patient with dermatomyositis receiving prednisolone and azathioprine who developed multiple cerebral abscesses from which *Nocardia asteroides* was cultured. These were clinically silent and proved to be fatal.

A 51 year old female presented in October 1987 when, she developed proximal muscle weakness, myalgia and an erythematous rash over the proximal interphalangeal and metacarpophalangeal joints. The creatine kinase was elevated at 7420 IU/l and polymyositis was confirmed by a needle muscle biopsy. She was commenced on high dose oral prednisolone. Azathioprine was added to the regime but reduced after 3 months because of leucocytopenia. In July 1988, she developed severe oral candidiasis which was treated with oral fluconazole.

Muscle power gradually improved over the next 12 months, but in February 1989, she was re-admitted complaining of lassitude and increasing weakness over the preceding month. At that time she was receiving prednisolone 30 mg on alternate days and azathioprine 50 mg daily. She was mildly cushingoid and drowsy but afebrile. There was a small 0.5 cm diameter abscess on the anterior abdominal wall below the umbilicus. Her moderate proximal muscle weakness and generalized wasting were unchanged from when she was reviewed 2 months earlier. There was no evidence of pyramidal or cerebellar dysfunction. The total white cell count was $8.7 \times 10^9/l$. Grey-green pus was aspirated from the abdominal abscess. This and a set of blood culture bottles were sent for microbiological examination but no organisms were identified or cultured. The patient was commenced on intravenous metronidazole and flucloxacillin on admission and the azathioprine stopped.

Her clinical condition remained unchanged over the next 4 days and no new neurological signs developed. She then suffered 2 generalized tonic/clonic seizures which were terminated with intravenous diazepam. Several hours later, she had a fatal cardiopulmonary arrest. Necropsy revealed that the abdominal abscess extended down to the peritoneum. There were numerous metastatic abscesses beneath the parietal pleura over the upper 4 ribs on the right side, each measuring approximately 2 cm in diameter. Multiple cerebral abscesses were also found. The largest were situated in the right occipital lobe, left frontal lobe and the right cerebellar hemisphere. The liver showed marked steatosis but no active inflammatory process and low-grade polymyositis was noted in several muscle samples. No evidence of malignancy was uncovered. Subsequent microbiological studies demonstrated *Nocardia asteroides* in abscesses from each site.

This case illustrates the need for constant vigilance for infection in immunocompromised patients. There was no evidence for malignancy and we therefore assume that the treatment of dermatomyositis with steroids and azathioprine predisposed to nocardiosis. Detailed microbiological studies should be undertaken in any similar patient who presents with a non-specific illness, particularly when there is evidence of infection such as the cutaneous abscess in this case. It has been suggested that more invasive investigations are warranted when nocardiosis is suspected, such as bronchoscopy with bronchial brush biopsy or even percutaneous or surgical lung biopsy.^{1,2} Interestingly, in spite of neurological examination on several occasions, no signs of the cerebral abscesses were found throughout her admission up to 12 hours prior to death. The possibility of cerebral involvement should

always be considered in patients known to have nocardia infection and detailed neuroradiological investigation undertaken, preferably with cranial computed tomography.

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Discharge from osteomyelitis sinus with heparin therapy

Sir,

Heparin has been in use for around 40 years for the treatment and prevention of thrombosis. Despite its widespread use, there has been a surprisingly small range of adverse effects. We describe a previously unreported reaction to the use of subcutaneous heparin and discuss a possible aetiology.

A 62 year old man was admitted to the coronary care unit with chest pain suggestive of myocardial infarction. Cardiac enzymes did not rise and he was discharged after 5 days with a diagnosis of angina. Whilst in the coronary care unit he was given heparin 5000 units subcutaneously twice daily as prophylaxis against deep venous thrombosis.

At the age of 30 he had suffered from severe osteomyelitis affecting both femora and both humeri. He had been left with discharging sinuses which had necessitated numerous operative explorations and he was on long term flucloxacillin which was necessary to prevent discharge.

Six hours after the first dose of heparin he noticed a serous discharge from his right femoral sinus. This persisted whilst he was on heparin and he stated that a similar phenomenon had occurred previously with heparin. He continued on flucloxacillin, but the discharge continued until 24 hours after he had stopped the heparin.

He was readmitted 10 days later with a further episode of chest pain which was subsequently confirmed to be a myocardial infarction. He was again given heparin whilst in the coronary care unit and again developed a discharge from his sinus. He refused further heparin; the sinus became dry within 24 hours and remained so for the duration of his 10-day stay in hospital.

Although heparin does not possess intrinsic fibrinolytic activity, it does, in combination with anti-thrombin III, inhibit the formation of thrombin, and also inhibit the activation of fibrin stabilization factor.¹

In our patient, it is possible that chronic infection in the osteomyelitis sinuses led to a dynamic balance of fibrin

formation and breakdown. The administration of heparin in this situation may have swung the balance to a predominance of fibrinolysis over fibrin breakdown.

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Metypapone-induced alopecia

Sir,

Metypapone, the adrenal 11-beta hydroxylase inhibitor is occasionally used to treat pituitary Cushing's syndrome when other means are considered inappropriate.^{1,2}

An 85 year old female with a history of tiredness, forgetfulness, facial pigmentation and hypokalaemia was investigated. Her 09.00 h cortisol was 977 nmol/l, mid-night was 952 nmol/l (normal range less than 250 nmol/l). The 24 hour urinary cortisol was 764 nmol/24 hours, (normal range less than 350 nmol/24 hours). A 3-day dexamethasone suppression test at 2 mg four times a day showed minor suppression with a 09.00 h cortisol of 766 nmol/l. A subsequent contrast enhanced cranial computed tomographic (CT) and abdominal CT scan showed adrenal hyperplasia more marked on the left. No pituitary tumour was demonstrated.

She refused pituitary irradiation or yttrium implants and was started on metypapone 750 mg four times/day

reducing to 500 mg twice daily. After a year her serum cortisol had fallen to 320 nmol/l. Following a subsequent illness (a complete heart block secondary to an anterior myocardial infarct), her metypapone was reduced further to 250 mg twice daily. Her urinary cortisol was subsequently 1427 and 1513 (normal range less than 350). Her metypapone was increased to 500 mg twice daily. Two months later her urinary cortisol had fallen back to 646 nmol/l, over 24 hours. She developed a frank alopecia at this time. Her only other drugs were frusemide and amiloride (Frumil) two tablets mane and paracetamol and dihydrocodeine (Co-dydramol) 2 tablets 6 hourly as required.

There is one other report linking metypapone with alopecia.³ This was dose related and reversible. Our patient died of an unrelated illness before the metypapone could be withdrawn. The cortisol response to metypapone suggests that she had Cushing's disease rather than ectopic ACTH. Metypapone is well known to cause nausea, vomiting, dizziness, headache and hypotension but alopecia is not a well recognized association. The exact cause remains unknown.

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