investigation was stopped for fear of perforation. Histological examination was consistent with ulcerative colitis of high inflammatory activity. The predominance of mixed inflammatory cells and the presence of large numbers of E. coli serotypes O26, O111, and O157 by slide agglutination was negative. However, DNA colony blot hybridisation with synthetic oligonucleotide probes constructed from the sequences reported for shiga-like toxin type 1 and 2 genes gave positive signals with both probes for 40 out of 55 E. coli colonies selected at random from an 'Endo' agar plate inoculated with the stool specimen. As a consequence the patient, who had been started 4 days earlier on 5-aminosalicylic acid and methylprednisolone, was also given ciprofloxacin 500 mg twice a day for 10 days. The patient improved rapidly and after another week his bowel habits had returned to normal. Control stool specimens taken 1, 3, and 9 weeks after antibiotic therapy were negative for VTEC by colony blot hybridisation.

In any colony blot hybridisation, we have detected VTEC strains in 3 more stool specimens from 17 patients with a diagnosis of ulcerative colitis. In contrast none of 53 stools from healthy individuals, all tested for at least 50 E. coli colonies, were positive. Interestingly serotyping yielded O2:H5 in all 4 cases. This O2 serotype has been listed as a verocytotoxin-producing strain.1

The fact that all 4 VTEC strains we found in association with ulcerative colitis were O2:H5 and that more VTEC strains found in association with haemorrhagic colitis and HUS are O157:H7 suggests that the production of verocytotoxin I and/or II, though a prominent feature of these strains, may not be their only pathogenic property. Burke et al described special adhesive properties of E. coli from patients with ulcerative colitis and Cronh's disease. Ljungh et al observed collagen type II and fibronectin binding properties as well as vero cytotoxicity in E. coli from similar patients. Neither group, however, reported serotyping. Ljungh et al have also presented a case report of a patient with ulcerative colitis from whom they isolated VTEC O7:H7. After treatment with mesilamine the patient improved. However, unlike our patient, VTEC continued to be isolated from the stool during and after antibiotic treatment. The role of antibiotics in the treatment of other VTEC-associated diseases, such as haemorrhagic colitis or HUS, is still unclear, and it has even been suggested that the use of antibiotics is a risk factor for acquiring the infection. We administered ciprofloxacin because this drug decreases verocytotoxin synthesis in vitro and, in clinical studies, eliminates enteric pathogens from the gut mucosa.

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BREAST CANCER AND ORAL CONTRACEPTIVES

Sir,—Dr Le Fanu (June 3, p 1258) criticises the Committee on Safety of Medicines (CSM) for failing to provide a "dispassionate presentation of the facts" on breast cancer and oral contraceptives (OC) usage. Specifically, he takes the Committee to task for appearing to be "influenced by the proposition" (Profession First: A metadata analysis (March 11) p 550) of the CASH study and for failing to give prominence to the increase in breast cancer registrations, amongst women aged 25-34 years, by two regional UK cancer registries.

Doctors and the public expect more from the CSM than a dispassionate presentation of facts. Over a year ago the Committee established a working party to review the scientific evidence, and to monitor all new findings on the subject. The working party and the CSM took account of all the available information in its recent assessment of the risks and benefits of OC use. In formulating its advice to the profession (Current Problems no 26) the CSM was aware, through its international contacts, that Professor Stadel and his colleagues (June 3, p 1257) were unable to confirm Peto's reanalysis of the CASH study. The Committee was also aware that the increase in breast cancer registrations noted by the Southern Thames and West Midlands registries began in the 1960s, too early to be explained by OC usage. These changes have not, moreover, been replicated in the UK as a whole.

When faced with the need to balance risks and benefits, the CSM, like any individual prescriber, has to make a judgment based on all the available evidence. Amongst the benefits of OC usage are not only its contraceptive efficacy but also the protection it offers against ovarian and perhaps cervical cancer.

