A 23 year old man presented to the casualty department with right periorbital oedema. A diagnosis of urticaria was made, antihistamines were prescribed, and he was discharged home. Within 24 hours he returned complaining of increased facial swelling and dysphagia, and a medical opinion was sought. He denied recent facial trauma, or insect stings. Further inquiry revealed that he had suffered a similar episode nine months earlier which had involved swelling of his hands and feet. These areas were not itchy or red. His past history included recurrent bouts of abdominal pain associated with distension and vomiting requiring numerous hospital admissions under the care of different consultants over the previous 14 years. A diagnosis of abdominal migraine was frequently recorded. There were no obvious precipitating factors and the bouts resolved spontaneously over a period of a few days. Detailed family history uncovered several members with similar symptoms and an inheritance pattern along the maternal line. Examination revealed a slim built, normotensive 23 year old man with bilateral periorbital, perioral, and pharyngeal oedema. He was comfortable at rest with no drooling, dyspnoea, or wheeze (fig 1). Routine investigations showed a normal full blood count, urea and electrolytes, liver function tests, and chest x ray film. The suspected diagnosis of C1 esterase inhibitor (C1 INH) deficiency was confirmed with low C1 INH and C4 concentrations at 0.08 g/l (normal 0.15–0.35) and <0.06 g/l (normal 0.20–0.60) respectively.

In view of the frequency and severity of his symptoms he was started on prophylactic treatment with danazol. He was advised that he would require intravenous infusions of C1 INH concentrate as prophylaxis before any future surgical intervention and review would be needed before future dental work. He was discharged with a Medic Alert bracelet and arrangements were made to screen other family members. To date, three years later, there have been no further relapses.
A rare coincidence and recurrent urinary tract infections

D Debnath, D G Richards

A 68 year old woman was referred for recurrent episodes of urinary tract infection and weight loss of four months' duration. She gave a history of intermittent brownish discharge from her urethra for the same duration but was otherwise asymptomatic. There was no significant past medical history. Laboratory evaluation revealed a haemoglobin level of 100 g/l, leucocyte count of $11.0 \times 10^9$/l, and a positive urine culture (Escherichia coli). A rigid cystoscopy was performed which readily confirmed the diagnosis. A biopsy specimen, which was taken during cystoscopy, showed transitional cell carcinoma.

Computed tomography of abdomen and pelvis (fig 1) was arranged. There was no nodal spread or liver metastasis. She subsequently underwent laparotomy that revealed the fistulous communication between sigmoid colon and roof of the bladder. A defunctioning colostomy was performed. She was recalled after six weeks for a second operation that entailed a total cystectomy (along with ileal conduit formation) and low anterior resection with closure of the rectal stump and left iliac fossa colostomy. Her postoperative recovery was uneventful.

The whole specimen was sent to the pathologist for further evaluation (fig 2 is the microphotograph of relevant section of the histology).

Questions
(1) What is the initial diagnosis?
(2) What and how common are the histological findings?
(3) What is the prognosis?
Obtunded sensorium in a trauma patient

A Mazumdar, S Kumar, S P Balasubramanian, A K Sharma

A 36 year old man, a victim of road traffic accident, with head injury and epistaxis, was taken to a district hospital. He was intubated with an orotracheal tube and his scalp injury was dressed, and he was referred to this tertiary care institute accompanied by his relatives. Three hours after the injury, when he was brought to the emergency room, he was noted to have intercostal recession while breathing, a systolic blood pressure of 95 mm Hg, and Glasgow coma score (GCS) was 2/10. Air entry on both sides of the chest was minimal and equally diminished on both sides, the percussion note on either side was not dull, and the neck veins were empty. Flow from the endotracheal tube was hardly audible. An endotracheal suction catheter was inserted but it could not be pushed beyond 20 cm. Arterial blood gases were sampled while trying hard to ventilate with an Ambu bag and were: oxygen tension 10.4 kPa, carbon dioxide tension 6.9 kPa, and pH 7.26. As per referral note, his systolic blood pressure at the time of referral was 110 mm Hg and GCS 5/10. There was no apparent external loss of blood. (Monitoring by pulse oximetry was not possible because no pulse oximeter was available.)

Questions
(1) What is the most likely cause of deterioration of GCS in this case?
(2) What should be the next step?
(3) What is the most probable cause of hypotension in this case?
(4) What is the finding shown in fig 1?
(5) What is the most likely explanation for the development of blockage of this endotracheal tube?

Acute appendicitis: an unusual cause

S K Clark, T Qureshi, M Sen

A 52 year old woman presented with a two day history of worsening central abdominal pain, with nausea, and vomiting. Over the previous month she had been treated for a flare up of rheumatoid arthritis. Her only medication was methotrexate 10 mg/week and buprenorphine 200 µg three times a day. On examination she looked unwell and had a pyrexia of 37.4°C. Her pulse was 110 beats/min and her blood pressure was 110/54 mm Hg. Her abdomen was distended and she had generalised peritonism; bowel sounds were absent. She had a mild leucocytosis of 11.2 × 10⁹/l but her full blood count and serum electrolytes were otherwise normal. Plain abdominal radiography revealed multiple central loops of small bowel which were not dilated.

At laparotomy there was free pus in the pelvis, and a pelvic appendix was inflamed and perforated distally; the only other abnormalities were a 10 cm nodular cyst of the right ovary and inflammation of the omentum. Appendicectomy, right salpingo-oophorectomy, and omentectomy were performed. These organs were non-adherent and were therefore removed separately.

Questions
(1) Describe the histological features (see p 131).
(2) What further treatment is indicated?
Is spiral computed tomography the imaging modality of choice for renal colic?

N Sarath Krishna, L Morrison, C Campbell

A 59 year old women was admitted with left loin pain of three days’ duration. There was no radiation of pain to her groin. She had no dysuria, urinary frequency, or vaginal discharge and was afebrile. On examination she had no loin tenderness. She was treated with analgesics, which relieved her pain. Her urine analysis was positive for blood. A midstream specimen of urine showed no growth of organisms. Full blood count, electrolytes, urea, and creatinine were all within normal limits. Intravenous urography was performed which revealed no obvious calculus in the line of the urinary tract and a normal right kidney. A delayed dense nephrogram was seen on the left side. There was no contrast excretion into the left ureter. Subsequently spiral computed tomography of the abdomen was performed to exclude a calculus as the cause of the obstruction (see fig 1).

