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The bacteriological examination of urine: a computer-aided study

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SUMMARY

For 6 months details of every patient who had his or her urine sent to a laboratory for bacteriological examination and the result of such examination were entered on a computer-card. A total of 15,606 cards were completed with information in code recording the sex and age of a patient, the origin of the request, the presence or absence in the urine of an excess of protein or cells, the culture result and the name of any significant organism isolated together with its sensitivity to various antimicrobial drugs. This information was interrelated in a computer, and in some cases the resulting numerical details were expressed as rates so as to eliminate the effect of uneven sex and age distribution. In this way the occurrence of urinary tract infection and the type of infecting organism in persons of either sex at various ages was examined according to whether the patient was in hospital or general practice. The sensitivity pattern of each type of significant organism isolated was established according to its source. The association between patients of either sex and various ages who had, or did not have, bacteriologically evident infections and the presence in their urine of an inflammatory exudate was investigated. Finally, the capacity of each type of infecting organism to produce such an exudate was estimated.

It was shown that hospital and general practice experience of urinary tract infections differed widely, with regard both to the age and sex distribution of those suffering from it, and to the causative organisms concerned and their sensitivities to antimicrobial drugs. It is suggested that these differences were so great that conclusions drawn from any study of this subject conducted in one of the two areas cannot be applied to the other, and that those derived from a mixture of the two will vary according to the relative sizes of each of the components.

INTRODUCTION

A computer-card was punched with coded details of each urine specimen sent to the Hospital Microbiology and Public Health Laboratory, Plymouth, during the 6 months from October 1972 to March 1973. No publicity was given to the study so that there would be no change in the way specimens were submitted. They were examined by simple methods appropriate in a busy laboratory, and the cards

which resulted were put into an IBM 1130 computer, which sorted the information and extracted certain relations.

The laboratory serves 400,000 people, more than half of whom live in the City of Plymouth. Specimens are accepted from hospitals and from general practice, and as the nearest similar laboratory is 40 miles away it may be assumed that all bacteriology for this population is done in one place. It was therefore possible to apply population statistics for the area to the information collected and so allow comparisons to be made of the incidence of infection and distribution of infecting organisms in patients of either sex at various ages.

METHODS

Clean-catch or mid-stream urine specimens were passed, or were transferred immediately after passing, into sterile plastic screw-capped 1 fl-oz. (28 ml.) bottles, each containing 0·5 g. of boric acid powder (Porter & Brodie, 1969). They were brought to the laboratory by hand, or sent there by post or by public or other transport, depending on the distance and the communications available. In many cases specimens were examined within 4 hr. of being passed, but some which came through the post were as much as 36 hr. old by the time they were dealt with.

Examination began by centrifuging 7 ml. of urine at 500 *g* in a 12 × 100 mm. glass tube for 7 min. The supernatant resulting was decanted, and the deposit resuspended in the amount of urine adhering to the glass by flicking the bottom of the tube. A drop of this was examined microscopically under a coverslip, at first at low power. A representative area was chosen and pus cells were counted in not less than five fields each of 0·31 mm. diameter, at a magnification of 280. The average number of cells per field was graded into one of four classes for reporting, though for the computer four or less cells were recorded as negative, and five or more as positive. Each specimen was tested for the presence of protein by adding 3 vol. of 3% sulphosalicylic acid to 1 vol. of urine; any turbidity which developed was compared with proteinometer standards (Gallenkamp Ltd). Four degrees of positivity were reported, but for the computer less than 10 mg. of protein per 100 ml. was recorded as negative, and more than this as positive. When indicated a direct sensitivity test was done by spreading about 0·03 ml. (three calibrated loopfuls) of urine on 'Wellcotest' sensitivity-test agar (Wellcome Reagents Ltd) in a Petri dish and adding one of the 'Multodisks' described below. Whether a direct sensitivity was done or not, a half Petri dish of cystine–lactose–electrolyte-deficient (CLED) medium (Mackey & Sandys, 1966) was spread with 0·01 ml. urine, using a fused calibrated loop. After overnight incubation the dishes were examined and the results on CLED medium were reported and coded according to the following conventions:

Culture negative	No growth	No colonies in the spread area
	No significant growth	Less than 100 colonies in the spread area
	Culture of doubtful significance	More than 100 colonies made up of two or more different organisms

Culture positive	Single pathogen	More than 100 colonies* in pure or near pure culture
	Mixed growth of two or three pathogens	More than 100 colonies each of two or rarely three organisms
	Mixed growth with one predominant pathogen	More than 100 colonies of the predominant organism, together with a mixed background growth

* Urines aspirated suprapubically were reported as positive if they gave any growth. Specimens collected via an indwelling catheter were regarded as positive if they gave more than 10 colonies when cultured as described.

