Testosterone, the major androgenic hormone, is secreted mainly by the interstitial (Leydig) cells of the testis in males and, to a minor extent, from the adrenal cortex and from the ovaries in females. Testosterone circulates in the plasma, bound primarily to sex hormone-binding globulin (SHBG) and albumin. Less than 4% of total testosterone circulates as free hormone.

Historically, only the free testosterone was thought to be the biologically active component. However, testosterone is weakly bound to serum albumin and dissociates freely, becoming available for tissue uptake through the capillary bed. Accordingly, both free and albumin-bound testosterones are considered “bioavailable.”

Serum SHBG concentration increases with age and, in males, testosterone levels start declining in the fifth decade of life with the lowest levels seen in men 70 years of age and older. The decrease in free and bioavailable testosterone levels may be greater than the decrease in total testosterone.

Bioavailable testosterone measurement may give a more accurate assessment of hyperandrogenic and hypoandrogenic states than total testosterone. Furthermore, individuals with SHBG abnormalities may require measurement of bioavailable testosterone. The bioavailable testosterone assay requires a smaller specimen volume and is reported more rapidly than the free testosterone assay (#8508 Testosterone, Total and Free, Serum).

**Useful For**
- A second-order test for evaluating sexual dysfunction, gonadal failure, sarcopenia, hirsutism, and monitoring hormonal replacement therapy
- Evaluating testosterone levels in individuals with SHBG abnormalities
- Assessing level of biologically active testosterone

**Interpretation**
- Low levels of bioavailable testosterone may be seen in gonadal failure.
- When gonadal failure occurs in the presence of conditions with abnormally high concentrations of SHBG, total testosterone levels may be normal while bioavailable testosterone levels are decreased.
- Bioavailable testosterone concentrations less than 70 ng/dL in adult males of any age may merit additional investigation.
- High levels of bioavailable testosterone are often seen in women with hirsutism and polycystic ovarian syndrome.

**Cautions**
- Oral estrogen treatment increases serum SHBG with a resultant increase in SHBG-bound testosterone. Patients receiving oral estrogens, such as in reproductive contraceptives or hormonal replacement therapies, will have lower bioavailable testosterone than patients not receiving estrogens.
- Total testosterone measurements are often sufficient for the evaluation of hypogonadal states in males and hirsutism and virilism in females.
Test Title: Testosterone, Total and Bioavailable, Serum

#80065

Supportive Data

Correlates well with free testosterone by equilibrium dialysis (r = 0.9606; n = 199)

References


Method

The method is based on the differential precipitation of SHBG by ammonium sulfate following equilibration of the serum specimen and tracer amounts of tritium-labeled testosterone. The results are expressed as the percent of testosterone free or albumin bound (not precipitated with SHBG) compared with an albumin standard. The product of this percentage and the total testosterone measurement is the total bioavailable testosterone. (Wheeler, MJ: The determination of bio-available testosterone. Ann Clin Biochem 1995;32:345-357)

Specimen Required: Draw blood in a plain, red-top tube(s) or an SST tube(s). Spin down and send 1.0 mL of serum refrigerated.

NOTE: PATIENT'S AGE AND SEX ARE REQUIRED ON REQUEST FORM FOR PROCESSING.

Reference Values:

<table>
<thead>
<tr>
<th>TESTOSTERONE, TOTAL</th>
<th>TESTOSTERONE, BIOAVAILABLE</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Males:</strong></td>
<td><strong>Females (non-oophorectomized):</strong></td>
</tr>
<tr>
<td>&lt; 1 year: not established</td>
<td>&lt; 19 years: not established</td>
</tr>
<tr>
<td>1-9 years: &lt; 40 ng/dL</td>
<td>20-29 years: 83-257 ng/dL</td>
</tr>
<tr>
<td>10-11 years: &lt; 200 ng/dL</td>
<td>30-39 years: 72-235 ng/dL</td>
</tr>
<tr>
<td>12-13 years: &lt; 800 ng/dL</td>
<td>40-49 years: 61-213 ng/dL</td>
</tr>
<tr>
<td>14 years: &lt; 1200 ng/dL</td>
<td>50-59 years: 50-190 ng/dL</td>
</tr>
<tr>
<td>15-16 years: 100-1200 ng/dL</td>
<td>60-69 years: 40-168 ng/dL</td>
</tr>
<tr>
<td>17-18 years: 300-1200 ng/dL</td>
<td>≥ 70 years: not established</td>
</tr>
<tr>
<td>19-40 years: 300-950 ng/dL</td>
<td></td>
</tr>
<tr>
<td>≥ 40 years: 240-950 ng/dL</td>
<td></td>
</tr>
<tr>
<td><strong>Females:</strong></td>
<td></td>
</tr>
<tr>
<td>&lt; 1 year: not established</td>
<td>&lt; 19 years: not established</td>
</tr>
<tr>
<td>1-9 years: &lt; 40 ng/dL</td>
<td>20-50 years (on oral estrogen): 0.8-4.0</td>
</tr>
<tr>
<td>10-11 years: &lt; 75 ng/dL</td>
<td>20-50 years (not on oral estrogen): 0.8-10</td>
</tr>
<tr>
<td>12-16 years: &lt; 120 ng/dL</td>
<td>≥ 50 years: not established</td>
</tr>
<tr>
<td>17-18 years: 20-120 ng/dL</td>
<td></td>
</tr>
<tr>
<td>≥ 19 years: 12-72 ng/dL</td>
<td></td>
</tr>
</tbody>
</table>

