

# THE MANAGEMENT OF CHRONIC NON-GONOCOCCAL URETHRITIS

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## ABSTRACT

Non-gonococcal urethritis (NGU) is one of the most common sexually transmitted diseases today. Oral tetracyclines and erythromycin are well established choices of treatment. Despite adequate treatment, about 30-35% of NGU persist or recur. The cause of persistence or recurrence remains unknown. Prostate gland involvement has to be ruled out where indicated. A 4 to 6 week course of tetracyclines or erythromycin is suggested for persistent or recurrent NGU. Counselling to emphasize that chronic NGU is probably a self limited disorder would be of help.

**Keywords:** Recurrent non-gonococcal urethritis, persistent non-gonococcal urethritis, chronic non-gonococcal urethritis, management.

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## INTRODUCTION

Non-gonococcal urethritis (NGU) is the most common sexually transmitted disease in many developed countries. It is also becoming an increasingly important sexually transmitted disease in Singapore. There has been a steady increase in the incidence of NGU over the last few years and it is now the second most common sexually transmitted disease in Singapore.

It is well established that *Chlamydia trachomatis* is responsible for 30-40% of NGU and *Ureaplasma urealyticum* implicated in another 10-20% of cases. However, no known etiological agents could be found in perhaps half the cases. Furthermore, about 30% of NGU persist or recur despite "adequate" treatment<sup>(1)</sup>. NGU, therefore, remains an enigma in many ways. In fact, the management of persistent or recurrent NGU is one of the most difficult problems facing venereologists today.

## PATHOGENESIS

Non-gonococcal urethritis (a more appropriate term than non-specific urethritis since some of the NGU do have specific causes) is known to be caused by certain pathogens as shown in Table I. Recommended treatment regimens include 1 to 2 weeks of tetracycline 500 mg orally four times daily or doxycycline 100 mg orally twice

daily. Alternative choices when tetracyclines are not tolerated or contraindicated are 1 to 2 weeks of an erythromycin base or stearate 500 mg orally four times daily. Despite drug compliance and non re-exposure to infection, about 30% to 35% of patients with NGU will have recurrences or incomplete resolution of pyuria when followed for 4 to 6 weeks after the initiation of treatment<sup>(1)</sup>. About half of these men will have symptoms of urethritis.

**Table I**  
**Etiology of Non-Gonococcal Urethritis**

<i>Chlamydia trachomatis</i>	
<i>Ureaplasma urealyticum</i>	
Others:	
<i>Trichomonas vaginalis</i>	- rare
Yeasts	- rare
Herpes simplex virus	- rare
<i>Bacteroides ureolyticus</i> ?	
<i>Mycoplasma genitalium</i> ?	
Others??	

What is then the underlying etiology of chronic NGU which implies either persistent or recurrent NGU? Is drug resistance responsible for persistent disease? Is reinfection the cause of recurrent disease where contact tracing has been inadequate or asymptomatic contacts not treated? Or are there some non infective pathological factors at work?

Tetracycline resistant *C. trachomatis* has not been described and although about 10% of *Ureaplasmas* are resistant to tetracyclines *in vitro*<sup>(2)</sup>, this probably accounts

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for only a small percentage of persistent NGU<sup>(3)</sup>.

Wong et al<sup>(4)</sup> isolated *Trichomonas vaginalis* from 3 out of 53 men with persistent or recurrent NGU. *T. vaginalis* probably also accounts for only a minority of persistent NGU.

The majority of persistent or recurrent NGU are culture negative for *C.trachomatis* and *U.urealyticum*<sup>(5)</sup>.

Re-infection does not appear to be an important cause of recurrent disease. Re-infection would seem likely when contact tracing has not been carried out or asymptomatic contacts not treated and there is re-exposure to such contacts or new partners. But treating contacts does not seem to greatly reduce the rate of recurrence<sup>(1,6)</sup>. Failure to re-isolate chlamydiae also suggests that re-infection is not an important cause of recurrent disease even when re-exposure is admitted<sup>(5)</sup>.

It has been suggested that re-infection of the urethra could occur when there is a focus of persistent infection in a contiguous site such as the prostate gland. Wong et al<sup>(4)</sup> found that in those men with persistent or recurrent NGU where the urethral culture was negative for known uropathogens, there was a high frequency of symptoms of prostatitis (ie. perineal pain, low back pain, testicular pain and hesitancy). There was also a higher number of leucocytes in the prostatic fluid and a more frequent evidence of prostatitis on ultrasound. A prostatic focus could act as a source of persistent or recurrent urethritis in a similar manner that chronic bacterial prostatitis frequently leads to recurrent cystitis.

