Emerging Technology in Clinical Microbiology

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October 9, 2015
Disclosures

• No financial or research relationships to disclose
Backgrounds

- “Imported” from Taiwan in 1998
- An island in eastern Asia (Mandarin Chinese)
- Cases of Dengue Fever multiply in S. Taiwan
Backgrounds

• Indiana University Health Pathology Laboratory
  • Centralized testing facility
    • IU Health University Hospital
    • IU Health Methodist Hospital
    • Riley Hospital for Children at IU Health
    • Numerous other IU Health and non-IU Health hospitals in Indiana
    • Numerous IU Health and non-IU Health clinics and physician’s offices

• 12 - 14 million laboratory tests per year
Objectives

• Identify and describe commonly concerned organisms that are related to healthcare-associated infections

• Describe the differences between traditional methods and molecular methods for clinical microbiology testing

• Describe the latest molecular technology in clinical microbiology
5 Moments of Hand Hygiene

1. Before touching a patient
2. Before clean/aseptic procedure
3. After body fluid exposure risk
4. After touching a patient
5. After touching patient surroundings

World Health Organization
# The “Big Players”

<table>
<thead>
<tr>
<th>Abbrev.</th>
<th>Full Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>VRE</td>
<td>Vancomycin-resistant Enterococcus</td>
</tr>
<tr>
<td>MRSA</td>
<td>Methicillin-resistant Staph. Aureus</td>
</tr>
<tr>
<td>ESBL</td>
<td>Extended-spectrum β-Lactamases</td>
</tr>
<tr>
<td>CRE or CP-CRE</td>
<td>Carbapenem-resistant Enterobacteriacea or Carbapenemase-producing CRE</td>
</tr>
<tr>
<td>C diff</td>
<td>Clostridium difficile</td>
</tr>
<tr>
<td>TB</td>
<td>Mycobacterium tuberculosis</td>
</tr>
<tr>
<td>Influenza</td>
<td>Human influenza viruses A, B, and C</td>
</tr>
</tbody>
</table>
ESBL

• First discovered in Europe in the mid 80s
• GN bacteria, mostly Enterics such as *E. coli*, *K. pneumoniae*, & *K. oxytoca*
• Produce enzymes, **Extended Spectrum Beta-Lactamases**, breaks down and destroys:
  - Penicillins
  - Expanded-spectrum cephalosporins (*Cefotaxime*, *Ceftriaxone*, and *Ceftazidime*)
  - Oxyimino-Monobactam *Aztreonam*

→ Treatment failure
ESBL

• Derived from many plasmid encoded genes, such as TEM, SHV, CTX-M, OXA
  o Transferable—Plasmid transfer bacterial resistance

• Diagnose challenges:
  o Current best method still relies on traditional culture and susceptibility test
  o Many genes
  o Compete for attention

• Limited treatment options:
  o Nitrofurantoin
  o Fosfomycin (UTI only)
  o Chloramphenicol
  o For serious infections: Carbapenem (Ertapenem) or gentamicin injections
• What are carbapenem antibiotics available in the US?
  
  o Primaxin (Imipenem, Merk, 1985)
  o Merrem (Meropenem, AstraZenica, 1996)
  o Invanz (Ertapenem, Merck, 2001)
  o Doribax (Doripenem, Johnson & Johnson, 2007)

  o All 4 drugs are injectable (IV) only
  o Broad-spectrum: active against GP, GN, anaerobes, non-fermenters
  o Drugs of choice for severe ESBL infections
CRE or CP-CRE

Guidance for Control of Carbapenem-resistant Enterobacteriaceae (CRE)

2012 CRE Toolkit

CRE or CP-CRE

CDC CRE Toolkit 2012 Definition of CRE:

- **Enterobacteriaceae** that are:
  - Non-susceptible to one of the following antibiotics: Doripenem, Meropenem, or Imipenem**
  - AND...
    - Resistant to all of the extended-spectrum (3rd generation) cephalosporins tested (Cefotaxime, Ceftriaxone, Ceftazidime)

