We also studied 10 fit women volunteers aged 21-36 two to four days before and six to eight days after the onset of menstruation. Height, weight, and leg volume were measured at the beginning and end of a working day, and leg symptoms at the end of the day were recorded.

Almost every subject had lost height and weight after menstruation, but leg volume increased in some and decreased in others and the changes were not significant. The amount of leg swelling and severity of symptoms at the end of the day were no different before and after menstruation. There were no differences in basal leg volume and leg swelling between those taking oral contraceptives (n=6) and those not.

Comment

We found a significant increase in leg volume during the day in fit young adults, and almost three quarters of this swelling occurred in the morning. The legs that ached were those that swelled most. The increase in leg volume may be due to increased interstitial fluid and venous distension, and accumulation of metabolites or passive stretching of skin, fascia, and veins may cause aching.

Body weight increases before menstruation due to salt and water retention induced by oestrogen and progesterone.[1 2] An increase in total body water might result in greater leg volume. It is therefore surprising that in our study neither basal leg volume nor leg swelling were greater before menstruation. This finding may be related to the fact that none of our subjects experienced any premenstrual symptoms.

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Lung abscess and reactive arthritis: rare complications of leptospirosis

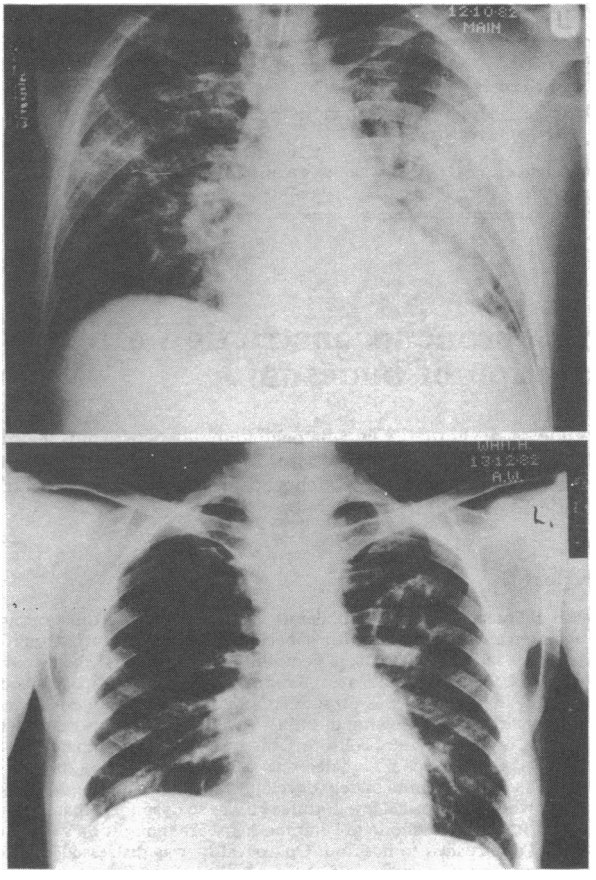
Leptospirosis is rare, about 60 cases being diagnosed each year in the United Kingdom, with a mortality of 5%.[1] We have found only one previous report of reactive arthritis and none of lung abscess complicating leptospirosis. We report on a patient with both complications.

Case report

A 52 year old civil engineer presented with a six day history of abdominal pain, headache, nausea, and vomiting. Fourteen days previously he had cut his hand in a drain. On admission to hospital he was shocked with an unrecordable blood pressure, jaundiced, and tachypnoeic. Haemoglobin concentration was 14·3 g/dl; white cell count $1{\cdot}6\times10^9$/l (73% neutrophils); platelet count 55×10^9/l; prothrombin ratio 1·6; and concentrations of fibrinogen degradation products 10-40 mg/l, urea 12 mmol/l (72·1 mg/100 ml), sodium 130 mmol(mEq)/l, potassium 3·4 mmol(mEq)/l, and bilirubin 170 μmol/l (10 mg/100 ml); liver enzyme activity was slightly raised. An electrocardiogram showed no abnormality other than sinus tachycardia. An *x* ray film showed bilateral basal shadowing. A leptospiral complement fixation test showed a rise in titre from 1/10 on the third day in hospital to 1/2560 on the 15th day. Agglutination tests showed cross reaction with several serotypes. Multiple blood cultures gave negative results, and there was no serological evidence of other pathogens.

