The prevalence of renal abnormalities in women with urinary tract infection

A study from general practice

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THE aims of the study were to investigate the frequency of renal abnormalities in women with urinary infection and to study the interrelationships of asymptomatic bacteriuria, acute bacterial pyelonephritis, and bacterial cystitis.

The subsequent occurrence of acute pyelonephritis in women with asymptomatic bacteriuria of pregnancy (Kass, 1959) and the relationship between dysuria and asymptomatic bacteriuria (Sussman *et al.*, 1969; Asscher *et al.*, 1969) have been recorded. Frequent abnormalities of renal function and structure have been shown in the long-term follow-up of asymptomatic bacteriuria of pregnancy (Zinner and Kass, 1971).

Earlier studies from general practice (Manners *et al.*, 1970; Manners *et al.*, 1972) have suggested that there is a close relationship between asymptomatic bacteriuria and acute pyelonephritis, and that women with either of these disorders form a different group from women who experience cystitis.

Method

A. Definitions

The definition of significant bacteriuria is based on that of Kass (1957) i.e. a reproducible pure growth of more than 100,000 organisms per ml of early morning urine. Allowance is made for frequency and the time of day at which urine is collected.

Women with significant bacteriuria are placed in one of three groups according to their symptoms and signs—cystitis, acute pyelonephritis, or asymptomatic bacteriuria. Cystitis is defined as the presence of dysuria without loin tenderness. Acute pyelonephritis depends on the presence of loin pain and loin tenderness, usually but not invariably associated with dysuria, frequency and general symptoms such as nausea and fever. Asymptomatic bacteriuria is defined as significant bacteriuria occurring in the absence of dysuria, loin pain, loin tenderness, and general symptoms.

B. Collection of cases

The work was conducted prospectively for three years from June 1968 to June 1971 in a single general practice of known age and sex structure.

The dip inoculum spoon (Mackey and Sandys, 1965 and 1966) has been found a convenient device for detecting bacteriuria in general practice (Grob *et al.*, 1970). A dip inoculum composed of a plastic spoon filled with Oxoid number two MacConkey medium was used to detect bacteriuria. This was given to the patient, with a sterile universal container and printed instructions for the collection of a clean specimen of urine. The specimen was collected by the patient in her home: the dip spoon was inoculated with urine immediately after voiding and was returned to the surgery where it was incubated for 24 hours at 37°C. Dip inocula showing significant growth were taken to the laboratory for identification and antibiotic sensitivity testing. Serotyping of *Escherichia coli* was performed using a panel of 13 ' O ' antisera.

The dip inoculum method was used for the detection of asymptomatic bacteriuria and for the investigation of women with urinary symptoms. Hence this study was a combination of screening and diagnostic work.

Urines were collected from women visiting the surgery for whatever reason. If acute urinary symptoms were present, at least two successive urines were examined before treatment began. If bacteriuria was found on screening a single specimen, the patient was recalled and three further consecutive morning urines examined; the patient was accepted as having true asymptomatic bacteriuria only if significant bacteriuria was found in all these specimens. If bacteriuria was not reproducible, the patient was not included in the survey.

Once bacteriuria had been detected, urines were examined weekly for one month, then monthly for three months, and then at three-monthly intervals for the remainder of the survey. Patients were instructed to report any urinary symptoms to the surgery, when further urines were examined.

C. Investigations of bacteriuric women

Evidence of renal abnormality was sought by the following methods:

