Drug resistance and choice of antibiotics

Paul Bonnar MD, FRCPC

Jan 10, 2018

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http://www.cdha.nshealth.ca/nsha-antimicrobial-stewardship
No disclosures

• Off-label antibiotic recommendations will be declared

• This speaker has been asked to disclose to the audience any involvement with industry or other organizations that may potentially influence the presentation of any education material

• Receiving evaluations is critical to the accreditation process. After the program, please provide feedback at https://surveys.dal.ca/opinio/s?s=40278
Objectives

• Utilize an antimicrobial stewardship approach for prescribing antibiotics.

• Appreciate the risks and potential harms of antibiotic use.

• Review the treatment recommendations for common infectious syndromes.
Outline

• Intro to AMS & why we care about AMR

• Antibiotic use in the community

• Syndromes
Approach to infections

Is there an infection?

Likely pathogens?
- Is it bacterial?
- Resistance issues?

Urgency to treat?
Non-pharm options?

Assessment plan
- How long should I treat?
- Goal of therapy
What is Antimicrobial Stewardship?

Coordinated interventions designed to improve and measure the appropriate use of antimicrobials

- Right drug
- Right dose
- Right duration
- Right route
TEAM MEMBERS

Andrea Kent
Paul Bonnar
Ian Davis
TEAM MEMBERS

Kim Abbass

Jason Reynolds

Stephen Smith

Valerie Murphy
VISION

Safe and effective use of antimicrobial agents in patients cared for in NSHA
# Inpatient Antimicrobial Use

## Canadian Inpatients Receiving Abx

<table>
<thead>
<tr>
<th>Year</th>
<th>Proportion (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2002</td>
<td>36.5%</td>
</tr>
<tr>
<td>2009</td>
<td>40.1%</td>
</tr>
</tbody>
</table>

## Piperacillin-tazobactam as Proportion of Penicillin Class

<table>
<thead>
<tr>
<th>Year</th>
<th>Proportion (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2002</td>
<td>20%</td>
</tr>
<tr>
<td>2009</td>
<td>43%</td>
</tr>
</tbody>
</table>

- **Vancomycin**
- **Carbapenem**
- **Antifungal Agents**

A Point Prevalence Survey of Antimicrobial Use at Hospitals in Nova Scotia

Emily Black, Heather Neville, Mia Losier, Megan Harrison, Kim Abbass, Kathy Slayter, Lynn Johnston, and Ingrid Sketris

<table>
<thead>
<tr>
<th>Antimicrobial</th>
<th>Use Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ampicillin</td>
<td>2.0%</td>
</tr>
<tr>
<td>Amoxclav</td>
<td>2.0%</td>
</tr>
<tr>
<td>Moxifloxacin</td>
<td>2.1%</td>
</tr>
<tr>
<td>Imipenem</td>
<td>2.6%</td>
</tr>
<tr>
<td>Levofloxacin</td>
<td>3.0%</td>
</tr>
<tr>
<td>Fluconazole</td>
<td>3.3%</td>
</tr>
<tr>
<td>SMX/TMP</td>
<td>3.6%</td>
</tr>
<tr>
<td>Cephalexin</td>
<td>4.4%</td>
</tr>
<tr>
<td>Vanco</td>
<td>5.5%</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>7.4%</td>
</tr>
<tr>
<td>Piptazo</td>
<td>8.0%</td>
</tr>
<tr>
<td>Ceftriaxone</td>
<td>8.9%</td>
</tr>
<tr>
<td>Cefazolin</td>
<td>10.9%</td>
</tr>
<tr>
<td>Metronidazole</td>
<td>11.1%</td>
</tr>
</tbody>
</table>

30% NS inpatients on antimicrobials

47% ICU

~2/3 IV

60% NO documented duration of therapy

<table>
<thead>
<tr>
<th></th>
<th>Patients on abx</th>
<th>Abx in the IV PO Conversion Policy given IV</th>
<th>Orders with an indication</th>
<th>Orders with duration or reassessment date</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>TOTAL</strong></td>
<td>34%</td>
<td>41%</td>
<td>77%</td>
<td>44%</td>
</tr>
<tr>
<td><strong>Central</strong></td>
<td>34%</td>
<td>30%</td>
<td>83%</td>
<td>34%</td>
</tr>
<tr>
<td><strong>Western</strong></td>
<td>29%</td>
<td>30%</td>
<td>87%</td>
<td>53%</td>
</tr>
<tr>
<td><strong>Northern</strong></td>
<td>37%</td>
<td>44%</td>
<td>79%</td>
<td>47%</td>
</tr>
<tr>
<td><strong>Eastern</strong></td>
<td>42%</td>
<td>55%</td>
<td>58%</td>
<td>39%</td>
</tr>
</tbody>
</table>

