

Oral Contraceptives and Thromboembolic Disease

SIR,—Dr. M. P. Vessey and Dr. Richard Doll (27 April, p. 199) presented data showing that thromboembolic patients were on the average heavier cigarette smokers than control patients, but discounted the difference as being statistically not quite significant. They further stated that their data provided no evidence that smoking could have accounted for the association between the use of oral contraceptives and the development of thromboembolism.

Their data do indicate an association between use of oral contraceptives and thromboembolism. By ignoring contraceptive use in their chi-square analysis of the statistical significance of the association of smoking and thromboembolism, Dr. Vessey and Dr. Doll may have overlooked a potentiating effect of cigarette smoking on any aetiological role of oral contraceptives relative to thromboembolism. Such potentiating effect is suggested when their data are retabulated to facilitate evaluation of possible separate or combined effects of smoking and oral contraceptives on thromboembolism. The data indicate a possible role of smoking in the pathogenesis of thromboembolism in combination with the use of oral contraceptives (Table 1).

TABLE I.—Relative Distribution of Thromboembolic and Control Patients by Use of Oral Contraceptives and Number of Cigarettes Smoked

Oral Contraceptives	Number Cigarettes Smoked per Day	Thromboembolic Patients (n = 58)	Control Patients (n = 116)	Ratio of Thromboembolic to Control Patients
Not used	0-14	43.1%	72.4%	0.6 to 1
Not used	15+	12.1%	19.0%	0.6 to 1
Used ..	0-14	20.7%	6.9%	3.0 to 1
Used ..	15+	24.1%	1.7%	14.2 to 1

Source of basic data: Vessey, M. P., and Doll, R. Investigation of Relation between Use of Oral Contraceptives and Thromboembolic Disease. *Brit. med. J.*, 1968, 2, 199.

Moreover, retabulation of the data indicates the lack of association between use of oral contraceptives and smoking in the control patients (Table II).

TABLE II.—Observed and Expected Distributions of Control Patients by Number of Cigarettes Smoked and Use of Oral Contraceptives

Number of Cigarettes Smoked	Oral Contraceptives			
	Not Used		Used	
	Observed	Expected	Observed	Expected
0-14	84	84.1*	8	7.9
15+	22	21.9	2	2.1

Source of basic data: same as Table 1.

$$*84.1 = \frac{(84 + 22)(84 + 8)}{(84 + 22 + 8 + 2)}$$

The U.S. Public Health Service has reported that cigarette smoking may cause an acceleration of the *in vitro* thrombus formation of human blood.^{1,2} Platelet adhesiveness, as measured by *in vitro* tests, also appears to be increased by cigarette smoking. The Public Health Service cites findings that platelet survival time is shortened, and that platelet turnover rate is increased in smokers. There is also an increased tendency for the platelets to adhere to the vascular endothelium.

Unless and until a potentiating effect of cigarette smoking on any aetiological role of oral contraceptives can be ruled out, our findings suggest that it would be prudent to consider heavy smoking as a contraindication to the prescription of oral contraceptives.—We are, etc.,

HARALD FREDERIKSEN.

Chief, Population and Program Analysis Division, Population Service.

R. T. RAVENHOLT.

Director, Population Service.

Department of State, Agency for International Development, Washington, D.C. U.S.A.

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- ¹ *The Health Consequences of Smoking. A Public Health Service Review, 1967, Public Health Services Publication No. 1696, Revised, 1968. Washington, D.C.*
- ² *Supplement to Public Health Service Publication No. 1696, 1968. Washington, D.C.*

Squatting in Heart Disease

SIR,—In your leading article (23 November, p. 470) you use the term squatting as synonymous with the knee-chest position. The genu-pectoral posture was described long before squatting was recognized in cyanotic congenital heart disease as characteristic of acute pericardial effusion. It was originally applied to the attitude of the Mohammedan's prayer described by Zehetmayer in 1845, later by Hirtz, and well portrayed by Blechmann.¹ However, it was more often applied to the posture adopted by children with pericardial effusion confined to bed in hospital; the child sits up, leaning forwards with the knees drawn up to the chest, and with the head and arms resting on the knees—as portrayed by Blechmann—and I have seen children asleep in this position, which is not identical with squatting, though the French term "accroupissement" (translated in the dictionary as squatting) is used for both. Squatting is usually practised by cyanotic children who are ambulant, and appears when they first start to walk. The genu-pectoral posture is encountered in children confined to bed with acute pericardial effusion, and they often fall asleep in this position.

