which probably resulted in a bacteraemia was comprehensive and included all common gastrointestinal and genitourinary operations, endoscopic procedures (including bronchoscopy), and common infections; cases also followed the insertion of a vaginal pessary, liver biopsy, acupuncture, parturition, blood donation, phlebography, haemodialysis, fractures, and cardiac catheterisation. There were also six drug addicts among the 541 patients.

How should the results of this survey influence future practice? Firstly, the authors call for better routine dental care. The dominance of *Str viridans* infection in cases of infective endocarditis even when no recent dental procedure has been performed and the reported high prevalence of periodontal disease in the community argue strongly in favour of this recommendation.¹⁷ Would, however, the risk from the increased number of dental procedures required to achieve this goal of improved dental hygiene counterbalance the expected benefit? Secondly, though the risk of dental procedures (not merely extractions) does not appear so great as traditionally believed the investigators decided that prophylaxis must still be given to patients at risk. They supported the recommendations of the British Society for Antimicrobial Chemotherapy (amoxycillin for dental procedures; erythromycin for those allergic to penicillin; and a combination of amoxycillin and gentamicin against bowel organisms) and called for wider publicity for these recommendations.²⁰ Thirdly, the numbers of cases associated with infection from the alimentary, genitourinary, and respiratory tracts and skin indicate the need for antibiotic prophylaxis for patients with cardiac defects at the time of any surgical procedure or endoscopy.

These aims are prudent and are likely to be endorsed. There remains, however, the problem of a group of patients (43% in this survey) with normal or apparently normal hearts who develop infective endocarditis. Within this group elderly patients seem to be at particular risk, and Bayliss *et al* argue that antibiotic cover should be considered when any surgical, alimentary, or genitourinary procedure (including endoscopy) is performed in an elderly patient—whether or not a cardiac defect is present. Other groups at enhanced risk include diabetics, alcoholics, the immunosuppressed, drug addicts, and patients with malignant disease or any serious illness.

The provision of antibiotic cover at times of suspected risk to any group of patients with apparently normal hearts in an attempt to prevent infective endocarditis would be treading new ground. The number of surgical, investigatory, and dental procedures performed each year on patients aged 60 and over with apparently normal hearts must be enormous, and the advantages of prophylaxis for this group might accrue more to the manufacturers of antibiotics than to the patients. Indeed, such a policy may not be without risk. The difficulties of mounting a controlled trial to assess the benefits and risks of prophylaxis in such patients would be as great as the event rates would be small, but surely objective evidence must be obtained before this untested recommendation is adopted.

Finally, Bayliss *et al* point to the need for doctors and dentists to appreciate that the pattern of infective endocarditis has changed considerably in the past 50 years. There has been no shortage of publications on the subject, but perhaps we need a new method of maintaining awareness of the problem and a watch for further changes. This might be achieved by treating deaths attributed to infective endocarditis in the same way as maternal deaths and subjecting them to detailed and confidential inquiry. The annual

number of deaths from the disease would not preclude this, and from the regular information provided we might get closer to the truth about the number of patients dying from infective endocarditis for want of prophylaxis—or despite it.

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Fixed drug eruptions

Fixed drug eruptions continue to puzzle dermatologists. A drug may be well tolerated by a patient for weeks, months, or even years, and then a further dose of the drug produces—usually within a few hours—the appearance of one or more raised, erythematous, sharply demarcated, round or oval plaques, often pruritic and sometimes bullous. The lesions may occur on any part of the skin; less commonly they may appear on mucous membranes. A lesion appearing on the lip simulating herpes labialis has recently been reported in the *BMJ*.¹

The skin lesions heal with scaling, and finally all that is left is a sharply demarcated area of pigmentation. Further administration of the drug causes a recurrence of the lesion in the same area, though new lesions may develop elsewhere. There are usually no constitutional disturbances. The susceptible areas have no obvious characteristics to suggest why they become affected whenever the drug is taken while the surrounding skin continues to appear normal. Fixed drug eruptions must presumably be due to local abnormalities in the skin, which determine the sites of the lesions; and since their round or oval shape might correspond with the distribution of terminal vessels or nerves either or both of these may be implicated.

