leggio L, Ferrulli A, et al. Effectiveness and safety of baclofen for maintenance of alcohol abstinence in alcohol-dependent patients with liver cirrhosis: randomised, double-blind controlled study. Lancet 2007;370:1915–22.
24. Forrest EH, Evans CD, Stewart S, et al. Analysis of factors predictive of mortality in alcoholic hepatitis and derivation and validation of the Glasgow alcoholic hepatitis score. Gut 2005;54:1174–79.
25. Mendenhall CL, Anderson S, Weesner RE, Goldberg SJ, Crolic KA. Protein-calorie malnutrition associated with alcoholic hepatitis. Veterans Administration Cooperative Study Group on Alcoholic Hepatitis. Am J Med 1894;76:211–22.
26. Saja MF et al. The coagulopathy of liver disease: does vitamin K help? Blood Coagul Fibrinolysis 2013;24:10–17.
27. Cattau EL Jr, Benjamin SB, Knuff TE, Castell DO. The accuracy of the physical examination in the diagnosis of suspected ascites. JAMA 1982;247:1164–66.
28. Runyon BA. Evaluation of adults with ascites. UpTodate 2014: Topic 1261 Version 19.0. Available at www.uptodate.com/contents/evaluation-of-adults-with-ascites [Accessed 5 March 2014].
29. Berzigotti A, Ashkenazi E, Reverter E, Abraldes JG, Bosch J. Non-invasive diagnostic and prognostic evaluation of liver cirrhosis and portal hypertension. Dis Markers 2011;31:129–38.
30. Gastrointestinal Expert Group. Advanced liver disease: Ascites. In: eTG Complete [Internet]. Melbourne:Therapeutic Guidelines Ltd, 2013. Available at www.tg.org.au [Accessed 14 April 2014].
31. Liou IW. Management of end-stage liver disease. Med Clin North Am 2014;98:119–52.
32. García-Pagán JC, Gracia-Sancho J, Bosch J. Functional aspects on the pathophysiology of portal hypertension in cirrhosis. J Hepatol 2012;57:458–61.
33. Kuiper JJ, van Burren HR, de Man RA. Ascites in cirrhosis: a review of management and complications. Neth J Med 2007;65:283–88.

CASE 4

SHIRLEY ASKS FOR REPEAT SCRIPTS

Shirley Smith, aged 75 years, has just moved to a local retirement village and comes to your practice for the first time. She presents 'just for repeat scripts'. Her medical history includes stable, medically treated ischaemic heart disease, hyperlipidaemia, depression and severe osteoarthritis affecting her back, hips and knees.

Her current medications are rosuvastatin 5 mg, isosorbide mononitrate 60 mg, aspirin 100 mg and meloxicam 15 mg, each daily, and sertraline 50 mg at night. She also takes paracetamol 500–1000 mg as neeeded. She is a non-smoker and rarely drinks alcohol.

QUESTION 1

What is your initial assessment of Shirley's situation?

FURTHER INFORMATION

On specific questioning, Shirley says she has had some mild indigestion, nausea and anorexia intermittently over the last few weeks. She has not noticed any weight loss. She has not had much indigestion before. Her bowel motions are normal. Shirley says that her other doctor advised her to stop taking meloxicam but she 'couldn't move' without it. Her previous doctor had also recommended exercise but she hates aqua aerobics. Examination reveals reduced mobility due to low back pain. Abdominal examination is normal. Her weight is 55 kg and BMI 23 kg/m^2.

QUESTION 2

Does Shirley need investigation(s)? If so, what will you arrange initially?

FURTHER INFORMATION

Full blood examination is normal. Biochemistry shows normal renal function and liver chemistry, which are unchanged from past results. Gastroscopy reveals mild erosive antral gastritis but no ulcer. Gastric biopsies show active chronic gastritis but no intestinal metaplasia. *H. pylori* is present.

QUESTION 3

What should happen next?

FURTHER INFORMATION

After determining that Shirley is not allergic to penicillin, you treat her with triple therapy comprising esomeprazole, amoxicillin and clarithromycin for 1 week, in accordance with current recommendations[1] for first-line *H. pylori* eradication therapy. She is apparently compliant but when a breath test is done some weeks later, the the infection is still present.

QUESTION 4

What do you do now?

FURTHER INFORMATION

Shirley was referred to a specialist and was given second-line *H. pylori* eradication therapy. When re-tested some weeks later, the breath test was negative. Her symptoms had diminished but were not abolished.

QUESTION 5

Is Shirley now adequately protected if she needs ongoing NSAID therapy? What changes to her management would you recommend now?

