MICROBIOLOGY
UPDATES:
V.3.0  3/07

Robert C. Jerris, Ph.D., D-ABMM
Director, Clin. Micro, CHOA
Assoc. Clin. Prof.
Emory Univ. School of Medicine
CDC

Rotavirus vaccine

ABC Core Surveillance

Population Based epidemiology

Biomedical Industry

BD

Inverness

Blood Cultures

Limited Resource Labs

CDC

Resp Virus-coronavirus metapneumovirus

Rollins School Public Hlth

ICARE Project

WHO Influenza Surveillance Site

CLSI Documents

AAP Visual Red Book

Mercer School Of Pharmacy

CF Center

Support of Fellows, Interns, Residents

U of Iowa

Logitudinal assessment of Risk actors for Impact of Ps. aerug. and impact of early aggressive Rx

Emory

Multiplex PCR Viral Resp

PCR pertussis

D-Zone test MRSA

Cytokine activation post Pneumococcal resp infection and progression to systemic disease

Evolve supports Fellows, Interns, Residents

Ntl presentations

AAP Visual Red Book

U of Iowa

Ga. State Univ

WHO Influenza Surveillance Site

Yellow text; in discussion
Track a Specimen

• Receipt in Lab
• Plate on specific media
  – Incubate overnight
• Look at plates for significant organisms
  – Perform Id and Susceptibility
• Results overnight
5% Horse-Blood
Brucella Base
Chocolate Agar
Helicobacter pylori
“Splashed water colonies”
Small, clear, pinpoint colonies
*Data

• MISYS (LIS), sort parameters:
  – All Locations
  – Duplicate isolates excluded
  – All Physicians

• Revenue Statistics

• MicroScan Lab-Pro

*, limitations with each
ID and Antimicrobial Susceptibility

» Automated
» Standardized

<table>
<thead>
<tr>
<th>SCOTTISH</th>
<th>EGLESTON</th>
</tr>
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<tbody>
<tr>
<td># TESTS</td>
<td># Δ ORG*</td>
</tr>
<tr>
<td>5888</td>
<td>115</td>
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</tbody>
</table>

*, if you see an organism with which you are not familiar (*Delftia acidovorans*), call me x54543
CDC: 12 Steps to Prevent Antimicrobial Resistance

- Do NO Harm
- Get some cultures
- Treat to cure: optimal drug, dose, route
- Know when to say “no”
- Don’t treat colonization

www.cdc.gov/getsmart
## Biochemicals

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<th>G</th>
<th>P4</th>
<th>GLU</th>
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<th>URE</th>
<th>LYS</th>
<th>TDA</th>
<th>CIT</th>
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<td>H2S</td>
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<td>ESC</td>
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<td>8</td>
<td>32</td>
<td>64</td>
<td>Ed</td>
<td>SOR</td>
<td>ARA</td>
<td>MEL</td>
<td>IND</td>
<td>ORN</td>
<td>VP</td>
<td>ONPG</td>
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<td>T/E</td>
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<td>4</td>
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<td>16</td>
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## Antibiotics

25 on this panel

### Antimicrobial Agents

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<th>Antibiotic/Drug</th>
<th>Dilutions</th>
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<tr>
<td>Amikacin (Ak)</td>
<td>16 - 32</td>
</tr>
<tr>
<td>Amoxicillin (Amx)</td>
<td>8/4 - 16/8</td>
</tr>
<tr>
<td>Augmentin (Aug)</td>
<td>8/4 - 16/8</td>
</tr>
<tr>
<td>Amoxicillin/clavulanate (Aug/Amx)</td>
<td>8/4 - 16/8</td>
</tr>
<tr>
<td>Gatifloxacin (Gatifloxacin)</td>
<td>2 - 4</td>
</tr>
<tr>
<td>Gatifloxacin (Gatifloxacin)</td>
<td>2 - 4</td>
</tr>
<tr>
<td>Imipenem (Imipenem)</td>
<td>4 - 8</td>
</tr>
<tr>
<td>Levofloxacin (Levo)</td>
<td>2 - 4</td>
</tr>
<tr>
<td>Piperacillin (Piperacillin)</td>
<td>8 - 64</td>
</tr>
<tr>
<td>Piperacillin/tazobactam (PT/Pi)</td>
<td>16 - 64</td>
</tr>
<tr>
<td>Tazocin (Tazocin)</td>
<td>8 - 64</td>
</tr>
<tr>
<td>Tobramycin (Tobramycin)</td>
<td>1 - 8</td>
</tr>
<tr>
<td>Trimethoprim (Trimethoprim)</td>
<td>8</td>
</tr>
<tr>
<td>Trimethoprim/sulfamethoxazole (T/SS)</td>
<td>2/38</td>
</tr>
</tbody>
</table>