Organisms leading to positive culture reports were divided into 12 named types which were separately coded for entry on computer-cards, according to the following criteria:

Gram-negative bacilli	
1. *Escherichia coli*	Characteristic colonial morphology, lactose positive, indole positive
2. *Klebsiella* spp.	Characteristic colonial morphology, lactose positive, indole negative
3. *Proteus* spp.	Characteristic colonial morphology, lactose negative, strong urease production
4. Paracolons	Variable colonial morphology, lactose negative, negative or weak urease production
5. Coliforms	Variable colonial morphology, lactose positive
6. *Pseudomonas* spp.	Characteristic colonial morphology and pigment (oxidase positive)
Gram-positive cocci	
7. Faecal streptococci	Characteristic colonial morphology (catalase negative)
8. *Staphylococcus albus*	Characteristic colonial morphology, coagulase negative, novobiocin sensitive (catalase positive)
9. *Micrococcus* spp.	Characteristic colonial morphology, coagulase negative, novobiocin resistant (catalase positive)
10. *Staphylococcus aureus*	Characteristic colonial morphology, coagulase positive (catalase positive)
Others	
11. *Candida* spp.	Characteristic morphology
12. Other organisms	

(Criteria in parentheses were only used in cases of doubt.)

Where a direct sensitivity test had been done a report was issued after 24 hr. but to code the organism for the computer it was subjected to any additional tests needed so as to allocate it to one of the types listed.

Strains other than *Candida* spp. from positive cultures were tested for their sensitivity to a selected group of antimicrobial drugs. Where a direct sensitivity had not been done, representative colonies of the organism were suspended in peptone-water to an optical density judged by eye as being sufficient to produce a semi-confluent growth on sensitivity-test agar inoculated with about 0·03 ml. of the suspension, spread with a bent glass rod. A 'Multodisk' (Oxoid Ltd) was added, bearing the antimicrobial drugs listed below, at the concentrations noted. A disk with the first eight drugs was used for the Gram-negative types, excluding

Pseudomonas spp., and for faecal streptococci. A second disk from which the next two antibiotics on the list were reported routinely was used for the remaining Gram-positive organisms. The last three antibiotics on the list were used for strains of *Pseudomonas* spp.:

Cotrimoxazole	25 μg.	Tetracycline	50 μg.
Kanamycin	30 μg.	Penicillin	1·5 units
Cephalexin	30 μg.	Erythromycin	10 μg.
Nitrofurantoin	200 μg.	Gentamicin	10 μg.
Nalidixic acid	30 μg.	Colistin	200 μg.
Ampicillin	25 μg.	Carbenicillin	100 μg.
Sulphonamide	500 μg.		

After about 18 hr. incubation, sensitivity results were read according to the sizes of the zones of inhibition of bacterial growth produced by the drugs. These were measured by eye where the results were clear-cut or by using a ruler when the size of any zone was close to the measurement separating sensitive from resistant strains. The reading for each drug was reported and coded as sensitive or resistant according to whether the zone was larger or smaller than the critical size decided for the organism concerned. This had been determined for each drug by testing a large number of isolates together with a known sensitive reference strain of each type of organism under the same conditions as used in the test. The zone sizes measured in this way usually had a bimodal distribution corresponding to sensitive and resistant organisms, and the critical size dividing sensitive from resistant strains was chosen at a point between the two peaks. When a drug failed to produce a biphasic curve when tested in this way its minimum inhibitory concentration against a number of the organisms concerned was measured, and the critical zone size chosen by reference to the results. The 'Multodisk' used for testing Gram-positive species included novobiocin (5 μg.). This antibiotic was used to divide coagulase-negative staphylococci into *Staphylococcus albus* (sensitive) and *Micrococcus* spp. (resistant) (Mitchell & Baird-Parker, 1967) for this study.

In addition to the laboratory results other information was entered on the computer-cards. This included the patient's sex and age, the latter coded in one of the eight groups shown in the 'Results' section, or where necessary as 'not given'. The origin of the specimen, from a medical in-patient (MIP), surgical in-patient (SIP), hospital out-patient (OP), or from the patient of a general practitioner (GP), was added.

