

## Answer 26

a. Blood cultures.

The eye demonstrates a conjunctival haemorrhage. The rash is a necrotic purpuric rash, which is typical of meningococcal septicaemia. The patient has septic shock and requires immediate therapy. The recognition that he has meningococcal septicaemia is important for the choice of antibiotics that you will use. In medical emergencies, the reader must be familiar with the drugs that are used in that particular emergency, but not necessarily the dosage, as this can be found in the British National Formulary or the equivalent. Although most *Neisseria meningitidis* strains are sensitive to benzyl penicillin, it is prudent to cover the patient with additional cephalosporin or aminoglycoside antibiotic therapy until the sensitivities of the organism are known. The circulation must be restored to prevent hypoperfusion of vital organs, particularly the kidneys. The presence of low platelets, high fibrinogen degradation products and abnormal clotting is suggestive of DIC, which should be treated with fresh-frozen plasma to prevent haemorrhage.

*Neisseria meningitidis*, the causal Gram-negative diplococcus, can be cultured from the CSF in over 80% of cases with evidence of neurological involvement. However,

the presence of very low levels of platelets and DIC is contraindicated because of the dangers of bleeding into the spinal canal, particularly because the yield is just as high from nasal swabs. It is also possible to isolate the meningococcal antigen from blood before blood culture results are available. This test is particularly useful if antibiotics have been given before the patient is brought to hospital (negative blood cultures).

Meningococcal meningitis and septicaemia are caused by serogroups B and C. Septicaemia is associated with widespread petechial haemorrhage. Conjunctival haemorrhage may be the first physical manifestation. Shock is common owing to the production of a circulating endotoxin. DIC is a commonly recognized complication that may result in adrenal haemorrhage (Waterhouse–Friderichsen syndrome). Meningitis is often characterized by a myalgia, headache, photophobia, neck stiffness, nausea and vomiting. In the absence of DIC, the diagnosis is made rapidly by performing a Gram stain on the CSF. Blood cultures are positive in the majority of patients with meningitis. Focal neurological signs are less common than in pneumococcal meningitis.

Note: individuals in contact with affected patients must receive rifampicin chemoprophylaxis.

## Answer 27

1. c. Oral activated charcoal.  
f. IV N-acetyl cysteine.
2. c. Arterial pH.

The drug should be given within 8–10 hours of ingestion of the overdose, and continued while the liver function is abnormal. It is useful because it replenishes cellular glutathione stores and reduces oxidative damage caused by the toxic metabolite, NAPQI. An alternative to this is methionine. Gastric lavage is useful if performed within 1 hour of the overdose.

The patient has taken 20 g of paracetamol. An ingestion of 15 g is considered potentially serious in most patients. The toxicity of paracetamol is related to the production of a toxic metabolite of paracetamol. This is NAPQI, which usually is immediately conjugated with glutathione and excreted. In paracetamol overdose, the toxic metabolite is produced in excess and depletes

cellular glutathione. The liver is unable to deactivate NAPQI, which is responsible for massive hepatic necrosis and hepatic failure. Patients may have nausea, anorexia or vomiting on the first day. After 72 hours, features of liver and renal failure may ensue.

