*J. clin. Path.*, 1976, **29**, 292-295

# Susceptibility of urinary pathogens to various antimicrobial substances: a four-year study

R. N. GRÜNEBERG

*From the Department of Microbiology, University College Hospital, London WC1*

SYNOPSIS The results of testing all urinary pathogens from general practice and hospital practice for their sensitivity to a range of antimicrobial agents over the four years 1971-74 are presented. The changes observed in each situation with the passage of time are discussed. Resistance has become more frequent to those drugs to which resistance is commonly R factor-mediated. Less change has been observed in resistance to other antimicrobial agents.

A clinician wishing to make a choice of antimicrobial drugs for the treatment of urinary tract infections requires information about the patient, the infecting organism, and the drugs available. The most important piece of information required about the urinary pathogen is its susceptibility to a range of antimicrobial substances. Choice of treatment should be made after the sensitivities of the causative organisms have been determined *in vitro*, but there will always be circumstances in which sensitivities cannot be determined (as in domiciliary practice remote from laboratories) or when the results of tests cannot be obtained before the start of treatment. In such circumstances it is important to have up-to-date information on the sensitivities of urinary pathogens in general, so that a 'best guess' choice can be made. Since variation, both geographical and temporal, can be expected in the sensitivity of urinary pathogens, clinical laboratories should keep a continuous record of their findings in this field. This paper reports the findings in one laboratory in London in the years 1971-74.

## Methods

Since the beginning of 1971 records have been kept of the antibacterial sensitivities of all urinary pathogens isolated by the Bacteriology Laboratory at St. Pancras Hospital. The urine samples are derived from various sources:

(1) Patients in the wards or attending outpatient clinics at the following hospitals: St. Pancras Hospital, The Hospital for Tropical Diseases, and the National Temperance Hospital. No attempt has been made to differentiate between inpatient- and outpatient-derived strains, all being classified as 'hospital strains'.

(2) Patients attending general practitioners in the neighbourhood whose specimens are sent to the laboratory. All these strains are classified as 'general practice strains'.

The diagnostic methods used are the same for all urine samples. A urine sample is regarded as showing significant bacteriuria if it is shown to contain more than 100 000 organisms/ml of a single type by a surface viable counting method on plates of layered blood agar and of cysteine-lactose electrolyte-deficient medium (CLED). Antibacterial sensitivities are determined using Stokes' method (1968) in which the zone size given by the test strain is compared on every plate with that given by a known sensitive control organism. The culture medium is either (in the case of sulphonamide, trimethoprim or co-trimoxazole) 5% lysed blood plus 5% whole blood layered over Oxoid DST medium or (in the case of all other drugs) 5-10% whole blood layered over Oxoid DST medium.

## Results

The types of organisms isolated from infected urines from general practice in the years 1971-74 are shown in table I; table II presents similar observations from hospital practice. The proportions of all urinary pathogens fully sensitive to various antimicrobials in general practice in the years 1971-74 are shown in table III, which also ranks the antimicrobials in order of *in vitro* effectiveness for each year. Table IV presents similar observations for the urinary pathogens from hospital practice. Table

Received for publication 23 September 1975

| *Organism* | *1971* | | *1972* | | *1973* | | *1974* | |
|---|---|---|---|---|---|---|---|---|
| | *No.* | *%* | *No.* | *%* | *No.* | *%* | *No.* | *%* |
| *Escherichia coli* | 340 | 78·5 | 308 | 73·6 | 390 | 76·0 | 451 | 77·1 |
| *Proteus mirabilis* | 40 | 9·2 | 42 | 10·0 | 40 | 7·8 | 38 | 6·5 |
| *Klebsiella-Enterobacter* spp. | 10 | 2·3 | 14 | 3·3 | 22 | 4·3 | 27 | 4·6 |
| Enterococci | 10 | 2·3 | 16 | 3·8 | 12 | 2·8 | 17 | 2·9 |
| Staphylococci | 22 | 5·1 | 24 | 5·7 | 34 | 6·6 | 41 | 7·0 |
| *Pseudomonas aeruginosa* | 4 | | 4 | | 3 | | 2 | |
| All other organisms | 7 | | 10 | | 12 | | 9 | |
| Total | 433 | 100 | 418 | 100 | 513 | 100 | 585 | 100 |

