Clostridium difficile (C. diff), Human Papilloma Virus (HPV) and Gonorrhea and Chlamydia trachomatis (GC/CT)

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UT Southwestern Medical Center
Dallas, TX
Learning Objectives

• After this session you should be able to...

1. Discuss the advantages and disadvantages of *C. difficile* testing methods

2. Understand the clinical significance of Human Papilloma Virus and its diagnosis

3. Understand the diagnosis of GC/CT infections
Clostridium difficile

The bug

• Anaerobic Gram-positive spore forming bacilli
• Spores very resistant to killing
  – Not killed by hand sanitizers
• Makes two exotoxins
  – Toxin A and Toxin B (important for diagnosis)
  – There are non-toxigenic strains

• Not to be confused with
  – C. botulinum – botulism
  – C. perfringens – food poisoning and gas gangrene
  – C. tetani - tetanus

C. Difficile Statistics

• Causes up to 25% of antibiotic associated disease
• $1 Billion in annual health-care associated costs in US
• An estimated 50% of antibiotics are given unnecessarily

Table 92-1: Antimicrobial and Chemotherapeutic Agents Associated with Clostridium difficile Diarrhea or Colitis

<table>
<thead>
<tr>
<th>More Frequently Associated Agents</th>
<th>Less Frequently Associated Agents</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cephalosporins (especially second- and third-generation agents)</td>
<td>Ticarcillin-clavulanate</td>
</tr>
<tr>
<td>Ampicillin and amoxicillin</td>
<td>Chloramphenicol</td>
</tr>
<tr>
<td>Clindamycin</td>
<td>Metronidazole</td>
</tr>
<tr>
<td>Other penicillins, including</td>
<td>Ampicillin B</td>
</tr>
<tr>
<td>β-lactamase–stable penicillins</td>
<td>Quinolones</td>
</tr>
<tr>
<td>Erythromycin and other macrolides</td>
<td>Rifampin</td>
</tr>
<tr>
<td>Tetracyclines</td>
<td>5-Fluorouracil</td>
</tr>
<tr>
<td>Trimethoprim-sulfamethoxazole</td>
<td>Methotrexate</td>
</tr>
<tr>
<td>Doxorubicin</td>
<td>Cyclophosphamide</td>
</tr>
<tr>
<td>Cyclophosphamide</td>
<td>Aminoglycosides</td>
</tr>
<tr>
<td>Aminoglycosides</td>
<td>Sulfonamides</td>
</tr>
</tbody>
</table>

Data from Bartlett,2 Kelly et al., and Thielman and Guerrant.251

Principles and Practices of Infectious Disease: Mandel 6th Ed.

www.cdc.gov/
C. difficile Infection (CDI)

Clinical Significance

- Common symptoms
  - watery diarrhea
  - fever
  - loss of appetite
  - nausea
  - abdominal pain/tenderness

- Disease
  - pseudomembranous colitis (PMC)
  - toxic megacolon
  - perforations of the colon
  - sepsis
  - death (rarely)
C. difficile Treatment

- If possible discontinue antibiotic that produced CDI in the first place
- Supportive
  - Fluid replacement
- Avoid antiperistaltic agents
- Avoid vancomycin if possible
  - Try to reserve for severe cases

- Mild Disease - **Metronidazole**
  - Characteristics
    - Oral meds OK
    - WBC <15,000
    - No increase in creatinine

- More Severe Disease – **Vancomycin (PO)**
  - Characteristics
    - Oral meds OK
    - WBC >15,000
    - >50% increase in creatinine

- Post-op or Severe Disease – **Metronidazole and Vancomycin (PO)**
  - Characteristics
    - Post-op ileus
    - Severe disease with toxic megacolon
C. difficile

Transmission
• C. diff is shed in the feces and the spores may contaminate anything that they come in contact with.
• Primarily spread through contact with these surfaces
  – Hands of healthcare workers
  – Patient direct contact
• Contact/colonization with C. diff does not equal disease
• Disease occurs when the normal flora of a patient has been altered (usually) through antibiotic usage and C. diff then causes a variety of diseases (discussed on next slide)

Epidemiology
• Found world-wide in the environment
• Commonly found in sewage, soil and feces
• Commonly found in hospital environments
• Alcohol does not kill the spores
  – EPA registered disinfectants with a sporicidal claim should be used
Diagnosis of CDI

Controversies

• Colonization
  – **Pediatrics** – up to 30% of healthy neonates colonized
  – **Hospitalized patients** – up to 21% of hospitalized adults acquire C. diff
    • Only 37% of those develop CDI