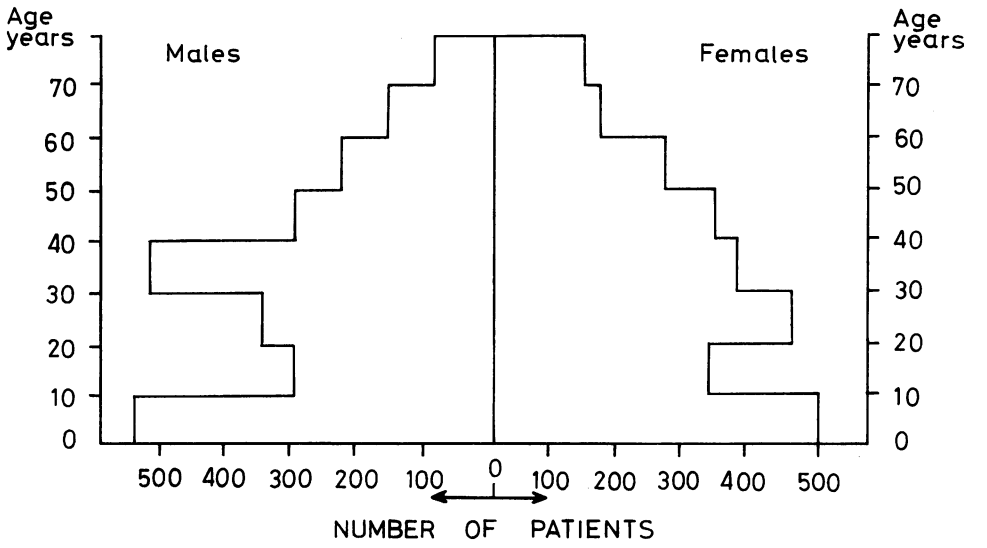
1. Clinical: Examining the resting blood pressure, measured on two occasions by the same observer.
2. Chemical: Measuring the blood urea, the urine concentrating ability after 15 hours overnight fluid deprivation.
3. Immunological: Serum agglutinating antibody titres to the infecting strain of *E.coli* were measured 12 days and one month after the detection of bacteriuria (Leigh, 1969; Percival *et al.*, 1964).
4. Radiological: Intravenous pyelograms (IVP) were performed on all women with asymptomatic bacteriuria or acute pyelonephritis, and in women who had two or more episodes of bacterial cystitis (i.e. recurrent bacterial cystitis). The IVPs were done following fluid deprivation using either 100 ml ' Hypaque ' 45 per cent or 100 ml 'Conray 325'. Films of the kidneys were taken before, during and after release of abdominal compression. Tomograms and oblique films of the kidneys were also performed.

Treatment

Women with symptoms of cystitis were given sulphadimidine 0·5 grams q.d.s. regardless of the result of urine culture. Women with acute pyelonephritis were given ampicillin 2·0 grams *stat* and 500 mg q.d.s. for one week. Women with asymptomatic bacteriuria were treated with sulphadimidine only if they were pregnant, if they later developed acute urinary symptoms, or if they had evidence of severe renal disease. Coincidental treatment for infection of sites other than the urinary tract was noted.

Results

The age-sex structure of the practice is shown in figure 1. Of 1,642 women aged 15 to 59 years, 1,409 (86 per cent.) submitted urine on at least one occasion. Bacteriuria, with

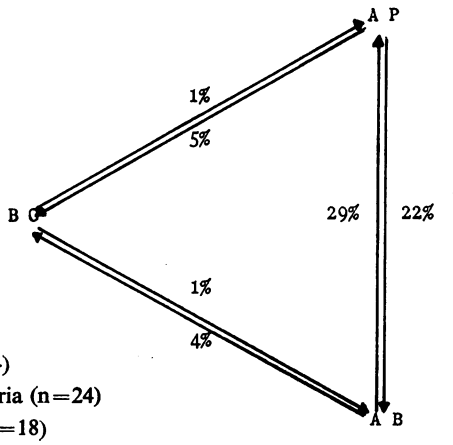


AGE AND SEX DISTRIBUTION IN A GENERAL PRACTICE OF 5,130 PATIENTS

Figure 1

or without urinary symptoms, was found in 126 women (seven per cent). The presenting feature was cystitis in 84 women, and acute pyelonephritis in 18; the remaining 24 had asymptomatic bacteriuria and had been found by screening.

The interrelationships between the symptom complexes of 126 women over a mean follow-up period of 2·0 years are shown in figure 2. Of the women presenting with bacterial cystitis, 29 per cent had a second episode, (recurrence) of bacterial cystitis



BC = Bacterial cystitis (n=84)
AB = Asymptomatic bacteriuria (n=24)
AP = Acute pyelonephritis (n=18)

Figure 2

Natural history of bacteriuria in women

during the follow-up, and 40 per cent experienced an episode of non-bacterial cystitis (19 per cent of the cystitis cases had recurrences both of bacterial cystitis and non-bacterial cystitis). Only one per cent developed either asymptomatic bacteriuria or acute pyelonephritis.