**Exceptions: Proteus/Providencia/Morganella are intrinsically resistant to imipenem**
CRE or CP-CRE

Two general mechanisms cause CRE:

1) **Other non-carbapenemases in conjunction with other structural change of bacteria**
   - Such as ESBL or AmpC + porin loss
   - Low-level carbapenemase activity
   - Seen in most of the CRE before 2000

2) **Carbapenemase** production: β-lactamases that can destroy carbapenems
   - Carbapenemases = enzymes derived from plasmid encoded genes
   - Transferrable!
   - After 2000, CRE incidence increased rapidly
   - Much of this increase appears to be caused by the spread of Carbapenemase-Producing CRE
CRE or CP-CRE

• GNR Carbapenemase genes are:
  o **KPC**
    • First discovered in *K. pneumoniae*
    • Also commonly seen in other Enterics
  o **SME**
    • First discovered in *S. marcescens*
  o Metallo-β-Lactamases (MBL)
    • **NDM, VIM, IMP, GIM, SPM**
    • Enterics, *P. aeruginosa*, *Acinetobacter*, *S. maltophilia*

• Carbapenemase genes are often linked to other resistance genes → Organisms often become **multi-drug resistant**
  • Most commonly quinolones, SXT, and at least one aminoglycoside
CRE or CP-CRE

- Diagnostic challenge:
  - CRE definition
  - Traditional Microbiology method vs. Molecular diagnostic method

- Treatment: Combo therapy
  - 2 drugs are better than 1
CRE or CP-CRE

• Positive patients may carry CRE for a LONG time even after discharge (as long as 387 days!)

• Patients carry CRE may also carry carbapenem resistant Enterobacteriacea, Pseudomonas and Acinetobacter

• LTACH and ECF are often the reservoir for local hospital’s CRE patients.
C diff

- GP anaerobes, ubiquitous in the environment
- Produce spores to survive in harsh environment
- May become part of the flora in human colon (2-5% of adult population)
- **GDH** (glutamate dehydrogenase) enzyme produced by ALL strains of C. difficile
- **Toxins** produced by pathogenic (toxigenic) C. difficile strains cause CDI
  - Presence of toxin is necessary for CDI
  - Colonization of toxin-producing C. diff does not always causes CDI
  - Lead to confusing test results (more later...)
C. diff

• Diagnostic challenge:
  o Method selection
  o Result interpretation

• Treatment:
  o Without symptoms is not recommended
  o Medications (Metronidazole, Vancomycin)
  o Probiotics
  o Fecal transplant
  o Colectomy
TB

- *Mycobacterium tuberculosis*
- “GP” or may not retain Gram stain
- Traditionally stained by acid fast stain (hence, acid fast bacilli, acid fast culture)
- MDR-TB = resist to Isoniazid (INH) and Rifampin (RIF)
- MDR plus TB = resist to INH, RIF, and Fluoroquinolone (FQ)
- XDR-TB (extensively drug-resistant TB) = resist to INH, RIF, FQ, and injectable aminoglycosides (Amikacin, Gentamycin, and Tobramycin)
TB

- Still with high prevalence in the world (1/3 of the world population)
  - No effective vaccination
  - Diagnostic challenge: slow grower
  - Treatment challenge: long term treatment and lack of new drug since 1968

- Only 50% successful rate to treat MDR TB
- On 12/28/12, FDA accelerated to approve Bedaquiline for MDR TB or XDR TB (Controversial!)
TB

• Out of all the positive acid fast culture, only 50% of their corresponding AFSM are negative.