• What is the best diagnostic algorithm?
  – Many different approaches

Test Methods

<table>
<thead>
<tr>
<th>Method</th>
<th>Target</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cell-cytotoxicity assay</td>
<td>C. diff toxin</td>
</tr>
<tr>
<td>Immunoassays (EIA and others)</td>
<td>C. diff toxin</td>
</tr>
<tr>
<td>Culture</td>
<td>C. diff</td>
</tr>
<tr>
<td>Antigen detection (GDH)</td>
<td>C. diff</td>
</tr>
<tr>
<td>Cytotoxigenic culture</td>
<td>Toxigenic C. diff</td>
</tr>
<tr>
<td>PCR</td>
<td>Toxigenic C. diff</td>
</tr>
</tbody>
</table>

McFarland. 1989. NEJM
Diagnostic Approaches

• Only test unformed stool (unless ileus suspected)
• GOLD STANDARD – stool culture followed by toxin identification (slow)
• EIA – rapid but lacks sensitivity
  – Some believe more clinically significant (see next slide)
• PCR – rapid, sensitive and specific
  – Repeat testing discouraged
• GDH – C. diff common antigen
• Two-step
  – EIA detection of GDH -> confirm with toxin detection
Toxin Detection

• Since it was discovered that toxin A and B were the cause of CDI most tests have been designed to target toxins
  – Toxin B shown in animals to be the primary cause of disease
  – Some strains lack toxin A
• Toxin EIA’s suffer from poor sensitivity and specificity
• Toxigenic culture is slow and labor intensive
• GDH does not detect the toxin
• PCR
  – Highly sensitivity and specific
    • Too sensitive for diagnosing disease
The two-step

• GDH screen. If +ve, followed by toxin-based confirmatory test

Considerations

• GDH test variability

• GDH is cheap – 75-85% of specimens are negative and only require one test
  – Significant cost savings
  – Some question the sensitivity and therefore its utility as a screen
Based on the premise that most studies lack information on disease severity and outcome

Clinical symptoms and test positivity were used as a combined gold standard for CDI

<table>
<thead>
<tr>
<th>Method</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
<th>NPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>EIA</td>
<td>75</td>
<td>96</td>
<td>73</td>
<td>96</td>
</tr>
<tr>
<td>PCR (Xpert)</td>
<td>100</td>
<td>90</td>
<td>62</td>
<td>100</td>
</tr>
<tr>
<td>2-step (GDH +PCR)</td>
<td>100</td>
<td>91</td>
<td>64</td>
<td>100</td>
</tr>
<tr>
<td>2-step (GDH + EIA)</td>
<td>90</td>
<td>95</td>
<td>73</td>
<td>98</td>
</tr>
</tbody>
</table>

19% of patients had received a laxative 48 hours prior to testing
Human Papilloma Virus (HPV)

- Small nonenveloped DNA virus
- Clustered into five genera
  1. Alpha
  2. Beta
  3. Gamma
  4. Mupa
  5. Nupa
- >100 different genotypes
- E6 oncogene binds p53 protein
  - P53 protein is a negative regulator
  - E6 mutates p53 protein and removes its protective function

FACTS
- 20 million Americans currently infected
  - 6 million new infections each year
- Almost all cervical cancers are HPV associated
  - 12,000 women in US with cervical cancer
- 1,500 men and 2,700 women get HPV-associated anal cancer in the US each year.
- 5,600 men get HPV-associated oropharyngeal cancers each year

http://www.cdc.gov/std/HPV/STDFact-HPV.htm
HPV Disease and Transmission

• Symptoms
  – Most people who are infected with HPV clear the virus within 2 years
  – In ~10%
    • Genital warts
    • Warts in throat – recurrent respiratory papillomatosis
    • Cervical cancer and other cancers
• HPV types that cause genital warts are not the same as those that cause cancers.
• No treatment to clear HPV
  – Treatment is supportive