CASE 4 ANSWERS

ANSWER 1

Her current medications put her at a very high risk of peptic ulceration and bleeding in addition to the cardiovascular and renal risks of her non-steroidal anti-inflammatory drug (NSAID). All NSAIDs confer some risk of peptic ulceration (odds ratio [OR] up to 18) and gastrointestinal bleeding (OR up to 5).[2] Meloxicam, although often considered a COX-2-selective agent, is more a traditional non-selective NSAID. It is at the mid-to-high end of the risk spectrum, compared with some other NSAIDS, and the higher dose that Shirley is using further increases risk.[3] In any case, her use of low-dose aspirin would abolish any gastrointestinal-protective effect of COX-2-selective NSAIDs.[3,4] Aspirin confers a modest independent risk of gastrointestinal bleeding, additive with her NSAID risk.[5]

Selective serotonin reuptake inhibitors (SSRIs) increase the risk of gastrointestinal bleeding[6] independently of (OR 2.36) and synergistically with NSAIDs (OR 6.3).[7] The increased bleeding may be due to reduced serotonin uptake by the platelets leading to impaired platelet function and aggregation.[7] Enquiry should be made as to whether she is also using over-the-counter NSAIDs.

Lastly, it would be important to re-assess the indication for low-dose aspirin. A cardiovascular opinion could be sought if there was any doubt about the suitability of ceasing aspirin for Shirley.[4]

ANSWER 2

Shirley's symptoms need investigation given her age, medications and new-onset gastrointestinal symptoms. Upper abdominal pain or discomfort has been reported in up to 50% of people who use NSAIDs but symptom assessment cannot distinguish between NSAID-related dyspepsia and pain due to peptic ulceration. Up to 30% of people who use NSAIDs have ulcers at endoscopy. Many of these people are asymptomatic until complications occur.[1,8]

Blood tests that should be done include full blood examination, iron studies to exclude anaemia and biochemistry for renal function, liver chemistry and lipids. As she is elderly, has new upper gastrointestinal symptoms and is at high risk, she should be referred for gastroscopy. Her past medical file should be obtained for details of past investigations and management of her arthritis and comorbidities.

ANSWER 3

Shirley should have eradication therapy for *H. pylori*. This infection independently increases the risk of ulceration and bleeding and the risk is synergistic with NSAID use.[2] There is a 60-fold increase in the risk of peptic ulcer detected by endoscopy in those who are infected and take NSAIDs; the risk of bleeding is increased more than 6-fold, compared with those without either risk factor.[2] Moreover, the risk of complications (bleeding and perforation) is very much higher in the elderly, particularly those aged ≥75 years and those with comorbidities.[8]

Evidenced-based clinical guidelines recommend testing for and treating *H. pylori* in at-risk patients taking NSAIDs even in the absence of symptoms, as eradication has been shown to reduce the risk of ulceration and bleeding.[1,9,10] Presentation to hospital with complications is frequently the first manifestation of ulcer disease, especially in the elderly.

Despite the evidence of benefit, surveys show that *H. pylori* testing and treatment are often overlooked in this context.

Testing for the outcome of eradication therapy is required, usually with a urea breath test done more than 4 weeks after the end of therapy.[1] To minimise the chances of a false-negative result, antibiotics and bismuth should not be taken for a at least 1 month and proton pump inhibitors (PPIs) should be ceased for at least 1 week (preferably 2 weeks) before breath testing. Histamine H_2-receptor antagonist treatment may be continued as it does not interfere with testing.[1]

ANSWER 4

Eradication of *H. pylori* remains highly desirable as a risk-reduction strategy. Failure of first-line therapy is not uncommon in general practice. Clinical trials report success rates of 85–90% for first-line eradication; however, lower rates are achieved in practice.[11] Unfortunately, repeating the same triple therapy is a poor strategy as secondary clarithromycin resistance usually occurs after failed therapy and the likelihood of treatment success with the same therapy is slim (<10%).[1,9,10] This creates a dilemma for GPs as there is only one combination *H. pylori* triple therapy registered in Australia. In practice, some GPs repeat first-line therapy and others try ad hoc combinations that are either not evidenced-based or have been shown to be ineffective; such attempts are usually unsuccessful.

There are a number of proven second-line therapies to treat first-line eradication failures but these combinations require approval through the Special Access Scheme, as components of these therapies are not registered in Australia and often have to be brought in from abroad. Unless a GP has particular expertise in this area, patients with difficult-to-eradicate *H. pylori* should be referred for expert advice. These therapies are outlined in the current edition of *Therapeutic Guidelines: Gastrointestinal*[1] and elsewhere.[9,10]

ANSWER 5

Although eradication of *H. pylori* reduces her risk of gastrointestinal problems, Shirley remains at a significant ongoing risk of ulceration and gastrointestinal bleeding as she is elderly, has comorbidities and is taking an NSAID and an SSRI (her aspirin was ceased). She has ongoing NSAID-related cardiovascular risks also.

