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A New Look at the Aetiology of Urinary Infection

Introduction

It is proposed in this review to reassess two separate aspects of the aetiology of urinary infection. First, on the basis of data collected in our own Urinary Infection Clinic over the past six years, we will suggest that the different conditions associated with "significant bacteriuria" (defined here as $\geq 10^5$ bacteria per ml of properly-collected mid-stream urine [1]) have separate, and distinct aetiological patterns. Second, we will summarize recent studies which throw some light upon the possible role of micro-organisms in the causation of the "dysuria and/or frequency syndrome without significant bacteriuria" (formerly known as the "urethral syndrome"). The latter term has now been discarded owing to the lack of a precise definition of the term (1).

Aetiology of Urinary Infections Associated with Significant Bacteriuria

In the domiciliary situation, urinary infections may be subdivided into three distinct clinical groups.

A Simple dysuria and/or frequency with infection. These patients show a high cure rate (around 90%) when treated with an appropriate antibiotic and they do not often relapse. The bacterial species causing the infection follow a well-defined pattern (Table 1). Infections are usually due to *Escherichia coli* but occasionally *Proteus mirabilis* is responsible. Together they are the causative organisms in over 80% of the patients. However, in some reports, in up to 10–13% of patients, a gram-positive organism is responsible, most often *Staphylococcus saprophyticus* (this species was formerly known as *Micrococcus sp.* type 3 under the Baird-Parker classification scheme [2]) *S. saprophyticus* – which outnumbers *S. epidermidis* and *Streptococcus faecalis* as an aetiological agent in this type of patient – causes infections almost exclusively in women aged 18–40 who are sexually active (3). Other workers (4) have reported an incidence due to this organism of up to 20% in similar patients but only in small studies.

B Domiciliary patients with recurrent infections. This group is characterized by a long history of symptomatic attacks, ranging in frequency from twice per year to twelve or more. A substantial minority of such patients have evidence of abnormalities (e. g. renal scarring, calculus or other acquired abnormality). In these patients the cure rate is initially only slightly lower than that found in patients with "simple" infections (Group A above) namely 65–80% – but up to 30% of those free of bac-

teriuria one week after the end of treatment relapse during the next four weeks. This type of patient is helped by long-term, low-dose chemoprophylaxis with such agents as trimethoprim, nitrofurantoin or a formaldehyde releasing agent (e. g. methenamine salts). Analysis of more than 400 infections in these patients (whom we have categorised "difficult" [5]) whom we have treated over the past six years shows a rather similar pattern (Table 1) to that observed in Group A. However, there are some important differences: *S. epidermidis* is more common than *S. saprophyticus*, and all types of streptococci – but especially those of Group D and B – are more often found in "difficult" than in "simple" patients. The overall incidence of gram-positive species is almost 20%.

C Bacteriuria in pregnancy. These patients, most of whom are asymptomatic, have a cure rate (65–75%) which is significantly lower than that in non-pregnant patients. In our experience the overwhelming majority of infections are caused by fully antibiotic sensitive *E. coli* (Table 1). Interestingly, gram-positive bacteria seem to have a negligible part to play in the pregnant patient, adding weight to the belief that such infections have a different aetiology. The reason for the lower cure rate is unknown.

D Infections in patients in hospital. It is interesting to compare the aetiological patterns found above with that found in patients in hospital. Again, *E. coli* infections predominate, but *Klebsiella pneumoniae*, *S. epidermidis* and faecal (Group D) streptococci each cause about 10% of infections. *S. saprophyticus* is almost non-existent as a pathogen in this group, although gram-positive bacteria account for virtually 20% of all the infections. However, great care should always be taken when collecting and interpreting data on causative agents in patients in hospital, because outbreaks of cross-infection may distort the figures: relatively unusual pathogens, such as *Serratia marcescens* (6), indole-positive *Proteus spp.* (7) and *Providencia stuartii* (8) may cause such outbreaks, and many patients may be involved in a particular episode.

