

# CONTAGIOUS COMMENTS

## Department of Epidemiology

### Drug Resistant Bacteria- What's It All About?

*John James, PhD, MPH, D(ABMM), CIC*

You probably have been hearing about antimicrobial resistance as a growing problem in healthcare. While standard precautions and isolation are imperative to prevent the spread of these organisms, knowledge of the complex resistance mechanisms is essential to understanding why there is such a significant problem.

Multiple antibiotic resistance mechanisms in both Gram-positive and Gram-negative bacteria have been inexorably increasing. This increase has been driven by the selection pressure of unnecessary or inappropriate antibiotic use, both in hospitals and the community.

Bacteria acquire antibiotic resistance genes through genetic mutation or more commonly by receiving genetic material (DNA) from an already resistant bacterium. The most common mechanisms of DNA transfer are conjugation (bacterial sex), or

transduction (DNA acquired from a bacteriophage -a bacterial virus) infection of the recipient bacteria.

The genes encoding antimicrobial resistance mechanisms may reside on large extrachromosomal self replicating transmissible DNA elements (plasmids). Plasmid or bacteriophage DNA may contain smaller mobile elements (transposons), which in turn may contain even smaller elements (integrons). These integrons are the building blocks of antimicrobial resistance, and may contain multiple antibiotic resistance genes positioned side by side as mobile gene cassettes. The cassettes are under the control of a strong promoter gene. This physical arrangement accounts for antibiotic cross-resistance, in that the antimicrobial resistance products of all the adjacent integrons may be expressed. Both enzymatic resistance genes and drug efflux pump genes are found on integrons. This Darwinian selection process is strongest in hospital intensive care units of both adult and pediatric hospitals.

### Major and Emerging Gram-negative Antibiotic Resistance:

| <u>Resistance Type</u>  | <u>Active Against</u>  | <u>Inhibited By</u> | <u>Drug of Choice</u>  | <u>Found In</u>  |
|---|--|---------------------|--|--|
| <b>mecA (PBP2) positive Methicillin Resistant <i>Staphylococcus aureus</i> (MRSA)</b>               | All $\beta$ -lactams   |                     | Variable, but<br>Vancomycin<br>Bactrim<br>Clindamycin and rifampin<br>(not as single drug therapy)<br>used   | <i>S. aureus</i> and<br>other<br>staphylococci   |
| <b>Vancomycin Resistant Enterococci (VRE)</b><br><br>vanA gene<br><br>vanB gene                     | <br><br>Vancomycin and<br>teicoplanin<br><br>Vancomycin  |                     | High levels of intrinsic<br>resistance to many<br>antibiotics<br><br><i>E. faecalis</i> -ampicillin<br><br><i>E. faecium</i> -linezolid,<br>quinupristin/dalfopristin<br>(Synercid), daptomycin,<br>tigecycline, and combined<br>therapy | <i>E. faecalis</i> and <i>E. faecium</i>   |
| <b>Extended spectrum <math>\beta</math>-lactamases(ESBL).<br/>Hundreds of different<br/>enzymes</b> | 3 <sup>rd</sup> -generation<br>cephalosporins, all<br>penicillins and<br>cephalosporins<br>except the<br>cephamycins<br>(cefoxitin and<br>cefotetan) | Clavulanic acid     | Carbapenems- Resistance<br>is rare but increasing.<br>Cross-resistance to<br>ciprofloxacin, TMP/SMX,<br>gentamicin and ceftriaxone.  | Klebsiella, <i>E. coli</i> ,<br>Proteus,<br>Enterobacter,<br>Salmonella,<br>Pseudomonas,<br>and others |