Though Dr. Helen Taussig herself used both terms, the novelty of her discovery was the squatting posture in ambulant cyanotic children as a means of relieving respiratory distress provoked by exercise. I venture to suggest that the term genu-pectoral should be preserved for the posture encountered in pericardial effusion, and that the term squatting should be applied to the posture of children with cyanotic congenital heart disease in which Dr. Taussig first described it.—I am, etc.,

D. EVAN BEDFORD.

London W.1.

REFERENCE

- ¹ Blechmann, G., *Les Péricardites Aiguës*, 1922. Paris.

Damages against Doctors

SIR,—In Mr. G. H. Alabaster's letter (30 November, p. 576) he says that when he reads "from time to time reports on cases in which doctors have been ordered to pay heavy damages, despite good intention" he has been "led to wonder whether the best is

being made out of the defence in action for malpraxis . . ." either by individual doctors, ". . . or by the medical profession as a collective body."

However, in the *Lancet* as recently as 16 November a reviewer was writing: "Reading the annual reports of the medical defence organizations it is hard not to sympathize with some of the patients who incautiously try to sue their doctors. In short, one sometimes wonders guiltily whether the profession is too ably represented." Perhaps this oblique tribute to the defence societies will reassure Mr. Alabaster, even if his letter does not have any reciprocal effect on the *Lancet's* reviewer.

Mr. Alabaster also refers to "the tremendous burden of mind which a doctor must endure who is threatened with a legal penalty of possibly obliterative dimensions." Inevitably, a doctor accused of professional negligence is distressed, but if he is a member of a defence society he certainly need not feel threatened by an overwhelming legal penalty, for he is wholly indemnified against all costs and damages. The doctor defendant is often conscious of human ingratitude, but sometimes without any gross carelessness a patient suffers grievously by reason of human fallibility. Wisely, the law in civil claims does not distinguish between varying degrees of culpability, but awards damages to the plaintiff strictly related to any harm or injury suffered when it has been adjudged that the doctor or doctors have not exercised reasonable skill and care. It should not be necessary to remind doctors that standards in this respect are set by the profession itself, and judge or jury determine these matters on the basis of expert medical evidence tendered on behalf of defendant and plaintiff.

The foregoing paragraphs were written before Professor M. F. A. Woodruff's letter was published in the *B.M.J.* (7 December, p. 643), but what he says emphasizes how important it is that doctors should have an informed and balanced appreciation of their obligations to patients, colleagues, and the community. It is perhaps a pity that Professor Woodruff's hope has not been realized—namely, that his university might appoint a professor of forensic medicine, "who would devote a substantial part of his time and energy to developing joint research by doctors and lawyers" in this field. As yet not all medical faculties and teaching hospitals include in their forensic medicine courses lectures devoted specifically to the subject, but the Medical Protection Society has through its president over the past years let the deans of medical schools know that the Society itself is ever ready to provide suitable lecturers.—I am, etc.,

H. A. CONSTABLE,
Secretary,
Medical Protection Society

London W.1.

REFERENCE

- ¹ *Lancet*, 1968, 2, 1088.

Rickettsial Endocarditis

SIR,—The account of four cases of rickettsial endocarditis described in the Clinico-pathological Conference (5 October, p. 40) is of great interest and prompts me to record the following brief case history.

A 38-year-old schoolmaster working in Western Nigeria developed recurrent attacks

or fever which were treated as malaria in 1964. He then returned to England and lived in the Isle of Wight. When seen in October 1967 he stated that he had had two or three attacks of fever each year since he came home, and the doctor who referred him to the Hospital for Tropical Diseases stated that investigation for infective endocarditis had proved negative.

