

anovulating cycles and consequent unopposed oestrogen effect. The population today is thus different, enjoying less continuous progestational influence.

The combined oral contraceptive may be an artificial way of supplying progesterone to those women who, owing to anovulation or obesity and ectopic production of oestrogen, do not produce their own ovarian progesterone. While it would be ridiculous to suggest treating 99 985 normal women for the 15 who develop endometrial carcinoma,¹ prophylactic treatment in a high-risk group may one day prove more feasible.

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¹ Office of Population Censuses and Surveys. *Cancer statistics 1972-73*. London: HMSO, 1979.

Temples, tubes, and plastic bags

SIR,—I was intrigued by Dr George Dunea's comments (29 May, p 1622) on the mnemonic for the differential diagnosis of coma. I seem to remember it slightly differently as "AEIOUDDD." Although I am not sure I am correct in my memory of what the vowel sounds stand for, I do remember rather clearly the drastic ending in the three Ds of "drugs, diabetes, and death." For us A stood for apoplexy, not alcoholism; E for epilepsy; I for insulin, a hypoglycaemic coma; O I seem to remember as standing for opium as an indicator of drugs in general but this would seem superfluous if my memory of D for drugs is correct, and occlusion would fit very well; U of course stood for uraemia, and Y was not included in the mnemonic we used in Tyne-side in the '30s. Perhaps your readers have other versions of the mnemonic, perhaps even including what must surely be the commonest cause of coma—trauma such as being hit by a motor car?

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Serum lipids during the menstrual cycle

SIR,—We write to re-enforce the conclusion reached by Dr P N M Demacker and colleagues (24 April, p 1213) that the time of blood sampling during the menstrual cycle is critically important in interpreting changes in serum lipids and also to take them slightly to task for not being even more precise.

We studied the cyclical changes in plasma lipids 30 years ago¹ and, by taking twice weekly samples over five weeks in 12 young healthy women and by identifying ovulation by a rise in oral temperature by one degree, related changes in serum lipids to the time of ovulation and to the preovulatory and postovulatory phases. Serum cholesterol concentrations were 15% lower over the 72 hours represented by ovulation compared with the preovulatory and postovulatory weeks. Apart from providing the first report of serial changes in serum lipids during the menstrual cycle, our findings indicated very clearly how transitory is the fall in serum cholesterol at ovulation. It is essential to relate the timing of blood samples to the day of ovulation of each individual.

Dr Demacker and colleagues report measure-

ments of total serum cholesterol and high-density lipoprotein cholesterol in two groups of women. Among eight women using an oral contraceptive, blood samples were taken twice weekly in six and once weekly in two. Among 10 women not using an oral contraceptive, blood samples were taken twice weekly in seven and once weekly in three. The results are presented as means with arbitrary division of the cycle in four phases comprising 2-8, 9-15, 15-22, and 23-28 days, but no attention has been paid either to the possibility of differences in the time of ovulation between the groups or to the influence of variation of length of the cycle of those not on oral contraceptives. The authors are unwise to conclude, without relating sampling time to ovulation, that fluctuations in serum lipids are greater in women taking oral contraceptives than those not doing so.

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¹ Oliver MF, Boyd GS. *Clin Sci* 1953;12:217-22.

Smoking, coffee, and cancer of the pancreas

SIR,—The recent review by Professor Melvin A Bernarde and Professor William Weiss (6 February, p 400) concluded that the reported¹ association between pancreatic cancer and coffee consumption is not one of cause and effect but rather an association confounded by other factors such as cigarette smoking and selected occupational exposures. This prompted us to review data from a recently completed case-control study which was part of an attempt to assess the possible carcinogenic effects of asbestos in drinking water.² In this study all patients with cancers of selected sites (including pancreas) diagnosed from November 1977 to December 1980 were identified through a population-based cancer registry which is part of the Surveillance, Epidemiology and End Results Program (SEER) of the National Cancer Institute. Eligible cases were aged 40-79 years at diagnosis and resided in selected low-migration census tracts north of Seattle. Eligible controls were 40-79 years of age at interview and were randomly selected from the same population in which the cases arose.

