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Drug resistance among *Escherichia coli* strains isolated from cerebrospinal fluid

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SUMMARY

One hundred and thirty-one strains of *Escherichia coli* isolated from the cerebrospinal fluid of patients in the United Kingdom were tested for resistance to 13 antimicrobial drugs. Sixty-four strains (49 %) were resistant to one or more drugs and 44 (34 %) were resistant to three or more drugs. Resistance to ampicillin, sulphonamides, streptomycin and tetracycline occurred most frequently.

INTRODUCTION

Members of the *Enterobacteriaceae* are the most common cause of meningitis in the neonate and, in most surveys, *Escherichia coli* predominates (Christie, 1980). These organisms have a wide variety of antibiotic sensitivity patterns and treatment must be guided by laboratory investigations. Nevertheless, prompt treatment is essential and is likely to begin before the infecting organism and its sensitivities are known. The choice of initial treatment should therefore be guided by a knowledge of the incidence of antimicrobial drug resistance among the likely causative organisms. In the present survey we report the incidence of resistance to commonly used drugs in a series of 131 strains of *E. coli* isolated from cerebrospinal fluid (CSF).

MATERIALS AND METHODS

Bacterial strains. One hundred and thirty-one strains of *E. coli* isolated from CSF were examined. All the strains were isolated in the United Kingdom during the period 1975–81. The exact age of the patients was not always known but 109 were known to be infants less than 3 years old and at least 69 of them were neonates.

Serotyping and K1 antigen determination. The 0 antigens of the strains were determined by the methods of Ørskov & Ørskov (1975) using antisera for *E. coli* 0 groups 01 to 0169. The presence of the K1 antigen was determined using the immunodiffusion method of Sarff *et al.* (1975) and specific bacteriophages described previously (Gross, Cheasty & Rowe, 1977).

Drug resistance tests. Initial screening for resistance to ampicillin, cephaloridine,

Table 1. *O group and K1 antigen in* 131 *isolates of* E. coli *from* CSF *in the U.K.*

O group	K1+	K1−	Total
0 rough	22	3	25
018ac	13	5	18
07	11	3	14
016	11	0	11
01	7	1	8
06	1	5	6
02	2	3	5
04	0	5	5
083	4	0	4
Others	7	28	35
Total	78	53	131

Table 2. *Drug resistance of* 131 E. coli *isolated from* CSF *in the U.K.*

Drug	(Concentration mg/l)	No.	%
Ampicillin	(8)	42	32·1
Cephaloridine	(4)	35	26·7
Cephalexin	(4)	11	8·4
Chloramphenicol	(8)	10	7·6
Furazolidone	(20)	2	1·5
Gentamicin	(4)	2	1·5
Mecillinam	(2)	27	20·1
Nalidixic acid	(20)	1	0·8
Neomycin	(8)	5	3·8
Streptomycin	(16)	31	23·7
Sulphonamides	(100)	40	30·6
Tetracycline	(16)	22	16·8
Trimethoprim	(0·5)	9	6·9
No. fully sensitive		67	51·1

cephalexin, chloramphenicol, gentamicin, neomycin/kanamycin, mecillinam, streptomycin and tetracyclines was performed by the strip diffusion method described by Anderson & Threlfall (1974). Strains found to be resistant using the strip method were further tested by an agar dilution method (Haltalin, Markley & Woodman, 1973). Resistance to sulphonamides, trimethoprim, furazolidone and nalidixic acid were also tested by the agar dilution method. The drug concentrations used in the agar dilution tests are shown in Table 2.

Drug resistance transfer and mobilization. Sixty-three resistant strains were tested for drug resistance transfer using a nalidixic acid-resistant strain of *E. coli* K12, F^-lac^+ (DEP strain no. 14R525) as the recipient (Anderson & Lewis, 1965). Where no direct transfer was detected, mobilization of resistance was attempted using auto-transferring plasmids of several different compatibility groups (Anderson, 1965).

Plasmid characterization. Autotransferring and non-autotransferring plasmids were characterized by the methods of Anderson & Threlfall (1974) and were tested for incompatibility with suitable representatives of the plasmid compatibility groups listed by Willshaw *et al.* (1980).

RESULTS

Serotyping and K1 antigen. The most common 0 groups of the strains are shown in Table 1, together with the number of strains in each 0 group which possessed the K1 antigen.

Drug resistance tests. Sixty-four strains (49 %) were resistant to one or more drugs. Resistance to ampicillin, sulphonamides, streptomycin and tetracycline occurred most frequently (Table 2). Forty-four strains (34 %) were resistant to three or more drugs.

Resistance transfer and plasmid characterization. Of the 63 strains tested for transfer of resistance, 24 (39 %) were able to transfer resistance directly and resistance could not be mobilized in any of the remaining strains. Of the 24 autotransferring plasmids, 15 were F-like, five were I-like and four belonged to compatibility group B.

DISCUSSION

Strains of *E. coli* which cause meningitis should be considered as a distinct group. Strains which cause diarrhoeal disease belong to particular serogroups (Rowe, 1979), do not possess the K1 antigen and rarely cause meningitis. Strains isolated from CSF tend to fall into a different range of serogroups and frequently possess the K1 antigen (Sarff *et al.* 1975); in the present study 78 (60 %) strains possessed this antigen. Furthermore, neonates who develop meningitis usually do so before leaving the hospital of their birth and the causative organisms may therefore be hospital-acquired. Knowledge of the incidence of drug resistance among, for example, strains of *E. coli* from the faeces of patients with diarrhoea, or from the urine of patients in the community with urinary trace infection, tell us little about the likely incidence of drug resistance in *E. coli* causing meningitis.

Neonatal meningitis caused by Gram-negative bacilli is associated with a high mortality rate and survivors often have neurological or developmental abnormalities. Antibiotic therapy is merely one factor important for survival. Nevertheless, when neonatal meningitis is diagnosed, treatment must be instituted immediately and before the bacteriological cause is certain. Two alternative regimes are usually recommended for initial treatment; either an aminoglycoside and a penicillin or chloramphenicol alone. Each of these has certain disadvantages. Aminoglycosides penetrate the blood-brain barrier poorly and even when given intrathecally may not reach the ventricular fluid adequately (McCracken & Mize, 1976). Intraventricular administration carries its own risks and has been shown to cause a higher mortality rate than systemic therapy alone (McCracken, Mize & Threlkeld, 1980). Chloramphenicol treatment, on the other hand, is accompanied by the problem of overdosage and the potentially fatal grey-baby syndrome (Burns, Hodgman & Cass, 1959). The present study suggests that neither of these regimes is likely to be frequently beset by problems of drug resistance, since resistance to gentamicin was found in only two strains and resistance to chloramphenicol was also uncommon. Nevertheless, *E. coli* strains resistant to both drugs were found and the importance of reserving these drugs for use in severe infections, such as meningitis and typhoid fever, should be emphasised. The observation that 32 %

of strains were resistant to ampicillin confirms that this drug is inadequate if used alone for the initial treatment of neonatal meningitis.

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