[4] O'Tauma LA, Kirkman HN, James PM. Raised intracranial pressure after hyperalimentation. *Lancet* 1973;ii:1101.
[5] Saxena VK, Heilpern RJ, Murphy SF. Pseudomotor cerebri. A complication of parenteral hyperalimentation. *JAMA* 1976;**235**:2124.

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Pleurisy and pulmonary granulomas after treatment with acebutolol

Many patients currently take beta-blockers to control hypertension or angina and such medication is often continued for years. Side effects are uncommon but reports of ocular, cutaneous, and serosal damage led to the withdrawal of the cardioselective beta-blocker practolol from long-term use. We report a case in which treatment with acebutolol was followed by recurrent attacks of pleurisy necessitating withdrawal of the drug.

Case report

A 47-year-old woman presented with a three-month history of intermittent pleuritic chest pain. The bouts of pain each lasted a few days but the site varied; for the last two weeks she had had a non-productive cough. She was not short of breath and was otherwise well with no previous history of respiratory disease. Two years before, she had been found to be hypertensive and had taken acebutolol (200 mg daily) and xipamide (20 mg daily) regularly since then.

Examination showed no sign of fever, clubbing, or cyanosis. A prominent pleural rub was heard in the left axilla and at other times rubs were heard in other areas of both lung fields. No other abnormalities were evident. Investigation showed a normal white cell count and differential but the erythrocyte sedimentation rate was 70 mm in the first hour. Antinuclear and rheumatoid factors were not detected and serum immunoglobulin and DNA-binding antibody values were normal. Sputum and urine samples were sterile and acid-fast and alcohol-fast bacilli were not present; results of viral studies were negative. Peak expiratory flow rate was 480 l/min, forced expiratory volume in one second 2·2 l (95% predicted), and vital capacity 2·7 l (100% predicted). Repeated chest *x*-ray pictures were normal, as was a ventilation-perfusion lung scan. *X*-ray computed tomography of the chest showed irregular subpleural densities at the lung bases, particularly on the right. These were thought to be intrapulmonary, though there was also patchy pleural thickening. Schirmer's test gave an abnormal result, the right eye producing 10 mm saturation at five minutes and the left eye 4 mm (normal $>$ 15 mm). Rose bengal staining was negative.

Disabling bouts of pleurisy for five months eventually necessitated an open-lung biopsy of the right lower lobe, disclosing patchy fibrosis and slight thickening of the visceral pleura. Histological studies showed granulomas in the lung with fibrosis; the granulomas were unlike those of sarcoidosis and contained scattered groups of degenerate eosinophils. Angiitis was not present and the tissue was thought to show an inflammatory condition. There was no evidence of fungal or tuberculous infection and cultures grew no pathogens.

Acebutolol was withdrawn and cyclopenthiazide substituted for xipamide. Over the next nine months the attacks of pleural pain became less frequent, the rubs disappeared, the erythrocyte sedimentation rate fell to 5 mm in the first hour, and a repeat Schirmer's test gave values of 38 mm and 28 mm at five minutes for the right and left eyes respectively. Follow-up pulmonary function tests gave normal values and the patient became asymptomatic.

Comment

Despite widespread use, there are only sporadic reports of oculomucocutaneous side effects from beta-blockers other than practolol. With that drug patients developed keratoconjunctivitis sicca, corneal opacities, rashes, and serositis.[1] Included in this last category were cases of "plastic peritonitis" and pleurisy[1–3] and one report of fatal interstitial pulmonary fibrosis.[4] The possibility remains that other drugs of this class might cause similar reactions.

Our patient suffered severe pleurisy necessitating a diagnostic thoracotomy. When acebutolol was withdrawn her symptoms gradually disappeared and there was no obvious cause apart from a drug reaction. It seems unlikely that xipamide was responsible, and it is worth noting that acebutolol resembles practolol more closely than any other beta-blocker, being cardioselective, an anilide, and having partial agonist activity.[5] The manufacturers of acebutolol and the Committee on the Safety of Medicines have had no reports of pleurisy or pulmonary granulomas associated with the drug.

We thank Professor H Spencer for help in interpreting the lung biopsy findings.

[1] Wright P. Untoward effects associated with practolol administration: oculomucocutaneous syndrome. *Br Med J* 1975;i:595-8.
[2] Marshall AJ, Baddeley H, Barritt DW, *et al.* Practolol peritonitis. *Q J Med* 1977;**46**:135-49.
[3] Mackay AD, Axford AT. Pleural effusions after practolol. *Lancet* 1976;i:89.
[4] Erwteman TM, Braat MCP, Van Aken WG. Interstitial pulmonary fibrosis: a new side effect of practolol. *Br Med J* 1977;ii:297-8.
[5] Cruickshank JM. The clinical importance of cardioselectivity and lipophilicity in betablockers. *Am Heart J* 1980;**100**:160-78.

