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.

We thank Dr K Greenlaw of Stock, Essex, who referred this patient.

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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.

Over the ensuing seven months she had three more clinical relapses, each accompanied by reappearance in the stools of either the organism or its cytotoxin, or both. Each improvement after vancomycin (eight to 14-day-courses) was accompanied by disappearance of the organism. At one point she was given cholestyramine, but she was unable to tolerate it. Her illness was punctuated by malnutrition and episodes of heart failure. She was given no other antibiotics. After the sixth relapse maintenance treatment with oral vancomycin 125 mg eight-hourly was begun. With this regimen diarrhoea was controlled and stools over the next 10 weeks remained negative for *C difficile* and its cytotoxin. There was no adverse reaction to vancomycin throughout.

Comment

C difficile as the sole factor in the pathogenesis of pseudomembranous colitis has been questioned.[4] Man can harbour this organism and its cytotoxin without ill effects.[1 5] Moreover, ischaemia on the basis of capillary microthrombosis may be important in producing the mucosal necrosis seen in this condition.[2 3] Pseudomembranous colitis is more common among patients with underlying cardiovascular diseases. In this case pseudomembranous colitis was associated with faecal presence of *C difficile* in a patient with severe chronic bowel ischaemia. She had not received antibiotics. The relapses after adequate courses of vancomycin point strongly to the role of ischaemia, which may encourage recolonisation or reproliferation of *C difficile*. The patient responded well clinically to each course of vancomycin, so that development of resistant strains is unlikely.

Antibiotics should be used with caution in patients with ischaemic bowel disease. In patients presenting with the disease stools should be tested for *C difficile*. When patients with pseudomembranous colitis relapse after adequate treatment an underlying ischaemic process should be considered. As pseudomembranous colitis may be contagious patients with ischaemic bowel disease might warrant protective isolation. Finally, in this patient a small maintenance dose of vancomycin appeared to be effective and safe in preventing relapses.

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Two-, six-, and 12-minute walking tests in respiratory disease

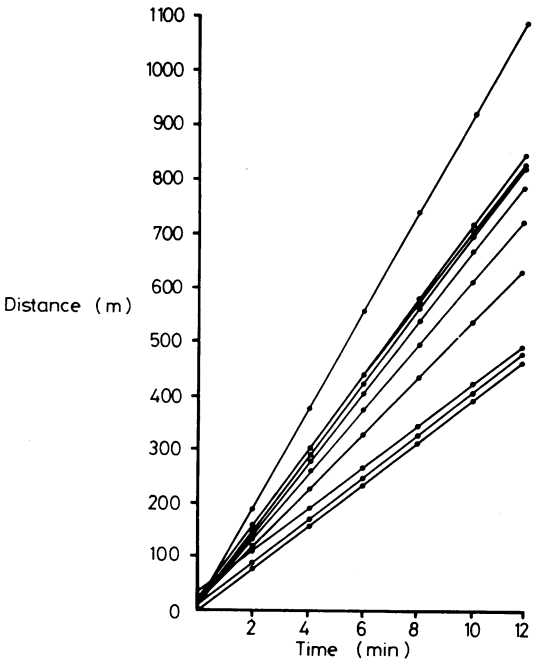
The 12-minute walking test[1] is a useful and reproducible[1 2] measure of exercise tolerance. It provides a simple, practical guide to everyday disability and does not require expensive apparatus. Nevertheless, it is both time consuming for the investigator and exhausting for the patient. We therefore explored the possibility of using walking tests of shorter duration to assess exercise tolerance.

Patients, methods, and results

Walking tests were conducted as described by McGavin *et al*,[1] but the timing (at two, six, and 10 minutes) and the wording of encouragement were standardised. All patients performed two practice 12-minute tests before entry into the first two studies.

Study 1. Pacing during 12-minute test—Ten patients of mean age 61 (±SD 11) years with limited exercise tolerance owing to stable chronic airflow obstruction were studied. Their 12-minute walking distance ranged from 400 to 1100 m. The test was performed on five occasions at four-week intervals, always at the same time of day. The distance covered at two-minute intervals throughout the test was noted. Patients generally walked further during the first two minutes of the test (figure) than during any subsequent two-minute period, when they covered remarkably constant distances (mean correlation coefficient=1·000, range 0·996 to 1·000, n=50).

Study 2. Comparison of two-, six-, and 12-minute tests—Thirty patients of mean age 61 (±12) years with stable chronic respiratory disability owing to various diseases were studied (forced expiratory volume in one second =1·28±0·66 l, forced vital capacity=2·29±0·78 l). Twelve-minute walking distances ranged from 345 to 1215 m. Each patient performed one two-minute, one six-minute, and one 12-minute test in a randomised cross-over design. The walks were made on three consecutive days but at the same time of day. The mean distances walked during the tests were 149±35 m, 413±107 m, and 774±229 m, respectively. The three tests were highly correlated: six-minute *v* 12-minute, r=0·955; two-minute *v* 12-minute, r=0·864; and two-minute *v* six-minute, r=0·892 (n=30). The linear regression equations were: 12-minute distance=2·04 (six-minute distance) −67·7 m; 12-minute distance=5·70 (two-minute distance) −73·3 m; six-minute distance=2·76 (two-minute distance) +3·12 m. The variance (=100 SD/mean) for the two-minute, six-minute, and 12-minute tests respectively was 23·4, 26·0, and 29·6 m.



Distance walked during 12-minute walk test, measured at two-minute intervals. Each line represents mean of five walks in a particular patient.

Study 3. Reproducibility of two-minute test—Thirteen patients of mean age 51±14 years with a range of respiratory disease (forced expiratory volume in one second 0·98±0·25 l, forced vital capacity 2·24±1·02 l) and exercise tolerance (two-minute walking distance 54-215 m) were studied. No patient had performed a walking test previously. Patients performed four two-minute tests, with at least an hour in between walks; mean distances of consecutive walks were 137±46 m, 141±43 m, 146±41 m, and 147±40 m.

Comment

The 12-minute walking test was based on a 12-minute running test described by Cooper[3] as a guide to physical fitness in healthy young men. We thought that in patients with severe disability a test of shorter duration might be adequate. Our first study, of the 12-minute test, showed that, after a slight initial burst of speed, patients walked at constant speed, suggesting that shorter tests would be as good. Subjects showed a remarkable ability to pace themselves during this test.

The high correlation coefficients between the two-minute, six-minute, and 12-minute tests indicated that they were similar measures of exercise tolerance. The variance of the 12-minute test was slightly greater than that of the six-minute test, which was slightly greater than that of the two-minute test—that is, the longer the patients walked the greater was the spread of results. Although this might reflect greater random variation, it probably indicates that the longer tests are more discriminating. In practice the differences were not large.

The 12-minute distance is highly reproducible.[2] The two-minute distance is equally reproducible and similarly requires two practice