measure of cross-allergenicity with the penicillins is debatable. Are not penicillin-allergic patients liable to show increased incidences of hypersensitivity to many substances? How does one use a cephalosporin "with caution"? Does this mean the use of an oral cephalosporin rather than an injectable one?

(5) The importance of β -lactamase is unfortunately obscured by generalisation; certain β -lactamase enzymes have a high capacity to hydrolyse certain compounds. But these antibiotics are indifferent to other enzymes. The key questions are: (a) To what extent is β -lactamase produced *in vivo*? (b) To what extent does this β -lactamase damage the antibiotic *in vivo*? (c) To what extent do laboratory sensitivity testing methods reflect the milieu of the patient as far as β -lactamase is concerned?

Much of the confusion over the cephalosporins has come from the use of loose terms such as "activity" and the failure of the manufacturers and others to perform controlled trials showing superiority of a newly introduced product. At a very recent promotional meeting about a new cephalosporin that I attended the results of treatment of 1400 patients were given, yet not a single trial comparing it with other cephalosporins was cited.

I suggest that in the use of cephalosporins, unless a specific indication exists for another agent, the drug for routine use should be selected on (1) availability as both an oral and a parenteral compound and (2) cost. It is hoped that before further agents are introduced in the future not only will they appear improved on selected *in vitro* evaluation but patients will also be seen to have benefited.

R W LACEY

West Norfolk and King's Lynn
General Hospital,
King's Lynn

¹ Lacey, R. W., and Stokes, A., *Journal of Clinical Pathology*, 1977, **30**, 35.

Antibiotic resistance in *Haemophilus influenzae*

SIR,—We agree with the suggestion of Dr A J Howard and his colleagues (24 June, p 1657) that ampicillin (and hence amoxycillin) are "unsuitable as first-line treatment for severe haemophilus infections in children." We have studied the resistance of haemophilus isolates (mainly in specimens of respiratory origin—all from children) over the past three months.

Primary isolation was performed using an Oxoid Columbia agar-based selective media containing 0.25% lysed horse blood, 12.5 mg/l NAD, 0.00025% haematin, and 5000 U/l bacitracin. All isolates were characterised by dependence on purified haematin and NAD and by the production of haemolysis. Sensitivity to ampicillin was tested by a disc diffusion method using Oxoid IST agar supplemented with lysed horse blood, NAD, and haematin in the same concentrations present in the selective medium. Organisms that showed a reduced zone of inhibition

to a 2- μ g ampicillin disc by comparison with the Oxford staphylococcus (NCTC 6571) were all tested for β -lactamase production using the phenol red penicillin technique.¹ The identity and resistance to ampicillin of the 588 haemophilus strains isolated are shown in the table below.

The relatively high incidence of β -lactamase-producing *Haemophilus influenzae* found in our isolates contrasts markedly with the absence of such strains reported from Birmingham by Dr Howard and his colleagues. The differences are unlikely to be due to local geographical variations, since our hospital and the Birmingham centre in the study serve the same area of the city. It would therefore be interesting to know what percentage of *H influenzae* in Dr Howard's study was isolated from children. Unfortunately we do not routinely serotype *H influenzae*, but in view of the noted higher incidence of ampicillin resistance in type b strains it is possible that a greater percentage of our isolates were of this serotype. It is worth emphasising, therefore, that although the overall incidence of ampicillin resistance in *H influenzae* noted by Dr Howard was only 1.6%, the incidence was 11.8% in type b strains. These are the strains usually responsible for the life-threatening infections, notably acute epiglottitis and meningitis.

Finally, it is interesting to note that in haemophilus species other than *H influenzae* the incidence of β -lactamase-producing strains may approach 50%. It has been shown by Sykes *et al*² that the R-factor mediating β -lactamase production in *H influenzae* passes relatively easily into *H parainfluenzae*. Should the β -lactamase in *H parainfluenzae* be mediated by the same R factor and pass as easily from *H parainfluenzae* to *H influenzae* then the presence of this reservoir of resistance may lead to a further increase in ampicillin/amoxycillin resistance in *H influenzae* in the future.

