diglycerides are secreted in the bile. Cholesterol in the bile is almost exclusively in free form and only about 4% is esterified (gall-bladder bile).⁹ After stopping smoking the resulting nicotinic absence in stimulation of antidiuretic hormone release probably causes an increase in bile flow, and this might have caused the decrease in plasma concentration of free cholesterol, phospholipid, and triglycerides. As free cholesterol is constantly removed by high-density lipoprotein from the tissues there is no significant decrease in its concentration.⁷ Since esterified cholesterol forms only 4% of the total cholesterol present in the gall-bladder bile, the concentration of high-density-esterified cholesterol in the plasma might have increased owing to the increase in bile flow after stopping smoking. In the patients studied by Dr Stubbe and others alcohol intake might have partly contributed to this effect by suppressing the release of antidiuretic hormone.

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Claims about compression treatment for venous disease

SIR,—Your journal of 29 May included an advertisement (opposite p vii) for compression hosiery written in the form of an authoritative statement and carrying the following heading: "Relief and reversal of the effects of venous disease by compression therapy. Possible only when pressure levels are within the range 30 to 60 mm Hg?"

The authors have assembled evidence to support their claim that graduated garments providing compression at the ankle of 30-60 mm Hg will reverse disorders of venous function in the legs. However, there are few investigations which will support their contention that lower levels of compression have little therapeutic value. The lowest levels of compression which will correct various forms of venous function remain to be determined. This is an important gap in our knowledge of this subject since patients' compliance declines with increasing compression. Indeed, my colleagues and I have previously demonstrated^{1,2} that the Laplace relationship operates to the advantage of the patient. Because pressure is proportional to the tension in the garment but inversely proportional to the radius over which the tension is acting the small radius of superficial veins experiences greater compression than the surface of the limb itself. A garment providing 6 mm Hg around the calf will reduce the distension of superficial varicose veins.² Furthermore, the dangers of providing compression greater than 40 mm Hg were discussed in this journal at the time when inflatable splints were introduced.³ Thus this statement goes beyond the evidence when it claims that relief and reversal of dysfunction are "possible only" with the high compression quoted.

The authors do acknowledge in the body of the text that the severity of venous disorders varies and "that it is vitally important to choose the compression which matches the condition." Readers

may wish to know that it is against this background that a subcommittee of the British Standards Institution is preparing a performance specification for graduated compression hosiery. Previously these garments have been prescribed against a description of their construction. The introduction of this standard will allow the clinical and physiological evaluation of hosiery according to the compression which they provide and will permit a better match between the amount of compression required and that provided. It will be unfortunate if the pattern of usage in other EEC countries should be allowed to obscure the need for a re-evaluation of this problem. In West Germany and Switzerland, in particular, garments have for some time been described by the compression which they provide. However, the pattern of their prescription by doctors appears to be influenced by, among other considerations, the levels of compression that qualify for reimbursement of the purchase price by the private medical insurance schemes, which are relatively high.

The claim that appeared in the journal is premature and anticipates studies which have not been undertaken.

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Recurrent cancer after restorative resection of the rectum

SIR,—Dr B J Cummings (8 May, p 1405) rightly emphasises the dangers of inadequate resection of rectal cancer—becoming perhaps more prevalent in the wake of the stapler salesman. It is, however, simplistic and almost certainly incorrect to equate this problem with the traditional 5-cm distal margin. Most pelvic and suture line recurrences arise *outside* the anastomosis and represent missed extramural foci—probably in perirectal lymphatics: that is, rectal cancer spreads outwards like the mushroom cloud of a nuclear bomb rather than directly downwards like gastric cancer. This led us to the idea that total mesorectal excision might improve results by encompassing all the fatty lymphovascular perirectal tissue, much of which is left behind in orthodox anterior resection. Our preliminary results will appear in the *British Journal of Surgery* in October; they include 31 cases with distal margins of 3 cm or less and 10 poorly differentiated lesions—all followed three monthly for a minimum of two years. No case in the initial series of 50 has yet manifested a local recurrence, although two out of our second 50 cases have done so. These figures have been achieved without adjuvant therapy and are better than we are currently obtaining in the few (possibly less favourable) cases selected for abdominoperineal excision. They suggest to us that wide accurate perirectal dissection from above is the essence of good rectal cancer surgery, that the levators and the anus are not relevant to the proper excision of most tumours, and that the 5-cm margin may be safely reduced provided that the perirectal clearance is adequate.

Abdominoperineal excision is an entrenched part of the general surgeon's repertoire and produces reasonable cure rates without lengthy specialist training. The newer and lower anterior resections offer improved hopes for potency, bladder function, and avoidance of permanent colostomy; they are, however,

introducing a wide variation in results from centre to centre and from surgeon to surgeon. The scene is becoming further confused by the threatening tide of experimental permutations and combinations of adjuvant therapy, which may well be unnecessary in the majority of patients for whom cure is possible.