On examination he looked unwell, and showed finger-clubbing and palpable enlargement of the spleen. A long, rough systolic murmur appeared to arise at the aortic valve, and was accompanied by a soft diastolic murmur. It seemed probable that, despite negative blood cultures previously, the patient had in fact got infective endocarditis of a congenitally deformed aortic valve.

On admission to the Hospital for Tropical Diseases the patient showed a daily remittent pyrexia up to 101° F. (38.3° C.). Four further blood cultures grew no bacteria after three weeks' incubation, and brucella agglutinations were negative. The erythrocyte sedimentation rate was 31 mm. in one hour.

Treatment was initiated with intramuscular injections of methicillin 2 mega units six-hourly with probenecid 500 mg. q.d.s. This was continued for 26 days without influencing the pyrexia. Penicillin V 500 mg. t.d.s. was then given, and ampicillin 250 mg. four-hourly was added, probenecid being continued. After 14 days on this treatment the pyrexia was unaffected. At this stage the results of complement fixation test to *Coxiella burnetii* were received from the Public Health Laboratory Service at Colindale. This showed a positive titre to 1:640 to Phase I and 1:1,280 to Phase II of this rickettsia. Treatment was then changed to tetracycline 500 mg. q.d.s. and Albamycin (novobiocin calcium and sulphamethizole) 500 mg. q.d.s. The pyrexia subsided on the fifth day of this treatment and did not return. The treatment was maintained for 24 days, after which the tetracycline, 2 g. a day, was continued as an outpatient for the next six weeks. Two months after the date of the first test there was no change in the titres of *Coxiella burnetii* complement-fixation tests. One year later the patient wrote to me to say that he remained in good health, though his capacity for exertion was somewhat limited.

I feel it is justifiable to diagnose in this patient rickettsial endocarditis of the aortic valve, and, despite the reported tendency of this infection to recrudescence, I hope that he is cured.

I wish to acknowledge the assistance given me by Dr. Arthur Hollman and Dr. Joan Stokes, of University College Hospital, in the management of this patient.

—I am, etc.,

JOHN WALTERS.

Hospital for Tropical Diseases,
London N.W.1.

SIR,—This question was discussed at a Clinicopathological Conference (5 October, p. 40). Commenting on Case 2, Dr. Celia Oakley wondered if tetracycline had cured him, and suggested that he may have been the first patient cured of rickettsial endocarditis. I should like to report a similar earlier case.

In August 1963 a Scottish migrant, a cleaner at the Brisbane abattoir, presented with a swollen leg, the result of a venous thrombosis 10 weeks earlier. He could recollect no antecedent illness consistent with Q fever. Temperature of 38° C., clubbed fingers, aortic stenosis and incompetence, an E.S.R. of 82 mm. in one hour, and increased gammaglobulin pointed to subacute bacterial endocarditis, but blood cultures were sterile and treatment with penicillin and streptomycin for five weeks was ineffectual.

When positive agglutinations for Q fever were reported treatment was changed to rolitetracycline 275 mg. b.d. intravenously for five weeks. There was a prompt fall of temperature to normal, and the E.S.R. was 22 mm. in one hour on his discharge in January 1964. In March 1964 fever recurred and the E.S.R. rose to 62. Intravenous rolitetracycline was repeated, again with rapid improvement; the E.S.R. fell to 7. In July a third course of this treatment was given, and followed with 1 g. of tetracycline by mouth daily for four months. Later congestive heart failure and progressive renal insufficiency developed, leading to death in October 1966. Phase-I antibody titres were 1,024 in October 1963, 512 in March 1964, and 32 in April 1966. At necropsy the aortic valve edge was thick and rough, the junction of the right coronary and non-coronary cusps being fused; behind this area a false aneurysm 2 cm. deep extended upwards posterior to the aorta in the pericardial fat. Histology showed moderate thickening of the cusps, with foci of calcification, but no rickettsiae on Macchiavello stain, and guinea-pig inoculation was negative. The presence of Phase-I antibodies in this case indicated chronic Q fever, while the high titre suggested endocarditis, which was demonstrated at necropsy. It seems reasonable to conclude that he had rickettsial endocarditis, which was cured—at least in the microbiological sense.