Table I *Organisms isolated from general practice urinary tract infections, 1971-74*

| *Organism* | *1971* | | *1972* | | *1973* | | *1974* | |
|---|---|---|---|---|---|---|---|---|
| | *No.* | *%* | *No.* | *%* | *No.* | *%* | *No.* | *%* |
| *Escherichia coli* | 306 | 55·4 | 456 | 55·4 | 312 | 52·3 | 382 | 58·3 |
| *Proteus mirabilis* | 63 | 11·4 | 108 | 13·3 | 92 | 15·4 | 68 | 10·4 |
| *Klebsiella-Enterobacter* spp. | 93 | 16·8 | 126 | 15·3 | 98 | 16·4 | 91 | 13·9 |
| Enterococci | 22 | 4·0 | 28 | 3·4 | 29 | 4·8 | 35 | 5·3 |
| Staphylococci | 18 | 3·3 | 24 | 2·9 | 18 | 3·0 | 21 | 3·2 |
| *Pseudomonas aeruginosa* | 15 | 2·7 | 43 | 5·2 | 14 | 2·3 | 25 | 3·8 |
| *Candida* spp. | 11 | 2·0 | 4 | 0·5 | 8 | 1·3 | 11 | 1·7 |
| All other organisms | 24 | | 33 | | 25 | | 22 | |
| Total | 552 | 100 | 822 | 100 | 596 | 100 | 655 | 100 |

Table II *Organisms isolated from hospital urinary tract infections, 1971-74*

| *Drug* | *Percentage of strains fully sensitive (ranking)* | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | *1971 (433 strains)* | | *1972 (418 strains)* | | *1973 (513 strains)* | | *1974 (585 strains)* | |
| Ampicillin | 88·2 | (4) | 84·4 | (6) | 82·4 | (7) | 81·2 | (7) |
| Co-trimoxazole | 96·6 | (1) | 96·4 | (1) | 94·9 | (1) | 93·2 | (1) |
| Cephaloridine | 87·5 | (5) | 85·1 | (4) | 86·6 | (5) | 83·1 | (6) |
| Colistin sulphamethate | 85·0 | (7) | 82·3 | (7) | 86·8 | (4) | 87·9 | (4) |
| Nalidixic acid | 90·7 | (3) | 87·6 | (3) | 88·2 | (3) | 86·0 | (5) |
| Nitrofurantoin | 85·6 | (6) | 85·1 | (4) | 85·5 | (6) | 88·4 | (3) |
| Sulphonamide | 76·4 | (8) | 73·2 | (8) | 75·6 | (8) | 73·7 | (8) |
| Tetracycline | 72·5 | (9) | 69·6 | (9) | 73·3 | (9) | 73·6 | (9) |
| Trimethoprim | 94·0 | (2) | 94·4 | (2) | 90·0 | (2) | 89·5 | (2) |

Table III *Percentage of all urinary pathogens from general practice, 1971-74, fully sensitive to various antimicrobials*

| *Drug* | *Percentage of strains fully sensitive (ranking)* | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | *1971 (552 strains)* | | *1972 (822 strains)* | | *1973 (596 strains)* | | *1974 (655 strains)* | |
| Ampicillin | 66·1 | (7) | 64·2 | (7) | 66·6 | (8) | 61·2 | (7) |
| Co-trimoxazole | 83·9 | (2) | 81·7 | (2) | 82·2 | (1) | 76·2 | (3) |
| Cephaloridine | 69·9 | (6) | 68·1 | (6) | 68·7 | (5) | 63·2 | (6) |
| Colistin sulphamethate | 76·8 | (4) | 78·6 | (4) | 74·1 | (3) | 78·0 | (2) |
| Nalidixic acid | 84·8 | (1) | 82·6 | (1) | 81·6 | (2) | 80·6 | (1) |
| Nitrofurantoin | 70·3 | (5) | 71·8 | (5) | 68·3 | (6) | 72·7 | (4) |
| Sulphonamide | 61·9 | (8) | 62·2 | (8) | 67·7 | (7) | 57·4 | (8) |
| Tetracycline | 55·8 | (9) | 56·1 | (9) | 53·4 | (9) | 48·6 | (9) |
| Trimethoprim | 79·9 | (3) | 80·7 | (3) | 73·9 | (4) | 71·5 | (5) |