• Rapid ID for TB is important:
  o Rapid ID of TB will improve diagnosis/treatment, prevent TB transmission, and help clinical trial of new TB drug development
MDx v.s. Traditional Methods

- Traditional microbiology diagnostic methods
  - Inoculate patient samples to agar plates
  - Incubate for certain amount of time
  - Analyze growth on agars to determine additional testing
  - Additional testing = biochemicals
  - If applicable, perform susceptibility
  - TAT:
    - Typical bacteria 3-7 days if positive
    - Two to six weeks for fungus and AFB
  - Subjective
  - Cheaper
  - Allow to detect unexpected infection
MDx v.s. Traditional Methods

- Molecular diagnostic (MDx) methods
  - Different techniques to analyze or detect targets in genome or proteome
  - Some allow direct pathogen detection from a clinical specimen (eliminating culture/incubation process)
  - Specific, Sensitive
  - Some are high-throughput
  - Faster TAT
  - Objective
  - More expensive
  - Target specific
MALDI-TOF Mass Spectrometry

• **Matrix-assisted laser desorption/ionization time-of-flight** (mass spectrometry)

• Identification based on protein contents of the organism

• Culture $\rightarrow$ Colony $\rightarrow$ MALDI $\rightarrow$ 10-15 minutes later $\rightarrow$ high-level of confidence identification
MALDI-TOF Mass Spectrometry

Bruker Biotyper

bioMerieux Vitek MS
MALDI-TOF Mass Spectrometry

FDA approved for clinical use on:
- GN
- Yeasts (Vitek MS only)
- GP (Vitek MS only)
- Anaerobes (Vitek MS only)

Soon in the future:
- Mold identification
- Acid fast bacilli identification
- Bacteremia identification
- Identify presence of resistant enzymes, such as ESBL or Carbapenemases
Bacteremia/Sepsis Identification

• Bacteremia and fungemia are very serious infections
  - Mortality: 14% (community) – 34% (nosocomial)
  - >50% of bloodstream infections are nosocomial

• 2001 – 2007 condition with the highest increase in incidence²
  - 675,000 cases / year (increase of 97%)

• Financial burden
  - $28,000 (community) - $105,000 (nosocomial)
  - Average of $18,500 / patient

References:
Bacteremia/Sepsis Identification

• Traditional culture methods rely on cultivation of pathogens:
  o 1-3 days: preliminary results
  o 3-5 days: definitive result, especially for MDRO such as CRE or VRE

• Not effective for modification/de-escalation of antimicrobial therapy

• Not effective for transmission prevention of MDRO

→ Increased mortality, emergence of MDRO, chance to spread of MDRO
Bacteremia/Sepsis Identification

- Microbial identification based on detection of organism-specific nucleic acids
  - Microscopic detection - PNA-FISH®
  - NAAT - BioFire™ Diagnostics, Cepheid® Xpert® MRSA/SA BC
  - Nanoparticle-based detection – Nanosphere, Inc. Verigene® System

- Microbial identification using proteomic information
  - Mass spectrometry

Note: A Gram stain is still required to guide decision of these rapid identification assay.
Bacteremia/Sepsis Identification

- PNA-FISH® AdvanDx
  - Peptide Nucleic Acid Fluorescence In Situ Hybridization
  - Examine using fluorescence microscopy
  - Still somewhat subjective
  - Unable to determine resistant mechanism

*S. aureus* (g) and CoNS (r)
Bacteremia/Sepsis Identification

- BioFire™ Diagnostics FilmArray BCID
  - Multiplex nucleic acid amplification-based platform
    - Blood Culture IDentification

- Identification of 24 microbial pathogens, bacteria and yeast, as well as detection of 3 genes encoding antimicrobial resistance mechanisms

- Uses a 100-µl aliquot of positive blood culture broth

- Hands-on time, 2 minutes; assay time ~ 1 h
BioFire™ Diagnostics FilmArray BCID

**Gram + Bacteria**
- Enterococcus
- *Listeria monocytogenes*
- Staphylococcus
- *Staphylococcus aureus*
- Streptococcus
- *Streptococcus agalactiae*
- *Streptococcus pyogenes*
- *Streptococcus pneumoniae*

