arises with false calls from patients but rather the reverse in that severe chest pain lasting 20 minutes or longer is reported neither soon enough nor frequently enough.

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Allergic reaction to chlormethiazole

SIR,—I noted with interest the reports of allergic reactions to chlormethiazole (Heminevrin) by Dr A A Khan (6 November, p 1105) and more recently by Drs N A Halstead and J S Madden (25 December, p 1563). In both instances quoted the dose form referred to was the capsule, in which it is known that the colouring agent tartrazine is used to provide the characteristic yellow appearance.

Among reactions listed to tartrazine are generalised pruritus,¹ generalised urticaria,¹⁻⁴ oedema of the lips and tongue or uvula,¹ vascular purpura,² and severe asthmatic attacks.³ It is possible to speculate that these patients would not have reacted in the same way to the alternative uncoloured white tablet distributed by the same manufacturer.

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¹ Lockey, S D, *Annals of Allergy*, 1959, 17, 719.

² Creip, L H, *Journal of Allergy and Clinical Immunology*, 1971, 48, 7.

³ Juhlin, L, et al, *Journal of Allergy and Clinical Immunology*, 1972, 50, 92.

⁴ Michaelsson, G, and Juhlin, L, *British Journal of Dermatology*, 1973, 88, 525.

Antibodies to spermatozoa

SIR,—The discussion of the immunological sequelae of vasectomy in your leading article on this subject (2 October, p 774) requires comment.

While certain types of antibody to sperm are detected in normal children (not adults) with an incidence approaching 90%,¹ this need not obscure the importance of substantial increases in other types of antisperm antibody after vasectomy. The 86% incidence in children was attributable to two specific types of antibody detected by immunofluorescence and these types were found to cross-react with antigens of common micro-organisms.¹⁻² Presumably these antibodies resulted from exposure to infectious agents, not to sperm. In considering the effects of vasectomy comparisons should be made between the same types of antibody.

Data on the frequencies of specific types of antisperm antibody before and after vasectomy are now becoming available from several prospective studies. These studies are in agreement that (1) sperm-agglutinating antibodies occur in low titre in 2-5% of men before vasectomy and in higher titres in 55-75% of men within a year after vasectomy³⁻⁵; (2) sperm-immobilising antibodies occur in low titre in 1-2% of men before vasectomy and in higher titres in 30-60% of men within a year after surgery³⁻⁵; and (3) several types of antibody detected by immunofluorescence also increase in frequency after vasectomy, some from a very low prevasectomy incidence and others from a higher baseline.⁵⁻⁶ The immunoglobulin nature of all of these antibodies has been demonstrated.¹⁻⁶⁻⁷ Contrary to the suggestion in your article there is actually quite

good agreement among different laboratories when the incidences of specific types of antibody are compared.

You suggest that immune responses to sperm may result from inflammatory or atrophic changes in the testis after vasectomy. However, it seems more likely that such responses may result from small ruptures of the occluded epididymis or vas deferens and formation of sperm granulomas. This hypothesis is supported by data on internal pressures in the epididymis and testis⁸⁻⁹ and the occurrence of focal ruptures of the epididymis or vas¹⁰ in vasectomised animals and on the frequency of sperm granulomas in vasectomised men.¹¹

No clinical effects of antisperm autoantibodies have been demonstrated in vasectomised men, but Bigazzi¹² has documented the occurrence of immune complex disease of the testis and kidney in vasectomised rabbits with high antibody titres. The relevance of this finding to other species, including man, remains to be determined, as do other possible consequences of immune responses to vasectomy.

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¹ Tung, K S K, et al, *Clinical and Experimental Immunology*, 1976, 25, 73.

² Tung, K S K, *Clinical and Experimental Immunology*, 1976, 24, 292.

³ Mumford, D M, and Ansbacher, R, personal communication.

⁴ Bernstein, G S, personal communication.

⁵ Rose, N R, personal communication.

⁶ Tung, K S K, *Clinical and Experimental Immunology*, 1975, 20, 93.

⁷ Rose, N R, et al, *Clinical and Experimental Immunology*, 1976, 23, 175.

⁸ Johnson, A L, and Howards, S S, *American Journal of Physiology*, 1975, 228, 556.

⁹ Johnson, A L, and Howards, S S, *Biology of Reproduction*, 1976, 14, 371.

