first trimester, the pregnancy was uneventful as determined by hormonal and ultrasound evaluations. The treatment was well-tolerated and no adverse effects were noted.

Commercially available urinary FSH preparations all contain LH activity, but this case shows that during concomitant intranasal buserelin treatment rhFSH alone can induce adequate folliculogenesis and steroidogenesis in normal ovulatory women undergoing IVF-ET.

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Adenomatous colonic polyps and colon cancer

SIR,—Most cases of colonic cancer are thought to arise from pre-existing polyps.[1] This polyp-cancer sequence is suggested by the association between polyps and cancer in resected specimens, and the demonstration of cancer changes in adenomatous polyps.[2] However, the incidence of colonic polyps is much greater than the incidence of colon cancer, and there is also a change in the predominance of adenomas from the distal to the proximal colon with increasing age,[3] which is not seen with cancers. The pathological relation between colonic polyps and cancer may not be a simple one.

Over a three-year period, data collected prospectively for the Australian Polyp Prevention Project (a study of the effects of dietary modification on the recurrence rate of adenomas), were available for analysis. Inclusion criteria were total colonoscopy to the caecum, a clean colon enabling accurate assessment, and histologically proven adenomatous polyps. Exclusion criteria were metaplastic polyps, no histology, an incomplete examination due to dirty bowel or failure to reach the caecum, a history of colonic cancer, inflammatory bowel disease or familial polyposis, and synchronous large-bowel cancer. 390 patients (426 polyps) fulfilled the criteria. The anatomical distribution of the polyps was determined from the colonoscopy report. Over the same period, 296 patients underwent surgery for colorectal cancer at this hospital. Data on these patients had been collected prospectively and the site of the cancer was identified from the database.

The distribution of polyps and cancers in the different colonic segments is shown in the table. There was an association between the distribution of polyps and cancers from the region of the hepatic flexure to the rectum. Both cancers and polyps were most frequently seen in the rectosigmoid region. There was a significant difference between the incidence of polyps and cancers in the right colon (caecum and ascending) (χ^2, $p < 0.001$):

	% distribution	
Site	Polyps (n = 426)	Cancer (n = 296)
Caecum	5·6	13·8
Ascending colon	6·1	9·1
Hepatic flexure	2·8	4·1
Transverse colon	8·7	6·1
Splenic flexure	1·2	3·4
Descending colon	3·8	3·4
Sigmoid colon	48·6	34·1
Rectum	23·2	26·0

These data support the polyp-cancer sequence for cancers in the distal colon but suggest that factors other than polyps are responsible for the development of right-sided cancers. DeLattre et al[4] have demonstrated different frequencies of genetic alterations in the proximal and distal colon and have suggested that proximal and distal tumours differ in their initiation or progression. Polypectomy may well be influential in reducing the incidence of colon cancer in the distal colon but its value in the proximal colon may be less pronounced. This is of concern in the elderly where there is a shift towards proximal tumours, and in whom total colonoscopy may be more difficult and less acceptable.

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Clinical importance of HCV confirmatory testing in blood donors

SIR,—Hepatitis C virus (HCV) is better characterised by its genome than by its serology or pathogenicity. This has caused confusion when information obtained by detection of HCV genome does not match serological findings. HCV infection is usually, but not always, persistent,[1-3] and there is clinical, histological, and serological evidence that a few infected individuals can recover.[2,3] This confusion should be clarified so that proper advice can be given.

Recent *Lancet* letters[4-6] convey conflicting interpretations of serological data: some suggest that a blood donor with an indeterminate result on the Ortho confirmatory recombinant immunoblot (RIBA) may well be truly infected with HCV[4] (or a particular subtype[5]) while others propose a false reaction[6] as a likely cause of this frequent pattern.

During the past six months we have screened 50 077 blood donors by second-generation enzyme immunoassay (Abbott). 138 (0·28%) repeatedly reactive samples were tested by RIBA and by a confirmatory assay that is still under development and that is based on recombinant HCV antigens similar to RIBA (MATRIX, Abbott).[3] The MATRIX sample to cut-off ratio was 5. Alanine aminotransferase (ALT) values were judged abnormal if above 40 IU/l.

32 samples (17 with raised ALT) that were reactive with two or more non-overlapping HCV recombinant proteins were taken as confirmed. 33 samples were indeterminate by RIBA, 30 by MATRIX, and 17 by both (c100 = 1, c33 = 1, c22 = 15). The 29 samples with discrepant results were either 1 + or 2 + with RIBA or below a ratio of 20 with MATRIX on a scale ranging from 1 to 300. By contrast, of 17 samples reactive with both assays, 7 were 3 + or 4 + with RIBA and 12 scored between 20 and 237 (median 81) with MATRIX. All individuals with confirmatory indeterminate results had normal ALT values.

