Mean (± 1 SD) vascular permeability (as mean areas of blueing) caused by cultured lymphocytes taken from normal subjects and from patients during relapse of minimal change nephropathy before treatment with steroids

	Mean areas of blueing (mm ²)
R ₁ : reconstituted supernatant from cultures from controls	32.8 $\pm$ 22.2
R ₂ : reconstituted supernatant from cultures from patients	105.4 $\pm$ 32.7
S ₁ : supernatant from PHA stimulated cultures from controls	60.2 $\pm$ 38.1
S ₂ : supernatants from PHA-stimulated cultures from patients	113.8 $\pm$ 24.9

PHA = Phytohaemagglutinin.

that for PHA-stimulated supernatant (S₁ v S₂; $p < 0.005$). In seven control assays S₁ was significantly higher than R₁ ($p < 0.05$, Student's dependent t test). The difference in values for R₂ and S₂ was not significant; nor was there any difference in production of vascular permeability factor between cells taken from patients in remission and those taken from controls.

Comment

Our results show that lymphocytes taken from patients during relapse of minimal-change nephropathy produced significantly more vascular permeability factor than lymphocytes of normal subjects when both sets of cells were stimulated with PHA in vitro (S₁ v S₂). This confirms the findings of Lagrue *et al.*² The production of vascular permeability factor by patients' unstimulated cells, however, was not significantly lower than that by cells cultured with PHA (R₂ v S₂), which suggests that during relapse patients' lymphocytes are already stimulated to produce vascular permeability factor in vivo and cannot be further stimulated by PHA in vitro. Conversely, lymphocytes of normal subjects produced more vascular permeability factor when stimulated by PHA, though by small amounts (R₁ v S₁).

These data suggest that Shalhoub's hypothesis should be modified. If the main abnormality in minimal-change nephropathy were an overproduction of vascular permeability factor by lymphocytes this should have been detected in patients studied during remission. More probably, lymphocytes in controls and patients with MCN can produce vascular permeability factor but in the patients its production is not inhibited. Clinically, this may constitute the difference between febrile proteinuria and frank nephrotic syndrome. A factor has been detected in the sera of patients during relapse of minimal-change nephropathy that could substantially inhibit PHA-induced transformation of lymphocytes.⁴ This factor disappeared when patients went into remission and was absent from the sera of patients with other forms of nephrotic syndrome. This inhibitory factor may serve to stop production of vascular permeability factor, and the basic abnormality of minimal-change nephropathy may be unresponsiveness of vascular permeability factor-producing lymphocytes to this factor. Measles, which induces remission of minimal-change nephropathy, inhibits lymphokine production in vitro.⁵ The importance of these results rests on the ability of vascular permeability factor to induce proteinuria, which has yet to be confirmed.

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Requests for reprints should be sent to Dr J M Boulton Jones.

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Temporal arteritis in association with the Guillain-Barré syndrome

A symmetrical polyneuropathy and mononeuritis both occur as manifestations of temporal arteritis,^{1,2} but the Guillain-Barré syndrome has not been reported in association with this condition. The following is a report of such a case.

Case report

A 71-year-old woman presented with a four-week history of bilateral facial weakness followed by a gradually progressive proximal limb weakness, which had begun in the legs and spread to the arms. There were no associated sensory symptoms, nor did she have muscle or joint pains. From the onset of the facial weakness she had had sore red eyes, and for three months she had also complained of anorexia, weight loss, and mild bilateral deafness associated with giddiness. Throughout this time she had not suffered from headaches.

She had bilateral conjunctivitis but her fundi and visual acuity were normal. There was a slight perceptive deafness present bilaterally. She had an almost complete facial diplegia and a definite proximal weakness of the limbs. There were no sensory abnormalities in the limbs, but all her tendon reflexes were absent and the plantar responses were flexor.