**Gram – Bacteria**
- *Acinetobacter baumannii*
- *Haemophilus influenzae*
- *Neisseria meningitidis*
- *Pseudomonas aeruginosa*
- Enterobacteriaceae
- *Enterobacter cloacae complex*
- *Escherichia coli*
- *Klebsiella oxytoca*
- *Klebsiella pneumoniae*
- Proteus
- *Serratia marcescens*

**Yeast**
- *Candida albicans*
- *Candida glabrata*
- *Candida krusei*
- *Candida parapsilosis*
- *Candida tropicalis*

**Antibiotic Resistance**
- *mecA* - methicillin resistant
- *vanA/B* - vancomycin resistant
- *KPC* - carbapenem resistant
Bacteremia/Sepsis Identification

- **Cepheid® Xpert® MRSA/SA BC**
  - Qualitative, real-time PCR for detection of methicillin-resistant *Staphylococcus aureus* and *S. aureus* (MSSA) in blood culture

- **Cartridge-based platform that offers**
  - Automated/integrated sample extraction (cartridge manipulated, thermal cycled, etc. using the Cepheid® GeneXpert)
  - Uses a small sample volume
    - 50-μl aliquot of positive blood broth
  - 62-minute TAT
  - Targets include *spa*, *mecA*, and *SCCmec*
Bacteremia/Sepsis Identification

- Cepheid® Xpert® MRSA/SA BC

Note: Xpert® MRSA (nasal) & Xpert® MRSA/SA SSTI
Bacteremia/Sepsis Identification

- Nanosphere, Inc. Verigene® System
  - Array-based gold nanoparticle technology
  - Nanoparticles (gold, 13 – 20 nm) are coated with either oligonucleotides complementary to organism-specific DNA or RNA sequences OR they are coated with antibodies specific for protein targets
  - Uses a larger volume of blood culture broth for analysis
  - BC-GN kit: 700 µl
  - BC-GP kit: 350 µl
  - TAT is approximately 2 h
### Bacteremia/Sepsis Identification

- **Nanosphere, Inc. Verigene® System**

<table>
<thead>
<tr>
<th>Bacterial genera and species</th>
<th>Antimicrobial resistance genes</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Acinetobacter</em> spp.</td>
<td><em>bla</em>&lt;sub&gt;CTX-M&lt;/sub&gt;</td>
</tr>
<tr>
<td><em>Citrobacter</em> spp.</td>
<td><em>bla</em>&lt;sub&gt;KPC&lt;/sub&gt;</td>
</tr>
<tr>
<td><em>Enterobacter</em> spp.</td>
<td><em>bla</em>&lt;sub&gt;NDM-1&lt;/sub&gt;</td>
</tr>
<tr>
<td><em>Proteus</em> spp.</td>
<td><em>bla</em>&lt;sub&gt;VIM&lt;/sub&gt;</td>
</tr>
<tr>
<td><em>Escherichia coli</em></td>
<td><em>bla</em>&lt;sub&gt;IMP&lt;/sub&gt;</td>
</tr>
<tr>
<td><em>Klebsiella pneumoniae</em></td>
<td><em>bla</em>&lt;sub&gt;OXA&lt;/sub&gt;</td>
</tr>
<tr>
<td><em>Klebsiella oxytoca</em></td>
<td></td>
</tr>
<tr>
<td><em>Pseudomonas aeruginosa</em></td>
<td></td>
</tr>
<tr>
<td><em>Serratia marcescens</em></td>
<td></td>
</tr>
<tr>
<td>(not FDA-cleared in US)</td>
<td></td>
</tr>
</tbody>
</table>

