the Chinese." But despite the low local background risk table I of their report supports my case: a significant 10.5% of leg scans were positive after major surgery for benign conditions in those taking the pill (excluding the minilap sterilisations), not 4.6% as quoted. Among those not taking the pill there was not a single postoperative positive ^{125}I fibrinogen scan for deep vein thrombosis in that study or in the London study, which showed a 20% rate in those taking the pill. Sagar *et al* concluded, "Women on oral contraceptives constitute a high risk group for postoperative thromboembolism."¹¹

Mr Sue-Ling and Professor Hughes rightly emphasise the other side of the risk-benefit equation—unwanted pregnancy. But given a United Kingdom maternal mortality of less than 1 in 10 000¹² it is far from obvious that more women would die. Moreover, the choice implied is not correct: it is not "the pill" or "unwanted pregnancy." There are other effective methods, including injectable contraceptives, such as medroxyprogesterone.¹ At the Margaret Pyke Centre we now routinely offer this (with counselling). One or more injections each lasting three months will cover the time on any waiting list. The oral contraceptive may be resumed two or more weeks after surgery without regard to the time of the last injection. Progestogen only pills also do not increase the risk of deep vein thrombosis and pulmonary embolism and have a failure rate above age 35 of less than 1 per 100 woman years.¹³

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SIR,—We agree with Mr H Sue-Ling and Professor L E Hughes (13 February, p 447) that epidemiological studies showing an association between the combined oral contraceptive and venous thromboembolism can be criticised both for their methods and because the diagnosis of thromboembolism was made clinically.¹ Case-control and cohort studies, however, have almost uniformly found a positive association between the combined oral contraceptive pill and idiopathic venous thromboembolism. Furthermore, morbidity due to venous thromboembolism fell after the introduction of low dose oestrogen pills and the concomitant reduction in the use of higher dose pills.²

Venous thrombosis is the result of blood coagulation and fibrin deposition in the presence of venous stasis. The incidence of spontaneous and postoperative thromboembolism is unknown. One study has shown that 20% of women taking the combined pill developed a deep venous thrombosis, diagnosed by ^{125}I fibrinogen scans, after surgery.³

The new combined pills containing 30 µg ethinylloestradiol together with the latest "third generation" progestogens (desogestrel or gestodene) alter the coagulation system, although to a lesser extent than older, higher dose formulations.⁴ We have shown recently that triphasic combined oral contraceptives containing ethinylloestradiol (mean dose 32.4 µg) in combination with either levonorgestrel (mean dose 92.4 µg) or gestodene (mean dose 78 µg) induced prothrombotic changes which were apparent after the first treatment cycle and were consistent over the six cycle study period. Both these preparations induced increases in biological activities of procoagulant factors VII, X, XII, and fibrinogen and decreased activity of antithrombin III compared with pretreatment levels ($p < 0.05$ to $p < 0.001$). Furthermore, protein C activity remained unchanged. It is well documented that decreased antithrombin III or protein C activity is associated with thromboembolism. Our findings indicate that the procoagulant factor increases induced by oral contraceptives are not balanced by increased biological levels of the two most important coagulation inhibitors—antithrombin III and protein C. The extent to which these changes are balanced by changes in the fibrinolytic system is unknown.

Venous thromboembolism is life threatening, causes long term morbidity, and has serious implications for future pregnancies. When major surgery is planned the combined oral contraceptive pill should be stopped four to six weeks preoperatively and an alternative method of contraception provided. This will enable the changes in the coagulation system to revert to normal and thereby not add to the risks of thromboembolism already present. In view of the morbidity and mortality associated with thromboembolism, we recommend prophylaxis with subcutaneous heparin when major surgery is unavoidable while a woman is taking the combined oral contraceptive pill. Surgery such as laparoscopy, dental extraction, and tonsillectomy, however, where the woman is mobile immediately, does not necessitate any alteration in contraceptive practice.

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SIR,—We would like to confirm the comments of Mr H Sue-Ling and Professor L E Hughes on the risk of pregnancy caused by the advice to stop oral contraceptives before surgery. We have a practice of 14 000 patients and in the past year two 19 year old unmarried women have become pregnant after being told to stop the contraceptive pill before surgery. The first underwent a nephrectomy and the other shaving of an exostosis of the clavicle.

They both conceived despite being advised to use other contraceptives until they had restarted the pill.