Questions
(1) What is the diagnosis, and what is spiral computed tomography?

A young woman with intractable diarrhoea

A S Kashyap, R Varadarajulu, S Kashyap

A 28 year old saleswoman reported loose motions of three years’ duration. She was symptomatic with recurrent copious watery loose motions five to six times a day, which had progressively worsened. Symptomatic treatment with antimotility agents had provided poor relief.

Moderate hypertension had been diagnosed seven years before, which was controlled with enalapril 5 mg/day. Over a period of four years her blood pressure settled to normal levels. Enalapril was discontinued three years ago and her blood pressure remained normal. Her father had died suddenly of hypertension and “abdominal tumour”.

On clinical examination her blood pressure was 130/76 mm Hg with no postural fall. The rest of the general and systemic examination was normal. Her packed cell volume, complete blood counts, peripheral blood smear, serum potassium, sodium, calcium, phosphate, albumin, glucose, serum creatinine, thyroid profile, stool microscopy and culture, fecal fat excretion, D-xynlose absorption test, upper gastrointestinal endoscopy, colonoscopy, small intestinal biopsy, small bowel barium follow through, abdominal and chest radiographs were normal. HIV antibodies were negative by enzyme linked immnosorbert assay. The serum and urine drug, toxicology, and laxative screen were negative. The serum concentrations of serotonin, gastrin, somatostatin, vasoactive intestinal peptide, and calcitonin were normal. Concentrations of urinary 5-hydroxyindole acetic acid and plasma norepinephrine and epinephrine were normal. The plasma dopamine concentration was 0.94 ng/ml (normal <0.03 ng/ml), and urine dopamine excretion was 12 000 µg/day (normal 50–480 µg/day). The urinary homovanillic...
Acid was 13 mg/day (normal <7 mg/day). Urinary adrenaline, noradrenaline, metanephrine, and normetanephrine concentrations were normal. A contrast enhanced computed tomogram of the abdomen was done (fig 1).

Questions
(1) What is the diagnosis?
(2) What is the cause of diarrhoea?
(3) What is the cause for remission of her hypertension?

A young man with tachycardia

R Sivakumar, A Eltrafi, J H Silas

Answers on p 134.

A 30 year old man was admitted with palpitations of sudden onset. There was no history of previous episodes. He was a non-smoker, did not take excess alcohol or any recreational drugs, and there was no family history of ischaemic or any cardiac disorders. He was breathless and was hypotensive; his electrocardiogram is given below (fig 1).

Questions
(1) What is the differential diagnosis?
(2) What is the most likely diagnosis?
(3) How will you manage this patient acutely?
(4) What is the long term management?

Figure 1 Electrocardiogram of patient.
A small axillary nodule—a therapeutic dilemma?

A 75 year, postmenopausal women presented with a lump in the left axilla associated with occasional pain for six months. There was no history suggestive of an increase in size, an awareness of a lump in either breast or the opposite axilla, or discharge from the nipple. Past medical history was not contributory as there was no family history of breast cancer. Examination showed a firm, mobile lump in the centre of left axilla (1 × 1 cm), subcutaneous in location. No other lump could be detected in the axilla or either of the breasts.

The patient had been seen earlier by a general practitioner who considered the lump of benign pathology. Fine needle aspiration cytology (FNAC) carried out in our hospital revealed features suggestive of metastatic carcinoma. Excision biopsy showed it to be an infiltrating duct carcinoma. Chest radiography, ultrasonography of the abdomen, and bilateral mammography were normal.

The patient underwent total mastectomy and axillary clearance with excision of the axillary scar. Histopathology revealed no primary focus in the entire breast or lymph nodes in the axilla. Sections from the excised scar tissue showed a very small focus of malignancy (fig 1). The postoperative period was uneventful. An oestrogen receptor study was positive. The patient is followed up regularly and taking tamoxifen 20 mg once a day.

Questions
(1) What is the significance of an axillary nodule in an elderly patient?
(2) What should be the diagnostic modality in a case of axillary nodule?
(3) What is the treatment modality in a case of axillary nodule with occult metastasis?
(4) What are the various histopathological considerations in such a case?

A farmer with artificial valve endocarditis

A 29 year old Yemeni man, a farmer, with St Vincent aortic and mitral prosthesis replaced in April 1996, was admitted to hospital in February 1997 with a nine month history of intermittent fever, general weakness, and loss of appetite. Three months before admission he developed right sided hemiparesis for which he was admitted to another hospital. No details of that admission could be obtained, however he had significant improvement in his weakness. Physical examination on admission revealed: temperature 39°C, blood pressure 120/60 mm Hg, pulse 104 beats/min, an early diastolic murmur at the left sternal border, and mild right facial, right upper, and lower limb weakness. Laboratory investigations revealed the following: haemoglobin 99 g/l, white cell count 4.3 × 10^9/l, platelet count 288 × 10^9/l, erythrocyte sedimentation rate (ESR) 33 mm in the first hour, and brucella agglutination test showed titres of 1: 5120 and 1:2560 respectively. Liver and renal function tests were normal. A transoesophageal echocardiogram revealed small
vegetation at the aortic prosthesis with moderate paravalvular leak, the mitral prosthesis was normal (fig 1). Six blood cultures grew Brucella melitensis. He was treated with oral doxycycline 100 mg twice daily, rifampin 450 mg twice daily, and intravenous co-trimoxazole 960 mg three times daily. Four days later he was taken for operation, two ring abscesses were found, they were drained, and the infected valve was replaced by a new one. Culture of specimen taken during surgery yielded B melitensis. He had an uneventful postoperative course and was discharged two weeks later on oral doxycycline, rifampin, and co-trimoxazole, which he took for a total of 20 weeks.

**Questions**

1. What are the most common organisms causing artificial valve endocarditis? What are other less common organisms should be considered?
2. How should the diagnosis be established?
3. What would be the best therapeutic approach?

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**Loss of weight in a female heavy smoker with diffuse interstitial pulmonary fibrosis**

A Al-Adsani, M H Dahniya, N Al-Adsani

A 75 year old hypertensive woman was admitted with a two month history of fever and cough with scanty sputum, loss of appetite and weight, and progressive exertional dyspnoea. She had habitually smoked 20–40 cigarettes a day since the age of 19 years. Her activities had become limited recently by dyspnoea and back pain. There was no history of exposure to tuberculosis. Chest radiography, done two years before, showed extensive diffuse reticulonodular shadowing with honeycombing and peripheral and basal accentuation (fig 1).