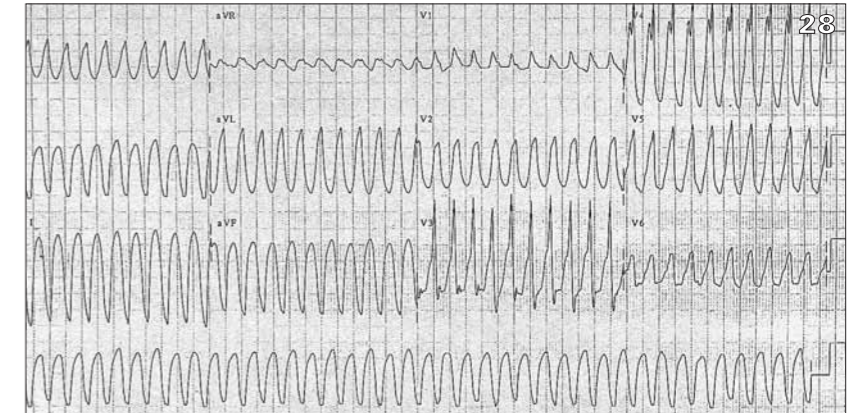
The three most important prognostic markers in paracetamol overdose are serum creatinine concentration, arterial pH and prothrombin time. A rise in serum creatinine level due to renal failure is a bad prognostic sign. A level of over 300 mmol/l is associated with over 70% mortality. Systemic acidosis (due to the failure of clearance of lactate by the liver) more than 24 hours after the overdose is associated with a poor prognosis. A pH of below 7.3 is associated with only a 15% chance of survival. The PT is usually the first liver test to become abnormal. A PT of >20 s at 24 hours after overdose is suggestive of significant hepatic damage, and a peak PT of >180 s is associated with a 90% mortality.

## Question 28

A 52-year-old female was brought into the Accident and Emergency Department after being found collapsed outside a public house. There was no one accompanying her, and there was no information regarding her next of kin.

On examination, she was very drowsy and had a Glasgow coma score of 6 out of 15. Her pupils were 10 mm each and reacted very sluggishly to light. On attempting to examine her fundi, she was noted to have coarse nystagmus, but a clear view of her fundi did not demonstrate any abnormalities. The tone in all her limbs was increased and her reflexes were brisk. The plantars were both upgoing. The heart rate was 135 beats/min, and regular. The blood pressure was 105/60 mmHg. The respiratory rate was 20/min. Examination of the precordium and lung fields was normal, but examination of the abdomen revealed a firm palpable mass 4 cm above the symphysis pubis. The patient was catheterized and drained of 2 litres of urine. Investigations are shown.

Shortly after the lumbar puncture, the patient had a generalized seizure which lasted 30 s. The attending nurse raised concerns about an arrhythmia on the cardiac monitor, and a 12-lead ECG was performed (28).



Hb	14 g/dl
WCC	$12 \times 10^9/l$
Platelets	$221 \times 10^9/l$
MCV	88 fl
Sodium	144 mmol/l
Potassium	4.0 mmol/l
Urea	13 mmol/l
Creatinine	100 $\mu$ mol/l
Bicarbonate	20 mmol/l
Chloride	108 mmol/l
Calcium	2.4 mmol/l
Phosphate	1.3 mmol/l
Bilirubin	12 $\mu$ mol/l
AST	33 iu/l
Gamma GT	28 iu/l
Alkaline phosphatase	120 iu/l
Plasma osmolality	333 mOsm/l
Urine osmolality	120 mOsm/l
Blood glucose	6 mmol/l
Chest X-ray	Normal-sized heart and clear lung fields
Skull X-ray	Normal; no fractures seen
Brain CT scan	Normal
Lumbar puncture:	
CSF pressure	100 cmH <sub>2</sub> O
Cells	3/mm <sup>3</sup>
Protein	0.35 g/l
Glucose	3 mmol/l
ECG	Sinus tachycardia; right axis deviation

1. Calculate the plasma osmolality.
2. Explain the discrepancy between the calculated plasma osmolality and the measured plasma osmolality.
3. Give two possible explanations for the low urine osmolality.
4. What is shown on the ECG?
5. What diagnosis best fits all the information given above?
6. What three investigations would you perform to help in this patient's management?

## Answer 28

- The plasma osmolality is calculated by the formula  $2 ([Na] + [K]) + [Urea] + [Glucose]$ . In this case, the calculated plasma osmolality is 315 mOsm/l.
- The measured plasma osmolality is higher than the calculated one, suggesting that the patient has ingested something which has not been measured, but has the effect of increasing the plasma osmolality. The most likely possibility in this case is alcohol ingestion. Although lithium contributes to plasma osmolality, it would be very unusual for the lithium concentration to be high enough to increase the plasma osmolality by 18 mOsm/l, considering that a serum lithium concentration of 2.5 mmol/l causes dangerous toxicity.
- Nephrogenic diabetes insipidus from lithium therapy or inhibition of ADH secretion as a result of alcohol ingestion.
- There is a broad-complex tachycardia with extreme axis deviation and concordance of the QRS complexes in the chest leads. These findings are suggestive of ventricular tachycardia.
- Tricyclic antidepressant drug overdose with alcohol.
- Arterial blood gases.
  - Serum lithium level.
  - Blood alcohol level.