ESBL - a is a Cephoxime 4 well.
Penicillin
FDA Approval 1946

Telithromycin
FDA Approval 2004

Quinolones 1962

Clarithromycin
FDA Approval 1991

Evolution of the Antibiotic Era

Ciprolin 1964

Erythromycin 1952

Azithromycin
FDA Approval 1991

Cefdinir
FDA Approval 1997

Cefaclor
FDA Approval 1979

Penicillin
FDA Approval 1946

Cephalosporins 1940s

Ciprofloxacin
FDA Approval 1987

Levofloxacin
FDA Approval 1996

Cefdinir
FDA Approval 1997

Gatifloxacin &
Moxifloxacin
FDA Approval 1999

Tigecycline
FDA Approval 2004

Daptomycin 2003

Antimicrobial Resistance

’06 Dalbavancin

’07 Ramoplanin

’08 Doripenem, Ceftibiprole

’06 Dalbavancin

’07 Ramoplanin

’08 Doripenem, Ceftibiprole

? Feropenem

? Ceftaroline

? Iclaprim
3. Find $x$.

Here it is.
Call # 1

• I have all of these drugs on the micro report, which ones are best.....do those numbers by the drugs mean something?

1rst year resident….who had no formal microbiology in Med School
How Is Resistance Measured?

Standardized (inoculum, time to determination, etc.)

- **Minimum Inhibitory Concentration (MIC):**
  - The most refined means of measuring in vitro antibacterial activity

- **Clinical Standards and Laboratory Institute (CLSI) (old NCCLS) establishes the MIC breakpoints:**
  - Susceptible (S)
  - Intermediate (I): Intermediate
  - Resistant (R): high level of resistance
This STD recommends which antibiotics to TEST & REPORT

•Publication # M100-S17 (2007)
Determination of S, I, R For Each Antimicrobial Based On:

Achievable serum OR CSF levels

Pkd/Pd addressing levels of antimicrobial in specific anatomic sites [EMERGING]
Determination of S, I, R For Each Antimicrobic

KEY CAVEATS:

1. THE BREAKPOINT VALUES DIFFER FOR EACH AGENT..... SO ...

2. YOU CAN’T COMPARE THE NUMBERS AMONG ANTIMICROBICS AND DEDUCE THAT THE LOWEST VALUE IS THE BEST!

These values may used for determination of POTENCY and SHIFTS in resistance
Peak/MIC Ratios and 24-hr AUC/MIC
Correlation of serum pharmacokinetics with MIC (susceptibility) of an organism

Peak/MIC ratio and AUC/MIC is correlated with outcome of infection, the magnitude required for success is known as the PD breakpoint and assesses POTENCY
Patterns of antimicrobial activity

- Time-dependent killing and minimal to moderate persistent effects ➔ Time above MIC (T>MIC)
  - Beta-lactams
  - Macrolides
- Time-dependent killing and prolonged persistent effects ➔ AUC/MIC ratio
  - Azithromycin
- Concentration-dependent killing and prolonged persistent effects ➔ AUC/MIC or Peak/MIC ratio
  - Quinolones (AUC/MIC),
  - Aminoglycosides (P:MIC)
Monitoring: Low Level Resistance and Trends

Shift slightly from WT; MIC Creep (subtle but significant), **dilutions must be low enough to detect
Genotype vs Phenotype

- A Genotype refers to a resistance mechanism encoded by a specific gene
  - *meca* is the genotype for methicillin resistant staphylococci; if + = ox R, if - = ox S
  - The Phenotype depicts how it is expressed and observed in testing
    - *meca* is observed as resistance to the beta-lactam antibiotics
- It is often possible to infer the genotype by observing the phenotype in testing: inducible RESISTANCE in GNRs
4c) Expand

\[(a+b)^n = (a + b)^n\]

\[= (a + b)^n\]

\[= (a + b)^n\]

\[= (a + b)^n\]

\[\text{x x}\]

\[\text{etc.}\]
Call # 2

• I didn’t get a culture, what drug should I use for a non-complicated UTI?

Evidence based data
Step 6. Use local data
Know your antibiogram

CDC’s Campaign to Prevent Antimicrobial Resistance

- Prevent infection
- Diagnose and treat infection
- Prevent transmission
- Use antimicrobials wisely
05- Urine

-SRH
- E.coli (835)
- Kl. pneumoniae (89)
- Proteus mirabilis (58)
- Enterococcus sp (99)
- Ps. aeruginosa (33)

