J Clin Pathol 1980;33:853-856

Antibiotic sensitivities of urinary pathogens, 1971-8

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SUMMARY The sensitivities of urinary pathogens from general practice and from hospital to a range of antimicrobial drugs have been recorded for the period 1971-8. There have been changes in the proportions of the different bacterial species and in their sensitivities to antibiotics. In particular, the position of ampicillin/amoxycillin and cephalosporins has deteriorated, partly because more resistant species have somewhat increased in prevalence and partly because the usually sensitive species, such as *Escherichia coli*, have become more resistant. Over the period 1971-8 the sensitivity of urinary pathogens, whether in general practice or in hospital, to co-trimoxazole and to trimethoprim has been maintained at a high level.

The organisms causing urinary tract infection (UTI) vary from place to place and from time to time, and so do their sensitivities to antibiotics. Presumably some of the variation reflects different antibiotic prescribing habits. Whatever the reasons for the differences, they determine the likely outcome of antibiotic treatment. There are, therefore, two main reasons for collecting the results of antibiotic sensitivity tests on urinary pathogens: to collect ecological information, and to predict the outcome of treatment of UTI when chemotherapy must be started before laboratory results are available.

Methods

For the last eight years, all urinary pathogens isolated from patients in the outlying hospitals in the University College Hospital group (hospital strains) and all those from samples sent to the hospital laboratory by general practitioners (general practice strains) have been examined. The numbers and types of organisms seen in 1971, 1972, and alternate years thereafter are shown in Tables 1 and 2. The proportions of all urinary pathogens from each source that were fully sensitive to a range of drugs in those years are presented in Tables 3 and 4. Sensitivity tests were performed using Stokes'[1] technique.

Received for publication 25 February 1980

Results and discussion

For a variety of reasons the mix of pathogens causing UTI in hospital is different from that in general practice. This alone will cause differences in the effectiveness of various drugs in the two situations. Two examples are the much greater prevalence of the inherently ampicillin-resistant *Klebsiella* spp. in hospital UTI, and the more frequent occurrence of the nalidixic acid-resistant staphylococci among GP urinary isolates than among hospital strains. Similarly, if the mix of bacterial pathogens causing UTI changes with time, there may be corresponding changes in the sensitivities of the bacterial flora.

In general, as can be seen from Tables 1 and 2, there has been a fairly stable relationship between the bacterial species causing UTI, whether in general

Table 1 *Organisms causing general practice UTI, 1971-8*

Organism	*1971*		*1972*		*1974*		*1976*		*1978*	
	No.	*%*	*No.*	*%*	*No.*	*%*	*No.*	*%*	*No.*	*%*
Esch. coli	340	78·5	308	73·6	451	77·1	502	73·6	454	74·9
Proteus mirabilis	40	9·2	42	10·0	38	6·5	38	5·6	30	4·9
Klebsiella-Enterobacter spp.	10	2·3	14	3·3	27	4·6	28	4·1	27	4·5
Enterococci	10	2·3	16	3·8	17	2·9	27	4·0	12	2·0
Staphylococci	22	5·1	24	5·7	41	7·0	67	9·8	59	9·7
Others	11	2·6	14	3·6	11	1·9	19	2·9	24	4·0
Total	433	100·0	418	100·0	585	100·0	681	100·0	606	100·0

Table 2 *Organisms causing UTI in hospital, 1971-8*

Organism	*1971*		*1972*		*1974*		*1976*		*1978*	
	No.	*%*	*No.*	*%*	*No.*	*%*	*No.*	*%*	*No.*	*%*
Esch. coli	306	55·4	456	55·4	382	58·3	367	49·3	339	50·7
Proteus mirabilis	63	11·4	108	13·3	68	10·4	87	11·7	71	10·6
Klebsiella-Enterobacter spp.	93	16·8	126	15·3	91	13·9	120	16·3	144	21·6
Enterococci	22	4·0	28	3·4	35	5·3	42	5·6	29	4·3
Staphylococci	18	3·3	24	2·9	21	3·2	51	6·9	18	2·7
Pseudomonas aeruginosa	15	2·7	43	5·2	25	3·8	31	4·2	19	2·8
Others	35	6·4	37	4·5	33	5·1	46	6·0	48	7·3
Total	552	100·0	822	100·0	655	100·0	744	100·0	668	100·0

Table 3 *Proportions of all urinary pathogens fully sensitive to various antimicrobials in general practice, 1971-8*

