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.

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[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-μg 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.

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[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.

Resistance to ampicillin in 588 strains of haemophilus

Organism	No of isolates	No (%) of β-lactamase-producing strains
H influenzae	168	13 (7·7)
H parainfluenzae	334	148 (44·3)
H haemolyticus	4	2 (50)
H parahaemolyticus	68	20 (29·4)
Other *Haemophilus* spp (X-dependent)	14	3 (21·4)
Total	588	186 (31·6)

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 (Sar[1]) (Ala[8]) 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 μg), Minovlar (norethisterone acetate 1 mg, ethinyloestradiol 50 μg), Loestrin-20 (norethisterone acetate 1 mg, ethinyloestradiol 20 μg), and Eugynon-30 (levonorgestrel 250 μg, ethinyloestradiol 30 μg).

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 μg/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 ± 2·2/99 ± 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.

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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