Sept 2017
Antibiotic use in the community 2014

- 23 million Rx dispensed
  - 93% dispensed from community pharmacies
  - $786M
  - 65% Canadians received abx
- Most often for respiratory tract infections

Canadian Antimicrobial Resistance Surveillance System Report 2016
Ambulatory care antibiotic use in US

Overall

- 506 antibiotic prescriptions/1000 pop/year
- >30% are unnecessary
  - 50% if include selection, dosing, duration
- Top 3: sinusitis, otitis media, pharyngitis

Acute respiratory conditions

- 221 antibiotic prescriptions/1000 pop annually
- 50% unnecessary

Fleming-Dutra. JAMA. 2016;315(17):1864-1873
CDC
27% patients received antibiotics

n= 1488

1 in 5 had antibiotic-associated ADE

Tamma. JAMA Intern Med. 2017 Jun 12
1 in 5 had antibiotic-associated ADE

Tamma. JAMA Intern Med. 2017 Jun 12
“Drugs of fear”

Our job is to adjust this fear and uncertainty
Observation

Specific therapy

Prophylaxis

Therapeutic trial

Empiric
the potential adverse effects have limited influence

Trainees are strongly influenced

4 themes culture of antibiotic prescribing

reluctance to provide critique, feedback, or advice

abx overuse is recognized but generally accepted

Audit and feedback

IV to PO policy
Redundant therapy policy
Formulary Review
Antimicrobial Handbook
Antibiograms
Beta-lactam Allergy
Microbiology Initiatives

http://www.cdha.nshealth.ca/nsha-antimicrobial-stewardship
STRATEGIES for COMMUNITY PRESCRIBERS

The behaviour of prescribing antibiotics is complex
Barriers in community stewardship

- Knowledge gaps
  - best practices and clinical practice guidelines
- Clinician perception of patient expectations
- Pressure to see patients quickly
- Clinician concerns about decreased patient satisfaction with clinical visits when antibiotics are not prescribed
Nudge, nudge

- RCT 5 primary care clinics
- Acute respiratory infections
- Poster: signed commitment letter
- Posted in exam rooms for 12 weeks
- 20% absolute reduction in inappropriate abx \((p=0.02)\)

Provision of social norm feedback to high prescribers of antibiotics in general practice: a pragmatic national randomised controlled trial

Michael Hallsworth, Tim Chadborn, Anna Sallis, Michael Sanders, Daniel Berry, Felix Greaves, Lara Clements, Sally C Davies

73 000 fewer antibiotic items dispensed
Effect disappeared after letters stopped

DELAYED PRESCRIPTIONS

• UK > 50% of ARI prescriptions are delayed
• RCT, multicenter in Spain
  • acute pharyngitis, rhinosinusitis, acute bronchitis, or AECOPD
• 4 groups
  • Patient-led prescription strategy
  • Prescription collection strategy
  • Immediate abx
  • No abx

### DELAYED PRESCRIPTIONS

**Patient-led prescription strategy**
- 32%

**Prescription collection strategy**
- 23%

**Immediate abx**
- 91%

**No abx**
- 12%

P < .001

10 key points

1. Appropriate microbiological samples and interpretation

2. Avoid the use of antibiotics to ‘treat’ fever

3. When indicated, start empirical antibiotic treatment after taking cultures, tailoring it to the site of infection, risk factors for MDR bacteria, and the local microbiology and susceptibility patterns.

4. Prescribe drugs at their optimal dose, route, duration adapted to each clinical situation and patient characteristics.

5. Use abx combinations only in cases where the current evidence suggests some benefit.

10 key points

6. Avoid antibiotics with a higher likelihood of promoting drug resistance or HAI

7. Control the infection source.

8. Always try to de-escalate/streamline antibiotic treatment; switch to the oral route as soon as possible.

9. Stop antibiotics as soon as a significant bacterial infection is unlikely.

10. Do not work alone

Five Things Physicians and Patients Should Question
1. Don’t routinely prescribe intravenous forms of highly bioavailable antimicrobial agents for patients who can reliably take and absorb oral medications.