Arrhythmias usually settle on correction of hypoxia and acidosis. Administration of class I antiarrhythmic agents may paradoxically worsen arrhythmias, with the exception of phenytoin. Status epilepticus should be corrected with intravenous diazepam.

Epileptic seizures and ventricular arrhythmias in a patient found collapsed should raise the suspicion of tricyclic antidepressant drug overdose. The low urine osmolality suggests that the patient has probably taken the overdose together with alcohol, and it is possible that she may have also taken lithium. The normal CT scan of the brain and normal CSF are against pathology in the central nervous system. She has dilated pupils, which is against narcotic abuse. Indeed, the combination of dilated pupils, tachycardia and urinary retention are all suggestive of the anticholinergic side-effects of tricyclic antidepressants. Severe lithium toxicity is associated with seizures, coma and ventricular arrhythmias, but

anticholinergic effects are not a feature. In addition, lithium toxicity is associated with ataxia and dysarthria. Chronic lithium ingestion may cause hypothyroidism. Sodium-depleting drugs such as diuretics lead to excess absorption of lithium by the kidney, and predispose to toxicity.

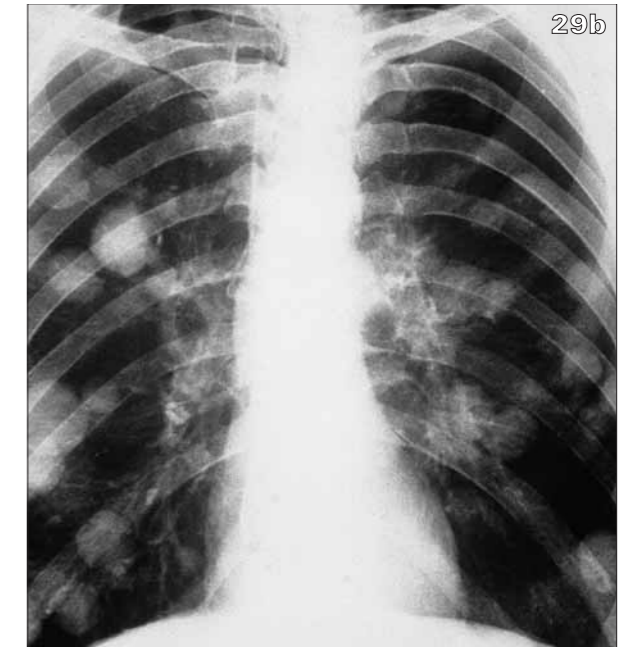
The arterial blood gases are an important investigation because they will identify hypoxia and acidosis, both of which precipitate ventricular arrhythmias in patients with tricyclic antidepressant overdose. The serum lithium level will be useful to determine whether lithium has been ingested, and will help decide whether the patient should have forced diuresis. In general, patients with a serum lithium of  $>3$  mmol/l should have forced diuresis. Haemodialysis is recommended if serum lithium exceeds 4 mmol/l.

The management of the patient is outlined below.

#### The management of tricyclic antidepressant overdose

- Protect the airway, and give oxygen via a mask
- Gastric lavage under anaesthetic supervision (within 12 hours of ingestion) followed by activated charcoal via a nasogastric tube
- Monitor on a high-dependency unit
- Correct hypoxia
- Correct acidosis with IV sodium bicarbonate
- Intravenous fluids to improve blood pressure
- Epileptic seizures should be corrected with IV lorazepam or diazepam. Phenytoin is contra-indicated
- Ventricular arrhythmias respond to correction of acidosis and hypoxia. IV sodium bicarbonate is the mainstay of prevention and treatment of ventricular arrhythmias and should be administered in all patients with ventricular tachycardia or acidosis or in patients with a QRS duration  $>110$  msec