- CMV (112)
<table>
<thead>
<tr>
<th><strong>Organism</strong></th>
<th><strong>Antibiotic</strong></th>
<th><strong>Susceptibility</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;100,000 COL/ML ESCHERICHIA COLI (MIC)</td>
<td>AMIKACIN</td>
<td>8 BLOOD SUSCEPTIBLE</td>
</tr>
<tr>
<td></td>
<td></td>
<td>URINE SUSCEPTIBLE</td>
</tr>
<tr>
<td></td>
<td>AMOX/CLAVULANATE</td>
<td>&lt;=8/4 BLOOD SUSCEPTIBLE</td>
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<tr>
<td></td>
<td></td>
<td>URINE SUSCEPTIBLE</td>
</tr>
<tr>
<td></td>
<td>AMPICILLIN</td>
<td>&gt;128 BLOOD RESISTANT</td>
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<td></td>
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<td>URINE RESISTANT</td>
</tr>
<tr>
<td></td>
<td>CEFAZOLIN</td>
<td>&lt;=8 BLOOD SUSCEPTIBLE</td>
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<tr>
<td></td>
<td></td>
<td>URINE SUSCEPTIBLE</td>
</tr>
<tr>
<td></td>
<td>CEFTRIAXONE</td>
<td>&lt;=4 BLOOD SUSCEPTIBLE</td>
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<tr>
<td></td>
<td></td>
<td>URINE SUSCEPTIBLE</td>
</tr>
<tr>
<td></td>
<td>CEFUROXIME</td>
<td>4 BLOOD SUSCEPTIBLE</td>
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<td></td>
<td></td>
<td>URINE SUSCEPTIBLE</td>
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<tr>
<td></td>
<td>CEPHALOTHIN</td>
<td>32 BLOOD RESISTANT</td>
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<tr>
<td></td>
<td></td>
<td>URINE RESISTANT</td>
</tr>
<tr>
<td></td>
<td>CIPROFLOXACIN</td>
<td>&lt;=1 BLOOD SUSCEPTIBLE</td>
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<tr>
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<td></td>
<td>URINE SUSCEPTIBLE</td>
</tr>
<tr>
<td></td>
<td>GENTAMICIN</td>
<td>&lt;=1 BLOOD SUSCEPTIBLE</td>
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<tr>
<td></td>
<td></td>
<td>URINE SUSCEPTIBLE</td>
</tr>
<tr>
<td></td>
<td>NITROFURANTOIN</td>
<td>&lt;=32 URINE SUSCEPTIBLE</td>
</tr>
<tr>
<td></td>
<td>SULF/TRIMETHOPRIM</td>
<td>&gt;2/38 BLOOD RESISTANT</td>
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<td></td>
<td></td>
<td>URINE RESISTANT</td>
</tr>
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</table>
# Gram-Negative Surveillance

<table>
<thead>
<tr>
<th>Organism</th>
<th>n</th>
<th>LVX</th>
<th>CIP</th>
<th>AMP</th>
<th>CRO</th>
<th>PTZ</th>
<th>GEN</th>
<th>SXT</th>
</tr>
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<tbody>
<tr>
<td>E. coli</td>
<td>171</td>
<td>89.7</td>
<td>89.6</td>
<td>60.6</td>
<td>97.9</td>
<td>96.7</td>
<td>94.5</td>
<td>81.0</td>
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<tr>
<td>K. neumoniae</td>
<td>992</td>
<td>94.3</td>
<td>93.2</td>
<td>2.0</td>
<td>95.3</td>
<td>94.4</td>
<td>96.1</td>
<td>88.9</td>
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<tr>
<td>E. cloacae</td>
<td>589</td>
<td>92.5</td>
<td>91.2</td>
<td>10.0</td>
<td>76.4</td>
<td>79.6</td>
<td>93.7</td>
<td>89.6</td>
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<tr>
<td>P. mirabilis</td>
<td>963</td>
<td>84.3</td>
<td>78.1</td>
<td>78.1</td>
<td>99.6</td>
<td>100</td>
<td>88.3</td>
<td>75.0</td>
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<tr>
<td>S. marcescens</td>
<td>320</td>
<td>93.4</td>
<td>88.8</td>
<td>8.4</td>
<td>95.9</td>
<td>96.6</td>
<td>95.6</td>
<td>96.9</td>
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<tr>
<td>S. maltophilia</td>
<td>299</td>
<td>77.3</td>
<td>30.1</td>
<td>-</td>
<td>0.0</td>
<td>14.7</td>
<td>17.4</td>
<td>92.0</td>
</tr>
<tr>
<td>P. aeruginosa</td>
<td>166</td>
<td>63.3</td>
<td>66.8</td>
<td>-</td>
<td>12.2</td>
<td>84.4</td>
<td>78.2</td>
<td>5.0</td>
</tr>
</tbody>
</table>

In vitro activity does not necessarily correlate with clinical results. Data on file, Ortho-McNeil. Yellow numbers show pathogens with levo 4-6% higher susceptibility than cipro.

