

The Case for Increased Chlamydia and Gonorrhea Screening of the At-Risk Male Population Worldwide

It is of concern to see recent dramatic increases in preventable, communicable, sexually transmitted infections (STIs) worldwide. Two STIs, chlamydia and gonorrhea, which are increasing at an alarming rate, have been somewhat forgotten and given poor resource allocation worldwide.

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While chlamydia and gonorrhea may have attracted less attention and, indeed, resources in recent years, their insidious health effects, coupled with the negative social and economic impact, need to be recognized. The good news is that thanks to both research and industry, we have the tools to mitigate the effects of these diseases. Sensitive tests are permitting early detection and allowing us to reach and treat the at-risk male population.

The medical and social burden of sexually transmitted *Chlamydia trachomatis* (Ct) and *Neisseria gonorrhoeae* (Ng) infections is well known.¹ While much literature regarding Ct disease in women has led to increased attention to the negative health outcomes of genital tract infection in women and the usefulness of subsequent screening programs, less information is available regarding the effects of Ct disease in men. Recently, Cunningham and Beagley suggested that up to 39.5 percent of prostatitis cases may be due to Ct.²

The authors note there is compelling evidence of an association between Ct infection and the development of prostatitis and other less-known genital tract diseases in men. The authors go on to discuss further considerations for the role of Ct infection and infertility.

The Value of Screening Programs

Because both Ct and Ng can cause asymptomatic infections, it is important to realize that screening programs have been shown to be the most effective means to control asymptomatic disease.^{3,4} Utilizing non-invasive specimens such as first-catch urine (FCU) has advantages, and the use of this specimen type is well-documented.^{5,6}

Urine screening has broadened STI-testing capabilities from the traditional public health STI clinic to innovative locations, such as juvenile detention centers, dance clubs, mobile clinics, and other venues frequented by adolescents, to reach the main reservoir of infection.

Coupled with nucleic acid amplification tests (NAATs), urine-based screening provides superior assay performance which is also well-documented.^{7,8} This is particularly important for screening programs where asymptomatic patients are most vulnerable to silent infection which advances to more serious disease. Individuals with asymptomatic infection continue to serve as a source of infection, and the argument can be made that asymptomatic patients are those most important to identify in order to decrease the overall prevalence of disease. Because current efforts have not adequately controlled these diseases, public health officials must consider additional means.

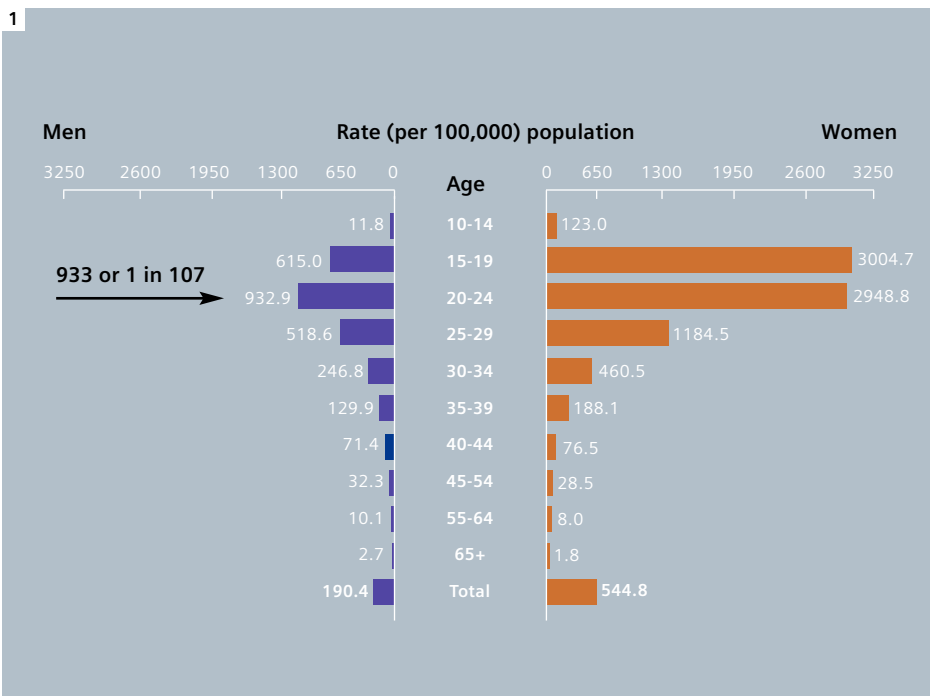
The latest national data with respect to the most affected groups in the US mirrors the pattern we have seen for some time now (Figure 1).

Molecular Diagnosis Using NAAT Testing

In vitro diagnostic tests can specifically identify individuals infected with Ct/Ng. Nucleic acid amplification tests (NAAT) are not only more sensitive than other methods but are also more effective for screening non-invasive clinical samples such as first-catch urine.^{5,7,10} NAAT assays, designed to operate on high-throughput platforms, are sensitive for screening programs to identify infected individuals.