In the group presenting with acute pyelonephritis, there was a recurrence of the condition in 33 per cent and 22 per cent later developed asymptomatic bacteriuria. Only five per cent later developed bacterial cystitis. Of the women found to have asymptomatic bacteriuria, seven out of 24 (29 per cent) later developed acute bacterial pyelonephritis—two while pregnant and five while not pregnant: only four per cent later developed bacterial cystitis. Apparently ' spontaneous ' clearance of asymptomatic bacteriuria was sometimes due to coincidental antibiotic treatment for infections other than those of the urinary tract.

Abnormal IVPs were found in 75 per cent of the acute pyelonephritis group, in 48 per cent of the asymptomatic bacteriuria group, and four per cent of women with recurrent bacterial cystitis (table 1). The difference in frequency of abnormalities in either of the former groups is significantly greater ($p<0.001$) than in the bacterial cystitis group. Blunting of calyces and dilated pelvicalyceal systems were the most common abnormalities: these changes were subdivided into ' dilated calyces ' when seen in films taken prior to abdominal compression, and ' distensible calyces ' when seen only during compression.

TABLE 1

FINDINGS ON IVP

Group	*Number of IVPs performed*	*Scars*	*Calculus*	*Dilated calyces*	*Distensible calyces*	*Sponge kidney*	*Other*	*Normal*	*Percentage abnormal*
Acute bacterial pyelonephritis	16	2	0	4	2	1	3	4	*75*
Asymptomatic bacteriuria	23	1	2	3	2	2	1	12	*48*
Recurrent bacterial cystitis	24	0	0	1	0	0	0	23	*4*

Nature of abnormalities detected by intravenous pyelography on bacteriuric women

The results of testing serum for agglutinating antibody to *E.coli* are shown in histogram form (figure 3). If a titre of 1:80 is taken as abnormal, and suggestive of renal parenchymal infection, such titres were found in three per cent (2/66) of the bacterial cystitis group compared with 39 per cent (5/13) of the acute pyelonephritis group and 50 per cent (11/22) of the asymptomatic bacteriuria group. The number of women with titres of either 1:80 or more is significantly higher ($p<0.001$) in the acute pyelonephritis and asymptomatic bacteriuric groups than in the cystitis group.

The mean values for age, parity, blood pressures, blood urea and urine concentrating ability in the three groups are shown in table 2. The mean age of both the acute pyelonephritis group (30 years) and asymptomatic bacteriuria group (38 years) differ from the mean age (34 years) of the cystitis group. When the two former groups are combined to form group 1, there is no significant difference ($p<0.5$) in mean age or in age distribution when compared with the cystitis group (group 2). Blood pressure and blood urea mean levels are significantly higher ($p<0.001$) and urine concentrating ability significantly lower ($p<0.001$) in group 1 compared with group 2.