LVX = levofloxacin; CIP = ciprofloxacin; AMP = ampicillin; CRO = ceftriaxone; PTZ = piperacillin/tazobactam; GEN = gentamicin; SXT = trimethoprim/sulfamethoxazole
## UTI 2005 Profiles

<table>
<thead>
<tr>
<th></th>
<th>% Susceptible</th>
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<th>PED</th>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N</td>
<td></td>
<td>650</td>
<td>1070</td>
</tr>
<tr>
<td>AM</td>
<td></td>
<td>53</td>
<td>47</td>
</tr>
<tr>
<td>SXT</td>
<td></td>
<td>81</td>
<td>69</td>
</tr>
<tr>
<td>E. coli LEVO</td>
<td></td>
<td>77</td>
<td>100</td>
</tr>
<tr>
<td>NITROFURAN</td>
<td></td>
<td>97</td>
<td></td>
</tr>
<tr>
<td>N</td>
<td></td>
<td>190</td>
<td>174</td>
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<tr>
<td>AM</td>
<td></td>
<td>90</td>
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<tr>
<td>SXT</td>
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<td>84</td>
<td>92</td>
</tr>
<tr>
<td>P. mirabilis LEV</td>
<td></td>
<td>80</td>
<td>98</td>
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<tr>
<td>NITR= NOT ACTIVE</td>
<td></td>
<td></td>
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<tr>
<td>N</td>
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<td>157</td>
<td>142</td>
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<tr>
<td>AM</td>
<td></td>
<td>0</td>
<td>0</td>
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<td>SXT</td>
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<td>77</td>
<td>89</td>
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<tr>
<td>K. pneumoniae LEV</td>
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<td>98</td>
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<tr>
<td>NITROFURAN</td>
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# Trend Ecoli % S CHOASR

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</tr>
<tr>
<td>SXT</td>
<td>95</td>
<td>84</td>
<td>82</td>
<td>78</td>
<td>84</td>
<td>81</td>
<td>82</td>
<td>85</td>
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<td>79</td>
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<td>76</td>
<td>78</td>
<td>76</td>
<td>76</td>
<td>73</td>
</tr>
</tbody>
</table>
Love? vs. Spanking……

Do not get upset; Rather evaluate the situation from a RATIONAL PERSPECTIVE

So, you behaved inappropriately and I can’t handle it. Let’s both calm down by taking a little DRIVE. It always seems to settle you; now I think it will settle me too!
Call #3

• We’re reviewing for productivity, do you have any data that we can use for a meeting in the next 30 minutes?

From Administration (bean counters anonymous)
## Year to Date Summary Raw Data 2005

<table>
<thead>
<tr>
<th>Specimen</th>
<th>SRH</th>
<th>ECH</th>
<th>Grand T</th>
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<tbody>
<tr>
<td></td>
<td>IP</td>
<td>OP</td>
<td>T</td>
</tr>
<tr>
<td>Blood</td>
<td>8863</td>
<td>5320</td>
<td>14183</td>
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<td>Urine</td>
<td>3425</td>
<td>9576</td>
<td>13001</td>
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<tr>
<td>Wounds</td>
<td>864</td>
<td>708</td>
<td>1572</td>
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<tr>
<td>CSF</td>
<td>1581</td>
<td>567</td>
<td>2148</td>
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<tr>
<td>Stool</td>
<td>652</td>
<td>842</td>
<td>1494</td>
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<tr>
<td>Respiratory</td>
<td>793</td>
<td>142</td>
<td>935</td>
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<tr>
<td>Body Fluids (X CSF)</td>
<td>268</td>
<td>30</td>
<td>298</td>
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No adjustments for patient visits/days, etc.
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<th>Grand T</th>
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<td>IP</td>
<td>OP</td>
<td>T</td>
<td>IP</td>
<td>OP</td>
</tr>
<tr>
<td>Viral Culture</td>
<td>656</td>
<td>162</td>
<td>818</td>
<td>805</td>
<td>291</td>
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<tr>
<td>Resp Viral Panel FA</td>
<td>877</td>
<td>122</td>
<td>999</td>
<td>1120</td>
<td>193</td>
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<tr>
<td>Rapid RSV</td>
<td>883</td>
<td>1081</td>
<td>1964</td>
<td>428</td>
<td>386</td>
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<tr>
<td>Rapid Influenza</td>
<td>274</td>
<td>899</td>
<td>1173</td>
<td>192</td>
<td>386</td>
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<td>Rotavirus</td>
<td>791</td>
<td>613</td>
<td>1404</td>
<td>622</td>
<td>139</td>
</tr>
<tr>
<td>C.difficile</td>
<td>937</td>
<td>319</td>
<td>1256</td>
<td>806</td>
<td>122</td>
</tr>
<tr>
<td>Strep screen</td>
<td>352</td>
<td>5443</td>
<td>5795</td>
<td>247</td>
<td>3082</td>
</tr>
<tr>
<td>[Valid for Throats ONLY]</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>B. pertussis</td>
<td>126</td>
<td>120</td>
<td>246</td>
<td>76</td>
<td>70</td>
</tr>
<tr>
<td>AFB</td>
<td>144</td>
<td>90</td>
<td>234</td>
<td>349</td>
<td>124</td>
</tr>
</tbody>
</table>

No adjustments for patient visits/days, etc.
ASM Staffing Document 2006

- 7,011 CPT codes per FTE/Year
- Adjusted for Complexity of lab
  - Mycology
  - Mycobacteriology
  - Virology
  - Molecular

We can now compare apples to apples in micro
Call # 5

- I just collected a blood culture about an hour ago, is it positive?