Drug	*Percentage of strains fully sensitive (ranking)*				
	1971 n = 433	*1972 n = 418*	*1974 n = 585*	*1976 n = 681*	*1978 n = 606*
Ampicillin/Amoxycillin	88·2 (4)	84·4 (6)	81·2 (7)	80·9 (7)	79·4 (7)
Cephalosporin	87·5 (5)	85·1 (4)	83·1 (6)	81·6 (6)	84·5 (6)
Colistin sulphamethate	85·0 (7)	82·3 (7)	87·9 (4)	85·0 (4)	90·3 (4)
Co-trimoxazole	96·6 (1)	96·4 (1)	93·2 (1)	96·7 (1)	97·0 (1)
Nalidixic acid	90·7 (3)	87·6 (3)	86·0 (5)	83·0 (5)	85·5 (5)
Nitrofurantoin	85·6 (6)	85·1 (4)	88·4 (3)	90·1 (3)	90·6 (3)
Sulphonamide	76·4 (8)	73·1 (8)	73·7 (8)	78·1 (8)	73·6 (9)
Tetracycline	72·5 (9)	69·6 (9)	73·6 (9)	74·5 (9)	75·7 (8)
Trimethoprim	94·0 (2)	94·4 (2)	89·5 (2)	92·7 (2)	90·9 (2)

Table 4 *Proportions of all urinary pathogens fully sensitive to various antimicrobials in hospital, 1971-8*

Drug	*Percentage of strains fully sensitive (ranking)*				
	1971 n = 552	*1972 n = 882*	*1974 n = 655*	*1976 n = 744*	*1978 n = 668*
Ampicillin/Amoxycillin	66·1 (7)	64·2 (7)	61·2 (7)	53·7 (9)	51·2 (9)
Cephalosporin	69·9 (6)	68·1 (6)	63·2 (6)	57·2 (7)	58·2 (8)
Colistin sulphamethate	76·8 (4)	78·6 (4)	78·0 (2)	74·7 (4)	80·4 (3)
Co-trimoxazole	83 9 (2)	81·7 (2)	76·2 (3)	81·2 (1)	82·5 (2)
Nalidixic acid	84·8 (1)	82·6 (1)	80·6 (1)	75·3 (3)	85·5 (1)
Nitrofurantoin	70·3 (5)	71·5 (5)	72·7 (4)	73·2 (5)	74·4 (4)
Sulphonamide	61·9 (8)	62·2 (8)	57·4 (8)	58·9 (6)	58·5 (7)
Tetracycline	55·8 (9)	56·1 (9)	48·6 (9)	54·0 (8)	59·3 (6)
Trimethoprim	79·9 (3)	80·7 (3)	71·5 (5)	76·4 (2)	74·1 (5)

practice or in hospital. In general practice, the main changes have been a reduction of *Proteus mirabilis* (which is resistant, or moderately resistant, to nitrofurantoin and is resistant to colistin and the tetracyclines) and an increase in staphylococci (which are resistant to nalidixic acid) in the last eight years. It is not known why staphylococcal isolates have increased in urinary material but the explanation does not lie in increased laboratory awareness of the possible pathogenic role of micrococci. In hospital there has been an increase in *Klebsiella-Enterobacter* spp. (which are inherently ampicillin-resistant) during the period of the study.

The general practice strains (Table 3) are much more antibiotic-sensitive than the hospital strains (Table 4). The main changes in general practice (Table 3) have been the steady decline in ampicillin/amoxycillin sensitivity (88·2% sensitive in 1971 and 79·4% in 1978) and some decline in nalidixic acid sensitivity, reflecting the increased number of staphylococci isolated over the review period. The sensitivity of GP strains to trimethoprim and to co-trimoxazole has been maintained throughout the period, co-trimoxazole being the 'best guess' for unguided chemotherapy in every one of the eight years from 1971 to 1978.

Among the hospital strains (Table 4), ampicillin/amoxycillin sensitivity has declined from 66·1% sensitive in 1971 to 51·2% sensitive in 1978, and cephalosporin from 69·9% to 58·2% between 1971 and 1978. Despite some reduction in trimethoprim sensitivity in the review period, the sensitivity of hospital strains to co-trimoxazole has hardly changed, and this drug has been first, second, or third 'best guess' in every one of the eight years reviewed.

In an attempt to remove the distorting effect of varying proportions of different bacterial species, Tables 5 and 6 show an analysis of one organism only, the usually antibiotic-sensitive *Esch. coli*, which is the commonest pathogen causing UTI, whether in general practice or in hospital. Examination of Table 5 shows that general practice *Esch. coli* from UTI has on the whole become less sensitive to ampicillin/amoxycillin and cephalosporins and perhaps sulphonamides but not significantly so to other drugs, including trimethoprim and co-trimoxazole. Similar examination of *Esch. coli* from hospital UTI (Table 6) again shows increased resistance to ampicillin/amoxycillin, cephalosporins, and sulphonamides, but not to other drugs, including trimethoprim and co-trimoxazole. Thus it can be seen that the declining position of ampicillin/amoxycillin and the cephalosporins is due partly to an increased prevalence of more resistant bacterial species, and partly to increasing resistance within bacterial species.