Her arthritis and pain management need revision. The next steps are to determine if she can do without regular NSAID therapy by substituting regular analgesics (rather than prn), typically paracetamol. Note that this strategy reduces the risks of ulceration and bleeding but, anecdotally, may be associated with liver toxicity, particularly in a low-weight older patient. However, a recent review suggests that the risk of hepatotoxicity from therapeutic doses of paracetamol is extremely low.[12] Non-drug physical therapies or other therapies to treat her pain and reduced mobility should be fully explored.

If Shirley cannot manage without NSAID therapy, an agent that balances gastrointestinal and cardiovascular risk is required. At present, naproxen has been associated with the lowest cardiovascular risk profile and, given her history of ischaemic heart disease, is preferred over a COX-2-selective agent, even though the latter have a somewhat lower risk of adverse gastrointestinal effects.[13] Naproxen is considered mid-range for gastrointestinal risk.[3] The lowest necessary dose should be used with review as to whether it is needed regularly or intermittently.

Her need for an SSRI should be reviewed, as it is an independent risk factor for bleeding, as discussed earlier, and should be ceased if possible.

Lastly, given Shirley's multiple ongoing risk factors for peptic ulcer disease and bleeding, a standard dose of a PPI once daily should be prescribed as prophylaxis if NSAIDs are continued. The evidence shows that such primary prophylaxis reduces ulceration in patients treated with either non-selective or COX-2–selective NSAIDs, and it is recommended for patients at higher risk.[14–16] Treatment with PPIs can be ceased if NSAIDs are no longer required.

REFERENCES

1. Expert Group for Gastrointestinal. Gastric disorders. Therapeutic Guidelines. In: eTG Complete [Internet]. Melbourne: Therapeutic Guidelines Ltd, 2013. Available at www.tg.org.au [Accessed 24 March 2014].
2. Huang JQ, Sridhar S, Hunt RH. Role of *Helicobacter pylori* infection and non-steroidal anti-inflammatory drugs in peptic-ulcer disease: a meta-analysis. Lancet 2002;359:14–22.
3. Castellsague J, Riera-Guardia N, Calingaert B, et al. Safety of non-steroidal anti-inflammatory drugs (SOS) project. Individual NSAIDs and upper gastrointestinal complications: a systematic review and meta-analysis of observational studies (the SOS project). Drug Safety 2012;35:1127–46.
4. National Vascular Disease Prevention Alliance. Absolute cardiovascular disease management. Quick reference guide for health professionals, 2012. National Stroke Foundation. Available at http://strokefoundation.com.au/site/media/NVDPA-Managment-Guideline-Quick-Reference-Guide.pdf [Accessed online 24 March 2014].
5. Sørensen HT, Mellemkjaer L, Blot WJ, et al. Risk of upper gastrointestinal bleeding associated with use of low-dose aspirin. Am J Gastroenterol 2000;95:2218–24.
6. Expert Group for Psychotropic. Management of antidepressant adverse effects. In: eTG Complete [Internet]. Melbourne:Therapeutic Guidelines Ltd, 2013. Available at www.tg.org.au [Accessed 24 March 2014].
7. Loke YK, Trivedi AN, Singh S. Meta-analysis: gastrointestinal bleeding due to interaction between selective serotonin uptake inhibitors and non-steroidal anti-inflammatory drugs. Aliment Pharmacol Ther 2008;27:31–40.
8. Gutthann SP, García Rodríguez LA, Raiford DS. Individual nonsteroidal antiinflammatory drugs and other risk factors for upper gastrointestinal bleeding and perforation. Epidemiology 1997;8:18–24.
9. Fock KM, Katelaris P, Sugano K, et al. Second Asia-Pacific Consensus Guidelines for *Helicobacter pylori* infection. J Gastroenterol Hepatol 2009;24:1587–600.
10. Malfertheiner P, Megraud F, O'Morain CA, et al. European Helicobacter Study Group. Management of *Helicobacter pylori* infection – the Maastricht IV/Florence Consensus Report. Gut 2012;61:646–64.