IV TO PO

- Fluoroquinolones
- Metronidazole
- Trimethoprim-sulfamethoxazole
- Fluconazole
- Clindamycin
- Linezolid
**MEDICATION MANAGEMENT Policy**

<table>
<thead>
<tr>
<th>TITLE:</th>
<th>Pharmacist Initiated IV to PO Conversion of Antimicrobials</th>
<th>NUMBER:</th>
<th>NSHA MM-SR-025</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sponsor:</td>
<td>NSHA Drugs &amp; Therapeutics</td>
<td>Page:</td>
<td>1 of 9</td>
</tr>
<tr>
<td>Approved by:</td>
<td>NSHA HAMAC</td>
<td>Approval Date:</td>
<td></td>
</tr>
<tr>
<td>Applies To:</td>
<td>Pharmacists, physicians, nursing staff</td>
<td>Effective Date:</td>
<td></td>
</tr>
</tbody>
</table>
2. Don’t prescribe alternate second-line antimicrobials to patients reporting non-severe reactions to penicillin when beta-lactams are the recommended first-line therapy.
SYNDROMES
Symptom free pee...

- 82 year old female admitted for nausea & vomiting
- Cloudy urine, foul smelling
- Urine culture: *Pseudomonas aeruginosa*
What if

Dipstick: leuk esterase +

E. coli

Candida

Pregnant
ASYMPTOMATIC BACTERIURIYA

• COMMON

• Dipstick NOT helpful

• MOST receive antibiotics

• Mental status changes alone
  • Can rehydrate and r/a 24 hours


Nicolle LE. ICHE 2001;22(3):167-75
NITROFURANTOIN

• Beers: previously ‘high’ severity risk
  • ‘potential for renal impairment’
  • ’safer alternatives available’

• NOT nephrotoxic
  • Excreted by kidneys
    • Low eGFR: less drug in urinary tract; risk of non-renal toxicities
    • 1st line by IDSA
Beers - update

• Avoid if ClCr <30mL/min

• Avoid long term use

(also should avoid if interstitial lung disease)

• Low quality of evidence
• Strong strength of recommendation

13,421 NTF cases

Cure

- CrCl <30: 97.1%
- CrCl 30-60: 97.3%
- CrCl >60: 96.6%

Among those with possible AE:

- 54% eGFR > 60
- 46% eGFR < 60

0.15% high suspicion for nitrofurantoin adverse drug effect

Chronic use (4/5 cases)

Claussen. JAGS 65:1316–1320, 2017
Cystitis:

- Nitrofurantoin 5 days (A-I)
- Fosfomycin 3g 1 dose (A-1)
- *TMP/SMX 1DS po BID 3 days (A-I) (off label)*
- Amoxclav 875/125mg BID 5-7days (B-I)
NSHA Antimicrobial Stewardship

Antimicrobial stewardship is an activity that includes appropriate selection, dosing, route, and duration of antimicrobial therapy and may include a number of interventions. NSHA’s Antimicrobial stewardship program is interdisciplinary; involving pharmacists, infectious diseases physicians, infection control specialists, physicians, microbiology staff, nursing staff, hospital administrators, and information system specialists. The program includes interventions to optimize antimicrobial use, such as audit and feedback, a formulary of targeted antimicrobials and approved indications, education, antimicrobial order forms, guidelines and clinical pathways for antimicrobial utilization, strategies for streamlining or de-escalation of therapy, dose optimization, and parenteral to oral conversion of antimicrobials.