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|---|--|---|---|--|
| <b><u>CTX-M</u></b><br>More than 50 different enzymes derived from <i>Kluyvera sp</i>   | Cefotaxime<br>ceftazidime  |   | Cephamycins (cefoxitin, cefotetan), carbapenems                         | Klebsiella, Salmonella, <i>E. coli</i> and other enteric bacteria    |
| <b>Carbapenase</b><br>KPC Producing<br><i>Klebsiella pneumoniae</i> )<br>3 types (KPC 1,2,3)  | 3 <sup>rd</sup> generation cephalosporins and carbapenems                                      |   | aztreonam   | Klebsiella, Salmonella   |
| <b>Metallo <math>\beta</math>-lactamases</b><br><b>OXA</b><br><b>VIM</b><br><b>IMP</b><br><b>And other types</b>  | All $\beta$ -lactam, carbapenems   | Not inhibited   | Monobactams (aztreonam).<br><br>Some azteronam resistance               | <i>Pseudomonas aeruginosa</i> ,<br>Acinetobacter<br>Enteric bacteria |
| <b>AmpC <math>\beta</math>-lactamase</b>  | Hydrolizes 3 <sup>rd</sup> generation cephalosporins and cephamycins (cefoxitin and cefotetan) | <b>Not</b> inhibited by clavulanic acid                                 | Carbapenems, but cross resistance can occur.<br>Higher MICs to cefepime | Citrobacter, Serratia, Enterobacter, <i>E. coli</i>                  |
| <b>Inhibitor Resistant <math>\beta</math>-lactamases</b><br>Over 20 known enzymes   | Ampicillin, amoxicillin, ticarcillin   | Resistant to clavulanic acid and sub-lactam but inhibited by tazobactam | tazobactam<br>piperacillin/tazobactam                                   | <i>E. coli</i> ,<br>Citrobacter,<br>Klebsiella,<br>Proteus           |
| <b>Hospital Acquired Pan-Resistance</b><br>Due to multiple resistance mechanisms acting in the same strain, especially ESBL, carbapenemases, aminoglycoside modifying enzymes, hyperproduction of AmpC, OprD2 porin loss, and upregulation of efflux pumps. |  |   | Resistant to all available antibiotics except Polymyxin- B and Colistin | Acinetobacter and <i>Pseudomonas aeruginosa</i>                      |

At TCH, a variety of Infection Control and Microbiology Laboratory efforts are utilized to reduce the incidence of hospital-associated infections with antibiotic resistant Gram-positive and Gram-negative bacteria.

- Clinical laboratory surveillance to detect infection and colonization with drug resistant organisms and guide selection of appropriate antibiotic therapy

- Tracking the increasing antibiotic resistance over time by use of antibiograms

- A multi-disciplinary process (Laboratory, Infectious Disease, Pharmacy, and Epidemiology) to foster appropriate antibiotic use

- Education of hospital staff and physicians as to the nature and extent of the problem of antibiotic resistance in our hospital

- Reduce the use of both prophylaxis and therapy with vancomycin

- Reduce the use of extended spectrum cephalosporins

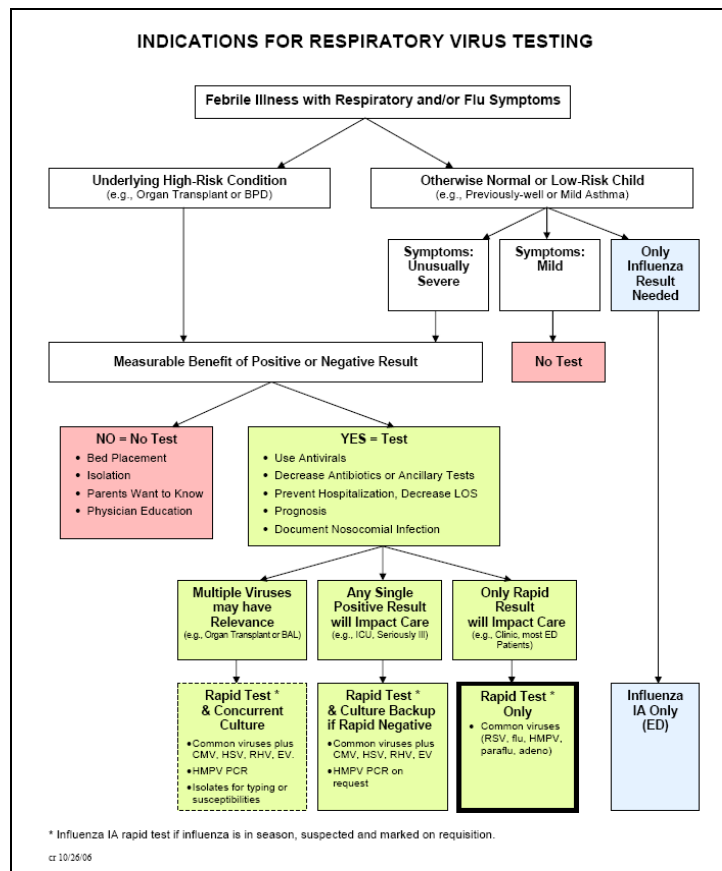
- Reduce the overuse of fluoroquinolones and carbapenems
- Standard Infection Control measures (chart flagging on re-admission, drug resistant organism (DRO) isolation precautions, environmental sanitation, patient cohorting )
- **Remember to always wash your hands with soap and water or alcohol hand wash between patient visits.**

By partnering together with the efforts above we can continue to keep antibiotics in our armamentarium and keep drug resistant bacteria from spreading within the hospital. The next time you care for a patient with a drug resistant organism (DRO), I hope you will have a better appreciation for how “smart” these organisms are, and that you will practice meticulous isolation technique to prevent DRO transmission.