11. Antibiotics Expert Group. Antibiotics: eradication of *Helicobacter pylori* and ulcer healing. In: eTG Complete [Internet]. Melbourne: Therapeutic Guidelines Ltd, 2013. Available at www.tg.org.au [Accessed 3 March 2014].
12. Graham GG, Davies MJ, Day RO, Mohamudally A. Scott KF. The modern pharmacology of paracetamol: therapeutic actions, mechanism of action, metabolism, toxicity and recent pharmacological findings. Inflammopharmacol 2013;21:201–32.
13. Coxib and traditional NSAID Trialists' (CNT) Collaboration. Vascular and upper gastrointestinal effects of non-steroidal anti-inflammatory drugs: meta-analyses of individual participant data from randomised trials. Lancet 2013;382:769–79.
14. Scheiman JM, Yeomans ND, Talley NJ, et al. Prevention of ulcers by esomeprazole in at-risk patients using non-selective NSAIDs and COX-2 inhibitors. Am J Gastroenterol 2006;101:701–10.
15. Rostom A, Muir K, Dube C, Lanas A, Jolicoeur E, Tugwell P. Prevention of NSAID-related upper gastrointestinal toxicity: a meta-analysis of traditional NSAIDs with gastroprotection and COX-2 inhibitors. Drug Health Patient Saf 2009;1:47–71.
16. Rostom A, Moayyedi P, Hunt R; Canadian Association of Gastroenterology Consensus Group. Canadian consensus guidelines on long-term non-steroidal anti-inflammatory drug therapy and the need for gastroprotection: benefits versus risks. Aliment Pharmacol Ther 2009;29:481–96.

CASE 5

KEN IS REJECTED BY THE BLOOD BANK

Ken, an electrician aged 35 years, lives with his wife and two sons aged 12 and 10 years. He was a regular plasma donor for many years, but stopped several years ago because of time pressures at work. He decides to resume donating blood after hearing about the shortage of plasma donations at the blood bank. Before his donation, the blood bank informs him that his blood count (from a skin prick test) is at the lower limit of normal.

A few days after the donation, he receives a follow-up letter from the blood bank informing him that his ferritin levels are low and that a blood film showed hypochromic microcytic changes. The letter advises him to see his GP and informs him that he cannot make further blood donations at the present time. He is annoyed about this and comes to see you, his wife's GP. He hasn't seen a GP for 10 years, is not vegetarian and says he is otherwise well.

When asked about other symptoms, he admits to feeling a bit tired. He has also been having mild intermittent flatulence, bloating and loose stools for many years. He has always attributed his bowel symptoms to irritable bowel syndrome (IBS) because his mother has the same problem. Ken's weight has been stable for many years.

Ken's physical examination is normal. His BMI is 20 kg/m^2.

QUESTION 1

What is the most likely diagnosis?

QUESTION 2

What specific investigations will you order for Ken to make the diagnosis you think is most likely?

QUESTION 3

What are common presenting symptoms of coeliac disease?

FURTHER INFORMATION

Ken undergoes all of the investigations you recommended and returns for the results. The tests confirm the diagnosis you thought was most likely.

QUESTION 4

How would you explain Ken's condition to him using lay terms?

QUESTION 5

Outline your management of Ken's condition using the following subheadings: initial, ongoing monitoring, follow-up and annual review.

QUESTION 6

Who in Ken's family should be offered screening?

CASE 5 ANSWERS

ANSWER 1

The most likely diagnosis is coeliac disease as Ken has a range of symptoms commonly associated with this condition.[1,2] Differential diagnoses include IBS with another cause of iron deficiency anaemia, non-coeliac gluten intolerance with another cause of iron deficiency anaemia, inflammatory bowel disease, diverticular disease and bowel cancer (unlikely).[1]

Coeliac disease is a common, yet underdiagnosed condition that has a broad spectrum of presentations. Diagnosing coeliac disease, therefore, requires a high level of suspicion. It affects at least one in 100 Australians;[3,4] however, about three in four patients remain undiagnosed.[3] The age of onset ranges from 6 months to >90 years.[2]

ANSWER 2

Investigations to diagnose coeliac disease include serological testing for coeliac-specific antibodies and duodenal mucosal biopsy confirmation.[1,3] The most sensitive and specific blood tests for coeliac disease are tissue transglutaminase antibody (tTG) and deamidated gliaden peptide (DGP) antibody.[1,2] It is also important to order a total immunoglobulin A (IgA) level[1] because 2–5% of patients with coeliac disease have IgA deficiency, which makes their coeliac antibody tests unreliable.[3]

Patients must be consuming sufficient gluten (equivalent of four slices of bread per day for 6 weeks) for coeliac serology and small bowel biopsy to be accurate diagnostic investigations.[1,2,5] If a patient is already on a gluten-free diet and refuses to re-introduce gluten into the diet because they feel so much better without it, genetic testing for HLA DQ8 and HLA DQ2, performed by taking a buccal smear or blood sample, may help. However, the result is only useful if it is negative (99.6% of patients with coeliac disease have one of HLA DQ8 or HLA DQ2, but so do one-third of the general Australian population[3]). In other words, the genetic test is one of exclusion only. Only one in 30 people with these genes develop coeliac disease.[3,6] In Ken's case, it is also appropriate to order a full blood examination, iron studies and assess vitamin B12, folate levels and vitamin D.[2]