Why Is Antimicrobial Stewardship Important?
Threshold of 20% resistance (B-III)
<table>
<thead>
<tr>
<th>Organism (in-patient isolates)</th>
<th>No. of isolates</th>
<th>Ampicillin</th>
<th>Cefazolin</th>
<th>Ceftriaxone</th>
<th>Ciprofloxacin</th>
<th>Gentamicin</th>
<th>Tobramycin</th>
<th>Sulfamethoxazole-trimethoprim</th>
<th>Nitrofurantoin**</th>
<th>Piperacillin-tazobactam</th>
<th>Meropenem</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Escherichia coli</em></td>
<td>536</td>
<td>53</td>
<td>87</td>
<td>91</td>
<td>73</td>
<td>92</td>
<td>88</td>
<td>82</td>
<td>94</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td><em>Enterobacter cloacae</em></td>
<td>91</td>
<td>NA</td>
<td>NA</td>
<td>0</td>
<td>90</td>
<td>100</td>
<td>99</td>
<td>86</td>
<td>48</td>
<td>NA</td>
<td>83</td>
</tr>
<tr>
<td><em>Klebsiella pneumoniae</em></td>
<td>155</td>
<td>NA</td>
<td>87</td>
<td>87</td>
<td>88</td>
<td>91</td>
<td>86</td>
<td>84</td>
<td>46</td>
<td>NA</td>
<td>98</td>
</tr>
<tr>
<td><em>Klebsiella oxytoca</em></td>
<td>43</td>
<td>NA</td>
<td>65</td>
<td>100</td>
<td>97</td>
<td>100</td>
<td>100</td>
<td>97</td>
<td>88</td>
<td>NA</td>
<td>100</td>
</tr>
<tr>
<td><em>Proteus mirabilis</em></td>
<td>76</td>
<td>89</td>
<td>79</td>
<td>93</td>
<td>93</td>
<td>96</td>
<td>94</td>
<td>88</td>
<td>0</td>
<td>NA</td>
<td>97</td>
</tr>
<tr>
<td></td>
<td># tested</td>
<td>Amoxicillin/Clavulanate</td>
<td>Ampicillin</td>
<td>Cefazolin (Cephalaxin&lt;sup&gt;1&lt;/sup&gt;)</td>
<td>Ceftazidime</td>
<td>Ceftriaxone</td>
<td>Piperacillin/Tazobactam</td>
<td>Ertapenem</td>
<td>Meropenem</td>
<td>Ciprofloxacin</td>
<td>Nitrofurantoin&lt;sup&gt;1&lt;/sup&gt;</td>
</tr>
<tr>
<td>---------------------</td>
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<td>-------------------------</td>
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<td>-----------</td>
<td>----------------</td>
<td>-----------------------------</td>
</tr>
<tr>
<td><em>E. coli</em></td>
<td>9636</td>
<td>87</td>
<td>62</td>
<td>90</td>
<td>97</td>
<td>96</td>
<td>96</td>
<td>100</td>
<td>100</td>
<td>87</td>
<td>97</td>
</tr>
<tr>
<td><em>Klebsiella pneumoniae</em></td>
<td>1733</td>
<td>96</td>
<td>R</td>
<td>98</td>
<td>98</td>
<td>96</td>
<td>100</td>
<td>100</td>
<td>98</td>
<td>43</td>
<td>91</td>
</tr>
<tr>
<td><em>Klebsiella oxytoca</em></td>
<td>342</td>
<td>91</td>
<td>R</td>
<td>61</td>
<td>100</td>
<td>94</td>
<td>92</td>
<td>100</td>
<td>99</td>
<td>85</td>
<td>96</td>
</tr>
</tbody>
</table>
Summary

• Make sure the patient has an infection
  • Asymptomatic bacteriuria is a colonization state NOT an infection
  • Antibiotics are NOT indicated
  • Bacteriuria and pyuria are expected findings in the elderly

• Cipro resistance is high

• Use as short a course as necessary
Respiratory infections
Respiratory syndromes

Acute bronchitis

Pneumonia
### Case: LK with cough

<table>
<thead>
<tr>
<th>ID:</th>
<th>LK, 45 yo female, weight 90kg</th>
</tr>
</thead>
<tbody>
<tr>
<td>CC:</td>
<td>Cough with productive sputum</td>
</tr>
<tr>
<td>HPI:</td>
<td>LK presents with 3 days of cough productive for green sputum. Started after runny nose and sore throat. No dyspnea, sweats, or chills. She did not measure temperature.</td>
</tr>
<tr>
<td>PMHx:</td>
<td>Hypertension, coronary artery disease</td>
</tr>
<tr>
<td>Meds:</td>
<td>ASA, Perindopril, metoprolol, atorvastatin</td>
</tr>
<tr>
<td>Allergies:</td>
<td>Penicillin allergy</td>
</tr>
<tr>
<td>Social Hx:</td>
<td>Lives with husband. Nonsmoker</td>
</tr>
<tr>
<td>Vitals</td>
<td>120/70 mmHg, 90bpm, RR 20, afebrile</td>
</tr>
<tr>
<td>Phx</td>
<td>Normal</td>
</tr>
</tbody>
</table>
## Case: LK with cough

<table>
<thead>
<tr>
<th>ID:</th>
<th>LK, 45 yo female, weight 90kg</th>
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<td>Meds:</td>
<td>ASA, Perindopril, metoprolol, atorvastatin</td>
</tr>
<tr>
<td>All:</td>
<td>Penicillin allergy</td>
</tr>
<tr>
<td>Social Hx:</td>
<td>Lives with husband. Nonsmoker</td>
</tr>
</tbody>
</table>

