PROPHYLAXIS OF URINARY TRACT INFECTION

by

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THERE is still much suffering from urinary tract infection (UTI). Consultation rates vary between 12-60 per thousand 1-3 and, as shown in Table 1, it is also a common cause of absenteeism from work. Prophylaxis is therefore indicated both on medical and economic grounds. It is less clear whether effective prophylaxis would have an impact on the mortality associated with UTI since long-term follow-up studies of patients with UTI have shown how rarely these infections progress to impairment of kidney function in the absence of obstruction. 4 However, the same benign course of UTI may not occur in childhood and in this age group effective prophylaxis may reduce both morbidity and mortality. 5

Most UTIs arise by ascent of the endogenous bowel flora so that, theoretically at least, prophylaxis could be achieved by eradicating the source of the pathogens or by interfering with the ascent of the organisms. The alternative approach to prophylaxis is to aid the natural defences against UTI.

Table 1. Disability due to genitourinary tract and respiratory infections* (days per 100 persons per year) .

|                         | Female | Male  | Total |
|-------------------------|--------|-------|-------|
| Genitourinary infections| 45.3   | 11.2  | 28.8  |
| Respiratory infections  | 408.1  | 327.3 | 369.1 |

*Data from HNS survey 1970-71
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TACKLING THE PROBLEM AT SOURCE

Since there is no evidence that the bowel organisms which cause UTI possess special pathogenicity for the urinary tract, it follows that nothing short of elimination of the normal bowel flora would constitute effective prophylaxis. Needless to say attempts to achieve this on a long-term basis would merely result in bowel colonization by more resistant strains. A more promising approach might be to
advise a policy of good perineal hygiene. This might include regular bathing, correct cleansing after defecation, avoidance of nylon underwear and sanitary towels and in babies regular nappy changes. None of these measures has been subjected to the rigours of controlled trials and they are all, therefore, part of medical folklore which I would not wish to dismiss. The only procedure which has been studied with care is the application of chlorhexidine ointment to the perineum, but this was found to be ineffective. Although perineal colonization precedes invasion of the urinary tract, it appears to be impossible to prevent it and the defect may well reside in the perineal cells of the host. In this regard it is of particular interest that Stamey et al and Kallenius and Winberg have shown that bacteria adhered more readily to vaginal and perineal cells of subjects liable to recurrent UTI than to those obtained from controls. It has also been suggested by Svanborg Edén and Svennerholm that secretory IgA antibody directed against Escherichia coli can prevent the attachment of bacteria to uroepithelial cells. Local immunization might therefore prove valuable and is certainly worth investigating. It is also interesting that bacterial adherence to perineal cells can be inhibited by D-mannose and a-methyl-D-mannoside. Here again new therapeutic avenues may be opening up to help the unfortunate sufferers from UTI.

Attacks of UTI are frequently precipitated by sexual intercourse. Good sexual technique together with the advice to empty the bladder after intercourse may suffice to prevent ‘honeymoon cystitis’. Sometimes a single dose of a suitable antibacterial agent taken after intercourse is also necessary. There is now good scientific justification for this because intercourse has been shown to produce bacteriuria in women whose perineum is colonized with E. coli. The practice of prescribing an antibacterial agent after intercourse is therefore comparable to the antibiotic cover for dental operations given to patients with rheumatic heart disease.

Climatic factors may also be important in the pathogenesis of UTI. There have been several reports to suggest that UTI shows a higher incidence in cold weather. The most recent study suggests that UTI is particularly likely to occur when the patient dresses in a manner inappropriate to weather conditions or as Angela Kilmartin put in her book Understanding cystitis, ‘If you do decide to go to Greenland, take some woollen combinations.’

Perhaps the most obvious way of interfering with the ascent of organisms relates to the infections which follow catheterization and instrumentation. Here good technique, avoidance of trauma and closed drainage systems are the keys to success.

In young boys the source of urinary pathogens may be the subprepuccial sac which is often colonized by Proteus spp. Here again good hygiene and in some cases circumcision, can make a contribution to prophylaxis. In middle aged men urinary pathogens may lurk in the prostate. It can be particularly difficult to eliminate organisms from the prostate gland. Only some antibacterial agents (e.g. trimethoprim, erythromycin and other macrolides and tetracyclines) penetrate the
prostatic fluid in sufficient concentration and are sufficiently active at the low pH of prostatic fluid to be useful. In elderly males the problem of UTI is usually related to prostatic enlargement, and repeated infections which cannot be controlled by medical means may be an indication for surgical treatment.