The gold standard for the diagnosis of coeliac disease is currently a small bowel biopsy.[1,2] However, more sensitive and specific blood tests may be available in future. The key finding on small biopsy is villous atrophy. Small bowel damage is usually patchy, so four samples, taken from different points of the duodenum, are required to ensure the result is not a false negative.[3]

If there is a strong clinical suspicion of coeliac disease and serology is negative, a small bowel biopsy should still be considered.[2]

ANSWER 3

Common symptoms of coeliac disease may include:

- IBS-type symptoms:[1,2,5]
  - bloating, flatulence and a variation in bowel habit (eg loose

stools/diarrhoea or constipation, or a combination of both)
  - abdominal pain and/or discomfort
- nausea[3]
- fatigue[3]
- iron deficiency anaemia[3] (eg discovered by the blood bank)
- nutritional deficiencies[3] (eg iron and folate, zinc, vitamin B12 and vitamin D)
- failure to thrive in children.[3]

Less common but important presentations include:

- osteoporosis – onset may be early due to a lack of absorption of calcium and vitamin D[5]
- infertility[3]
- recurrent miscarriage[5]
- mood disorders (eg depression, bipolar)[5]
- recurrent mouth ulcers[5]
- polyneuropathy/peripheral neuropathy[5]
- cerebellar ataxia[3]
- dermatitis herpetiformis[7]
- abnormal liver function tests.[5]

ANSWER 4

The following text is an example of how you might explain the diagnosis to Ken.

'Ken, coeliac disease is a condition in which the body reacts to gluten, a protein found in wheat, barley, rye and oats. The reaction causes damage to the small bowel. If you look at a part of the small bowel under a microscope, it has tiny fingers called villi that line the bowel. They have an important role in absorbing nutrients from the food we eat after being broken down. In coeliac disease, the villi are flat and inflamed, so you are not absorbing the required nutrients from your food. This has caused you to be low in iron and possibly other nutrients, which we need to test you for.'

You could use a diagram and/or your fingers to illustrate this.

ANSWER 5

Initial management[2,3,6]

Ideally, this should involve the person in the family who does most of the cooking and shopping, in this case, Ken's wife. The cornerstone management of coeliac disease is a lifelong gluten-free diet. This allows the damaged villi to recover and grow back, leading to an improvement in symptoms. It also prevents long-term complications, such as bowel lymphoma, osteoporosis, infertility and chronic ill-health in symptomatic or asymptomatic patients with coeliac disease. For a person with coeliac disease who maintains a gluten-free diet, the risk of these complications is no greater than that for people without coeliac disease.

Ken should be advised to join the Coeliac Society in his state or territory (www.coeliac.org.au or phone 1300 GLUTEN) as soon as possible. He also needs a doctor's letter confirming his diagnosis for the Coeliac Society.

The Coeliac Society offers various resources, including a list of gluten-free foods and coeliac-friendly restaurants, recipes and gluten-free products, an ingredient book that indicates whether or not something is gluten-free, dietitians with a special interest in coeliac disease, support groups, a magazine with updates on research, supermarket tours that explain how to read food labels and tips for travelling.

Additional initial management steps for Ken include:

- Commencement of a gluten-free diet, starting with 1) naturally occurring gluten-free foods (eg fruit, vegetables, eggs and meat), and 2) products labelled 'gluten-free'. Further information is available from the Gastroenterological Society of Australia (GESA) website[2] and the Coeliac Society.[6] It is essential that patients and their partners/carers learn how to read food labels accurately so they can avoid the accidental ingestion of gluten, which may be present in less obvious sources such as sausages, processed meats, soups, ice creams, sauces, dressings and stock cubes.
- Identify gluten-free foods using, for example, the ingredients list booklet (available for members from the Coeliac Society) or the Coeliac Society of Australia's smartphone app that identifies gluten-free products not marked as such but contain only gluten-free ingredients.
- Diagnose and treat any nutritional deficiencies (eg iron, vitamin B12, folate, calcium, phosphate, magnesium, zinc and vitamin D).
- Educate Ken to check that all of his medications are gluten-free. These medications include all over-the-counter medicines, vitamins and herbal preparations. He may need to ask his doctor or pharmacist to check if a product is gluten-free. Useful resources for this include MIMS or Consumer Medical Information (www.nps.org.au or phone 1300 633 424).
- Screen Ken for the more common conditions associated with coeliac disease. These include type 1 diabetes mellitus, hypothyroidism, thyrotoxicosis, glomerulonephritis and pernicious anaemia. Investigations for these conditions include renal function tests (urea, electrolytes and creatinine), liver function tests, thyroid function tests and fasting blood glucose.[5]
- Perform a bone mineral density test (DEXA) of the hips and spine. All adults with coeliac disease should have a DEXA scan to screen for osteoporosis or osteopenia at the time of diagnosis.[2] People with medically diagnosed coeliac disease are able to claim the Medicare rebate for a DEXA scan done every 2 years if required (one in three adults with newly diagnosed coeliac disease has decreased bone density).
- Refer Ken to a dietitian, preferably one who specialises in coeliac disease (contact the Coeliac Society or the Dieticians Association of Australia for a list). Patients tend to gain weight after their villi regenerate as they absorb more nutrients.
- Assess and monitor Ken's mental state. Emotional reactions to the diagnosis of coeliac disease can vary from relief to shock, despair, grief, disbelief, guilt for passing it on to one's children, or a feeling of being overwhelmed.