Table IV *Percentage of all urinary pathogens from hospital practice, 1971-74, fully sensitive to various antimicrobials*

| Year | No. of Strains | Drug | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | Nitro-furantoin | Sulphon-amide | Ampicillin | Trimetho-prim | Colistin sulpha-methate | Nalidixic acid | Tetra-cycline | Cepha-loridine | Co-tri-moxazole |
| 1971 | 340 | 97·6 | 77·3 | 91·4 | 98·5 | 100 | 99·1 | 81·2 | 91·2 | 99·2 |
| 1972 | 308 | 97·0 | 75·3 | 88·9 | 99·6 | 99·6 | 99·0 | 81·2 | 88·7 | 99·6 |
| 1973 | 390 | 96·9 | 75·1 | 87·4 | 97·9 | 100 | 98·4 | 79·3 | 87·7 | 99·0 |
| 1974 | 451 | 98·3 | 74·3 | 85·6 | 97·9 | 100 | 97·8 | 80·0 | 85·6 | 98·9 |

Table V *Percentage of urinary* Esch. coli *from general practice urinary tract infections, 1971-74, fully sensitive to various antimicrobials*

| Year | No. of Strains | Drug | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | Nitro-furantoin | Sulphon-amide | Ampicillin | Trimetho-prim | Colistin sulpha-methate | Nalidixic acid | Tetra-cycline | Cepha-loridine | Co-tri-moxazole |
| 1971 | 306 | 95·7 | 69·6 | 84·4 | 96·8 | 100 | 98·1 | 75·8 | 86·6 | 97·0 |
| 1972 | 456 | 97·7 | 68·9 | 81·3 | 96·8 | 100 | 98·4 | 78·3 | 81·9 | 95·2 |
| 1973 | 312 | 96·5 | 78·6 | 82·4 | 97·2 | 99·7 | 100 | 76·9 | 83·0 | 98·1 |
| 1974 | 382 | 97·8 | 66·4 | 74·3 | 91·7 | 100 | 97·1 | 67·8 | 74·3 | 93·4 |

Table VI *Percentage of urinary* Esch. coli *from hospital urinary tract infections, 1971-74, fully sensitive to various antimicrobials*

V and VI show the antimicrobial sensitivities of urinary *Escherichia coli* alone from general practice and hospital practice, respectively.

## Discussion

The organisms isolated from urinary infections in general practice and in hospital are shown in tables I and II respectively. For each source of material, the distribution of organisms shows little variation from year to year, and the proportions of each are typical of general experience and similar to published series (McAllister *et al*, 1971; Gillespie *et al*, 1971). There are substantial differences in the proportions of infections caused by various organisms in general practice and in hospital. Thus, the usually antibiotic-sensitive *Esch. coli* was responsible for 73-78% of infections in general practice but only 52-58% of hospital urinary tract infections. This difference in the species distribution could be the underlying cause of the difference in antibiotic sensitivity of the infecting urinary flora in the two situations. An analysis of the degree of antibiotic resistance of *Esch. coli* causing urinary tract infection in general practice and in hospital practice is presented in tables V and VI respectively. It can be seen from these tables that there are still differences in antibiotic sensitivity in the two situations when organisms of the same species are compared, but that the major cause of differences in sensitivity is variation in species distribution. Thus, in 1974, 85·6% of *Esch. coli* causing urinary tract infection in general practice were sensitive to ampicillin, compared with 74·3% sensitive in hospital. Comparing all urinary pathogens in 1974, 81·2% of general practice strains were sensitive to ampicillin whereas only 61·2% of hospital strains were sensitive.

Tables III and IV show that urinary pathogens, whether in general practice or in hospital, are in general very antibiotic-sensitive. Urinary *Esch. coli* are more sensitive to antimicrobials than are most urinary organisms, despite their potentiality for the accumulation of plasmid-mediated resistances (R factors). In general practice the provisional treatment of a clinically diagnosed urinary tract infection with any of the antimicrobials tested (table III) could readily be justified. Some of these choices are more apparent than real: trimethoprim is not used independently of sulphonamide, and colistin and cephaloridine require parenteral administration which is often not convenient in general practice. A choice made solely on the basis of breadth of antimicrobial spectrum in general practice in 1974 would rank the drugs in decreasing order of preference thus: co-trimoxazole, nitrofurantoin, nalidixic acid, a cephalosporin, ampicillin, a sulphonamide, a tetracycline. The choice of treatment would not be made solely on these grounds, of course, since considerations such as frequency of administration, nature and frequency of side effects, acceptability to the patient, and cost must be taken into account.

