The pharmacokinetics of cyclosporin A are not fully understood,³ and the present method of monitoring the drug is not always satisfactory²; hence concentrations in the blood may not accurately reflect tissue concentrations, particularly in the cerebrospinal fluid and brain. This aspect of cyclosporin A usage needs further investigation. Nevertheless, the epileptic fits were associated with predose cyclosporin A blood values above the recommended range.

We suggest that if epileptic fits occur in patients receiving cyclosporin A after renal transplantation the drug should not be stopped but the blood concentrations brought within the recommended range and the fits controlled with anticonvulsants.

- 1 Atkinson K, Biggs J, Darveniza P, *et al*. Cyclosporin A associated central nervous system toxicity after allogeneic bone marrow transplantation. *N Engl J Med* 1984;310:527.
- 2 Rolles K, White DJG, Thiru S, *et al*. Cyclosporin A initially as the only immunosuppressant in 34 recipients of cadaveric organs: 32 kidneys, 2 pancreases and 2 livers. *Lancet* 1979;ii:1033-6.
- 3 Durrant S, Chipping PM, Palmer S, *et al*. Cyclosporin A, methylprednisolone and convulsions. *Lancet* 1982;ii:829-30.
- 4 Gross MLP, Pearson R, Sweny P, *et al*. Rejection encephalopathy. *Proc Eur Dial Transplant Assoc* 1981;18:461-4.
- 5 Joss DV, Bassett AJ, Kendr JP, *et al*. Hypertension and convulsions in children receiving cyclosporin A. *Lancet* 1982;ii:906.

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Sucking wound of the knee: not gas gangrene

Sucking wounds develop when a one way valve and negative pressure allow air to enter the tissues; they are commonly seen in chest and neck injuries.¹ We report a case of air entrapment in the leg and discuss the differential diagnosis of gas gangrene.

Case report

An eight year old boy presented in the casualty department with pain in the back of the right thigh. Eight hours earlier, while playing football, he had felt something penetrate the skin at the back of the right knee. He removed a 2 cm splinter and discarded it without paying any attention to its nature. He continued playing football and did not experience any pain until the middle of a karate session seven hours later.

When seen in casualty he was irritable, tired, and mildly feverish (37.6°C). There was a 2 mm puncture wound over the lateral aspect of the popliteal fossa with associated fullness and crepitus extending proximally up the thigh. No foreign body was palpable, and he had slight limitation of knee movements alone. There was no evidence of cellulitis, lymphadenopathy, or neurovascular injury. A radiograph of the knee (figure) confirmed the presence of gas in the soft tissues. This finding raised the suspicion of gas gangrene, but further radiography two hours later confirmed the diagnosis of air entrapment in the tissues (figure). He was treated with parenteral antibiotics and discharged from hospital 48 hours later. On review in the outpatient department four days after injury he was asymptomatic and radiography showed complete resorption of the gas (figure).

Comment

Air entrapment in the leg after small puncture wounds is extremely rare. In this case knee flexion may have opened up the skin wound and increased the volume of the popliteal fossa, creating subatmospheric conditions and sucking in air; knee extension may then have sealed the skin wound and forced the air into the tissue planes deep and proximally.

Gas gangrene is rarely seen in civilian practice and is characterised by swollen, crepitant tissues. Its early diagnosis and treatment are essential to avoid serious complications. The incubation period may be as short as four hours but is on average one to two days.² Gas

Radiographs in boy with small puncture wound (a) at admission, showing gas in soft tissues, (b) two hours later, showing (arrow) air entrapment, and (c) four days later, showing complete resorption of gas.

forming clostridia may be introduced into wounds as spores, which, in the presence of tissue necrosis or foreign particulate matter, especially calcium and silicates, germinate and produce toxins. It is diagnosed clinically, being characterised by swollen, oedematous, painful tissues with a scanty serosanguinous exudate and crepitus. Rapid spread along the length of skeletal muscles and associated systemic effects, reflected in a rise in temperature and pulse rate, lead ultimately to death. Treatment includes the administration of penicillin, polyvalent antitoxin, surgical debridement, and hyperbaric oxygen.

