LETTERS TO THE EDITOR

Staphylococcus lugdenensis and endocarditis

Further to the recent correspondence regarding *Staphylococcus lugdenensis* we report a further case of endocarditis due to this organism.

A 32 year old man presented with a history of fever, rigors for one week preceded by malaise, and weight loss for one month. He described a transient pain and weakness in the right forearm and hand (ulnar aspect) two days before admission. A toolmaker by profession, with no history of rheumatic fever or drug abuse, his only surgery (dental or otherwise) had been a vasectomy three months earlier.

Examination showed that his temperature was 38°C and blood pressure was 130/40 mmHg. Splinter haemorrhages were present on all fingers of both hands. A collapsing pulse was noted. On auscultation signs consistent with aortic regurgitation were found without obvious outflow obstruction, but no signs of cardiac failure. Clinical examination yielded otherwise normal results. Investigations included a white cell count of 12.9 x 10^9/l, haemoglobin concentration of 13.8 g/dl, platelets 152 x 10^9/l, erythrocyte sedimentation of 70 mm/hour, and C-reactive protein of 19-6 mg/dl. Serum biochemistry and urine examination yielded normal results. An echocardiogram showed a tricuspid aortic valve with a single vegetation.

Staphylococci were isolated from a total of eight blood culture bottles. The slide coagulase test was positive with human plasma and negative with rabbit plasma. The tube coagulase test was negative with both plasmas.

Both Staphylofase (Oxoid) and Staphaurex (Wellcome) tests were positive. The plate DNA was negative after overnight incubation but positive at five days. API Staph (API Products Ltd, Basingstoke, Hampshire) identified the organism as *Staphylococcus hominis* biotype 1. A positive ornithine test identified it as *Staphylococcus lugdenensis*.1 The organism was fully sensitive to penicillin, methicillin, aminoglycosides and vancomycin. It was non-phage typeable, using the standard set of phages.

The patient started intravenous fluoxacillin (2 g every four hours) plus gentamicin 120 mg twice daily, but within five days he developed early signs of cardiac failure, necessitating urgent valve replacement. At operation a grossly damaged and perforated aortic valve was replaced with a St Jude bileaflet mechanical prosthesis. Postoperative cidal concentrations were inadequate and the patient was changed to benzylpenicillin 1-2 g every four hours plus gentamicin 120 mg twice daily. After three weeks on this regimen he developed a severe allergic reaction to penicillin requiring a change to vancomycin 1 g twice daily plus netilmicin 80 mg twice daily for a further week. The patient made a steady recovery and remains well to date.

Coagulase negative staphylococci cause 5% of native valve endocarditis1 and of these 28% are on previously normal valves.2 At 32 years of age this is the youngest reported case of *Staphylococcus lugdenensis* native valve endocarditis.3 It followed the same aggressive course as those described.1,4 The transient weakness in the patient’s arm suggests an embolic phenomenon not previously reported in this condition and uncommon in other coagulase negative staphylococci endocarditis.4 The source of the organism remains unknown, although it is interesting to speculate that it may relate to his vasectomy. Further research is needed to establish the skin distribution and pathogenesis of endocarditis due to this organism.

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References


Lack of in vitro activity of omeprazole against Campylobacter pylori

There is considerable evidence linking *Campylobacter pylori* infection with gastritis, peptic ulceration, and ulcer relapse.5 We investigated the presence of *C pylori* in 15 patients undergoing diagnostic upper gastrointestinal endoscopy and tested the antibacterial activity of omeprazole, a new anti-ulcer agent, against cultures of *C pylori* obtained from these patients.

Cytology brushings were used to obtain the Gram negative, urease and catalase positive, highly motile bacteria which were cultured microaerophilically (7-8 days at 37°C) for up to five generations on Wilkins-Chalgren agar containing defibrinated horse blood (70 ml/l), amphotericin B (0.02 g/l), cycloheximide (0.5 g/l), trimethoprim (0.25 g/l), vancomycin (0.06 g/l) and nalidixic acid (1 g/l). Electron microscopic examination confirmed that the bacteria were *C pylori* (figure), and was performed on bacteria fixed for one hour in glutaraldehyde (2% in phosphate buffer, 0.1 M, pH 7.4), then washed for 30 minutes in the buffer, resuspended in ammonium molybdate (2%, in distilled water), and then applied to formvar films coated with carbon and wetted with bactracin.

