the removal of irrelevant pack inserts should be as much a part of the supply of medication as ensuring the clear and concise labelling of the product for the patient.

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Streptococcus bovis endocarditis with carcinoma of the colon

SIR,—With reference to Dr Celia Oakley's excellent article on endocarditis (12 August, p 489) we would like to comment on the association of *Streptococcus bovis* endocarditis with carcinoma of the colon. *Str bovis* is a non-enterococcus and is sensitive to penicillin and streptomycin. This association has drawn a lot of attention recently in North America.

Klein *et al*[1] reported the increased incidence of positive faecal cultures for *Str bovis* in patients with colonic carcinoma. Since then several other case reports have appeared confirming this association. The recent literature emphasises the importance of differentiating group D streptococci by species in patients with infective endocarditis and the need for investigating patients with *Str bovis* endocarditis for bowel carcinoma.[2]

We hope this letter will heighten the clinical awareness of this "syndrome" in the UK.

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[1] Klein, R S, *et al*, *New England Journal of Medicine*, 1977, **297**, 800.
[2] Levy, B S, *et al*, *New England Journal of Medicine*, 1978, **298**, 527.

Link between hepatoma and hepatitis B

SIR,—In your leading article on this subject (9 September, p 718) you state that HBs antigenaemia is more common in hepatoma secondary to cirrhosis than in hepatoma unrelated to cirrhosis. For sub-Saharan Africa, where hepatoma is so common, the evidence for this is tenuous—patients present late, often with huge tumours which have all but replaced normal liver tissue, and neither needle biopsy nor post-mortem study may reveal the pre-existing cirrhosis. An underestimate of the prevalence of cirrhosis in hepatoma is therefore likely. Furthermore, you have ignored HBs antigenaemia in cirrhosis itself. A number of studies have shown that in cirrhosis antigenaemia occurs as frequently as, or more frequently than, in hepatoma. No African studies I know have shown that the prognosis of these HBs-positive cirrhotics is worse than the HBs-negative cirrhotics nor that the positive patients are more likely to develop an HBs-associated hepatoma.

The studies of Larouze *et al*[1] suggest that maternal transmission of hepatitis B virus (HBV) may be of importance in the development of hepatoma but is not sufficient by itself. Since a cocarcinogen (? environmental) is required, prevention of hepatoma would more logically be directed to the elimination of this, since not all hepatomas are HBV-related. The costs of HBV vaccine development, coupled with the well-known problems of immunisation in the tropics (where most hepatomas are found) make it unlikely that an effective vaccination campaign could be mounted. Epidemiologically, the mycotoxins remain important probable co-carcinogens: intervention studies based on lowering mycotoxin contamination through improved storage of cereals will probably prove substantially cheaper than vaccination and may well provide an answer to hepatoma within the next 20 years.

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[1] Larouze B, *et al*, *Lancet*, 1976, **2**, 534.

Paraldehyde and plastic syringes

SIR,—In response to a query last year all locally available makes of disposable syringe and needle were closely examined after exposure to paraldehyde for several minutes. All needle hubs tested were unchanged, but of the five makes of syringe tested the clear plastic Gillette Sabre and Steriseal showed immediate signs of damage and the piston stuck firmly to the barrel within 2½ minutes. Becton Dickinson, Brunswick, and Everest Medical syringes, which are of a more opaque plastic, appeared undamaged within five minutes. Therefore we do not agree with the statement made by Dr D P Addy (16 September, p 81) that plastic syringes may be used provided the paraldehyde is drawn up immediately before injection. In practice it would take some time to draw up the required volume, identify a suitable site, keep the child still, and insert quite a large volume of fluid.

As syringe packs carry a warning against use with paraldehyde and manufacturers may change their specifications without notice, doctors will need to check their plastic syringes carefully to ensure that they will actually be able to make an injection of paraldehyde in an emergency.

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Interaction of warfarin with antacid constituents

SIR,—It has been suggested that antacids may affect warfarin absorption from the gastrointestinal tract[1]; in clinical studies by other authors[2 3] no change in warfarin absorption has been reported during concomitant administration with magnesium and aluminium hydroxides. A report by Talbot and Meade,[4] however, implicated dimethicone, a constituent of certain cooking oils, as causing decreased absorption of warfarin in several patients. Activated dimethicone is now used extensively as an antifoaming agent in antacid preparations. Consequently it was thought important to determine if, and to what extent, an interaction occurs between antacid constituents (including activated dimethicone) and warfarin and between kaolin (an adsorbent) and warfarin. The study employed an in-vitro technique which has already been clinically evaluated with the tetracycline-metal ion[5] and the digoxin-antacid[6] interactions.

Effects of antacid constituents on warfarin absorption in vitro

Antacid constituent	Percentage decreased absorption of warfarin
Aqueous emulsion of activated dimethicone (35%)	0
Bismuth carbonate	6·9
Kaolin	0
Magnesium trisilicate	19·4

The results (see table) indicate that for clinically equivalent doses of antacid constituent and warfarin sodium there was a small decrease in warfarin absorption when in combination with magnesium trisilicate and bismuth carbonate; however, kaolin and activated dimethicone showed no decreased absorption. These findings suggest that warfarin absorption kinetics may be affected by concomitant administration of certain antacid constituents. We would suggest that the patient should be made aware of this.

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[5] D'Arcy, P F, Muhyiddin, H A, and McElnay, J C, *Journal of Pharmacy and Pharmacology*, 1976, **28**, 33P.
[6] McElnay, J C, *et al*, *British Medical Journal*, 1978, **1**, 1554.

Absence of interaction of digoxin with antacids under clinical conditions

SIR,—We have read with interest the letter from Mr J C McElnay, and others (10 June, p 1554) concerning the interaction of digoxin with antacids. It substantiates the earlier in-vitro study of Khalil,[1] who noted a high level of adsorption of digoxin by magnesium trisilicate. Brown and Juhl[2] demonstrated in healthy volunteers what they claimed to be a severe reduction (30%) in the absorption of oral digoxin by magnesium trisilicate, although they studied single large doses (750 μg digoxin and 2·8 g magnesium trisilicate).

In a preliminary study we have investigated the effects of smaller amounts of two antacid preparations on the absorption of more normal doses of digoxin (250-500 μg) in four patients on chronic medication. Bioavailability was estimated by the quantity of digoxin excreted in the urine during the final 24 h of three seven-day periods. The seven-day drug administration schedules were digoxin alone (schedule A), digoxin with aluminium hydroxide mixture *BPC* 10 ml thrice daily (schedule B), and oral digoxin with magnesium trisilicate mixture *BPC* 10 ml thrice daily (schedule C). Patients thus acted as their own controls in a crossover fashion. Neither antacid significantly reduced the bioavailability of these oral doses of digoxin and none of the patients showed any reduction in the control of their symptoms.

The investigation would suggest that interaction between digoxin and magnesium trisilicate may not be significant in most

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