• Transmission
  – Passed through genital contact during genital-to-genital or oral sex
  – Transmitting person does not have to be symptomatic to be infectious
  – Rare transmission during delivery

http://www.cdc.gov/std/HPV/STDFact-HPV.htm
<table>
<thead>
<tr>
<th>Disease</th>
<th>Frequent Association</th>
<th>Less Frequent Association</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plantar warts</td>
<td>1, 2</td>
<td>4, 63</td>
</tr>
<tr>
<td>Common warts</td>
<td>2, 1</td>
<td>4, 26, 27, 29, 41, 57, 65, 77</td>
</tr>
<tr>
<td>Common warts of meat, poultry, and fish handlers</td>
<td>7, 2</td>
<td>1, 3, 4, 10, 28</td>
</tr>
<tr>
<td>Flat and intermediate warts</td>
<td>3, 10</td>
<td>26, 27, 28, 38, 41, 49, 75, 76</td>
</tr>
<tr>
<td>Epidermodysplasia verruciformis</td>
<td>2, 3, 10, 5, 8, 9, 12, 14, 15, 17</td>
<td>19, 20, 21, 22, 23, 24, 25, 36, 37, 38, 47, 50</td>
</tr>
<tr>
<td>Condylomata acuminata</td>
<td>6, 11</td>
<td>30, 42, 43, 44, 45, 51, 54, 55, 70</td>
</tr>
<tr>
<td>Intraepithelial neoplasia, unspecified</td>
<td>30, 34, 39, 40, 53, 54, 57, 59, 61, 62, 64, 66, 67, 68, 69, 71, 72, 82</td>
<td>51, 54, 55, 70</td>
</tr>
<tr>
<td>Low grade</td>
<td>6, 11</td>
<td>16, 18, 31, 33, 35, 42, 43, 44, 45, 51, 52, 54, 61, 70, 72, 74, 81, 83, 84, 86, 87, 89, 90, 91</td>
</tr>
<tr>
<td>High grade</td>
<td>16, 18</td>
<td>6, 11, 26, 31, 34, 33, 35, 39, 42, 44, 45, 51, 52, 54, 61, 53, 56, 58, 66</td>
</tr>
<tr>
<td>Cervical carcinoma</td>
<td>16, 18</td>
<td>26, 31, 33, 35, 39, 45, 51, 52, 53, 56, 58, 59, 68, 73, 82</td>
</tr>
<tr>
<td>Recurrent respiratory papillomatosis</td>
<td>6, 11</td>
<td>16, 18, 31, 33, 35, 39</td>
</tr>
<tr>
<td>Focal epithelial hyperplasia of Heck</td>
<td>13, 32</td>
<td></td>
</tr>
<tr>
<td>Conjunctival papillomas and carcinomas</td>
<td>6, 11, 16</td>
<td></td>
</tr>
<tr>
<td>Other cutaneous lesions</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
HPV Vaccine

Prevention

• Vaccine
  – Recommended for girls and boys at age 11 or 12

• Two forms
  – Bivalent (Cervarix)
    • Prevents serotypes 16 and 18 that cause ~70% of cervical cancers
  – Quadrivalent (Gardasil)
    • Serotypes 6, 11, 16 and 18 that cause 90% of genital warts
    • Only one licensed for males
    • Been shown to protect against cancer of the anus, vagina and vulva

• Vaccines do not have a therapeutic effect

• Made from non-infectious particles and do not contain thimerosal or mercury

Efficacy

• Bivalent
  – 99% developed antibody to HPV 16 and 18
  – 93% vaccine efficacy

• Quadrivalent
  – 100% vaccine efficacy for preventing precancers
  – 90% vaccine efficacy for preventing genital warts

• Vaccines do not prevent cancer from developing in those who are already infected.

• Duration
  – At 6 years – vaccine is new – there is no evidence of waning immunity
Screening for HPV and Cervical Cancer

- Screening recommended in women 21-65 years.
- Screening in 30-65 to include both cytology and HPV detection
- Screening to continue for now in vaccinated individuals

<table>
<thead>
<tr>
<th>TABLE 1. ACS/ASCCP/ASCP Screening Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age to initiate screening: 21 y old</td>
</tr>
<tr>
<td>No screening in women younger than 21</td>
</tr>
<tr>
<td>regardless of age of coitalarche or risk factors</td>
</tr>
<tr>
<td>Screening in women 21-29 y old</td>
</tr>
<tr>
<td>Pap every 3 y</td>
</tr>
<tr>
<td>No HPV testing in this population</td>
</tr>
<tr>
<td>Screening in women 30-65 y old</td>
</tr>
<tr>
<td>Pap every 3 y OR</td>
</tr>
<tr>
<td>Pap and HPV cotesting every 5 y (preferred method)</td>
</tr>
<tr>
<td>Age to stop screening: &gt; 65 y old if:</td>
</tr>
<tr>
<td>Adequate screening has been negative</td>
</tr>
<tr>
<td>No history of CIN 2/3 or adenocarcinoma in situ,</td>
</tr>
<tr>
<td>otherwise this population should continue</td>
</tr>
<tr>
<td>screening for 20 y after diagnosis/adequate</td>
</tr>
<tr>
<td>management</td>
</tr>
<tr>
<td>Screening after hysterectomy: no screening if</td>
</tr>
<tr>
<td>Cervix has been removed</td>
</tr>
<tr>
<td>No history of CIN 2/3 or cervical cancer</td>
</tr>
<tr>
<td>Screening in HPV 16/18 immunized patients</td>
</tr>
<tr>
<td>continue to screen per age-specific guidelines</td>
</tr>
<tr>
<td>for the general population</td>
</tr>
<tr>
<td>ACS/ASCCP/ASCP does not recommend annual</td>
</tr>
<tr>
<td>screening for women of any age</td>
</tr>
</tbody>
</table>