We make no apology for taking a broad view of the effects of modern medicines and will continue to monitor all work on breast cancer and OC usage.

Committee on Safety of Medicines, Market Towers, London SW8 5NQ

WILLIAM ASSCHER, Chairman

PROPORTION OF NEWLY OBESE AND CHRONIC OBESE AT DIFFERENT AGES

Sir,—Most studies of obesity are purely cross-sectional in nature, comparing parents and children, or obese probands with other family members. However, the obese do not necessarily remain obese, and obesity may be attained at any age from childhood through middle age.1 Accordingly, we do not know what proportion of obese people has been obese for long (ie, chronic obesity) and what proportion represents the newly obese (recent obesity). Nor do we know whether the newly obese and the chronic obese have a different familial origin.

To answer these questions we have made a retrospective study of 1140 obese people derived from a total population sample with over 95% compliance.2 All were obese at the time of a later examination, obesity here being defined with respect to the 84th percentile (+1Z) or chronic obesity while those not obese at the previous examination were defined as newly obese. The study was therefore retrospective, using fully longitudinal data and the same diagnostic criterion at all age groups from childhood (5-9 years) through the 4th decade (30-39). Problems of skewness and kurtosis for the summed skinfolds (triceps and subscapular) were obviated by the use of centiles and normalised Z-scores throughout.

At least half of the 220 obese children, 468 obese adolescents, and 452 obese adults were not obese at a previous examination. Moreover, the percentage deemed newly obese was highest (76%) in the 5-9 age group, and 50% in the 10-14 and 15-19 age groups. The trend was similar for both sexes. Using 5-9 years as a cut-off for the young age group, the proportion of newly obese was 76% in both sexes and 78% in the combined sexes. By the age of 14-15 years, the proportion of newly obese was 27% and 13% in girls and boys respectively. By the age of 15-19 years, the proportion of newly obese was 4% and 3% in girls and boys respectively.

We are aware that the proportion of newly obese individuals is a function of the interval between examinations, just as the prevalence of obese individuals is necessarily a function of the obesity criterion used. However, our findings were based on the same obesity criteria remain obese, and obesity may be attained at any age from childhood through middle age.12 Accordingly, we do not know what proportion of obese people has been obese for long (ie, chronic obesity) and what proportion represents the newly obese (recent obesity). Nor do we know whether the newly obese and the chronic obese have a different familial origin.

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We are aware that the proportion of newly obese individuals is a function of the interval between examinations, just as the prevalence of obese individuals is necessarily a function of the obesity criterion used. However, our findings were based on the same obesity criteria and the same examination intervals. These findings are also...
consistent with prospective data indicating that the obese do not necessarily remain obese and that the cadre of obese individuals is continually replenished by recruitment from the ranks of the non-obese. Even in the middle years, at least half of the obese comprise the newly obese, thus providing an indication of the incidence of obesity (new cases per 5 year interval) rather than its prevalence.

These data, that effectively divide the obese into the newly obese and the chronic obese, hold major implications for the study of obesity, especially in family studies. We would not expect the newly obese and the chronic obese to be identical in socioeconomic origins or to derive from families of comparable parental and sibling fatness. Indeed, parent-child and sibling similarities in measured fatness may well be different for the newly obese and for those with long-established obesity. The living-together or cohabitational factor in familial obesity may also be different for the newly and the chronic obese. Years of living in an obese family may have a greater bearing on chronic obesity than on obesity of recent onset.

Source: Tecumseh, Michigan, community health survey, examination rounds.

The chronic obese. Years of living in an obese family may have a greater bearing on chronic obesity than on obesity of recent onset.