A P GILLET
D E HEALING
R H GEORGE

Children's Hospital,
Birmingham

¹ Escamilla, J., *Antimicrobial Agents and Chemotherapy*, 1976, **9**, 196.

² Sykes, R. B., Matthew, M., and O'Callaghan, C. H., *Journal of Medical Microbiology*, 1975, **8**, 437.

Hypertension and oral contraceptives

SIR,—We read with interest your leading article on this subject (17 June, p 1570). We are currently undertaking an investigation into the role of the renin-angiotensin system in the mechanism of this process, using the specific angiotensin II (AII) antagonist (Sar¹) (Ala⁸) angiotensin II (Saralasin; Eaton Laboratories, Norwich, NY). So far four patients have been studied and our preliminary results support the hypothesis that the renin-angiotensin system is not directly

involved in the pathogenesis of this form of hypertension.

Four Caucasian women aged 28-38 years have been studied. Two were nulligravid and two were multiparous. There was a positive family history of hypertension in two cases, but no patient was known to be suffering from renal or metabolic disease. Negative pregnancy tests were obtained from all patients. Contraceptive therapy given was: Gynovlar-21 (norethisterone acetate 3 mg, ethinyloestradiol 50 μ g), Minovlar (norethisterone acetate 1 mg, ethinyloestradiol 50 μ g), Loestrin-20 (norethisterone acetate 1 mg, ethinyloestradiol 20 μ g), and Eugynon-30 (levonorgestrel 250 μ g, ethinyloestradiol 30 μ g).

Three were known to have been normotensive (blood pressure <140/90 mm Hg) immediately before starting contraceptive therapy; no initial blood pressure recording had been made for the fourth patient. At the time of investigation the patients were known to have been hypertensive (blood pressure >140/90 mm Hg) for 3-12 months.

Blood pressure was monitored at 2-min intervals using an automatic blood pressure recorder (Arteriosonde, Roche). Saralasin was infused into an antecubital vein at doses ranging from 0.1-24.9 μ g/kg/min in stepwise increments. Blood samples were taken for plasma renin and AII measurements before, during, and at the end of the infusion. The maximum fall in blood pressure was taken as the mean of the three lowest consecutive points. Percentage fall was calculated by comparison with the initial and final blood pressures. Mean resting blood pressure was $145.4 \pm 2.2/99 \pm 1.8$ mm Hg. Only in one instance did the diastolic blood pressure fall consistently to below 90 mm Hg. Proportional falls in diastolic blood pressure ranged from 3.5 to 8.7%, and in systolic blood pressure from 3.1 to 6.1%. The plasma AII concentration rose in three patients, showing that adequate blockade of the renin-angiotensin system had been achieved; it fell slightly in the fourth patient.

Thus specific blockade of angiotensin receptors results in only small decreases in blood pressure in women presumed to have "pill-induced" hypertension. These preliminary results therefore add further support to the suggestion that the renin-angiotensin system is not immediately involved in the pathogenesis of this form of hypertension.

F BROUGHTON PIPKIN
J C HUNTER
JEREMY OATS
MALCOLM SYMONDS

Department of Obstetrics and
Gynaecology,
City Hospital, Nottingham

Children who cannot read

SIR,—Your leading article under this title (1 July, p 3) has considerable value, particularly in stressing the need for comparative appraisal of teaching methods, and so does the Warnock Report,¹ which recommends giving "dyslexia," whatever we call it, formal recognition. This is encouraging to me, since I have been personally aware of its importance since I analysed it correctly in myself 38 years ago and see it in my family. I am far less happy about your sentence, "While uncommon, it has generated a disproportionate amount of

Resistance to ampicillin in 588 strains of *haemophilus*

Organism	No of isolates	No (%) of β -lactamase-producing strains
<i>H influenzae</i>	168	13 (7.7)
<i>H parainfluenzae</i>	334	148 (44.3)
<i>H haemolyticus</i>	4	2 (50)
<i>H parahaemolyticus</i>	68	20 (29.4)
Other <i>Haemophilus</i> spp (X-dependent)	14	3 (21.4)
Total	588	186 (31.6)

publicity in recent years," and the implication that "dyslectics," like me, should be considered together with other children with reading backwardness.

