TABLE—*Changing susceptibility of sequential N gonorrhoeae isolates to six antibiotics using high (10^5cfu) and low (10^3cfu) inocula. (Figures with the lower inoculum are given in parentheses)*

Date of isolation	Minimum inhibitory concentrations (mg/l)					
	Penicillin	Ampicillin	Spectinomycin	Streptomycin	Tetracycline	Cefuroxime
2.11.81	8 (4)	>64 (32)	32 (16)	>512 (>512)	16 (8)	0·12 (0·06)
6.11.81	>64 (16)	>64 (32)	32 (16)	>512 (>512)	16 (8)	0·12 (0·06)
1.11.81*	>64 (16)	>64 (32)	>512 (512)	512 (512)	16 (8)	0·12 (0·06)
7.11.81*	>64 (16)	>64 (32)	>512 (>512)	512 (512)	16 (8)	0·12 (0·06)
14.11.81*	>64 (16)	>64 (32)	>512 (>512)	512 (512)	16 (8)	0·12 (0·06)

*After spectinomycin treatment.

antibiotics for all five isolates were determined using sensitivity agar (DST, Oxoid) supplemented with 1% IsoVitalex and 5% lysed blood inoculated with 10^5 and 10^3 colony forming units (cfu). After 24 hours' incubation at 36°C in 7% CO_2 the minimum inhibitory concentration was determined as the point of complete inhibition. All isolates were screened for plasmids using a rapid screening method.[5] The samples were electrophoresed in 0·6% agarose and stained with ethidium bromide.

Neisseria gonorrhoeae isolates from the urethral exudate were oxidase-positive, Gram-negative cocci, utilising glucose alone, and requiring proline for growth. The minimum inhibitory concentrations of benzyl penicillin, ampicillin tetracycline, spectinomycin, streptomycin, and cefuroxime for these strains, using high (10^5cfu) and low (10^3cfu) inocula, are shown in the table. Although penicillin-resistant, the first isolate (obtained before treatment with ampicillin) had a minimum inhibitory concentration of benzyl penicillin lower than the other four. The chromogenic cephalosporin test, performed after one subculture, showed that β-lactamase was produced by only 7% of the colonies from the first isolate but by all the colonies from the other four. The first two isolates showed zones of inhibition to a 30 μg disc of spectinomycin while the remaining isolates did not. This difference in disc sensitivity to spectinomycin was reflected in the minimum inhibitory concentrations (see table). Although disc testing suggested sensitivity to tetracycline, all isolates had relatively high minimum inhibitory concentrations. On plasmid analysis three plasmids with molecular weights of 2·6, 4·4, and 24·5 megadaltons were found.

Comment

Only one other report of a spectinomycin-resistant β-lactamase-producing strain of *N gonorrhoeae* has been published.[2] In that report and in our own both spectinomycin-resistant strains were isolated after spectinomycin treatment, both contained plasmids of 2·6, 4·4, and 24·5 megadaltons, and both required proline for growth. Although we have no further information about the source of the strain the initial infection was probably caused by a mixed population of *N gonorrhoeae*, only some of which produced β-lactamase. Treatment with ampicillin and probenecid selected the β-lactamase producers, which resulted in the increase in the minimum inhibitory concentration of benzyl penicillin for the subsequent isolates.

The emergence of spectinomycin resistance could be the result of either selection or induction, although the increasing minimum inhibitory concentration suggested induced resistance. We investigated neither the mechanism of spectinomycin resistance in our isolates nor its genetic control, but the similarity of the plasmids to those of the recently reported strain[2] indicated a chromosomal change.

Tetracycline treatment was unsuccessful in our patient, as in the previous instance.[3] The discrepancy between sensitivity results by disc testing (by the Stokes method) and minimum inhibitory concentrations highlighted the difficulty in interpreting this disc method with *N gonorrhoeae*. The most suitable antibiotics for these strains are probably the second and third generation β-lactamase-resistant cephalosporins. They are, however, relatively expensive and have been rarely used in gonorrhoea, particularly in single-dose regimens.