- Provide supportive counselling and/or refer Ken to a psychologist if needed.
- Consider preparing a care plan for Ken.

Ongoing monitoring and follow-up after initial diagnosis[2,3,6]

People with coeliac disease require regular monitoring and follow-up, focusing on nutritional deficiencies and dietary compliance. Gluten can sometimes be ingested unintentionally, and this is the most common cause of persistently elevated coeliac serology tests.

At 6 months repeat coeliac serology (tTG DGP and total IgA) and other relevant blood tests, depending on abnormalities at diagnosis (eg low nutrients).

At 12 months repeat relevant tests (ie full blood examination [FBE], iron studies, vitamin B12, folate, calcium, phosphate, magnesium, zinc, vitamin D, thyroid function tests [TFTs], liver function tests [LFTs], urea, electrolytes creatinine [UEC], fasting blood glucose and coeliac serology) to monitor long-term progress and adherence to the gluten-free diet.

At 12–24 months repeat duodenal biopsy to review the histology of villi.[6] Some debate exists as to whether this should be standard practice for patients who are responding well to a gluten-free diet.[3]

Annual review[2]

Coeliac serology and repeat blood tests should be ordered on a 12-monthly basis to assess dietary compliance, nutritional deficiencies and possible complications. Follow-up with a referral to a dietitian if needed.

ANSWER 6

All first-degree relatives of a patient with confirmed coeliac disease should be advised to have screening using coeliac serology.[1] In Ken's case, first-degree relatives are his parents, any siblings and his children. It is particularly important to screen his mother if she has never been screened, given she has been told she has IBS. The risk of coeliac disease in an individual who has a family member with this condition is 10%.[3,6,8] The identical twin of a patient with coeliac disease has a 70% chance of developing coeliac disease, indicating a multifactorial aetiology for coeliac disease.[6]

REFERENCES

1. Rubio-Tapia A, Hill, ID, Kelly CP, Calderwood AH, Murray JA. ACG clinical guidelines: diagnosis and management of celiac disease. Am J Gastro 2013;108:656–76.
2. Gastroenterological Society of Australia. Coeliac Disease: clinical update. Sydney: Digestive Health Foundation, 2007. Available at www.gesa.org.au/files/editor_upload/File/Professional/Coeliac_Disease4Ed07.pdf [Accessed 24 March 2014].
3. Ellard K, Shepherd, S. Coeliac disease. How to Treat. Australian Doctor 2012;pp 31–8.
4. Anderson RP, Henry MJ, Taylor R, et al, A novel serogenetic approach determines the community prevalence of celiac disease and informs improved diagnostic pathways. BMC Med 2013;11:188–203.
5. National Institute for Health and Clinical Excellence. Coeliac disease: recognition and assessment of coeliac disease. Quick reference guide. NICE clinical guideline 86, issued May 2009. Available at www.nice.org.uk/nicemedia/live/12166/44355/44355.pdf [Accessed 5 March 2014].
6. Coeliac Society of Australia. Available at www.coeliacsociety.com.au/coeliac-disease (Accessed 4 March 2014).
7. Welsh, B. Blistering skin conditions. Aust Fam Physician 2009;38:484–90.
8. Rubio-Tapia A, van Dyke CT, Lahr BD, et al. Predictors of family risk for celiac disease: a population-based study. Clin Gastroenterol Hepatol 2008;6:983–87.

RESOURCES FOR PATIENTS AND DOCTORS

- Coeliac Australia has a number of useful resources. www.coeliac.org.au/resources/
- Gastroenterological Society of Australia. www.gesa.org.au/consumer.asp?id=45

RESOURCES FOR DOCTORS

- Welsh, B. Blistering skin conditions. Aust Fam Physician 2009;38:484–90. This article contains information about the features and management of dermatitis herpetiformis, a rare but important presentation of coeliac disease.
- Gibson P. Irritable bowel syndrome. How to Treat. Australian Doctor 13 April 2012:27–34 (includes fructose malabsorption).