Physical examination revealed an afebrile emaciated women with respiratory rate of 20 breaths/min, and a blood pressure of 150/90 mm Hg (after medication). Heart sounds were normal and there were bilateral fine basal crackles over the lungs. There was no palpable peripheral lymphadenopathy or pedal oedema but there was clubbing of both fingers and toes. A new posteroanterior chest radiograph was done (fig 2). Investigations revealed mild hypochromic anaemia and a normal white cell count with eosinophilia of 16.4%. Her erythrocyte sedimentation rate was raised at 121 mm/hour. Arterial blood analysis revealed an oxygen tension of 8.96 kPa, carbon dioxide tension 3.99 kPa, and pH 7.39. Microscopic examination of the sputum was negative for acid-fast bacilli.

**Questions**

1. What does the chest radiograph in fig 2 show?
2. Suggest two causes that would explain the new radiological finding in fig 2.
3. What three further investigations would you request?
4. What is the final diagnosis and what is the relative risk of its development in patients with diffuse interstitial pulmonary fibrosis?
5. In your opinion, what is the major risk factor for the final diagnosis in this case?
SELF ASSESSMENT ANSWERS

**Q1: Is always associated with peripheral angio-oedema and urticaria**
*False*

C1 INH deficiency is not associated with urticaria but the angio-oedema may be preceded by a serpiginous erythematous rash which is non-pruritic. Peripheral angio-oedema is a well recognised presentation but mucosal angio-oedema can be life threatening and may involve the bowel.

**Q2: Symptoms can be precipitated by the oral contraceptive pill**
*True*

The oral contraceptive pill and menstrual cycle have been linked to exacerbations of the condition but the most commonly reported precipitating factors are trauma, dental extraction, and emotional stress.

**Q3: Is the most commonly described genetic defect of the complement system and is characterised by a reduction in complement proteins C3 and C4**
*False*

It is the most commonly described genetic defect of the complement system in which C4 and C2 are reduced due to the unchecked activity of C1, but C3 is invariably normal. This is because C3 convertase is not generated due to C4b and C2b being rapidly inactivated in the plasma.

**Q4: Is inherited in an autosomal recessive manner and usually presents in the first decade of life**
*False*

C1 INH deficiency may be inherited in an autosomal dominant (chromosome 11, p11.2–q13), manner where it usually appears early in life, or acquired presenting in the fourth decade or later. Quantitative (85%) and qualitative (15%) deficiencies of C1 INH are responsible for the inherited variety while an increased catabolic rate and autoantibodies to C1 INH are responsible for the two acquired forms.

**Q5: Is primarily treated with fresh frozen plasma which has replaced steroids and antihistamines as the treatment of choice during acute episodes**
*False*

C1 INH concentrate is preferred for the acute episode, because fresh frozen plasma contains C1 and C2 which may aggravate symptoms.

**Q6: May be treated by antifibrinolytic drugs, particularly in the acquired variety or in those not responding to androgens**
*True*

Prophylactic treatment is by substituted androgens (stanozolol) and antifibrinolytic drugs (tranexamic acid). Antifibrinolytics are the treatment of choice before puberty and in women trying to conceive.

**Discussion**

Angio-oedema was originally documented by Milton in 1876, while Osler described hereditary angioneurotic oedema in 1888. Donaldson et al first recognised that a deficiency of C1 INH was the cause of hereditary angio-oedema in 1963. C1 INH is a 104 kDa protein and its deficiency is the most commonly described genetic defect of the complement system. It acts as a serine protease inhibitor upon the C1qrs enzyme complex of the classical complement pathway as well as those of the kallikrein and plasminogen pathways. It is believed that angio-oedema is a result of reduced C1 INH function through a reduced inhibition of kallikrein, complement system activation, and kinin generation.

A common presentation of C1 INH deficiency is that of recurrent episodes of acute, colicky abdominal pain associated with vomiting. Reports exist of patients undergoing operative exploration in the mistaken belief that a surgical emergency underlies the abdominal pain. Findings at operation include a large amount of serous fluid and intestinal wall oedema, which can lead to intussusception and hypovolaemic shock. Our case was saved from laparotomies because the diagnosis of “abdominal migraine” had been made repeatedly. Non-mucosal angio-oedema is usually well demarcated, localised, and most commonly found affecting skin on the extremities. The mucous membranes of the mouth, pharynx, and larynx may be involved. Trauma, dental extractions, and emotional stress are among the most common precipitating factors, while the menstrual cycle and oral contraceptive pill have also been linked to exacerbations of the condition.

Initial investigations of suspected C1 INH deficiency should include measurement of the complement components C2, C3, C4, and C1 INH. Further immunological investigations may include assays for functional C1 INH, C1, and C1 autoantibodies. If acquired C1 INH is suspected serum electrophoresis may identify the monoclonal paraprotein of a B cell lymphoproliferative condition. Barium studies during abdominal pain may show a classical “stacked coin appearance”, but confirmation is achieved by quantitative and qualitative measurement of C1 INH.

Treatment of the acute episode is preferentially with C1 INH concentrate which should also be used prophylactically before surgery.
Learning points
C1 esterase inhibitor deficiency:
- Commonest complement deficiency
- Significant morbidity and mortality
- Easy and cheap to diagnose
- Eminently treatable
- Should be considered in any case of recurrent abdominal pain for which no obvious cause can be found

The use of fresh frozen plasma is controversial because it contains C1 and C2, which may aggravate symptoms.

Prophylactic treatment is by substituted androgens (stanozolol) and antifibrinolytic drugs (tranexamic acid). Antifibrinolitics may be effective in the acquired variety, those not responding to androgens, and are indicated before puberty and in women trying to conceive. Treatment of associated conditions may lead to symptomatic improvement in acquired C1 INH deficiency.

Affected individuals should wear Medic Alert bracelets. Genetic counselling and screening should be offered to their families, even those apparently not affected, because the clinical course of the disease can be so varied.

The diagnosis of C1 INH deficiency is frequently missed, as happened in our patient over a period of 14 years. It should be considered in any case of recurrent abdominal pain for which no obvious cause can be found.