Several groups of workers have investigated the mechanism which determines the localisation of the skin

lesions by transplanting skin from an affected site to an area of normal skin in the same patient and taking the normal skin which had been removed to provide a bed for the affected skin and transplanting it to the site from which the affected skin had been removed. If the lesions were due to a local abnormality of some constituent of the skin then it might be expected that the skin from the affected area would continue to react and that the normal skin would remain unreactive. Bruinsma's well known *Guide to Drug Eruptions* states that the normal skin will become sensitised, whereas the skin from the affected area, though it will retain its sensitivity for a short time, will lose it and within about a month the affected skin will have lost its capacity to react while the normal skin will have become reactive.² Ryan, on the other hand, in the *Oxford Textbook of Medicine*, states the exact opposite: "The affected area can be transplanted and will not lose its responsiveness."³ The facts, however, are even more complex than these incompatible statements would suggest, for in the hands of different workers autotransplantation has produced virtually every possible result.

In patients with eruptions due to antipyrine⁴ and phenolphthalein⁵ split skin grafts of previously affected skin retained their reactivity when transplanted, but grafts of normal skin transplanted to an affected area did not become reactive. Porter and Comaish obtained similar results five months after exchanging full thickness skin grafts in a patient with a fixed eruption due to sulphadimidine.⁶ Knowles *et al* obtained similar results initially in a patient sensitive to phenolphthalein, though about three months after full thickness autografting the transplanted affected skin showed no reaction to an oral challenge and the transplanted normal skin "seemed to react slightly."⁷

Other workers who have used full thickness grafts in cases due to phenolphthalein⁸ and allyl isopropyl barbituric acid⁹ have reported a reaction in the normal transplanted skin but no reaction in the abnormal skin transferred to a non-reactive area when the patients were challenged with the appropriate drug about seven weeks after the grafts had been interchanged. Chargin and Leifer transplanted skin in three patients with fixed eruptions due to arsphenamines.¹⁰ In two, a lesion was excised and an adjacent area of normal skin (full thickness) was slid into the area previously occupied by the affected skin. In this way, presumably, the vascular and nervous supply of the grafts would have been preserved. In neither case did the transplanted (normal) skin develop a reaction when the patient was repeatedly given the drug, though other areas of the skin did react. In a third patient these workers exchanged full thickness grafts of normal and affected skin, but reported that neither transplant developed a reaction when the patient was repeatedly challenged with the drug over three years, although other areas of skin continued to react.

Finally, Baker, in a case due to antipyrine, reported that normal skin (full thickness) transplanted to an affected site developed a bright erythema when the patient was challenged with antipyrine three and a half, 10, and 14 weeks after transplantation, whereas previously affected skin transplanted to a normal area showed no change.¹¹ Baker speculated that the erythema which developed in the normal transplanted skin might have been due to passive vasodilatation of vessels in the graft which would have been in communication with the dilated vessels in the fixed eruption in the surrounding skin. Although this might explain the apparent transfer of sensitivity to normal skin in

the experiments quoted above, it would not explain the finding of Porter and Comaish that normal skin transplanted to an affected area remained unreactive,⁶ nor would it explain the entirely negative results of Chargin and Leifer.¹⁰

Patch testing with the causative drug in areas of unaffected skin appears almost always to have produced negative results, whereas patch testing of quiescent reactive areas has occasionally produced a positive response.¹² The significance of these apparently exceptional positive reactions is uncertain. Early studies included occasional claims that the causative drug had been shown in the cutaneous lesions,¹² but radioactive tracer techniques have failed to show any such localisation.^{6, 11}

At least three groups of workers have produced evidence of a humoral factor in the patient's serum, but the existence of such factors does not explain the striking localisation of the lesions.¹³⁻¹⁵

Despite a considerable amount of investigation, the pathogenesis of fixed drug eruptions is as obscure as it was when the condition was first described by Brocq, 90 years ago.¹⁶

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In our issue of 6 April (p 1024) we published an article under the title "Pseudomonas aeruginosa and whirlpools." We have been asked by Jacuzzi Inc and Jacuzzi Europe SpA to point out that the word Jacuzzi is a registered trade mark and may only be used in connection with products manufactured and sold by that company.

These companies have also asked us to make clear that none of the incidents referred to in the article involved whirlpools manufactured by them and that our use of the word Jacuzzi in the article was not intended to be a reference to their products.