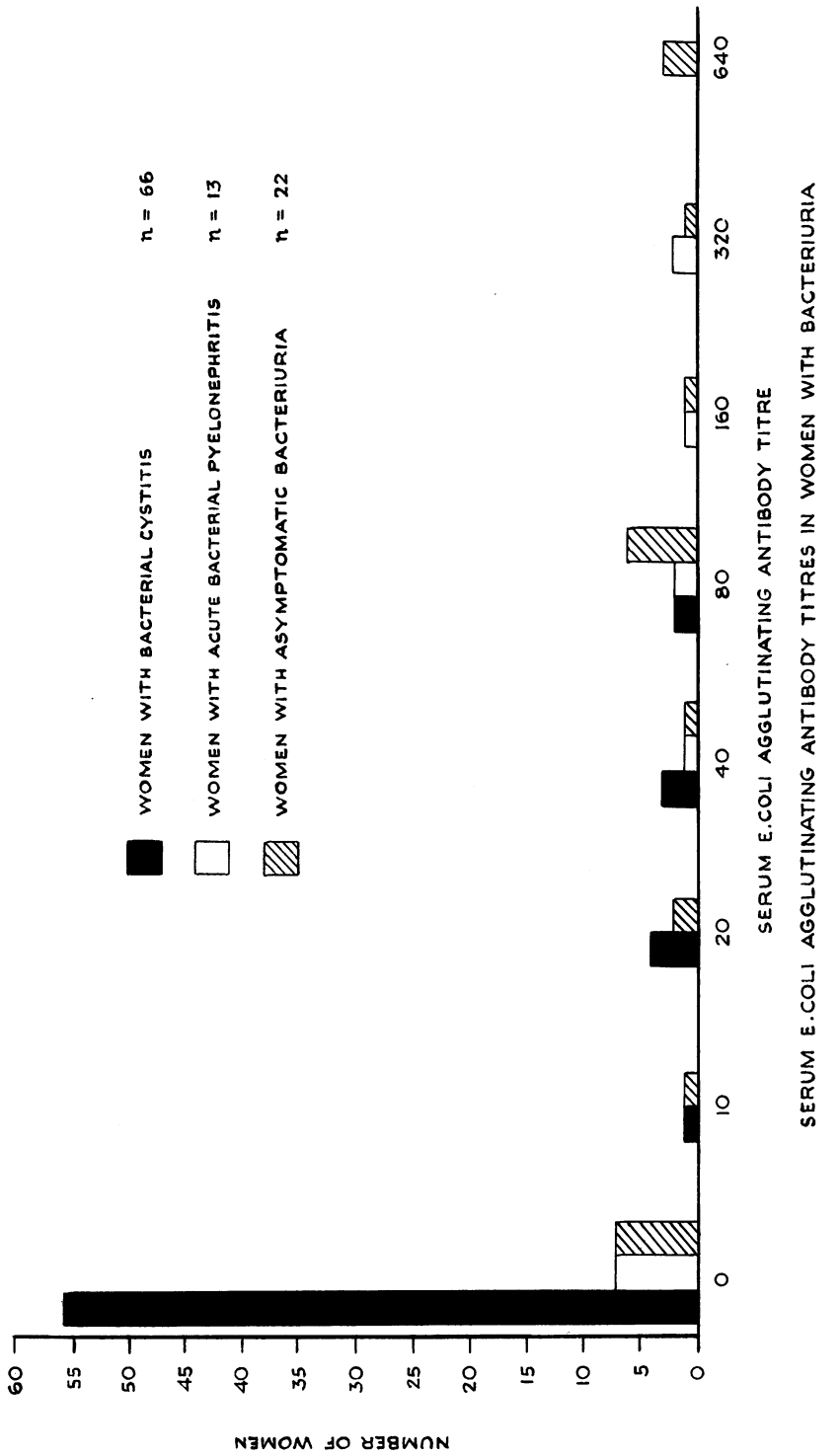

WOMEN WITH BACTERIAL CYSTITIS n = 66
WOMEN WITH ACUTE BACTERIAL PYELONEPHRITIS n = 13
WOMEN WITH ASYMPTOMATIC BACTERIURIA n = 22
NUMBER OF WOMEN
60
55
50
45
40
35
30
25
20
15
10
5
0
0
10
20
40
80
160
320
640
SERUM E.COLI AGGLUTINATING ANTIBODY TITRE
SERUM E.COLI AGGLUTINATING ANTIBODY TITRES IN WOMEN WITH BACTERIURIA

Figure 3

TABLE 2
COMPARISON OF ACUTE BACTERIAL PYELONEPHRITIS, ASYMPTOMATIC BACTERIURIA AND BACTERIAL CYSTITIS

	Mean+S.E. of measurement in group				
Measurement	*Acute bacterial pyelonephritis*	*Asymptomatic bacteriuria*	*Combined acute pyelonephritis & asymptomatic bacteriuria (Group 1)*	*Bacterial cystitis (Group 2)*	*Group 1 against Group 2 " p "*
Number of patients	18	24	42	84	—
Age (years)	30±2·1	38±2·5	35±1·8	34±1·2	Not significant
Parity	2·2±0·3	2·2±0·3	2·2±0·3	1·6±0·1	<0·10>·05
Months in trial	24±2·7	26±1·8	25±1·5	24±1·1	Not significant
Systolic BP (mm/Hg)	126±3·5	137±6·9	133±4·3	115±1·6	<0·001
Diastolic BP (mm/Hg)	74±2·3	80±3·5	77±2·1	68±0·9	<0·001
Blood urea (mg/100ml)	27±1·5	32±2·5	30±1·6	23±1·8	<0·001
Urine concentrating ability (mOsm/kg)	742±25	774±41	761±26	920±13	<0·001

