Lung cancer and chronic bronchitis

SIR,—Dr D Davies's criticism (11 October, p 100) of the paper by Drs M Caplin and Freda Festenstein (20 September, p 678) is incomplete, for even if the correct comparison, which he describes, between the obstructed and unobstructed bronchitics is made the difference in frequency of lung cancer between them is still significant. What is missing is any statement of the period of survival of the two groups of men. Since 40% of the obstructed but only 18% of the unobstructed bronchitics died in the seven years of follow-up, the latter had many more man-years in which to develop lung cancer.

Apart from this, the clinical approach is incapable of providing any reliable data on the presence or absence of a real association between two diseases which have different fatality rates and different likelihoods of inclusion in the clinical series.¹ The only way of deciding this would be by a prospective study of a sample of the general population to determine the attack rate of lung cancer in men with and without airways obstruction. The fact that Drs Caplin and Festenstein found that 17% of their lung cancer patients had severe airways obstruction (forced expiratory ratio < 50%), while we found only 5% in cigarette smokers in a sample of working men in West London,² appears to conflict with their conclusion that there is a "lack of association" between lung cancer and airways obstruction—but it does not prove the opposite because of the unpredictable effects of selection in any clinical series.

Dr Ian Gregg (11 October, p 100) comments on the apparently small relationship in prevalence surveys between amount smoked and severity of airways obstruction. In our study we found a significant tendency for men with airways obstruction to reduce their cigarette consumption.² In prevalence surveys subjects are usually classified by their current smoking habits so that subjects with low and medium consumption will include many of the former heavier smokers with airways obstruction and the group of current heavier smokers will contain chiefly those who are not susceptible to the development of airways obstruction. This effect will also presumably distort the true relationship between smoking habits and deaths from bronchitis, although these do show a pretty steep gradient in relation to cigarette consumption.

C M FLETCHER

Royal Postgraduate Medical School,
Hammersmith Hospital,
London W12

¹ Mainland, D, *American Heart Journal*, 1953, **45**, 644.

² Fletcher, C M, *Community Health*, 1975, **7**, 70.

SIR,—If, as reported by Drs M Caplin and Freda Festenstein (20 September, p 678), there is an absence of association between lung cancer and airways obstruction, then Dr I Gregg's interpretation (11 October, p 100) can be taken a stage further.

The power of a carcinogen to produce cancer is related to its concentration in or on the susceptible tissue as well as the frequency and length of exposure of the tissue to it. In obstructive airways disease due to chronic bronchitis the underlying factor is hypersecretion of mucus. It seems reasonable to postulate that such mucus would perform

its physiological function and trap some, or much, of the carcinogen in the tobacco smoke, so reducing the concentration of the carcinogen that actually reaches the bronchial mucosa. In addition, since mucus is being constantly secreted, the carcinogen which does reach the mucosa may very well be removed after only a short period of contact. Some of the carcinogen would be trapped in the mucus and expectorated before making contact with the mucosa, so reducing the frequency of the mucosa's exposure to it.

Thus the three factors influencing the effect of a carcinogen—namely, concentration, length of exposure of tissue, and frequency of contact, may all be reduced by the presence and continued secretion of bronchial mucus. If this is so, it would seem that, as suggested by Dr Gregg, those smokers who, owing to host factors, develop obstructive airways disease may be protected against lung cancer whereas those smokers who do not produce hypersecretion of mucus are most at risk.

O MORTON

London NW6

SIR,—Drs Maxwell Caplin and Freda Festenstein (20 September, p 678) found obstructive bronchitis less often in patients with lung cancer and simple bronchitis than in those with simple bronchitis alone. This lack of association between lung cancer and severe airways obstruction, they say, requires an explanation.

Any one of the answers suggested by the authors is, of course, possible. On the other hand spurious association due to differences in the way in which the various samples have been selected from the parent population must not be overlooked. In a study described by Berkson¹ as "a paradigm of what, according to widely held opinion, are the essentials for a perfectly performed experiment of statistical comparison" Pearl² found active tuberculosis in 6.6% of 816 persons with malignant tumours and in 16.3% of 816 persons without malignant tumours but of the same race, sex, and age. The conclusion that tuberculosis and cancer are biologically antagonistic "was accepted with utmost seriousness" and a programme of treating cancer patients with tuberculin was instituted. Nevertheless, Pearl's conclusion was not valid. As Berkson^{1,3} demonstrated with a number of worked examples it foundered because of an important statistical fallacy which ensures that the appearance of association of diseases, either positive or negative, will arise in subpopulations "except in special circumstances" although no association exists in the general population. This he claimed to be true even in prospective studies.

P E BROWN

Department of Community Medicine,
University of Sheffield Medical School,
Sheffield

¹ Berkson, J, *Proceedings of the Staff Meetings of the Mayo Clinic*, 1955, **30**, 319.

² Pearl, R, *American Journal of Hygiene*, 1929, **9**, 97 (cited by Berkson).

³ Berkson, J, *Biometrics Bulletin*, 1946, **2**, 47.