Initial treatment included intravenous methylprednisolone, fluid replacement, azlocillin, gentamicin, and metronidazole. He had anuria with evidence of acute tubular necrosis, and peritoneal dialysis was started. After 24 hours a chest *x* ray film showed extensive pneumonitis (figure (top)), and because of increasing respiratory distress mechanical ventilation with positive end inspiratory pressure was started. Profuse amounts of heavily bloodstained secretions were aspirated from the endotracheal tube throughout the following 15 days. After 28 days the pneumonitis had partially resolved, which permitted extubation, although cavitation in the left upper lobe rapidly developed into a large abscess (figure (bottom)). On fibreoptic bronchoscopy the left upper lobe bronchus was patent, although the mucosa throughout appeared floridly haemorrhagic. Bronchial washings yielded *Pseudomonas aeruginosa*; anaerobic culture was negative and dark ground microscopy showed no leptospira. After 21 days' treatment with chloramphenicol and metronidazole his symptoms had resolved completely, and he was discharged from hospital with normal hepatic and renal function.

After three weeks he presented again with severe arthritis of acute onset affecting the spine, shoulders, and knees, and morning stiffness lasting three hours. There was generalised muscle wasting; limitation of movement of the spine, shoulders, and knees; and prominent bilateral heel tenderness. Erythrocyte sedimentation rate was 47 mm in the first hour. Tests for rheumatoid factor and antinuclear factor were negative. *X* ray films of the hands, knees, heels, and lumbar spine were normal. He was negative for HLA B27. His symptoms did not improve after treatment with a series of non-steroidal anti-inflammatory drugs, but partially responded to high doses of prednisolone.



Chest *x* ray film showing (top) extensive pulmonitis before ventilation and (bottom) cavitation and large abscess in left upper lobe.

Comment

Lung disorders have been reported in 11% of patients with leptospirosis, often as incidental findings[2] but occasionally, as the major manifestation of the disease, presenting as haemoptysis[3] or adult respiratory distress.[4] Pathologically the pulmonary lesions are pneumonitis with interstitial oedema and haemorrhage, and the likely mechanism is a direct toxic effect on the vascular endothelium, exacerbated in this case by prolonged caogulation times and thrombocytopenia.

Although Heath *et al* frequently found arthralgia in the prodromal phase of leptospirosis,[2] we have found only one report of acute arthritis after the initial infection.[5] Uveitis and prostatitis have been described after leptospirosis,[2] which provides further evidence of "reactive" responses to the acute infection. Hypertrophic osteoarthropathy but not reactive arthritis may be associated with lung abscess, and our patient's lung disease alone is unlikely to have accounted for his arthritis. We suggest that leptospirosis should be added to the increasing number of infectious diseases that lead to reactive arthritis.

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Pyrexia of undetermined origin, diarrhoea, and primary cerebral lymphoma associated with acquired immunodeficiency

We report on a heterosexual man who presented with chronic diarrhoea and fever associated with acquired immunodeficiency. Investigation, which included extensive serological studies, failed to show a cause for his fever.

Case report

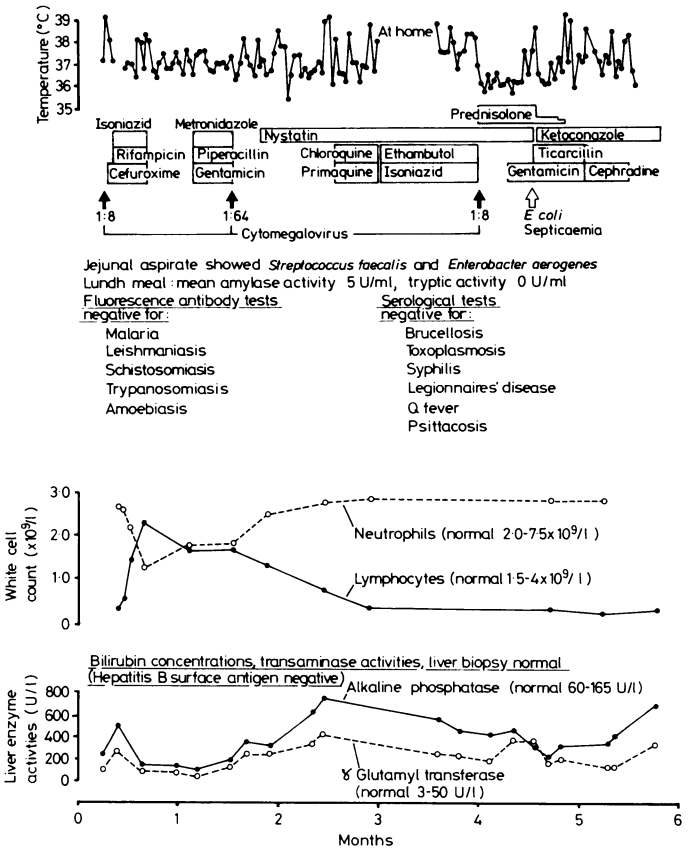
A 47 year old Scotsman, who had returned to the United Kingdom after working in East Africa for many years, presented with profuse diarrhoea, weight loss, and consolidation in the right lung. Eighteen months previously he had presented to another hospital with fever, lymphadenopathy, and hepatosplenomegaly. He was also known to have had recurrent malaria. Initial tests showed haemoglobin concentration 7·8 g/dl, white cell count $4{\cdot}5 \times 10^9$/l, and platelet count 77×10^9/l. The peripheral blood lymphocyte count was depressed (figure), recovered transiently, and then declined to a very low value. Erythrocyte sedimentation rate was 137 mm in the first hour. A Mantoux test yielded a negative result. T cell marker studies were not performed. Serum IgG concentration was slightly increased at 1·67 g/100 ml, and serum concentrations of IgA, IgM, IgE, and complement were all within normal limits.