Investigations showed: haemoglobin concentration (Hb) 9.9 g/dl, red blood cells normochromic and normocytic; white blood count $7.8 \times 10^9/l$, neutrophils 86%, lymphocytes 14%; erythrocyte sedimentation rate (ESR) 125 mm in one hour; plasma urea, electrolytes, and calcium concentrations normal; and plasma albumin concentrations 25.8 g/l. Serum protein electrophoresis showed: albumin low, a pronounced increase in α_1 - and α_2 -globulins with a diffuse increase in γ -globulins, and no paraprotein band. Serum concentration of IgG was raised, but that of IgA and IgM normal. She was positive for antiparietal cell antibodies but negative for other autoantibodies. Serum iron concentration 8.5 mmol/l (47.5 $\mu g/100$ ml), iron binding capacity 37.5 mmol/l (209.4 $\mu g/100$ ml), and vitamin B₁₂ concentration 354 pmol/l (480 ng/l). Bone marrow examination showed an increase in stainable iron but was otherwise normal. Glucose tolerance was normal and the Wassermann reaction was negative. Muscle enzymes values were normal. The cerebrospinal fluid was acellular and contained 0.1 g/l protein. Sputum cytology and a chest radiograph showed nothing abnormal. Barium meal showed a hiatus hernia and barium enema diverticulosis. A skeletal survey was normal, as were nerve conduction studies and slit lamp examination of the eyes. Audiometry showed a bilateral sensorineural hearing loss.

After admission there was a gradual spontaneous improvement in her symptoms and signs, and the Guillain-Barré syndrome was diagnosed. Extensive investigations for an underlying neoplasm were carried out in view of the weight loss, anaemia, and raised ESR but all proved negative. Two weeks after discharge, however, she developed severe bilateral fronto-temporal headaches followed within a week by an appreciable deterioration in the vision of the left eye and blurring of vision on the right. When examined she could not distinguish light from dark with the left eye and had greatly reduced visual acuity in the right eye (J 14). She had bilateral papilloedema, which was more pronounced on the left. The left retina was generally pale, indicating the presence of retinal oedema, and there were some haemorrhages close to the optic disc. Both temporal arteries were tender to touch. She still had a mild left facial weakness, a mild proximal limb weakness, and absent tendon reflexes. Her haemoglobin concentration was 10 g/dl and her ESR 134 mm in one hour. Temporal arteritis was diagnosed and steroid treatment started immediately (prednisolone 80 mg/day). By the next day her headache had improved greatly and after three days her haemoglobin concentration had risen to 13.4 g/dl and her ESR fallen to 52 mm in one hour. Her visual acuity improved progressively to J4 on the left and J2 on the right after six weeks. Her ESR continued to fall and her symptoms were subsequently controlled by a reduced dose of prednisolone (10-20 mg daily).

Comment

The patient presented initially with the clinical picture of the Guillain-Barré syndrome, a diagnosis which was acceptable despite the presence of a normal protein concentration in the cerebrospinal fluid and normal results of nerve conduction studies.³ She also gave a three-month history of anorexia and weight loss and had an unexplained anaemia associated with a high ESR. It was only some weeks later, when her facial diplegia and polyradiculoneuropathy had greatly improved, that she developed the clinical features of temporal arteritis. This association does not seem to have been reported and, although it may be a mere coincidence, both disorders are thought to have an immunological pathogenesis.^{4,5} The neuropathies reported in association with temporal arteritis have been attributed to ischaemic lesions of the nerves due to an arteritis of the vasa nervorum.^{1,2} Nevertheless, the clinical picture in this patient, with a symmetrical

polyradiculoneuropathy of subacute onset, seems to be more in keeping with an immunologically induced demyelination.

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Pregnancy attributable to interaction between tetracycline and oral contraceptives

Various drugs, including antibiotics, may cause failure of contraception and breakthrough bleeding in patients on oral contraceptives.¹ Early reports implicated rifampicin,² which was later shown to increase the rate of hepatic metabolism of ethinylloestradiol and norethisterone.¹ There have been three cases of pregnancy in women taking ampicillin.³ We cannot find any report of either breakthrough bleeding or pregnancy attributable to tetracycline in a woman taking oral contraceptives. We report such a case.

Case history

The patient, a 20-year-old student, had been taking oral contraceptives for four years. Her only complaint had been of an increase in left-sided headaches. For the last two years she had taken Microgynon 30 (ethinylloestradiol 30 µg, norgestrol 150 µg) and had had no breakthrough bleeding. On 16 October 1978 she had a normal withdrawal bleed. On 20 October she started the next course of Microgynon and also (for sinusitis) a five-day course of tetracycline 500 mg six hourly for three days and 250 mg six hourly for two days. She completed the course on the 24 October. She did not forget to take her oral contraceptive. She had no diarrhoea or vomiting but had only a very light two-day withdrawal bleed on 14 and 15 November 1978. She continued to take her oral contraceptive for a further two months until seen at the family planning clinic on 8 January 1979. Her uterus was then the size of at least a 12-week pregnancy. This would have corresponded with a previous menstrual period on about the 15 October, and indicated that she must have ovulated either when she was taking the tetracycline or in the week after. Termination confirmed the clinical assessment of the duration of pregnancy.