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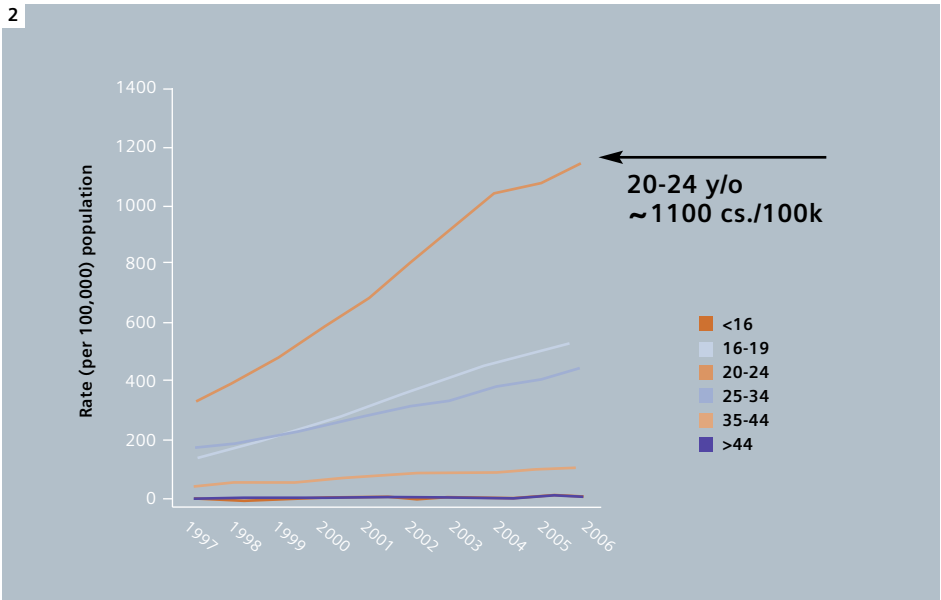


1 Chlamydia: age- and sex-specific rates in the US, 2007 (Centers for Disease Control, US)

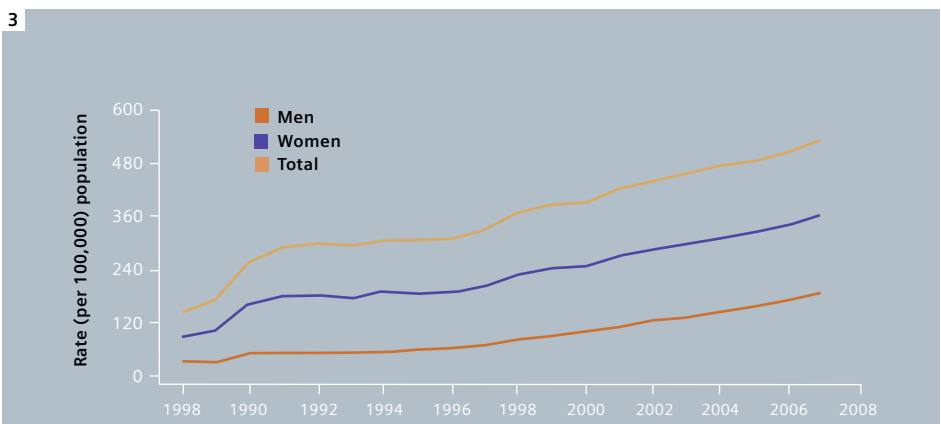
Women and men in the 15 to 24 year old age group are those most affected, according to the most recent data available from the Centers for Disease Control (CDC). The UK has also collected STI rate data that give us some insight into disease trends outside of the US. In fact, when we drill down to specific age groupings and rates, we see similar patterns of Ct disease within the UK as in the US regarding Ct increases in men (Figure 2).

Increasing Ct rates in both women and men, and ever-present Ng infections in women, have given rise to consideration of a targeted national male screening program to address the silent male reservoir. Given the continued increases in disease burden, one could wonder if the emphasis on screening, identifying, treating women, and not aggressively attacking the male reservoir, has been the best public policy.

Unfortunately, even with significant infusion of public funds, Ct disease rates continue to rise for both women and men in the US (Figure 3). Initially, public health officials and researchers considered the rise in rates to have been due to the introduction of significantly more sensitive NAAT assays. However, this theory has given way to the realization that the significant and sustained increase, especially of Ct disease rates, is due to a combination of social and economic factors, as well as questions concerning the biology of the organism and the disease it causes. In turn, this has led to questions as to the best approach for national screening programs.



2 Rates of diagnosis of uncomplicated genital chlamydial infection in males according to age group in the UK, 1997-2006 (Genitourinary Clinics, Health Protection Agency, UK)



Note: As of January 2000, all 50 states and the District of Columbia had regulations requiring the reporting of chlamydia cases.

3 Chlamydia rates: total and by sex in the US, 1988-2007 (Centers for Disease Control, US)

Expert Consultation

To that end, and to their credit, the CDC held an Expert Consultation in 2007 that brought together opinion leaders from state and local public health organizations and key members of the research field. The aim was to review the literature, share experiences, and develop consensus information to guide US policy regarding Ct screening in men. The first documents from the Consultation were made available and distributed by the CDC in May 2007 and are available on the CDC's website.⁹ A summary of the Consultation findings is found in Figure 4.