The emergence of spectinomycin resistance in *N gonorrhoeae* after treatment may not in fact be a rare event but rather a reflection of laboratory procedures. Since continuity of care in sexually transmitted diseases can be limited both clinicians and laboratory workers may easily fail to recognise resistant strains. The number of β-lactamase-producing isolates detected in the Praed Street Clinic has increased and will lead to a greater use of spectinomycin. Surveillance programmes are needed to determine the prevalence of spectinomycin resistance among strains of *N gonorrhoeae* by presumptive disc sensitivity techniques.

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Diclofenac hepatitis

Diclofenac (Voltarol, Geigy Pharmaceuticals), a derivative of phenylacetic acid, is a non-steroidal anti-inflammatory agent. It is at least as effective as indomethacin in relieving symptoms of inflammatory arthritis in clinical trials and is generally well tolerated.[1] Some patients, however, have developed abnormalities of serum liver function tests during treatment with diclofenac,[2] but there have been no documented cases of acute hepatitis caused by this drug. The Committee on Safety of Medicines and the manufacturer have received a few reports of hepatocellular damage in patients taking diclofenac, but none where other causes could be excluded.

Case report

A 52-year-old man began taking diclofenac for painful pseudogout in the right knee in November 1980. His pain was relieved, but in March 1981 he developed nausea and vomiting, followed within a few days by dark urine, pale stools, and jaundice. He was admitted to his local hospital and found to have an enlarged liver, palpable 4 cm below the right costal margin; serum liver function tests gave results consistent with acute hepatitis. Serum bilirubin concentration was 126 μmol/l (7·4 mg/100 ml) (normal 5-17 μmol/l (0·3-1·0 mg/100 ml)) and aspartate aminotransferase activity 1375 IU/l (normal 15-40). There was no history of blood transfusion, tattoos, injection, or recent foreign travel, and he was not homosexual. He did not abuse alcohol and took no regular medication besides diclofenac. Tests for hepatitis B surface antigen and hepatitis A IgM antibody yielded negative results. Diclofenac was withdrawn, and the jaundice resolved completely over seven days, although he remained weak and lethargic.

It was assumed that he had recovered from an acute viral hepatitis when he began treatment with diclofenac again in late April. Five weeks later he started to vomit and again became jaundiced. On admission to this hospital his liver was enlarged 2 cm below the right costal margin but there were no signs of chronic liver disease. Serum bilirubin concentration was 201 μmol/l (11·8 mg/100 ml) and aspartate aminotransferase activity 1150 IU/l. Hepatitis B surface antigen and hepatitis A IgM antibody were again undetectable by radioimmunoassay, and serological tests for recent infection with Epstein-Barr virus and cytomegalovirus again yielded negative results. Liver biopsy specimens showed a moderately severe actue hepatitis with canalicular cholestasis and Kupffer-cell proliferation, and plasma cells and eosinophils in the inflammatory infiltrate.

Diclofenac was stopped, and his symptoms again resolved over a few days. Results of serum liver function tests returned to normal within six weeks and were still normal three months later.

Comment

There is no doubt that this patient had acute hepatitis. Diclofenac or non-A non-B hepatitis are the most likely causes. In the absence of specific tests non-A non-B hepatitis can be diagnosed only by exclusion. The presence of eosinophils in the inflammatory infiltrate seen on liver biopsy favours a drug aetiology, but this feature may also be seen in relapsing or prolonged acute viral hepatitis, which may be indistinguishable histologically.[3] This patient had not, however, been exposed to any of the known risk factors for non-A non-B hepatitis. Furthermore, relapsing non-A non-B hepatitis usually follows a more chronic course,[4] whereas our patient was completely well with normal serum liver function tests between the two episodes of hepatitis, which resolved rapidly and totally after diclofenac was stopped.

The gap between starting diclofenac and the onset of hepatitis is incompatible with a drug-induced liver injury of the "hypersensitivity" type but is in keeping with an idiosyncratic drug-induced hepatitis of the "metabolic aberration" type.[5] Diclofenac has been reported to cause abnormalities in serum liver function tests,[2] and it was the only drug our patient was taking. This fact and the temporal relation of the two episodes of hepatitis to ingestion of diclofenac strongly suggest that the drug was responsible for the liver injury.

This case emphasises the difficulties encountered in separating viral hepatitis from that caused by drugs.