It is apparent from the above that, although there are certain resemblances between the patterns observed in the various patient groups considered above (for instance, the predominance of *E. coli* throughout), there are distinct and important differences. It has been shown (9) that the same O-serotypes of *E. coli* predominate in all the patient groups. Thus we suggest that the observed differences in the incidence of infection by *E. coli* O-serotypes are best explained by their prevalence in the

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Table 1: Incidence of infecting organism in urinary infections in various groups of patients.

Bacterial species	Incidence in different patient groups			
	Simple dysuria/frequency syndrome	Recurrent infections	Pregnant women	Hospital patients
<i>Escherichia coli</i>	71.7%	66	89.2	53.1
<i>Proteus mirabilis</i>	7.3%	9.5	3.5	10.4
<i>Staphylococcus saprophyticus</i>	5.7	2.9	0.4	0.4
<i>Staphylococcus epidermidis</i>	4.2	3.9	0.4	10.4
<i>Klebsiella pneumoniae</i>	3.1	1.7	1.7	9.7
Faecal-type streptococci	2.7	8	0.4	3.2
Non-faecal streptococci	2.5	4	—	5.4
Others	2.8	4	4.3	7.4
Total number of strains studied	953	411	231	2022

bowel flora (9). The same may well apply to the other infecting species; clearly, this problem has been widely studied but clarification especially of host factors is awaited.

Possible Microbial Aetiology of Symptoms in the Absence of Significant Bacteriuria

One of the major unsolved problems in the field of urinary infection concerns the reason for symptoms in the 50% of symptomatic patients who do not have a significant bacteriuria (i. e. $\geq 10^5$ per ml). There have been several recent attempts to prove that this condition (which should properly be called [1] "dysuria and frequency without infection") may have a conventional microbial aetiology. A common feature of recent reports is that the concept that "significant bacteriuria" means 10^5 or more micro-organisms per ml of urine is not necessarily true. Gleckman et al. (10) and Stamm et al. (11) both suggest that "conventional" pathogens – such as *E. coli*, *Proteus mirabilis* etc. – in concentrations of 10^4 per ml, or less, may cause a true infection and be responsible for the symptoms. Thomsen (12) has found, on the basis of culture and of antibody assays, that *Mycoplasma hominis* was responsible for symptomatic pyelonephritis. Birch et al. (13) report isolating a related organism, *Ureaplasma urealyticum*, in numbers exceeding 10^3 per ml in 34 of 190 patients with "sterile pyelonephritis" where the urine was collected by suprapubic puncture. Maskell, Pead and Allen (14) have made the more controversial suggestion that lactobacilli may cause dysuria and frequency: however, our own work (15) casts doubt on the validity of this

hypothesis. It seems likely that the lactobacilli found by Maskell et al. (14) were in fact contaminants arising from the vaginal flora.

The importance of specimen collection for the proper diagnosis of urinary infection is again emphasised. It is impossible to stress too strongly the importance of adequate cleansing of the intralabial area prior to collecting a mid-stream specimen of urine for microbiological analysis. In view of the above, it is clear that it is imperative to take great care to exclude the possibility of a microbial infection in a symptomatic patient before alternative causes are considered. In view of symptoms being due to infection of the urethra attention should be directed to isolation of bacteria from this structure as well as from bladder urine. Thus, in clinics dealing with urinary infection the collection of the first 5 ml of urine passed (which washes out the urethra) is being reintroduced. This, of course, is in addition to collection of a conventional mid-stream urine specimen.

Alternative causes of the dysuria and/or frequency syndrome, without infection, include physiological disturbances (16) as well as psychological disorders (17). For this reason we are carrying out a trial on patients with such symptoms, using a long-acting benzodiazepine. This has an action on the smooth muscle of the bladder (16) as well as having a tranquillizing effect. Recently the introduction of flunarizine for the control of incontinence is an interesting development, which may be of benefit to patients suffering symptoms of lower tract urinary infection in the absence of significant bacteriuria.

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