### Vitals

- 120/70 mmHg, 90bpm, RR 20, afebrile

### Phx

Normal
Acute Bronchitis

Nasal congestion, rhinitis, sore throat, malaise
↓
Acute cough +/- sputum
10d to >3weeks

Inflammation large and mid airways

No signs of pneumonia

Most commonly **viruses**
- Rhinovirus
- Influenza
- RSV
- Metapneumovirus
- Coronaviruses
- Adenovirus
- <10% *M. pneumoniae, C. pneumoniae, B. pertussis*

No antibiotics (but 60-80% of patients receive abx)

Pt reassurance, Vaccinations, smoking cessation

Principles and Practice of Infectious Diseases 2014
### Antibiotics for bronchitis

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>RR (95% CI)</th>
<th>NNT for an additional beneficial outcome (NNTB)= 22</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical improvement at follow-up</td>
<td>1.07 (0.99 – 1.15)</td>
<td>22</td>
</tr>
<tr>
<td>Adverse effects in the antibiotic group</td>
<td>1.20 (1.05 to 1.36)</td>
<td></td>
</tr>
</tbody>
</table>

**Bordetella pertussis**

- All adults should receive one dose of Tdap vaccine

- Acellular pertussis-containing vaccine (Tdap) for all pregnant women ≥26 weeks who have not received a dose of a pertussis-containing vaccine in adulthood
# Case: LK with cough

<table>
<thead>
<tr>
<th>ID</th>
<th>LK, 89 yo female, weight 90kg</th>
</tr>
</thead>
<tbody>
<tr>
<td>CC</td>
<td>Cough with productive sputum</td>
</tr>
<tr>
<td>HPI</td>
<td>LK presents with 3 days of cough productive for green sputum. Also increasing dyspnea. Some sweats and chills. She did not measure temperature.</td>
</tr>
<tr>
<td>PMHx</td>
<td>Hypertension, coronary artery disease</td>
</tr>
<tr>
<td>Meds</td>
<td>ASA, Perindopril, metoprolol, atorvastatin</td>
</tr>
<tr>
<td>Allergies</td>
<td>Penicillin allergy</td>
</tr>
<tr>
<td>Social Hx</td>
<td>Lives with husband. Nonsmoker</td>
</tr>
<tr>
<td>Vitals</td>
<td>120/70 mmHg, 100bpm, afebrile</td>
</tr>
<tr>
<td>Phx</td>
<td>Crackles left lower base</td>
</tr>
<tr>
<td>Invest.</td>
<td>Chest Xray: Left lower lobe opacity</td>
</tr>
</tbody>
</table>
MANAGEMENT OF OUTPATIENT PNEUMONIA

<table>
<thead>
<tr>
<th>Controversial</th>
<th>$S.\ pneumoniae$ most common bacterial pathogen</th>
<th>$\text{Amoxicillin:}$ best oral beta-lactam against $S.\ pneumoniae$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Doxycycline:</td>
<td>$\text{Macrolides:}$ increasing pneumococcal resistance</td>
<td>Role of “atypical pathogens” debatable</td>
</tr>
<tr>
<td>less pneumo resistance</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
# Outpatient therapy

<table>
<thead>
<tr>
<th>Infectious Diseases Society of America and the American Thoracic Society 2007</th>
</tr>
</thead>
</table>
| **1.** Previously healthy and no use of antimicrobials within the previous three months | Macrolide (strong, level I)  
**or** doxycycline (weak, level III) |
| **2.** Presence of comorbidities such as chronic heart, lung, liver, or renal disease; diabetes mellitus; alcoholism; malignancies; asplenia; immunosuppressing conditions or use of immunosuppressing drugs; or use of antimicrobials within the previous 3 months (in which case an alternative from a different class should be selected): | Respiratory fluoroquinolone (strong, level I)  
**Or**  
Beta-lactam (high-dose amoxicillin, amoxicillin-clavulanate; alternative agents: ceftriaxone, or cefuroxime)  
**PLUS** a macrolide (strong, level I) |

*Clinical Infectious Diseases* ; 2007 ; 44 : S27 -S72
Antimicrobial stewardship is an activity that includes appropriate selection, dosing, route, and duration of antimicrobial therapy and may include a number of interventions. NSHA’s Antimicrobial stewardship program is interdisciplinary; involving pharmacists, infectious diseases physicians, infection control specialists, physicians, microbiology staff, nursing staff, hospital administrators, and information system specialists. The program includes interventions to optimize antimicrobial use, such as audit and feedback, a formulary of targeted antimicrobials and approved indications, education, antimicrobial order forms, guidelines and clinical pathways for antimicrobial utilization, strategies for streamlining or de-escalation of therapy, dose optimization, and parenteral to oral conversion of antimicrobials.