*C pylori* were obtained, by culture, from five out of six gastric ulcer or gastritis samples, all four duodenal ulcer or duodenitis samples, and five out of eight oesophagitis samples. These findings correlated well with the histopathological inflammatory changes, assessed by haematoxylin and eosin staining (six out of six gastric ulcer or gastritis, two out of three duodenal ulcer or duodenitis, and seven out of seven oesophagitis samples), detected in biopsy samples taken at an adjacent site to the cytology brushings. Detection of this bacterium in the biopsy specimens using Giemsa staining, however, was much poorer (three out of six, none out of three, and none out of seven of the respectively grouped complaints). Twelve out of 15 patients were *C pylori* positive by the culture method; only three out of 13 (two not assessed) were positive by the Giemsa method. Histopathological changes were present in 13 out of 14 patients (one not assessed).

The antibacterial activity of omeprazole (synthesised by Fisons plc) was compared with that of furazolidone (Norwich Eaton Pharmaceuticals, New York, USA), a known inhibitor of the bacterium, against four isolates of *C pylori* using a surface inoculated agar-well technique. Whereas furazolidone inhibited growth of the bacterium, neither omeprazole nor the vehicle control (4%, polyethylene glycol 4000 in physiological saline) had any effect (table).

Like others,6 we found that the organism was present in a high proportion of patients with peptic ulcers or gastritis or duodenitis, as well as in those with reflux oesophagitis.

The superiority of microbiological culture in our hands compared with Giemsa staining for identifying the bacterium may have been related to the sample techniques used. Given the patchy distribution of *C pylori*, it is more likely that the bacterium will be found by cytology brushing than by biopsy.

If *C pylori* is responsible for ulcer relapse2 then it seems unlikely on this score that

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omeprazole will be any more effective than H$_2$ antagonists in preventing recurrence.

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2 Marshall BJ, Goodwin CS, Warren JR, et al. Prospective double-blind trial of duodenal ulcer relapse after eradication of Campylo-

bacter pyloridis. Lancet 1988;ii:1347-42

4 Howden A, Boswell P, Tovey F. In-vitro sensitivity of Campylobacter pyloridis to furazolidone. Lancet 1986;i:1035.

Eelective surgery in a haemophilic patient with high titre inhibitors: use of extracorporeal protein A immunoadsorption

About 12% of congenital haemophiliacs develop IgG factor VIII inhibitors, and in these cases it is difficult or impossible to achieve haemostatic concentrations of factor VIII.c. In emergencies animal factor VIII, high dose human factor VIII, and activated plasma products such as FEIBA have been used with some success. Immune tolerance induction using regular doses of factor VIII can reduce concentrations of inhibitor over a prolonged period but this is impractical if surgery is urgent. In these circumstances plasmapheresis is useful in reducing concentrations of inhibitor. This becomes relatively inefficient, however, at low concentrations of inhibitor and requires replacement treatment with donor plasma products. These disadvantages are overcome with extracorporeal antibody immunoadsorption in which extensive plasma treatment is feasible without recourse to the use of donor plasma. Patients with Christmas disease with inhibitors have been successfully treated in this way, but as yet there have been no reports in cases of haemophilia A.

A 36 year old haemophiliac with 0 IU/dl factor VIII, 250 New Oxford U/ml human factor VIII inhibitor, and negative tests for HIV antibodies presented with recurrent dental abscesses. He experienced increasing pain needing prolonged courses of antibiotics and it was felt that he required urgent surgery. Previous minor bleeding had been treated with bed rest alone, but a calf haematoma three years previously had required four months of factor VIII treatment, and a life threatening retroperitoneal haematoma six months previously had been treated with 934 000 U human factor VIII, following which his inhibitors rose to 2890 U/ml. These then fell slowly to 250 U/ml in six months in response to regular factor VIII treatment.