Analytic Time: Same day/1 day
Days Set Up: Monday through Friday
Fee: $124.90
CPT Code:
84402- testosterone, bioavailable
84403- testosterone, total
Chlamydiae are gram-negative, obligate intracellular bacteria. *Chlamydia trachomatis* causes cervicitis, urethritis, salpingitis, proctitis, and endometritis in women and urethritis, epididymitis, and proctitis in men. In the United States, the prevalence of genital *Chlamydia trachomatis* infections among persons 15-44 years of age is estimated to be approximately 4 million infected, and it is considered the most common sexually transmitted disease. Importantly, it is estimated that about 25% of women who have acute salpingitis become infertile, and chlamydial infection is the most common cause of acute salpingitis.1,2

*N. gonorrhoeae* are gram-negative, oxidase-positive diplococci. *Neisseria gonorrhoeae* causes acute urethritis in males, which if untreated can develop into epididymitis, prostatitis, and urethral stricture. In females, the primary site of infection is the endocervix. An important complication in females is development of pelvic inflammatory disease, which contributes to infertility.1,2

Culture of *Neisseria gonorrhoeae* can be difficult because the organism does not survive for long periods outside its host and it is highly susceptible to adverse environmental conditions, such as drying and extreme temperatures.

The combined detection of *Chlamydia trachomatis* or *Neisseria gonorrhoeae* from a single swab or urine specimen

**Clinical**

Chlamydiae are gram-negative, obligate intracellular bacteria. *Chlamydia trachomatis* causes cervicitis, urethritis, salpingitis, proctitis, and endometritis in women and urethritis, epididymitis, and proctitis in men. In the United States, the prevalence of genital *Chlamydia trachomatis* infections among persons 15-44 years of age is estimated to be approximately 4 million infected, and it is considered the most common sexually transmitted disease. Importantly, it is estimated that about 25% of women who have acute salpingitis become infertile, and chlamydial infection is the most common cause of acute salpingitis.1,2

*Neisseria gonorrhoeae* are gram-negative, oxidase-positive diplococci. *Neisseria gonorrhoeae* causes acute urethritis in males, which if untreated can develop into epididymitis, prostatitis, and urethral stricture. In females, the primary site of infection is the endocervix. An important complication in females is development of pelvic inflammatory disease, which contributes to infertility.1,2

Culture of *Neisseria gonorrhoeae* can be difficult because the organism does not survive for long periods outside its host and it is highly susceptible to adverse environmental conditions, such as drying and extreme temperatures.

Useful For

The combined detection of *Chlamydia trachomatis* or *Neisseria gonorrhoeae* from a single swab or urine specimen

**Interpretation**

- A positive result indicates the presence of DNA of *Chlamydia trachomatis* and/or *Neisseria gonorrhoeae*.
- A negative result indicates that DNA for *Chlamydia trachomatis* and/or *Neisseria gonorrhoeae* was not detected in the specimen.
- The predictive value of an assay depends on the prevalence of the disease in any particular population. In settings with a high prevalence of sexually transmitted disease, positive assay results have a high likelihood of being true positives. In settings with a low prevalence of sexually transmitted disease, or in any setting in which a patient’s clinical signs and symptoms or risk factors are inconsistent with gonococcal or chlamydial urogenital infection, positive results should be carefully assessed and the patient retested by other methods (eg, culture for *Neisseria gonorrhoeae*) if appropriate.

**Cautions**

- This method has been tested only with endocervical swabs, male urethral swabs, and male and female urine specimens. Performance with other specimens has not been assessed.
- Optimal performance of the test requires adequate specimen collection and handling.
- Testing of urine specimens is not intended to replace cervical exam and endocervical sampling for diagnosis of urogenital infection. Cervicitis, urethritis, and urinary tract infections may result from other causes or concurrent infections may occur.
- Urine testing should be performed on first-catch random urine specimens (ie, the first 15-20 mL of the urine stream). During the clinical evaluation of the testing method, urine volumes up to 60 mL were included in the performance estimates. The effects of other variables such as midstream collection have not been determined.
The effects of other potential variables, such as vaginal discharge, use of tampons, douching, and specimen collection variables have not been determined.

A negative test result does not exclude the possibility of infection because improper specimen collection, technical error, specimen mix-up, concurrent antibiotic therapy, or the number of organisms in the specimen (which may be below the sensitivity of the test) may affect test results.

As with many diagnostic tests, results should be interpreted in conjunction with other laboratory and clinical data available to the physician.

The assay does not detect plasmid-free variants of Chlamydia trachomatis.

This assay should not be used for the evaluation of suspected sexual abuse or for other medico-legal indications. Additional testing is recommended in any circumstance when false-positive or false-negative results could lead to adverse medical, social, or psychological consequences.

This assay cannot be used to assess therapeutic success or failure, since nucleic acids from Chlamydia trachomatis and Neisseria gonorrhoeae may persist following antimicrobial therapy.