AIDING THE NATURAL DEFENCES

As already mentioned, immunization to prevent bacterial colonization of the perineal floor is a possibility for the future which so far has not materialized. At present the main methods of aiding natural defences are by a high fluid intake (in excess of 3 litres/day) and by emptying the bladder frequently and completely. This aids the hydrokinetic defences and enables polymorphs to function better since these cells do not phagocytose bacteria as readily in urine of high osmolality as in urine which approximates to the osmolality of blood. The dilution of antibacterial agents by such a high fluid intake is not important since the urinary concentrations of most of the commonly used agents far exceeds the minimal inhibitory concentration (MIC) required to deal with the average urinary pathogen.

Another possible method of aiding natural defences is to reduce the urinary pH, for example by a high protein intake. At low pH the organic acids in normal urine are undissociated and able to penetrate the bacterial cell and so produce their bactericidal effect.\textsuperscript{13} It is difficult, however, to reconcile the production of an acid urine with a high fluid intake since the hydrogen ion concentration of dilute urine is reduced accordingly. Because the hydrokinetic defence is of greater importance than reduction of urinary pH, we do not normally make use of urinary acidification as a method of prophylaxis. Yet according to American folklore, eating cranberries prevents UTI presumably because of their high hippuric acid and ascorbic acid content.

TREATMENT OF SYMPTOMLESS INFECTIONS

The pioneering work of Kass revealed that for every patient with symptomatic infection there are at least three apparently healthy people who harbour covert infection. The question therefore arises to what extent these covert infections lead to symptomatic infection on the one hand and to progressive kidney damage on the other. Could these symptomless infections be the submerged part of the iceberg which accounts for the continuing morbidity associated with UTI?

The prevalence of these covert infections in different population groups is shown in Table 2. It must be recognised that these are point prevalences and that covert bacteriuria is a dynamic state. Figure 1 illustrates the various possible sequelae of covert infection. The frequency with which the events indicated occur varies from one population to another, for example, during one year 25% of adult women with covert infections will be spontaneously cured and 10% of children. However, since the point prevalence is static, it is clear that the number of women and children who acquire infection must equal the number who are cured. This is a very important observation because if it were true that detection and treatment of covert
infection is beneficial, it would be necessary to screen the whole apparently healthy population at frequent intervals in order to make those benefits available to all; this would be quite impossible. It follows that there is a need to define high risk groups within the bacteriuric population. Most bacteriuric subjects are 'fitters' and only in a small percentage (about 10%) does the condition persist. Perhaps these are the ones who require treatment, or it may be that in these patients the

| Population      | Age range | Prevalence |
|-----------------|-----------|------------|
| Adult women     | 21-65     | 5          |
| Pregnant women  | 16-40     | 3          |
| Schoolgirls     | 5-12      | 2          |
| Adult males     | 21-65     | 0.5        |
| Schoolboys      | 5-12      | 0.03       |
| Infants         | 0-5       | 0.001      |

**Fig. 1** Dynamics of covert bacteriuria.  
After Kunin CM. Detection, prevention and management of urinary tract infection. 3rd ed. Philadelphia: Lea and Febiger, 1979.
bacteria emanate from the kidney. The advent of a simple non-invasive test of localization which detects antibody coating on bacteria of renal origin \(^{15}\) may prove helpful. There is certainly a need to study the fate of women with renal bacteriuria separately from that of women in whom the bacteria are confined to the bladder. In the past, because we did not have a non-invasive method of localization of UTI we tended to lump all bacteriuric subjects together. It is now clear that bacteriuric populations are not homogenous and that we need additional markers to identify subjects who are at high risk of developing symptomatic UTI and/or kidney damage.