Why Is Antimicrobial Stewardship Important?
## Gram Positive Isolates - % Susceptible

<table>
<thead>
<tr>
<th></th>
<th># tested**</th>
<th>Amoxicillin/Cloxacillin</th>
<th>Ampicillin</th>
<th>Penicillin</th>
<th>Cloxacillin</th>
<th>Ceftriaxone</th>
<th>Clindamycin</th>
<th>Enthromycin</th>
<th>Ciprofloxacin</th>
<th>Levofloxacin</th>
<th>Nitrofurantoin³</th>
<th>SXT/TMP</th>
<th>Tetracycline⁵</th>
<th>Vancomycin</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Staphylococcus aureus¹</strong></td>
<td>1551</td>
<td>100</td>
<td>-</td>
<td>-</td>
<td>100</td>
<td>-</td>
<td>79</td>
<td>73</td>
<td>91</td>
<td>-</td>
<td>100</td>
<td>98</td>
<td>98</td>
<td>100</td>
</tr>
<tr>
<td>MRSA</td>
<td>196</td>
<td>R</td>
<td>R</td>
<td>R</td>
<td>R</td>
<td>R</td>
<td>58</td>
<td>17</td>
<td>27</td>
<td>-</td>
<td>100</td>
<td>98</td>
<td>96</td>
<td>100</td>
</tr>
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<td>Coagulase negative</td>
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<td>43²</td>
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<td>64</td>
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<td>98</td>
<td>95</td>
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<tr>
<td><strong>Staphylococcus</strong></td>
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<td><strong>Enterococcus faecalis</strong></td>
<td>966</td>
<td>98²</td>
<td>98</td>
<td>-</td>
<td>R</td>
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<td>R</td>
<td>81</td>
<td>-</td>
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<td>R</td>
<td>29</td>
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<tr>
<td><strong>Enterococcus faecium</strong></td>
<td>296</td>
<td>10²</td>
<td>10</td>
<td>-</td>
<td>R</td>
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<td>R</td>
<td>R</td>
<td>-</td>
<td>15</td>
<td>R</td>
<td>35</td>
<td>99</td>
</tr>
<tr>
<td>Streptococcus pyogenes</td>
<td>79⁴</td>
<td>100³</td>
<td>100³</td>
<td>100³</td>
<td>100³</td>
<td>100³</td>
<td>87</td>
<td>86</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>R</td>
<td>-</td>
<td>100³</td>
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<tr>
<td>(Group A Streptococcus)</td>
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<tr>
<td><strong>Streptococcus pneumoniae⁵</strong></td>
<td>61</td>
<td>-</td>
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<td>71</td>
<td>-</td>
<td>95</td>
<td>71</td>
<td>-</td>
<td>99</td>
<td>-</td>
<td>R</td>
<td>78</td>
<td>100³</td>
<td></td>
</tr>
</tbody>
</table>
BTS / NICE

• CAP treated in community: amoxicillin 500mg po TID x 5days [1a]

• Alternative: doxycycline [4b] or clarithromycin [1b]
Duration

- Admitted patients, moderate to severe
- Amoxicillin 3 days vs 8 days
- Clinical success at d10: 93% in both groups
- Adverse events: 11% placebo; 21% treatment group

el Moussaoui. BMJ. 2006 Jun 10;332(7554):1355.
afebrile for 48 hours
no more than one clinical instability factor
  • defined as HR >100 beats/min
  • RR >24 breaths/min
  • SBP ≤90 mmHg
  • Sats < 90% on room air

Success at 30 days was 92.6% (long) and 94.4% (short); p=.54

Uranga et al. JAMA Intern Med. 2016;176(9):1257-1265
Minimizing collateral damage

• Acute bronchitis is usually VIRAL

• Use as narrow a spectrum agent as possible
  • Evidence supports amoxicillin for mild CAP

• Use as short a course as necessary
  • Evidence supports azithromycin for 3 days
  • Evidence supports levofloxacin 750 mg for 5 days
Sinusitis