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Fatal acute immune haemolytic anaemia caused by nalidixic acid

Haemolytic anaemia in subjects with glucose-6-phosphate-dehydrogenase deficiency is the only reported haematological complication of treatment with nalidixic acid.[1] We describe the onset of fatal immune haemolytic anaemia after administration of nalidixic acid.

Case report

A 74-year-old woman had a 10-year history of episodes of haemolytic anaemia. Results of direct Coombs test during each attack were positive becoming negative between each episode. The patient took no drugs apart from occasional nalidixic acid for a recurrent urinary infection. She was admitted to the department of general medicine on 29 March 1980 with a haemolytic crisis. Laboratory tests showed red cell count of $2{\cdot}59\times10^7$/l, haemoglobin concentration of 9·8 g/dl, mean cell volume 107 fl, leucocytes $2{\cdot}7\times10^5$/l, reticulocytes 8·4%, total bilirubin 2·97 mg/100 ml (51 μmol/l), direct Coombs test gave weakly positive results; serum lactate dehydrogenase activity was 850 U/l and haptoglobin concentration less than 0·2 g/l. Tests for glucose-6-phosphate-dehydrogenase, sideraemia, transferrinaemia, Waaler-Rose reaction, lupus erythematosus cells, antinuclear factors, complement fixation for *Mycoplasma pneumoniae*, osmotic fragility, and autohaemolysis gave negative results, as did Ham-Crosby and Donath-Landsteiner tests. The myelogram showed a pronounced erythropoiesis. Haemolysis was controlled with betamethasone.

On 17 April 1980 the patient complained of dysuria and pollakiuria and nalidixic acid was prescribed. After the first dose of 1000 mg the patient suffered a serious attack of intravascular haemolysis and died after a few hours despite high doses of steroids and a blood transfusion with compatible blood. The haemogram was illegible for autohaemolysis; result of indirect Coombs test was weakly positive and of the direct Coombs test strongly positive. It was impossible to determine the antibodies for autopanagglutination of erythrocytes. Results of tests with monospecific sera showed a clear positivity with anti IgG and anticomplement.

Comment

A positive result to the direct Coombs test in one of the earlier haemolytic crises, negative results between attacks, and clearly positive results during the terminal attack suggested a haemolytic anaemia of immunological pathogenesis. The absence of infection with *M. pneumoniae* and of autoimmune diseases or underlying lymphoproliferative disorders, together with a fatal intravascular haemolytic attack after administration of nalidixic acid points to a clear connection between drug and haemolysis. Retrospectively, we deduce that the previous haemolytic attacks were caused by nalidixic acid, which the

patient took periodically. The presentation and clinical aspect in the form of an acute intravascular haemolytic episode, the small doses of drug sufficient to cause the attacks, the brief time lapse between administration and onset of symptoms, and the positive result of direct Coombs test, with notable components on the erythrocyte surface at the time of the attacks, all indicate that the mechanism responsible is of stibophen or "innocent bystander" type.[2-5]

Nalidixic acid should therefore be added to the list of drugs responsible for immune haemolytic anaemia.

[1] Mandal BK, Stevenson J. Haemolytic crisis produced by nalidixic acid. *Lancet* 1970;i:614.
[2] Garratty G, Petz LD. Drug-induced immune hemolytic anemia. *Am J Med* 1975;**58**:398.
[3] Vila JM, Blum L, Dosik H. Thiazide-induced immune hemolytic anemia. *JAMA* 1976;**236**:1723.
[4] Wintrobe MM. *Clinical hematology*. Philadelphia: Lea and Febiger, 1981: 943-7.
[5] Worlledge SM. Immune drug-induced hemolytic anemia. *Semin Hematol* 1973;**10**:327.

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Campylobacter colitis associated with erythema nodosum

When erythema nodosum and mouth ulcers occur in a patient presenting with bloody diarrhoea in whom there is sigmoidoscopic and histological evidence of "colitis" the colitis is usually due to either Crohn's disease or ulcerative colitis. We describe a patient in whom these cutaneous manifestations paralleled the course of campylobacter colitis. Erythema nodosum has not been described previously in association with campylobacter infection. This association may have implications for the pathogenesis of inflammatory bowel disease, infective colitis, and transient colitis syndrome.[1]

Case report

A 24-year-old woman gave a week's history of frequent watery, bloody diarrhoea associated with colicky lower abdominal pain, which had started six days after she had arrived in Spain. She had also developed tender raised areas on both shins, which she ascribed to insect bites. Ovranette, an oral contraceptive containing ethinyloestradiol and levonorgestrel, was the only medication.

