normal in post-secretin volume and maximum bicarbonate concentration, with a decrease in amylase output. Although the biliary juice in post-cerulein fractions did not contain *G intestinalis*, post-secretin pancreatic juice contained lots of the protozoa. The patient was treated with 750 mg three times daily of metronidazole for 7 days. The CST after treatment was normal and no giardia was found in any fraction of duodenal juice. Ultrasonography showed reduction of the cyst size after treatment.

To our knowledge, there has been no previous report of pancreatic infection with giardia, but the mechanism of diarrhoea and malabsorption in giardiasis has been explained by decreased pancreatic function,[1] which has been shown to be secondary to the inhibitory effect of giardia on trypsin[2] and lipase[3] by in-vitro studies. In our case, diabetes might have predisposed to an immunocompromised state or severe diabetic neuropathy might have affected the tone of Oddi's sphincter to allow infection with the protozoa.

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Response to specific anti-oestrogen (ICI182780) in tamoxifen-resistant breast cancer

SIR—Howell and colleagues' data (Jan 7, p 29) on the novel steroidal anti-oestrogen are encouraging. However, the cited response rate of 13/9 (69%), albeit striking, should be interpreted with care in relation to other published data. First, although there are biological and clinical arguments to include patients with 6 months of no change with objective responders, this approach is uncommon. Second, the group of patients that they selected for treatment would generally be regarded as favourable in relation to treatment with a second-line agent such as an aromatase inhibitor.

We have reanalysed the response rate of our two phase I/II studies[1,2] of two new triazole aromatase inhibitors (vorozole and letrozole), which are potent suppressants of plasma oestrogen concentrations in postmenopausal patients. In this reanalysis we have included only patients who fitted Howell and co-workers' entry criteria. Thus, patients were excluded if they had received chemotherapy in addition to tamoxifen, failed on adjuvant tamoxifen after less than 2 years treatment, or showed intrinsic resistance to tamoxifen in the metastatic setting. We have also included patients with no change for 6 months in the group of responders.

6 of 21 and 12 of 24 patients were acceptable for this reanalysis from the letrozole and vorozole studies, respectively. There were 5 and 9 responders, respectively, giving a combined response rate of 78% (14/18), which is clearly not significantly different from that with the new anti-oestrogen. The response rate cited in each of the original papers without this selection was 33% (7/21 and 8/24, respectively). Also in accord with Howell and colleagues' findings, several of our patients' responses were of prolonged duration (for >21 months in 5 of 14).

The new anti-oestrogen looks likely to be more effective than the other mixed agonist/antagonist toremifene. It remains to be seen whether it will be more effective than other non-steroidal anti-oestrogens with less agonist activity than tamoxifen or toremifene, such as idoxifene.[3] Our data suggest that it may not be substantially more effective in terms of response rate than aromatase inhibitors, with which it is conceptually similar in its pure deprivation of the oestrogenic signal.

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Budd-Chiari syndrome and factor V Leiden mutation

SIR—Budd-Chiari syndrome is characterised by hepatic venous outflow obstruction. Although myeloproliferative diseases are usually responsible for this obstruction,[1] deficient or abnormal inhibitors of the haemostatic system, antithrombin III, protein C, and protein S, and anti-phospholipid antibodies can be involved. A defect in anticoagulant response to activated protein C (APC) is a new mechanism for thrombophilia.[2] The anticoagulant function of APC lies in its capacity to inactivate coagulation co-factors Va and VIIIa. APC resistance is linked to a single basepair mutation on the factor V gene, resulting in Arg^{506}→Gln substitution in the APC cleavage site and characterising factor V Leiden.[3,4]

A 21-year-old trisomic woman was admitted in November, 1994, with fulminant hepatic failure, ascites, and peripheral oedema. Aspartate aminotransferase was 8745 U/L, prothrombin time 34 s (normal 12), fibrinogen 0·65 g/L, and D dimers 3·2 μg/mL (normal ≤0·4 μg/mL). 2 years before, she had had an ilio-femoral thrombosis and bilateral pulmonary embolism. At that time, protein C, antithrombin III, and antiphospholipid antibodies were normal or negative, but free protein S was low at 46% (normal 65–120). She had been treated with unfractionated heparin, followed by vitamin K antagonists for 6 months.

Hepatic doppler ultrasonography showed occluded hepatic veins and Budd-Chiari syndrome was histologically confirmed. The patient was treated with low-molecular-weight heparin (Enoxaparin) and then with vitamin K antagonists when prothrombin time reached about 15 s, and she was discharged. Coagulation studies would not have been informative because of the severe hepatocellular insufficiency. We therefore examined the family although there was no familial history of thrombosis. The father, mother, and two brothers did not have deficiency in antithrombin III, proteins C or S, or plasminogen. Resistance to APC, assessed by the APC-dependent prolongation of the activated partial thromboplastin time,[2] was found in the mother (ratio 2·11, normal 2·48–3·66). DNA analysis was done with *MnlI* digestion of amplified factor V DNA fragment.[3] Both our patient and her mother were heterozygous for the Arg^{506}→Gln mutation.

The deficiency of free protein S seen previously seems to have been acquired, since it was not detected in the family.