As I understand it, "dyslexia" can only be identified by a disparate performance in reading (A) as against other intellectual modalities (B)—a low value of a ratio A:B. This is, of course, discernible only if A is low and B is high, so we cannot possibly have any idea of the number of children who have the positive attributes of dyslexia leading to a low value of A if it is not discernible because B is not high enough. The children who are identifiable by present techniques must be a small minority of the real problem, so it is unlikely to be uncommon.

The problem deserves special stress not only because of its size but because it is aggravated by arbitrarily imposed social policy. There are many ways of communicating, and the stress on the written word in education and above all in examination has led to a vicious spiral of selection for opportunities for those good at these functions. There is some reason to believe that they will become less relevant, and the deprivation of able dyslectics of opportunity purely on these grounds is surely morally unjustified, and possibly damaging, not only to us but also perhaps to the community if our different attitudes provide another perspective of things. We are not talking about a disease but about a difference.

Egalitarian approaches to education are clearly biologically unsound, and the principal problem for the dyslectic. These policies are readily reversible, and the dyslectic's potential may be so great that any implication of disability is obvious nonsense. Still the talk is of "remedial education" when what many of us need is "appropriate education," accentuating and making full use of our strengths. These are the reasons why both the size and the nature of the problem fully justify special consideration, and the publicity so far has been quite inadequate.

J F SOOTHILL

Department of Immunology,
Institute of Child Health,
London WC1

¹ Department of Education and Science, *Report of the Committee of Enquiry into the Education of Handicapped Children and Young People*. London, HMSO, 1978.

Contamination of sterile fluids

SIR,—In their letter on this subject (8 July, p 123) Dr G Ayliffe and his colleagues imply their acceptance of the concept that "if it's sterile it's clean." As a pharmacist I apply the reverse concept that "if it's clean enough it's also likely to be sterile."

Microbiological contamination of intravenous fluids has led to spectacular and unpleasant problems. General contamination of fluids manufactured in an unclean environment or used in an unclean way rarely leads to spectacular or "headline" problems. The damage¹ to patients in these circumstances is insidious and might well have long-term deleterious effects.

To produce fluids acceptably free from micro-organisms is easy—your correspondents admit that the likeliest contaminant organisms are easily killed by moist heat. To produce fluids sufficiently free from rubbish of clinical significance is not easy. A very clean working

environment in the fluid production area helps. Such fastidiousness is not simply designed to reduce hospital infection, as your correspondents imply, but to reduce morbidity of patients generally, be it from micro-organisms, cotton fibres, or plastic going down the cannula.

Therefore I believe that at least one high standard "manufacturing" centre is required per area health authority.

I W MARSHALL

St James's Hospital,
Leeds

¹ Dimmick, J E, *et al*, *New England Journal of Medicine*, 1975, 202, 685.

Hazard of chemical sympathectomy

SIR,—It is a pity that enthusiasts for a technique cannot admit that there are other methods which are equally effective and safe if properly performed. We did not wish to decry the use of the image intensifier for chemical sympathectomies (29 April, p 1143), and where it is readily available some operators may well find its use of considerable assistance. However, where it is not easily available it was our intention to suggest that the procedure can be done safely without it. Our experience and that of many others in Britain (without scouring the world for support!) give credence to this contention.

Hoxton¹ stated that "the whole technique of inserting the needles with accuracy should be mastered by careful practice in many cases before any injections of phenol are undertaken." Reid *et al*² and Hoxton stressed the need for the needle to be deeply inserted, a point we also made in our original letter. Dr R A Boas and others (24 June, p 1700) doubtless noted too that the technique to which we referred³ included a test injection of lignocaine which would reveal inadvertent intrathecal injection. Incidentally, we also follow the injection of phenol in water with a small volume of radio-opaque dye and the patient is then sent to the x-ray department for posteroanterior and lateral views of the lumbar spine.

