resembling those of gonococcaemia.² There have also been reports from the United States of a child with leukaemia who had bacteraemia, arthritis, and skin lesions due to *K kingae*³ and another child with moraxella endocarditis.⁴ The organism may enter the bloodstream from the respiratory tract.⁵

Kingella, *Moraxella*, and *Neisseria* genera all belong to the *Neisseriaceae* family, and all can cause disseminated infection with similar clinical manifestations.

We thank Miss J Midgley of the microbiology department at this hospital and the National Collection Type Culture, Public Health Laboratory Service, Colindale, for help with the final identification of the blood culture isolate.

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(Accepted 5 July 1984)

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Agranulocytosis caused by spironolactone

Spironolactone has been in widespread use for over 20 years, and so far as we know it has never been documented unequivocally as the cause of agranulocytosis. In only one report was the possible association mentioned briefly, and no details were given.¹ The manufacturer has received a few reports of agranulocytosis over the years but in none was a causal role of spironolactone convincing (H van der Hulst, Searle Pharmaceuticals, personal communication, 1984). We have observed a patient in whom complete agranulocytosis was induced by spironolactone on two occasions.

Case report

A 70 year old woman was admitted for cardiac failure and renal dysfunction. On admission she had dyspnoea, chest pain on exertion, peripheral oedema, and hepatomegaly. She had not been using any medicines. Abnormal haematological findings were: urea concentration 22.4 mmol/l (135 mg/100 ml) (normal < 7.5 mmol/l; < 45 mg/100 ml); creatinine concentration 162 µmol/l (1.8 mg/100 ml) (normal < 110 µmol/l; < 1.2 mg/100 ml); γ-glutamyl-transferase activity 88 IU/l (normal < 40 IU/l); alanine aminotransferase activity 36 IU/l (normal < 30 IU/l); lactate dehydrogenase activity 550 IU/l (normal < 320 IU/l). Leucocyte counts were repeatedly normal with normal differentiation. Electrocardiography showed multiple ventricular extrasystoles. X ray film of the chest disclosed cardiomegaly and pulmonary congestion.

Treatment was instituted with digoxin 0.5 mg, frusemide 80 mg, and triamterene 50 mg daily and a sodium and protein restricted diet. She showed slow but definite improvement and digoxin and frusemide were decreased to 0.125 and 40 mg daily. Renal function remained impaired. Because of hyperkalaemia triamterene was discontinued. Once the serum potassium concentration had returned to normal spironolactone 100 mg daily was instituted (see figure). Five weeks later a routine blood count disclosed leucopenia ($2.6 \times 10^9/l$) with complete agranulocytosis, relative lymphocytosis, and eosinophilia (15%). Bone marrow biopsy showed normal red cell and platelet production but many immature myelocytes in the absence of mature granulocytes. Spironolactone was discontinued. Within one week the granulocyte count was normal ($4.9 \times 10^9/l$; 75% neutrophils) and two weeks later she was discharged.

One month after discharge the patient was readmitted because of dyspnoea and peripheral oedema. Frusemide was increased to 80 mg daily and digoxin to 0.25 mg daily and the importance of the diet re-emphasised. All signs and symptoms of congestive heart failure disappeared. Leucocyte counts were repeatedly normal. Renal function remained stable and the patient was discharged again. Two months later she was admitted for the third time. She had the same symptoms as before. In addition to her treatment regimen, which she had adhered to, she was again given spironolactone (50 mg/day). Three

Changes in white cell counts in relation to treatment with spironolactone.

weeks later the leucocyte count (normal on admission and with normal differentiation) had fallen to $1.6 \times 10^9/l$. Differentiation showed complete agranulocytosis. The causal relation between spironolactone and the agranulocytosis was then recognised and the drug discontinued. Nine days later the leucocyte count was $4.5 \times 10^9/l$ and showed normal differentiation.

Comment

In our opinion there is no doubt that spironolactone caused the agranulocytosis in this patient. All other drugs were continued without difficulty and no other cause was found. The temporal relation with the administration of spironolactone was clear on both occasions (see figure). In view of the apparent rarity of the reaction it may be idiosyncratic. Probably the mechanism is immunoallergic and acts by destroying granulocytes in the peripheral blood. The complete absence of granulocytes in the presence of many myelocytes in the bone marrow, the accelerated reaction to rechallenge, and the rapid and complete recovery after discontinuation of spironolactone on both occasions were compatible with a drug dependent antibody mediated reaction.

Even common drugs that have been used safely for years may unexpectedly cause life threatening adverse effects. Plainly drug monitoring should not be restricted to new drugs only.

We thank Dr A W F M van Leeuwen for the bone marrow biopsy report.

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(Accepted 9 July 1984)

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Relation between use of tampons and urogenital carriage of group B streptococci

Although infection with group B streptococci in man was described in 1943, these bacteria were unfamiliar to clinicians until their association with neonatal infection was established in the 1960s.¹ The reason for this apparent increase in the incidence of infections due to group B streptococci remains obscure. In the study reported here we found a positive correlation between the use of tampons and the carriage of group B streptococci, which might have contributed to the increase.