In laboratory studies, blood >5% was shown to cause indeterminate (inhibitory) results in both urine and swab specimens and false-negative results in urine specimens. Blood >5% also may cause false-negative results in swab specimens. Specimens with moderate to gross blood may interfere with assay results.

The presence of highly pigmented substances in urine, such as bilirubin (10 mg/mL) and phenazopyridine (10 mg/mL), may cause indeterminate or false-negative results.

Leukocytes in excess of 250,000 cells/mL may cause indeterminate or false-negative results (swab specimens).

The assay may cross-react with Neisseria cinerea and Neisseria lactamica and may cause false-positive results.

Performance characteristics for detecting Neisseria gonorrhoeae in males are based on testing patients with infection rates of 27-43%. The male populations sampled were from sexually transmitted disease (STD) clinics where the prevalence of Neisseria gonorrhoeae is higher than in other clinical settings. Likewise, the majority of females in the study with Neisseria gonorrhoeae infections were from STD clinics. In the low prevalence setting (1.2% prevalence), only 6 gonococcal infections were identified. Positive results in low prevalence populations should be interpreted carefully in conjunction with clinical signs and symptoms, patient risk profile, and other findings and the understanding that the likelihood of a false positive may be higher than a true positive.

Testing urine specimens as the sole test for identifying female patients with chlamydial or gonococcal infections may miss infected individuals (17/100 or 17% of females with Chlamydia trachomatis-positive cultures, and 11/80 or 13.8% of females with Neisseria gonorrhoeae-positive cultures had negative results when urine only was tested) with the BD Probe Tec ET Chlamydia trachomatis/Neisseria gonorrhoeae Amplified DNA Assay.

The BD Probe Tec ET Neisseria gonorrhoeae assay has not been evaluated with a sufficient number of specimens from asymptomatic males to estimate sensitivity in this population.

Supportive Data

BD Probe Tec detection of Chlamydia trachomatis was twice as sensitive as culture with urine and swab specimens obtained from patients with genitourinary infections. In a study of 4,130 specimens (urine and swabs from men and women) the sensitivity for detection of Chlamydia trachomatis and Neisseria gonorrhoeae (compared with LCx and culture) was >93% from all specimens. Urine specimens yielded the lowest sensitivities for both Chlamydia trachomatis (80.5%) and Neisseria gonorrhoeae (84.9%) from women. These results were similar to those obtained by LCx testing.

Of 825 male and 399 female urine specimens tested for both Chlamydia trachomatis and Neisseria gonorrhoeae with the BD Probe Tec ET system, the overall sensitivity was 95.3% (Chlamydia trachomatis) and 100% (Neisseria gonorrhoeae) compared with the Roche Amplicor PCR test for both organisms.
**Test Title:** *Chlamydia trachomatis* and *Neisseria gonorrhoeae* by Nucleic Acid Amplification

#81094

**Specimen Required:** SUBMIT ONLY 1 OF THE FOLLOWING SPECIMENS:

**NOTE:**
1. SPECIMEN SOURCE IS REQUIRED ON REQUEST FORM FOR PROCESSING.
2. Spermicidal agents and feminine powder sprays interfere with the assay and should not be used prior to collection.
3. Please complete a “Microbiology Request Form” (Supply T244) or a “Mayo Connect Additional Test Information” form (Supply T357), and forward it with the specimen.

**Method**
The BD Probe Tec ET *Chlamydia trachomatis* and *Neisseria gonorrhoeae* Amplified DNA Assay uses homogenous strand displacement amplification technology as the amplification method and fluorescent energy transfer as the detection method to test for the presence of *Chlamydia trachomatis* and *Neisseria gonorrhoeae* DNA in clinical specimens. The BD Probe Tec ET test is FDA-approved.5

References


**Endocervix (Females Only)**
Collect specimen using the NAT Swab Specimen Collection System (Supply T501) supplied as follows:
1. Remove excess mucus from the exocervix with the medium cleaning swab provided in the NAT Swab Specimen Collection System (Supply T501) and discard.
2. Insert the second medium swab into the endocervix and rotate the swab for 15-30 seconds to ensure adequate sampling.
3. Withdraw the swab.
4. Holding the tube upright, verify that all NAT medium is at the bottom of the transport tube. Unscrew the cap of the transport tube, fully insert the swab into the tube, and break the swab at the score line. Screw the cap on securely.
5. Send specimen refrigerated.

**Urethra (Males Only)**
Collect specimen using the NAT Swab Specimen Collection System (Supply T502) supplied as follows:
1. The patient should not have urinated for at least 1 hour prior to specimen collection.
2. Insert the small-tipped specimen swab 2-4 cm into the urethra and rotate the swab for 3-5 seconds to ensure adequate sampling.
3. Withdraw the swab.
4. Holding the tube upright, verify that all NAT medium is at the bottom of the transport tube. Unscrew the cap of the transport tube, fully insert the swab into the tube, and break the swab at the score line. Screw the cap on securely.
5. Send specimen refrigerated.

Continued on next page.
Test Title: *Chlamydia trachomatis* and *Neisseria gonorrhoeae* by Nucleic Acid Amplification

#81094

**Specimen Required:**

**Urine (Males and Females)**

1. Patient should not have urinated for at least 1 hour prior to specimen collection.
2. The patient should collect the first 15-20 mL of voided urine (the first part of the stream-NOT MIDSTREAM) in a screw-capped, sterile, plastic, preservative-free specimen container.
3. Send specimen refrigerated.