A rare coincidence and recurrent urinary tract infections

Q1: What is the initial diagnosis?
Enterovesical fistula secondary to bladder carcinoma complicated by urinary tract infection. Common causes of enterovesical fistula are:
- Diverticular disease of colon
- Colonic malignancy
- Granulomatous bowel disease
- Iatrogenic (for example, radiation therapy)

Clinical symptoms and signs are varied, mainly urinary tract infection (100%), pneumaturia (66%), and faecaluria (50%). Awareness of the possibility of an enteric origin of recurrent urinary tract symptoms should help prevent the long delays in diagnosis.

Cystoscopy is regarded as the most useful diagnostic procedures in detecting fistula.

Other modes of investigation are barium enema, cystography, colonoscopy, and computed tomography. In this case computed tomography distinctly showed (A) gas in the bladder (B) mass involving the bladder.

Treatment depends on the aetiology, localisation, and the patient’s general condition. Commonly used technique is resection of the fistulous tract and the compromised intestinal segment, followed by repair of the bladder. The procedure can be performed as a single stage when the aetiology is diverticular or granulomatous bowel disease. Staged repairs are more judicious in patients with a large intervening pelvic abscess or those in whom advanced malignancy or radiation changes are present. Insertion of colonic stent, laparoscopic repair, and use of human fibrin glue for a recurrent fistula have also been described in the literature.

Q2: What and how common are the histological findings?
Unexpectedly, pathological assessment showed that the fistula was formed by two distinct primaries: adenocarcinoma from the colon and transitional cell carcinoma from the bladder. Note fig 2 (see page 122): (A) colonic adenocarcinoma and (B) poorly differentiated transitional cell carcinoma.

Malignancy is a known cause (35%–66%) of enterovesical fistula. The latter is most commonly vesicosigmoidal by location (50%). In this case the site of fistula was between dome of the bladder and sigmoid colon in deed. However, occurrence of two unrelated primaries of adjacent organs at the same site, which collided to form a fistula, was an extremely rare coincidence. We have not found any published reports of a similar nature, which makes this case unique.

Q3: What is the prognosis?
When the fistula is of malignant origin, the long term prognosis remains poor, as it is for any colonic (or bladder) carcinoma extending beyond the serosa and involving a contiguous organ. Fistulas secondary to radiation necrosis and recurrent tumour have also been described in the literature.

This patient sadly died eight months after the operation from distant metastases.

Final diagnosis
Malignant vesicosigmoidal fistula due to collision between two distinct primary tumours arising from the colon and bladder respectively.

Obtunded sensorium in a trauma patient

Q1: What is the most likely cause of deterioration of GCS in this case? Hypoxia is the most important preventable cause of obtunded sensorium in a trauma patient. It may manifest in the form of non-purposeful motor responses, and, therefore, is a strong indication for the need for definitive airway. Hypoxia and hypotension are to be ruled out before incriminating intracranial events or drugs (alcohol) as a cause of deterioration in GCS score.

Q2: What should be the next step? Extube the patient because the tube is blocked. Oxygenate him with mask, and establish a definitive airway once again. The cuff of the endotracheal tube was immediately deflated and the patient was extubated. The oral cavity and pharynx were cleaned and he was put on an oxygen mask. He was reintubated with another endotracheal tube and ventilated. Immediately thereafter, a bottle of saline (500 ml) was infused over 15 minutes. After 30 minutes of reintubation his blood pressure improved to 105 mm Hg systolic. Two hours after reintubation and ventilation, his arterial blood gases were: oxygen tension 13.6 kPa, carbon dioxide tension 5.6 kPa, and pH 7.32. About five hours after admission his blood pressure was 110 mm Hg and GCS score improved to 4/10. By this time the fluid infusion was limited to 800 ml (since admission) in view of the head injury and lack of any apparent blood loss (internal/external).

Q3: What is the most probable cause of hypotension in this case? In a trauma setting, hypoxia is the most important preventable cause of death. Myocardial contractility is reduced in the presence of hypoxia or acidosis. Correction of hypoxia and acidosis (respiratory) after reintubation and ventilation resulted in improvement in blood pressure. Only an 800 ml fluid infusion over five hours was needed to raise his blood pressure; this indicates that it was not hypovolaemia that was the main cause of the lower blood pressure.

Q4: What is the finding shown in fig 1 (see p 123)? The tube is blocked with a blood clot.

Q5: What is the most likely explanation for the development of blockage of this endotracheal tube? Aspirated blood would block the endotracheal tube. It is an important possibility in this case as the patient had epistaxis at the time of presentation to the district hospital. Endotracheal suctioning, during transfer, could have saved him from such a catastrophe. Blocked or displaced endotracheal tubes are an important cause of hypoxia in trauma during transfer. Whenever a patient is shifted from one ward/hospital to other, one must ensure patency and correct positioning of the endotracheal tube. This can be easily accomplished by a trained paramedic.

Discussion It is not surprising that there is deterioration in the sensorium because of a blocked or displaced tube. What is surprising is the lack of awareness, and desire to take appropriate measures (pre-hospital trauma care), among the public, administrators, and medical professionals that hypoxia can kill very quickly. Ali et al reported much improved care after introduction of the pre-hospital trauma life support program (PHTLS), on the principles of Advanced Trauma Life Support. PHTLS has been shown to be effective when compared to care before introduction of PHTLS in, for example, the frequency of airway control (99.7% v 10%). Failure to monitor the endotracheal tube resulted in the lumen being compromised by blood clots, a preventable complication. The major clinical problem in this case is that it took three hours for the patient to arrive at a tertiary centre and the patient was not accompanied by medical or paramedical staff. Besides the medical lessons learnt from this case, an even more important message is for planners of medical care. They should be aware that tertiary care hospitals cannot treat patients effectively until and unless primary and secondary care is made effective. Good communication and a safe paramedical escort to a further referral centre is the key as trauma patients with a compromised airway cannot wait.

Final diagnosis
Hypoxia causing obtunded sensorium.

Acute appendicitis: an unusual cause

Q1: Describe the histological features Histopathological examination of the appendix (fig 1) shows deposits of adenocarcinoma associated with acute inflammation. Examination of the ovary (fig 2) and omentum (fig 3) confirm the presence of papillary adenocarcinoma of the ovary with spread to the omentum as well as the appendix.