Alpha-chain disease cured with antibiotics

SIR,—Dr O N Manousos and others (25 May, 1974, p 409) reported a case of alpha-chain disease¹ with "Mediterranean lym-

phoma" which was cured by combined treatment with prednisone, cyclophosphamide, and antibiotics. Laroche *et al*² and Zlotnick and Levy³ obtained similar results with or without antibiotics.

In 1970 we reported a complete regression of the clinical, anatomical, and immunological signs of this disease in a patient who received antibiotics only.⁴ Tetracycline and oleandomycin were given by mouth in doses of 2 g of each daily for 10 months and then 1 g daily for one year. No drugs have been given since June 1971.

Now, six years since the onset, he remains in complete clinical remission (although he developed diabetes mellitus in July 1973). For the past five years the disappearance of the abnormal serum IgA has been verified each year. The last small-intestinal biopsy showed villi of normal architecture and a normal cell population in the lamina propria. The deep lamina propria was only moderately sclerotic. By immunofluorescence the jejunal mucosa was essentially normal.

It appeared interesting to us to report the long-term evolution of this case since, to the best of our knowledge, this is the only example of alpha-chain disease with "Mediterranean lymphoma" cured by antibiotic therapy alone and still in complete remission after six years.

J ROGÉ

P DRUET

C MARCHÉ

F SILVEREANO DE ROISSARD

J P CAMILLERI

Hôpital Broussais,
Paris 14

¹ Seligmann, M, *et al*, *Science*, 1968, **162**, 1396.

² Laroche, C, *et al*, *Presse Médicale*, 1970, **78**, 53.

³ Zlotnick, A, and Levy, M, *Archives of Internal Medicine*, 1971, **128**, 432.

⁴ Rogé, J, *et al*, *Pathologie et Biologie*, 1970, **18**, 851.

Artificial insemination (donor)

SIR,—It was with great interest that we read your leading article (4 October, p 2) on donor insemination. A service of this type, broadly based within the National Health Service, started in this centre approximately two years ago as a natural extension of a large infertility investigation and treatment clinic. Many of the difficulties outlined in your article have been successfully overcome.

We would entirely agree that secrecy and confidentiality are essential; hence all records of our patients are kept separate from their normal hospital records and are retained within our own unit at all times. In necessary correspondence to all other medical authorities the word "donor" is deliberately deleted, reference being made only to "insemination procedures." This, we believe, helps to protect the patient from casual non-medical observers who have access to the letters. The procedure itself is carried out in our clinically oriented laboratory unit in a special room set aside for treatment procedures. This is an ideal arrangement, for in a busy gynaecological clinic treatments of this type are impracticable for the reasons outlined in your article.

We have a substantial semen bank available and are often able to inseminate with both fresh and frozen semen from the same donor within the same cycle. We do not agree that donors should always match the husband's physical characteristics in all re-

spects. It is not always practicable, and it should be remembered that the physical attributes of a husband and wife are not always passed on to their children. It would seem more appropriate to us to match only the broad outlines of physical appearance in terms of height and stature.

All of our donors are screened in terms of a series of medical and laboratory tests and are also paid at the rate of £4 for each sample of semen they provide. Most are university students and are thus assumed to be of reasonable intelligence. The couple requiring insemination are asked to make a contribution of between £5 and £10 into a research fund administered by the local treasurer under our control. This is used to pay the donors. Under normal circumstances the payment covers a woman for up to six consecutive monthly inseminations. It is our impression that the fertility potential of frozen semen is less than that of the fresh.

Knowledge of the service has quickly spread and we now have a substantial waiting list of nearly 200 couples either undergoing investigation, waiting for treatment, or having insemination. We note that various authors have reported variable chances of success. The following facts might prove interesting:

Total No of couples referred ...	193
No currently undergoing insemination ...	23
No awaiting treatment ...	44
No currently being investigated before treatment ...	30
No who have received six courses of treatment without a pregnancy occurring ...	25
No who for personal reasons have decided not to proceed further (of these, six received treatment) ...	51
No of pregnancies ...	20

Excluding those patients who have not yet finished their course of treatment (23) it is apparent that 20 pregnancies have occurred, while 25 have had six courses of treatment without pregnancy. If in addition the six who received treatment and do not wish to proceed further are taken into consideration, it is apparent that the 20 pregnancies have occurred from 51 treated women, an approximate 40% success rate. An analysis in greater detail is now being carried out and it is hoped to publish this in the near future.

G W PENNINGTON
SANDRA NAIK

Sheffield and Region Endocrine Investigation Centre,
Jessop Hospital for Women,
Sheffield

SIR,—I was interested in your leading article on AID (4 October, p 2). Very little has been published because of the sensitive nature of this work, and the impression is given that this is a new concept when in fact we are already treating second-generation AID women.

The lack of information has also created the impression that this procedure is relatively unsuccessful. In practice there is little difficulty in achieving a pregnancy by this method in normally fertile women; 49% of my patients conceived within three months of treatment, 412 pregnancies being achieved with an average of 4.4 inseminations. Of the first 100 patients, 58 have returned for a second baby, two are expecting a third, and one has four children.

