627), all earlier workers failed to demonstrate specific antibodies in the serum of patients.¹⁻⁷ Even Hermans' group,^{8,9} as you mention, failed to detect antibodies to cartilage or chondrocytes using very elegant methods, but the increased lymphocyte transformation detected by them occurred in all of three cases of relapsing polychondritis and also in nine out of 12 cases of rheumatoid arthritis and in one of two cases of gouty arthritis among the control subjects, in the presence of the same antigens. Increased lymphocyte transformation by itself is not accepted as an indisputable index of cell-mediated immunity because a humoral or a cell-mediated mechanism, or both in combination, or a "non-specific" mitogenic effect could each transform lymphocytes.¹⁰ The possibility of the occurrence of a "non-specific" mitogen in the antigenic material used was not excluded. Further, as the increased lymphocyte transformation occurred in many cases of rheumatoid arthritis and one of gouty arthritis, the operation of a factor common to all these arthritides (including relapsing polychondritis) seems likely.

Hughes *et al.*¹¹ have recently demonstrated, by the immunofluorescent technique, positive human fetal cartilage staining in two out of three cases of relapsing polychondritis and in all of 12 cases of rheumatoid arthritis but no staining in 32 control subjects. Again, like Herman's findings, their results seem to indicate the occurrence of an antibody in the serum of patients with these chronic arthritides. We¹² have shown the presence of cell-mediated immunity to human laryngeal cartilage proteoglycan (kindly supplied by Dr. Helen Muir of the Kennedy Institute) by two in vitro methods—macrophage migration inhibition¹³ and lymphocyte transformation—in two patients with relapsing polychondritis, whereas nine control subjects suffering from a variety of arthritides gave negative results. Further, we were unable to show the presence of humoral antibodies to cartilage in the serum of these two patients by immunofluorescent staining (kindly done by Dr. G. Loewi, Dr. G. Johnson, and Mr. D. Kingston of this unit separately) or to proteoglycan by gel immunodiffusion. Subsequently we were in a position to study three other cases of relapsing polychondritis (to be published). The following results were obtained in them when the same four tests were applied. The first case showed no cell-mediated immunity and in the two humoral tests showed positive immunofluorescent staining of fetal cartilage but negative immunodiffusion with proteoglycan. The second case showed positive cell-mediated immunity and weakly positive immunofluorescent staining of cartilage but negative immunodiffusion with proteoglycan. The third case showed positive cell-mediated immunity but negative humoral tests like the two reported cases.¹² These findings are difficult to interpret. We feel that humoral immunity could be an early manifestation of the disease, while cell-mediated immunity could be a late manifestation. The interesting feature is the development of cell-mediated immunity against a normal biochemical constituent of the tissues affected in the disease process.

His-chemical studies indicate that the chondromucoprotein of the cartilage ground substance is affected in the pathological process of the disease. There is some evidence^{14,15} to suggest that the arterial walls may contain a similar substance and this could perhaps

explain the involvement of the arteries in the disease. One of the two patients under our care referred to above¹² (in fact, the first) presented as a case of Takayasu's syndrome, and over the years she developed both arthritis and finally chondritis. She showed a marked degree of cell-mediated immunity to human laryngeal cartilage proteoglycan. Another patient referred for our opinion had angiographically established Takayasu's disease but had no evidence of arthritis or chondritis clinically or radiologically. She showed a mild degree of cell-mediated immunity to the same proteoglycan antigen. It could well be that the arteritis of Takayasu's type and polychondritis of relapsing type are variants of the same disease or disease process.—We are, etc.,

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The Blind in Hospital

SIR,—Some years ago I spent three months in a surgical ward. During that time the sister spoke to me exactly once. Doubtless she was often in the ward, but I never knew because I am totally blind. It would have been a help because the nurses were continually changing. Over a period of two or three weeks I was asking nurses to ask Dr. X. to see me, without success. Eventually I phoned him from my bed and asked him if he had had a holiday. He was furious and said that he had been in the ward every day. The staff often forget that you are blind and completely fail to communicate. The situation was desperate for me and I would prefer to die in the gutter rather than go back.

If I am blind I never know who you are and rarely if you are there at all, because of background noise. People think I do not want to speak because I cannot speak first. Would it not be possible to hang up a little label saying, perhaps, "Blind but not deaf," or "Tell me you are here"?—I am, etc.,

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Clinical Experience with the Dalkon Shield

SIR,—We were interested to read Dr. J. S. Templeton's letter (8 September, p. 542) concerning our preliminary report on our clinical experience with the Dalkon Shield (21 July, p. 143) and would like to comment on some of the points that he has raised.