It takes 9 months to have a baby
BacT/Alert Continuous Monitor Blood Culture System

Detection of Positives:
@ 80% day 1
90% day 2, 95% day 3

Monitors every 10 minutes

Wafer with pH sensor

Photodiode, Amplification Colorimeter
BLOOD CULTURES

• RATE OF POSITIVITY:
  – SRH = 13.5 %
  – ECH = 13.9 %

• AVG CONTAM RATE:
  – SRH = 2.8 %
  – ECH = 2.6 %
05-BC Orgs

• SRH
  – Staphylococcus epidermidis (522)
  – Yeast (Candida sp.) (164)
  – Enterococcus faecalis (105)
  – SPICE & M (108)
  – S.aureus (108)
  – MRSA (40)
  – E.coli (45)
  – Klebsiella sp. (64)
  – S.pneumo (32), Acinetobacter sp. (33)
  – H. influenzae (2)

Source: Misys Incidence query
Slime Layer with UNKNOWN bacteria

Role of 16s rRNA
Test Procedure

Nasal Swab

<2 hours Total Process Time

SmartCycler Detection and Results (60 min)

Sample Buffer

Lysis Tube

SmartCycler Tube

DNA
Molecular Target

- SCCmec types I - IV detected:
  - Community acquired
  - Hospital acquired
- Detects junction between orfX (*S. aureus*) and SCCmec cassette (carries the resistance determinants)
  - Does not get false-positives from coagulase negative Staphylococci
Studies have demonstrated that large-volume culture methods for sterile body fluids other than blood increase recovery compared to traditional plated-medium methods. BacT/Alert is a fully automated blood culture system for detecting bacteremia and fungemia. In this study, we compared culture in BacT/Alert standard aerobic and anaerobic bottles, BacT/Alert FAN aerobic and FAN anaerobic bottles, and culture on routine media for six specimen types, i.e., continuous ambulatory peritoneal dialysate (CAPD), peritoneal, amniotic, pericardial, synovial, and pleural fluids. Specimen volumes were divided equally among the three arms of the study. A total of 1,157 specimens were tested, with 227 significant isolates recovered from 193 specimens. Recovery by method was as follows: standard bottles, 186 of 227 (82%); FAN bottles, 217 of 227 (96%); and routine culture, 184 of 227 (81%). The FAN bottles recovered significantly more gram-positive cocci \((P < 0.001)\), \textit{Staphylococcus aureus} \((P = 0.003)\), coagulase-negative staphylococci \((P = 0.008)\), gram-negative bacilli \((P < 0.001)\), \textit{Enterobacteriaceae} \((P = 0.005)\), and total organisms \((P < 0.001)\) than the routine culture. There were no significant differences in recovery between the standard bottles and the routine culture. The FAN aerobic bottle recovered significantly more gram-positive cocci \((P < 0.001)\), \textit{S. aureus} isolates \((P < 0.001)\), coagulase-negative staphylococci \((P = 0.003)\), and total organisms \((P < 0.001)\) than the standard aerobic bottle, while the FAN anaerobic bottle recovered significantly more gram-positive cocci \((P < 0.001)\), \textit{S. aureus} isolates \((P < 0.001)\), \textit{Enterobacteriaceae} \((P = 0.03)\), and total organisms \((P < 0.001)\) than the standard anaerobic bottle. For specific specimen types, significantly more isolates were recovered from the FAN bottles compared to the routine culture for synovial \((P < 0.001)\) and CAPD \((P = 0.004)\) fluids. Overall, the FAN bottles were superior in performance to both the standard bottles and the routine culture for detection of microorganisms from the types of sterile body fluids included in this study.
**Blood Products and Stem Cell Screening**

- **BacT/Alert-FDA selection-allows institution to set policy**
  - **Platelets** (Dr. Cassandra Josephson, AssocDir,.BB-CHOA)
    - Allow bag to inc for 24h
    - Place 4-10 ml into BPA and BPN
    - Hold 5 days (shelf life of a platelet)

- **Stem Cells** (Diana Worthington-White-Mgr. Cellular Therapies Lab, Blood /Bone Marrow Transplant-CHOA)
  - Place 4-10ml into **iAST** (Industry Aerobic bottle, for processed or aseptically prepared products)
  - Place 4-10 ml into **iNST** (Industry Anaerobic bottle)
  - Hold 14 days
Call # 6

- Patient referral form outside physician.....
- My child has had a recurrent Strep throat and we don’t know what to do?