Comment

The time course of this history in a woman who had been taking oral contraceptives for four years with no problems strongly suggests that the tetracycline contributed to the failure in contraception. In addition to the reports of pregnancies associated with rifampicin² and ampicillin,³ pregnancies have been reported in two women taking either sulphamethoxypyridazine or chloramphenicol⁴ and also an increased incidence of breakthrough bleeding in women on phenoxymethylpenicillin, neomycin, or nitrofurantoin.¹ The mechanism of the interaction is unknown but a decrease in urinary oestriol output has been noted in pregnant women taking ampicillin,⁵ phenoxymethylpenicillin, or neomycin.¹ Therefore the enterohepatic circulation of contraceptive steroids may be interrupted by inhibition of the gut bacteria normally responsible for hydrolysis of steroid conjugates.⁴ This would result in lower-than-normal concentrations of circulating steroids. There seems no reason why tetracycline should not cause a similar change.

With the widespread use of low-dose oestrogen contraceptives such interactions may well occur more often. Tetracyclines are used for a wide range of infections including pelvic inflammatory disease and non-specific urethritis. One of us has seen a second case of breakthrough bleeding associated with a course of tetracycline. We therefore think that doctors should be aware of the potential problem. We would advise that women taking low-dose oral contraceptives should take extra precautions against conceiving in any cycle during which antibiotics are given.

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Diet and ulcerative colitis

The apparent rarity of ulcerative colitis in developing countries together with the ability of dietary fibre to affect colonic function and bacterial metabolism have led to suspicions that a low intake of fibre may be a causal factor in this disease.^{1,2} People who develop Crohn's disease (a closely related condition) show significant differences in diet from matched controls, eating less raw fruit and vegetable fibre and more refined sugar.³ To investigate whether ulcerative colitis is preceded by an unusual diet we have compared the diet before illness of patients with newly diagnosed colitis with that of closely matched, healthy subjects.

Subjects, methods, and results

Thirty consecutive newly diagnosed patients (17 men, 13 women) were studied. The diagnosis of ulcerative colitis was based on the findings of barium radiology, sigmoidoscopy, and rectal biopsy. In 10 patients the disease extended proximal to the splenic flexure, in five it was limited to the rectum, and in the remaining 15 it was of intermediate extent. The median duration of symptoms before diagnosis was two months (range 1-18).

All patients were interviewed within three months of diagnosis. A single dietitian used the dietary history method⁴ to question each patient about his or her habitual diet before illness. Using a specially designed questionnaire, she determined the frequency of consumption and size of helpings of each of a comprehensive range of foods and drinks.³ The data were analysed to determine the average daily intake of different food components with the use of a computer programme compiled from McCance and Widdowson's food tables.⁵

Dietary intake of 30 patients with ulcerative colitis before their illness and that of 30 matched, healthy controls. Results given in g/day as means $\pm$ SE of mean unless stated otherwise

	Patients	Controls
Total dietary fibre	19.9 $\pm$ 1.1	18.3 $\pm$ 1.2
Cereal fibre*	8.6	7.2
Total fruit and vegetable fibre	10.1 $\pm$ 0.6	10.5 $\pm$ 0.8
Raw fruit and vegetable fibre	1.4 $\pm$ 0.2	1.4 $\pm$ 0.2
Refined sugar	96 $\pm$ 9	97 $\pm$ 9
Total carbohydrate	291 $\pm$ 20	269 $\pm$ 16
Protein	78 $\pm$ 4	82 $\pm$ 3
Fat	109 $\pm$ 7	106 $\pm$ 5
Energy (MJ/day)	10.2 $\pm$ 0.6	10.0 $\pm$ 0.5

*Median value.

Conversion: SI to traditional units—Energy: 4.2 MJ $\approx$ 1000 kcal.