It did not prove possible to identify second or third specimens coming from the same patient during the trial, so duplicate or multiple entries were not excluded from the computer except in the case of those sent for examination only for *Mycobacterium tuberculosis*. Some clinicians regularly re-examined patients' urine after treatment, and a few patients had repeated tests carried out on their urine during the 6 months of the survey.

Before the beginning of the study proper, the whole system was put into operation for a month to practise methods and to prove the computer programme. Thereafter the cards produced were summarized monthly in the computer, and the

Table 1. *Details of urines examined, according to the sex of the patients and the sources of the specimens*

Source		Males	Females	Totals	
Hospital	MIP*	1,504	2,667	4,171	10,044 (64·4)
	SIP*	1,935	2,320	4,255	
	OP*	458	1,160	1,618	
GP*		1,208	4,354	5,562	(35·6)
Totals		5,105 (32·7)	10,501 (67·3)	15,606	

* (Percentages are given in parentheses. * MIP, Medical in-patient; SIP, surgical in-patient; OP, out-patient; GP, patient of a general practitioner.)

Table 2. *The distribution, percentage, of the six varieties of culture result which led to positive or negative reports*

Result reported	Percentage			
	Males	Females	Both	
Culture negative				
No growth	67·8	51·6	57·0	80·2
No significant growth	16·4	26·1	22·9	
Culture of doubtful significance	0·3	0·3	0·3	
Culture positive				
Single pathogen	13·2	19·2	17·2	19·8
Mixed growth with two or three pathogens	1·4	1·3	1·3	
Mixed growth with one predominant pathogen	0·9	1·5	1·3	

results used to check the internal reproducibility of the study, which proved to be high. Full interrelationships were established after the third and the sixth months.

RESULTS

A total of 15,606 specimens of urine were examined and were recorded on computer-cards during the study. Two-thirds were from female patients and one-third were sent by general practitioners; Table 1 gives their sources more completely. The distribution of the six defined types of culture result is given in Table 2. In all, one specimen in five was culture-positive. This ratio held almost exactly when three of the four sources were considered individually, but specimens from hospital out-patients produced only one positive in eight examined. Urines from females were positive more often than those from males, and they had a higher incidence of results indicating contamination.

Fig. 1 shows the rate at which examinations of urine were carried out and positive results found in various groups of patients defined by sex and age. The actual numbers observed have been converted into rates per 10,000, using the Registrar General's population figures (*The Registrar General's Statistical Review of England and Wales for the Year 1970*) for the area as a basis. In Table 3 the number of organisms of each type which led to a positive culture report is given, first as a simple total and then as a rate of such isolations per 1000 patients having their

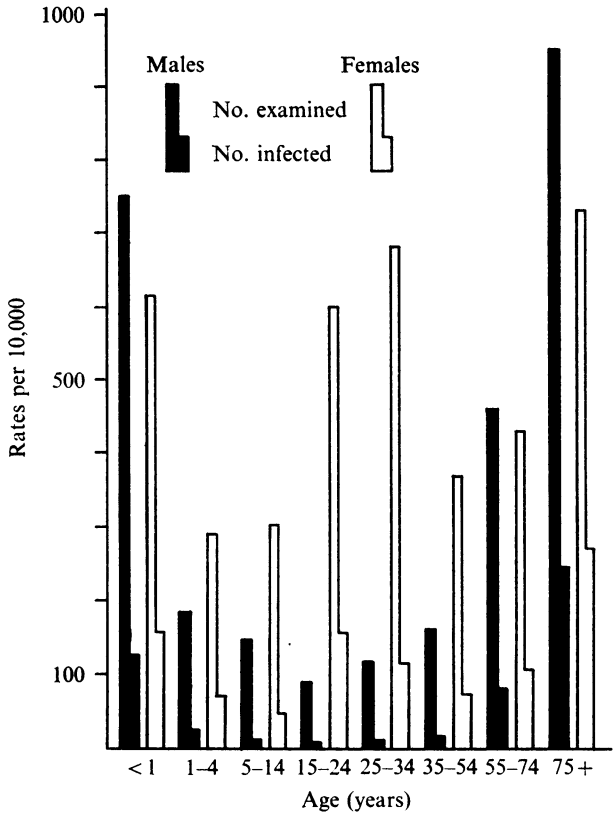

Fig. 1. The number of bacteriological examinations of samples of urine from a population divided into 16 groups by sex and age, expressed as a rate per 10,000 patients in each group (whole column) together with the incidence of bacteriologically proved infections, similarly divided and expressed (broad lower part of each column).

urines examined from each of the sources, divided according to the sex of the patients. This table does not include four isolations which did not fit into any of the 11 named groups. They were classified for the computer as 'other organisms'; all were non-faecal streptococci. Table 4 shows the rate of isolation of each type of organism per 10,000 patients in each of several groups defined by sex and age. At the bottom of this table is given the rate per 10,000 at which patients in each of the sex and age groups had their urine examined, divided to show whether they were being seen in hospital or in general practice.