Q2: What further treatment is indicated? Total abdominal hysterectomy and left salpingo-oophorectomy (right salpingo-oophorectomy and omentectomy having already been performed) to “debulk” the tumour mass, followed by cytotoxic chemotherapy.
(with cisplatin and either paclitaxel or cyclophosphamide)\(^1\) is indicated.

**Discussion**

Epithelial cancer of the ovary is characterised by exfoliation of malignant cells and early dissemination throughout the peritoneal cavity. The appendix is a common site of such metastasis, both macroscopically apparent and occult, and appendicectomy is performed by some gynaecologists as part of surgical staging and to reduce tumour burden before chemotherapy. In one study of women with epithelial ovarian tumours, 39% overall and 49% with FIGO stage III (disease outside the pelvis) or IV (distant metastases) had appendiceal secondaries; about one third of these were occult (that is, microscopic only).\(^2\) In three cases appendices involved with tumour were found to be acutely inflamed microscopically, but none of these was symptomatic. In another series, appendiceal metastases were found in 63% overall and in 80% with stage III or IV ovarian disease.\(^3\)

In three cases appendices involved with tumour were found to be acutely inflamed microscopically, but none of these was symptomatic. In another series, appendiceal metastases were found in 63% overall and in 80% with stage III or IV ovarian disease.\(^3\)

The aetiology of appendicitis is not entirely clear, but obstruction of the lumen is thought to play an important part in some cases. This may be due to lymphoid tissue, foreign body, or, in an older age group, caecal carcinoma. We have found only one previous report of a case of ovarian carcinoma presenting with acute appendicitis.\(^4\) While metastatic ovarian cancer is a very rare cause of appendicitis, these cases emphasise the importance of thorough examination of the abdomen and pelvis at appendicectomy, even in the presence of unequivocal appendicitis.

**Final diagnosis**

Acute appendicitis due to metastases from papillary carcinoma of the ovary.

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Is spiral computed tomography the imaging modality of choice for renal colic?

Q1: What is the diagnosis, and what is spiral computed tomography?
The patient was diagnosed as having left sided renal colic due to a calculus in her left proximal ureter. A spiral computed tomogram allows imaging of the entire abdomen and pelvis during one breath hold, eliminating respiratory artefacts. The entire technique of performing spiral computed tomography takes approximately 30 seconds to complete.

Q2: What are the findings on the spiral computed tomogram?
A spiral computed tomogram of the abdomen was performed. No intravenous contrast medium was used during the procedure. It showed a normal right renal tract. There was a 6 mm calculus in the proximal left ureter and an 8 mm calculus in the inferior pole calyx of the left kidney (fig 1; see p 124). These calculi were not visualised in the intravenous urogram.

Q3: What are the advantages of spiral computed tomography in evaluating a case of renal colic?
There are several advantages in performing a spiral computed tomogram to evaluate acute flank pain. As the imaging with spiral computed tomography is performed without contrast medium, the stones are not masked by the presence of radio-opaque contrast. With conventional computed tomography stepwise slices are taken and therefore it is possible to miss a stone. Spiral computed tomography provides a continuum profile of the urinary tract and therefore is unlikely to miss a stone. Like an intravenous urogram but unlike an ultrasound scan, a spiral computed tomogram gives good imaging of the ureter and has the same advantage as an intravenous urogram to be able to delineate the level of obstruction. Unenhanced spiral computed tomography is reported to have more than 95% sensitivity and specificity in the diagnosis of obstructing ureteral calculi. Within the next few years spiral computed tomography may replace intravenous urography in the evaluation of renal colic.

Discussion
Intravenous urography has been the procedure of choice for evaluation of renal colic since it was first performed in 1923. It provides structural as well as functional information of the urinary tract. In addition it gives us information regarding the site, degree, and the nature of obstruction. There are a few disadvantages with intravenous urography. The incidence of contrast induced allergic reactions is 5%–10%. There is 25% risk of contrast induced nephrotoxicity in people with pre-existing renal failure and diabetes mellitus. Intravenous urography is more time consuming. On the other hand spiral computed tomography has several advantages. As the imaging with spiral computed tomography is performed without contrast medium, the stones are not masked by the presence of radio-opaque contrast. Total time taken to perform a spiral computed tomography is less than a minute. Like an intravenous urogram, but unlike an ultrasound scan, a spiral computed tomogram gives good imaging of the ureter and has the same advantage as an intravenous urogram to be able to delineate the level of obstruction. The sensitivity and specificity of unenhanced spiral computed tomography in the diagnosis of renal colic is reported to be more than 95%. Evaluation of spiral computed tomography and intravenous urography revealed comparable radiation dosages and with a lower gonadal dose provided by the spiral computed tomography. The main disadvantage of unenhanced spiral computed tomography compared with intravenous urography is the absence of evaluation of renal function and the lining epithelium of the urinary tract. Rarely phleboliths in the pelvis could be confused with ureteral stones on spiral computed tomography.

Learning points: advantages of spiral computed tomography
- No bowel preparation or contrast medium is required
- It requires less time than intravenous urography. Entire technique of spiral computed tomography takes approximately 30 seconds
- It scans the entire abdomen and pelvis during one breath hold, eliminating respiratory artefacts
- It is highly accurate in identifying the size and location of ureteral and renal calculi
- Uric acid calculi could be accurately diagnosed
- The degree of obstruction to the kidney can be assessed by the severity of hydronephrosis, perinephric, and perirectal stranding and perinephric fluid collection indicating fornical rupture
- In addition other abdominal organs can be evaluated
- Radiation dosage is comparable to that of intravenous urography (4.6 ± 4.4 rad, respectively), with a lower gonadal dose provided by the spiral computed tomography.

References
A young woman with intractable diarrhoea

Q1: What is the diagnosis?
The diagnosis is a dopamine secreting pheochromocytoma. The abdominal computed tomogram (p 124) shows a left adrenal mass (8 × 6 cm) with haemorrhagic and necrotic areas. A 123I-metadobenzylguanidine scintigram showed uptake in the left adrenal gland.

A histopathologically proved benign pheochromocytoma was resected. Immunohistochemical study revealed enhanced expression of tyrosine hydroxylase and low expression of dopamine β-hydroxylase in the tumour. These findings are consistent with the secretion of dopamine, as dopamine β-hydroxylase is the enzyme that synthesises norepinephrine from dopamine. An increased production of enzyme that synthesises norepinephrine from dopamine, as dopamine findings are consistent with the secretion of tyrosine hydroxylase and low expression of chemical study revealed enhanced expression of phaeochromocytoma.