37 available samples indeterminate by RIBA or MATRIX for c22 or c33 (20 from the prospective screening of blood donors and 17 samples from another study) were further analysed with a peptide-based EIA (UBI, Organon) and cDNA PCR with a primer pair from the 5' non-coding region.[7] 12 of 26 (46%) samples reacting with c22 and none of 11 reacting with c33 were positive with UBI EIA. 4 samples strongly reactive with c22 (all positive with UBI EIA) and 1 sample reactive with c33 were positive for HCV RNA by cDNA PCR:

	Confirmatory assay			
Specificity	RIBA	MATRIX	UBI EIA pos/neg	PCR pos
c-22	+	+	10*/9	4
	+	–	1/3	0
	–	+	1/2	0
c-33	+	+	0/7*	1
	+	–	0/0	..
	–	+	0/4	0

*1 sample confirmed with MATRIX.

Our findings suggest that about half of all HCV RIBA indeterminate results are likely to be false reactions since the level of reactivity is consistently low and not detected by an alternative

confirmatory assay of similar sensitivity under the study conditions based on almost identical antigens. As suggested,[4] a minority of samples with indeterminate c22 or c33 reactivities are hepatitis C viraemic, as indicated by PCR. Chan et al[5] have suggested that incomplete serological patterns are related to infection with divergent HCV variants (type 3), and recommended a rigorous exclusion of these donors as potentially infectious. This hypothesis would be more convincing if some patients had clinical evidence of liver disease, if an HCV type-3 acute post-transfusion hepatitis could be identified, and if such donors were proved to be able to transmit HCV. We have an alternative explanation, based on longitudinal studies of patients with haemophilia. We have shown that c22-only reactivity resulted from the sequential loss of c100 and, later, c33 antibodies in 2 individuals apparently recovering from HCV infection and no longer viraemic.[2] Blood donors with high reactivity to c22, normal ALT, and negative PCR may correspond to this setting. Virologically, the emergence of type 3 HCV may be the result of effective immunological pressure selecting out over time a non-infectious or less infectious escape mutant highly divergent from the initial, dominant quasi-species. The data reported by Chan et al may reflect a temporary state between viraemic type 1 or 2 HCV cases with full serological profile and recovering individuals who are no longer viraemic but have residual anti-c22 reactivity. A careful longitudinal study of patients and/or infectivity studies of informative donor-recipient pairs should provide a firm answer to this critical question. Until then, although donors with HCV confirmatory indeterminate results should still be excluded, their counselling should include the possibility of a benign long-term outcome.

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Magnetic resonance imaging in cobalamin deficiency

SIR,—Clinically, cobalamin deficiency resembles demyelinating disease[1,2] and the two disorders also have pathological changes in common. Spinal-cord findings have, however, only been described at necropsy. We have seen a patient with pernicious anaemia presenting with neurological findings in whom magnetic resonance imaging (MRI) revealed an unexpected finding that resolved with cobalamin treatment.

A 36-year-old woman was referred with progressive paraesthesiae. She had been in good health until 1 year before admission, when she had a sharp pain in her feet when she flexed her head anteriorly (Lhermitte's sign). 2 months before admission, numbness developed in her fingertips, radiating to her palms and arms. Numbness in her heels had then progressed to her legs. She had normal cranial nerve, motor, proprioceptive, temperature, and pinprick examination. She had an impaired sensory level below C5, deep tendon reflexes slightly diminished in the right arm only, and Lhermitte's sign.

She was anaemic (Hb 8·1 g/dl, mean corpuscular volume 110 fl). Her cerebrospinal fluid was negative for oligoclonal bands and myelin-basic protein. She had a normal electromyogram and evoked potentials. Her serum vitamin B_{12} was 9 pg/dl with a positive test for intrinsic factor antibodies. Bone marrow studies revealed megaloblastic changes and diminished iron stores. MRI of her cervical spine revealed a bright signal at C3–C6 (figure, top).

MRI of cervical spine.

Top, symptomatic state before cobalamin treatment. Bottom, after 4 months' therapy with cobalamin.

The patient was given intramuscular injections 1 mg vitamin B_{12} daily for 7 days, then 1 mg a week for several weeks, and then 1 mg monthly. Progression of her symptoms halted. 1 month later, minor residual numbness in her fingertips was her only difficulty and she was no longer anaemic. Follow-up cervical spine MRI 4 months later was normal (figure, bottom).

A striking difference between the demyelinating disorders and cobalamin deficiency is the reversiblity of neurological changes in