For four months attempts to detect an infective cause for his fever were unsuccessful (figure). All viral titres except, transiently, titres to cytomegalovirus yielded negative results. There were no malarial parasites on the blood film. Serum alkaline phosphatase and γ-glutamyltransferase activities were raised (figure). The common and right hepatic ducts were dilated. Cholangitis could not be confirmed bacteriologically, and a cause for the dilated ducts was not established. Inflammatory bowel disease was excluded. In November he developed septicaemia due to *Escherichia coli* during a brief trial of treatment with prednisolone; in December his condition deteriorated considerably with the sudden onset of focal neurological signs. Computed tomography and a brain biopsy were undertaken. He died on 24 December.

At necropsy a poorly differentiated lymphocytic cerebral lymphoma centred on the left lentiform nucleus was found as well as toxoplasma cysts throughout both cerebral hemispheres. A lung abscess 4 cm long was present, from which *Klebsiella pneumoniae* and *Candida albicans* were isolated. The larger hepatic ducts were dilated and contained concretions of bile crystals. Cytomegalovirus inclusion bodies were found within epithelial cells of the bile ducts, periductal endothelial cells, the submucosa of the gall bladder and gut, and epithelial cells of the pancreas, thyroid, and lungs.

Comment

A previously healthy heterosexual man developed an illness characterised by prolonged fever, chronic diarrhoea, mucosal candidiasis, tuberculin anergy, lymphopenia, widespread multiple opportunistic infections, and primary lymphoma of the central nervous system. These features suggest a disorder of cell mediated immunity but give no insight into its cause.[1] In retrospect it would have been interesting to have studied T lymphocyte subpopulations.[1] Similar disturbances of immunity, however, have been seen in high risk groups—namely, in patients with viral, fungal, or mycobacterial infections or apparently after exposure to ultraviolet light—who do not develop opportunistic infections or unusual tumours.[2] Our patient fulfilled the criteria for the acquired immunodeficiency syndrome.[3] This term has become linked with "an outbreak of disease" undoubtedly related to immunodeficiency in the homosexual population of the United States of America,[1] but similar abnormalities have been reported, not necessarily with manifestation of immunodeficiency, in drug abusers, Haitian immigrants, and patients with haemophilia, among others.[1-4] In spite of this diversity a common aetiological agent has been suggested.[1 2] Acquired immunodeficiency is not new; its manifestations are not unexpected, as evidenced by



Summary of clinical findings showing daily temperature (measured at 1800), drug treatment, titre of antibodies to cytomegalovirus, serial white cell count, and liver enzyme activities.

the unusual infections seen in patients receiving cytotoxic treatment and by the occurrence of primary cerebral lymphoma in recipients of renal transplants.

Fever and diarrhoea commonly develop in homosexuals with the acquired immunodeficiency syndrome.[1 3 5] Our patient was unusual in that no organisms accounting for his fever were isolated during four months of investigation. In this respect his impaired antibody responses to cytomegalovirus and toxoplasma indicate that the results of serological tests may be misleading when antibody production depends on the cooperation of T cells. A similar explanation may account for the absence of malarial antibodies. We did find evidence, however, of colonisation of the small bowel and pancreatic insufficiency (figure), which may have contributed to his diarrhoea. The distribution of cytomegalovirus in the liver without hepatic parenchymal change represents an unusual form of infection by cytomegalovirus in adults.

Our patient's illness may have resulted from the combined immunosuppressive effects of cytomegalovirus, malaria or other infections, and, latterly, malnutrition. Serological tests may be inappropriate for diagnosis when antibody production depends on the cooperation of T cells. Our study emphasises the importance of considering acquired immunodeficiency as a cause of fevers of undetermined origin, particularly in view of the reliance normally placed on serological tests.

We thank Dr G Watkinson, Dr G G Birnie, and Professor M R Bond for their help in the management of this patient, Dr J F Boyd for performing