When the results of the examinations of urine for protein and cells were looked at in detail, it became clear that no purpose would be served by dealing with the four possible types of finding separately. The summary given in Table 5 keeps some separation of protein and cell results but otherwise any specimen with an excess of protein or cells or both was regarded as containing an inflammatory exudate and was called 'exudate positive'. The proportion of patients who were exudate positive in each of the groups defined by sex and age is shown in Fig. 2, where those with a positive culture result have been separated from those found to be negative. Table 6 displays the association between each type of pathogen and the presence or absence of an exudate.

Table 3. *The number of each type of organism isolated expressed as a total and as a rate per* 1000 *patients from each source who were examined for the presence of a urinary infection*

No. of isolations	Types of organism	Isolations/1000 examinations from each source							
		MIP*		SIP*		OP*		GP*	
		M	F	M	F	M	F	M	F
1509	*Escherichia coli*	46	130	41	107	35	79	60	135
472	*Proteus* spp.	37	47	27	36	15	8	29	24
290	Faecal streptococci	22	22	23	22	17	11	17	14
203	Paracolons	9	13	11	12	11	8	12	18
155	*Staphylococcus albus*	16	7	29	10	4	6	8	3
144	Coliforms	12	15	8	13	2	4	7	6
133	*Klebsiella* spp.	11	15	10	8	2	7	3	6
116	*Micrococcus* spp.	1	3	6	3	0	5	3	18
108	*Candida* spp.	7	10	11	18	0	2	2	1
94	*Pseudomonas* spp.	12	8	9	7	4	4	7	1
47	*Staphylococcus aureus*	7	1	8	3	9	0	2	0

* See key at foot of Table 1.

Table 7 gives the results of sensitivity tests done between the antimicrobial drugs listed and the organisms isolated. These have been divided according to whether the specimen yielding each organism came from general practice, or from one of the hospital (MIP, SIP, OP) sources.

Finally, 20 organisms identified as paracolons, together with 20 coliforms and 25 *Proteus* spp. randomly isolated and initially identified according to the criteria given, were examined in rather greater detail so as to discover the major species making up these types. Fifteen of the paracolons (75%) proved to be lactose-negative *Escherichia coli*; the remainder were *Enterobacter* spp. or lactose-negative *Klebsiella* spp. Twelve (60%) of the coliforms were *Esch. coli* of atypical morphology on CLED medium, and the remainder were atypical *Klebsiella* spp., half of them being indole positive. Of the *Proteus* spp., 23 (94%) were *Pr. mirabilis*, and there was one *Pr. vulgaris* and one *Pr. morgani*.

DISCUSSION

The 1-to-4 positive-to-negative ratio of culture results observed here is artificially small because the study includes patients whose urine was examined more than once, often as a test of cure. Others (Gallagher, Montgomerie & North, 1965; Mond, Percival, Williams & Brumfitt, 1965; Steensberg *et al.* 1969; Brooks & Maudar, 1972; Dove *et al.* 1972) have noted ratios of about 1-to-1 in smaller series where repeat examinations were excluded and in which there was likely to have been critical patient selection. There are a number of studies (Fry, Dillane, Joiner & Williams, 1962; Loudon & Greenhalgh, 1962; Steensberg *et al.* 1969) from general practice in which urinary tract infection is seen predominantly as a disorder of young and middle-aged women. When the general practice component in the

Table 4. *The number of isolations of the types of organism named per* 10,000 *males or females in the age-groups shown, together with a comparison of the rates of presentation of patients from these sex and age groups in hospital and general practice*