IN-VITRO STUDY OF IMMUNE RESPONSES IN LOIN PAIN/HAEMATURIA SYNDROME

SIR,—In loin pain/haematuria syndrome recurrent unilateral or bilateral loin pain is accompanied by frank or microscopic haematuria,1 Renal biopsy often reveals abundant granular deposits of C3 in arteriolar walls,2 and angiography may demonstrate abnormalities in intrarenal vessels.3 Exaggerated type 3 hypersensitivity reactions after intradermal injections of recall antigens have been described in patients with this condition and suggest that it may represent a hypersensitivity state.4 We have examined cellular and humoral immune responsiveness in vitro of eight patients with the syndrome, using antigens shown to cause abdominal skin reactions.

The diagnosis was based on clinical and renal biopsy findings. We looked at T-cell proliferation and serum antibody levels in response to antigen and at T-cell phenotype in the patients and in 4 healthy volunteers. Peripheral blood mononuclear cells were cultured for 5 days with the non-specific T-cell stimulator concanavalin A (3–50 μg/ml), and streptodornase 25 U/ml and streptozotocin 25 U/ml. The cells were then pulsed with tritiated thymidine. T-cell phenotype was determined by incubating mononuclear cells with mouse monoclonal antibodies to human lymphocyte surface markers T4, T8, and T1. The cells were washed and resuspended with fluorescein isothiocyanate anti-human Ig and immunoglobulin and analysed in a fluorescence-activated cell sorter. Serum antibody levels to PPD or varidase were measured by ELISA. Serum was incubated on micropore plates coated with antigen (10 μg/ml) and bound antibodies were reacted with goat anti-human-immunoglobulin alkaline phosphatase conjugate. After incubation with phosphate substrate absorbance at 405 nm was read on a ‘Multiscan’ plate reader.

T-cell proliferation, expressed as a stimulation index, was no different in patients and controls. Although T4 counts were low in three patients, patients and controls did not differ as a group; nor did the T4/T8 ratio. Antibodies to human and bovine PPD were present in sera from all patients and there was no difference between the mean absorbance values. Cutaneous hypersensitivity in four of the patients has already been reported4 and has since been studied in a fifth patient. There was no clear relation between the skin and the in-vitro responses or between in-vitro responses and symptom severity. Indeed in two patients whose symptoms were severe enough to merit renal autotransplantation, one produced no T-cell response to any of the antigens whilst the other responded to all of them.

The cutaneous hypersensitivity seen in patients with the loin pain/haematuria syndrome was unequivocal4 and similar observations have subsequently been made by others (Clarkson AR, personal communication). It is therefore surprising that a study of the mechanisms involved in such responses provides no evidence of hypersensitivity. However, 3–4 years had elapsed between the skin tests and the in-vitro analyses reported here. Also the patients were all well at the time of this study, and perhaps the tests should be repeated during episodes of pain. Since a relative increase in T-helper response would heighten immune responsiveness, the low T8 values in three of the patients is of interest. However, this must be interpreted with caution because the group mean was not significantly reduced and T-cells cannot be confidently assigned to helper or suppressor subgroups solely on the basis of their T8 and T4 phenotype. Furthermore one patient who had a low T8 count produced a strong cutaneous reaction to varidase but none to PPD, and no T-cell proliferative response to either antigen.

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NURSERY-ACQUIRED ASYMMPTOMATIC B HEPATITIS

SIR,—L. Gray Davis and colleagues (April 22, p 889) suggest that horizontal transmission of hepatitis B virus (HBV) may occur in pre-school day-care centres. The following case-report could support this view.

A previously healthy 11-year-old boy was brought to the paediatric ward showing signs of contact with eye-shadow on his lips and tongue. On examination the only striking finding was mild hepatosplenomegaly. However, laboratory tests revealed raised levels of aspartate (AST 912 IU/l) and alanine (AST 1284 IU/l) aminotransferase. These results were confirmed 2 days later. Alkaline phosphatase (1028 IU/l), y-glutamyltransferase (76 IU/l), and lactate dehydrogenase (445 IU/l) activities were also increased. Total bilirubin was 0.03 mg/dl.

Tests for HBV serum markers pointed to active HBV infection (HBsAg, HBeAg, and HBV-DNA all positive). Viral culture