ACS indicates the American Cancer Society; ASCCP, the American Society for Colposcopy and Cervical Pathology; ASCP, the American Society for Preventive Oncology.
HPV Laboratory Testing Methods

• HPV detection
  – Two FDA cleared tests for testing of residual liquid-based cytology materials
    • Hybrid Capture 2 (HC2) (Qiagen)
    • Cervista HPV HR (Hologic)

• Specimen collection
  – Exfoliated cells collected with cervical brush or spatula
  – Stable at RT up to 12 weeks
  – No standardized tests from other specimens

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- HPV detection
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  - Exfoliated cells collected with cervical brush or spatula
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- Hybrid Capture 2 (HC2)
  - In vitro nucleic acid hybridization assay
    - Uses signal amplification and chemiluminescence
    - Does not use HPV DNA amplification

Priebe. 2013. Clinical Obstetrics and Gynecology
Genotyping

• Genotyping of all HPV not clinically useful
• HPV 16, 18 and 45 is recommended
  – These genotypes are associated with increased risk for progression cervical intraepithelial neoplasia (CIN) 2+ within 2 to 3 years
• Only the Cervista is FDA cleared as a reflex to genotyping
  – Qiagen is developing an assay using their hybrid capture technology
• Abbott RealTime High Risk HPV test
  – Detects 14 HPV types and differentially identifies HPV 16 and 18
HPV Serology

- Detection of HPV antibodies is a marker of exposure
  - Does not provide information about site of exposure or time of infection
- Research serologies have limited sensitivity
  - Antibody only detected in 60% of women with DNA positive testing
- No diagnostic clinical utility
- Can be used to assess immunity

Schiller. 2009. CID
Neisseria gonorrhoea and Chlamydia trachomatis

Neisseria gonorrhoea
- Gram negative diplococci
- Catalase and oxidase positive
- More than 700,000 new infections every year

Chlamydia trachomatis
- Most commonly reported STD in the US.
- Obligate intracellular organism
- Does not grow in normal bacterial culture
- Requires cell line inoculation to grow

BOTH
Transmitted through sexual contact
Can be transmitted to infants during birth
Neisseria gonorrhoeae - Epidemiology

...but as long as people are still having promiscuous sex with many anonymous partners without protection while at the same time experimenting with mind-expanding drugs in a consequence-free environment, I’ll be sound as a pound!

CDC implementation of GC control program in the mid 70’s.
- Decreased incidence of GC in the US by 74%
- However, 5.5% increase from 2005-2006
**Gonococcal Isolate Surveillance Project (GISP)**

The Gonococcal Isolate Surveillance Project (GISP) was established in 1986 to monitor trends in antimicrobial susceptibilities of strains of *N. gonorrhoeae* in the United States in order to establish a rational basis for the selection of gonococcal therapies. GISP is a collaborative project among selected sexually transmitted diseases (STD) clinics, five regional laboratories, and the Centers for Disease Control and Prevention (CDC).

In GISP, *N. gonorrhoeae* isolates are collected from the first 25 men with urethral gonorrhea attending STD clinics each month in approximately 28 cities in the United States. At regional laboratories, the susceptibilities of these isolates to penicillin, tetracycline, spectinomycin, ciprofloxacin, ceftriaxone, ceftaxime, and azithromycin are determined by agar dilution. Minimum inhibitory concentrations (MICs) are measured, and values are interpreted according to criteria recommended by the National Committee for Clinical Laboratory Standards (NCCLS).