One outcome of the CDC Expert Consultation process included a recent publication by Consultation attendees Gaydos, Ferrero, and Papp regarding a review of Ct laboratory aspects. In the paper, key recommendations for advancing male Ct screening in the US were made.¹⁰ The review supports the notion that NAATs are the test of choice for Ct screening of males and that the use of non-invasive FCU specimens best advances the potential for increased screening of males. The review concludes that increasing the number of at-risk males screened may provide potential reduction in overall disease burden in both men and women.

Screening the Male Population

Just as health maintenance organizations, (HMOs), family planning organizations, the military, and numerous professional organizations came to realize that screening for certain STIs was in their best economic interest and was the

proper health policy for women, it will come to pass that many of the same cost-effective policy measures will be put in place for men. Finding ways to have men avail themselves of simple, relatively inexpensive, accurate, easy-to-do NAAT screening tests will lead to increased cost-savings versus treating male-acquired sequelae and infertility, while advancing the mission to protect women. Public health cannot do this in a vacuum.

clinical laboratories. Without all provider sectors engaged, the necessary screening of both women and men in sufficient numbers to affect disease trends will never be realized. We must foster a partnership combining public health sector expertise with access to special populations outside the public sector. Robust data collection and analysis is needed, coupled with an economic incentive for the military,

country, but somehow we have managed to do just that in male Ct rates during the most recent five-year period (Figure 5).

Reducing Transmission

Several articles published in late 2008 following the CDC's Expert Consultation on male screening have led the way to a better understanding of where we need to consider enhanced screening activities. Clearly, we cannot veer from any policy aimed at reducing morbidity in women; however, enhanced screening of selected male populations can only enhance efforts toward women.

In an article published in 2008, Dunne et al. noted that male infection can result in transmission to female partners and they suggested that screening men should be considered as a means of reducing transmission risk to female partners. They further suggested that rescreening men found to be infected could impact Ct morbidity in males, as currently recommended for women.¹¹ Dunne et al. also posed the question in a recent editorial: "Key activities that lead to significant reductions in morbidity are needed, and enhancing activities to identify and treat men with Ct infection might be a step to reducing Ct morbidity."¹² Others have pointed out that Ct infections in men serve as a reservoir for transmission to females.^{13,14}

Economic considerations, as well as moral obligations, led to more robust screening activities directed toward women 12 years ago. This was accompanied by a significant infusion of federal dollars. Similar discussions have occurred regarding the need to increase attention toward men.

Regarding Ng infection in males we have more work to do here as well lest we think the battle against genital tract infections due to Ng has been won. In the US, while significant strides were made from the late 1970s to now, it is predicted that the US will not meet the 2010 Healthy People goal for Ng disease. As a matter of fact for men we are very far from the goal of 19 cases per 100,000 with 113.7 cases per 100,000 recorded in 2007.

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Recommendation	Strength
Urine specimen using NAATs are preferred	Strongly Recommend
Males attending STI clinics	Strongly Recommend
Males attending National Job Training Program	Strongly Recommend
Males in military	Strongly Recommend
Males entering juvenile facilities	Recommend
Communities with high Ct prevalence should consider screening men	Recommend

4 Compilation of the Centers for Disease Control 2007 Expert Panel's Recommendations regarding male screening

Ct: *Chlamydia trachomatis*; NAATs: nucleic acid amplification test; STI: sexually transmitted infection

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Age	Sex	2002	2007	% Increase
15-19 years	Female	2619.1	3004.7	14.7%
	Male	408.4	615.0	50.6%
20-24 years	Male	691.5	932.9	35.0%
Total	Female	456.5	544.8	19.3%
Total	Male	130.4	190.4	46.0%

5 Increase in *Chlamydia trachomatis* rates in selected age groups and total by sex in the US, 2002–2007

While the case can be made that a high percentage of positive test findings do come from the public sector, the numbers of tests rendered to many of the at-risk populations come from the military, HMOs, family planning, and other non- and for-profit sectors via military, hospital, and independent

HMO, family planning, and other non- and for-profit sectors who will be important in providing this access.

Normally it would be unacceptable to have preventable disease rates that increase by over 50 percent during a five-year time frame in any developed

Furthermore, when one delves into the data available, we find regional outbreaks occurring,¹⁵ sustained Ng activity in certain sectors, and case rates for some age groups increasing. For the two-year period 2005–2007, we saw case rates increase by 9.5 percent for males aged 15 to 19; from 261.2 per 100,000 to 286 per 100,000.

Dual Screening

It is important to realize that many women and men (up to 50 percent of those infected) are dually infected with both Ct and Ng. One significant armament we have in the arsenal for battle is the fact that all major NAAT assays have the capability to simultaneously test both Ct and Ng from the same FCU specimen.

To summarize, much of the evidence today points to the realization that we need to find innovative ways to reach the at-risk male population to identify and treat significant disease potential in the male population and at the same time better protect the female population worldwide. Fortunately, with state-of-the-art NAAT assays, we have the ability to provide the most sensitive means to detect Ct and Ng disease using easy-to-obtain non-invasive specimens.



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