Gastroenterology

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

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

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

The expected time to complete this activity is 3 hours.

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

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

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

QUESTION 1

Which statement about coeliac disease is CORRECT?

A. Coeliac disease affects at least one in 1000 Australians, the age of onset ranges from 6 months to ≥90 years and the risk of coeliac disease in an individual with an affected family member is around 70%.

B. Coeliac disease affects at least one in 10,000 Australians, the age of onset ranges from 6 months ≥90 years and the risk of coeliac disease in an individual with an affected family member is around 10%.

C. Coeliac disease affects at least one in 100 Australians, the age of onset ranges from 6 months to ≥90 years and the risk of coeliac disease in an individual with an affected family member is around 70%.

D. Coeliac disease affects at least one in 1000 Australians, the age of onset ranges from 6 months to middle age (40–50 years) and the risk of coeliac disease in an individual with an affected family member is around 10%.

E. Coeliac disease affects at least one in 100 Australians, the age of onset ranges from 6 months to ≥90 years and the risk of coeliac disease in an individual with an affected family member is around 10%.

QUESTION 2

Jade, aged 18 years, and her boy friend Flyn, aged 19 years, are planning to take a gap year and travel around the world. They plan to visit a number of regions and countries, including South East Asia, the United States of America, Brazil (for the soccer World Cup), England, France, Spain and Portugal, as well as Germany to visit Jade's relatives. Initially, they will spend 2 months travelling through South East Asia. They have come to see you for a pre-travel consultation under advice from Jade's mother who is a registered nurse. Which of the following is CORRECT?

A. Any travel medicine advice provided to them should take into account their destinations, duration of travel, time of year, activities to be undertaken and their personal health.

B. It will be important to ensure that Jade and Flyn receive appropriate vaccinations, given the diversity of the regions/countries that they are travelling to.

C. Jade and Flyn should be provided with detailed information on preventative measures and be given detailed printed information on problems they might encounter (eg traveller's diarrhoea) as well as medications for the treatment of diarrhoea.

D. Answers A, B and C are correct.

E. Answers A and B are correct.

QUESTION 3

David is a retired lawyer, aged 67 years, who presents complaining of burning pain in his abdomen, nausea and indigestion-like symptoms that he believes have crept up on him over a period of months. He has hypertension, which was diagnosed 3 years ago and for which he takes ramipril 10 mg daily. In recent years he has been taking paracetamol and ibuprofen for joint pain. David claims the pain was pretty bad this winter and he was using a lot more painkillers than usual. He used to take low-dose aspirin until recently, when a GP in your practice advised him to stop taking it. He was treated for *Helicobacter pylori* infection last year. On questioning, he thinks his current gastric symptoms are mild, compared with his symptoms prior to diagnosis of *H. pylori* infection. Which of the following statements is the most CORRECT?

A. David's symptoms are due to his use of ibuprofen or some other gastric problem, not *H. pylori* infection.

B. David should have baseline blood investigations and *H. pylori* testing and, depending on the outcomes of these investigations, might need a referral for gastroscopy; he could also benefit from referral to a rheumatologist to assess his joint pain.

C. David should be asked to cease use of his ibuprofen and see you again in 2 weeks for a review.

D. On the basis of David's history and presenting symptoms, he should be tested for *H. pylori* infection, treated, if positive, and referred to a rheumatologist to get assess his joint pain.

E. On the basis of David's history and presenting symptoms, he should be prescribed a proton pump inhibitor and referred to a rheumatologist to assess his joint pain.

QUESTION 4

Which of the following statements regarding NAFLD/NASH is CORRECT?

A. By definition, NAFLD is a condition that involves hepatic steatosis on imaging or by histology and occurs in patients with little or no history of alcohol consumption.

B. NASH may progress to cirrhosis in up to 80% of patients.

C. The prevalence of NAFLD has tripled in last the 20 years and its major risk factors (eg central obesity, type 2 diabetes mellitus, dyslipidaemia, and metabolic syndrome) are increasingly prevalent.

D. Screening for NAFLD in high-risk groups is recommended and this could be incorporated into the health assessment for people aged 45–49 years who are at risk of developing chronic disease.

E. Evidence-based drug therapy for NASH includes the use of diabetes drugs targeting insulin resistance.

QUESTION 5

Which of the following statements regarding alcoholic liver disease is CORRECT?

A. In the case of suspected alcoholism or alcohol-related conditions, it is not necessary to obtain a patient's permission to interview family members to help determine the patient's alcohol consumption.