**Antimicrobial resistance genes**

- *mecA*
- *vanA*
- *vanB*

<table>
<thead>
<tr>
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</tr>
</thead>
<tbody>
<tr>
<td><em>Staphylococcus</em> spp.</td>
<td><em>Streptococcus pyogenes</em></td>
</tr>
<tr>
<td><em>Staphylococcus aureus</em></td>
<td><em>Streptococcus agalactiae</em></td>
</tr>
<tr>
<td><em>Staphylococcus epidermidis</em></td>
<td><em>Streptococcus anginosus</em></td>
</tr>
<tr>
<td><em>Staphylococcus lugdunensis</em></td>
<td><em>Enterococcus faecalis</em></td>
</tr>
<tr>
<td><em>Streptococcus</em> spp.</td>
<td><em>Enterococcus faecium</em></td>
</tr>
<tr>
<td><em>Streptococcus pneumoniae</em></td>
<td><em>Listeria monocytogenes</em></td>
</tr>
</tbody>
</table>
Bacteremia/Sepsis Identification

- All of these methods still rely on a sample from a positive blood culture.
- A positive blood culture may take 3 hours to days to be positive and detectable on a blood culture instrument.
- New MDx test—Direct detection from blood sample without the step of blood culture
  - T2Biosystem® T2 Candida Panel (FDA cleared)
  - T2Biosystem® T2Bactera Panel
  - Eliminate blood culture incubation
MDx Fecal Tests

- BioFire™ Diagnostics FilmArray GI Panel

**Bacteria**
- Campylobacter (jejuni, coli and upsaliensis)
- Clostridium difficile (toxin A/B)
- Plesiomonas shigelloides
- Salmonella
- Yersinia enterocolitica
- Vibrio (parahaemolyticus, vulnificus and cholerae)
  - Vibrio cholerae
- **Diarrheagenic E. coli/Shigella**
  - Enteraggregative E. coli (EAEC)
  - Enteropathogenic E. coli (EPEC)
  - Enterotoxigenic E. coli (ETEC) It/st
  - Shiga-like toxin-producing E. coli (STEC) stx1/stx2
  - E. coli O157
  - Shigella/Enteroinvasive E. coli (EIEC)

**Parasites**
- Cryptosporidium
- Cyclospora cayetanensis
- Entamoeba histolytica
- Giardia lamblia

**Viruses**
- Adenovirus F 40/41
- Astrovirus
- Norovirus GI/GII
- Rotavirus A
- Sapovirus (I, II, IV and V)
### MDx Fecal Tests

- **Nanosphere, Inc. Verigene® System Enteric Panel**

<table>
<thead>
<tr>
<th>TARGETS</th>
<th>US/FDA Cleared</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bacteria</td>
<td></td>
</tr>
<tr>
<td>Campylobacter Group</td>
<td>![ ]</td>
</tr>
<tr>
<td>Salmonella spp.</td>
<td>![ ]</td>
</tr>
<tr>
<td>Shigella spp.</td>
<td>![ ]</td>
</tr>
<tr>
<td>Vibrio Group</td>
<td>![ ]</td>
</tr>
<tr>
<td>Yersinia enterocolitica</td>
<td>![ ]</td>
</tr>
<tr>
<td>Toxins</td>
<td></td>
</tr>
<tr>
<td>Shiga Toxin 1 (stx1)</td>
<td>![ ]</td>
</tr>
<tr>
<td>Shiga Toxin 2 (stx2)</td>
<td>![ ]</td>
</tr>
<tr>
<td>Viruses</td>
<td></td>
</tr>
<tr>
<td>Norovirus</td>
<td>![ ]</td>
</tr>
<tr>
<td>Rotavirus</td>
<td>![ ]</td>
</tr>
</tbody>
</table>
MDx Fecal Tests

- Luminex xTAG® Gastrointestinal Pathogen Panel (GPP)

**Bacteria**
- Campylobacter
- Clostridium difficile
- Toxine A/B
- Escherichia coli O157
- Enterotoxigenic E.coli (STEC) LT/ST
- Shiga-like Toxin producing E.coli (STEC) stx1/stx2
- Salmonella
- Shigella
- Vibrio cholerae
- Yersinia enterolitica