BRIDGETT MASON

London W1

Sterilisation of minors

SIR,—Your legal correspondent (27 September, p 775) urges legislation to assist doctors in this difficult area. Mr William Nash, legal officer of the National Council of Civil Liberties, who acted for Mrs Hamidi in the case of the Sheffield girl, also pointed out that "there is a clear gap in the law which must be filled."

As a possible solution to this lacuna in the law we would like to bring to your attention the proposal made by the Second International Conference on Voluntary Sterilisation and recently endorsed and amended by the law panel and central medical committee of this federation. It reads as follows:

Applicable to incompetents—The following shall apply with respect to any person who does not have legal capacity to consent: if the parents or guardian of such a person and a physician have decided that temporary measures will be ineffective, they may apply for a procedure to render that person permanently infertile to a Board, duly appointed by the appropriate authority, which may, after full consideration, grant their application. . . . The Board shall consist of at least five persons, both lay and professional of both sexes, which shall act by a majority vote. The Board shall also include a person or persons representative of the particular ethnic, religious or philosophical group of which the person who is the subject of the application is a member."

We hope that the above suggestions will be constructive in the formulation of guidelines with respect to irreversible sterilisation until such time as fully reversible sterilisation methods are developed. We note that the use of injectable steroids and oral contraceptives can be valuable in such cases.

REBECCA J COOK
MALCOLM POTTS

International Planned Parenthood Federation,
London SW1

Survival of infants with unoperated myelocoeles

SIR,—It is interesting to read the experience of Dr M F Robards and his colleagues in Liverpool that 30% of the infants denied early closure of their myelocoeles survived at least a year (4 October, p 12). This is very different from the findings reported from Oxford,¹ where 92 of 99 infants with unoperated myelocoeles had died within the first year. Subsequent experience in Oxford and Swindon has shown a similar outcome in the unoperated group.

The outcome clearly varies from centre to centre and perhaps it is worth considering why this might be. As one who has been associated with a very low survival rate I should like to outline a personal approach to the care of such infants.

If, after discussion as fully as possible with the parents, surgeon, and family doctor, it is agreed that early surgery is not in the baby's best interest the hospital undertakes to provide care. It is unusual for the parents to ask to take the baby home, although, of course, they are free to do so. It would be wrong to ask for standards of nursing care to be in any way less than for any other infant. So the back wound is dressed and general care given. Nothing is done to prolong the infant's life. The infant is fed on demand but is not given tube feeds or parenteral nutrition. Antibiotics are not pre-

scribed. I am prepared to sedate the baby when necessary. Most of these infants die with minimal suffering to them and their family. The cause of death has more often been infection than hydrocephalus in our experience.

I am well aware of the difficult moral and ethical area into which I venture. However, this approach, which is, I believe, similar to that carried out by many paediatricians, does have the support of our colleagues who nurse these babies and, above all, satisfies the demands of the parents that their grossly handicapped infant "shall not suffer."

DAVID W HIDE

St Mary's Hospital,
Newport, Isle of Wight

¹ Hide, D W, Williams, M P, and Ellis, M L, *Developmental Medicine and Child Neurology*, 1972, 14, 304.

Tibial shaft fractures

SIR,—Your leading article on tibial fractures (4 October, p 4) glosses over the important problem of skin cover which bedevils a small proportion of these injuries. As the blood supply below the knee is relatively poor and no loose skin is available there is a temptation to suture under tension, particularly if damaged skin has been excised. There is a basic conflict—namely, that the wound is lacerated and should not be closed primarily but the fracture is compound and should be converted into a simple one. If the fracture is unstable the temptation to introduce some form of hardware is almost irresistible.

I would like to take this opportunity to ask those who carry out the primary care and are unable for one reason or another to obtain assistance with difficult repairs to spare a thought or two for those who may be called in later to salvage limbs in the event of breakdown: (1) A single pedicle flap will probably slough, leaving two problems instead of one. A double pedicle flap is safer but moves very little. (2) The application of a closed plaster for some weeks in the presence of skin of doubtful viability may be followed by skin breakdown, suppuration, and necrosis of exposed bone. A window must be cut to allow wound inspection during the first few days. (3) A decision whether or not to use a cross-leg or muscle flap should be made within 48 hours of injury if possible—certainly within the first week. Skin-graft-covered muscle flaps are useful in small defects with minimal muscle damage, particularly in the over-40s for primary or secondary repair. (4) In unstable fractures I agree that a method of fixation which allows the knee to bend, gives access to the wound, and avoids introducing foreign material into the fracture site should be chosen.

B S CRAWFORD

Plastic and Jaw Department,
Royal Hospital Annexe,
Fulwood, Sheffield

SIR,—It is a pity that, in an otherwise well-balanced leading article (4 October, p 4) you should perpetuate a myth. It is just not true that encirclage wires "act like a tourniquet on the bone, interfering with local blood supply and delaying or preventing union." When encirclage wires fail, as in the case of tibial fractures they usually will, it is because they have been applied too loosely or with-