## Question 29

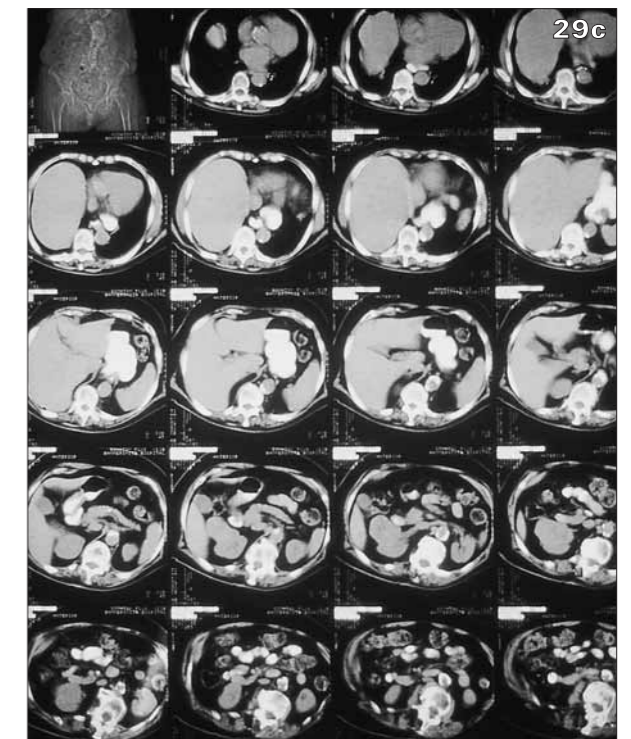


A 76-year-old male presented with a three-month history of anorexia, weight loss and fever. Apart from sweating excessively at night and feeling very thirsty, he did not have any other symptoms. He was a non-smoker and had been a schoolteacher for 40 years before retiring.

On examination, he was thin. The finding on inspection of his hands is shown (29a). The heart rate was 100 beats/min and the blood pressure 180/105 mmHg. His temperature was  $37.8^{\circ}\text{C}$  ( $100^{\circ}\text{F}$ ). Examination of the cardiovascular system and the respiratory system was normal. Abdominal examination revealed minimal tenderness and some fullness in the right loin. Examination of the genitalia revealed some oedema of the scrotum. The lower limbs were oedematous.

Investigations are shown.

Hb	18 g/dl
WCC	$10 \times 10^9/l$
Platelets	$300 \times 10^9/l$
ESR	110 mm/h
Sodium	140 mmol/l
Potassium	3.1 mmol/l
Creatinine	120 $\mu\text{mol/l}$
Calcium	2.6 mmol/l
Albumin	36 g/l
Chest X-ray (29b)	
CT scan of abdomen (29c)	
Urinalysis	Blood +++
	Protein +
	Bilirubin 0



- Give two explanations for the serum calcium level.
- What is the most probable diagnosis?
- List three important tests you would perform to help achieve a diagnosis.
- What is the management?

### Answer 29

1. i. Bone metastases.  
ii. PTH-related peptide secretion from a right-sided renal carcinoma.
2. Right-sided renal carcinoma.
3. i. Renal angiography.  
ii. Renal venography and inferior vena cavogram.  
iii. Bone scan to detect bony metastases.
4. Surgical removal of the right kidney if his general health will allow.