• 38 year old with a history of asthma
• Facial congestion x 5 days
• Feverish x 24 hours, now resolved
• Rhinorrhea: “yellow”
Clinical Manifestations

**Viral**
- 5-10 days
- peak d3-6
- nasal d/c and congestion are prominent
- mild fever 1st 48 h

**Bacterial**
1) Persistent symptoms
2) Onset of severe symptoms
3) “Double sickening”

Bacterial Rhinosinusitis

- Symptoms 10 days without improvement (strong, low-mod)

- Severe symptoms: fever >39°C + purulent nasal discharge or facial pain for at least 3-4 days (strong, low-mod)

- Initial viral infection that improved with subsequent worsening: new fever, headache, nasal discharge (strong, low-mod)

Rhinosinusitis - management

1. Amoxicillin*
   Amox-clav recommended by IDSA: (weak, low)

2. Allergy
   • Doxycycline (off-label) or fluoroquinolone

3. Duration
   • 5-7 days (weak, low-moderate)

Sinusitis is over treated

- 10% Bacterial
- 90% Viral

70% resolve spontaneously

Skin and soft tissue infections
**Cellulitis**

- Gp A streptococcus
- Gp C/G streptococcus
- Gp B streptococcus
- *S. aureus*

Adding clindamycin **Does Not** improve outcomes
Doubles the risk of diarrhea

<table>
<thead>
<tr>
<th>Erysipelas</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gp A streptococcus</td>
</tr>
<tr>
<td>Gp C or G streptococcus</td>
</tr>
<tr>
<td>Gp B streptococcus</td>
</tr>
<tr>
<td>S. aureus</td>
</tr>
</tbody>
</table>

Beta-hemolytic strep:  
Predictably penicillin susceptible  

*Streptococcus pyogenes*  
Penicillin, amoxicillin, 1st generation cephalosporin
Predisposing factors

• Lymphedema, venous stasis, obesity, diabetes mellitus

• Tinea pedis

• Management of cellulitis and erysipelas should include
  • elevation of the affected area and treatment of underlying conditions.
  • The skin should be sufficiently hydrated to avoid dryness and cracking without interdigital maceration.
No evidence for routine systemic antibiotics

Commonly colonized
- Gram positive and Gram negatives

Consider dermatitis

Monitor for signs of cellulitis
- Local heat and tenderness
- Increasing erythema of the surrounding skin
- Lymphangitis (red streaks traversing up the limb)
- Rapid increase in the size of the ulcer
- Fever

Venous Stasis
Cochrane Database Syst Rev. 2014 Jan 10;(1):CD003557
<table>
<thead>
<tr>
<th>Mimickers of infection</th>
</tr>
</thead>
<tbody>
<tr>
<td>DVT</td>
</tr>
<tr>
<td>Contact dermatitis</td>
</tr>
<tr>
<td>Venous stasis</td>
</tr>
<tr>
<td>Drug reaction</td>
</tr>
<tr>
<td>Gout</td>
</tr>
<tr>
<td>Erythema migrans</td>
</tr>
<tr>
<td>Pyoderma gangrenosum</td>
</tr>
<tr>
<td>Neuropathic arthropathy (Charcot joint)</td>
</tr>
</tbody>
</table>
Mimickers of infection-related bilateral inflammation:

- Usually not infection
- Venous stasis
- Contact dermatitis
- Lymphedema with chronic inflammation
- Neuropathic arthropathy (Charcot joint)
- Peripheral vascular disease
Duration

• Levofloxacin
• 5 days vs 10 days
• Outcome measure was resolution at 14 days, with absence of relapse by 28 days
• 98% resolution in both groups

A case was considered a clinical success even with mild residual erythema, hyperpigmentation or edema

Nail punctures

- *Pseudomonas*: rubber-soled shoe
- Debridement
- Tetanus
- Foreign bodies
## A point on bone scans

<table>
<thead>
<tr>
<th>Diagnostic method</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Probe to bone</td>
<td>0.60 (0.46-0.73)</td>
<td>0.91 (0.86-0.94)</td>
</tr>
<tr>
<td>Plain radiography</td>
<td>0.54 (0.44-0.63)</td>
<td>0.68 (0.53-0.80)</td>
</tr>
<tr>
<td>*chronicity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MRI</td>
<td>0.90 (0.82-0.95)</td>
<td>0.79 (0.62-0.91)</td>
</tr>
<tr>
<td>Bone Scan</td>
<td>0.81 (0.73-0.87)</td>
<td>0.28 (0.17-0.42)</td>
</tr>
</tbody>
</table>