To suggest that the use of the image intensifier is a foolproof method of ensuring correct needle placement and is devoid of all risks is hardly true. Furthermore, it is surely a little presumptuous and certainly unfair, without further details of the case, of Drs A P Rubin and B R Master (25 March, p 790) to suggest that the complication described by Mr R C Smith and others (4 March, p 552) in their report "is entirely preventable" by its use. It may express the authors' convictions, but it has very serious medicolegal implications and its accuracy is open to question since the absence of reports of mishaps may not necessarily mean that there have not been any.

In summary, we believe that there is more than one way of performing a satisfactory chemical sympathectomy but that none is entirely free from hazard. Whatever technique is adopted considerable experience and care are necessary in order to reduce the risks to a minimum. We feel it is unreasonable that a patient should be denied the benefit of a chemical sympathectomy merely because the facility of an image intensifier is not available. In those cases in which complications have occurred it would be necessary to examine every detail of technique before one could

claim either that it was avoidable or that an image intensifier could have prevented it.

JAMES M B BURN
L LANGDON

Shackleton Department of Anaesthetics,
Southampton General Hospital,
Southampton

¹ Hoxton, H A, *British Medical Journal*, 1949, 1, 1026.

² Reid, W, Watt, J K, and Gray, T G, *British Journal of Surgery*, 1970, 57, 45.

³ Mehta, M, *Intractable Pain*, p 213. Philadelphia, Saunders, 1973.

Thrombocytopenia and subclavian cannulation

SIR,—The safe placement and efficient function of catheters for long-continued venous access are important practical considerations in clinical medicine. The problem arises when superficial veins are not available and here direct puncture of large vessels may be unavoidable. One site that is popular for central venous cannulation is the percutaneous introduction of the catheter into the subclavian vein, and to those experienced in the technique the subclavicular approach is useful, reliable, and quick. However, complications may arise, including pneumothorax and bleeding from the vessel wall. The latter may assume significance in the patient with disturbed haemostasis and we have recently encountered the development of large haemothoraces in two thrombocytopenic patients following apparently technically successful introduction of the catheter.

The first patient was a 14-year-old girl with severe acute aplastic anaemia. She had previously sustained a cerebral haemorrhage from which recovery had been complete and was referred for bone marrow transplantation because no haematological response had followed conservative therapy. Superficial veins were inaccessible and the subclavian vein was easily cannulated by a surgeon experienced in the procedure. The platelet count was $19 \times 10^9/l$ ($19\,000/mm^3$) and since neither bleeding nor purpura was present and the patient was scheduled for transplantation allogeneic platelets were not infused. Some hours later a large haemothorax developed requiring blood and platelet transfusion. The patient subsequently died from a second cerebrovascular accident before transplantation could be performed.

The second patient was a 42-year-old woman with stage IV lymphocytic lymphoma. She was admitted with uterine bleeding and a platelet count of $19 \times 10^9/l$ ($19\,000/mm^3$) following cytotoxic chemotherapy. Since no superficial veins were accessible and no other bleeding was evident subclavian cannulation was undertaken by one of us (SCM). The procedure was uneventful, but over the next few hours a large haemothorax appeared, requiring surgical drainage.

We have now come to consider thrombocytopenia to be a relative contraindication to percutaneous subclavian cannulation, particularly in patients who have already bled. When this technique offers the only route of venous access allogeneic platelet transfusion appears a sensible prophylactic procedure.

In the light of this experience we now introduce a large-bore cannula under direct vision, particularly when long-continued venous access will be required as in patients with acute leukaemia and those undergoing bone marrow transplantation. To date we have experienced no difficulties with the latter procedure and even when retained for periods over 30 days infection has not been