Box 1: Common mechanisms for loose motions in pheochromocytoma
- Ectopic production by pheochromocytoma of: vasoactive intestinal peptide (watery diarrhoea), hypokalaemia, achlorhydria syndrome; serotonin, somatostatin; calcitonin.
- In pheochromocytoma as part of multiple endocrine neoplasia 2A and 2B syndromes; calcitonin, serotonin, and prostaglandin production from medullary thyroid carcinoma may lead to diarrhoea.
- Pheochromocytoma may be associated with gastrinoma of Zollinger-Ellison syndrome, leading to presentation with diarrhoea.

Box 2: Gastrointestinal manifestations of pheochromocytoma

- Nausea (with or without vomiting)
- Constipation
- Abdominal pain
- Ileus
- Pseudo-obstruction
- Diarrhoea
- Ischaemic enterocolitis
- Gastrointestinal bleeding
- Cholelithiasis
- Acute abdomen with hyperamylasaemia
- Hunger

Learning point
Intractable diarrhoea may be the only manifestation of a dopamine secreting pheochromocytoma.

Q2: What is the cause of diarrhoea?
The cessation of diarrhoea after tumour resection suggests that dopamine may cause diarrhoea, perhaps via D1-like receptors in the gastrointestinal tract. Diarrhoea is an uncommon sole manifestation of pheochromocytoma. A literature search revealed only one other report of dopamine secreting pheochromocytoma presenting solely with diarrhoea.

Q3: What is the cause for remission of her hypertension?
The dopamine receptors in peripheral tissues are of two functional classes: D1 and D2-like receptor. Stimulation of postsynaptic, D1-like receptors or presynaptic D2-like receptors may cause vasodilatation. Stimulation of D1-A receptors promotes natriuresis and lowers blood pressure in humans. A deficient renal dopamine formation or action may contribute to hypertension,

Box 3: Common mechanisms for loose motions in pheochromocytoma

A deficient renal dopamine formation or action may contribute to hypertension, and a deficient dopaminergic response to salt loading may play an aetiological part in patients with a salt sensitive form of hypertension. D1-A receptor deficient mice have been shown to have hypertension, suggesting a hypotensive action from dopamine. This is consistent with the spontaneous lowering of blood pressure initially and the increase in blood pressure after resection of dopamine secreting pheochromocytoma seen in our patient.

Follow up
Two months after surgery she continues to be asymptomatic. Her blood pressure is 140/80 mm Hg. The urinary 24 hour catecholamines, urinary dopamine and urinary homovanillic acid concentrations returned to normal. Her blood pressure one week later was 140/80 mm Hg.

Final diagnosis
Dopamine secreting benign pheochromocytoma.

A young man with tachycardia

Q1: What is the differential diagnosis?
The important differential diagnosis for a irregular broad complex QRS tachycardia is:
- Atrial fibrillation with aberrant conduction
- Atrial fibrillation with pre-excitation
- Atrial fibrillation with pre-existing bundle branch block
- Polymorphic ventricular tachycardia

Q2: What is the most likely diagnosis?
The rapid ventricular rates and the absence of cardiovascular risk factors should make one suspect atrial fibrillation with pre-excitation (conduction via the accessory pathway). Wolff-Parkinson-White syndrome was confirmed in this patient in the electrocardiogram taken during sinus rhythm after treatment.

Q3: How will you manage this patient acutely?
In view of the hypotension DC cardioversion is the best choice.

Q4: What is the long term management?
Patients with Wolff-Parkinson-White syndrome with symptomatic arrhythmias, particularly life threatening ones like atrial fibrillation, should be referred for radiofrequency ablation for elimination of the accessory pathway. Flecaïnide, propafenone, and sotalol are prophylactic antiarrhythmic drugs of choice while the patient is awaiting the procedure.

Discussion
Atrial fibrillation is the second commonest (10%–30%) arrhythmia in patients with Wolff-Parkinson-White syndrome after orthodromic atrioventricular (AV) re-entrant tachycardia (AVRT) which is a narrow QRS regular tachycardia almost identical to AV nodal re-entrant tachycardia. The cardiac features of atrial fibrillation in Wolff-Parkinson-White syndrome are the irregularity and the rapid ventricular rates as well as the varying QRS configuration. Ventricular rate is an aggregate of conduction over the normal AV node and accessory pathways and it can approach 300 to 350 beats/min. QRS configuration is determined by the refractory period of the accessory pathway.

If the refractory period of the accessory pathway is short, the antegrade conduction occurs via the accessory pathway to produce an irregular wide QRS tachycardia as in this case, while it is no different from usual atrial fibrillation if conduction takes place via the AV node. Varying degrees of fusion beats can also be found. Short effective refractory period of accessory pathway and short R-R interval between consecutive pre-excited complexes are associated with rapid ventricular rates that can degenerate into ventricular fibrillation and sudden death.

The pathogenesis of atrial fibrillation in Wolff-Parkinson-White syndrome is poorly understood. It is more common in patients with multiple accessory pathways. Though the accessory pathway is important in the pathogenesis of atrial fibrillation, it is probably not required for the initiation of atrial fibrillation and the accessory pathway is usually a passive bystander. However some reports suggest that accessory pathways are branched and can support microre-entry.

Atrial fibrillation is almost always associated with concomitant inducible AVRT, and spontaneous degeneration of AVRT into atrial fibrillation has been reported to represent the most frequent mode of initiation. It is unclear why all patients with AVRT do not develop atrial fibrillation. Intrinsic atrial electrophysiological abnormalities and exaggerated sympathoadrenal discharge have all been blamed in the pathogenesis of atrial fibrillation. Associated abnormalities like mitral valve prolapse and Ebstein’s anomaly can be found.

Electrical cardioversion is the treatment of choice in pre-excited atrial fibrillation as it can degenerate into ventricular fibrillation. However if haemodynamically well tolerated, chemical cardioversion can be tried. Though intravenous flecaïnide, propafenone, procainamide, sotalol, and amiodarone have all been shown to be effective in cardioverting pre-excited atrial fibrillation or reducing the ventricular rate, class Ic drugs (flecainide and procainamide) are popular choices. Verapamil and digoxin are contraindicated as they block conduction via the AV node enhancing conduction via the accessory pathway thereby actually increasing the ventricular rate. Intravenous amiodarone should be used with caution in pre-excited atrial fibrillation as increase in the ventricular rates and ventricular fibrillation have been reported. Radiofrequency ablation is the treatment of choice in patients with symptomatic arrhythmias. It is usually but not always successful in preventing atrial fibrillation. However it will eliminate the life threatening rapid ventricular rates which can be associated with it.