In hospital practice the choice of urinary antimicrobial agents (table IV) is wider, since parenteral treatment can be undertaken, although oral therapy

is usually preferred. The choice of initial treatment before laboratory results are available, if based solely on the antimicrobial spectrum in 1974 (table IV) would be, in decreasing order of preference: nalidixic acid, colistin, co-trimoxazole, nitrofurantoin, a cephalosporin, ampicillin, a sulphonamide, a tetracycline. It should be repeated that the choice would not be made solely on these grounds.

In view of the concern felt about the possibility of deterioration in the efficacy of antimicrobial agents in the face of plasmid-mediated resistance (R factors), it is interesting to note (tables III to VI) the relatively small changes in sensitivities observed in the four years 1971-74. In the treatment of general practice urinary pathogens of all kinds only ampicillin has shown a marked decline, from 88·2% to 81·2% of all strains fully sensitive. When urinary *Esch. coli* from general practice is considered alone (table V) it can be seen that the decline of ampicillin sensitivity is again shown to be from 91·4% to 85·6%, but that it is mirrored by a similar decline of sensitivity to cephalosporins, from 91·2% to 85·6%. In hospital (table VI) the urinary *Esch. coli* shows similar declines in sensitivity, between 1971 and 1974, in the case of ampicillin (84·4% to 74·3%), cephalosporins (86·6% to 74·3%), and tetracyclines (75·8% to 67·8%). Resistances to these three agents, ampicillin, cephalosporins, and tetracyclines, may all be plasmid-mediated. In general (tables V and VI), the susceptibility of urinary pathogens to antimicrobial agents, resistance to which is not plasmid-mediated (nitrofurantoin and nalidixic acid), has been maintained with little change. In general practice there has been no significant change in the proportion of urinary *Esch. coli* fully sensitive to trimethoprim and therefore also sensitive to co-trimoxazole (table V).

It has been shown that resistance to trimethoprim can be plasmid-mediated (Fleming *et al*, 1972) but this has not been reflected in the general practice urinary flora. Table VI, however, shows a decline in the sensitivity of urinary *Esch. coli* in this hospital (where the R factor mediating trimethoprim resistance was first recognized) from 96·8% to 91·7% between 1971 and 1974. This experience is not general since most hospitals do not at present have the R factor concerned (Jobanputra and Datta, 1974). Experience in this hospital shows, so far, that antibiotic prescribing policies, limiting the use of sulphonamide, ampicillin, and co-trimoxazole, are capable of eradicating R factor-mediated trimethoprim resistance from the hospital flora (Grüneberg *et al*, 1975).

It appears, therefore, that there is a slow change in the pattern of susceptibility of urinary pathogens to various antimicrobial agents, that this change may be more marked in the case of drugs, resistance to which is R factor-mediated, but that this situation can be modified by appropriate action. Urinary pathogens are still generally sensitive to most antibiotics, and in nearly all cases there is a wide choice of chemotherapeutic agents.

**References**

Fleming, M. P., Datta, N., and Grüneberg, R. N. (1972). Trimethoprim resistance determined by R factors. *Brit. med. J.*, **1**, 726-728.

Gillespie, W. A., Lee, P. A., Linton, K. B., and Rowland, A. J. (1971). Antibiotic resistance of coliform bacilli in urinary infection acquired by women outside hospital. *Lancet*, **2**, 675-677.

Grüneberg, R. N., Leakey, A., Bendall, M. J., and Smellie, J. M. (1975). The bowel flora in urinary tract infection: the effect of chemotherapy with special reference to co-trimoxazole. *Kidney int.* **8**, suppl. 4, p. 5122.

Jobanputra, R. S., and Datta, N. (1974). Trimethoprim R factors in enterobacteria from clinical specimens. *J. med. Microbiol.*, **7**, 169-177.

McAllister, T. A., Percival, A., Alexander, J. G., Boyce, J. M. H., Dulake, C., and Wormald, P. J. (1971). Multicentric study of sensitivities of urinary tract pathogens. *Postgrad. med. J.*, **47**, September Supplement, 7-14.

Stokes, E. J. (1968). *Clinical Bacteriology*, 3rd ed., p. 179. Arnold, London.