Examination showed a well woman with classical erythema nodosum on both shins. A 0·5 cm shallow ulcer was present on her lower lip, but there was no eye or genital disease. Direct and rebound tenderness were present in the left iliac fossa. Sigmoidoscopy showed abnormal rectal mucosa with diminished vascularity and contact bleeding. Histology of a rectal biopsy specimen gave appearances of an infective colitis. *Campylobacter jejuni* was cultured from stool samples, which were negative for *Salmonella, Shigella,* and *Yersinia* spp and enteropathogenic *Escherichia coli. Clostridium difficile* and its toxin were not detected. Virus particles were not detected by direct electron microscopy or culture. A full blood count was normal. A Monospot slide test was negative; yersinia antibodies were absent; and titres of antistreptolysin O, antideoxyribonucleotidase B, antihyaluronidase, and antibodies to cytomegalovirus and *Chlamydia psittaci* showed no abnormality. A Mantoux test (100 old tuberculin units) was negative. A chest radiograph was normal. Throat swab and blood culture were sterile.

Both the colitis and the cutaneous lesions resolved spontaneously, and she continued taking Ovranette. The erythema nodosum did not reappear, and she remained well three months later.

Comment

Campylobacter infections have been associated with colitis, and several extraintestinal manifestations including septic and reactive arthritis, cholecystitis, and endocarditis are well recognised. Cutaneous manifestations have not, to our knowledge, been described. A causal relation between the appearance of erythema nodosum, mouth ulcer, and colitis appears to have existed in this patient, and the lesions regressed as the colitis settled. Continuing challenge with Ovranette was not associated with recrudescence, which eliminates this potential cause.

Mouth ulceration and erythema nodosum are both well-recognised cutaneous associations with inflammatory bowel disease. Infective bowel disease has previously been reported only in association with yersinia infections. There was no supportive clinical or pathological evidence for inflammatory bowel disease in our patient. If stool samples had not been sent for microbiological analysis or had been negative for campylobacter (due to previous antibiotic treatment, for example) inflammatory bowel disease such as ulcerative colitis would probably have been diagnosed. She would probably then have received quite inappropriate treatment and become subject to the implications of long-term follow-up.

It has been suggested that there is a form of colitis, possibly of infective aetiology, transient in nature, that may be mistaken for inflammatory bowel disease and that accounted for almost 20% of one series of patients with acute colitis.[1] The occurrence of mouth ulcer and erythema nodosum in this patient with campylobacter colitis raises the possibility that a common pathological or immunological mechanism may function in some cases of inflammatory disease and infective colitis.

We thank Dr B C Morson, consultant pathologist, St Mark's Hospital, London, for the histopathology report of the rectal biopsy specimen.

[1] Mandal BK, Schofield PF, Morson BC. A clinico-pathological study of acute colitis: the dilemma of transient colitis syndrome. *Scand J Gastroenterol* (in press).

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Orthogeriatric rehabilitation ward in Nottingham: a preliminary report

Orthogeriatric wards have been advocated for many years,[1 2] and the concept was supported in the Duthie report.[3] In Nottingham there have been problems with coping with the numbers of orthopaedic patients, and at the peak time of the year in February 1977, 70 orthopaedic patients were "sleeping out" in other departments. The main source of difficulty was the large number of aged patients with trauma, mainly fractured neck of femur. In Nottingham the geriatric service has lacked resources (six beds/1000 patients over 65 years compared with the Department of Health and Social Security norm of 10 beds/1000 patients). In October 1978 an 18-bed orthogeriatric rehabilitation ward was opened in a hospital three miles away from the acute hospital. This orthogeriatric ward was a collaborative project between the orthopaedic and geriatric departments with combined ward rounds and a close working relationship. It was also an attempt to put the available resources of both departments to the most effective use.

We have made a preliminary evaluation of the success of the project by comparing the length of stay for all female patients admitted to the Nottingham hospitals with fractured femur in 1977 (the last complete year before the ward opened) with that in 1979 (the first complete year after the ward opened).

Patients, methods, and results

Female patients were selected for transfer to the rehabilitation ward 48 hours after operation or as soon as a bed became available. Basically fit patients who were expected to do well without special measures were not sent, nor were those with gross physical or mental defects which would prevent mobilisation. Patients who were expected to respond to a well-staffed rehabilitation team were selected for the ward; a "triage" system thus operated. Most patients had a fractured neck of femur complicated by other disease or disability, but elderly patients with trauma and any major rehabilitation problem also qualified for the ward.