**Virus**
- Adénovirus 40/41
- Norovirus GI/GII
- Rotavirus A

**Parasites**
- Giardia
- Cryptosporidium
- Entamoeba histolytica
MDx Fecal Tests

• Cepheid® Xpert® C. difficile
  o Detect toxigenic C. difficile

• Cepheid® Xpert® C. difficile/Epi
  o Detect toxigenic C. difficile
  o If positive, detect 027/NAP1/BI strain
MDx Fecal Tests

- BD MAX™ System C. difficile
- BD MAX™ System Enteric Bacterial Panel
  - Salmonella spp.
  - Campylobacter spp. (jejuni / coli)
  - Shigellosis disease causing agents
    - Shigella spp. and Enteroinvasive E. coli (EIEC)
  - Shiga-toxin producing E. coli

Note: BD MAX also has panels for MRSA (nasal) & StaphSR (SSI)
# CDI Diagnosis

Currently available *C. difficile* Laboratory Tests:

<table>
<thead>
<tr>
<th>Test</th>
<th>Target Detected</th>
<th>TAT</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Culture with Cytotoxin</td>
<td>Toxigenic <em>C. difficile</em></td>
<td>3-5 days</td>
<td>&gt;95</td>
<td>80-90</td>
</tr>
<tr>
<td>Cytotoxin</td>
<td>Toxin B</td>
<td>1-3 days</td>
<td>95</td>
<td>90-95</td>
</tr>
<tr>
<td>EIA Toxin A or A/B</td>
<td>Toxin A or Toxin A&amp;B</td>
<td>Hours</td>
<td>75-80</td>
<td>97-98</td>
</tr>
<tr>
<td>GDH</td>
<td><em>C. difficile</em></td>
<td>Hours</td>
<td>95-100</td>
<td>70-80</td>
</tr>
<tr>
<td>GDH + EIA Toxin A/B</td>
<td><em>C. difficile</em> + Toxin A&amp;B</td>
<td>Hours</td>
<td>95-100</td>
<td>97-98</td>
</tr>
<tr>
<td>MDx (PCR)</td>
<td>Toxigenic <em>C. difficile</em></td>
<td>Hours</td>
<td>&gt;98</td>
<td>80-99</td>
</tr>
</tbody>
</table>

- Barlett J. ICHE 2010, 31:S35
CDI Diagnosis

• What do the results mean?
  o Positive GDH = *C. difficile* present (non-toxigenic and/or toxigenic strains)
  o Positive Toxin A/B = the toxin(s) that causes CDI present (true positive CDI)
  o Positive PCR = Toxigenic strain *C. difficile* present

• Presence of toxin(s) = CDI
• Presence of toxigenic strain *C. difficile* does not necessary = CDI
CDI Diagnosis

• MDx (PCR) C diff test will pick up asymptomatic carriers
  o Carrier of the toxigenic C. diff without active CDI
  o >50% of CDI patients after treatment continue to shed C. difficile organisms

• From infection prevention standpoint
  o An asymptomatic C. diff carrier may still present a risk of transmission
  o The current best way to screen for carriers is MDx method
  o Screen all patients for C. diff? Isolate asymptomatic carriers? Controversial!