One of the prime objectives of our paper was to point out that in our hands the Dalkon Shield results were not as good as those reported by Davis¹ and his colleagues who had developed the intrauterine device (I.U.D.). We therefore presented our data in a similar way to that which they had done, using the Pearl index and the life table method.² It is possible that their results might be related to the use of a spermicide, which Davis recommends in the first few months of use. Furthermore, in the multicentre analysis reported by the family planning unit at the University of Exeter, there is no information on spermicide usage either.³ We quoted the use of spermicide in 5% of our cases. Variation in spermicide usage may be one of the factors related to the widely differing pregnancy rate in these 10-12 clinics, of which, incidentally, ours is one (the pregnancy rate in these clinics varies from 0.8 to 8.4%). We, too, have little doubt that valuable complementary data are derived from studies such as the multicentre trial quoted as well as experience in an individual clinic.

We have used the accepted definition of parity as a pregnancy which has gone beyond 28 weeks. Therefore our nulliparous patients were those who had been pregnant and had had a pregnancy terminated; thus they were able to accommodate the larger Dalkon Shield without any difficulty. It was in the two patients in whom the uterine cavity was small that we used the smaller Dalkon Shield.

As far as the training of doctors in the insertion of I.U.D.s is concerned, we accept that this may well contribute to a higher pregnancy rate, bearing in mind that if an I.U.D. is to be inserted in large numbers, it is to be expected that the skill of individual operators will vary.

We have since had our data analysed according to the currently recommended cumulative life table method⁴ and our pregnancy rate findings with this method of analysis were not dissimilar from those reported.—We are, etc.,

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One Thousand Vasectomies

SIR,—With reference to the report by the staff of the Margaret Pyke Centre (27 October, p. 216) I was interested to note that it was considered unreasonable to insist on sperm-free specimens before taking the responsibility of pronouncing sterility.

I have performed some 5,000 vasectomies

during the past 13 years in Canada where, possibly because an actual fee for the surgery is involved, the situation is more individualized and contractual, with the consequent possibility of litigation in the event of failure. Therefore for personal and legal reasons I could not guarantee sterility if any spermatozoa—motile or non-motile—were present in the semen. In the early years I required only one negative specimen but later increased this to two. Because of two pregnancies, with motile spermatozoa, I have for the past five years followed a routine of two negative specimens, two weeks apart, two months after the operation followed by a third negative specimen one month later. Thus the patient and I are satisfied that every reasonable precaution has been taken. If a specimen shows any sperm, then specimens are repeated monthly for 8-12 months. At the end of this variable period a second operation is performed as before under local anaesthetic with no difficulty, using a fresh site on the vas if there is any granulomatous tissue formation from the previous surgery. A total of 14 patients, 12 with non-motile sperm and two with large motile sperm counts, had repeat vasectomies performed and in every case was aspermic one month after operation.

It was noted that, generally speaking, the older the patient, the longer the period required to attain azoospermia, the oldest (75 years) taking 18 months. While I have a routine based on a period of time, the vital factor is the frequency of coitus, which in the older patient with failing sexual function requires more time and more ejaculations to complete evacuation of the spermatozoa. The time schedule was strictly adhered to in order that if recanalization takes place, which is more probable in the first two months, it will show up in the routine tests. It would appear that sperm present in the semen after 50 intercourses indicates recanalization, and reoperation should be considered. Intermittent aspermia may be due to a temporary blockage of a recanalizing vas. No third vas was encountered and it is probable that its functional existence is to provide the surgeon with a reason to give the patient for failure to attain sterility.

It is unlikely and unethical that the question whether a patient with non-motile sperms in his specimen is capable of impregnation—other specimens may contain motile spermatozoa—will be resolved as it is not in the interest of the patient, his wife, or the child to prove that the husband is not the father. If the doctor is not aware of this the patient and his wife are, and will refuse the confrontation and consequences.—I am, etc.,

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Lung Cancer and Smoking

SIR,—After the latest depressing news about the increase in cigarette smoking I consider it inevitable that eventually legislation will have to be introduced prohibiting the use of tobacco or limiting its use to registered addicts only.

Should not the B.M.A. start now and lobby the Government seriously to consider legislation, or at least increase the prices so much that children under 14 years would

have great difficulty in affording to smoke?—I am, etc.,

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Female Sterility Produced by Investigation

SIR,—The letter of Dr. F. W. Wright and Sir John Stallworthy (22 September, p. 632) prompts me to draw attention to another danger in the investigation of infertility in the female, possibly leading to subsequent tubal blockage.

Methylene blue is commonly used to demonstrate tubal patency during diagnostic laparoscopy. The usual preparation is methylene blue injection, U.S.P., 1% in water in 10-ml ampoules (Harvey Laboratories, Inc., Philadelphia). The pH is 6.07. I wish to emphasize that this should be diluted liberally. Because the colour is very strong 1 ml diluted in 1000 ml of sterile normal saline is sufficient to show clearly after spill into the peritoneal cavity.