Types of organism or source	Numbers per 10,000 in each sex and age group															
	<1		1–4		5–14		15–24		25–34		35–54		55–74		75+	
	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F
Escherichia coli	60	106	8	44	2	32	1	54	4	64	6	45	23	56	67	125
Proteus spp.	10	11	6	8	5	3	1	10	0	12	1	11	13	19	65	49
Faecal streptococci	7	14	5	5	1	2	1	9	2	11	2	5	12	7	31	28
Paracolons	7	0	0	3	2	4	0	9	1	7	2	5	5	7	14	15
Staphylococcus albus	23	4	2	2	0	1	0	7	1	4	2	1	9	2	28	5
Coliforms	3	18	1	4	0	1	0	1	1	4	0	2	5	6	20	18
Klebsiella spp.	0	7	0	0	0	1	0	2	0	4	1	1	6	5	8	24
Micrococcus spp.	3	0	2	0	0	1	0	20	0	10	0	1	2	1	3	2
Candida spp.	0	0	1	2	0	1	0	2	0	1	0	2	4	6	15	14
Pseudomonas spp.	13	4	0	6	0	1	0	0	0	1	2	1	4	2	11	11
Staphylococcus aureus	7	0	2	0	0	1	0	0	1	0	0	0	4	1	6	5
MIP* SIP* OP*	706	567	111	122	77	134	63	305	71	333	101	176	386	317	875	614
GP*	44	46	71	167	69	168	25	290	45	341	58	187	65	108	76	108

* See key at foot of Table 1.

Table 5. *Results, percentage, of the examination of male and female urines for protein and for excess cells, related to culture findings*

		Percentage		
		Culture positive	Culture negative	Totals
Males	Protein positive	10	24	100
	Protein negative	5	61	
	Protein and/or cells positive	13	27	100
	Protein and cells negative	3	57	
Females	Protein positive	12	15	100
	Protein negative	10	63	
	Protein and/or cells positive	16	20	100
	Protein and cells negative	6	58	

Table 6. *The percentages of patients with infections due to the organisms named who also had either protein or an excess of cells or both (inflammatory exudate) in their urine*

Types of organism	Inflammatory exudate %	Types of organism	Inflammatory exudate %
Micrococcus spp.	92	*Klebsiella* spp.	76
Staphylococcus aureus	87	Coliforms	76
Candida spp.	86	*Pseudomonas* spp.	75
Paracolons	84	*Escherichia coli*	72
Proteus spp.	81	*Staphylococcus albus*	70
Faecal streptococci	76		

present study is examined on its own by referring to the last two rows of Table 4 and to Fig. 1 good agreement with these studies is seen even though the effect of using rates for greater comparability alters the shape of the curve. However, when hospital and general practice experience is combined and in particular when rates are used to even out the disparity in the sizes of the various age groups, a different picture emerges. Examination for urinary tract infection and its bacteriological diagnosis is seen in Fig. 1 to have affected both sexes almost equally at the extremes of age. Table 4 shows that most of these young and old patients were in hospital. Fig. 1 also confirms the higher incidence of examination for and diagnosis of urinary infection in females in the early years of sexual activity not seen in males. It must be added that because bacteriological help in the diagnosis and treatment of urinary tract infections is more likely to be sought in hospital than in general practice, the relative heights of the columns in Fig. 1 must not be taken as absolute indices of these infections in a community. The preponderance of females in middle life seen in general practice must outweigh hospital experience of involvement of both sexes at the extremes of age, but the absolute incidence of such cases has not been established in this study. However, this does not invalidate a comparison between the occurrence of urinary symptoms leading to a bacteriological examination, and the diagnosis of an infection in males and females of different ages illus-

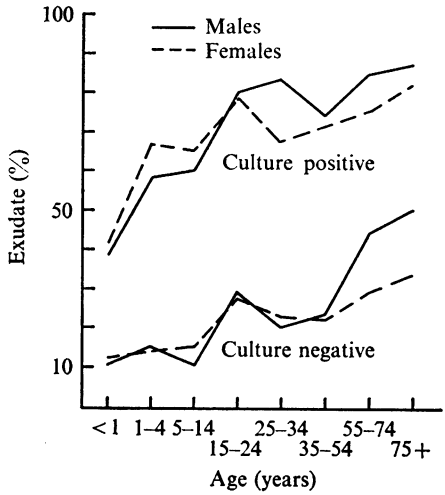

Fig. 2. The incidence of an inflammatory exudate (excess protein or cells or both) in urine, by sex and age, divided according to the presence or absence of significant bacteriuria.

trated in Fig. 1. Table 2 shows that the suspicion of urinary tract infection proved to be bacteriologically correct more often in women (22·0%) than in men (15·5%), and this table also gives an indication of the degree of contamination in specimens from females, whose urines gave rise to a greater incidence of reports of 'no significant growth' and 'mixed growth with one predominant pathogen' than did specimens from males, though the difference between the sexes was less than might have been expected. This, together with the generally low incidence of doubtful results, is thought to have been due to the use of boric acid, which had the effect of turning urine into its own bacteriostatic transport medium.

