

Use of Gonozyme on Urine Sediment for Diagnosis of Gonorrhea in Males

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We compared enzyme immunoassay (Gonozyme; Abbott Laboratories, North Chicago, Ill.) for detection of gonococcal antigen in urine sediments with urethral swab culture for diagnosis of gonorrhea in men attending a venereal disease clinic. The prevalence of infection was 14% by culture (27/196). The sensitivity of enzyme immunoassay was 93% (25/27) compared with the culture method, and the specificity was 99% (167/169). The ability to detect gonococcal antigen in urine sediment may provide the basis for a noninvasive method of screening for gonococcal infection.

Much information is available on the prevalence of sexually transmitted disease agents in asymptomatic female populations being routinely screened for such infections. These data are accumulated because women have routine pelvic examinations in which the cervix is readily accessible and can be sampled for the presence of *Neisseria gonorrhoeae* and *Chlamydia trachomatis* (the two most common sexually transmitted pathogens). It is not uncommon in screening high-risk populations to find prevalence rates of 15 to 25% for these agents. Obviously, when identified, infected women and their male partners are treated.

Unfortunately, similar prevalence data cannot be generated for males, because there are no convenient noninvasive methods of sampling male urethras. Studies in selected settings have shown that asymptomatic gonococcal or chlamydial infections are common in male urethras (6).

It is clear that we must identify asymptomatic male carriers if we are to impact on the reservoir for sexually transmitted disease. However, it is impractical to consider urethral swabbing as a routine technique. It is possible that urine could be an appropriate specimen for screening asymptomatic males (3). A previous study of adolescent males found that pyuria in first-catch urine specimens had a high predictive value for recovery of chlamydiae or gonococci from urethral swabs (1). Obviously, it would be desirable if the same specimen could be used for both screening (pyuria) and diagnosis (culture or antigen detection). If urine were an appropriate holding medium for gonococci and *Chlamydia* spp., it might be possible to screen first-catch urine specimens for the polymorphonuclear leukocytes and then make appropriate cultures. However, results obtained with urine as a holding medium for gonococcal cultures have been variable, and urine or urine sediment are clearly not the specimens of choice for chlamydial culture (5). Antigen detection may offer a viable alternative. Rudrik et al. have shown that gonococcal antigens could be detected by the Gonozyme (Abbott Laboratories, North Chicago, Ill.) test in urine specimens from men with gonococcal urethritis (2). We have been evaluating a similar approach and now report our results for gonorrhea diagnosis by using Gonozyme in the detection of gonococcal antigen in urine sediment.

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MATERIALS AND METHODS

Patient population. Males attending the Contra Costa County sexually transmitted disease clinic were evaluated for the presence of urethral infection with gonococci. These men either were symptomatic, were requesting checkups, or were named contacts.

Specimen collection. The routine procedure for evaluating the men included a Gram stain of urethral discharge or smear made by a urethral swab. A second swab was streaked on modified Thayer-Martin medium. After these specimens were collected, approximately 30 ml of urine was collected into a container and refrigerated. Urine specimens were held for approximately 18 h before being processed. This holding period probably reflects a "real-world" situation, in which the test is performed the morning after an afternoon or evening clinic.

The urine specimen was split and centrifuged (approximately 500 × g for 10 min), and each sediment was suspended in 0.2 to 0.5 ml of urine. A smear of one sediment was prepared and evaluated for the presence of polymorphonuclear leukocytes. A cotton swab of that sediment was streaked onto Thayer-Martin medium for detection of *N. gonorrhoeae*. The second sediment was suspended in 0.5 ml of Gonozyme specimen dilution buffer, and 0.20 ml of the suspension was transferred to a well in a reaction tray for processing in the Gonozyme test.

Presumptive diagnosis of gonococcal infection was based on identification of gram-negative intracellular diplococci by the Gram stain. Culture was performed on all specimens, and gonococci were identified as gram-negative cocci and by the oxidase reaction and sugar utilization patterns.

Gonozyme test. The Gonozyme procedure used was as described previously (4), except that the incubation periods were 45 min, as in the current recommended protocol.

RESULTS

A comparison of results of the Gonozyme test with those of the culture showed that the two tests had a 98% (192/196) agreement. The prevalence of gonococcal infection indicated by the culture method was 14% (27/196). The sensitivity of Gonozyme compared with that of the culture method was 93% (25/27), and the specificity was 99% (167/169). The

predictive value of a positive Gonozyne test was 93%; the predictive value of a negative Gonozyne test was 99%.

Of the 27 culture-confirmed gonococcal infections, only 20 (74%) yielded gonococci by culture of the urine sediments 18 to 24 h after they had been collected.

The Gonozyne test was also applied to some whole, unspun urine specimens (processed with an equal volume of specimen dilution buffer). Of 15 specimens that were positive when sedimented, we found that only 12 (80%) uncentrifuged urines were positive.

The majority (23/27) of the men with positive cultures were symptomatic. Only two of the culture-positive specimens did not show high (>10 per high-power field) polymorphonuclear leukocyte counts in resuspended urine sediments.

As expected, the Gram stain was a reliable diagnostic test. All 25 men with gram-negative intracellular diplococci seen on smear were culture positive. Of the 171 samples giving negative smears, 2 had positive cultures. Thus, the gram-stained smear was 93% sensitive and 100% specific, with a positive predictive value of 100% and a negative predictive value of 99%.

One false-positive reaction in the Gonozyne test showed an optical density of 0.465 (the cutoff point for positivity was approximately 0.070). This specimen was negative by both culture and Gram stain. The other false-positive specimen grew *Neisseria meningitidis*.

DISCUSSION

Nonculture methods for diagnosing sexually transmitted disease represent an attractive modality for screening asymptomatic infections in males. In previous studies, the Gonozyne assay was found to be virtually the equivalent of the Gram stain in diagnosis of symptomatic gonococcal urethritis (4). Obviously, the Gram stain is the method of choice for initial evaluation of symptomatic urethritis in men, but it is not accurate in asymptomatic infections. Rudrik et al. found the enzyme immunoassay to be relatively efficient in diagnosis of gonorrhea with uncentrifuged urine (2). Our experience with specimens that were held overnight was less satisfactory. We did not find this procedure as sensitive as the initial Gram stain or urethral swab culture. Neither did we find the culture of the stored urine sediment to be as sensitive as direct urethral swab culture. Rapid processing might have improved our results, but it may not be possible in a screening test.

Enzyme immunoassay performed well in detecting infection. With a performance profile of approximately 93%

sensitivity and 99% specificity, the results with urine sediment are similar to those one would expect with routine use of Gram stain. We cannot extrapolate our results to an asymptomatic population, because most of the men with gonococcal infections were symptomatic. Of the four asymptomatic men with gonococcal infections that were detected by culture, three were Gonozyne positive.

Our results suggest that a screening approach for detection of gonococcal infection may be based on the use of urine as a specimen. It is possible that an initial screen could be done by use of esterase or other indicators for the presence of polymorphonuclear leukocytes. That initial cut would allow for identification of those specimens to be further tested for specific pathogens. Thus, after the initial screen, urine specimens with positive esterase tests could be centrifuged and sediments could be tested for gonococcal antigen. If a similar test could be developed for chlamydial infection, we could be in a position to evaluate screening methods for chlamydial and gonococcal infections in males. Availability of such screening measures could have important public health implications and aid in control programs for these important organisms.

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