**Reference Values:**

*Chlamydia trachomatis* DNA not detected
*Neisseria gonorrhoeae* DNA not detected

**Analytic Time:** 1 day

**Days Set Up:** Monday through Saturday

**Fee:** $138.90

**CPT Code:**

87491- *Chlamydia trachomatis*
87591- *Neisseria gonorrhoeae*
Neisseria gonorrhoeae are gram-negative, oxidase-positive diplococci. Neisseria gonorrhoeae causes acute urethritis in males, which if untreated can develop into epididymitis, prostatitis, and urethral stricture. In females, the primary site of infection is the endocervix. An important complication in females is development of pelvic inflammatory disease, which contributes to infertility.1,2

Culture of Neisseria gonorrhoeae can be difficult because the organism does not survive for long periods outside its host and it is highly susceptible to adverse environmental conditions, such as drying and extreme temperatures.

The detection of Neisseria gonorrhoeae from a swab or urine specimen

• A positive result indicates the presence of DNA of Neisseria gonorrhoeae.
• A negative result indicates that DNA for Neisseria gonorrhoeae was not detected in the specimen.
• The predictive value of an assay depends on the prevalence of the disease in any particular population. In settings with a high prevalence of sexually transmitted disease, positive assay results have a high likelihood of being true positives. In settings with a low prevalence of sexually transmitted disease, or in any setting in which a patient's clinical signs and symptoms or risk factors are inconsistent with gonococcal or chlamydial urogenital infection, positive results should be carefully assessed and the patient retested by other methods (eg, culture for Neisseria gonorrhoeae) if appropriate.

Clinical
Neisseria gonorrhoeae are gram-negative, oxidase-positive diplococci. Neisseria gonorrhoeae causes acute urethritis in males, which if untreated can develop into epididymitis, prostatitis, and urethral stricture. In females, the primary site of infection is the endocervix. An important complication in females is development of pelvic inflammatory disease, which contributes to infertility.1,2

Culture of Neisseria gonorrhoeae can be difficult because the organism does not survive for long periods outside its host and it is highly susceptible to adverse environmental conditions, such as drying and extreme temperatures.

Useful For
The detection of Neisseria gonorrhoeae from a swab or urine specimen

Interpretation
• A positive result indicates the presence of DNA of Neisseria gonorrhoeae.
• A negative result indicates that DNA for Neisseria gonorrhoeae was not detected in the specimen.
• The predictive value of an assay depends on the prevalence of the disease in any particular population. In settings with a high prevalence of sexually transmitted disease, positive assay results have a high likelihood of being true positives. In settings with a low prevalence of sexually transmitted disease, or in any setting in which a patient's clinical signs and symptoms or risk factors are inconsistent with gonococcal or chlamydial urogenital infection, positive results should be carefully assessed and the patient retested by other methods (eg, culture for Neisseria gonorrhoeae) if appropriate.

Cautions
• This method has been tested only with endocervical swabs, male urethral swabs, and male and female urine specimens. Performance with other specimens has not been assessed.
• Optimal performance of the test requires adequate specimen collection and handling.
• Testing of urine specimens with this assay is not intended to replace cervical exam and endocervical sampling for diagnosis of urogenital infection. Cervicitis, urethritis, and urinary tract infections may result from other causes or concurrent infections may occur.
• Urine testing should be performed on first-catch random urine specimens (ie, the first 15-20 mL of the urine stream). During the clinical evaluation of this method, testing urine volumes up to 60 mL was included in the performance estimates. The effects of other variables such as midstream collection have not been determined.
• The effects of other potential variables, such as vaginal discharge, use of tampons, douching, and specimen collection variables have not been determined.
• A negative test result does not exclude the possibility of infection because improper specimen collection, technical error, specimen mix-up, concurrent antibiotic therapy, or the number of organisms in the specimen (which may be below the sensitivity of the test) may affect test results.
• As with many diagnostic tests, results should be interpreted in conjunction with other laboratory and clinical data available to the physician.
• This assay does not detect plasmid-free variants of Chlamydia trachomatis.
• This assay should not be used for the evaluation of suspected sexual abuse or for other medico-legal indications. Additional testing is recommended in any circumstance when false-positive or false-negative results could lead to adverse medical, social, or psychological consequences.

• This assay cannot assess therapeutic success or failure, since nucleic acids from *Chlamydia trachomatis* and *Neisseria gonorrhoeae* may persist following antimicrobial therapy.

• In laboratory studies, blood >5% was shown to cause indeterminate (inhibitory) results in both urine and swab specimens and false-negative results in urine specimens. Blood >5% may cause false-negative results in swab specimens. Specimens with moderate to gross blood content may interfere with assay results.

• The presence of highly pigmented substances in urine, such as bilirubin (10 mg/mL) and phenazopyridine (10 mg/mL), may cause indeterminate or false-negative results.

• Leukocytes in excess of 250,000 cells/mL may cause indeterminate or false-negative results (swab specimens).

• The assay may cross-react with *Neisseria cinerea* and *Neisseria lactamica* and cause false-positive results.

