started; it rose to 10% in the late 1970s, between 1980 and 1985 it was 9·7%, and it rose steadily to 23% in 1989. The hospital authorities submitted the matter to a review committee. Measures suggested to check the high CS rates were obtaining a second consultation before CS was decided, reducing the obstetrician's fee for CS (which was hitherto substantially higher than for vaginal delivery), and raising the fee for vaginal delivery (assisted or otherwise) so as to virtually equalise the two. These measures seemed to work: the CS rate dropped to 16% in 1990 and to 12% in 1991, at which level it has stabilised. Lastly, faith in astrology is widespread in India and some families, realising that childbirth can be timed (by CS) to occur at the most propitious hour, have persuaded pliable obstetricians to do the needful.

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Rectal cancer in FAP patient after sulindac

SIR—Sulindac (Clinoril) reduces the number and size of colorectal adenomas in patients with familial adenomatous polyposis (FAP). However, its effect is incomplete and drug therapy will probably not replace prophylactic colectomy for long-term management.[1] Tonelli and Valazano (Oct 30, p 1120) describe reduced efficacy with increased length of sulindac therapy. Two of their patients developed large, sessile adenomas after 25 and 107 months of treatment; both needed transanal resection and both adenomas harboured severe dysplasia. We report a case of malignant degeneration during long-term sulindac therapy.

A 68-year-old woman with FAP was followed with periodic sigmoidoscopy since undergoing a colectomy with ileorectal anastomosis 35 years ago. Scattered rectal polyps were intermittently identified and electrocoagulated. 3 years ago she developed a large villous adenoma that needed transanal excision. A year later, her rectum contained many polyps. These were electrocoagulated, but 4 months later, over 100 rectal polyps were recorded. Oral sulindac was initiated at a dose of 150 mg twice daily according to the North Central Cancer Treatment Group protocol 909251. Nearly complete polyp regression was noted 3 months later at sigmoidoscopy. Sigmoidoscopy was continued every 3 months. On each occasion, only 1 or 2 polyps were noted and were treated with electrocoagulation. 15 months after initiating sulindac, a 1–2 cm flat ulcerated lesion was identified at sigmoidoscopy. Biopsy confirmed adenocarcinoma. Preoperative transrectal ultrasound identified a UT-3 lesion that had invaded beyond the bowel wall. Preoperative chest radiography, liver function test, and carcinoembryonic antigen were normal. The patient underwent completion protectomy with ileostomy. The specimen contained a moderately differentiated adenocarcinoma of the rectum that had invaded through the bowel wall into the perirectal fat. 6 of 20 perirectal lymph-nodes were involved with tumour. DNA analysis of the tumour showed a single diploid cell line with high proliferative activity. The rectal mucosa also contained a flat villous adenoma, a flat tubular adenoma with high-grade dysplasia, and at least 10 additional foci of adenomatous change in flat mucosa.

This case is the first documented occurrence of rectal cancer in a patient with FAP after regression of visible polyps with continuous oral sulindac therapy. This pattern of occurrence is consistent with the natural history of FAP after ileorectal anastomosis (without sulindac) as described by Nugent and Phillips[2] who showed increased risk of carcinoma after age 50, malignant degeneration despite twice yearly sigmoidoscopy, and a high incidence of lymph-node or distant metastases despite the small size of primary tumours. Sulindac inhibits the formation of polypoid masses, but does not block the development of adenomatous change or interrupt the adenoma-carcinoma sequence. Our findings strongly indicate the need for continuing surveillance of FAP patients undergoing sulindac chemoprevention. Random biopsies may be a necessary adjunct.

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Guillain-Barré syndrome associated with hantavirus infection

SIR—In eastern Netherlands hantavirus infections (Puumala-like virus) is frequent, especially so in 1993.[1] The virus causes nephropathia epidemica (NE), the mild European variant of haemorrhagic fever with renal syndrome.[2] Manifestations of the infection are usually dominated by transient renal failure. Recently one of our NE patients developed a neurological syndrome while recovering from renal failure.

A previously healthy 46-year-old woman was admitted to hospital with fever, nausea, reduced diuresis, and increasing malaise over the previous 7 days. She complained of numbness in her hands and feet. 3 weeks earlier she had been exposed to bank voles while cleaning a caravan at a camp site. There was no history of recent illness. Physical examination was normal except for flank pain on palpation and widespread hyporeflexia. Laboratory findings were: erythrocyte sedimentation 58 mm over 1 h, normal blood cell count (including platelets), urea 33·5 mmol/L, creatinine 817 μmol/L, potassium 5·8 mmol/L, albumin 33 g/L, and normal liver enzymes. Urine analysis was: erythrocytes greater than 150/μL, white-cells 10–50/μL, hyaline casts, few cell cylinders, and 24 h protein excretion 1·4 g (940 mL). Chest radiograph and kidney ultrasonography were normal. A renal biopsy specimen (second day after admission) contained only cortical tissue with 18 glomeruli and showed no abnormalities on light microscopy or immunofluorescence. Puumala-virus-specific antibodies were detected in serum by indirect immunofluorescence assay (IFA) on the ninth day after the onset of illness (IgA titre 60, IgM 180, IgG 1620), confirming recent hantavirus infection.[3] Renal function returned to normal within 2 weeks.