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Personal computers in the Third World

SIR,—Our experience of using a personal computer in administration, teaching, and research in a university teaching department in the Third World is similar to that of Drs I H Wilson and D A K Watters (23 January, p 255). We too have used a BBC model B for three years, and it has broken down only once. This reliability may be due to the extra protection of a spike suppressor plug. A printer that allows single sheet printing saves us buying expensive fanfold computer paper, and a printer ribbon reinking machine (Computer Friends, USA) makes the cost of a ribbon negligible. Surprisingly, we find it cheaper, and sometimes quicker, to order equipment from British retailers.

We put our machine to many uses. A spreadsheet for examination marks has eliminated tedious calculation of totals and averages. Students use a self teaching program developed by the University of Leeds which we have modified slightly to help those with poor English. It is very popular as students prefer to make silly mistakes with an impersonal computer rather than in a tutorial. A program for marking multiple choice question papers is very useful. It used to be almost impossible to prepare a correctly typed multiple choice question paper, but now it is made "word perfect" on the word processor and the stencil is cut on the dot matrix printer. The script of transparencies for overhead projection is fed into the word processor, printed in enlarged type with a special chip (PMS Multifont), and then photocopied on to the transparency. The transparency can be wiped clean and reused while the scripts are stored on the disk. We use a large capacity database (System Delta) for our drug audits. The students themselves enter the data, a useful first step in becoming computer literate. Calculation of pharmacokinetic variables is done using specially written software.¹

We have had no formal training but have found a user group (BEEBUG) and its magazine very helpful. The biggest barriers to wider acceptance of computers in medicine in Sri Lanka appear to be "technophobia" and the misconception that using computers means learning computer programming.

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Carbon monoxide poisoning

SIR,—Drs T Meredith and A Vale (9 January, p 77) emphasise the importance of treatment with hyperbaric oxygen in the prevention of serious neuropsychiatric complications of carbon monoxide poisoning. This treatment is itself dangerous as reactive oxygen metabolites worsen the tissue damage of anoxia on subsequent reoxygenation. An increased rate of auto-oxidation, lipid peroxidation, and formation of superoxide and hydrogen peroxide mitochondria have been shown

to follow treatment with hyperbaric oxygen.¹ A reperfusion injury mediated by these metabolites is thought to cause the reported side effects.

The delayed neurological complications of carbon monoxide poisoning may in fact be due to secondary oxidative damage which occurs during the resuscitation of patients with hyperbaric oxygen or high concentrations of inhaled oxygen.² Pretreatment with α tocopherol to protect against the effects of toxic oxygen metabolites has been shown to reduce the incidence of convulsions.² The role of xanthine oxidase in the mediation of anoxic reperfusion damage has led to the use of the xanthine oxidase inhibitor allopurinol in its prevention. Allopurinol may be a simple and effective treatment in the prevention of severe neuropsychiatric complications of carbon monoxide poisoning in combination with hyperbaric oxygen or with high concentrations of inspired oxygen at normal pressures.³

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AUTHORS' REPLY.—Dr Howard emphasises the potential hazards of treatment with hyperbaric oxygen and suggests that delayed neuropsychiatric sequelae after carbon monoxide poisoning may be due to oxygen toxicity incurred as a result of treatment. This is difficult to accept because these complications occur in the absence of oxygen treatment¹ and hyperbaric oxygen prevents their occurrence when used prophylactically and abolishes those that are present even when used up to 21 days after exposure to carbon monoxide.² Indeed, Dr Howard and colleagues recently stated that "the incidence of neuropsychiatric complications in carbon monoxide intoxication may be reduced by hyperbaric oxygen."³

Dr Howard suggests that xanthine oxidase may be involved in the development of neurological damage because in animals allopurinol and a sulphhydryl based free radical scavenger have been shown to ameliorate oxidative damage during hypoxic reperfusion injury.^{4,5} Dr Howard and colleagues have recently reported a case in which there was an apparent temporal relation between recovery from coma due to carbon monoxide toxicity and the use of allopurinol and N-acetylcysteine.³ If the proposed mechanism of toxicity is correct the same treatment should be effective in any form of postanoxic brain damage and undoubtedly more information is needed about this. However, we cannot recommend the use of allopurinol either alone or in conjunction with N-acetylcysteine for the treatment of carbon monoxide poisoning as a result of experience in one patient since full neurological recovery may occur after even prolonged coma due to carbon monoxide exposure.⁶

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SIR.—In their leading article on carbon monoxide poisoning (9 January, p 78) Drs Tim Meredith and Allister Vale underestimate the frequency of hospital admission with this diagnosis by failing to take into account victims of smoke inhalation.