• Performance characteristics for detecting *Neisseria gonorrhoeae* in males are based on testing patients with infection rates of 27-43%. The male populations sampled were from sexually transmitted disease (STD) clinics where the prevalence of *Neisseria gonorrhoeae* is higher than in other clinical settings. Likewise, the majority of females in the study with *Neisseria gonorrhoeae* infections were from STD clinics. In the low prevalence setting (1.2% prevalence), only 6 gonococcal infections were identified. Positive results in low prevalence populations should be interpreted carefully in conjunction with clinical signs and symptoms, patient risk profile, and other findings and the understanding that the likelihood of a false positive may be higher than a true positive.

• Testing urine specimens as the sole test for identifying female patients with chlamydial or gonococcal infections may miss infected individuals (17/100 or 17% of females with *Chlamydia trachomatis*-positive cultures and 11/80 or 13.8% of females with *Neisseria gonorrhoeae*-positive cultures had negative results when urine only was tested) with this assay.

• This assay has not been evaluated with a sufficient number of specimens from asymptomatic males to estimate sensitivity in this population.

In a study of 4,130 specimens (urine and swabs from men and women) the sensitivity for detection of *Neisseria gonorrhoeae* (compared with LCx and culture) was >93% from all specimens. Urine specimens yielded the lowest sensitivities for *Neisseria gonorrhoeae* (84.9%) from women. These results were similar to those obtained by LCx testing.\(^3\)

Of 825 male and 399 female urine specimens tested for *Neisseria gonorrhoeae* with the BD Probe Tec ET system, the overall sensitivity was 100% compared with the Roche Amplicor PCR test.\(^4\)

References

Test Title: Neisseria gonorrhoeae by Nucleic Acid Amplification
#81095

Method
The BD Probe Tec ET Chlamydia trachomatis and Neisseria gonorrhoeae Amplified DNA Assay uses
homogenous strand displacement amplification technology as the amplification method and
fluorescent energy transfer as the detection method to test for the presence of Chlamydia trachomatis and
Neisseria gonorrhoeae DNA in clinical specimens. The BD Probe Tec ET test is FDA-approved.4

Specimen Required: SUBMIT ONLY 1 OF THE FOLLOWING SPECIMENS:

NOTE: 1. SPECIMEN SOURCE IS REQUIRED ON REQUEST FORM FOR PROCESSING.
2. Spermicidal agents and feminine powder sprays interfere with the assay and should not be used prior to collection.
3. Please complete a “Microbiology Request Form” (Supply T244) or a “Mayo Connect Additional Test Information” form (Supply T357), and forward it with the specimen.

Endocervix (Females Only)
Collect specimen using the NAT Swab Specimen Collection System (Supply T501) supplied as follows:
1. Remove excess mucus from the exocervix with the medium cleaning swab provided in the NAT Swab Specimen Collection System (Supply T501) and discard.
2. Insert the second medium swab into the endocervix and rotate the swab for 15-30 seconds to ensure adequate sampling.
3. Withdraw the swab.
4. Holding the tube upright, verify that all NAT medium is at the bottom of the transport tube. Unscrew the cap of the transport tube, fully insert the swab into the tube, and break the swab at the score line. Screw the cap on securely.
5. Send specimen refrigerated.

Urethra (Males Only)
Collect specimen using the NAT Swab Specimen Collection System (Supply T502) supplied as follows:
1. The patient should not have urinated for at least 1 hour prior to specimen collection.
2. Insert the small-tipped specimen swab 2-4 cm into the urethra and rotate the swab for 3-5 seconds to ensure adequate sampling.
3. Withdraw the swab.
4. Holding the tube upright, verify that all NAT medium is at the bottom of the transport tube. Unscrew the cap of the transport tube, fully insert the swab into the tube, and break the swab at the score line. Screw the cap on securely.
5. Send specimen refrigerated.

Urine (Males and Females)
1. Patient should not have urinated for at least 1 hour prior to specimen collection.
2. The patient should collect the first 15-20 mL of voided urine (the first part of the stream-NOT MIDSTREAM) in a screw-capped, sterile, plastic, preservative-free specimen container.
3. Send specimen refrigerated.

Reference Values: Neisseria gonorrhoeae DNA not detected
Analytic Time: 1 day
Days Set Up: Monday through Saturday
Fee: $74.10
CPT Code: 87591
Chlamydiae are gram-negative, obligate intracellular bacteria. *Chlamydia trachomatis* causes cervicitis, urethritis, salpingitis, proctitis, and endometritis in women and urethritis, epididymitis, and proctitis in men. In the United States, the prevalence of genital *Chlamydia trachomatis* infections among persons 15-44 years of age is estimated to be approximately 4 million infected, and it is considered the most common sexually transmitted disease. Importantly, it is estimated that about 25% of women who have acute salpingitis become infertile, and chlamydial infection is the most common cause.1,2

The detection of *Chlamydia trachomatis* from a swab or urine specimen

• A positive result indicates the presence of DNA of *Chlamydia trachomatis*.
• A negative result indicates that DNA for *Chlamydia trachomatis* was not detected in the specimen.
• The predictive value of an assay depends on the prevalence of the disease in any particular population. In settings with a high prevalence of sexually transmitted disease, positive assay results have a high likelihood of being true positives. In settings with a low prevalence of sexually transmitted disease, or in any setting in which a patient’s clinical signs and symptoms or risk factors are inconsistent with chlamydial or gonococcal urogenital infection, positive results should be carefully assessed and the patient retested by other methods (eg, culture for *Neisseria gonorrhoeae*) if appropriate.