This patient presents with anorexia, weight loss, and a fever that may represent sepsis or malignancy. The right loin tenderness and haematuria are suggestive of renal involvement. The chest X-ray reveals multiple opacities in both lungs which represents a cannon-ball metastases from the right kidney. CT scan of the abdomen reveals a carcinoma of the right kidney which is invading the inferior vena cava; hence the scrotal and lower-limb oedema. Hypernephroma characteristically presents with a triad of haematuria, loin pain and swelling. Haematuria is present in 50% of cases, but pain and swelling are less frequent. Non-specific symptoms such as anorexia, weight loss and fatigue may be present for several

months before the diagnosis is made. The neoplastic cells often produce peptide hormones such as erythropoietin, renin, ADH and PTH-related peptide. This patient has a relative polycythaemia, hypercalcaemia, hypokalaemia and hypertension, which reflect erythropoietin, PTH-related peptide and renin secretion, respectively. Fever is present in approximately 20% of patients and is probably secondary to the secretion of a pyrogen by the tumour. Hypertension is present in approximately 30% of patients. Metastases usually occur via the bloodstream, although direct invasion of the renal veins or the inferior vena cava is relatively common. Some 10% of hypernephromas are bilateral, so close attention is given to the contralateral kidney when reviewing the CT scan. Venography and arteriography allow assessment of invasion of the veins and the vascularity of the tumour, respectively. Urine cytology may reveal malignant cells but the diagnostic yield is low. Removal of the hypernephroma (even when distant metastases are present) improves survival and causes regression of the metastases in many, but not all, patients. Radiotherapy and chemotherapy have been used in the treatment of this tumour, but the results are not very encouraging. The overall survival rate is 30–50%.

### Question 30

An 84-year-old female was referred to clinic with increasing forgetfulness. Her GP had commenced her on a small dose of haloperidol for agitation eight months ago. According to the staff at the nursing home where she resided, she had become increasingly confused over the past few months and more recently had developed odd movements affecting her face, arms and legs. Her GP had reviewed her two weeks previously and stopped the haloperidol; however, she remained confused and the movement disorder had become much more pronounced. She was not taking any other medication.

On examination, she had a mental test score of 4/10. Her vital parameters were normal. She exhibited intermittent yawning motions of the mouth, with occasional tongue protrusion. There were semi-purposeful

movements of her arms and legs. There was also clinical evidence of increased tone and cogwheel rigidity on neurological examination of her limbs.

A CT scan of the brain revealed generalized cerebral atrophy and calcification of the basal ganglia.

What is the cause of her movement disorder?

- a. Multi-infarct dementia.
- b. Lewy body dementia.
- c. Extrapiramidal side-effects of haloperidol.
- d. Pseudohypoparathyroidism.
- e. Hypoparathyroidism.

### Question 31

A 33-year-old Iranian male was investigated for a six-month history of general malaise, weight loss, fever, pain in his knees, ankles and wrists and a sore mouth. On systematic enquiry, he gave a two-year history of a recurrent sore mouth that made it difficult for him to eat. Just before the onset of all his symptoms he had experienced an attack of abdominal pain and bloody

diarrhoea which resolved after a week. He was seen by a gastroenterologist shortly afterwards, who diagnosed an inflammatory colitis, possibly secondary to infection. A rectal biopsy was performed by the gastroenterologist, and this was reported as a non-specific colitis. The patient had never experienced any abdominal symptoms after this, but had several episodes of soreness affecting the mouth. In

addition, he developed painful eyes and pain on intercourse and on voiding urine. There was no history of urethral discharge. Shortly afterwards he was admitted to hospital with a femoral vein thrombosis, which was treated with anticoagulants and thought to be secondary to dehydration and immobility from his diarrhoeal illness. During the past six weeks his health had deteriorated. He had arthralgia and a fever. He had been married for five years. He denied extramarital sex. His wife was well, and had not experienced any similar symptoms.

On examination, the patient appeared unwell.

Examination of his oral cavity revealed an abnormality (31a). His eyes were sore (31b). He had submandibular lymphadenopathy. His ankle, wrist and knee joints were tender, and joint movements were restricted. In addition, he had painful lesions on his legs (31c). Examination of his genitalia and anal areas are shown (31d, e). He also pointed out an erythematous lesion approximately 2 cm in diameter that had developed at the site of venepuncture during a blood test performed by his GP two days earlier. All other aspects of the physical examination were normal. Investigations are shown.



Hb	9.8 g/dl
WCC	$13 \times 10^9/l$
Platelets	$450 \times 10^9/l$
MCV	82 fl
CRP	200 g/l
Rheumatoid factor	Absent
Antinuclear antibody	Absent
Radiology of painful joints	Normal

What is the most probable diagnosis?