TABLE 3
DRUG SENSITIVITY PATTERNS OF INFECTING ORGANISMS

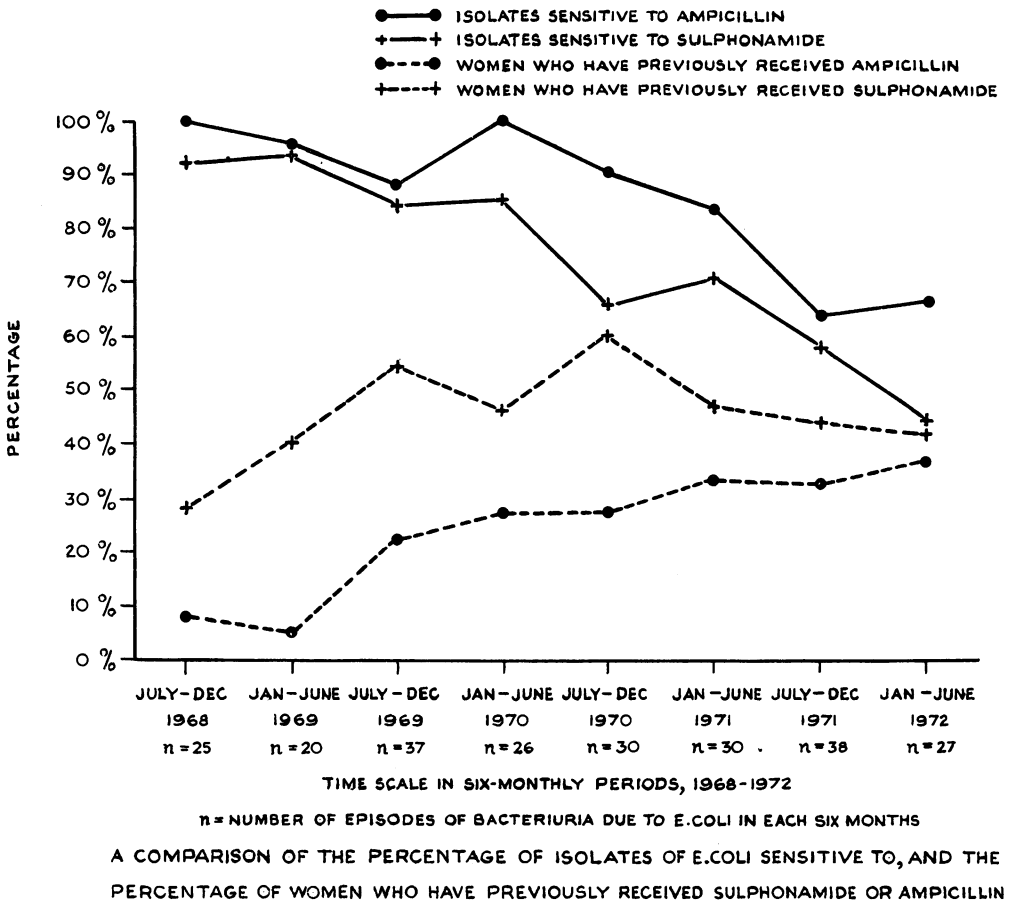
		Percentage of organisms sensitive to			
Species	*Number of isolates*	*Sulpha*	*Ampicillin*	*Nalidixic acid*	*Cotrimoxazole*
E.coli	178 (*86*)	*82*	*93*	*99*	*98*
Proteus	21 (*10*)	*57*	*86*	*100*	*93*

Other isolates (9) *Staph.albus, Klebsiella, Strep.faecalis*

The species and antibiotic sensitivity of the infecting organisms are shown in table 3. The frequency of *E.coli* strains resistant to sulphonamide or ampicillin has increased steadily during the period of the survey (figure 4). The emergence of resistant *E.coli* has been associated with increasing previous exposure to sulphonamide or ampicillin.

TABLE 4
ASSOCIATION OF SEROTYPING OF *E.coli* WITH SYMPTOM-COMPLEX

Serotype	*Bacterial cystitis*	*Asymptomatic bacteriuria*	*Acute bacterial pyelonephritis*	*Total*
Not typable	53	25	8	86
075	20	5	1	26
07	8	6	0	14
02	6	3	1	10
01	3	1	2	6
039	4	1	1	6
04	2	2	1	5
018	3	0	0	3
011	3	0	0	3
09	2	0	1	3
05	1	1	0	2
06	2	0	0	2
Total	107	44	15	166



A COMPARISON OF THE PERCENTAGE OF ISOLATES OF E.COLI SENSITIVE TO, AND THE PERCENTAGE OF WOMEN WHO HAVE PREVIOUSLY RECEIVED SULPHONAMIDE OR AMPICILLIN

Figure 4

The time scale of this figure has been extended to include a further one year of the survey and shows the pattern more clearly.