2 days after her admission severe limb paraesthesia developed, with ataxia and areflexia, and over the next 2 weeks this progressed to severe sensory loss in hands and feet with loss of vibration and joint position sense. A mild proximal arm and leg weakness was noted. Cerebrospinal fluid examinations revealed increasing protein concentrations (0·80 to 3·7 g/L) without cells, and rising hantavirus antibody titres (IgG 8 to 32). Isoelectric focusing revealed one oligoclonal band in the IgG region with an IgG index of 0·84, which is compatible with intrathecal IgG production. Nerve conduction studies at 2 weeks demonstrated total absence of sensory responses and H-reflexes. F and motor responses were completely normal, as was needle examination. Slow spontaneous recovery from the proximal weakness, paraesthesia, ataxia, and sensory loss occurred after the third week, and nerve conduction studies showed improvement in H-reflexes. An extensive search for systemic illnesses and viral infections associated with Guillain-Barré syndrome was negative.

We conclude that our patient had a predominantly sensory Guillain-Barré syndrome associated with hantavirus infection. Serious neurological complications during NE have been reported before[4,5] but to our knowledge this is only the second case of Guillain-Barré syndrome.

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Antibodies to different strains of hantavirus in end-stage renal disease in USA and Japan

SIR—Glass et al[1] reported an association between end-stage renal disease (ESRD) and antibodies to hantaviruses by enzyme immunoassay (EIA) based on viral lysate antigens (Hantaan virus strain 76–118) and by plaque reduction neutralisation (Baltimore rat virus). We have studied patients with azotaemia in the United States and Japan, using a capture EIA for IgM antibodies and an indirect EIA for IgG antibodies reactive with recombinant nucleocapsid antigens of Puumala and Hantaan strains of the hantaviruses (Progen Biotechnik, Heidelberg).[2,3]

The EIA cut-off (mean + 5 SD) was established in sera from 150 healthy donors in four geographical areas (Florida, Arizona, California, Tokyo) and results were expressed as a ratio of patient value to assay cut-off (around 0·3 optical density [OD] for IgM and 0·6 OD for IgG). All sera were tested in duplicate in antigen and no-antigen wells to check for "sticky" sera. The signal with the no-antigen well was subtracted from the OD obtained with the antigen well. In a direct comparison with sera from confirmed cases of Hantaan-virus-associated Korean haemorrhagic fever ($n = 18$) and Puumala-virus-associated nephropathia epidemica ($n = 16$), the EIA proved 2–5 times more sensitive than indirect fluorescent antibody (IgG and IgM) assay, which uses whole viruses in Vero cells (data not shown). Specificity was studied by testing a separate set of sera with increased antibody titres against various viral and bacterial antigens as well as autoimmune disease sera. None of these 50 sera was positive for IgM or IgG antibodies to Hantaan and Puumala viruses.

Three lots of sera were tested to investigate the association between hantaviruses and renal disease—81 consecutive sera with raised blood urea nitrogen and creatinine values and 80 normal sera during the same period, all from a large clinical laboratory in Florida, and similar groups of consecutive abnormal and control sera from Tokyo ($n = 60$ and $n = 30$, respectively) and California ($n = 94$ for both). All patient and control sera were age and sex matched, the average age being 60.

8 of the 81 (10%; $p < 0{\cdot}001$, Fisher's exact test) renal disease sera from Florida had raised antibody levels against Puumala virus; 3 were positive for IgG alone, 4 for IgM alone, and 1 for both. Of the 4 IgG Puumala-positive sera, 2 were also positive for Hantaan IgG (although with weaker signals, probably due to cross-reactivity). The average age of the 8 hantavirus-positive, azotaemic patients was 65; this accords with the observation that seroprevalence of antibodies to hantavirus is higher in patients older than 60.[1] 1 of 80 normal sera assayed had a borderline increase in IgG Hantaan-reactive antibody titre; this patient was 71. The sera from California also had similar results: 9 of 94 (10%; $p < 0{\cdot}001$) ESRD sera had increased antibody levels to the Puumala virus; 5 were positive for IgM and 4 for IgG. None of the 94 normal sera was positive for Hantaan or Puumala reactive antibodies (IgG or IgM).

In Japan, 7 of 60 (12%, $p < 0{\cdot}001$) renal disease sera had antibodies to the Hantaan strain, of which 5 were IgM and 2 were IgG. None of the normal sera from Japan was positive for Hantaan or Puumala reactive antibodies. None of the Hantaan-positive sera in this set showed any reactivity with the Puumala antigen, confirming the reported one-way cross-reactivity seen in Hantaan-reactive sera.[4-6] The presence of one-way cross-reactivity in 2 of the sera positive for IgG Puumala antibodies from the US indicates the need to test for antibodies against both strains wherever indicated.

Our data suggest that the reported association of hantavirus antibodies with renal disease is widespread. The viral strains involved differ geographically so testing for antibodies to more than one strain is necessary to ascertain the associations of hantavirus antibodies and renal disease.

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Molecular genetic testing of a fetus at risk of Gerstmann-Sträussler-Scheinker syndrome

SIR—Genetic diseases with known causative mutations can be eliminated in as little as a single generation by the judicious application of molecular genetic testing of DNA from fetal cells. Numerous mutations in a gene on chromosome 20 that encodes an amyloid precursor (proteinase-resistant protein, PRP) have been shown to be linked to the occurrence of disease in families affected with transmissible spongiform encephalopathy.[1] We report the first instance in which molecular genetic testing of an at-risk fetus has been used for this group of diseases.

For the past few years, we have provided genetic testing and counselling for an American family of German-Danish ancestry, afflicted with the form of Gerstmann-Sträussler-Scheinker disease linked to the proline→leucine mutation in codon 102 of the gene. The disease shows the usual fully