- a. Crohn's disease.
- b. Ulcerative colitis.
- c. Reiter's syndrome.
- d. Behçet's syndrome.
- e. Gonococcal septicaemia.

## Answer 30

c. Extrapyramidal side-effects of haloperidol.

The woman has clinical evidence of dyskinesia and parkinsonism. The most common cause of her neurological signs is drug-induced extrapyramidal disease. Neuroleptic drugs which include haloperidol are extensively used in treating agitation in the elderly. By blocking dopamine receptors in the basal ganglia, these drugs can offset extrapyramidal side-effects which include tremor, dystonia, akathisia, parkinsonism and tardive dyskinesia. Acute dystonic reactions appear within the first few hours or days, and consist of oculogyric crises, torticollis or trismus. Fortunately, they are uncommon, and resolve as soon as the drug is withdrawn. Chronic tardive dyskinesias are the most serious complication and affect 20% of patients on chronic neuroleptic therapy. They usually occur after a patient has been on treatment for at least three months, and can be made worse in the first few weeks after stopping the offending drug. In 60% of cases the dyskinesia resolves over three years after drug withdrawal; however, in the remainder of patients the movement disorder persists and is very difficult to treat. Characteristic features involve lip smacking, tongue protrusion, orofacial mouthing, trunk rocking and distal chorea of the hands and feet. A combination of any of these features may be present.

Cerebral calcification is an incidental finding in 0.5% of CT scans in the elderly. About 20–30% of patients with widespread calcification of the basal ganglia exhibit



neurological signs which include parkinsonism, chorea, epilepsy, ataxia and dementia. There is an association between calcification of the basal ganglia and hypoparathyroidism or pseudohypoparathyroidism. Rare causes of basal ganglia calcification (30, arrowed) are cerebral irradiation and mitochondrial diseases.

## Answer 31

d. Behçet's syndrome.

The patient has oral, genital and anal ulcers (31a, d and e, respectively), conjunctivitis (31b), arthritis, erythema nodosum (31c) and features of a systemic illness. There has been a single episode of bloody diarrhoea and a previous femoral vein thrombosis. The differential diagnoses include Crohn's disease, Reiter's syndrome and Behçet's syndrome (Table A). Reiter's syndrome is classically a triad of conjunctivitis, urethritis and arthritis 1–4 weeks after an episode of bacterial dysentery or a sexually transmitted urethritis. Other features include plantar fasciitis, Achilles tendinitis, keratoderma blennorrhagica, circinate balanitis, stomatitis, hepatitis, cardiac and neurological involvement, and occasionally amyloidosis. It is possible that the diarrhoeal illness may have been dysenteric and offset the reactive features of Reiter's disease. There is no history of promiscuity or urethral discharge. Venous thrombosis affects about 4% of patients with Reiter's disease and occurs early in the disease. Mouth ulcers are common in Reiter's disease and are painless. Erythema nodosum is not a feature of Reiter's syndrome. Arthritis is asymmetrical and usually

affects the knee and ankle joints. The most common joint to be affected in the upper limb is the wrist, as in this case; however, joint involvement occurs early, whereas in this case the disease has been present for two years.

Crohn's disease is a chronic granulomatous inflammatory disease of the gastrointestinal tract of unknown cause, and is a strong possibility in this case. Bloody diarrhoea is a recognized feature of Crohn's colitis. Colonic disease is associated with perianal disease in just over 30% of patients. A seronegative reactive arthritis is a recognized complication of Crohn's disease. Erythema nodosum occurs in some cases. Genital ulcers are rare, as is deep-vein thrombosis. Urethral involvement and dysuria only occur when an inflammatory fistula develops between the colon and the ureter. Recurrent urinary tract infections due to faecaluria can cause urethral stricture.