The difficulty of the surgical technique and the orchestration of adjuvant modalities is now so complex that rectal cancer should perhaps no longer be considered to lie within the province of the general surgeon. It is certainly our belief that results have been improved because consultant colleagues have been prepared to encourage specialisation within our district hospital by referring all rectal cancers to one surgeon. We would suggest that specialisation along these lines in the "Cinderella specialty" offers a real chance of improvement in results in this common and important disease.

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Heartburn in pregnancy

SIR,—I have with great interest read the editorial by Mr J G Feeney (17 April, p 1138) on heartburn in pregnancy.

In our study in 40 patients¹ in early pregnancy with or without heartburn we found that there was a significant decrease in the mean barrier pressure (lower oesophageal sphincter pressure minus gastric pressure) in patients complaining from heartburn when compared with both pregnant patients without heartburn and non-pregnant patients (45 in number). Furthermore, we found that there was an increase in gastric pressure in the two pregnant groups which could not be attributed to the presence of an enlarged uterus. However, the average weights of the groups of pregnant patients were significantly heavier than that of the non-pregnant controls. The difference in gastric pressure may be a weight-related phenomenon. In Hey's article² no mention was made of the average weights of the two pregnant patients' groups or of the non-pregnant controls.

Further studies looking at this aspect and the possible hormonal control of lower oesophageal competence are imperative.

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¹ Brock-Utne JG, DOW TGB, Dimopoulos GE, Welman S, Downing JW, Moshal MG. *Br J Anaesth* 1981;53:381-4.

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Side effects of benoxaprofen

SIR,—Like Drs J R Marsden and M G C Dahl (12 June, p 1782), I have observed reversible nail changes other than onycholysis in patients treated with benoxaprofen (Opren). In addition to flattening and dishing (koilonychia), I have noted warping and increased ridging of the nail plate, and originally drew these features to the attention of the manufacturers (Dista Products Ltd) at a special workshop on benoxaprofen during the XVth International Congress of Rheumatology in June last year.

With regard to photosensitive skin reactions,

these are common and for the most part give rise to few problems and can be easily managed or avoided. Some patients, however, have experienced intensely unpleasant and prolonged reactions continuing for up to several weeks after returning from holidays abroad. Several have commented that treatment with wax baths or washing in hot water has produced similar, milder symptoms. Many of us have listened to accounts of patients applying chilled bottles, ice, or wet towels to their skin, or resorting to a cold shower or bath. Others have thought they were "wind burnt"; others having sought medical or pharmaceutical advice have unfortunately been told that their symptoms could not possibly be drug related. It is now my practice to advise patients who have had a photosensitive cutaneous reaction, especially if experienced in a British spring, to stop the drug before going abroad for a summer or skiing holiday. In my experience the drug needs to be stopped about a fortnight before the intended vacation, and I have seen patients who, stopping the drug only a week before departure, have still experienced a marked photosensitive reaction.

Like Dr M L Snaith (29 May, p 1630), I have no particular brief for the manufacturers, but the loyalty of many patients to the drug despite nail or cutaneous reactions has been impressive. I wonder if there has not been a tendency to relative over-reporting of reactions, by comparison with some of the other recently released non-steroidal anti-inflammatories? Could it be that benoxaprofen, which has a unique profile of side effects, has been the victim of a backlash, perhaps from some of those who were not a little distressed by the publicity which attended its general release and therefore scrutinised it more closely than would normally have been the case?

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Fatal cholestatic jaundice in elderly patients taking benoxaprofen

SIR,—We noted with interest the report by Drs Hugh McA Taggart and Joan M Alderdice of cholestatic jaundice and renal failure in elderly patients taking benoxaprofen (8 May, p 1372). We report here two similar cases.

Case 1 A 70-year-old woman presented with a two-week history of increasing jaundice and massive bruising. She had a long history of rheumatoid arthritis, having had bilateral Sheehan knee replacements some years previously. Benoxaprofen 300 mg twice daily had been started 10 months before admission, her other drug therapy being prednisolone 5 mg daily, frusemide 80 mg daily, and spironolactone 100 mg daily. There was no history of excessive alcohol intake. On admission she was deeply jaundiced with hepatomegaly, the liver being 4 cm below the costal margin; but there were no stigmata of chronic liver disease. There was generalised bruising with massive haematomas over the jaw and right thigh. She was profoundly oliguric. Investigations on admission showed the following: serum creatinine 600 $\mu\text{mol/l}$ (6.8 mg/100 ml); bilirubin 88 $\mu\text{mol/l}$ (5.1 mg/100 ml); aspartate transaminase 364 IU/l; γ -glutamyl transpeptidase 563 IU/l. Coagulation studies showed depletion of liver-dependent clotting factors and a qualitative platelet defect. Tests for autoantibodies gave negative results, there was no evidence of viral hepatitis, and serological tests for leptospirosis were negative; ultrasonic examination of the liver and biliary tree showed no obstruction. All drugs except prednisolone were stopped and haemodialysis was commenced four