The result of serotyping of *E.coli* and the nature of serotypes associated with the three symptom-complexes are shown in table 4. There was no correlation between a particular serotype or the presence of typable organisms and the occurrence of a particular symptom-complex. Of 159 non-typable isolates, 72 (84 per cent) were sensitive to sulphonamide and 87 (94 per cent) were sensitive to ampicillin. Of 126 typable isolates, 58 (73 per cent) were sensitive to sulphonamide and 68 (85 per cent) were sensitive to ampicillin. These differences between typable and non-typable groups were not significant ($p<0{\cdot}05$).

A different organism (judged by species difference or dissimilar serotype) was found in 22/37 (60 per cent) of recurrences of bacterial cystitis, and in 11/21 (53 per cent) of recurrence in the combined acute pyelonephritis and asymptomatic bacteriuria group ($p>0{\cdot}05$). Early recurrence (less than three months after the initial episode) occurred in 4/21 (19 per cent) recurrent episodes in the acute pyelonephritis and asymptomatic bacteriuria group; by contrast early recurrence occurred in 19/37 (51 per cent) recurrent episodes in the bacterial cystitis group ($p<0{\cdot}05$).

Discussion

Abnormalities of renal function or structure can be found most often in women with either acute pyelonephritis or asymptomatic bacteriuria. Women with cystitis are unlikely to have such abnormalities. The younger mean age (30 years) of the women with acute pyelonephritis compared to the mean age (38 years) of the women with asymptomatic bacteriuria, and the frequent interchange between these two conditions during a mean follow-up period of 2·0 years, suggest that asymptomatic bacteriuria may be a late sequel of acute pyelonephritis. This view is supported by our observation that there is a past history (before June 1968) of acute pyelonephritis in 29 per cent of the women found to have asymptomatic bacteriuria. It is these women who have abnormal renal function and structure. A past history of acute pyelonephritis was obtained in three per cent of women with bacterial cystitis.

It has been suggested by Brumfitt (1968) that recurrence of infection by the same organism (relapse) may indicate renal involvement, whereas recurrence due to a dissimilar organism (reinfection) argues against a persistent focus of infection in the kidney. However, in our series, episodes of recurrent infection due to a similar organism occurs no more often in the group with renal abnormalities (group 1) than in a group without renal abnormalities (group 2). Further, rapid relapse (within 12 weeks of the first infection) occurred more frequently in group 2 than in group 1; similar differences were found when the time factor for rapid relapse was reduced to either ten or eight weeks (Gruneberg, 1970). Thus rapidity of relapse and the persistence of a similar organism in recurrence of infection have not been helpful in detecting a group of women with renal abnormalities.

Conclusion

Women with renal abnormalities can most easily be detected in general practice by investigating patients with either acute pyelonephritis or asymptomatic bacteriuria. Asymptomatic bacteriuria should be sought particularly by screening the urine in pregnancy and in women with a past history of acute pyelonephritis.

Summary

A three-year study of urinary infection in women aged 15 to 59 years from a single general practice is described. Bacteriuria was found in 126 out of 1,642 women (seven per cent), in this age group. Of these 84 presented with cystitis, 18 presented with acute pyelonephritis, and 24 were found to have asymptomatic bacteriuria.

Evidence of renal abnormality was sought by measuring blood pressure, blood urea, urine concentrating ability, *E.coli* antibodies, and IVP. A close relationship between asymptomatic bacteriuria and acute pyelonephritis was found; renal abnormalities occurred significantly more frequently ($p<0·001$) in these women than in women with cystitis. Recurrent infection by *E.coli* of similar serotype was not associated with increased likelihood of renal abnormality.

There are two groups of women who have urinary tract infection; in one there are women with the recurrent and interchangeable conditions of acute pyelonephritis and asymptomatic bacteriuria; in the other there are women with the recurrent and interchangeable conditions of bacterial cystitis and non-bacterial cystitis.

Acknowledgements

Our thanks are due to Dr J. Liddell for arranging urine concentration tests, Professor F. O'Grady and Dr A. Asscher for their advice, to Mrs H. Lane and Mr J. Grimshaw for their help in statistical analysis, to Mr F. J. Gibbs for assistance in bacteriology and to the Research Foundation Board of the Royal College of General Practitioners for financial aid.

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