of observation were available for analysis. In total, 46 women had been diagnosed during the follow up period by the consultant responsible for their care as suffering from a first stroke (ICD (8th revision) codes 430-438). Thirteen had suffered a subarachnoid haemorrhage, of whom four died; eight had an aneurysm or arteriovenous malformation detected by angiography or at necropsy. Two other women (who are not considered further here) suffered definite intracranial haemorrhage (a fatal intracerebral haemorrhage in one and a chronic bilateral subdural haematoma in the other). The remaining 31 women developed strokes of thrombotic, embolic, or unknown pathogenesis (hereafter referred to as "non-haemorrhagic" strokes). Of these 31, only two died, while so far as could be ascertained from the available records another nine were left with an important disability. Arteriography or brain scanning was undertaken in 17 women and an abnormality was found in nine. The diagnosis of stroke in the non-haemorrhagic group was thus usually on the basis of the clinical picture.

We analysed the data concerning subarachnoid haemorrhage and non-haemorrhagic stroke separately, taking into account the woman's age, whether or not she had been referred to hospital for management of hypertension before the stroke occurred, her smoking habits, and her use of oral contraceptives. The table summarises the results. Numbers were small, but the data suggest that hypertension and smoking were strongly related and that pill use was weakly related to the risk of subarachnoid haemorrhage.

Incidence of subarachnoid haemorrhage and "non-haemorrhagic" stroke in relation to age, history of hospital referral for hypertension, cigarette smoking, and oral contraceptive use. (Data given for each variable adjusted for effects of all other variables by indirect standardisation)

Variable	Subarachnoid haemorrhage		"Non-haemorrhagic" stroke	
	No of women	Incidence rate per 1000 woman years	No of women	Incidence rate per 1000 woman years
Age (years):				
25-34	3	0.04	6	0.07
35-39	5	0.08	9	0.15
40-44			9	0.24
≥45	5	0.08	7	0.51
Past hospital referral for hypertension:				
No	10	0.05	31	0.17
Yes	3	1.08	0	0
Cigarette smoking:				
Never smoked	4	0.04	15	0.14
Ex-smoker	2	0.09	4	0.18
Current smoker	7	0.12	12	0.19
Oral contraceptive use:				
Never	3	0.05	10	0.13
Ex-user	7	0.09	7	0.10
Current user—up to 36 months			6	0.41†
Current user—over 36 months	3	0.06	8	0.30†

*In addition there was evidence in the records that two patients with subarachnoid haemorrhage and four patients with "non-haemorrhagic" stroke had hypertension for which they had not been referred to hospital.

†"Non-haemorrhagic" stroke: current users v never and ex-users $\chi^2_1 = 8.7$ ($p < 0.01$).

The pattern seemed to be quite different for non-haemorrhagic stroke; there was little indication of an adverse effect of hypertension or smoking, but current oral contraceptive use emerged as a clear risk factor, duration of use appearing to be unimportant. We also examined the risk of non-haemorrhagic stroke in current oral contraceptive users in relation to the type of pill used. No strokes were observed during 9100 years of observation in women using the modern pills containing less than 50 µg oestrogen, while 13 strokes were observed during 39 400 years of observation in women using pills containing a higher dose of oestrogen. These data are encouraging but too few to be conclusive.

Comment

The findings in the Oxford Family Planning Association study agree with those of the other major studies in that they suggest that any increase in the risk of subarachnoid haemorrhage in oral contraceptive users is modest, probably not more than about 1.5-fold to 2-fold.²⁻⁵ They also suggest that the increase in the risk of non-haemorrhagic stroke is greater and is confined to current users. This conclusion supports the results of the collaborative group study² conducted in the United States from 1969 to 1971, which remains by far the largest investigation concerned with this particular question. That we have yet to observe a stroke among women using modern low oestrogen pills is encouraging but must be interpreted cautiously.