A report of the first four years' findings of this study[2] indicated that some of the antibiotic choices implied in the observations were more apparent than real, because trimethoprim was at the time not available independently of sulphonamide, and because colistin has to be given parenterally, which is often not convenient. Trimethoprim is now available for use on its own. A choice made solely on the basis of breadth of antimicrobial spectrum in general practice in 1978 would rank the drugs in decreasing order of preference as follows: co-trimoxazole, trimethoprim, nitrofurantoin, nalidixic acid, a cephalosporin, amoxycillin, a tetracycline, a sulphonamide. Clearly, the choice of treatment would not be made solely on this basis, since considerations such as frequency of administration, nature and frequency of side effects, acceptability to the patient, ecological effects, and cost must be taken into account. This ranking in 1978 is almost identical with that which applied in 1974.

In hospital, parenteral therapy is more feasible than in general practice, although oral treatment is preferred. The choice of treatment, if made solely on the basis of breadth of spectrum in 1978, would rank the drugs in decreasing preference thus: nalidixic acid, co-trimoxazole, colistin, nitrofurantoin, trimethoprim, a tetracycline, a sulphonamide, a cephalosporin, amoxycillin. There are no very striking changes at the top of this list compared with the situation in 1974. Sulphonamides and tetracyclines have been moved from the bottom of the list by the arrival there of amoxycillin and the cephalosporins.

There has been only a very slight decline in the sensitivity of urinary pathogens, whether in general practice or in hospital, to both trimethoprim and sulphonamides in the period 1971-8. This has not had any deleterious effect on the usefulness of co-trimoxazole in either environment. How sensitivities of urinary isolates will be affected by the marketing in the United Kingdom in 1979 of trimethoprim on its own remains to be seen.

It can be seen from the results here presented that, despite some slow deterioration, the generality of urinary pathogens remains sensitive to many antibiotics. Antibiotic resistance is rarely a bar to effective treatment. The time may, however, have come to start testing newer products such as mecillinam to assess their usefulness.

I am grateful to my colleagues in the microbiology

Table 5 *Percentage of urinary* Esch. coli *from hospital practice 1971-8 fully sensitive to various antimicrobials*

Year	*No. of strains*	*Ampicillin/ Amoxycillin*	*Cephalosporin*	*Colistin sulphamethate*	*Co-trimoxazole*	*Nalidixic acid*	*Nitrofurantoin*	*Sulphonamide*	*Tetracycline*	*Trimethoprim*
1971	340	91·4	91·2	100	99·2	99·1	97·6	77·3	81·2	98·5
1972	308	88·9	88·7	99·6	99·6	99·0	97·0	75·3	81·2	99·6
1974	451	85·6	85·6	100	98·9	97·8	98·3	74·3	80·0	97·9
1976	502	83·4	84·1	100	98·4	98·4	97·7	79·4	80·5	97·4
1978	454	86·3	87·0	100	98·2	99·3	98·2	72·5	81·5	96·5

Table 6 *Percentage of urinary* Esch. coli *from hospital practice 1971-8 fully sensitive to various antimicrobials*

Year	*No. of strains*	*Ampicillin/ Amoxycillin*	*Cephalosporin*	*Colistin sulphamethate*	*Co-trimoxazole*	*Nalidixic acid*	*Nitrofurantoin*	*Sulphonamide*	*Tetracycline*	*Trimethoprim*
1971	306	84·4	86·6	100	97·0	98·1	95·7	75·3	75·8	96·8
1972	456	81·3	81·9	100	95·2	98·4	97·7	68·9	78·3	96·8
1974	382	74·3	74·3	100	93·4	97·1	97·8	66·4	67·8	91·7
1976	367	68·3	67·8	99·8	96·1	97·1	97·1	64·6	61·2	96·1
1978	339	73·2	73·5	100	95·9	97·9	97·1	69·6	73·5	94·7

laboratories who have cheerfully undertaken extra work on these studies. The work was supported by a grant from Messrs F Hoffmann-La Roche and Co, Basel, Switzerland.

References

[1] Stokes EJ. *Clinical Bacteriology*. 3rd ed. London: Arnold, 1968;179.

[2] Grüneberg RN. Susceptibility of urinary pathogens to various antimicrobial substances; a four-year study. *J Clin Pathol* 1976;**29**:292.

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The August 1980 Issue

THE AUGUST 1980 ISSUE CONTAINS THE FOLLOWING PAPERS