days after admission. Despite full supportive therapy she became progressively more jaundiced (bilirubin 294 $\mu\text{mol/l}$ (17.2 mg/100 ml)), remained oliguric, and developed severe sepsis in the liquefying haematomas. She died three weeks after admission.

Case 2 came to our attention from the pathologists. An 86-year-old woman had fallen and fractured her left neck of femur. At that time she was taking bumetanide, chlormethiazole, and benoxaprofen 300 mg twice daily. The head of the femur was replaced under a general anaesthetic but no halothane was used. She initially made a good postoperative recovery but subsequently became jaundiced. She had been taking benoxaprofen for two months by this time. All drugs were stopped, but she developed progressive hepatic and renal failure and died 14 days later.

At necropsy the liver pathology was identical in the two cases. There was no extrahepatic obstruction, but histological examination showed intrahepatic cholestasis with extensive, mainly centrilobular, liver-cell necrosis (figure). There was

Case 1: Liver showing extensive centrilobular necrosis. (Haematoxylin and eosin $\times 24$.)

little chronic inflammatory reaction, which was confined to the portal triads, and no evidence of regeneration or fibrosis. In each case the kidneys showed multiple bile casts but no evidence of acute tubular necrosis; the kidneys in case 1 were small (8 cm).

Although the clinical picture of fulminating liver failure with associated acute renal shutdown is identical to that described by Drs Taggart and Alderdice, and similar to other cases described by Goudie *et al.*,¹ the histological findings differ somewhat in that liver-cell necrosis was prominent. As was pointed out by Dr W I H Shedden (29 May, p 1630) on behalf of the manufacturers of benoxaprofen, intrahepatic cholestasis alone is rarely fatal. On the other hand, the histological findings in our cases readily explain the fatal outcome.

The fact that in case 1 small kidneys were found at necropsy highlights again the major problem of prescribing for the elderly. As with many drugs, the half life of benoxaprofen is prolonged in renal failure; if indeed this predisposes to jaundice and hepatic failure,

extreme caution must be exercised in prescribing the drug for the elderly, in whom mild-to-moderate renal failure is common and almost invariably undiagnosed.

We have reported these cases to the Committee on Safety of Medicines.

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¹ Goudie BM, Birnie GF, Watkinson G, MacSween RNM, Kissen LH, Cunningham NE. *Lancet* 1982; i:959.

* * * We have received several other letters describing side effects of benoxaprofen but for reasons of space we suggest that further case reports should be forwarded to the Committee on Safety of Medicines.—Ed, *BMJ*.

Genitourinary medicine

SIR,—Professor M W Adler's article on genitourinary medicine (5 June, p 1677) brings a very important question before the profession. I refer to his last two paragraphs. I discern the points he puts forward in favour of not informing the patient's GP but suggest that his deliberations on them have landed him in a regrettable and untenable position.

Professor Adler undermines many key elements in the relationship of patients with their doctors. The absolute confidentiality of the doctor-patient relationship is debased; the crucial role of a complete view of the whole patient, in himself or herself and in relation to his family and environment, is set aside, and the Hippocratic precept of sharing knowledge and skills is forsaken. The patient loses by failing to be considered "in the round," and loss of the opportunity to enhance or create a constructive and empathetic relationship with his personal physician; his reticence or embarrassment about his condition or orientation is massively reinforced by the "special doctor's" connivance in keeping it quiet, and if so minded he will have to remember to maintain the falsehood with his GP indefinitely. Our profession suffers by the divisions engendered by the application unilaterally of the views of those with narrow sectional interests. The GP suffers in that extragenital manifestations of disease may fail to register immediately, as may the significance of illness in the family. He will fail to gain the invaluable assistance of hospital feedback for his own educational gain; and it is clear that those who do experience distaste or revulsion when considering sexually transmitted disease will be unable to develop a more useful approach while shielded from contact with the naughty world outside.

I applaud the promotion of self-referrals in this and one or two other areas—in particular, the peculiar facilities for rapid diagnosis, treatment, contact tracing, and the acquisition of statistical data are invaluable—but please let us present ourselves as a unified health care profession in which the patient may have whole confidence.

I have directed a couple of dozen patients to the local facility in the last 18 months, without