**\*\*\*\*\*AMENDMENT\*\*\*\*\***

*Note: The Bronchiolitis Care Path section in the November/December issue of Contagious Comments has been revised. Please review the following corrected version.*

**Indications for Respiratory Virus Testing:**



**Therapies**

**Supportive Therapy:** Hydration, oxygenation, and upper airway suctioning are the mainstay of treatment for most babies, even those who are hospitalized with pneumonia and bronchiolitis.

**Bronchodilators:** Consider these if Severity Classification is moderate or severe. First Choice: Racemic Epinephrine. Alternate Choice: Albuterol via nebulizer.. (See Clinical Care Guidelines, <http://planetch/policies/general/pdf/538.pdf>.)

**Evaluating Clinical Status and Response to Treatment:**

1. On initial assessment, determine Severity Classification.
2. Decide on intervention based on Care Algorithm (Figure. 2).
3. Repeat severity classification to determine if intervention was helpful.

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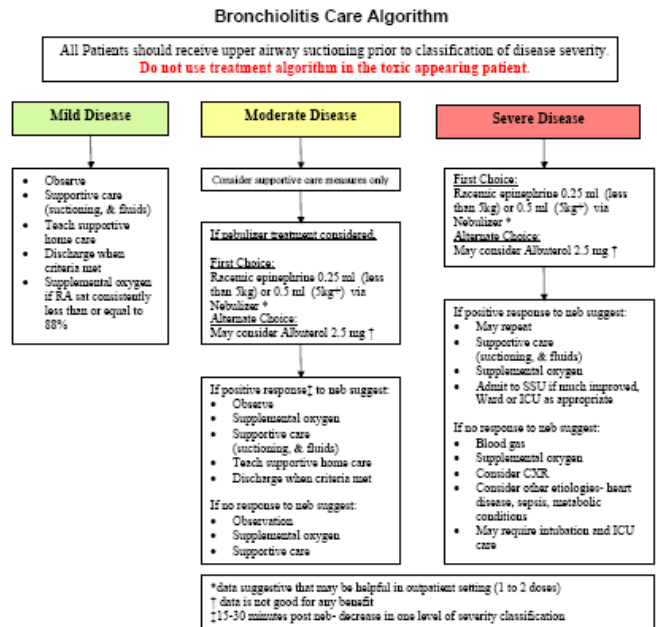
**Respiratory Severity Classification:**

|                         |   |
|-------------------------|---|
| <u>Mild Disease</u>     | <ul style="list-style-type: none"> <li>Alert, active, feeding well</li> <li>None to minimal retractions</li> <li>RR normal to mildly elevated (less than 50)</li> </ul>                               |
| <u>Moderate Disease</u> | <ul style="list-style-type: none"> <li>Alert, consoles, feeding decreased</li> <li>Minimal to moderate retractions</li> <li>RR is mildly to moderately elevated (50-70)</li> </ul>                    |
| <u>Severe Disease</u>   | <ul style="list-style-type: none"> <li>Fussy, difficult to console, poor feeding</li> <li>Moderate to severe retractions,</li> <li>RR is moderately to severely elevated (greater than 70)</li> </ul> |

**Supportive Care - Routinely Indicated:**

- Oxygen to achieve SaO<sub>2</sub> at or above 90%
- P.O. / I.V. fluids as needed
- Suction upper airway (use saline PRN):
  - Prior to feeding
  - Prior to clinical assessment
  - PRN evidence of upper airway obstruction

**Figure 2**



**Bronchiolitis Severity Classification**

|                         |   |
|-------------------------|---|
| <u>Mild Disease</u>     | <ul style="list-style-type: none"> <li>Alert, active, feeding well</li> <li>None to minimal retractions</li> <li>RR normal to mildly elevated (less than 50)</li> </ul>                               |
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