What about a non infective etiology? It has been proposed that persistent and recurrent NGU is inflammatory and not infective in nature. Yoxall<sup>(7)</sup> showed that there was a higher number of patients with a history of atopy among those who were less likely to respond to the initial course of antibiotics. He suggested that "NGU is initiated by an exogenous infection eg. *C. trachomatis*, which then sensitizes the urethra of a susceptible individual to a number of probably non infectious stimuli." This was however, a study of a small sample size.

## MANAGEMENT

The first step in managing a patient with persistent or recurrent NGU is to obtain objective evidence of urethritis ie. presence of an urethral discharge or significant leucocytosis (more than 5 polymorphonuclear leukocytes per high power field) on microscopy of an urethral smear. The patient has to be questioned on drug compliance including avoidance of milk products when taking tetracyclines. Re-infection by a new partner or an inadequately treated partner has to be ruled out. Many patients are anxious over their condition and frequently inspect their urine for haziness or squeeze their penises to look for discharge. This anxiety may have been contributed by doctors who treat the "pus cells" present on microscopy of the urethral smear despite the patient being asymptomatic.

If the above factors are non contributory, and there is genuine persistent or recurrent NGU, what further treatment should be given after an initial course of oral tetracyclines? Since tetracycline resistant *Ureaplasma* is a possibility, it is worthwhile prescribing a course of 1 to 2 weeks of oral erythromycin 500 mg four times daily. If this still fails, then treatment for *T. vaginalis* seems reasonable. Most patients will improve again with the

second course of treatment, but about 30% will have recurrence of symptoms albeit mild like intermittent itching of the urethra. Such patients at this time would probably be going from one doctor to another in search for a cure. Most doctors would, on the other hand, be likely to continue the patient on yet another course of antibiotics.

It is important at this point to review the patient's entire history and previous treatment. If there are no florid symptoms of urethritis, no further antimicrobial treatment should be prescribed. If there is florid disease or symptoms prolong, a suggested practical treatment regime consists of a 4- to 6- week course of tetracycline 500 mg four times daily, doxycycline 100 mg twice daily or erythromycin 500 mg four times daily<sup>(8)</sup>. It is, however, unknown whether a prolonged course of antibiotics would alter the ultimate outcome of the disease.

In those patients with symptoms of prostatitis, prostate gland evaluation is worthwhile. This evaluation includes microscopy of prostatic fluid using a haemocytometer chamber, microbiological studies and perhaps ultrasound of the prostate gland. Wong et al<sup>(4)</sup> believe that confirmation of any prostatic involvement would have some prognostic significance since it has been shown that such patients respond poorly to 3 weeks of antibiotics. By analogy to patients with chronic bacterial prostatitis who are often treated with two to three months of antibiotics, these men may require even longer courses of therapy.

Urethral strictures, foreign bodies and intraurethral lesions should be excluded by urethroscopy. This is especially essential when there is a concurrent or past history of genital warts.

Is there a need for repeated urethral cultures for *C. trachomatis* or *U.urealyticum*? As mentioned earlier, urethral cultures are usually negative in patients with chronic NGU. Therefore, microbiological diagnosis will not provide further therapeutic guidance.

Like treating any patient with a chronic disease, patients suffering from chronic NGU should be counselled and reassured. It is understandable that many of these patients become neurotic and obsessive since treatment does not seem to be successful most of the time. Complaints of mild symptoms should not always be regarded as psychological in origin. Patients should, in particular, be reassured that the physical sequelae of chronic NGU is very slight. Infertility from chronic NGU is uncommon. And it is certainly not a presentation of AIDS.

The other issue that worries patients endlessly is the risk of transmission to their spouses or regular sex partner. Since these men do not usually harbour *C.trachomatis* and other pathogens are usually not identified or are not important causes of sequelae in women, the risk of transmission is exceedingly low. As stated earlier, recurrences arise in patients who have not resumed sexual intercourse and also in those whose partners have received apparently adequate therapy. It is therefore important to emphasise that recurrence is not a sign of infidelity.

## CONCLUSION

Chronic NGU is generally believed to be a self limited disorder. And even if no prolonged treatment with antimicrobials is given, symptoms will probably disappear

with time in most men. More important to remember is the possible psychological impact of chronic NGU on the patients. Emphasis on the slight physical consequences

of the disease and discussion on the course of the disorder will help to alleviate the distress experienced by the patient.

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