

Prescribing...

Recurrent UTIs in women

- ✚ Around 40-50% of women experience at least one urinary tract infection (UTI) during their lifetime, of which 20-30% will have a recurrence within a few months.
- ✚ Recurrent UTI (usually defined as three episodes in the last 12 months or two episodes in the last 6 months) can have a considerable impact on a woman's quality of life.
- ✚ Antibacterial prophylaxis is effective in preventing recurrent episodes, but at the expense of unwanted effects and a risk of promoting bacterial resistance.
- ✚ This bulletin looks at the efficacy of different antibacterial regimens and non-antibacterial alternatives (oestrogens, cranberry, acupuncture and herbs) in the prevention of recurrent uncomplicated UTIs in women.

What is the background to this?

Risk factors associated with recurrent UTI in sexually active premenopausal women include frequency of sexual intercourse, age at first UTI (under 15 years indicates a greater risk) and history of UTI in the mother. After the menopause, risk factors include pelvic organ prolapse, incontinence, and post voiding residual urine. Before starting any prophylactic therapy, the infection needs treatment. UK guidelines recommend a 3-day course of trimethoprim (200mg twice daily) or nitrofurantoin (100mg twice daily). Asymptomatic bacteriuria appears to play a protective role in preventing symptomatic recurrence and so should not be treated, except in pregnant women.

What are the options for longer term treatment?

1. Continuous antibacterial prophylaxis

Public Health England (PHE) recommends a trial of low-dose antibacterial prophylaxis (trimethoprim 100mg or nitrofurantoin 50-100mg) nightly for women with frequent symptomatic recurrent infections, for 6 months.

A Cochrane systematic review of antibacterial prophylaxis for recurrent UTIs included 19 published randomised controlled trials. Continuous prophylaxis for 6-12 months, with trimethoprim, nitrofurantoin or a cefalexin, reduced rates of recurrent UTI when compared with placebo, the effect lasting only while the antibacterial was being taken. Unwanted effects included skin rash, nausea and vaginal itching. Dropouts and withdrawal were frequent, especially with nitrofurantoin. The rate ranges of microbiological recurrences per patient/year were 0.0-0.9 with antibacterial therapy and 0.8-3.6 with placebo. No conclusions could be drawn about the optimal duration of prophylaxis, schedule or doses.

2. Postcoital antibacterial prophylaxis

Postcoital therapy consists of a single dose of antibacterial following sexual activity. CKS, also known as Prodigy, recommends offering trimethoprim 100mg, taken within 2 hours of intercourse. A Cochrane review of antibacterial prophylaxis for recurrent UTIs found that in women with UTI associated with sexual intercourse, postcoital prophylaxis seemed to be as effective as daily prophylaxis.

3. Patient-initiated antibacterial prophylaxis

A randomised controlled trial of 83 postmenopausal women assessed the efficacy of a single dose of antibacterial (nitrofurantoin, co-trimoxazole, norfloxacin, amoxicillin or cefuroxime) taken after exposure to certain conditions associated with their UTI recurrence (such as sexual intercourse, travelling, working or walking for a long time, diarrhoea or constipation), compared with continuous low-dose daily antibacterial prophylaxis. Recurrent UTI in the intermittent group was reduced from 5.1 to 1.9 episodes per patient per year and in the continuous therapy group from 4.7 to 1.4 episodes per patient per year. The difference between the two groups was not significant. Women in the intermittent group were more likely to have more than one UTI. The proportion of women who experienced 0 or 1 episode per year was higher in the continuous treatment group (59% vs. 36% in the intermittent group, $p < 0.05$). In addition, there were more unwanted effects in the continuous group (93% vs. 64% in the intermittent group, $p < 0.05$).

What about cranberry products?

Cranberry products include juice, syrup, capsules and tablets. Research suggests that cranberries prevent bacteria (particularly *E. coli*) from adhering to uroepithelial cells that line the wall of the bladder. This effect is attributed to fructose and substances called proanthocyanidins contained in cranberries. PHE recommends cranberry products for recurrent UTIs.

In a Cochrane systematic review, among women with recurrent UTI (in four trials involving a total of 594 women) there was no significant reduction in risk of repeated symptomatic UTI with cranberry treatment compared to placebo or no treatment. However, when an outlying trial was removed (the largest, in 419 women, which used a lower threshold for defining UTI than other trials), the relative risk [RR] of recurrent UTI was 0.58 (95% CI 0.39 to 0.86). Analysis of two studies showed that cranberry products were as effective as antibacterial therapy in reducing the risk of repeat UTI in women. The results of three trials comparing high- vs. low-dose cranberry products found no difference between the two doses.

In another systematic review, pooling of data from two trials (involving a total of 250 women with recurrent infections) showed that cranberry-containing products were effective in reducing recurrent infections (RR 0.53, 95% CI 0.33 to 0.83). Cranberry juice was more effective than cranberry capsules or tablets. A better preventive effect from cranberry-containing products was noted with dosing frequency of more than twice daily.

A more recent double-blind, double-dummy randomised placebo-controlled trial (involving 221 premenopausal women with recurrent UTIs) found that co-trimoxazole (480mg daily) was more effective than cranberry capsules (500mg twice daily) in preventing recurrent UTIs. After 12 months, the mean number of clinical recurrences was 1.8 (95% CI 0.8 to 2.7) with co-trimoxazole vs. 4.0 (95% CI 2.3 to 5.6) with cranberry, $p=0.02$.

Are oestrogens in postmenopausal women effective ?

Oestrogens appear to promote the colonisation of the vagina with 'protective' lactobacilli and so loss of oestrogen after the menopause may make infection with pathogens more likely. Oral oestrogens appear to have no effect on recurrent UTIs. However, results from two randomised controlled trials show that vaginal oestrogens might reduce the number of recurrent UTIs, although the best mode of application (cream, pessary, vaginal ring) and duration of use are unclear. In one trial (in 93 women) with estradiol cream 0.5mg, the relative risk of recurrent UTI was 0.25 (95% CI 0.13 to 0.50); in the other trial, using a vaginal ring (in 108 women) the relative risk of recurrent UTI was 0.64 (95% CI 0.47 to 0.86). Unwanted effects (vaginal bleeding, discharge, irritation, burning, itching) were more frequent in women receiving oestrogens compared with placebo. Vaginal oestrogen therapies are indicated primarily for the treatment of local oestrogen deficiency symptoms, which may or may not include urinary symptoms.

What about other measures ?

Non-pharmacological measures such as vaginal *Lactobacillus* probiotics, acupuncture, herbs such as horseradish and nasturtium have been studied but did not show superiority over control in trials. However they may help individual patients.

In summary

The best evidence is for the prevention of recurrent UTIs is continuous daily antibiotics, but the benefit only lasts while the antibiotic is being taken. However the unpleasantness of a UTI needs to be weighed against the potential unwanted side effects. For some people intermittent antibacterial therapy is an option. Vaginal oestrogens for post menopausal women and a daily dose of cranberry juice may be considered. Acupuncture or herbal remedies may be helpful for individual women, but at present there is insufficient evidence to support their use.

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