

meter. Our preliminary results indicate that the method is suitable for measuring factor-VIII-related antigen. The method may well have other haematological applications.

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SHORT REPORTS

Meningitis due to relatively penicillin-resistant pneumococcus

Until recently pneumococci have been regarded as invariably sensitive to benzylpenicillin, but several recent reports have described resistant strains.¹⁻⁵ We report here a case of meningitis due to a penicillin-resistant *Pneumococcus*.

Case report

A 10-month-old Oxfordshire girl presented with meningitis in December 1974 after one day's illness. Cerebrospinal fluid had $2.5 \times 10^9/l$ ($2500/mm^3$) white cells, predominantly polymorphs, and Gram-positive diplococci were seen in the smear. She was treated immediately with 300 mg benzylpenicillin given intravenously every six hours. The pneumococci isolated were initially reported as sensitive to penicillin, sulphonamide, chloramphenicol, erythromycin, and lincomycin and resistant to tetracycline, using antibiotic discs. Despite an initial improvement, the child's clinical condition deteriorated on the fourth day and the dose of penicillin was therefore increased to 600 mg four-hourly (360 mg/kg/day). A further CSF specimen taken on the eighth day showed 4.75×10^9 white cells/l ($4750/mm^3$) and pneumococci were still present. A review of the original antibiotic sensitivities showed that the zone of inhibition around the 1-unit penicillin disc was diminished compared with zone sizes produced by random control strains. The strain appeared to be fully sensitive to a 25- μ g ampicillin disc, and as a report had indicated that pneumococci relatively resistant to penicillin were sometimes sensitive to ampicillin,² ampicillin 500 mg was given six-hourly (200 mg/kg) instead of penicillin. The patient improved immediately and all subsequent CSF specimens showed a progressive fall in white cell count and were sterile. Gentamicin (30 mg) was given intravenously each day during the last two days of treatment with penicillin and for the first four days of the course of ampicillin but is unlikely to have influenced the therapeutic result because of its poor penetration into the CSF. The child was well when discharged home on the 13th day and has remained so.

Family history—The patient's father and her 5-year-old brother had recently suffered from upper respiratory infections. The patient had not received penicillin before admission to hospital, but four weeks previously her brother had received penicillin drops for an ear infection. A few days after the girl left hospital a 6-month-old boy who lived in the neighbourhood was admitted to hospital with convulsions, but meningitis was excluded. Both families were in close social contact.

Further investigations—Nose and throat swabs were taken from all members of the girl's family and from the boy neighbour and cultured for pneumococci. Multiple colonies from each positive culture were serotyped, and the minimum inhibitory concentrations (MICs) of penicillin, ampicillin,

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cloxacillin, and cephalothin for all strains were determined by the plate dilution method, using a multipoint inoculator (table).

The MIC of penicillin for the patient's CSF strain was 0.31-0.62 units/cm³ (0.19-0.37 μ g) and the MIC of tetracycline was 12.5 μ g/cm³.

Discussion

Three strains of pneumococci relatively resistant to penicillin were isolated in Australia in 1967-70, and during the same period 12% of 530 pneumococci isolated in New Guinea were similarly resistant, with MICs ranging from 0.1 to 2.0 μ g/cm³.¹⁻³ A penicillin-resistant pneumococcus has been isolated from sputum in Alberta, Canada,⁴ with MIC values almost identical to those obtained for the present CSF strain. In the USA a case of meningitis due to a penicillin-resistant pneumococcus has been reported in a 3-year-old boy with sickle cell anaemia who was cured with a 27-day course of benzylpenicillin (600 mg/kg).⁵ No similar resistant strains appear to have been recorded in Britain.

The reasons for therapeutic success in our patient are not clear, and it is unfortunate that antibiotic levels in the CSF were not measured. It is not convincingly explained by a difference in MIC, and ampicillin may have penetrated the blood-brain barrier better than penicillin in this case. The source of the penicillin-resistant strain was not discovered. Pneumococcal meningitis is unusual at this age, and at any age is usually a complication of a pre-existing infection such as otitis media or pneumonia, both of which were excluded in our patient.

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² Hansman, D, Devitt, L, and Riley, I, *British Medical Journal*, 1973, **3**, 405.

³ Hansman, D, *et al*, *Medical Journal of Australia*, 1974, **2**, 353.

⁴ Dixon, J M S, *Lancet*, 1974, **2**, 474.

⁵ Naraqi, S, Kirkpatrick, G P, and Kabins, S, *Journal of Paediatrics*, 1974, **85**, 671.

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Pneumococci isolated from patients and associates: serotypes and MIC determinations

Subject	Date of isolation	Source	Serotype	MIC			
				Penicillin (U cm ³)	Ampicillin (μ g cm ³)	Cloxacillin (μ g cm ³)	Cephalothin (μ g cm ³)
Patient	28 Dec 74	CSF before treatment	14	0.62	0.15	5.0	0.62
Patient	4 Jan 75	CSF during treatment	14	0.62	0.15	5.0	0.62
Patient	13 Feb 75	Nose	14	0.039	0.039	0.31	0.078
		Nose	7				
		Nose	19				
Brother	3 Jan 75	Nose	47	0.02	0.039	0.15	0.039
		Nose	7	0.039	0.039	0.15	0.039
Mother	13 Feb 75	Nose	11	0.039	0.039	0.31	0.15
Neighbour	3 Jan 75	Throat	11	0.039	0.039	0.31	0.15
6 control strains of pneumococci	8 Jan 75	Nose	19	0.02-0.039	0.039	0.15-0.31	0.039-0.15
				0.039		0.31	0.15
Oxford H staphylococcus							