Scourge and Re-scourge of Pertussis
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*Bordetella pertussis* (whooping cough)
- Highly contagious respiratory disease
- Severe debilitating cough illness (100 day cough) in persons of all ages
- Highest morbidity and mortality
- Estimated > 300,000 deaths/year
- Poorly controlled despite high vaccine coverage
- First Us pertussis vaccine for adolescents and adults (Tdap) licensed in 2005
- Adolescents and adults waning immunity-(5-10 years) giving it to our kids

Antigenic and biological active components
- Pertussis Toxin (PT)
  - Major virulence factor
  - Immunogenic and protective
  - Elicits lymphocytosis
  - In all acellular pertussis vaccines
- Filamentous hemagglutinin (FHA)
  - Adhesion to ciliated epithelial cells
  - Immunogenic but not completely protective
- Pertactin-cell surface protein
  - Enhances cell binding and entry
- Trachael Cytotoxin
  - Major reason for cough
  - Cough can not be treated with antibiotics
- Adenylate Cyclase
  - Inhibits local immune response
- Dermonecrotic toxin
  - Cell damage and death

Picture of Pertussis in the ED
- Lymphocytosis
- Fever usually minimal throughout course
- Characteristic Cough-toxin mediated/antibiotics do not modify the cough

Clinical Stages and Clinical Course
- Catarrhal-watery eyes, low grade fever, malaise, runny nose, 3 weeks after cough onset
  - 1-2 weeks
- Paroxysmal-bursts of coughing during a single exhalation followed by inspiratory whoop sound,
  - 1-6 weeks
- Convalescent-weeks-months paroxysms gradually improve
Infant Pertussis
- Young infants-highest rate of disease
- Atypical symptoms: apnea (sometimes with seizures), sneezing, gagging, choking, vomiting

Pertussis among Adolescents and Adults
- Disease often milder than in infants and children
- Persons with mild disease can transmit
- Difficult to diagnose infection
- Pertussis immunity wanes 5-10 years after childhood vaccine series

Complicated Pertussis Laboratory Diagnosis
- Stage of Disease
- Antibiotic administration wipes out B. pertussis
- Vaccination status
- Quality/timely collection of clinical specimens
  - Nasopharyngeal aspirate, nasopharyngeal swab
  - Swabs not cotton or calcium alginate for PCR
- Transport
  - Regan Lowe, BG transport
  - PCR-universal transport media
- Culture
  - Gold Standard
  - 100% specific but low sensitivity
  - Highest yield in young patients, unvaccinated patients, patients early in cough illness prior to antimicrobials
  - Slow incubation time-up to 10 days
  - Freshly Prepared Regan-Lowe Media
- Identification
  - FA Testing
  - Biochemical not recommended
  - MALDI-TOF
- PCR
  - Primary diagnostic test
  - Potentially more sensitive than culture
  - Rapid
  - Disadvantages
    - Affected by disease phase and antibiotics
    - No national standard protocol
    - Potential for false positives
PCR Assays-Multiplex
- Focus-www.focusedx.com/
- Biofire-bioMerieux-www.biofiredx.com
- Vergene-Nansphere-www.nanosphere.us/
- Gen-Mark-e-Sensor-www.genmarkdx.com

PCR Assays-Single
  - LAMP Molecular Technology
  - Provides Results in less than 1 hour: test and treat the same day
- Amplivue-Quidel-www.Quidel.com
  - Helicase-dependent amplification assay

The Reds, the Blacks and the Ugly!!AFB/Mycology Case Studies
Betty Forbes, PhD., D(ABMM)
VCU Medical Center, Richmond, VA

Rapid Growing Mycobacteria (RGM’s)
- Do not stain well with Kinyoun
- Very susceptible to decontamination
- Reservoirs
  - Soil, water, dust
  - Extended habitats-grow in water including distilled water
  - Components of biofilms
  - In artificial water supplies
- Isolation of RGM’s does not imply disease

Case 1: *Mycobacterium goodii* isolated from a pocket formed around a dysfunctional pacemaker.

*M. goodii*
- Belongs to *M. smegmatis* group
- Recognized in 1999
- Associated with community acquired wound infections, respiratory and nosocomial infections
- Nosocomial outbreak of wound infections associated with surgical implants, (2004), pacemaker infections
- Treatment-*M. smegmatis* group= general lack of susceptibility to clarithromycin
Case 2: *M. porcinum* from a patient with several year history of bronchiectasis and cough

*M. porcinum*
- First recognized as a human pathogen in 2004
- Emerging rapid grower
- In *M. fortuitum* group
- Wound infections, IV catheter-related infections, osteomyelitis
- Can be drinking water contaminant serving as a long term reservoir

Common Infections associated with the Following RIGM’s
- Localized post-traumatic wound infections
- Catheter infections
- Surgical wound infections especially following augmentation mammoplasty, cardiac surgery
- Post traumatic or postsurgical corneal infections

*M. fortuitum* group
*M. chelonae* group
*M. abscessus* group
- *M. abscessus* ss *abscessus* group most drug resistant *Mycobacteria* inducible macrolide resistance

*M. smegmatis* group
*M. mucogenicum* group

Identification of RGM’s
- More than 70 species
- Biochemical identification-forget it
- Molecular Sequencing
  - 16S RNA
  - rpoB-based gene sequencing
  - MALDI-TOF