Am I paid to answer these kinds of questions.....?
Pharyngitis/Tonsillitis Overview

• Every day a family physician can expect to see at least one patient with a sore throat
  – One of the top 20 reasons for an office visit
  – Time burden on physician and office staff time
• Since the 1980s, the severity of group A streptococcal infection has changed in the United States
• Common therapies used
  – Penicillin or amoxicillin
  – Erythromycin for penicillin allergy
  – Cephalosporins

Etiology of Pharyngitis in Children

- **GABHS** 28%-40%
- Neisseria gonorrhoeae 0%-.01%
- Arcanobacterium haemolyticum 0%-.05%
- Chlamydia pneumoniae 0%-3%
- Mycoplasma pneumoniae 0%-3%
- Neisseria gonorrhoeae 0%-.01%
- Bacterial 30%-40%
- Idiopathic 20%-55%
- Viral 15%-40%

GABHS=group A β-hemolytic streptococci.
Improving Diagnosis

Streptococci Detection Methods

• Rapid antigen detection test (RADT) detects the presence of a carbohydrate antigen characteristic of group A streptococci

• Clinical application
  – Specificity: >95%\(^2,3\)
  – Sensitivity: 80% to 90%\(^1-3\)

• Positive result on RADT adequately confirms diagnosis\(^1\)

• Negative result on RADT in children/adolescents requires a throat culture for confirmation\(^1\)

Bacteriologic Failure Rates in GABHS Pharyngitis

Red Book: Pen 1rst

Failure Rate (%)

- Benzathine penicillin G: 6 to 25
- Penicillin G: 10 to 30
- Penicillin VK: 10 to 30
- Ampicillin/Amoxicillin: 10 to 20
- Erythromycin: 5 to 15
- Clindamycin: 5 to 20
- Cephalosporins: 2 to 10

GABHS=group A β-hemolytic streptococci.
Adapted from Pichichero ME. Am Fam Physician. 1990;42:1567-1576.
Possible Explanations for Treatment Failures in GABHS Pharyngitis

• Poor patient compliance with the antibiotic regimen\(^1\)
• Recurrent exposures (family/peers)\(^1\)
• Copathogenicity (\(\beta\)-lactamase–producing pharyngeal flora “protects” GABHS against penicillins)\(^1,2\)
• Coaggregation (\textit{M catarrhalis} adheres to throat cells and GABHS adheres to \textit{M catarrhalis})\(^3\)

\(\bullet\) Tonsillitis as a “slime layer model”- Aerobes and anaerobes

β-Lactamase Copathogenicity Description

Coaggregation Description

Advances in Pharyngitis Management
Potential Reasons for GABHS Pharyngitis Treatment Failures

- Early in the course of disease, antibiotic therapy suppresses immune response to infection
- Eradication of protective nonpathogenic pharyngeal flora
  - $\alpha$-hemolytic streptococci and their byproducts (bacteriocins)
- Penicillin tolerance
  - Inhibits but does not eradicate the pathogens
- GABHS carrier state; predominates in pediatric age-group
  - Penicillin cannot eradicate the carrier state
- HOST FACTORS-from toothbrushes to pets

Call # 7

• In a panicked voice; physician from his office…….
  – I have seen so much respiratory disease in my patients, how will I know if it's bird flu?

Take a good history, like you were taught in med school
Influenza A viruses periodically cause worldwide epidemics, or pandemics, with high rates of illness and death. Unlike other public welfare emergencies, an influenza pandemic will impact on multiple communities across the United States and require swift and coordinated action and cooperation by all levels of government. Advanced planning for a large scale and widespread health emergency is required to optimize health care delivery during a pandemic. In addition, prevention and preparedness activities facilitate the response and recovery during and after an influenza pandemic.

www.dhhs.gov/nvpo/pandemics
# Human Respiratory Viruses

## DNA Viruses
- **Adenoviridae**
  - adenovirus 1-49

## RNA Viruses
- **Orthomyxoviridae**
  - influenza viruses A, B, C
- **Paramyxoviridae**
  - respiratory syncytial viruses A, B
  - parainfluenza viruses 1 - 4
  - human metapneumovirus
- **Picornaviridae**
  - rhinovirus 1-100
  - enterovirus: echovirus 1 - 33; coxsackievirus A1-A24, B1-6
  - parechovirus 1, 2, 3
- **Coronaviridae**
  - coronavirus: 229E, OC43, SARS-CoV
  - NL63/NH, HKU1
Epidemiologic pattern of upper respiratory tract infection (URI) with human metapneumovirus and other virus infections. Data are combined from 20 years of surveillance in the Vanderbilt Vaccine Clinic.
Influenza A virus resistance to amantadine and rimantadine can emerge rapidly during treatment. On the basis of antiviral testing results conducted at CDC and in Canada indicating high levels of resistance, CDC and ACIP recommend that neither amantadine nor rimantadine be used for the treatment or chemoprophylaxis of influenza A in the United States until susceptibility to these antiviral medications has been re-established among circulating influenza A viruses. Oseltamivir or zanamivir can be prescribed if antiviral treatment of influenza is indicated. Oseltamivir is approved for treatment of persons aged \( \geq 1 \) year, and zanamivir is approved for treatment of persons aged \( \geq 7 \) years. Oseltamivir and zanamivir can be used for chemoprophylaxis of influenza; oseltamivir is licensed for use in persons aged \( \geq 1 \) year, and zanamivir is licensed for use in persons aged \( \geq 5 \) years.
Influenza Activity Peds

