the pathogenic insult.² Tissue death has therefore occurred before thrombosis and cannot be accounted for by fibrin deposition as suggested by Dr. Bonnar and others.—I am, etc.,

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JOHN SOPHIAN.

REFERENCES

- ¹ Sheehan, H. L., and Davis, J. C., *British Medical Bulletin*, 1968, 24, 59.
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Oral Contraceptives and Thromboembolic Disease

SIR,—I was most interested in the possible potentiating effect of smoking on oral contraceptive drugs (30 August, p. 529). The fact that these drugs contain an oestrogen together with the catalytic ability of certain oestrogenic phenols¹ and the demonstration of a high concentration of phenols in the smoke of cigarettes,² brings to mind recent work on the action of phenols on blood coagulation.³ Certain phenols evolve (activate) factor XII, accelerate thrombin-fibrinogen interaction, retard clot retraction, and inhibit plasmin.

Although any or all of these phenomena may play a part in the pathogenesis of thrombosis, it is worth noting that retarded clot retraction is also produced by a high level of factor VIII,⁴ which is seen in patients taking oral contraceptive drugs. Failure of clot retraction would aggravate the consequences of a thrombus by preventing or delaying re-establishment of circulation, thus offering an explanation of the apparently disastrous effect of thrombi seen in women on oral contraceptives.—I am, etc.,

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REFERENCES

- ¹ William-Ashman, H. G., Cassman, M., and Klavins, M., *Nature*, 1959, 184, 427.
- ² Carruthers, W., and Johnstone, R. A. W., *Nature*, 1960, 185, 762.
- ³ Nour-Eldin, F., *Journal of Biomedical Materials Research*, 1968, 2, 23.
- ⁴ Nour-Eldin, F., *Blood Coagulation Simplified*, 1967, London, Butterworths.

SIR,—Drs. D. L. Crombie and K. W. Cross (13 September, p. 654) have compared the results of the investigations carried out by the Royal College of General Practitioners¹ and by ourselves,^{2,3} and, in particular, have drawn attention to the difference between the estimates of the relative risk of developing "thromboembolism" when using oral contraceptives that were obtained in the two studies (3.0 to 1 and 6.3 to 1 respectively). The comparison is not, in fact, justifiable, as the investigations were largely concerned with different disorders: the College's with the common condition, superficial thrombophlebitis, and our own with the much rarer conditions, deep vein thrombosis and pulmonary embolism.

It may be noted that the results of the College's study offer some support to the view that our data are not biased, contrary to what Drs. Crombie and Cross suggest. The College's study included only six women aged 15–39 years who were recorded as having deep vein thrombosis or pulmonary embolism when neither pregnant nor in the puerperium.⁴ Of these, three had used oral contraceptives and three had not, and two in

each category of use were admitted to hospital. Thus there is no evidence from these data (nor from the other relevant data that we examined) that a history of the use of oral contraceptives increases the likelihood of a woman being admitted to hospital when she suffers deep vein thrombosis or pulmonary embolism.—We are, etc.,

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RICHARD DOLL.

REFERENCES

- ¹ Royal College of General Practitioners, *Journal of the College of General Practitioners*, 1967, 13, 267.
- ² Vessey, M. P., and Doll, R., *British Medical Journal*, 1968, 2, 199.
- ³ Vessey, M. P., and Doll, R., *British Medical Journal*, 1969, 2, 651.
- ⁴ Crombie, D. L., personal communication, 1967.

Awareness during Anaesthesia

SIR,—I have followed this correspondence (30 August, p. 532, and 20 September, p. 716) with interest, as in 20 years of practice of anaesthesia I have never yet suffered the mortification of discovering that a patient, supposedly under general anaesthesia, was in fact awake; nor have I ever lost a baby at caesarean section where there had been an audible foetal heart beat before induction of anaesthesia. As a practical rather than an academic anaesthetist I would be grateful if I could be allowed to state my simple views on this subject.

