by obstructing biliary drainage or, as is crucial to Keynes's hypothesis, by causing duodenopancreatic reflux? The mere presence of gall stones does not really help to establish this.

It is well known that ductal obstruction is extremely common in pancreatic carcinoma but is rarely complicated by distal pancreatitis, that in animals the entire biliary output of the liver can be routed through the pancreas without causing pancreatitis,^{3,5} but that duodenopancreatic reflux consistently induces acute pancreatitis. Infected bile seems to produce a severe pancreatitis,² thus behaving similarly to bile which has been exposed to the duodenal flora, and gall stones are not infrequently associated with infection. Acosta and Ledesma⁶ and Kelly⁷ certainly recovered gall stones from a large proportion of patients with acute pancreatitis, but Kelly also showed a much higher incidence (67%) of pancreatic reflux in the patients with pancreatitis from whom the stones were recovered than in controls (18%). He has also shown that pancreatitis did not occur in patients with large gall stones completely blocking the ampulla or pancreatic duct but did occur in those with smaller stones, which were associated with a greater dilatation of the biliary tree⁸—a finding confirmed by others.⁹

The data attributed to reference 4 should have been attributed to reference 8.

Undoubtedly, there are firmly held opinions which forcibly support the ductal obstruction hypothesis, but equally there are plenty of data, which cannot be dismissed, which suggest that obstruction alone may not be of major importance. Of course, the obstruction and the reflux hypotheses are both flawed—duodenopancreatic reflux cannot easily explain pancreatitis in the tail of an otherwise normal gland; neither can ductal obstruction explain the pancreatitis occasionally seen in heterotopic pancreatic tissue. The surgical dinosaur may continue to plod along its well trodden paths for some time to come, but it should pause occasionally to examine its changing environment. Keynes's ideas suggest that the time is ripe for such a review. I remain of the opinion that we need to establish the role and frequency of duodenopancreatic reflux and of primary infection in acute pancreatitis and that Keynes's ideas are worthy of further investigation.

Dr Benbow makes an important and valid point. Unfortunately, his reasoning is equally seductive if he intends to imply that a drug must be the cause of pancreatitis in patient B simply because it has been previously shown as the cause in patient A. Many case reports have not adopted the strict criteria on which Dr Benbow insists (resolution of the disease on drug withdrawal and recurrence of the disease on rechallenge with the drug). Many of the case reports therefore must remain suspect because it is wrong to assume that a drug did cause pancreatitis merely because it can.

R E BARRY

Department of Medicine,
Royal Infirmary,
Bristol BS2 8HW

- 1 Keynes WM. The mythology of acute pancreatitis. *Infections in Surgery* 1987;6:354-68.
- 2 Acosta JM, Pellegrini CA, Skinner DB. Etiology and pathogenesis of acute biliary pancreatitis. *Surgery* 1980;88:118-25.
- 3 Becker JM, Ti TK, Moody FG, McGreevy JM, Nelson AJ. A model of biliary pancreatic reflux. *Surgery* 1979;85:147-53.
- 4 Robinson TM, Dunphy JE. Continuous perfusion of bile and protease activators through the pancreas. *JAMA* 1963;183:530-3.
- 5 White TT, Magee DF. Perfusion of the dog pancreas with bile without production of pancreatitis. *Ann Surg* 1960;151:245-50.
- 6 Acosta JM, Ledesma CL. Gallstone migration as a cause of acute pancreatitis. *N Engl J Med* 1974;290:484-7.
- 7 Kelly TR. Gallstone pancreatitis: pathophysiology. *Surgery* 1976;80:488-92.
- 8 Kelly TR. Gallstone pancreatitis: local predisposing factors. *Ann Surg* 1984;200:479-85.
- 9 Armstrong CP, Taylor TV, Jeacock J, Lucas S. The biliary tract in patients with acute gallstone pancreatitis. *Br J Surg* 1985;72:551-5.

Should the pill be stopped preoperatively?

SIR,—Mr H Sue-Ling and Professor L E Hughes (13 February, p 447) believe that the problems of unwanted pregnancy outweigh the risks of postoperative venous thromboembolism. Others take the opposite view (12 March, p 786), but the use of prophylactic drugs does not appear to have been considered.

After even minor surgery in women taking oral contraceptives, there is a significant fall in antithrombin III activity, but this fall is prevented by a small dose of subcutaneous heparin.¹ It is likely, therefore, that women taking oral contraceptives would benefit from prophylactic subcutaneous heparin, as already shown for a wider group of patients.^{2,3} The increased risk of wound haematoma⁴ may be reduced by careful choice of injection site,⁴ but the overall balance of risks and benefits can be determined only by a prospective randomised clinical trial.