In pregnant women the risk of developing symptomatic UTI is clearly defined. Thirty per cent of those with covert bacteriuria in early pregnancy which is left untreated, will suffer from acute pyelonephritis later in the pregnancy. \(^{14}\) If the covert infections are treated, however, this can be prevented. Screening for and treatment of covert infections are worthwhile for three reasons:

- Spontaneous cures of covert infection in pregnancy are rare, possibly because the hydrokinetic defences are deranged
- Pregnancy is of short duration and it is easy to eradicate or suppress infection for 6-7 months
- No special clinic arrangements need to be made since it is only a trivial addition to routine antenatal care.

There may be other circumstances in which screening and treatment for bacteriuria could be worthwhile. For instance, in the elderly the urinary tract is a common source of Gram-negative septicaemia and this may prove fatal. Here one could vaccinate against core (Re) antigen of \textit{E. coli} to prevent endotoxin shock or one could screen and treat covert infections.

In schoolgirls screening cannot be justified because of the large turnover of bacteriuria. What is more, both in the adult woman and the schoolgirl with bacteriuria, short courses of treatment such as might be used on a large scale tend to precipitate symptomatic bouts of infection. This is because the reinfections which follow initially successful treatment are more commonly associated with the development of symptoms than are the persistent infections in untreated subjects. \(^{17}\) It would seem that in some subjects with covert infection the condition is a kind of symbiosis between host and parasite which is better left undisturbed.

In conclusion, therefore, the only group for which screening for covert infection has been proved valuable as a prophylactic measure is the pregnant population. It may be that additional methods will become available to identify high risk groups within the total bacteriuric population but as yet there is no proven method to achieve this.

**PREVENTION OF RECURRENT INFECTION**

After treatment some 50% of infections recur within one year. These recurrences are either due to the original infecting strain (relapse) and indicate that treatment has been ineffective, or they may be due to a different organism
(reinfection) and indicate defective host defences. Relapsing infections tend to be more common when the kidneys are involved and they may be prevented by identifying and dealing with the cause of the relapse. In Table 3 the cause of relapsing infection and suggested remedies are shown. When no cause or no

Table 3. Causes of relapsing urinary tract infection and suggested remedial action.

| Cause of relapse                                           | Action to be taken                                                                 |
|------------------------------------------------------------|------------------------------------------------------------------------------------|
| Sometimes it is necessary to start antibiotic treatment before the antibiotic sensitivity of the pathogen is known. In this case it is best to choose the drug on 'best guess' principle after consultation with the local bacteriologist. This may lead to a wrong choice of drug. | The pathogen should be identified as soon as possible and treatment started with the right drug. |
| Inadequate duration of treatment.                           | A 7-day course of treatment should be used. If compliance is likely to be poor, use a long-acting drug. |
| Emergence of minority resistant strain.                    | Retreat with an antibacterial agent to which the minority strain is sensitive.    |
| Inadequate concentration of drug.                          | Change to a high dose concentration.                                              |
| Stones                                                     | Remove the stones.                                                                |

treatable cause for relapsing infection is found, long-term prophylaxis is indicated. This is best achieved by prescribing a nightly dose of an antibacterial agent to which the organism is sensitive. This is because the longest time between successive urinary voidings is the night and, therefore, it is then that organisms are most likely to multiply in the urinary tract. It is important that the drug chosen for treatment should not produce resistance of the bowel flora otherwise breakthrough infections are likely. Suitable drugs include nitrofurantoin, since this drug is absorbed in the small intestine; nalidixic acid, since resistance transfer to this drug does not occur; or very low doses of cephalaxin, since these do not reach the colon. Trimethoprim and organic acids have also been used very successfully for long-term prophylaxis of frequently recurring symptomatic relapses.

The problem of symptomatic reinfections is less easy to overcome, although fortunately they are more widely spaced than the relapses. One way of coping at least partially with the morbidity they cause is to provide the patient with a dip-
slide and a suitable supply of an antibacterial agent to enable her (or him) to start treatment at the first evidence of the recurrence. At the same time a dip-slide might be inoculated and sent to the laboratory. In this way morbidity is reduced to a minimum and bacteriological supervision is retained.

There is still a very long way to go before morbidity from UTI is eliminated but if a careful assessment of precipitating factors is made by good history taking and wise use of conservative measures as well as antibacterial agents much can be done and there will only be a few patients who will need to be told they have to ‘live with the problem’.

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