Missed pill conception: fact or fiction?

Sir,—Following the correspondence (13 July, p 136) on the paper by Mr B G Molloy and others (18 May, p 1474) we would like to express a cautionary note. We would agree with the points expressed about ovarian folliculogenesis, which occurs to a similar extent in the first seven days of spontaneous cycles as in the seven pill free days of combined oral contraceptive cycles. Some women seem less susceptible to gonadotrophin suppression than others during their pill taking days. These points were made some considerable time ago by endocrine assessment.1 More recently ultrasonographic evidence for this has come from Mr Molloy and others and Van der Vaage et al (personal communication) and from our own results so far. It remains also to establish what potential for ovulation these ultrasonographically demonstrated ovarian cysts have. There are considerable difficulties in the design of research protocols to show this.

However, the suppression of gonadotrophin induced ovarian folliculogenesis is not the only mode of action of the combined oral contraceptive pill. Ancillary contraceptive effect is provided by impermeable cervical mucus, which inhibits sperm transport, and by rendering the endometrium unfavourable for implantation. Hence, follicular development cannot be the only factor implicated in the mechanism of pill failure and any study of the latter must ideally incorporate concurrent endocrine variables, ultrasonographic measurements, and assessments of cervical mucus. Recommendations to women who inadvertently miss pills must inevitably, for the time being at least, be severely empirical. However, within the constraints of the data available2 the following advice should be given. If the omission of a pill served to extend the pill free period and hence the time available for folliculogenesis and follicular growth, the next pill should be swallowed without break at all. Arbitrary rules that the prolonged use of barrier contraception in the women who occasionally omit their pills have a salutary effect on follicular development, their placing during the time of omission and until the progesterone effect on the cervical mucus has become manifest. From our published data and further studies in progress the current barrier effect persists even with one or two days of pill omission. The time taken for the development of these changes during a course of pills needs to be firmly established.

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4 Langer SA, Donofrio E. Hormonal consequences of missing pills during the first two or three consecutive artificial cycles. Contraception 1984; 30: 167-8.

Selective consumption of large platelets during massive bleeding

Sir,—Dr C B Thompson reported that the thrombocytopenia after massive trauma and blood loss is associated with a reduction in mean platelet volume (13 July, p 95). He attributed this reduction to the selective consumption of the larger more haemonarchically effective platelets from the tail of the platelet volume distribution. In addition he has implied that a preferred consumption of small platelets, proposed earlier,4 is unlikely after acute myocardial infarction. This latter statement echoes our own conclusions.5 Dr Thompson suggests therefore that the increased mean platelet volume after acute myocardial infarction arises from the prodduction of larger platelets, which supports our previous observations that large platelets arise from large megakaryocytes after acute myocardial infarction.6 Similarly, larger than normal megakaryocytes have been observed in the tail of the platelet distribution immediately after (within three hours) sudden cardiac death, suggesting that both megakaryocytes and their progeny are larger than normal at the time of acute myocardial infarction and sudden cardiac death and are not necessarily secondary to these events. Polymorphonuclear leucocytes provide a link between the large platelets and megakaryocytes.

This hypothesis raises a further question. Why should thrombocytopenia be observed before acute myocardial infarction in sudden cardiac death? Possible answers that occur to us are that (a) some people are genetically predisposed to large megakaryocytes and as a consequence are at increased risk of acute myocardial infarction; (b) the large megakaryocytes are transformed cells; (c) megakaryocytes may be larger than normal in response to increased platelet consumption associated with the development of atheromatous coronary disease; and (d) the megakaryocytes increase in size in response to some environmental factor. In support of (c) and (d) we showed recently that chronic hypoxia, experimentally induced by a high cholesterol diet, was associated with an increase in megakaryocyte size and changes in platelet production.7

SMOKING, SUGAR, AND INFLAMMATORY BOWEL DISEASE

Sir,—In their paper on smoking, sugar, and inflammatory bowel disease Dr J R Thorson and others (15 June, p 1786) emphasise again the recently reported relation between smoking and inflammatory bowel disease.8 The conclusion, however, that smoking may cause some protection against ulcerative colitis may still be premature and needs additional evidence. We would like to report on the smoking habits of 93 patients with ulcerative colitis. The control group consisted of 177 consecutive patients matched for age and sex from an orthopaedic clinic. Seventy one (76%) of the 98 patients with ulcerative colitis never smoked compared with 112 (58%) of the control group (p<0.05). Also significant was the difference among smokers: 9% (95%) with ulcerative colitis compared with 39 (22%) in the control group (p<0.05) smoked between a half and two packs of cigarettes daily.

Surprisingly, in the group of ex-smokers (those who stopped smoking at least one year before the onset of the disease) we found a lower morbidity than in the patients who never smoked. Does, therefore, smoking in the past confer some protection against the development of ulcerative colitis?

Is there any relation between smoking and the evolution of the disease? Apparently not. In our series 17 (7%) of 146 patients with total colitis were non-smokers compared with 40 (76%) of 52 who had proctitis or left sided colitis. Like Dr Thorson and others, we found smoking to be more common among our 10 patients with Crohn's disease than in the control group.

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Effects of aerobic exercise on depression

Sir,—I was interested to read the paper by Dr Egl J Martinson and others (13 July, p 109). There has been no evaluation or experience of such an approach in this country, although there have been several recent studies in America1 and some essays by psychiatrists and psychologists who use exercise as a form of psychotherapy;2 in this, there is even an organisation called Running Psychologists. The numbers in the authors' study, as in previous trials on exercise in depression, are remarkably small. There is no mention of power calculations to determine the number of patients in the trial. Depressed patients have a large number of variables that may affect outcome, and future trials must be large enough to overcome these potential biases between groups. The statistical analysis was not performed "by intention to treat" but by analysis of complete cases. There were six patients (four in the exercise group and two controls) who were not included in the analysis and the former may represent patients who are the most depressed and least motivated to comply with an exercise regimen.

The authors state, "for patients in the training group with a small increase in maximum oxygen uptake (<15%) the antidepressive effect was similar to that of the control group." These patients may, however, have less depressed and retarded subjects who would be less motivated to perform on a bicycle ergometer. The authors readily admit that there may be other non-specific factors to account for the antidepressive effect.

I hope that the paper stimulates further interest in Britain. A large scale randomised trial is required that incorporates an aerobic exercise group (30-60% of maximum oxygen uptake) and a "low exercise" group who would not improve their physical fitness as assessed by the maximum oxygen uptake. This should control for the non-specific benefit(s) such as the sense of achievement and enthusiasm of the coach, the group participation, and the sense of self mastery that is probably gained from an exercise programme.

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Editorial comment

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