Syndromic Testing for Infectious Diseases
Part 2: Gastrointestinal Infections

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Disclosures

- None

Utilization Message

- As you view this presentation, consider the following important points regarding testing:
  - How can a multiplex molecular panel for gastrointestinal pathogens be used in your practice?
  - When should the test be used?
  - How will results impact patient management?
Gastrointestinal Infections

- Primarily manifest with vomiting and diarrhea
- Infectious diarrhea is a significant source of morbidity and mortality:
  - 1.7 billion cases and 2.2 million deaths each year worldwide\(^1\)
  - In the United States, nearly 48 million cases and >3000 deaths\(^2\)
    - Estimated cost of $150 million dollars/year to the U.S. economy

Gastrointestinal Pathogens

- There are a number of bacteria, viruses, and parasites that can cause gastrointestinal infections
  - Includes preformed toxins that are formed by certain bacteria.
  - Many are acquired through consumption of contaminated food
- Prevalence varies with the host’s age, immune status, and travel/exposure history
Common Pathogens Causing Diarrheal Illness

- Overall cause of foodborne illnesses in 2011:
  - Norovirus is most common (58%)
  - Nontyphoidal *Salmonella* spp (11%)
  - *Clostridium* perfringens (10%)
  - *Campylobacter* spp (9%)
  - Data from passive and active collections, including outbreak investigations

Viral Pathogens

- Adenovirus (enteric types 40 and 41)
- Astrovirus
- Coxsackievirus
- Norovirus
- Rotavirus
- Sapovirus
Bacterial Pathogens

- *Bacillus cereus*
- *Campylobacter* spp
- *Clostridium difficile* (toxigenic)
- *Clostridium perfringens*
- Shiga-toxin producing *Escherichia coli* (STEC); O157:H7 and other strains
- Enterotoxigenic *E coli* (ETEC)
- Diarrheagenic *E coli* other than STEC and ETEC
- *Helicobacter pylori*

- *Listeria monocytogenes*
- *Plesiomonas shigelloides*
- *Salmonella enterica*, non-typhi
- *Salmonella enterica*, serotype typhi
- *Shigella* spp
- *Staphylococcus aureus*
- *Staphylococcus aureus*
- *Vibrio* and *Vibrio*-like spp
- *Yersinia enterocolitica* and other species

Parasitic Pathogens

- *Blastocystis* spp
- *Cryptosporidium* spp
- *Cyclospora cayetanensis*
- *Cystoisospora* (Isospora) *belli*
- *Dientamoeba fragilis*
- *Entamoeba histolytica*
- *Giardia duodenalis* (Syn. *G lamblia*, *G intestinalis*)
- Various helminths
- *Microsporidia* (actually fungi)
Evaluation and Diagnosis of Infectious Diarrhea

- Most cases are self-limited and do not require treatment or testing
- However, some pathogens can cause severe, life-threatening infections, especially in immunocompromised hosts
- Clinical evaluation alone cannot ID the causative agent
- Definitive ID is necessary to guide therapy and infection prevention and control measures

Approach to Laboratory Testing

- Should be based on a careful evaluation of the patient and assessment of disease severity and risk factors
  - Immune status
  - Signs and symptoms of severe disease: fever, bloody diarrhea, dysentery, abdominal pain, dehydration, hospitalization
  - Risk factors for severe disease: immunocompromised host, advanced age
- Testing should also be considered for select populations:
  - International travelers, food handlers, patients with persistent or relapsing disease, outbreak setting
Gastrointestinal Pathogens - Testing

- Traditional laboratory testing for these pathogens consists of exams performed on stool specimens, commonly including:
  - Bacterial stool culture
  - “Ova and parasite exam”
  - Antigen detection methods for Cryptosporidium, Giardia, and rotavirus
  - PCR tests for norovirus, adenovirus 40/41
- These tests range in price and can take several days until a result is produced.

Multiplex Molecular Gastrointestinal (GI) Panels

- Allows for simplified ordering
- Now several FDA-approved/cleared options
- Detect bacterial, viral, and protozoal pathogens
- Test results available in 1 shift
- Benefits of these panels are recognized by the American College of Gastroenterology (ACG)
  - “Molecular diagnostic tests can provide a more comprehensive assessment of disease etiology by increasing the diagnostic yield compared with conventional diagnostic tests.”

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Comparison of FDA-approved/Cleared GI Panels for Bacteria and Viral Pathogens, +/- Parasites

<table>
<thead>
<tr>
<th>Manufacturer / Test</th>
<th># Targets Detected</th>
<th>Types of pathogens</th>
<th>Through-put</th>
</tr>
</thead>
<tbody>
<tr>
<td>Luminex xTAG® Gastrointestinal Pathogens Panel (GPP)</td>
<td>14</td>
<td>Bacterial, viral and parasitic</td>
<td>24 specimens/~5 hours</td>
</tr>
<tr>
<td>Biofire Gastrointestinal Panel</td>
<td>22</td>
<td>Bacterial, viral and parasitic</td>
<td>1 specimen/hour</td>
</tr>
<tr>
<td>Verigene Enteric Pathogens Panel</td>
<td>9</td>
<td>Bacterial, viral</td>
<td>1 specimen/&lt;2 hours</td>
</tr>
</tbody>
</table>

Advantages of Molecular Panels

- Rapid
- Similar or increased sensitivity compared to conventional methods
- Detect viruses and bacteria for which testing isn’t routinely available
  - Sapovirus, astrovirus, enteroagglomerative *E.coli*
- Detect more potential pathogens than conventional methods
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Studies – Increased Detection

- Spina et al, 2015\(^5\)
  - Multicenter study across 10 European countries using the BioFire GI panel; 709 samples
  - Positivity rates (for at least 1 pathogen):
    - BioFire GIP – 54%
    - Conventional methods – 18%
- Khare et al, 2014\(^6\)
  - Positivity rates:
    - BioFire GIP – 33%
    - Luminex GPP – 30%
    - Conventional methods – 8%

Potential Disadvantages

- Expensive
  - A patient may be charged >$1000 for a single test
- Results may be difficult to interpret
  - Detection of multiple potential pathogens
  - Some targeted organisms may be commensal
  - Clinical correlation is required
- Bacterial isolates not available for public health testing (eg, typing assays)
  - Unfixed specimen should be saved when possible for additional testing
Main Points

- A variety of pathogens cause infectious diarrhea
- Most infections are self-limited and do not require treatment or testing
- A subset of patients are at risk for severe disease
- Clinical symptoms overlap and specific testing is needed to identify the causative agent
  - Identification is needed for treatment decisions and prevention and control efforts
  - Syndrome testing using multiplex molecular panels provides a rapid and cost-effective method for detecting the causative pathogens in settings where testing is indicated

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References

1. World Health Organization
2. Centers for Disease Control and Prevention (CDC)

Questions or requests…

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