Final diagnosis
Wolff-Parkinson-White syndrome.

A small axillary nodule—a therapeutic dilemma?

Q1: What is the significance of an axillary nodule in an elderly patient?
In an elderly patient, an axillary nodule may be a metastatic deposit from a known or unknown primary tumour. Axillary lymph node metastasis other than breast cancer, especially in males, includes lung, thyroid, gastric, colorectal, and pancreatic malignancy; however, in females the commonest is ipsilateral breast cancer.

Q2: What should be the diagnostic modality in a case of axillary nodule?
A suspicious nodule (particularly in an elderly person) should always have a histopathological diagnosis by FNAC and/or histopathology.

Q3: What is the treatment modality in a case of axillary nodule with occult metastasis?
Once diagnosed, routine haematological and biochemical investigations, chest radiography, ultrasonography of the abdomen, and bilateral mammography are undertaken. Additional investigation to locate the exact site of primary tumour is unrewarding. In most of the series on this subject, the sensitivity of mammography in the identification of the occult lesion is as low as 33%. Magnetic resonance imaging (MRI) may be helpful; however, the absence of abnormality on mammography and MRI does not exclude the diagnosis of primary breast cancer. A bone scan may be done as a part of metastatic work up.

Total mastectomy and axillary clearance are practised by the majority of surgeons. Recently some surgeons have suggested conservative surgery with or without radiation therapy. Ellerbroek et al treated such patients with irradiation alone and showed a 17% five year actuarial risk for locoregional recurrence. Advantages claimed are that the breast is preserved and survival is comparable to total mastectomy. The presence of extensive tumour burden and multifocality, even when the disease is clinically occult, may limit breast conservation therapy as it may not be feasible to excise the primary or deliver a boost dose of radiotherapy to the primary site. Moreover, in the absence of details of the primary tumour and lymph nodal status, it is not possible to evaluate tumour characteristics and prescribe adjuvant treatment.

Q4: What are the various histopathological considerations in such a case?
The pathologist should be alerted to the occult primary in the breast as more sections may be required to locate the tumour. A primary tumour is identified only in 64%–93% as reported in various series. Infiltrating duct carcinoma is the commonest tumour, while carcinoma in situ is seen in 8%–20% of cases. Rosen and Kimmel reported median tumour size of 1.5 cm (0.1–6.6 cm). Baron et al had noted 45% of their cases to be multifocal. A study of hormone receptors may be helpful in confirming the diagnosis as it is positive in 50%–60% of the cases and a negative result does not exclude breast carcinoma. A positive result can also be seen in other malignancies like renal cell carcinoma, melanoma, and colorectal carcinoma.

Learning points
- A small axillary nodule in an elderly woman can be metastatic tumour.
- A primary tumour is usually found in the breast; however, at times the primary tumour may be occult.
- Total mastectomy and axillary clearance are undertaken in the case of occult primary in the breast with lymph node metastasis where frequent follow up is not possible and the patient does not opt for breast conservation therapy.
- At times, the primary site is not detected even on histopathological examination and such cases remain a therapeutic dilemma.

Discussion
In 1907, William Stewart Halsted first described two patients with extensive carcinomatous involvement of the axilla caused by occult breast cancer. The incidence of occult carcinoma with axillary nodal metastasis varies from 0.35% (35 out of 10 014 patients) at the Memorial Sloan-Kettering Cancer Center to 0.5% (60/12 000) at the National Cancer Institute in Milan.

The commonest cause in females is ipsilateral breast cancer. No investigations can identify an occult primary lesion with accuracy. Total mastectomy and axillary clearance, conservative surgery with or without radiation, and primary radiation therapy are the various options available in elderly patients. Total mastectomy and axillary clearance are undertaken especially in patients where frequent follow up is not possible and the patient does not opt for breast conservation treatment. Since studies have shown significant survival advantage in patients with stage II breast cancer after adjuvant therapy, patients with occult carcinoma metastatic to the axilla should be treated as stage II disease and hence adjuvant systemic therapy instituted.

In an elderly postmenopausal patient only tamoxifen should be given as a treatment option especially in the case of an occult or small oestrogen receptor positive primary.

In our patient, no primary focus could be detected in the large number of sections that were studied, although it is not possible for us to completely rule out the presence of a small focus in the unexamined parts of the breast. The axillary metastasis was in the centre of the axilla in the subcutaneous tissue with no metastatic deposit found in the lymph nodes. It is difficult to predict whether the tumour was present in ectopic breast tissue or part of the axillary tail or it was an occult primary in the breast with metastasis to subcutaneous axillary tissue. Carcinoma has also been reported to arise primarily in the ectopic breast tissue inclusions present in an axillary lymph node. Our case demonstrated metastasis in the subcutaneous tissue, a rare event. This case gives an important message; however small a
small nodule may be, especially in an elderly patient, it should not be ignored.

Final diagnosis
Metastatic axillary nodule with occult breast cancer.

A farmer with artificial valve endocarditis

Q1: What are the most common organisms causing artificial valve endocarditis? What are other less common organisms should be considered?
The most common aetiological organism is *Staphylococcus epidermidis* which accounts for 29% of both early and late onset endocarditis, followed by viridans streptococci (17%), *Staphylococcus aureus* (14%), and enterococci (7%).

Q2: How should the diagnosis be established?
Relapsing brucella bacteraemia after appropriate treatment for acute brucellosis is an important clue for the diagnosis of brucella endocarditis in patients who have prosthetic valves.

Q3: What would be the best therapeutic approach?
Treatment for brucella endocarditis has not been well established, due basically to the low number of reported cases. Brucella organisms are susceptible to a variety of antibiotics including aminoglycosides, tetracyclines, chloramphenicol, quinolones, macrolides, rifampin, and trimethoprim-sulfamethoxazole (TMP-SMZ).