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Polymicrobial septicaemia due to *Clostridium difficile* and *Bacteroides fragilis*

We report a case of polymicrobial septicaemia due to *Clostridium difficile* and *Bacteroides fragilis*, which has not been reported previously.

Case report

A man aged 65 was admitted for urgent arteriography complaining of claudication at 100 m and a cold, painful, swollen left foot. No pulses were palpable below the right femoral artery, and the left femoral artery was not palpable at all. A gangrenous area was present on the left great toe. Arteriography showed an aortoiliac block, and a left axillofemoral bypass graft was performed. Cefuroxime 750 mg three times daily was started before the operation and continued because of suspected postoperative infection. Blood taken at this time and cultured with 0.1% glucose broth (two bottles), fastidious anaerobe broth (FAB, Lab M), and a pour plate was sterile.

On the sixth postoperative day diarrhoea developed. Pseudomembranous colitis was diagnosed presumptively, cefuroxime stopped, and oral vancomycin 125 mg four times a day started. Sigmoidoscopy was performed, a rectal biopsy specimen taken, and faecal samples analysed for the isolation of *C difficile* and its toxin. Examination for the presence of *C difficile* was by standard methods¹ using selective medium (Oxoid *C difficile* agar plus 7% defibrinated horse blood and Oxoid antibiotic supplement) and alcohol at a final concentration of 50% to select out clostridial spores. Toxin was investigated using a HEP₂ cell line (Flow Laboratories). *C difficile* and toxin were not detected. Sigmoidoscopy showed normal mucosa with liquid faeces coming from above. Histological examination of the rectal mucosa showed some congestion and extravasation of erythrocytes in the lamina propria. There was a small area without superficial epithelium, but specific features of ischaemic or pseudomembranous colitis were absent.

The diarrhoea gradually decreased until on the 10th postoperative day septicaemia developed, which was treated blindly with cefuroxime and metronidazole. A blood culture set taken before treatment with antimicrobials originally yielded *B fragilis*. On subsequent subculture three days later, however, fastidious anaerobe broth yielded a strain of *C difficile* that produced toxin. Formal identification of *C difficile* was made by volatile fatty acid profiles shown by gas-liquid chromatography in conjunction with a short set of biochemical tests.¹ Specificity of the cytopathic effect in HEP₂ cells was confirmed by neutralisation with *C sordelli* antitoxin (Wellcome Laboratories).

The patient recovered from this septicaemic episode without any additional treatment or recurrence of diarrhoea. On the 21st postoperative day a bed sore was sloughed and a subcutaneous abscess found that yielded a multi-resistant strain of *Staphylococcus aureus* sensitive only to vancomycin. Despite appropriate treatment the patient's general condition deteriorated and he died 46 days after operation.

Comment

C difficile is now firmly established as a leading cause of pseudomembranous colitis, and examination for the organism and production of toxin in faeces is a well established laboratory investigation. On this occasion Oxoid CCFA medium (cycloserine, cefoxitin, fructose,

and agar) was probably not sensitive enough to isolate *C difficile* in the original episode of diarrhoea. The absence of toxin in faeces does not reliably indicate the absence of an organism. Histological examination of the rectal biopsy specimen, however, showed no evidence of pseudomembranous colitis.

C difficile is rarely found outside the bowel,² though two recent reports have described its isolation from the frontal bone in a patient with osteomyelitis³ and from a splenic abscess,⁴ both cases being due to spread in the blood. There have also recently been increased reports of polymicrobial septicæmia, and some workers have recommended subsequent subculture of previous positive cultures.⁵ Our case shows that *C difficile* is indeed capable of dissemination from the gastrointestinal tract and the value of repeat subcultures of previous positive blood cultures.