Tables 3 and 4 taken together show the distribution of the various urinary pathogens in a population. A study of these tables and of Fig. 1 shows how widely different conclusions might be reached about the incidence of urinary tract infection and the distribution of its causative organisms by being selective in the choice of the patients surveyed. However, it is clear that *Escherichia coli* was the dominant pathogen in the urine of those of both sexes of all ages from all sources, with the single exception of males in the 5–14 age group, among whom *Proteus* spp. was more common. The dominance of *Esch. coli* is even more striking when the 75% of paracolons which proved to be lactose-negative strains of this organism and the 60% of coliforms which were also *Esch. coli*, though colonially atypical, are added. The number of lactose-negative *Esch. coli* that were found is nearly 10% of all the strains of this organism isolated, a proportion which agrees with the findings of another group (McAllister *et al.* 1971) and with an estimate of the incidence of such strains among *Esch. coli* in general (Edwards & Ewing, 1964). *Esch. coli* was quite evenly spread among patients from the different sources given in Table 3, and it produced almost the lowest incidence of associated inflammatory exudate (Table 6). The sensitivity to antimicrobial drugs of strains of this organism isolated

Table 7. *The percentage of strains which were resistant to various antimicrobial drugs among the organisms isolated, divided according to their origin in hospital or general practice*

Types of organism	Source	Resistant strains (%)												
		G	PN	SXT	TE	F	K	NA	CL	P (PN)	E	CN	CS	PY
Escherichia coli	Hospital	33	28	9	23	4	6	3	9	—	—	—	—	—
	GP	20	17	2	14	2	1	1	5	—	—	—	—	—
Proteus spp.	Hospital	12	10	7	98	99	2	6	15	—	—	—	—	—
	GP	10	6	8	99	99	2	3	10	—	—	—	—	—
Faecal streptococci	Hospital	98	3	9	50	1	92	98	95	—	—	—	—	—
	GP	96	1	2	43	4	95	99	96	—	—	—	—	—
Paracolons	Hospital	30	38	14	18	21	6	12	30	—	—	—	—	—
	GP	20	23	5	18	11	3	2	16	—	—	—	—	—
Coliforms	Hospital	49	67	28	43	17	14	15	26	—	—	—	—	—
	GP	41	47	6	35	26	6	9	24	—	—	—	—	—
Klebsiella spp.	Hospital	52	83	28	34	19	6	15	17	—	—	—	—	—
	GP	26	74	15	22	22	11	11	27	—	—	—	—	—
Staphylococcus albus	Hospital	20	—	21	66	1	26	99	—	72	27	—	—	—
	GP	14	—	19	43	0	19	95	—	62	5	—	—	—
Micrococcus spp.	Hospital	18	—	21	45	0	15	100	—	70	13	—	—	—
	GP	1	—	1	10	0	0	100	—	65	2	—	—	—
Staphylococcus aureus	Hospital	20	—	18	45	0	15	100	—	77	33	—	—	—
	GP	38	—	14	38	0	0	100	—	88	38	—	—	—
Pseudomonas spp.	Hospital	—	—	—	—	—	—	—	—	—	—	3	5	24
	GP	—	—	—	—	—	—	—	—	—	—	7	0	43

Key: G, sulphonamide; PN, ampicillin; SXT, cotrimoxazole; TE, tetracycline; F, nitrofurantoin; K, kanamycin; NA, nalidixic acid; CL, cephalexin; P, benzyl penicillin; E, erythromycin; CN, gentamicin; CS, polymyxin, colomycin; PY, carbenicillin.

from patients in general practice was quite different from that of those found in hospital (Table 7), the latter being noticeably more resistant.

Proteus spp., almost exclusively *Pr. mirabilis*, were distributed somewhat like *Esch. coli*, though with a slight predilection for males, particularly the old and the very young, and a tendency to be found in patients in medical wards in hospital more often than elsewhere. The organisms were more frequently associated with an inflammatory exudate than *Esch. coli*, and although they showed a smaller variation in sensitivity pattern between isolates from hospital and general practice, those from general practice were on the whole more sensitive. The position of *Proteus* spp. as the second most common organism isolated in urinary tract infections is usual (Loudon & Greenhalgh, 1962; Gallagher *et al.* 1965; Mond *et al.* 1965; McAllister *et al.* 1971) except in the series where selection of patients by age and sex or by source has been such as to impose a different pattern (Steensberg *et al.* 1969; Dove *et al.* 1972).