Treatment of RGM’s
- General lack of susceptibility to clarithromycin
- Duration of therapy: success depends on nature and severity of disease
- Localized infections: oral-single dose drug therapy for 4-6 months
- More severe: debridement, combination of oral and IV antimicrobials and then oral therapy for 6 months

Important to correctly identify and perform susceptibility testing on RGM’s to predict antibiotic susceptibility and patient outcome
Dematiaceous Fungi

- > 150 species and 70 genera
- Histology important in identification
  - Fontana-Mason stain: stain specific for melanin
  - Differentiated based on histologic findings
- Identification based on phenotypic studies
- Reference for dematiaceous fungi
  - Revankar, SG and Sutton, DA 2010, Clinical Microbiology Review 23:884-928

General Comments about Dematiaceous Fungi

- Common in environment
- Often isolated in laboratory but only 10% are likely to have clinical significance
- Clinical disease is uncommon

Clinical Syndromes of Dematiaceous Fungi

- Eumycetoma
  - Deep subcutaneous tissue infections of lower extremities, draining sinus tracts
- Chromoblastomycosis
  - Production of sclerotic bodies in subcutaneous tissue, tropical areas
- Phaeohyphomycosis-reserved for everything else
  - Generic name that encompasses pathologic conditions associated with dematiaceous fungi

Disseminated Phaeohyphomycosis

- *Scedosporium prolificans* is by far most common cause
- Primary Risk Factors
  - Immunocompromise of any kind
  - Known malignancy, neutropenia, HIV, Bone marrow transplant, solid organ transplant, cardiac hardware
- Body sites involved
  - Blood, lung, heart, skin, brain, kidney
- Overall Mortality 79%
Antimicrobial Testing Updates: What’s New and What’s Coming
Richard Van Enk, Ph.D., CIC
Bronson Methodist Hospital, Kalamazoo, Michigan

New Antibiotics
- 3 for MRSA
- 3 for ESBL and CRE in Gram negative rods
- Expensive
- Shorter course of therapy
- Unusual dosing regiments like single dose or weekly

Tedizolid (Sivextro™, Cubist)-Released June 2014
- Second generation linezolid (oxazolidinones)
- IV and PO
- Cellulitis drug
- For Gram positive cocci including MRSA and VRE
- More active than Linezolid about 4x and safer

Oritavancin (Orbactive™)-Released August 2014
- A lipoglycopeptide similar to vancomycin
- Skin and skin structure infections-1200 mg single-dose
- For Gram positive bacteria-MRSA and VRE

Dalbavancin (Dalvance™)-Released May 2014
- Vancomycin analog
- IV-2 doses (1,000 mg followed by 500 mg dose one week later)
- Approved for skin and skin structure infections
- Gram positive bacteria

Ceftaroline fosamil (Teflaro)-Released 2010
- 5th generation cephalosporin
- Skin and soft tissue infections
- Community acquired pneumonia
- Inhibits MRSA, MRSE, Pencillin R S. pneumoniae and E. faecalis
- Gram positive activity like vancomycin
- Gram negative activity like Ceftriaxone (Rocephin)
- Not active against ESBL, CRE or nonfermentors

Avibactam
- Best of all the beta-lactamase inhibitors
- Irreversible binding of enzyme
- Extends the spectrum of other drugs
- Inhibits ESBL’s and KPC’s
Ceftaroline-avibactam
• Avibactam extends spectrum for Ceftaroline to include ESBL’s and KPC’s
• Lowers MIC of ceftaroline against enterics at least 2X

Ceftolozane/tazobactam
• Phase III trials completed-submitted to FDA
• Most potent Gram negative cephalosporin seen
• Inhibits 98% Pseudomonas aeruginosa
• Active against ESBL’s not CRE
• IV
• Reserve for serious Pseudomonas infections

Updates on Susceptibility Testing CLSI
• Table 1-Drugs recommended for testing
  o Cefazolin tested on urine isolates from uncomplicated UTI predicts other oral cephalosporins
  o Cefoxitin surrogate test for Oxacillin Resistance in staphylococci. Detects Mec A better than oxacillin
  o Doripenem added to carbapenem box in Group A for Acinetobacter
  o Minocycline is added to Group B for Acinetobacter
    ▪ More active than tetracycline or doxycycline so if it is on your formulary you should test it rather than the others
• Table 2
  o For all disk diffusions testing; no more than 6 disks on a 100mm plate, disks should be 24 mm apart
  o Cefazolin predicts oral cephalosporins better than Cephalothin for urine cultures
  o For Acinetobacter and carbapenem comment specifies the dosing that interpretation refer to
  o Deleted vancomycin disk for staphylococci

• Susceptible Dose Dependent Category-SDD
  ▪ New category of interpretation for Enterobacteriaceae and Cefepime
  ▪ SDD replaces Intermediate
  ▪ Four different dosing regimens for different infections
  ▪ This is first drug CLSI is connecting dosing to MIC

<table>
<thead>
<tr>
<th>Old Breakpoints</th>
<th>Proposed Breakpoints</th>
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<tr>
<td>S = &lt; 8</td>
<td>S = &lt; 2</td>
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<tr>
<td>I= 16</td>
<td>SDD = 4-8</td>
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<tr>
<td>R= &gt; 32</td>
<td>R = &gt; 16</td>
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• Under SDD if MIC is 4 or 8 bump up to higher dosing
• Problem whether Doctors and pharmacists knowing how to interpret SDD result
• Need to have discussion with Pharmacy about SDD concept and result