Cautions

• This method has been tested only with endocervical swabs, male urethral swabs, and male and female urine specimens. Performance with other specimens has not been assessed.
• Optimal performance of the test requires adequate specimen collection and handling.
• Testing of urine specimens with this assay is not intended to replace cervical exam and endocervical sampling for diagnosis of urogenital infection. Cervicitis, urethritis, and urinary tract infections may result from other causes or concurrent infections may occur.
• Urine testing should be performed on first-catch random urine specimens (ie, the first 15-20 mL of the urine stream). During the clinical evaluation of this method, testing urine volumes up to 60 mL was included in the performance estimates. The effects of other variables such as midstream collection have not been determined.
• The effects of other potential variables, such as vaginal discharge, use of tampons, douching, and specimen collection variables have not been determined.
• A negative test result does not exclude the possibility of infection because improper specimen collection, technical error, specimen mix-up, concurrent antibiotic therapy, or the number of organisms in the specimen (which may be below the sensitivity of the test), may affect test results.
• As with many diagnostic tests, results should be interpreted in conjunction with other laboratory and clinical data available to the physician.
• This assay does not detect plasmid-free variants of *Chlamydia trachomatis*. 

With the introduction of this new test, #81665 *Chlamydia trachomatis* Detection by Nucleic Acid Amplification (Ligase Chain Reaction) has been deleted.
**Test Title:** Chlamydia trachomatis by Nucleic Acid Amplification 
#81096

**Cautions continued**

- This assay should not be used for the evaluation of suspected sexual abuse or for other medico-legal indications. Additional testing is recommended in any circumstance when false-positive or false-negative results could lead to adverse medical, social, or psychological consequences.
- This assay cannot be used to assess therapeutic success or failure since nucleic acids from *Chlamydia trachomatis* may persist following antimicrobial therapy.
- In laboratory studies, blood >5% was shown to cause indeterminate (inhibitory) results in both urine and swab specimens, and false-negative results in urine specimens. Blood >5% may cause false-negative results in swab specimens. Specimens with moderate to gross blood may interfere with assay results.
- The presence of highly pigmented substances in urine, such as bilirubin (10 mg/mL) and phenazopyridine (10 mg/mL), may cause indeterminate or false-negative results.
- Leukocytes in excess of 250,000 cells/mL may cause indeterminate or false-negative results (swab specimens).
- Testing urine specimens as the sole test for identifying female patients with chlamydial infections may miss infected individuals (17/100 or 17% of females with *Chlamydia trachomatis*-positive cultures had negative results when urine only was tested with this assay).

**Supportive Data**

BD Probe Tec detection of *Chlamydia trachomatis* was twice as sensitive as culture with urine and swab specimens obtained from patients with genitourinary infections. In a study of 4,130 specimens (urine and swabs from men and women) the sensitivity for detection of *Chlamydia trachomatis* (compared with LCx and culture) was >93% from all specimens. Urine specimens yielded the lowest sensitivities for *Chlamydia trachomatis* (80.5%) from women. These results were similar to those obtained by LCx testing.

Of 825 male and 399 female urine specimens tested for *Chlamydia trachomatis* with the BD Probe Tec ET system, the overall sensitivity was 95.3 compared with the Roche Amplicor PCR test.

**References**

Chlamydia trachomatis by Nucleic Acid Amplification
#81096

Test Title: Chlamydia trachomatis by Nucleic Acid Amplification

Specimen Required: SUBMIT ONLY 1 OF THE FOLLOWING SPECIMENS:

NOTE:
1. SPECIMEN SOURCE IS REQUIRED ON REQUEST FORM FOR PROCESSING.
2. Spermicidal agents and feminine powder sprays interfere with the assay and should not be used prior to collection.
3. Please complete a “Microbiology Request Form” (Supply T244), or a “Mayo Connect Additional Test Information” form (Supply T357), and forward it with the specimen. These forms are available upon request.

Endocervix (Females Only)
Collect specimen using the NAT Swab Specimen Collection System (T501) supplied as follows:
1. Remove excess mucus from the exocervix with the medium-cleaning swab provided in the NAT Swab Specimen Collection System and discard.
2. Insert the second medium swab into the endocervix and rotate the swab for 15-30 seconds to ensure adequate sampling.
3. Withdraw the swab.
4. Holding the tube upright, verify that all NAT medium is at the bottom of the transport tube. Unscrew the cap of the transport tube, fully insert the swab into the tube, and break the swab at the score line. Screw the cap on securely.
5. Send specimen refrigerated.

Urethra (Males Only)
Collect specimen using the NAT Swab Specimen Collection System (T502) supplied as follows:
1. The patient should not have urinated for at least 1 hour prior to specimen collection.
2. Insert the small-tipped specimen swab 2-4 cm into the urethra and rotate the swab for 3-5 seconds to ensure adequate sampling.
3. Withdraw the swab.
4. Holding the tube upright, verify that all NAT medium is at the bottom of the transport tube. Unscrew the cap of the transport tube, fully insert the swab into the tube, and break the swab at the score line. Screw the cap on securely.
5. Send specimen refrigerated.