Summary

• Utilize supportive measures

• Mimickers of infection
  • Venous stasis

• Duration 5-10 days
  • Often residual erythema, hyperpigmentation, or edema
C. difficile infection

- Diarrhea: 3 or more unformed stools in 24 hours
  +
  - A. Pseudomembranous colitis
  - Or
  - B. Stool testing for toxigenic C. difficile

Cohen. Infection Control and Hospital Epidemiology ; 2010 ; 31 : 431 -455
Clostridium difficile - Background

• Common nosocomial infection
• Recurrences common (10-30%), usually within 2 months
  • >60% if > 2 recurrences
• Treatment of recurrences expensive
  • Limited options
  • Vancomycin 6 wk taper ($1000)
  • Fidaxomycin (> $2000)
Treatment

• Discontinue inciting antibiotic if possible

• Avoid antiperistaltic agents

• The treatment of asymptomatic carriers of *C. difficile* is not necessary

• IV vanco does not work

Infection Control and Hospital Epidemiology; 2010; 31: 431-455
Treatment

• Non-severe: *metronidazole* 500mg po TID x10-14d (A-I) (off-label)

• Severe: vancomycin 125mg po QID x 10-14d (B-I)

• Severe
  • Zar score (CID,2007, 45:302) ≥ 2:
    • Age > 60
    • Temp > 38.3
    • Albumin < 25
    • WBC > 15,000
    • Pseudomembranous colitis (2 pts)
    • Tx in ICU (2 pts)

Infection Control and Hospital Epidemiology ; 2010 ; 31 : 431 -455
1\textsuperscript{st} Recurrence

- Same as first episode (dependent on severity) CIII

- Do not use metronidazole beyond the first recurrence of CDI or for long-term chronic therapy because of potential for cumulative neurotoxicity (B-II)

Infection Control and Hospital Epidemiology ; 2010 ; 31 : 431 -455
Recurrence

• Differentiate post infectious IBS vs relapse

• Test of cure not recommended (nor in asymptomatic patients)
  • False positives
  • Persistent positive

Cohen. Infection Control and Hospital Epidemiology ; 2010 ; 31 : 431 -455
2nd recurrence

• Vanco 125 mg 4 times per day for 10–14 days,
• 125 mg 2 times per day for a week,
• 125 mg once per day for a week
• 125 mg every 2 or 3 days for 2–8 weeks

• Cure may be higher in those tapered to Q3days
  • Q2days versus Q2d+Q3d: 60% vs 80% cure (P=0.03)
  • No difference with regimens longer than 10weeks

Am J Gastroenterol 1985;80:867-8
CID 2017;65(8):1396–9
Fecal microbiota therapy

- 2 weeks vanco + FMT vs 6 weeks vanco taper
- Cure: 44% vs 58%

CID 2017;64(3):265–71
C. difficile Prophylaxis

- OVP for those with prior CDI hospitalized for systemic antibiotics
- Control: no OVP
- OVP: 125mg BID or 250mg BID during systemic antibiotics and for up to 1 week after completion
- CDI 4% OVP vs 27% control
  - OR: 0.12 (95% CI .04-.4; P<0.00)

CID. 2016;63(5):651–3
10 key points

1. Appropriate microbiological samples and interpretation

2. Avoid the use of antibiotics to ‘treat’ fever

3. When indicated, start empirical antibiotic treatment after taking cultures, tailoring it to the site of infection, risk factors for MDR bacteria, and the local microbiology and susceptibility patterns.

4. Prescribe drugs at their optimal dose, route, duration adapted to each clinical situation and patient characteristics.

5. Use abx combinations only in cases where the current evidence suggests some benefit.

10 key points

6. Avoid antibiotics with a higher likelihood of promoting drug resistance or HAI

7. Control the infection source.

8. Always try to de-escalate/streamline antibiotic treatment; switch to the oral route as soon as possible.

9. Stop antibiotics as soon as a significant bacterial infection is unlikely.

10. Do not work alone

Summary

• Antibiotics are widely used
• Techniques to optimize antibiotic usage
• Approach to common syndromes
Piperacillin/tazobactam
FY 2016-17

DDD/1000pt-days  cost/1000pt-days
Imipenem/Meropenem
FY 2016-17

DDD/1000 pt-days
Cost/1000 pt-days
Ciprofloxacin
FY 2016-17

- DDD/1000 pt-days
- Cost/1000 pt days