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Oral rehydration without added bicarbonate for childhood gastroenteritis

Oral rehydration with glucose electrolyte solution has become recognised as the best treatment for childhood gastroenteritis.¹ The following unresolved problems were recently identified: (a) what formula is best? (b) who are the health care personnel best suited to give treatment? (c) how should it be packaged? (d) how to avoid the largest errors in final electrolyte concentration that arise from measuring the water rather than the salts? (e) what are the effects on morbidity and mortality?²

Unlike most solutions recommended for oral rehydration, those used for intravenous rehydration do not include bicarbonate and achieve results that are equally satisfactory.¹ Aqueous solutions of bicarbonate slowly decompose to form carbonate, and also attack glass containers. On heating glucose solutions become discoloured and produce furfural and other deposits. Bicarbonate accelerates these reactions making it difficult and expensive to produce sterilised preparations containing both bicarbonate and glucose.³ Prepacked powders containing bicarbonate must be reconstituted and diluted using water that has been boiled and cooled. For the past 14 years we have overcome this problem in Cardiff by using a prepacked sterile oral rehydration solution that is free of bicarbonate.

Methods and results

All children admitted with gastroenteritis during one year were studied prospectively. Oral rehydration was carried out with a solution containing sodium 34 mmol(mEq)/l, potassium 20 mmol(mEq)/l, chloride 54 mmol(mEq)/l, and glucose 183 mmol/l (3.2 g/100 ml). This is prepared and sterilised by the hospital pharmacy and supplied in sealed 500 ml glass bottles at a cost of 36p.

During one year 50 boys and 40 girls under 5 were admitted for gastroenteritis to this unit, which serves a population of about 250 000. Ten were under 1 month, 48 from 1 to 12 months, and 32 under 5 years. Four breast

Deaths from childhood gastroenteritis in England and Wales 1937-80. ICD 008-009. Data from Office of Population Censuses and Surveys.

fed infants were admitted, none of whom required intravenous fluids. Eighty two children were managed with oral rehydration fluids alone. None had received similar standard solutions at home. Eight were given intravenous fluids within two hours of admission of whom one was given intravenous bicarbonate. None of those managed with oral fluids required sodium bicarbonate supplements or intravenous fluids. After rehydration standard formula or low lactose feeding was resumed.

On admission the mean serum electrolyte concentrations and blood gases were: sodium 137 mmol/l, range 122-164 mmol/l; potassium 4.2 mmol/l, range 3.3-5.1 mmol/l; urea 6.4 mmol/l (38.4 mg/100 ml), range 1-12 mmol/l (6-72 mg/100 ml); pH 7.4, range 7.3-7.47; carbon dioxide pressure 4.1 kPa (31 mm Hg), range 2.5-5.4 kPa (19-41 mm Hg); standard bicarbonate 21 mmol(mEq)/l, range 16-24 mmol/l; base deficit 4 mmol(mEq)/l, range 0-9 mmol/l. Serum sodium concentration was over 150 mmol/l in two children and under 125 mmol/l in another two. Various pathogenic bacteria and viruses were detected. Fifty per cent of the children were home within four days and 78% within one week. No obvious neurological damage or deaths occurred.

Comment

Nowadays deaths from childhood gastroenteritis are rare in England and Wales (figure). The greatest reduction in mortality occurred between 1945 and 1955 before the introduction of oral rehydration treatment. Under 0.4% of all local children under 5 were admitted with gastroenteritis, but they constituted 10% of all admissions to our unit from this age group. Family doctors did not give oral rehydration powders to the patients they admitted, who were mainly infants or older children with severe attacks. Incorrect reconstitution of powdered milk, with which parents are familiar, has often been reported: many (occasionally fatal) mistakes are also made in the preparation of oral rehydration powders by parents under stress caring for an ill child.⁴

The use of sterile prepacked solutions stored at 4°C after opening minimises the problem of bacterial growth.⁵ We suggest that in Britain and probably other developed countries childhood gastroenteritis can be treated advantageously with a sterile prepacked oral rehydration solution that is free of bicarbonate.

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