The next most common organism at about 9% of all was the faecal streptococcus. The age, sex and source distribution of this organism follows that of *Proteus* spp. closely. As with other Gram-positive organisms, the reported incidence of infections with this agent in a number of series has been variable (Garrod, Shooter & Curwen, 1954; Loudon & Greenhalgh, 1962; McAllister *et al.* 1971) and although this may be due to patient selection, other possibilities exist which will be mentioned later.

The distribution of, and sensitivity test results on, the paracolons and coliforms followed those of the species into which the more detailed survey divided them. Thus the paracolons, most of which were lactose-negative *Esch. coli*, had a similar distribution to that organism, whereas the coliforms which included significant numbers of *Klebsiella* spp. as well as *Esch. coli* occupied an intermediate position between the two. *Klebsiella* spp. were found more commonly in hospital practice, were more resistant to antibacterial drugs, and compared with *Esch. coli* were more often found in the very old. *Pseudomonas* spp. were hospital strains with a predilection for the old and the very young, with a slight male preponderance.

The Gram-positive bacteria isolated from cases of urinary tract infection made an interesting study. The faecal streptococcus has been widely accepted as a pathogen and it figures in most published series, though with variations in its proportional incidence, as has been noted. This variation is much greater with the other Gram-positive species. For instance, one group found that 4·06% of 1556 causal organisms isolated from cases of urinary tract infection were Gram-positive (Arneil, McAllister & Kay, 1973); in making this statement the authors appear to be referring to a contribution to a collaborative study (McAllister *et al.* 1971) in which these Gram-positive organisms are given as *Streptococcus faecalis* 4·0% and *Staphylococcus aureus* 0·06%, with no isolations of coagulase-negative staphylococci. At the other end of the scale another group report that 24% of 55 organisms isolated from urine obtained by suprapubic aspiration from women aged between 16 and 60 were coagulase-negative staphylococci (Dove *et al.* 1972). This figure is notable, because it is almost identical with that which can be derived from Table 4 when infections due to *Staph. albus* and *Micrococcus* spp. for the age-

and sex-groups covered by the investigation quoted are combined. The pathogenic status of these organisms has been accepted by many for some time (Garrod *et al.* 1954; Gallagher *et al.* 1965; Mond *et al.* 1965; Steensberg *et al.* 1969), and they have been the subject of specific study (Pereira, 1962; Mitchell, 1965). In the series reported here 8·3% of all significant organisms were coagulase-negative staphylococci, divided by their sensitivity to novobiocin into *Staph. albus* (4·7%) and *Micrococcus* spp. (3·6%). Separated in this way these organisms had very different distributions, the *Micrococcus* spp. being the second most common pathogen in women aged between 15 and 34, while *Staph. albus* was found chiefly among male patients in surgical wards at the extremes of age. Of all organisms micrococci were the most productive of inflammatory exudate at 92%, whereas *Staph. albus* stood at the other end of the scale with only 70% associated exudate (Table 6). It may be that the latter organism frequently contaminated urine samples collected in infancy. Its remarkably high incidence in males under 1 year old might have been because it colonized the preputial sac and thus contaminated specimens collected in adhesive bags with significant multiplication before the urine reached boric acid in the final container. The remaining Gram-positive bacterial pathogen, *Staph. aureus*, follows *Staph. albus* in being found chiefly in old or very young males in hospital.

There are probably several reasons for the wide variation in the reported incidence of Gram-positive organisms in urinary tract infections. One is that a few bacteriologists would not accept *Staphylococcus albus* or *Micrococcus* spp. as pathogens, so that any growth of these was ignored. Another may result from the use of MacConkey's medium for urinary bacteriology. This medium was not designed for work with Gram-positive organisms, and its ability to support their growth is variable. The introduction of CLED medium, based on the electrolyte-deficient medium of Sandys (1960), provides a cheap non-inhibitory alternative which gives good colonial differentiation while suppressing the swarming of *Proteus* spp. A third possibility is that the *Micrococcus* spp. may be pathogenic in the so-called urethral syndrome, but that it is ignored if the figure of 100,000 organisms per ml. for an infection is rigidly applied and particularly if the small colonies which this organism produces are wrongly interpreted numerically when using the dip-inoculum technique. The efficient bacteriostatic action of boric acid has allowed the lower standard of 10,000 organisms per ml. to be adopted here with a confidence strengthened by the agreement just noted between the rates of isolation of significant coagulase-negative staphylococci in this study and those reported by Dove *et al.* (1972) who used suprapubic aspiration for the collection of their specimens.