R J FARRELL
J LAMB

Royal Postgraduate Medical School,
Hammersmith Hospital,
London W12 0HS

- 1 Sagar S, Stamatakis JD, Thomas DP, Kakkar VV. Oral contraceptives, antithrombin III activity and postoperative deep vein thrombosis. *Lancet* 1976;ii:509-11.
- 2 International Multicentre Trial. Prevention of fatal postoperative pulmonary embolism by low doses of heparin. *Lancet* 1976;ii:45-51.
- 3 Lamb J, Dodds R, Flaxman J, Scully MF, Kakkar VV. Haemostatic changes associated with general anaesthesia and surgical trauma: effect of low molecular weight heparin. *Thromb Haemostas* 1983;50:299.
- 4 Briel RC. Low-dose heparin prophylaxis and postoperative wound haematoma. *Int Surg* 1983;68:241-3.

SIR,—We are gratified at the response to our leading article (13 February, p 447) and appreciate the arguments presented (12 March, p 786). This is undoubtedly a controversial subject and almost inevitably differences of opinion will emerge. The first two replies, however, do not address our main proposition—that young women without other risk factors do not have a significant incidence of thromboembolism when undergoing general surgical procedures.

Mr J Guillebaud argues from parallel, non-surgical, whole population data that the risk of thromboembolism in this specific group is real and the problems of pregnancy are not. The balance of evidence derived from direct studies of this population is that the risk of thromboembolism is not important. (In our own unreported prospective study we have yet to see a single isotopic deep vein thrombosis, let alone a clinical thromboembolic event—a finding in keeping with the two studies quoted.) It is encouraging to hear that some centres can provide safe effective alternative contraception, but this does not happen across the country, as evidenced by the third letter from Dr G C Kassianos and others.

Dr G Robinson and colleagues draw attention to haematological consequences of the pill which are potentially thrombogenic but do not give equal prominence to the increased fibrinolysis associated with the pill.^{1,2} The volume of published reports is large and cannot be covered in correspondence columns. The only valid approach is to study the incidence of postoperative thrombotic episodes directly.

Having considered these letters, we can only reiterate our main conclusions. There is an urgent need for larger studies to quantify the risk of thromboembolism in young women taking the pill without risk factors for deep vein thrombosis—for example, malignancy, previous deep vein thrombosis, obesity—undergoing general surgical procedures. Until these data are available the

balance of evidence supports the view that the combined risks of anticoagulant therapy and unwanted pregnancy outweigh the risks of thromboembolism. Separate studies will be needed to answer the same question in young women with risk factors for deep vein thrombosis or who are undergoing orthopaedic or other non-general surgical operations.

HENRY M SUE-LING
L E HUGHES

Department of Surgery,
University of Wales College of Medicine,
Cardiff CF4 4XN

- 1 Jespersen J, Kluft C. Increased euglobulin fibrinolytic potential in women on oral contraceptives low in oestrogen—levels of extrinsic and intrinsic plasminogen activators, prekallikrein, factor XII, and C₁-inactivator. *Thromb Haemost* 1985;54:454-9.
- 2 Hedlin AM. The effect of oral contraceptive estrogen on blood coagulation and fibrinolysis. *Thrombosis et Diathesis Haemorrhagica* 1975;33:370-8.

Effect of stanozolol on itching in primary biliary cirrhosis

SIR,—The five patients of Dr R P Walt and others (27 February, p 607) seem to have been treated unusually. On their own admission, a C₁₇ substituted derivative of testosterone is contraindicated in patients with chronic progressive liver disease. Nevertheless, with no further explanation of the rationale for using stanozolol, or even that the work had been approved by the local ethical committee, the authors used this drug in five patients with chronic liver damage.

The graph for case 1 shows not only an increase in bilirubin concentrations over about four and a half years of stanozolol treatment, which might have occurred with the original condition, but also a large rise in alanine transaminase activity. The authors make no comment about this finding, which might indicate hepatocyte damage caused by the drug. Primary biliary cirrhosis itself would be unlikely to show a large rise in alanine transaminase activity in this time, unless the patient was in the very late stages of the disease. This is unlikely on the data shown, since the bilirubin concentrations, although raised, were not achieving the high values typical of end stage primary biliary cirrhosis.

This report is not only too preliminary; it also suggests that five patients were used for a drug trial without full explanation of the rationale of treatment or involvement of an ethical committee, which might have prevented this course of action.

CAROL A SEYMOUR
C B SUMMERTON

Department of Medicine,
Addenbrooke's Hospital,
Cambridge CB2 2QQ

AUTHOR'S REPLY,—Drs Seymour and Summerton have seen but failed to read our report. The rationale for treatment is alluded to in the opening paragraph and was the non-availability of norethandrolone, which had previously been used with success for itching in primary biliary cirrhosis. The penultimate sentence emphasises this. The rise in alanine transaminase activity shown in the graph is also discussed fully in the final paragraph. The original submission dealt more completely with these points and showed graphs for all patients, but editorial regulations resulted in a report somewhat less clear than planned. A full explanation of the rationale and expectation of increasing jaundice was given to each patient before treatment, but formal ethics committee approval was not sought. The guidelines from the