An Intro to Culture-Independent Diagnostic Tests for Gastrointestinal Pathogens

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Objectives of the Session

• Discuss the importance of reviewing and modifying local/state laws for mandatory isolate or clinical material submission

• Describe validation studies and workflow practices within public health laboratories in response to uptake of CIDT testing in clinical laboratories

• Explain current studies to address isolate recovery practices and long-term solutions for culture-independent public health surveillance testing
What is “CIDT”? 

• “Culture-Independent Diagnostic Test”
• Any diagnostic test that does not require the culture or isolation of a microorganism in order to arrive at a diagnostic test result
• May be any number of commercially-available or laboratory-derived test methodologies
Commercially Available CIDT’s-
Multi-target GI Pathogens

• A handful of multi-target assays are available and more are in development
• Variation among the available multi-target CIDT’s in which GI pathogens are targeted (Bacteria only vs bacteria and viruses vs bacteria, viruses and parasites)
• Common aspects of multi-target CIDT’s:
  ▪ Same day result
  ▪ Molecular/ PCR-based
Devices with GI Panels in Development or FDA Clearance Process

- BD Max
- BioFire FilmArray
- GenMark Dx eSensor XT-8
- Cepheid GeneXpert
- Nanosphere's Verigene Enteric Pathogens (EP) Test
- Applied Biocode
- Luminex xTag GPP
BioFire FilmArray® System

- Sample preparation, amplification, detection and analysis combined
- Add patient sample and reagents and walk away
- Detects 22 common bacterial, viral and parasitic GI pathogens
- Low throughput (single sample- can chain 8 instruments to a PC)
- Results in one hour
Prodesse Progastro™ SSCS Assay

- Detects the four common bacterial agents of gastrointestinal disease: *Salmonella*, *Shigella*, *Campylobacter* and Shiga toxin-producing *E. coli*
- Real time PCR kit run on the Cepheid SmartCycler II platform
- Results in four hours
BD MAX® Enteric Bacterial Panel

- Detects the 4 common enteric bacterial pathogens
- Virus and Parasite panels in development
- PCR-based
- Fully automated; 24 tests
- Flexibility to target pathogen class (B, V or P)
- Result in three hours
Nanosphere Verigene® Enteric Pathogens (EP) Test

- Detects 9 common bacterial and viral GI pathogens
- Combines automated extraction, purification, amplification and hybridization
- Single throughput; can chain up to 8 instruments
- Result in two hours
- Most recent platform to become available
Luminex xTAG GPP

- Both ASR and RUO kits available
- Detects 14-15 common bacterial, viral and parasitic gastrointestinal pathogens
- Bead-based technology
- Higher throughput; 96 well*
- More significant hands-on time
- Results in 5 hrs (~24 tests)
Advantages to CIDT Use

• Generally faster to result than traditional tests
• Classically-trained microbiologists not needed in many cases
• May be more cost-effective than traditional, conventional tests
• Syndromic-based testing approach possible with multi-target tests
• Ability to detect non-cultureable or fastidious pathogens
Advantages to CIDT Use

• Improved sensitivity and specificity?
  ▪ Compared with culture
  ▪ Need to assess the validity of the developer validation studies; specimens and/or isolates used may not have been optimal

• Detection of nonviable organisms*
  ▪ Only advantageous if truly pathogenic or a significant cause of GI illness
Disadvantages to CIDT Use

• Price of some CIDT platforms may be cost-prohibitive for laboratories

• Loss of culture isolates
  ▪ To clinical laboratories and PHL’s for AST
  ▪ To public health for surveillance

• Loss of classical microbiology experience; staff unable to determine when CIDT results don’t make sense
Disadvantages to CIDT Use

- Detection of nonviable organisms*
  - Problematic if not significant; not the cause of illness
  - Ineffective for test of cure; patient may shed nonviable organism or organism DNA well after the infection has passed

Red Herring!
Considerations of CIDT Results

• Interpretation of results
  ▪ What do the findings mean in relation to the clinical picture of the patient?
  ▪ What is the significance of multiple pathogens detected?
  ▪ How do epidemiologists apply the current reportable conditions guidelines to CIDT results?
    ▪ Confirmed?
    ▪ Suspect?
    ▪ Probable?
PHL Strategies for CIDT

• Partner with clinical laboratories in your jurisdiction
  • Work to ensure isolate/specimen submission continues
  • Communicate regularly- know who is using CIDT

• Assess impact of clinical lab CIDT implementation on your laboratory
  • Calculate number of additional cultures you will need to perform
  • Pursue funding (grants, general revenues, etc.) to cover rising costs of PH surveillance
PHL Strategies for CIDT

- Partner with epidemiologists
  - Discuss reporting issues
  - Educate them on what results may mean
- Monitor CIDT use and performance
  - What CIDT’s have become available?
  - Have there been published performance issues?
- Pursue mandatory specimen submission in your jurisdiction (in addition to isolate submission mandates)
- Partner with CIDT industry representatives
Summary

- There are a number of multi-target CIDT’s that have become available for detection of GI pathogens
- These CIDT’s offer definite advantages over traditional culture-based testing methods but considerations still must be taken into account when assessing their utility
- PH labs and epidemiologists must adapt to the ever-changing world of clinical diagnostics
- There are strategies PHL can utilize to address and adapt to the effects CIDT have on them