Starting 11/20/2006
Update: Resp Viruses
(Note: Virology 24/7)

• Three key essentials to diagnosis
  – Appropriate specimen
    • NP Swab > NP aspirate
  – Viral titer (highest early in disease)
  – Assay quality: sensitivity, specificity, PPV, NPV
    • Culture: R/Mix cells (mink lung/A549)
      – Read at 24h, final at 48h
    • DFA - 10:45 am cutoff
    • OIA - on demand
OIA (Rapid Influenza Test)

- NP Swab: Sensi 83.3%; Speci 76.2%
- NP Aspirate: Sensi 83.4%; Speci 69.4%

- ISSUE: Predictive Values + and –
  • Depend on prevalence
  - Bayesian Analysis:
    www.intmed.mcw.edu/clincalc/bayes.html
To internet site for analysis

http://www.intmed.mcw.edu/clincalc/bayes.html
## 05 - Virus Culture

*CUCM,CUVI,CUVR,*

<table>
<thead>
<tr>
<th>Virus</th>
<th>Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>HSV 1</td>
<td>10</td>
</tr>
<tr>
<td>Adeno</td>
<td>42</td>
</tr>
<tr>
<td>RSV</td>
<td>21</td>
</tr>
<tr>
<td>Influenza A</td>
<td>22</td>
</tr>
<tr>
<td>CMV</td>
<td>13</td>
</tr>
<tr>
<td>Influenza B</td>
<td>14</td>
</tr>
<tr>
<td>Adeno</td>
<td>13</td>
</tr>
<tr>
<td>Para 3</td>
<td>13</td>
</tr>
<tr>
<td>Para 1</td>
<td>9</td>
</tr>
<tr>
<td>Entero</td>
<td>11</td>
</tr>
<tr>
<td>HSV 2</td>
<td>4</td>
</tr>
</tbody>
</table>

Due to performance issues with the rapid tests, DFA and culture are recommended for INPATIENTS.

* ;CUVI-held 14d, CUCM-shell report at 48h,held 14d, CUHS-held 5 d,CUR-report at 48h
### Think Avian Flu!

**Protect yourself and your community**

**Prevent spread of avian influenza**

<table>
<thead>
<tr>
<th>Screen hospitalized/ambulatory patients</th>
<th>Screen hospitalized patients with CXR-confirmed pneumonia/ARDS or unexplained severe respiratory illness</th>
</tr>
</thead>
<tbody>
<tr>
<td>with T &gt;38°C (&gt;100.4°F) AND cough or sore throat or shortness of breath</td>
<td></td>
</tr>
</tbody>
</table>

**FOR**

Travel to an affected country* ≤10 days before symptom onset AND contact with potentially infected poultry** or suspect or confirmed human case of H5N1 influenza

**FOR**

Travel to an affected country* ≤10 days before symptom onset AND contact with potentially infected poultry** or suspect or confirmed human case of H5N1 influenza

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* As of February 28, 2006, H5N1-affected countries/territories include: Austria, Azerbaijan, Bosnia and Herzegovina, Bulgaria, Cambodia, China, Croatia, France, Germany, Greece, Hong Kong, Hungary, India, Indonesia, Iran, Iraq, Italy, Kazakhstan, Laos, Malaysia, Niger, Nigeria, Mongolia, Romania, Russia, Slovak Republic, Slovenia, Switzerland, Thailand, Turkey, Ukraine, and Vietnam. For an updated listing of affected countries, see the OIE website at [http://www.oie.int/eng/en_index.htm](http://www.oie.int/eng/en_index.htm), the WHO website at [http://www.who.int/en/](http://www.who.int/en/), or the CDC website at [http://www.cdc.gov/flu/avian/](http://www.cdc.gov/flu/avian/).

**Poultry exposure**: One of the following: direct contact with domestic poultry (e.g., touching sick or dead chickens or ducks or well-appearing ducks); consumption of uncooked poultry or poultry products; direct contact with surfaces contaminated with poultry feces. It does NOT include exposure to cooked or processed poultry.

---

- ✔️ Report patients with above exposure history immediately to **infection control** and **public health** as potential *Avian Influenza* patients.
- ✔️ Testing should include rapid testing for influenza A, and PCR of nasopharyngeal specimen for influenza at the Georgia Public Health Lab.
- ✔️ Viral culture should **NOT** be performed because of danger to lab workers and agriculture.
- ✔️ Acute- (within 1 week of illness onset) and convalescent-phase (after 3 weeks of illness onset) Serum sample should be collected and stored in case testing for antibody to the avian influenza virus should be needed.
- ✔️ **Infection control measures** for potential Avian Influenza patients:
  - Standard Precautions: Careful hand hygiene
  - Contact & Droplet Precautions: Gloves, gown, eye protection ≤3 feet from the patient
  - Airborne Precautions: Patient in negative pressure, airborne isolation room; use a fit-tested NIOSH-approved N-95 respirator in room.