A total of 22 cases of pancreatic cancer were identified. Information was obtained direct from two living patients and from next of kin for 20 deceased patients. Using the method of Mantel and Haenszel³ to adjust for age (in decades), sex, and coffee drinking (drinkers *v* non-drinkers), analysis of these 22 cases and 485 population controls showed a significantly increased risk for smokers *v* non-smokers (estimate of relative risk 6.4; 95% confidence interval of 1.6 to 25.1). Using Mantel's extended technique,⁴ and adjusting for the same three factors, we found a significant ($p=0.01$) dose-response relationship for cigarette smoking (see table). After adjusting for age, sex, and cigarette smoking, we found no excess risk for those who consumed coffee relative to those who did not (estimate of relative risk 1.0; 95% confidence interval of 0.2 to 4.5).

Although these findings are based on a small number of cases, they are of interest for

Risk of pancreatic cancer by number of cigarettes smoked per day

| Cigarettes/day | Risk estimate | 95% confidence interval | No of patients | No of controls |
|----------------|---------------|-------------------------|----------------|----------------|
| 0 | 1.0 | | 2 | 184 |
| 1-15 | 4.7 | 1.1-21.5 | 5 | 102 |
| 16-35 | 6.8 | 1.3-34.7 | 11 | 159 |
| ≥36 | 19.2 | 1.1-345.7 | 4 | 40 |

χ^2 for dose response: $p=0.01$.

several reasons. Firstly, we found a significantly increased risk of pancreatic cancer due to cigarette smoking while controlling for coffee consumption. In fact, our estimate of this risk is higher than those previously reported. Secondly, while controlling for cigarette smoking, we found no excess risk of pancreatic cancer due to coffee consumption, although the 95% confidence interval is wide enough to include those risks reported by MacMahon.¹ We feel that our results support the conclusion of Bernarde and Weiss and we hope this communication will provide additional impetus to their suggestion that additional case-control studies be carried out.

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¹ MacMahon B, Yen S, Trichopoulos D, Warren K, Nardi G. *N Engl J Med* 1981;304:630-3.

² Polissar L, Severson RK, Boatman ES, Thomas DB. *Am J Epidemiol* (in press).

³ Mantel N, Haenszel W. *J Natl Cancer Inst* 1959;22:719-48.

⁴ Mantel N. *Journal of the American Statistical Society* 1963;58:690-700.

Communicable disease associated with milk and dairy products

SIR,—I have read the review of Dr N S Galbraith and others (12 June, p 1761) on this subject with mixed feelings. It is reassuring to learn that—apart from an occasional costly slip—pasteurisation provides near-perfect protection from milk-related communicable disease. In the last 20 years covered by the review only two outbreaks associated with pasteurised milk have been reported, due either to imperfect heat treatment or to the transfer of the treated milk to contaminated containers. In a country where the provision of our daily pinta involves transporting immense quantities of milk, it cannot be reasonably expected that errors would never be committed, and two outbreaks in 20 years do not seem a bad record. The fact that one of these resulted in 3500 cases of campylobacter infection merely calls attention to the costliness of errors.

The lamentable fact brought to light by the review is that untreated milk (thought to be about 3% of the total production in this country) is responsible for something like 25% of all cases of milk-borne infection and 100% of the deaths from this cause. Untreated milk is likely to be consumed mainly by farmers and their families, who ought to have learned their lesson by now. If they have not they should be obliged to pasteurise milk by legislation, no matter how convinced they are that Tulip's milk needs no treatment.

However, the truly dark side of milk is not its known connection with communicable disease but its suspected connection with non-communicable ones, notably coronary disease. To put the matter in perspective, the review