Urine (Males and Females)
1. Patient should not have urinated for at least 1 hour prior to specimen collection.
2. The patient should collect the first 15-20 mL of voided urine (the first part of the stream—NOT MIDSTREAM) in a screw-capped, sterile, preservative-free specimen container.
3. Send specimen refrigerated.

Reference Values:
Chlamydia trachomatis DNA not detected

Analytic Time: 1 day
Days Set Up: Monday through Saturday
Fee: $75.10
CPT Code: 87491
Fatty acid oxidation (FAO) plays a major role in energy production during periods of fasting. When the body's supply of glucose is depleted, fatty acids are mobilized from adipose tissue, taken up by the liver and muscles, and step-wise oxidized to acetyl-CoA. In the liver, acetyl-CoA is the building block for the synthesis of ketone bodies, which enter the bloodstream and provide an alternative substrate for production of energy in other tissues when the supply of glucose is insufficient to maintain a normal level of energy.

The major clinical manifestations associated with individual FAO disorders include hypoketotic hypoglycemia, variable degrees of liver disease and/or failure, skeletal myopathy, dilated/hypertrophic cardiomyopathy, and sudden or unexpected death in early life. Signs and symptoms may vary greatly in severity and may appear at any age, from birth to adult life, and in variable combinations, frequently leading to life-threatening episodes of metabolic decompensation after a period of inadequate caloric intake and/or intercurrent illness.

In FAO disorders, characteristic metabolites accumulate in blood and bile as carnitine derivatives. Analysis of acylcarnitines in blood and bile spots represents the first level of evaluation in a complete postmortem investigation of a sudden and/or unexpected death of a child. The diagnosis of an underlying FAO disorder allows genetic counseling of the family, including the option of future prenatal diagnosis and testing of at-risk family members of any age.

Postmortem evaluation of infants or children who have died suddenly or unexpectedly

Testing is particularly recommended under the following circumstances (risk factors):
- Family history of sudden infant death syndrome (SIDS) or other sudden, unexpected deaths
- Family history of Reye syndrome
- Maternal complications of pregnancy (acute fatty liver pregnancy, HELLP syndrome [hemolysis, elevated liver enzymes, and low platelet count])
- Lethargy, vomiting, fasting in the 48 hours prior to death
- Allegation of child abuse (excluding obvious cases of trauma, physical harm)
- Macroscopic findings at autopsy
  - Fatty infiltration of the liver
  - Dilated or hypertrophic cardiomyopathy
- Autopsy evidence of infection that routinely would not represent a life-threatening event

Reports of abnormal acylcarnitine profiles will include an overview of the results and of their significance, a correlation to available clinical information, possible differential diagnoses, recommendations for additional biochemical testing and confirmatory studies (enzyme assay, molecular analysis) as indicated, name and telephone number of contacts who may provide these studies at Mayo Clinic or elsewhere, and a telephone number to reach one of the laboratory directors in case the referring physician has additional questions.

Abnormal results are not always sufficient to conclusively establish a diagnosis of a particular disease. To verify a preliminary diagnosis based on an acylcarnitine analysis, independent biochemical (eg, #81927 Fatty Acid Oxidation Probe Assay, Fibroblast Culture) or molecular genetic analyses are required using additional tissue such as skin fibroblasts from the deceased patient. If not available, molecular genetic analysis of a patient's parents usually enables the confirmation of a diagnosis.
Cautions

- Both blood and bile specimens must be collected in order to detect and independently confirm the largest possible number of disorders.
- In cases with a higher level of suspicion due to the recognition of 1 or more risk factors, collection of frozen liver and a skin biopsy is also recommended for further testing and enzymatic/molecular studies.
- In comparison to living individuals, profiles of postmortem blood specimens generally show a nonspecific increase of short chain species.
- Patients with secondary carnitine deficiency may display uninformative acylcarnitine profiles in blood, but not in bile.
- Several FAO disorders are not associated with abnormal acylcarnitine profiles (eg, carnitine palmitoyltransferase I deficiency, 3-hydroxy-3-methylglutaryl CoA synthase deficiency).

References


Method

Blood and bile are collected on the same filter paper card; newborn screening filter paper cards are used. Blood drawn into heparin-containing tubes and bile collected by direct puncture of the gallbladder are spotted on a filter paper card. Two circles at the one end of the card are used for blood, 2 circles at the opposite end for the bile (each 25 µL of volume). A 3/16” disk is punched out of the blood or bile spot into an Eppendorf tube. The acylcarnitines are extracted by the addition of methanol and known concentrations of isotopically labeled acylcarnitines as internal standards. The extract is transferred to a Raacti-Vial, dried under a stream of nitrogen and derivatized by the addition of n-butanol HCl. The acylcarnitines are measured as their butyl esters by electrospray tandem mass spectrometry (MS/MS). The concentration of the analytes are established by computerized comparison of ion intensities of these analytes to that of the respective internal standards. (Chace DH, DiPerna JC, Mitchell BL, et al: Electrospray tandem mass spectrometry for analysis of acylcarnitines in dried postmortem blood specimens collected at autopsy from infants with unexplained cause of death. Clin Chem 2001;47:1166-1182)

Specimen Required: BILE AND BLOOD SPOTS ARE REQUIRED FOR THIS TEST.