Candida spp. are absent from several lists of pathogens of the urinary tract, appearing only in larger or more specialized works (Seneca, Longo & Peer, 1968; Rocha, 1972). In the present series they were reported as significantly present more often than *Pseudomonas* spp. and *Staph. aureus*, with an incidence of 3·3% among all pathogens. The paucity of previous records may reflect the fact that many reports in this field have come from general practice, whereas significant isolations of *Candida* spp. are seen in Table 3 to have been hospital strains. The suggestion

that their presence in urine may follow contamination from the female genital tract is countered by the observation that they were isolated from either sex with equal frequency, and that as generators of inflammatory exudate *Candida* spp. were near the top of the list at 86%. The status of this organism as a potential pathogen in the urinary tract perhaps deserves more attention.

The distribution of inflammatory exudate in urine revealed by this survey shows once more how unreliable is the practice of using a test for an excess of either protein or cells as the sole criterion in diagnosing a urinary tract infection. Table 5 shows that on the basis of the presence of protein alone one-third of male and nearly half of female infections would have been missed, and that one-third of the males and a quarter of the females presenting with urinary symptoms would have been treated for bacteriologically non-existent infections. Table 5 also shows that when protein and cells were considered together the rate of error was diminished but that it remained unacceptably high. This fact has been publicized (Loudon & Greenhalgh, 1962; Mond *et al.* 1965; Brooks & Maudar, 1972), but the practice is still so widespread as to require the point to be made again. In Fig. 2 the incidence of inflammatory exudate by sex and age and the presence or absence of a positive culture result has been plotted. Those with symptoms referable to the urinary tract, but without bacteriologically demonstrable infection at the time of examination, had an incidence of inflammatory exudate which increased almost linearly with age. Males and females moved very similarly in this respect until the onset of prostatic enlargement in the male began to have an effect. In the presence of bacteriologically proved infection the incidence of exudate was increased by about 50% at all ages in both sexes, so that the 'infected' curves for both sexes remained almost parallel to the non-infected ones at all ages except in those under 1 year where there was a lower incidence of exudate in the presence of positive culture results. This may have been due to bacteriological mis-diagnosis in this age group, owing to the difficulty of collecting specimens aseptically. Those who have compared the results of the examination of urine samples gathered from infants by the usual methods with those of specimens withdrawn by suprapubic aspiration might agree. Clarification of this point is clearly important so long as urinary infection and chronic pyelonephritis are linked in that order as cause and effect.

It has been suggested that the choice of antimicrobial drug for use in clinically diagnosed acute urinary tract infection before a bacteriological diagnosis is available or where no laboratory examination is to be made, should be from a list of drugs arranged in order of preference as the result of studies of the sensitivity of a large number of urinary pathogens brought up-to-date from time to time (McAllister *et al.* 1971). The results presented here suggest that a single list should not be used for this purpose. The sensitivity of strains from general practice and hospital differed sufficiently widely for any single set of figures to depend on the relative sizes of the contributions from the two sources. Also, the distribution of the groups of pathogen involved in urinary tract infection changed according to the age, sex and source of the patients yielding them, so that by varying the composition of a trial group the pathogens concerned and hence the sensitivity results for all patients taken together alter. Finally, if one or other potential

pathogen is under-represented for any reason, remarkably misleading suggestions may result. It seems possible that the best advice can only be given if the sort of information in Tables 3 and 4 is available, so that the most likely pathogens can be identified according to the circumstances, and the 'best' antimicrobial drug chosen. For instance, the most likely cause of a urinary tract infection in a woman of 24 in general practice was either *Esch. coli* or *Micrococcus* spp. Turning to the antibiotic sensitivity pattern of these organisms in general practice (Table 7), it appears that cotrimoxazole represented the best choice of drug for this patient. It also seems that ampicillin might have failed in a significant number of cases, and that nalidixic acid was a poor choice because of the complete resistance of the *Micrococcus* spp. to this drug.

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