An average injection would be 10 ml and if given undiluted, straight from the ampoule, can provoke an acute reaction with signs of pelvic peritonitis lasting for some weeks, presumably following a "chemical salpingitis." There is also the problem of leakage into uterine blood vessels. The manufacturer's leaflet relating to intravenous administration of undiluted dye specifies the precaution of slow injection over minutes of a dose calculated on a body weight basis and mentions adverse reactions of nausea, abdominal and precordial pain, dizziness, headache, profuse sweating, mental confusion, and the formation of methaemoglobin.—I am, etc.,

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Type IV Hyperlipidaemia in Cord Blood

SIR,—Though Kwiterovitch *et al.*,¹ have recently reported triglyceride concentrations in cord blood averaging 37 mg/100 ml, with a standard deviation of only 15 mg, in 36 normal infants, evidence was published 11 years ago that a proportion of newborn babies have relative hypertriglyceridaemia. Brody and Carlson² measured triglycerides and other lipids in cord blood from 52 unselected newborn infants. The mean concentration of their plasma triglycerides was 0.38 mmol/l. (approximately 33 mg/100 ml) but the frequency distribution was significantly skewed to the right—so that a standard deviation could not be calculated—and values ranged up to 0.85 mmol/l. or 74 mg/100 ml. The upper tail of the distribution might, if one wished, be called relative type IV hyperlipidaemia in the newborn.

Brody and Carlson suggested that genetic factors could be responsible for this phenomenon. However, the last weeks of pregnancy and birth itself are a time of stress and metabolic changes whose intensity varies between individuals. Some degree of fatty liver appears to be quite common in the newborn.^{3,4} Pre- β -lipoprotein, which carries endogenous triglycerides in plasma, is the predominant lipoprotein in cord blood but its concentration falls off during the first few days of life, while that of β -lipoprotein increases.⁵ There are accompanying major

changes in the fatty acid pattern of serum lipids.⁶

The phenomenon to which Dr. F. M. Martins and his colleagues draw attention (8 September, p. 544) is interesting and deserves further study, but we cannot yet assume that those newborn babies with relatively high triglyceride levels in cord blood will be the individuals who show the better known primary type IV hyperlipoproteinaemia in middle age. Careful and prolonged follow-up is needed and it could yet turn out that the cause of "newborn type IV hyperlipoproteinaemia" is obstetrical (in the broadest sense of the word) rather than genetic.

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Drug-induced Platelet Antibodies

SIR,—We read with interest the letter of Drs. C. Davidson and S. M. Manohitharajah (8 September, p. 545), who reported the presence of specific platelet antibodies in a patient who developed thrombocytopenia while receiving phenylbutazone therapy. With the increasing incidence of drug-induced blood dyscrasias it would appear to be more and more relevant to search for mediating antibodies and we would like to report another illustrative case.

A 77-year-old woman presented with a 24-hour history of epistaxis and rectal bleeding, with spontaneous bruising for two weeks. She had been taking phenylbutazone regularly for 12 years to alleviate arthritic pain and for three years she had been taking quinine sulphate as treatment for nocturnal cramps. We were unable to ascertain any recent alteration in dosage or proprietary brand. Examination revealed a pale woman with generalized bruising and purpura over the limbs and trunk. Petechial haemorrhages in the mouth and a flame haemorrhage in the left fundus were noted, together with evidence of recent epistaxis and rectal bleeding. There were no other abnormal clinical findings.

Her haemoglobin level was 9.7 g/100 ml, total leucocyte count 1,200/mm³, and platelet count 10,000/mm³. Bone marrow aspiration revealed a mildly hypocellular marrow with macronormoblastic erythropoiesis and delayed maturation of granulopoiesis. Megakaryocytes showed reduced platelet budding. There was no evidence of bone marrow infiltration. Tests for antinuclear factor and L.E. cells were negative, as were Ham's test and screening for urinary haemosiderin. Serum vitamin B₁₂ and folate levels were normal. The Direct Coombs test was negative. Tests for leucocyte and platelet agglutinins were also negative, but a complement fixation test was strongly positive for incomplete platelet antibodies in the presence of quinine sulphate. This was negative in the presence of phenylbutazone.

All drugs were withheld and, apart from reverse barrier nursing, no active therapy was given. After eight days her haemoglobin level had risen to 10.3 g/100 ml, total leucocyte count to 4,600/mm³, and platelet count to 170,000/mm³.

It would appear that the pancytopenia resulted from the combined effects of phenyl-