The Hospital In-Patient Enquiry estimate of 475 admissions to and 10 deaths in hospital in 1985 due to carbon monoxide poisoning is misleading due to the nature of these statistics. The inquiry classifies cases under only their primary diagnosis and thus fire victims suffering concomitant carbon monoxide poisoning are often classified as suffering smoke inhalation or burns and not carbon monoxide poisoning. Fire victims who die from carbon monoxide poisoning will be correctly classified at necropsy since the unnatural mode of death requires a postmortem examination.

About half of early fire fatalities have lethal carboxyhaemoglobin concentrations,¹ while Clarke found that all admissions to hospital with major smoke inhalation had raised carboxyhaemoglobin concentrations.² The Hospital In-Patient Enquiry gives an estimate of 650 discharges and deaths in English hospitals for 1985 with a primary diagnosis of smoke inhalation, and 76 were recorded in Wales. While not all of these fire victims would require aggressive treatment for carbon monoxide poisoning, the degree of carbon monoxide poisoning, as judged by the carboxyhaemoglobin value on admission, has been shown to be an independent predictor of mortality in fire victims once age and percentage burns have been taken into account.³

The major adverse effects of smoke inhalation are often delayed for some hours after exposure⁴ and it is tempting to speculate how treatment for concomitant carbon monoxide poisoning with hyperbaric oxygen, as suggested in your leading article, would affect the prognosis. Indeed, there are many reports supporting this form of treatment but sadly these are all from abroad.⁵⁻⁸

Despite the recent plea by Dr J K Anand and others for independent studies in Britain to assess the cost effectiveness of hyperbaric treatment in carbon monoxide poisoning (6 February, p 432), it is noteworthy that to treat a patient with an intravenous infusion in situ or on ventilatory support requires a chamber capable of accommodating an attendant. No such NHS facility exists south of Newcastle upon Tyne.

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SIR.—The leading article by Drs Tim Meredith and Allister Vale (9 January, p 79) highlighted the mortality and morbidity associated with carbon monoxide poisoning.

In an attempt to identify biological features associated with depressive illness we have been carrying out necropsy studies on brain tissue from suicide victims with a history of depression. Five of the suicide victims died by carbon monoxide poisoning as a result of intentionally inhaling vehicle exhaust fumes (blood carboxyhaemoglobin saturations of 50-80% measured at necropsy). Activity of glutamic acid decarboxylase, the enzyme which catalyses the synthesis of γ -aminobutyric acid (GABA, the major inhibitory neurotransmitter in the mammalian central nervous system), was about 50% lower in the frontal and temporal cortex of these subjects than in that of 16 suicide victims dying by other methods and 20 subjects dying suddenly from accidents or natural causes. The last groups did not differ significantly in glutamic acid decarboxylase activity from each other. A further subject who died by accidental carbon monoxide poisoning as a result of a faulty bathroom water heater also had much reduced glutamic acid decarboxylase activity.

The mechanism of the loss of glutamic acid decarboxylase activity is unclear but was not related to the time between death and tissue storage or to the duration of tissue storage. Terminal illness associated with hypoxia—for example, bronchopneumonia—has been shown to lower glutamic acid decarboxylase activity measured after death.^{1,2} It is uncertain, however, if the brief but profound hypoxia associated with acute carbon monoxide poisoning would produce the same effects. A direct effect of carbon monoxide on glutamic acid decarboxylase activity is a possibility, although we have no direct evidence for this.

Although the present results relate to subjects who died by acute carbon monoxide poisoning, they suggest that sublethal poisoning may result in some loss of glutamic acid decarboxylase activity and hence reduced ability to synthesise γ -aminobutyric acid. Since abnormalities in neurotransmission mediated by γ -aminobutyric acid have been implicated in a number of neurological and psychiatric disorders, reduced synthesis of γ -aminobutyric acid might contribute to the delayed neurological and psychiatric sequelae associated with sublethal carbon monoxide poisoning.

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Newly registered elderly patients

SIR.—The paper by Drs Helen Graham and Brian Livesley on the delay in transferring the records of newly registered elderly patients (30 January, p 340) tells a tale that must be familiar to all general practitioners. It must ring particularly true to any