• From treatment standpoint
  o MDx (PCR) test overdiagnoses CDI → Set clinical criteria
  o A patient with GDH +/-Toxin – and/or PCR + C. diff result should not be treated

TB Diagnosis

Direct respiratory sample test:

- Roche COBAS® TaqMan® MTB test & Amplicor® MTB
- Cepheid® Xpert® MTB/RIF
- Hologic (Gen-Probe) Amplified MTD® test
TB Diagnosis

• CDC’s “Report of an Expert consultation on the Uses of Nucleic Acid Amplification Tests for the Diagnosis of Tuberculosis”

  [Link](http://www.cdc.gov/tb/publications/guidelines/amplification_tests/default.htm)

• Advantages of MDx TB Diagnosis:
  o Faster diagnosis (hours versus weeks)
  o Initiation of earlier treatment
  o Faster reporting to TB programs
  o Reduce transmissions
Influenza & Respiratory Viruses

- Large panels include different strains of respiratory viruses and/or bacteria:

<table>
<thead>
<tr>
<th>Nanosphere Verigene® RP Flex</th>
<th>BioFire™ FilmArray Respiratory Panel</th>
<th>GenMarkDx® eSensor® RVP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adenovirus</td>
<td>Adenovirus</td>
<td>Adenovirus B/E, C</td>
</tr>
<tr>
<td>Human Metapneumovirus</td>
<td>Human Metapneumovirus</td>
<td>Human Metapneumovirus</td>
</tr>
<tr>
<td>Influenza A</td>
<td>Influenza A</td>
<td>Influenza A</td>
</tr>
<tr>
<td>• &amp; Subtype H1, H3</td>
<td>• &amp; Subtype H1, H3, H1-2009</td>
<td>• &amp; Subtype H1, H3, H1-2009</td>
</tr>
<tr>
<td>Influenza B</td>
<td>Influenza B</td>
<td>Influenza B</td>
</tr>
<tr>
<td>Parainfluenza 1,2,3,4</td>
<td>Parainfluenza 1,2,3,4</td>
<td>Parainfluenza 1,2,3</td>
</tr>
<tr>
<td>Rhinovirus</td>
<td>Rhinovirus/Enterovirus</td>
<td>Human Rhinovirus</td>
</tr>
<tr>
<td>RSV A &amp; B</td>
<td>RSV</td>
<td>RSV A &amp; B</td>
</tr>
<tr>
<td>Bordetella pertussis</td>
<td>Coronavirus</td>
<td></td>
</tr>
<tr>
<td>B. parapertussis/bronchiseptica</td>
<td>HKU1, NL63, 229E, OC43</td>
<td></td>
</tr>
<tr>
<td>B. holmesii</td>
<td>Bordetella pertussis</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Chlamydomphila pneumoniae</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Mycoplasma pneumoniae</td>
<td></td>
</tr>
</tbody>
</table>
Influenza & Respiratory Viruses

Influenza based test:

- Roche COBAS® Liat Influenza A/B

- Alere™ i Influenza A & B

- Cepheid® Xpert® Flu & Flu/RSV XC
PFGE

PFGE = Pulsed Field Gel Electrophoresis

Relatively “older” technology
Compare strains of bacteria at genomic level
Applications:
- Outbreak studies (foodborne)
- Bacterial typing or characterization
- Nosocomial person-to-person transmission
More in the future…

• Direct sample to detect sepsis (such as T2Biosystem®)

• Rectal sample to screen for CRE by non-culture method (such as Cepheid®)

• Direct sample to organism identification/susceptibility without cultivation (GeneWEAVE™ Smarticles™)
Applications for MDx

• Specific pathogen identification for
  o Surveillance and other epidemiologic purposes
  o Organisms associated with nosocomial transmission
  o Organisms associated with disease outbreak
  o Organisms ID when conventional methods fail to achieve high-level of confidence

• Challenge to implement MDx in your lab:
  o COST, COST, COST!
  o Validation difficulty (need assistance from ID docs, ICP practitioners, and hospital epidemiologists to acquire samples)
  o Consider complexity and throughput of newly developed technology→ may only be available to large commercial or university-based diagnostic laboratories
  o Middleware allow for interfacing of HIS/LIS from multiple institutions
Acknowledgements

- Dr. Ryan Relich, Ph.D, MLS(ASCP) IUHPL
- Deidre Jarrett, MT(ASCP) Cepheid
- Steve Smith, Nanosphere
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