

in water and ethanol, insoluble in chloroform and ether, stable at pH 6.8, and moderately stable to heat.¹ He also consulted a number of colleagues in 1929 and subsequently about how to proceed with extraction. Two of them, Stuart Craddock and Frederick Ridley, evaporated extracts in vacuo without success. Fleming then consulted several chemists independently, including Harold King, head of the Medical Research Council's laboratory at Hampstead, who told me later that they "had not been able to do much work on penicillin." Harold Raistrick, professor of biochemistry at the London School of Hygiene, worked harder on the problem collaboratively with R Lovell and P W Clutterbuck, but they were equally unsuccessful.² I have in my possession a bottle of dried yellow pigment purified by Raistrick from the crude brew in 1930 and given to me later by one of his assistants. When tested many years ago it contained none of the stable degradation products of penicillin. From 1932 onward, there are no records of further attempts to extract any active principles from the penicillin mould or the crude brew.

In retrospect, it is very surprising that bacteriologists of the time ignored his findings, for filtrates of crude brew killed staphylococci and other organisms at dilutions of 1600, were non-toxic to leucocytes, and apparently eliminated sensitive organisms from burns, wounds, and ocular and other localised infections.³ Until 1936 Fleming continued to draw attention to these unique properties but no one in the domestic research councils or pharmaceutical industry, or internationally, evinced any interest.⁴ My reading of the record⁵ and my acquaintance (later) with Fleming himself leave me convinced that he did not surrender easily to Wright or anyone else, but that he was by 1936 at his wit's end. So he followed the only course open to an honest scientist by describing his findings in a manner which left open the track, accurately, for the subsequent discovery of the active principle at Oxford a few years later by Chain, Florey, and their colleagues.

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¹ Fleming, A, *British Journal of Experimental Pathology*, 1929, **10**, 226.

² Clutterbuck, P W, Lovell, R, and Raistrick, H, *Biochemical Journal*, 1932, **26**, 1907.

³ Wright, A D, *The Medical Society's Transactions*, 1945, **64**, 142.

⁴ Fleming, A, in *Proceedings of Second International Congress of Microbiology*, ed R St John Brooks, p 33. London, International Society for Microbiology, 1937.

⁵ Stewart, G T, *The Penicillin Group of Drugs*, Amsterdam, Elsevier, 1965.

Easy-rider sling

SIR,—For generations Africans, American Indians, and Australian Aborigines have carried their children close to them, mostly strapped to their backs. This technique of portage has been imported into the "developed" countries and the advantages in total mothering is obvious. I wish, however, to express some concern about this and to draw attention to a hazard of carrying babies in the front.

A 5-week-old child was brought to the accident and emergency department having been involved in a fall. She was being carried in a sling worn in front when her mother

tripped and fell on her face. On examination she had a large haematoma on the right side of the head and skull x-ray film showed a fracture on the right parietal bone. Skeletal survey revealed no other fractures. This is a particularly interesting case for a number of reasons. It made us aware of another differential diagnosis in non-accidental injury. The mother of this child was under treatment for postnatal depression. Our liaison health visitor recalled three other similar incidents when mothers had tripped and fallen forwards.

Most important is the dynamics of falling: it is rare to fall backwards from a trip. It is more usual to fall forwards, thereby involving a baby in the process. It will be interesting to know if any of your readers have been presented with similar problems. Should it not be possible for manufacturers of slings to state warnings and possible dangers?

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Compliance with drug treatment

SIR,—We were interested in the papers on drug compliance by Dr D A Ellis and others (17 February, p 456) and Dr A Smith and others (19 May, p 1335). Many elderly patients and some who are not so elderly have difficulties in remembering the exact daily dosage when they are on more than one drug. We have found it useful to give such patients a card to which is fixed by Sellotape an example of each tablet which the patient is taking with written instructions beside the tablet. We find that this simple step helps greatly to avoid confusion about dosage.

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Prophylaxis of tetanus

SIR,—Dr J F Stent (7 July, p 50) could not be more correct. For a non-immunised patient with a tetanus-prone wound neither tetanus toxoid nor antibiotics either together or singly provide necessary prophylaxis against tetanus intoxication.

The advocacy of such prophylaxis stems from the highly immunised and oversensitised communities of the West, among whom there may be more fatalities from the careless administration of antitetanus serum (ATS) than from tetanus. Nevertheless, the fact remains that one cannot rely on toxoid with or without antibiotics for a contaminated wound in someone whose previous immunisation is in doubt. The circumstantial evidence given by Dr Stent can be repeated many times.

Over some years in our north India rural 200-bed hospital where 10% of village-born babies develop tetanus and 1% of admissions are for tetanus, some 7000 severely contaminated wounds (late burns, compound fractures, tiger mauls, etc) had routine 500 units or 750 units prophylactic ATS and not one developed tetanus. At a hospital I knew, however, the specialist paediatrician, flushed with "recent advances" and without consultation, forbade the routine ATS and relied on only toxoid with penicillin. Two of the first three

(and last) children so treated developed tetanus and one died. For India's widespread vasectomy campaigns (at least up to 1975) Western advice prevailed in the instruction to give only toxoid and procaine penicillin at the time of operation. The resulting incidence of postoperative tetanus was sometimes as high as 1%. At the same time Indian surgeons in some big city hospitals insist on prophylactic ATS for their private patients.

I am convinced we need use only very small amounts of ATS prophylactically, certainly not more than 500 units and probably less than 100 units. One unit of ATS is capable of neutralising six minimal lethal doses to a 60 kg man. The question is, therefore, not how much ATS to use but how little and where and when. This also applies to the therapeutic use of ATS, where, as with the non-immunised tetanus prone wound, ATS should not be omitted (7 July, p 49).

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Oral metronidazole in *Clostridium difficile* colitis

SIR,—We were interested in the report by Mr N L Pashby and others (16 June, p 1605), describing two cases of *Clostridium difficile* colitis treated with oral metronidazole. Two of our cases cast doubt on the value of metronidazole for treatment of this condition. The first patient was given oral metronidazole for 11 days, during which time the faecal toxin titre did not fall. The second patient acquired *Cl difficile* and developed a low titre of faecal toxin while receiving metronidazole. He had also been given neomycin and metronidazole preoperative bowel preparation, and co-trimoxazole, gentamicin, and nitrofurantoin before the onset of colitis.

We believe that vancomycin should remain the treatment of choice in severe cases of colitis due to *Cl difficile*. Contrary to the statement made, vancomycin is not toxic when given orally, because it is not absorbed. An oral preparation consisting of coarse powder is available, which can be taken as a suspension in fruit juice. It is not necessary to use the parenteral preparation for oral therapy. Although vancomycin is expensive, we have found that a dose of only 125 mg four times daily achieves satisfactory levels in the colon.

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Mission hospital medicine

SIR,—I heartily agree with the sentiments and proposals clearly stated by Dr Anne Savage (14 July, p 111). As one of the several Glasgow clinicians who participated in a scheme to set up a medical school in Nairobi in the 1960s I can confirm the undoubted benefits to trainees—not only in widening their horizons in general, but equally in greatly extending their operative skills. There is no doubt that from the practical point of view a BTAf degree is far superior to BTA (been to America), and what are surgeons if they are not practical?

With the present rat race I know it is risky