We thank Mr R A Elson for allowing us to report this case.

- 1 Harris JH. The significance of soft tissue injury in the roentgen diagnosis of trauma. *C R C Critical Reviews in Clinical Radiology and Nuclear Medicine* 1975;6:295-368.
- 2 Wilson GS, Miles A. Gas gangrene: clostridial infections of man and animals. In: Topley WCC, Wilson GS, eds. *Topley and Wilson's principles of bacteriology, virology and immunology*. London: E Arnold, 1972:2258-77.

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Patterns of ovarian cyst hospital discharge rates in England and Wales, 1962-79

Ovarian cysts are the fourth most common gynaecological cause for admission to hospital in England and Wales, with 14 000 discharges annually. Little is known about their aetiology or distribution in the population. This report summarises the age distribution of women admitted to hospital with ovarian cysts and describes trends in hospital discharge rates in England and Wales from 1962 to 1979.

Methods and results

Hospital discharge data were obtained from the Hospital In-Patient Enquiry (HIPE), a 10% sample of discharges from NHS hospitals. Included were all discharges where the main diagnosis was either retention cyst or benign neoplasm of the ovary (9th ICD codes 620.0-620.2,220). From 1962 until 1979 the all ages hospital discharge rates for ovarian cysts have decreased by 15%—from 59.3 to 51.4 per 100 000—which is highly statistically significant ($p < 0.01$). The age specific discharge rates for the three year periods 1962-4, 1969-71, and 1977-9 are shown in the figure. The age pattern has been stable throughout the years, rates being low until puberty and peaking at 25-34. There is a dramatic decline from ages 45-54, but after 55 there is only a small further decline in the rates. Each age group except those 0-14 years old has experienced decreasing rates since 1962-4. These decreases were significant ($p < 0.01$) except in the 35-44 year olds.

Age specific ovarian cyst hospital discharge rates (per 100 000 women per year). The percentages are the % change between 1962 and 1964 and between 1977 and 1979 rates.

Comment

The age pattern of discharge rates suggests that the occurrence of ovarian cysts is strongly related to ovarian activity. That follicular stimulation and ovulation are important in their formation is supported by the observed decreased risk of ovarian retention cysts among women using oral contraceptives.^{1,2} The steep decline in discharge rates for perimenopausal women probably marks the disappearance of the formation of retention cysts coincident with the cessation of ovarian activity. Ovarian cysts diagnosed in women from the age of 55 onwards are mostly benign neoplasms. Unfortunately, retention cysts and benign neoplasms are usually inadequately distinguished in hospital records and so cannot be separated in these data.

The decreases in hospital discharge rates for ovarian cysts were gradual, and did not occur abruptly in 1968 or 1979, when newer revisions of disease classification were adopted. Furthermore, over a similar time period hospital discharge rates for pelvic inflammatory disease³ and ectopic pregnancy⁴ have increased. Thus the decrease in ovarian cysts is not simply part of a general decrease in hospital admissions for gynaecological disorders or in their ascertainment.

During the years considered here there has been a wide adoption of laparoscopy and ultrasound scans, and women have been encouraged to attend for screening checkups and cervical smears. Thus small or asymptomatic cysts may have been detected recently, but missed in earlier years. This increased detection of asymptomatic cysts should not have resulted in a reduction in hospital discharge rates (rather the reverse), but might have altered the type of case, with a decreasing proportion being admitted as emergencies. This may well have happened since discharge rates decreased by 24% for emergency cases, but only by 12% for non-emergency admissions. Thus the true prevalence of ovarian cysts may have declined even more rapidly than the data suggest.

Oral contraceptive use in Britain increased between 1962 and 1979,⁵ and our estimates based on their reported degree of protection suggest that the pill may be responsible for up to a half of the observed decrease in hospital discharge rates among women aged 15-44. Nevertheless, the relative decrease in discharge rates was greater in women older than 45, who were probably not taking oral contraceptives and were likely to have benign neoplasms rather than functional cysts. The increasing prevalence of hysterectomy and oophorectomy and the use of hormone replacement therapy may be protecting these older women from benign ovarian neoplasms, but we know of no published evidence to support these suggestions.