Discussion
Brucellosis is a zoonosis with a worldwide distribution, especially in the Mediterranean basin, the Arabian Peninsula, the Indian subcontinent, Mexico, Central and South America. It is a systemic disease, and almost every organ can be affected. The infection usually manifests itself as a febrile syndrome with no apparent focus, chills, sweating, arthralgia, and myalgia. About 30% of patients suffer from some localisation, most commonly bone and joint involvement. Brucella endocarditis is rare occurring in fewer than 2% of patients with brucellosis.

Prosthetic valve endocarditis caused by brucella species is very rare. *Brucella abortus*, *B suis*, and *B melitensis* have been reported to cause endocarditis. Brucella endocarditis produces highly destructive lesions of the valve structure. It usually involves a previously healthy native valve. The aortic valve is involved in more than 75% of cases. Mitral involvement occurs more rarely and usually affects a previously damaged valve. The valvular lesions have been described as bulky and ulcerative with gross abscesses of the myocardium, microabscesses within the cusps, destruction of commissures, and calcifications. These observations might...
Self assessment answers

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infection to cause fibrosis, hyalinisation, and has been attributed to the tendency of prosthetic valve endocarditis were rare; this has been attributed to the tendency of infection to cause fibrosis, hyalinisation, and calcification, rather than large vegetations. Diagnosis depend on isolation of brucella from blood culture or cardiac tissue, which are positive in 80% of cases. Combined antibiotic and surgical treatment is the best approach for treating brucella prosthetic valve endocarditis as the mortality rate is less than for medical treatment alone, and infection of the new prosthesis that has been placed is low.1

**Final diagnosis**

Brucella prosthetic valve endocarditis.

Loss of weight in a female heavy smoker with diffuse interstitial pulmonary fibrosis

Q1: What does the chest radiograph in fig 2 (see p 127) show?
In addition to the diffuse interstitial pulmonary fibrosis (DIPF), there is an irregular left upper lobe opacity and apical pleural fibrosis.

Q2: Suggest two causes that would explain the new radiological finding in fig 2 (see p 127)
Pulmonary tuberculosis and lung cancer are the two most likely causes of an opacity in the upper lobe of the lung.

Q3: What three further investigations would you request?
Sputum culture for acid-fast bacilli, sputum cytology for malignant cells, and high resolution computed tomography of the chest.

Sputum culture showed mycobacterium tuberculosis that was sensitive to rifampicin, ethambutol and streptomycin, but resistant to isoniazid. Sputum cytological examination of three specimens revealed squamous cell carcinoma. High resolution computed tomography confirmed DIPF with honeycomb reticulation and ground glass opacity. A large irregular cavitating mass was apparent in the anterior segment of the left upper lobe (fig 3 below).

Q4: What is the final diagnosis and what is the relative risk of its development in patients with diffuse interstitial pulmonary fibrosis?
Lung cancer with DIPF. It is well established that the occurrence of lung cancer is greatly increased in patients with DIPF.1 There is an excess relative risk of 14.1 of lung cancer in patients with DIPF compared with the general population of comparable age and sex.3 The development of lung cancer in DIPF seems to be related to DIPF itself, apart from smoking and no predicting factors for its development in the presence of DIPF have been identified.3 Lung cancer in this setting occurs predominantly in males, in smokers, in the lower lobes, and in the peripheral regions of the lung.2

Q5: In your opinion, what is the major risk factor for the final diagnosis in this case?
Cigarette smoking is the most important single aetiological factor in the development of lung cancer. The patient was an elderly women who smoked heavily for more than 50 years, and had a longstanding history of DIPF. The squamous cell carcinoma she developed was in the left upper lobe and was most probably the result of her heavy smoking. Her DIPF may have been a contributory factor.

Clinical course

The patient was considered unfit for surgical excision or therapeutic irradiation of her neoplasm, because of her pre-existing pulmonary fibrosis. She failed to respond to a quadruple regimen of antituberculous therapy (including rifampicin, pyrazinamide, ethambutol, and ciprofloxacin; streptomycin was not prescribed because she had renal impairment during her illness). She died 3.5 months after admission. There was no necropsy.
Although the association of lung cancer and DIPF is well established, little attention has been given to it. In comparison with the general population of lung cancer patients, lung cancer associated with DIPF occurs more commonly in males, and in smokers, and is predominantly located in the lower lobes and peripheral regions of the lungs. The precise role of DIPF as a predisposing factor for lung cancer is speculative. The fact that lung cancer occurs more frequently in the lower lobes where fibrosis is predominant supports the view that fibrosis and carcinoma are closely related. Bronchial squamous metaplasia as a precancerous state in DIPF is well recognised. Transition from atypical squamous metaplasia to carcinoma and anatomical correlation between sites of fibrosis and the carcinoma has been demonstrated in some instances.

The simultaneous occurrence of lung cancer and pulmonary tuberculosis has been reported by several authors. In a review of associated lesions in patients with lung cancer, pulmonary tuberculosis was the most frequent lesion, followed by scars, emphysema, and thickened pleura. A firm aetiological relationship between lung cancer and pulmonary tuberculosis has not, however, been established and recent analyses suggest that the association may be coincidental. When lung cancer does coexist with pulmonary tuberculosis, the diagnosis is typically delayed.

### Learning points

- The association of diffuse interstitial pulmonary fibrosis and lung cancer is well established.
- Lung cancer associated with DIPF occurs more commonly in males, and in smokers, and is predominantly located in the lower lobes and peripheral regions of the lungs.
- Cigarette smoking acts as an additive risk factor for the development of lung cancer in patients with DIPF.
- Clinical and radiological screening is important in patients with DIPF.

### Discussion

Although the association of lung cancer and DIPF is well established, little attention has been given to it. In comparison with the general population of lung cancer patients, lung cancer associated with DIPF occurs more commonly in males, and in smokers, and is predominantly located in the lower lobes and peripheral regions of the lungs. The precise role of DIPF as a predisposing factor for lung cancer is speculative. The fact that lung cancer occurs more frequently in the lower lobes where fibrosis is predominant supports the view that fibrosis and carcinoma are closely related. Bronchial squamous metaplasia as a precancerous state in DIPF is well recognised. Transition from atypical squamous metaplasia to carcinoma and anatomical correlation between sites of fibrosis and the carcinoma has been demonstrated in some instances.

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### Final diagnosis

Lung cancer with diffuse interstitial pulmonary fibrosis and pulmonary tuberculosis.

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Recurrent abdominal pain—the forgotten cause

Postgrad Med J 2001 77: 128
doi: 10.1136/pmj.77.904.128

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