Collect blood in a heparin-containing tube and collect bile by direct puncture of the gallbladder. Use the Mayo Supplemental Newborn Screen Card (Supply T493). Drop 25 µL of blood onto each circle on one end of the special card. Drop 25 µL of bile onto each circle on the opposite end of the card. Allow to dry at ambient temperature in a horizontal position for 3 or more hours. Fill out information on page 2 of collection card and send ambient.

Reference Values: Quantitative results are compared with a constantly updated range that corresponds to the 5-95 percentile interval of all postmortem cases brought to our attention.

Analytic Time: 2 days
Days Set Up: Varies
Fee: $36.00
CPT Code: 83788
Hereditary pancreatitis (HP) is a rare autosomal dominant disorder, with 80% penetrance, accounting for approximately 1% of all cases of pancreatitis and 2-3% of chronic pancreatitis. HP is characterized by early onset of acute pancreatitis during childhood or early adolescence. The acute pancreatitis in these patients generally progresses to chronic pancreatitis by adulthood and can eventually lead to both exocrine and endocrine pancreatic insufficiency. Furthermore, patients with HP are at increased risk for developing pancreatic cancer: the lifetime risk of developing cancer is estimated to be over 40%. Currently, treatment for HP is symptomatic, with surgery being used primarily to reduce the pain of recurrent pancreatitis.

HP cannot be clinically distinguished from other forms of childhood pancreatitis and is usually only diagnosed after ruling out other metabolic causes. Therefore, delay in diagnosis has been a problem for patients with HP. Recent advances in the detection of the genetic defects causative in HP can aid in earlier diagnosis for clinically affected individuals and the detection of at-risk family members.

Two mutations within the cationic trypsinogen gene, Arg122His (R122H) and Asn29Ile (N29I), have been identified as the primary causative defects in HP. Although the phenotype of patients with these 2 mutations is quite similar, sharing many clinical features, there does seem to be some differences. Data suggests that the R122H mutation results in a more severe disease and an earlier onset of symptoms. Although these 2 alterations, to date, account for greater than 90% of mutations detected in the cationic trypsinogen gene, the inability to identify mutations in approximately 30% of families with HP suggests the possibility of other loci or unidentified mutations in the cationic trypsinogen gene.

**Clinical**

Hereditary pancreatitis (HP) is a rare autosomal dominant disorder, with 80% penetrance, accounting for approximately 1% of all cases of pancreatitis and 2-3% of chronic pancreatitis. HP is characterized by early onset of acute pancreatitis during childhood or early adolescence. The acute pancreatitis in these patients generally progresses to chronic pancreatitis by adulthood and can eventually lead to both exocrine and endocrine pancreatic insufficiency. Furthermore, patients with HP are at increased risk for developing pancreatic cancer: the lifetime risk of developing cancer is estimated to be over 40%. Currently, treatment for HP is symptomatic, with surgery being used primarily to reduce the pain of recurrent pancreatitis.

**Useful For**

- Confirming the diagnosis of HP in patients with chronic pancreatitis
- Ruling out HP in patients with chronic pancreatitis
- Screening of at-risk individuals when the R122H, R122, or N29I mutation has been identified in an affected family member.

**Interpretation**

An interpretive report based on the test results, clinical presentation, and family history will be provided.

**Cautions**

Approximately 30% of families with HP will not have a mutation detected by this assay. Therefore, other clinical tests may be necessary to prove or exclude the diagnosis of HP.

The absence of a mutation for an unaffected individual with a family history of HP does not rule out the diagnosis, since these mutations account for only approximately 70% of cases. Therefore, the identification of a mutation in an affected family member is necessary before predictive testing can be offered. Additionally, predictive testing of an asymptomatic child is not recommended and should be done only after careful consideration of all issues.
Test Title: Hereditary Pancreatitis, Blood
#83019

References

Method
In this direct mutation analysis, a polymerase chain reaction (PCR)-based assay using LightCycler technology is used to test for the R122H (arginine to histidine) and N29I (asparagine to isoleucine) mutations within the cationic trypsinogen gene. (Method developed by the Molecular Genetics Laboratory at Mayo Clinic) (Ririe KM, Rasmussen RP, Wittwer CT: Product differentiation by analysis of DNA melting curves during the polymerase chain reaction. Analytical Biochemistry 1997;15;245(2):154-160)

Specimen Required: Specimen should include a “Molecular Genetics Congenital Disorders Request Form” (Supply T245) or a “MayoConnect Additional Test Information Form” (Supply T357) with information including relevant clinical and family history information. Specimen must arrive within 96 hours of draw.

Blood
Draw a lavender-top (EDTA) tube(s) or a yellow-top (ACD) tube(s) of whole blood (5.0 mL) and send in the original VACUTAINER(S). Invert several times to mix blood. Forward unprocessed whole blood promptly.

Reference Values: An interpretive report will be provided.
Analytic Time: 8 days
Days Set Up: Wednesday
Fee: $194.50
CPT Code: 83890/Molecular isolation or extraction
83896x2/Nucleic acid probe, each
83898x2/PCR amplification
83912/Interpretation and report