Intravenous rolitetracycline may be the best available treatment for rickettsial endocarditis, but it should be followed by oral tetracycline for several months to lessen the possibility of relapse.—I am, etc.,

DEREK MEYERS.

Brisbane,
Queensland, Australia.

Wastage of Equipment

SIR,—I work in a group of small scattered hospitals serving a large mixed urban and rural area, and our instrument committee meets regularly to decide priorities for new and replacement medical equipment within a pathetically small annual budget of a few hundred pounds. Its problems are exacerbated by the number of small units, each of which must carry at least the bare necessities for emergency work.

Remembering my own days as a teaching hospital registrar, I know it is not uncommon for a senior registrar engaged in specialist work to leave behind him equipment unused by both his chiefs and his successors, and then seek to order the same equipment somewhere else on his appointment as consultant. Similarly a great deal of apparatus, obsolete by university standards, is far more modern than that currently in use in peripheral units, and in many cases even broken equipment could be cannibalized to repair similar models often rendered useless by the non-availability of spares from the makers.

Thus I am sure it should be possible to devise some scheme whereby, rather than doing without altogether, we could effectively buy or exchange sound second-hand equipment with other hospitals or groups. Since it would be very difficult to arrange a direct and comparable swap, a system of cataloguing equipment available would have to be devised and circulated with the price asked by the vendor group to each other instrument committee and by them to their divisions.

Each group would have an incentive to turn out its cupboards if, by so doing, it could actually obtain something it needed more.

A pilot study in one regional area run by, say, a retired or disabled doctor, with an ex-theatre sister and some secretarial help, would soon show if the scheme could be of value.

If it were deemed desirable to expand such a scheme on a national scale, it would seem likely that this is just the sort of process that could well be computerized, or even extended to include aid to underequipped units in developing countries.—I am, etc.,

E. B. LEWIS.

Hythe, Kent.

Rhesus-sensitization During Pregnancy

SIR,—The suggestion of Dr. J. C. Godel and others (23 November, p. 479) that anti-D γ -globulin be used prophylactically in the last trimester of pregnancy is interesting.

While it seems unlikely in the light of recent trials that Zipursky's extreme view (expressed in a personal communication to Godel *et al.* 23 November 1968) that "delivery appeared to play an insignificant part in the production of foetal maternal haemorrhages" is acceptable, nevertheless it would appear that the foetal red cells found during pregnancy by Zipursky *et al.*¹ are enough in some individuals to start the sensitization process. The attempt to eliminate this risk by passively immunizing mothers in the last trimester is given credence by Chown's² analysis of the Columbia-Presbyterian second Sing Sing experiment of Freda *et al.*³ which suggests that anti-D γ -globulin confers some protection against sensitivity when challenged with Rh(D)-positive cells for up to 42 or even 81 weeks.

When we consider the position in the woman carrying an Rh(D)-positive foetus the situation is very different. There is known to be a very efficient transfer of γ -G antibodies across the placenta in both directions. It has been found by DuPan *et al.*⁴ that the level of γ -globulin in the foetal plasma was 50% of that in the maternal plasma within 24 hours. This is an equilibrium situation, whereas in the risk pregnancy the Rh(D)-positive cells would be expected to remove the anti-D γ -globulin from the foetal plasma very quickly and no equilibrium would be approached, thus the maternal depletion of anti-D γ -globulin would be even faster.

Although Rhesus disease in pregnancy has caused several immunological surprises already it is unlikely that anti-D given in the third trimester of pregnancy will be useful except perhaps for the immediate cover of antenatal situations known to be a risk—for example, external cephalic version.⁵—I am, etc.,

J. W. CRAWFORD.

Department of Obstetrics
and Gynaecology,
University of Dundee.

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