

burdens on overworked junior medical staff and insults the GPs in the area of Oldchurch Hospital, who made appropriate referrals in 85% of cases.

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#### 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.<sup>1,2</sup> More recently ultrasonographic evidence for this has come from Mr Molloy and others and Van der Vange *et al* (personal communication) and from our own results so far. It remains also to establish what potential for ovulation these ultrasonically 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 impenetrable 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 largely empirical. However, within the constraints of the data available<sup>3,4</sup> the following advice should be given. If the omission of a pill served potentially to extend the pill free period and hence the time available for folliculogenesis and effective sperm transport the next pack of pills should be started without a break at all. Arbitrary rules for the prolonged use of barrier contraception in the women who occasionally omit their pills have little scientific foundation, their place being during the time of omission and until the progestogenic effect on the cervical mucus 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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- 1 Elstein M, Briston PG, Jenkins M, Kirk D, Miller H. Effect of low oestrogen oral contraceptive on urinary excretion of luteinizing hormone and ovarian steroids. *Br Med J* 1974; 11:3.
- 2 Morris SE, Groom GV, Cameron ED, Buckingham MS, Everitt JM, Elstein M. Studies on low-dose contraceptives: plasma hormone changes in relation to deliberate pill (Microgynon 30) omission. *Contraception* 1969;20:61.
- 3 Nuttall ID, Elstein M, McCafferty E, Seth J, Cameron ED. The effect of ethinyl estradiol 20 mcg and Levonorgestrel 250 mcg on the pituitary-ovarian function during normal tablet taking and when tablets are missed. *Contraception* 1982;26:121-35.
- 4 Landgren B, Diezfalluy E. Hormonal consequences of missing the pill during the first two or three consecutive artificial cycles. *Contraception* 1984;29:437-46.

#### Smoking, sugar, and inflammatory bowel disease

SIR,—In their paper on smoking, sugar, and inflammatory bowel disease Dr J R Thornton and others (15 June, p 1786) emphasise again the recently reported relation between smoking and inflammatory bowel disease.<sup>1,2</sup> The conclusion, however, that smoking may confer some protection against ulcerative colitis may still be premature and needs additional evidence.

We would like to report on the smoking habits of 93 outpatients 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 93 patients with ulcerative colitis never smoked compared with 112 (63%) of the control group ( $p < 0.05$ ). Also significant was the difference among smokers; nine (9.6%) patients 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 extension of the disease? Apparently not. In our series 11 (78%) of 14 patients with total colitis were non-smokers compared with 60 (76%) of 79 who had proctitis or left sided colitis.

Like Dr Thornton and others, we found smoking to be more common among our 10 patients with Crohn's disease than in the control group.

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, just represent the more 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 (50-80% of maximum oxygen uptake) and a "low exercise" group who would not improve their physical fitness as measured by the maximum oxygen uptake. This should control for the non-specific benefits such as the attention 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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- 1 Simons AD, McGowan CR, Epstein LH, Kupfer DJ. Exercise as a treatment for depression: an update. *Clinical Psychology Review* (in press).
- 2 Sachs ML, Buffone WL, eds. *Running as therapy. An integrated approach*. Lincoln: University of Nebraska Press, 1984.

#### 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 haemostatically effective platelets from the tail of the platelet volume distribution. As a consequence he has implied that a preferential consumption of small platelets, proposed earlier,<sup>1,2</sup> is unlikely after acute myocardial infarction. This latter statement echoes our own conclusions.<sup>3,4</sup> Dr Thompson suggests therefore that the increased mean platelet volume after acute myocardial infarction arises from the production of larger platelets, which supports our previous observations that large platelets arise from large megakaryocytes after acute myocardial infarction.<sup>5</sup> Similarly, larger than normal megakaryocytes have been observed immediately after (within three hours) sudden cardiac death,<sup>6</sup> 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. Pulmonary platelet production<sup>7</sup> provides a link between the large platelets and megakaryocytes.

This hypothesis raises a further question. Why should thrombopoiesis be altered before acute myocardial infarction or 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 atherosclerosis; and (d) the megakaryocytes increase in size in response to some environmental factor. In support of (c) and (d) we showed recently that atherosclerosis, experimentally induced by a high cholesterol diet, was associated with an increase in megakaryocyte size and changes in platelet production.<sup>7</sup>

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- 1 Harries AD, David A, Rhodes J. Non-smoking: a feature of ulcerative colitis. *Br Med J* 1982;284:706.
- 2 Jick H, Walker AM. Cigarette smoking and ulcerative colitis. *N Engl J Med* 1983;308:261.
- 3 Somerville KW, Logan RFA, Edmond M, et al. Smoking and Crohn's disease. *Br Med J* 1984;289:954.

#### Effects of aerobic exercise on depression

SIR,—I was interested to read the paper by Dr Egil W Martinsen 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 America<sup>1</sup> and some essays by psychiatrists and psychologists who use running as a form of psychotherapy<sup>2</sup>; there is even an organisation called Running Psychologists.

The numbers in the authors' study, as in previous trials on exercise in depression, are regrettably 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 compliers. 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