We thank Dr J Ashley of the Office of Population Censuses and Surveys for providing unpublished HIPE tables.

- 1 Boston Collaborative Drug Surveillance Study. Functional ovarian cysts and oral contraceptives. *JAMA* 1974;228:68-9.
- 2 Vessey M, Doll R, Peto R. A long-term follow-up study of women using different methods of contraception—an interim report. *J Biosoc Sci* 1976;8:373-472.
- 3 Robinson N, Beral V. Risk of ectopic pregnancy. *Lancet* 1979;ii:1247-8.
- 4 Robinson N, Beral V, Ashley J. Trends in pelvic inflammatory disease in England and Wales. *J Epidemiol Community Health* 1981;35:265-70.
- 5 Kols A, Rinehart W, Piotrow PT, Doucette L, Guillen WF. Oral contraceptives in the 1980s. *Popul Rep [A]* 1982;10:189-222.

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Amputation for pseudotumour in acquired haemophilia

In patients with haemophilia haemorrhage into muscle with a wide periosteal attachment may lead to destruction of bone with the development of a pseudotumour.¹ Although well recognised in inborn haemophilia, this has never been described in a patient with acquired haemophilia. Acquired haemophilia may occur in both sexes and results from the development of antibodies to clotting factor VIII:c, which lead to spontaneous haemorrhages and may inactivate human factor VIII replacement. Though it occurs post partum and in association with malignancy, certain drugs, rheumatoid arthritis, and systemic lupus erythematosus, in nearly half the patients no underlying cause is apparent.

We report on a woman with acquired haemophilia who developed a life threatening pseudotumour in the thigh. Surgical management was made possible by replacement treatment with a new highly purified porcine factor VIII concentrate.

Case report

In 1971 a 56 year old woman presented with repeated spontaneous haemorrhages into muscles and joints. Investigation showed complete absence of factor VIII:c due to a specific antibody (400 new Oxford units/ml²), for which no cause could be identified. Immunosuppressive drugs were given in attempts to reduce the antibody level. Prednisolone was ineffective; azathioprine and cyclophosphamide resulted in lymphopenia and anaemia respectively.

In 1973 a large spontaneous bleed into the right quadriceps muscle failed to resolve completely and progressed to form a haemophilic pseudotumour. This gradually increased in size and eroded the femoral shaft, which fractured spontaneously in 1981. Despite protracted conservative management the pseudotumour did not regress. The bone ends resorbed and failed to unite. By 1983 the pseudotumour had invaded the length of the thigh and threatened the viability of the overlying skin. Computed tomography confirmed that it could still be resected by amputation.

At this stage the concentration of factor VIII:c antibody was 80 new Oxford units/ml, which would have inactivated infused human factor VIII. The concentration of antibodies to porcine factor VIII, however, was negligible. A test dose of 3000 units of highly purified porcine factor VIII (Hyate:C, Speywood Laboratories) gave a concentration of factor VIII of 670 IU/l 10 minutes after infusion. It was considered safe to undertake intertrochanteric amputation, and the whole pseudotumour was removed.

Postoperatively infusions of 50-70 units porcine factor VIII concentrate/kg were given every eight hours, the dose depending on the results of frequent assays of plasma factor VIII:c concentration. Satisfactory haemostasis was maintained. The dose and frequency of the infusions were gradually reduced, and they were stopped on the 30th postoperative day. By discharge she could walk with the help of a walking frame.

Comment

Management of haemorrhage in patients with antibodies to factor VIII:c is difficult. Replacement treatment with porcine factor VIII:c concentrate has often been complicated by anaphylaxis, allergic reactions, or thrombocytopenia. The highly purified preparation of porcine factor VIII concentrate now available is valuable in treating patients who have a high titre of antibodies to human factor VIII:c