¹⁰ Bedford, J M, *Biology of Reproduction*, 1976, 14, 118.

¹¹ Schmidt, S S, and Morris, R R, *Fertility and Sterility*, 1973, 24, 941.

¹² Bigazzi, P E, et al, *Journal of Experimental Medicine*, 1976, 143, 382.

Effect of cigarette smoking on thromboembolism

SIR,—We read with much interest the paper by Drs P A Emerson and P Marks (1 January, p 18) on the prevention of thromboembolism after myocardial infarction. We were in particular interested in their observations on the lower incidence of deep vein thrombosis (DVT) after myocardial infarction in cigarette smokers. We now write to point out that, in a recent paper (16 October 1976, p 910) in which we gave an account of the preoperative prediction of postoperative DVT after gynaecological surgery, we found that 48% (50 of 104 patients) of those who did not develop postoperative DVT were cigarette smokers but only 25% (5 of 20 patients) of the DVT-positive patients were smokers. The "protective" effect of smoking in patients at risk to DVT clearly extends beyond those who suffer myocardial infarction and is a phenomenon worthy of further study. In their penultimate paragraph Drs Emerson and Marks suggest that "patients who enter a coronary care unit with myocardial infarction may be drawn from two populations. One group may be intrinsically more susceptible to both arterial and venous thrombosis so will suffer myocardial infarction whether they smoke or not; the other group do not have this susceptibility to thrombosis but suffer a myocardial infarction because they smoke."

In the light of our observations in patients undergoing gynaecological surgery and the previous report from Pollock¹ on a higher incidence of postoperative DVT in non-smokers some other explanation for the effect of cigarette smoking must be found.

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¹ Pollock, A V, *British Medical Journal*, 1974, 3, 522.

Multiple courses of ancrod (Arvin) therapy

SIR,—In an effort to reduce the incidence of chronic and recurrent thromboembolic disease we have treated several patients¹ with a new regimen² including ancrod (Arvin), oral fibrinolytics, and standard anticoagulants. One of these patients has had so far five courses of ancrod therapy without any anaphylactic reaction. The first 24 h of the ancrod therapy were covered, however, with six hourly injections of 100 mg hydrocortisone sodium succinate intramuscularly. The clinical results of the therapy were encouraging, antibody formation was negligible, and defibrination was always complete.

The patient, a 34-year-old woman, was admitted in February 1968 with left deep vein thrombosis and haemoptysis. She had taken oral contraceptives until 18 months previously. A diagnosis of pulmonary embolism was made and she was given intravenous heparin for one week followed by warfarin. As she deteriorated streptokinase was given one week later and she improved thereafter. Symptoms of thromboembolism recurred two days after her discharge and she was readmitted for a further course of heparin, despite which her clinical state became critical. Several expert opinions were sought and ligation of the inferior vena cava was considered. Then the account by Reid and Chan of ancrod appeared³ and therapy with this was given shortly afterwards. The improvement was soon apparent. The haemoptysis stopped within two days, as did the chest pain. The pain and swelling in the right leg improved during the following week and she was discharged on a maintenance dose of warfarin and Fearnley's regimen.⁴⁻⁵

In August 1968 she was readmitted with bilateral calf vein thrombosis and pulmonary embolism. A second course of ancrod was given and she improved promptly. She was discharged on warfarin and Fearnley's regimen, but anticoagulant control was poor as she did not attend regularly.

In December 1968 right calf vein thrombosis recurred, for which she was given a seven-day course of ancrod. She improved slowly and was again discharged on warfarin and Fearnley's regimen.

She remained quite well until October 1972, when she was readmitted with pain and swelling in the right calf, for which she was given the fourth course of ancrod with satisfactory improvement.

In June 1973 left calf vein thrombosis recurred and this was followed 10 days later by right-sided pleurisy and haemoptysis. The warfarin had been stopped in September 1972 as the daily dose had risen to 130 mg and anticoagulant control was poor. She was then given 10 days' intravenous heparin and the signs in the calf and chest resolved slowly. Signs of right calf vein thrombosis appeared again in January 1974. There was no response to heparin and a further course of ancrod was given. Venepuncture was difficult now and strict dosage of ancrod was impracticable. The full dose was therefore not given on 26 and 27 of January. The signs and symptoms of the right calf vein throm-