**Protocol**
- GISP Protocol

**Annual Reports and Profiles**
- 2009 GISP Profiles

**Sentinel Sites and Regional Laboratories**

Click thumbnail for larger map

* indicates Regional Laboratories

- Albuquerque, NM
- Atlanta, GA *
- Miami, FL
- Minneapolis, MN
GC rates in your state...

Rate per 100,000 population

- <=19.0 (n= 7)
- 19.1-100.0 (n= 24)
- >100.0 (n= 23)

Guam 53.1
Virgin Islands 126.7
Puerto Rico 9.2

CDC GISP program
GC - Disease

- Transmitted through sexual contact
- Can be transmitted to infants during birth
# Current Neisseria gonorrhoeae

Treatment recommendations

<table>
<thead>
<tr>
<th>Infection</th>
<th>Primary</th>
<th>Alternative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urethritis, cervicitis and proctitis</td>
<td>Ceftriaxone or cefixime PLUS doxycycline or azithromycin</td>
<td></td>
</tr>
<tr>
<td>Conjunctivitis</td>
<td>Ceftriaxone IM</td>
<td></td>
</tr>
<tr>
<td>Disseminated gonococcal infection (DGI)</td>
<td>IM or IV Ceftriaxone</td>
<td>IV Cefotaxime or IV ceftizoxime</td>
</tr>
<tr>
<td>Pharyngitis</td>
<td>Ceftriaxone IM PLUS doxycycline or azithromycin</td>
<td></td>
</tr>
</tbody>
</table>

As of 2007, fluoroquinolones no longer recommended due to widespread emergence of resistance.

MMWR 2010 – Dec 17, 2010 – STD Treatment Guidelines
Resistance in Neisseria gonorrhoeae

Figure 34. Penicillin, Tetracycline, and Ciprofloxacin Resistance Among Neisseria gonorrhoeae isolates, Gonococcal Isolate Surveillance Project (GISP), 2011

NOTE: PenR = penicillinase producing Neisseria gonorrhoeae and chromosomally mediated penicillin-resistant N. gonorrhoeae; TetR = chromosomally and plasmid mediated tetracycline-resistant N. gonorrhoeae; and QRNG = quinolone-resistant N. gonorrhoeae.
Neisseria gonorrhoeae: Regional Treatment
Oklahoma City, OK

Figure D. Drugs used to treat gonorrhea among GISP participants, 2009

Figure E. Drugs used to treat Chlamydia trachomatis infection among GISP participants, 2009

Different in Dallas...

Figure E. Drugs used to treat *Chlamydia trachomatis* infection among GISP participants, 2009

Figure J. Distribution of Minimum Inhibitory Concentrations (MICs) to azithromycin among GISP isolates, 2005-2009

Chlamydia trachomatis

Figure 4. Chlamydia—Rates by County, United States, 2011

CDC GISP Surveillance Program 2011 Data
CT Disease and Risk Factors

- **Disease**
  - Like GC – often asymptomatic in women but can result lead to PID if left untreated
  - Transmission to infants during birth
    - Can lead to ophthalmia or pneumonia
  - Rate over 2.5 times higher in women...
    - Why would this be?

Rate (per 100,000 population)

Year

CDC STD Surveillance
Chlamydia Life Cycle

- Obligate intracellular pathogen
- Invades cell and forms elementary bodies
- Once inside the cell they convert to metabolically active reticulate bodies which replicate by binary fission.
- After 48-72 hours hundreds of particles are released and perpetuate the life cycle.

Treatment and Prevention of Chlamydia infection

Prevention

• Prevention programs have been implemented to reduce the burden of reproductive sequelae
  – Requires screening of at-risk females
  – Yearly in sexually active females <25
  – Yearly in females >25 if they are at increased risk (i.e. – new or multiple sex partners)

Treatment

• Highly effective
  – Single dose azithromycin
  – 1 week doxycycline
Diagnosis of Gonorrhoeae and Chlamydia Infection

**Neisseria gonorrhoeae**
- Culture
  - Grows well on blood and chocolate agars
  - Selective media often used to specifically culture GC
    - JEMBEC or Modified Thayer Martin
- Molecular methods

**Chlamydia trachomatis**
- Culture
  - In vitro culture in McCoy or HeLa 229 cells are most commonly used
- Direct Fluorescent Antibody (DFA) and EIA
- Molecular Methods
- Serology
Chlamydia Serology

• Can be helpful for diagnosing infections such as...
  – Ornithosis (C. psittaci)
  – Lymphogranuloma venereum
  – Neonatal pneumonia

• Should not be used for C. trachomatis genital infection or for screening asymptomatic individuals

• The assay is done as either complement fixation, MIF or EIA
  – Generally detect IgM, IgA, IgG or total antibody.