Using venous access via the antecubital vein, over five days, a total of 35 litres of plasma was generated on a Hemotronics V-50 cell separator machine and immunoadsorbed on protein A sepharose columns using a Citem 10 extracorporeal immunoadsorption treatment system (Excorim, Lund, Sweden). The figure shows that serum IgG concentrations and factor VIII inhibitor concentrations fell rapidly with each treatment. With about 30 machine cycles of 200 ml of plasma, the technique was very effective at reducing high concentrations of inhibitor but was less effective at lower concentrations. There were also slight overnight increases in IgG and VIII inhibitor concentrations which were probably explained by the equilibration of extravascular and intravascular IgG. On the fourth day the inhibitor concentrations had fallen to <0.3 IU/ml, but an infusion of human factor VIII calculated to raise the patient’s factor VIII concentrations by 200 IU/dl only achieved an increase from 0 to 6 IU/dl. After a further two days of plas-

mapheresis and immunoadsorption a further infusion of factor VIII increased the circulating factor VIII concentrations to 124 IU/dl. Oral tranexamic acid 1 g three times a day was started and the patient underwent extraction of four infected teeth including an impacted wisdom tooth. Immunosuppressive and normal human immunoglobulin replacement treatment were not administered. Piroperihaemostasis was normal, and the next day the patient’s factor VIII concentrations rose from 31 to 85 U/dl after a further infusion of factor VIII.

On the subsequent two days, similar infusions of factor VIII did not increase factor VIII concentrations and the inhibitor reappeared. To what extent this anamnestic response was modified by the factor VIII infusion on day 3 or the previous desensitisation regimen is uncertain. Factor VIII treat-

ment was continued for a total of seven days and when reviewed three weeks later he had made a full recovery.

Extracorporeal protein A immunoadsorption has been used to remove IgG inhibitors from patients with Christmas disease and to remove HLA antibodies before renal transplant.

A major application of this new technique would be to manage emergency bleeding in haemophiliacs with inhibitors, or to prepare such patients for urgent surgery. Previous workers treating Christmas disease have combined this with immunosuppressive treatment with cyclophosphamide and high dose intravenous immunoglobulin, and have shown long term diminution in factor IX inhibitor concentrations. The case we de-

describe shows that immunoadsorption alone can reduce factor VIII inhibitor to almost undetectable concentrations and that follow-
ing this, conventional factor VIII support is adequate for surgical procedures. This form of treatment would be particularly appropriate in emergency situations where extracorporeal immunoadsorption would avoid the cost and uncertain response to high dose human factor VIII treatment. Our patient was seronegative for HIV, but it should be borne in mind that seropositive patients could be immuno-

compromised by a period of hypogamma-

globulinemia and should perhaps receive normal IgG replacement treatment at the end of the immunoadsorption procedure.
ERRATA

Errata 1

In the indexed letter, "Lack of in vitro activity of omeprazole against Campylobacter pylori," A M Ghelleni et al (1990;43:171). The figure legend to the figure reproduced below was inadvertently omitted. We apologise for this error.

Electron micrograph showing C pylori negatively stained with ammonium molybdate. Although only two intact flagella are seen here, the basal portions of two other flagella are visible (arrowed). A terminal paddle is just visible on one of the two intact flagella. A terminal paddle from another specimen is shown enlarged in the inset.

Errata 2

Part of the Appendix in "Guidelines on oral anticoagulation: second edition" by the British Society for Haematology (1990;43:177-84) was incorrectly transcribed. The correct version is printed below. We apologise for this error.

Infections:

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intended for undergraduates and recently fledged doctors and there can be no doubt that this role is fulfilled most admirably in the specialty of forensic medicine through the commendable conciseness and clarity of text, the subdivision of the chapters by numerous subheadings, and the informative inclusion of simple illustrative line drawings—all at a price (slightly inflated from the last edition) easily accessible to a student's pocket.

The authors seem to have placed great faith on their previous reviewers and I therefore tentatively venture to suggest some changes in emphasis for the forthcoming edition: breath alcohol—assaying machines are here to stay—and child non-accidental injury and sexual abuse will persist in the limelight. The nuances of (Scottish) precognitions and fatal accident inquiries could be highlighted even further. I also hope that the pious hope expressed that the Procurator Fiscal "will always require an autopsy to be carried out" comes to pass by then. A BUSUTTL