Behçet's syndrome is the most probable diagnosis. Behçet's syndrome is a recurrent multifocal disorder that persists over many years. It is characterized by recurrent mouth and genital ulcers, ocular lesions, and skin, joint and neurological involvement. The incidence is high in Japan and in countries bordering the Mediterranean. Oral and genital ulcers are present in most patients.

Ulcers can affect the pharynx and cause dysphagia. Genital ulcers can cause dysuria and dyspareunia. Ocular lesions are the most serious development. Recurrent uveitis and iridocyclitis, retinal vascular lesions and optic atrophy can lead to loss of vision in 50% of patients with ocular involvement. Erythema nodosum is a recognized feature. Other skin manifestations include a diffuse pustular rash affecting the face, erythema multiforme. The pathergy is a useful diagnostic sign. Pricking the skin can lead to erythema around the affected part within 24–48 hours, which is a relevant feature in our patient.

A seronegative arthritis affects about 40% of patients and commonly involves knees, ankles and wrists. Recurrent thrombophlebitis of the legs is a significant feature of Behçet's syndrome, leading to venous thrombosis. Less often, superior or inferior cava thrombosis may occur. Abdominal pain and bloody diarrhoea have also been documented. Asymptomatic proteinuria is a recognized feature, but on a few occasions may reflect renal amyloidosis. Neurological complications occur in 20% of patients. Organic confusional states, meningoencephalitis, transient or persistent brainstem syndromes, multiple sclerosis and parkinsonian-type disorders are all recognized.

Behçet's syndrome is a clinical diagnosis. There is no specific diagnostic test. HLA-B51, B<sub>12</sub>, DR2, DR7 and Drw52 are associated with the syndrome. Acute-phase

proteins are elevated and immune complexes are present. The pathergy test is a simple useful test. Genital ulcers and oral complications are treated with topical steroids. In severe cases, systemic steroids become necessary, together with azathioprine, which acts as a steroid-sparing agent. Colchicine, cyclosporin and levamisole have also been used in the management of this condition. The causes of orogenital ulceration are given in Table B.

Table A Causes of orogenital ulcers

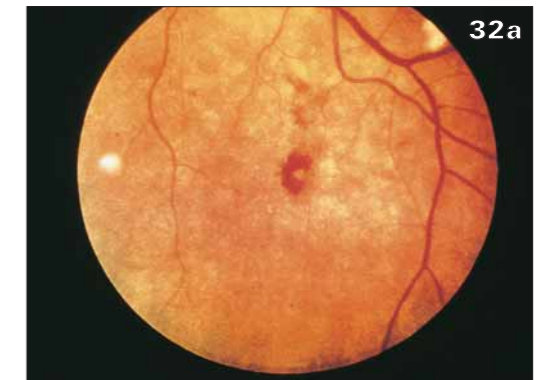
Behçet's syndrome	Syphilis
Crohn's disease	Gonococcal infection
Herpes simplex virus	HIV
Ulcerative colitis	Pemphigus pemphigoid
Reiter's syndrome	Stevens–Johnson syndrome
Lichen planus	

Table B Causes of orogenital ulcers and venous thromboses

Behçet's syndrome	Ulcerative colitis
Crohn's disease	Reiter's syndrome

## Question 32

A 16-year-old female was admitted with a six-month history of myalgia, loss of weight and night sweats. Over the past six weeks she had started to become breathless on exertion. On admission to hospital she had a temperature of 38.1°C (100.6°F). On auscultation of the precordium, there was an early diastolic murmur at the left lower sternal edge. Examination of the chest, abdomen and central nervous system was normal, with the exception of her fundi, one of which is shown (32a). An echocardiogram was performed to investigate the murmur (32b).



1. What is the diagnosis?
  - a. Systemic lupus erythematosus.
  - b. Polyarteritis nodosa.
  - c. Infective endocarditis.
  - d. Marantic endocarditis.
  - e. Libman–Sacks endocarditis.
2. What investigation would you perform to confirm the diagnosis?
  - a. Autoantibody screen.
  - b. Serum ANCA.
  - c. Serum complement.
  - d. Blood cultures.
  - e. Serology for atypical bacteria.