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Psittacosis presenting with Reiter's syndrome

Polyarthritis is a common feature of chlamydial respiratory infection in many animal species,[1] but this association, while recognised, is rarely reported in man.[2 3] We report such a case, which presented as Reiter's syndrome.

Case report

A 35-year-old woman was admitted in March 1981. Three weeks before admission she had developed a fever, general weakness, sore throat, cough, and purulent sputum. Ten days later she had bilateral conjunctivitis, back pain, and painful swollen knees. There was no dysuria or vaginal discharge. She visited a pet shop regularly but had no direct contact with psittacine birds. On examination gingivitis and purulent conjunctivitis were present. There were no clinical abnormalities of the respiratory, cardiovascular, or alimentary systems. Rotation of the cervical spine was limited with tenderness over C4/C5. The right first metacarpophalangeal joint, both knees, and the left ankle had tense effusions with pronounced tenderness and limitation of movement.

The initial results of investigations were as follows: full blood count normal; erythrocyte sedimentation rate 114 mm/first hour; Paul Bunnell test negative; antinuclear factor, DNA antibodies, and rheumatoid factor absent; antistreptolysin O titre less than 50 units; serum albumin 31 g/l (3·1 g/100 ml) (normal 35-55 g/l) (normal 3·5-5·5 g/100 ml); serum alanine aminotransferase 52 IU/l (normal 5-35 IU/l). A midstream specimen of urine showed no abnormality. Throat and conjunctival swabs and sputum grew commensal organisms only. Synovial fluid from the knee contained total protein 65 g/l (6·5 g/100 ml) and albumin 27 g/l (2·7 g/100 ml); 60% of the cells were lymphocytes and 40% neutrophils. The glucose content was 5·5 mmol/l (100 mg/100 ml). Chest *x*-ray films showed a raised right hemidiaphragm with increased basal markings. *X*-ray films of the sacro-iliac joints were normal. Complement fixation test for the psittacosis/lymphogranuloma venereum organism was positive at a titre of 1/256, which fell to 1/64 three weeks later. HLA-B27 antigen was present. The patient was treated with tetracycline and then prednisolone and recovered fully over the following eight weeks. To date no other cause for her polyarthritis has been discovered.

Comment

This patient had a characteristic psittacosis pneumonia, which was diagnosed retrospectively by serology. The lack of a history of a contact is characteristic of this disease, which is being increasingly reported.[4] Asymmetrical polyarthritis and conjunctivitis with the presence of the HLA-B27 antigen satisfied the criteria for the diagnosis of Reiter's syndrome.[5] This is, we believe, the first report of such an association.

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Spontaneous persistent pseudomembranous colitis related to Clostridium difficile in ischaemic bowel disease

Clostridium difficile is now considered to be a major factor in the pathogenesis of antibiotic-associated pseudomembranous colitis,[1] though in the past bowel ischaemia was considered to be important.[2 3] I describe a patient with chronic ischaemic bowel disease who developed spontaneous pseudomembranous colitis associated with *C difficile* infection.

Case report

A 69-year-old woman with a history of stroke affecting the right hemisphere, angina, and hypertension presented in December 1980 after three weeks of non-bloody diarrhoea. She had not received antibiotics in the preceding six months. Sigmoidoscopy and rectal biopsy showed the florid changes of pseudomembranous colitis. Barium enema showed a pancolitis with diffuse thumb-printing pattern. Vancomycin 500 mg six-hourly was given by mouth for eight days. Stools were not examined for *C difficile* before this course of vancomycin. Her diarrhoea responded dramatically.

Within three days of her stopping vancomycin the diarrhoea returned; faecal *C difficile* and its cytotoxin were isolated. Vancomycin was given for a further three weeks at the same dose and was stopped when repeated stool testing shown no *C difficile* and the diarrhoea had resolved. One week later *C difficile*, sensitive to vancomycin, was again isolated, though there was no detectable cytotoxin. Vancomycin was initially withheld. Two weeks later she developed rectal bleeding and diarrhoea. Both the cytotoxin and *C difficile* were then present in the stools.

A third two-week course of vancomycin was begun, again with improvement. Angiography was carried out because of the rectal bleeding and the appearance seen on the initial barium enema. Complete occlusion of the origin of the inferior mesenteric and severe stenosis of the superior and coeliac arteries were shown. Her symptoms again resolved with vancomycin.