The maintenance of unconsciousness in a patient anaesthetized by the nitrous oxide/oxygen relaxant technique depends on an adequate concentration of nitrous oxide supplemented by hyperventilation.

There is no justification or rational reason for administering a greater concentration of oxygen in the respired gases than that existing in the atmosphere, except in hyperbaric conditions.

If the technique includes "oxygen flushing" before delivery it should surprise no one if the patient wakes up.

Maintain a concentration of 75% nitrous oxide and awareness will not occur.—I am, etc.,

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Premedication for Hypotensive Anaesthesia

SIR,—Dr. P. J. Thompson (2 August, p. 300) states that a standard method of inducing hypotension failed when a droperidol/fentanyl mixture as in Thalamonal (1–2 ml. of droperidol 2.5 mg./ml., fentanyl 0.05 mg./ml.) was substituted as premedication. In fact his preoperatively normotensive patients became resistant to strenuous efforts to induce hypotension—namely, by increasing intermittent positive pressure ventilation from 10 to 15 l./min., and the halothane concentration from the 2–4% level previously found adequate up to 6%. He concludes that the systolic blood pressure could not be reduced below 90 mm. Hg despite all these measures.

Cardiovascular stability under anaesthesia with droperidol as a premedicant is widely reported. Prys-Roberts and Kelman¹ state, "The results of this study emphasize the

previous reports of cardio-vascular stability and relative lack of undesirable side effects." These findings have been supported by my clinical impression after five years' use of droperidol 10 mg. combined with either opioridine 1–2 mg. or fentanyl 0.05–0.1 mg. as standard premedication in adults, *except* those cases for induced hypotension. For these chlorpromazine is used to bring about a labile cardiovascular response. The compensatory tachycardia which occurs with the onset of hypotension can cause troublesome oozing in the operation field. In such resistant cases, improvement can be achieved by the use of an adrenergic beta blocking agent such as propranolol, to reduce the pulse rate.

I would also question the rationale of Dr. Thompson's use of 0.6 mg. atropine at induction of anaesthesia in the Thalamonal group. This will only accentuate the tachycardia in cases where hypotension is to be induced. My experience is that virtually the only contraindication to the use of a droperidol premedication is "induced hypotension."—I am, etc.,

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REFERENCE

- ¹ Prys-Roberts, C., and Kelman, G. R., *British Journal of Anaesthesia*, 1967, 39, 134.

Cost of Anaesthetic Agents

SIR,—Dr. C. Langton Hewer (16 August, p. 415) rightly draws attention to the significance of the cost factor in assessing the relative merits of various kinds of drugs and treatment. He would probably agree, however, that cost becomes paramount only after it has been satisfactorily demonstrated that other factors, especially relating to patient safety, are equal. The extensive trials recently conducted by Dr. P. L. Jones and others in which the relative merits of methoxyflurane, nitrous oxide, and trichloroethylene as analgesic agents for obstetrics were compared seem to show that these factors were roughly equal, and concluded that methoxyflurane was marginally the best analgesic (2 August, pp. 255–267).

On the other hand, it has been clearly demonstrated that a subatmospheric concentration of oxygen in the inhaled mixture constitutes a serious hazard to the foetus. Furthermore, there are strong indications that an oxygen-enriched mixture is beneficial, at least to the extent that the risk of intra-partum anoxia is reduced.¹

Entonox (made by the British Oxygen Company) is the only mixture of nitrous oxide/oxygen (50%/50%) premixed in one cylinder available in Britain, and the accuracy and consistency of the mixture is guaranteed, using dispensing equipment which is sufficiently simple and inexpensive for use by unsupervised midwives. The importance of this in marginal situations, such as might suddenly confront the midwife, must surely merit serious consideration before progressing to the simple question of comparative cost.—I am, etc.,

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REFERENCE

- ¹ World Health Organization Technical Reports Series, No. 300, p. 11.