---

For your 24-hour public health needs, call **1-866-PUB-HLTH** (782-4584)
<table>
<thead>
<tr>
<th>Avian influenza</th>
<th>Number of human cases of Avian Influenza A (H5N1) since January 1, 2006:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total: 126 cases (88 deaths) (10 cases, 8 deaths in 2007)</td>
</tr>
<tr>
<td></td>
<td>2 (2 deaths) in Cambodia</td>
</tr>
<tr>
<td></td>
<td>62 (51 deaths) in Indonesia (6 cases, 5 deaths in 2007)</td>
</tr>
<tr>
<td></td>
<td>12 (8 deaths) in China</td>
</tr>
<tr>
<td></td>
<td>12 (4 deaths) in Turkey</td>
</tr>
<tr>
<td></td>
<td>3 (2 deaths) in Iraq</td>
</tr>
<tr>
<td></td>
<td>8 (5 deaths) in Azerbaijan</td>
</tr>
<tr>
<td></td>
<td>20 (12 deaths) in Egypt (3 case, 2 death in 2007)</td>
</tr>
<tr>
<td></td>
<td>1 (0 deaths) in Djibouti</td>
</tr>
<tr>
<td></td>
<td>3 (3 deaths) in Thailand</td>
</tr>
<tr>
<td></td>
<td>1 (1 death) in Nigeria (1 case, 1 death in 2007)</td>
</tr>
<tr>
<td></td>
<td>Continued positive reports among poultry and wild birds in parts of Asia, the Middle East, Europe (Great Britain), and Africa</td>
</tr>
<tr>
<td></td>
<td>2/16/2007</td>
</tr>
</tbody>
</table>
Call #8

I’ve got these funny spider bite-like red spots all over me.....
What could it be?
Nodular lymphangitis or necrotizing fasciitis
**Swabs don’t do the job...**

- Out of every 100 bacteria absorbed on a swab, only 3 make it to culture.
- Anaerobes on swabs die upon exposure to air, but survive in tissues and fluids.
- Swabs hold only 150 microlitres of fluid.

**FOR QUALITY RESULTS, SEND TISSUE, FLUIDS, OR ASPIRATES**

(SAME SPECIMEN FOR PATHOLOGY BUT NOT IN FORMALIN)
Key Findings  Baba T. et al. 2002. Lancet. 359:1819

- Newly described genetic element: mec a gene on a mobile element (SCC-mec)
- “Only mec a “ gene, no additional resistance determinants
  - (to survive sporadic exposure to limited numbers of antibiotics in the environment: amox and underdosed ceph's as with non-compliance)
- Homology only 95% with HA-MRSA genome
  (whereas homology is 99.7% between HA-MRSA strains)
- Genomic/pathogenicity islands with key virulence factors: horizontal transfer  (18 toxins in MW2 conferring “fitness”), PVL Panton Valentine Leucocidin –key marker
- Growth rate: doubling time 23.5m vs 34.8 and 46.8m for HA-MRSA  (survival fitness)
<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>% Susceptible</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clindamycin*</td>
<td>92</td>
</tr>
<tr>
<td>Trim/Sulfa</td>
<td>100</td>
</tr>
<tr>
<td>Tetracycline</td>
<td>94</td>
</tr>
<tr>
<td>Linezolid*</td>
<td>100</td>
</tr>
</tbody>
</table>

*, D-zone test +, Avg: 2.7%
*, (2006-Resistant strains to Pfizer for analysis)
Public Health Dispatch: Outbreaks of Community-Associated Methicillin-Resistant *Staphylococcus aureus* Skin Infections -- Los Angeles County, California, 2002--2003

**Prevention Strategies in Health -Care setting:**

- Standard precautions
- Emphasis on hand hygiene between treating patients
- Clean surfaces of examination rooms with commercial disinfectant or diluted bleach (1 tablespoon bleach in 1 quart water)
- Careful disposal of dressings and other material that come into contact with pus, nasal discharge, blood and urine
Ironically, I had no calls about cruise ships, raspberries, bean sprouts, green onions, lettuce, peanut butter, or chicken strips.

**Poultry Cooking Temperatures:** FSIS is in the process of updating all the pages on its Web site to reflect new cooking recommendations for poultry. For safety, when cooking poultry, use a food thermometer to check the internal temperature. Poultry should reach a safe minimum internal temperature of 165 °F throughout the product.


(Food Safety and Inspection Service, FDA)
2. A 3-kg object is released from rest at a height of 5m on a curved frictionless ramp. At the foot of the ramp is a spring of force constant $k = 100 \text{ N/m}$. The object slides down the ramp and into the spring, compressing it a distance $x$ before coming to rest.

(a) Find $x$.

(b) Does the object continue to move after it comes to rest? If yes, how high will it go up the slope before it comes to rest?

\[ U = 3(9.81)(5) = 147.15 \]
\[ U_s = \frac{1}{2}(100)x^2 = 50x^2 \]

\[ \text{NO, there is an elephant in the way.} \]