• Interpretation
  – May be useful for above-mentioned conditions
  – No marker for chronic infection
  – Poor correlation between serology and PCR /culture.
  – Single point serology not useful – need paired sera
Chlamydia DFA, EIA Point of Care

• DFA
  – Use FITC labeled monoclonal antibodies against MOMP epitope of C. Trachomatis
  – Sensitivity = 75-85%
  – Specificity = 99%
  – Fast and practical for labs that have low volumes

• EIA and Point of Care tests
  – Detect similar antigens to DFA
  – In theory can detect all Chlamydiae but not well studied
  – Sensitivity = 62-72%
    • Not recommended anymore

• Point of Care
  – Use antibodies against LPS
  – Results in 30 minutes
  – Poor sensitivity ~ 35% compared to PCR

Newhall WJ. 1999. JCM
Mahilum-Tapay. 2007. BMJ
Johnson RE. 2002. JCM
Yin YP. 2006. Sex. Trans. Infect
# GC/CT Molecular Assays

## Specimen

<table>
<thead>
<tr>
<th>Specimen</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cervical swab</td>
<td>90-94%</td>
<td>98-99%</td>
</tr>
<tr>
<td>Female urine</td>
<td>80-95%</td>
<td>98-99%</td>
</tr>
<tr>
<td>Male urine</td>
<td>90-97%</td>
<td>91-99%</td>
</tr>
<tr>
<td>Male urethral swab</td>
<td>95%</td>
<td>94-98%</td>
</tr>
</tbody>
</table>

## Methodologies

- **PCR**
  - Roche Amplicor or Abbott RealTime CT/NG
    - Performed on the Cobas or Abbott m2000
- **Strand displacement**
  - BD ProbeTec
    - Performed on Viper
- **Transcription mediated amplification**
  - Aptima transcription-mediated amplification
    - Performed on the Tigris
- **New gold standard for GC/CT diagnosis**
  - 20-30% more sensitive than other methods

Taken from package inserts of commercially available products
GC/CT by PCR

Abbott RealTime CT/NG

- 96 sample batch size
- Compatible with many other assays
  - HBV, HCV, HIV, HPV

GC/CT by PCR

Roche Amplicor

• 188 results in 4 hours
• Single system can process 384 specimens in a day
• Walk Away technology

Competitive comparison: hands-on time (run of 96 tests)¹

- **Hands-On Time (min.)**
- **Total Cycle Time (min.)**
- **Walk-Away Time (% of total)**

![Graph showing competitive comparison of hands-on time among different systems.](https://www.mylabonline.com/products/hpv/docs/cobas_CTNG_test_51148.pdf)
GC/CT by Strand displacement

- **BD Probe Tec**

  - **BD FOX™ Extractor Module:**
    - Holds 96 single-dose BD FOX extraction tubes and permanent magnet assembly for on-board DNA extraction.

  - **Pipettor Head:**
    - For consumable check, fluid volume transfer, and microwell plate sealing.

  - **Sample Processing Station:**
    - Up to 96 specimens, including controls, can be loaded for walk-away capability.

  - **Amplification/Detection Staging Station:**
    - Up to two amplification microwell plates can be incubated for real-time amplification and detection.

  - **Priming Station:**
    - Two heaters incubate up to two priming microwell plates for hybridization of primers.

[Link to product page](http://www.bd.com/ds/productCenter/MD-Viper.asp)
GC/CT by Strand displacement

**BD Viper**
- 736 samples in 8.5 hours
- Done with less the one FTE

Schweitzer. 2001. Current Opinion in Biotechnology

APTIMA Combo 2 – Gen Probe: Transcription Mediated Amplification

Giachetti. 2002. JCM
Questions

What is the gene target of *C. difficile* PCR assays?

a) Toxin  

b) LPS  

c) Peptidoglycan  

d) Flagella  

What are the two genotypes of HPV that are associated with progression to cervical cancer?

a. 3 and 11  

b. 5 and 12  

c. 1 and 44  

d. 16 and 18  

What is the primary technique used to diagnosis Gonorrhoeae and Chlamydia infection?

a. Serology  

b. Culture  

c. DFA  

d. Nucleic Acid Amplification Testing  

What HPV are the serotypes most commonly associated with cervical carcinoma? Pick two.

a. 2  

b. 7  

c. 16  

d. 18