B. Patients with alcoholic fatty liver who are not malnourished on presentation do not require nutritional assessment.

C. In patients with alcoholic liver disease who have not progressed to cirrhosis, abstinence may allow for reversal of the hepatic changes induced by alcohol.

D. Alcoholic cirrhosis represents an early stage of progressive hepatic fibrosis and liver damage in those with alcoholic liver disease.

E. People with alcoholic liver disease and ascites do not need to restrict their use of dietary sodium.

QUESTION 6

Judy is a pianist, aged 29 years, and has a long history of irritable bowel type symptoms and anaemia. She has recently been diagnosed with coeliac disease. She presents with her partner to discuss her results and management. Which of the following statements outlines the BEST management plan for Judy?

A. Judy needs to be educated about coeliac disease.

B. Judy needs to be educated about coeliac disease and her first-degree relatives should be screened for the condition.

C. Judy's first-degree relatives need to be encouraged to be screened for the condition.

D. Judy needs to be educated about coeliac disease and its management (eg gluten-free diet, screening for associated conditions, regular review and screening of first-degree relatives).

E. Judy needs to commence a gluten-free diet immediately and be assessed for nutritional deficiencies, which if identified, should be treated.

QUESTION 7

Which of the following statements is CORRECT with regards to travel to India?

A. The risks of food-borne and water infections are potentially high in India and prevention strategies, including vaccinations, should be discussed and encouraged as a minimum.

B. For people travelling to India, antibiotic prophylaxis is not (routinely) recommended to prevent traveller's diarrhoea; however, where treatment is required, current antimicrobial resistance patterns support the use of azithromycin as a first-line antibiotic, at a dose of 500 mg twice daily for 3 days.

C. For people travelling to India, antibiotic prophylaxis is not (routinely) recommended to prevent traveller's diarrhoea; however, patients should be provided with information on traveller's diarrhoea and medications, should a problem arise.

D. Answers A, B and C are correct.

E. Answers A and C are correct.

QUESTION 8

Which of the following statements is CORRECT regarding gastric ulcers?

A. Up to 70% of people using NSAIDs are likely to have an ulcer on endoscopy but not all of these people are likely to be symptomatic.

B. Not all NSAIDs are associated with gastric ulcers and gut bleeding.

C. The potential benefits of prescribing a COX-2-selective NSAID are abolished when a person uses aspirin concurrently with the COX-2-selective NSAID.

D. H. pylori infection independently increases the risk of a gastric ulcer and gastric bleeding but concurrent use of NSAIDs attenuates this risk.

E. If testing shows that first-line *H. pylori* eradication has failed, triple therapy should be repeated.

QUESTION 9

Serena is a widow aged 57 years. She presents requesting repeat prescriptions for her blood pressure medications. She complains of tiredness and a nagging persistent pain in the upper right part of her abdomen. On examination her liver feels slightly enlarged. Her blood pressure is 151/81 mmHg today and her BMI is 33.6 kg/m^2. Since her husband's death a few years ago, Serena has gained weight and has gone up two dress sizes. She rarely drinks, perhaps consuming half a glass of champagne once or twice a year at a wedding or a christening. Which of the following statements is the most CORRECT?

A. Serena should have blood samples taken for investigation of her liver function and she may require additional investigations such as an ultrasound or biopsy, depending on the findings.

B. Given her presenting history, Serena may have NAFLD as most patients are asymptomatic and the symptoms she reports often occur in NAFLD.

C. If Serena is diagnosed with NAFLD/NASH she would need to be advised to lose weight and make other lifestyle modifications to slow progression.

D. Differential diagnosis for her presenting symptoms may need to include testing for hepatitis A, B and C.

E. All of the above are true.

QUESTION 10

Andrew, 45 years of age, is a divorced war veteran who suffered from post-traumatic stress disorder after the Afghanistan war and had major depression. He also has a longstanding drinking problem and alcoholic liver disease. He takes medication for his depression and uses paracetamol and a prescribed NSAID regularly to manage pain from a war injury. He takes a herbal product that his mother bought for him to help him sleep. His regular GP is on leave and he has come to see you to discuss the results of his recent liver ultrasound, which shows a cirrhotic liver. Which of the following statements is CORRECT?

A. Portal hypertension is a major complication of cirrhosis and it has been implicated in the development of ascites; however, ascites itself is a benign condition.

B. Patients with cirrhosis are at increased risk of medication adverse events because of impaired hepatic metabolism and some medications may require dose adjustments, while others should be avoided.

C. Patients with cirrhosis should not receive vaccinations.

D. While portal hypertension is a major complication of cirrhosis it has not been implicated in the development of ascites.

E. A diagnosis of ascites can be made on the basis of examination alone.

check

Independent learning program for GPs