AMMI CANADA PRESENTS:
DURATION OF ANTIBIOTIC THERAPY: HOW LONG IS ENOUGH, BALANCING RISK VERSUS BENEFIT.

All attendees will enter the meeting with their mic muted and will be unable to turn on their video.
Moderator:

Deborah Yamamura BSc, MD, FRCPC
AMMI Canada President-Elect
Webinar Housekeeping Notes

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Medical Microbiologist and Infectious Diseases Physician
Vancouver General Hospital
Medical Director, ASPIRES, Coastal Health
Clinical Associate Professor, The University of British Columbia
How Long Is Long Enough

New insights on duration of therapy for common infections
Jennifer Grant
Nicole Le Saux
Antibiotics

Thanks to PENICILLIN
...He Will Come Home!
Local treatment as indicated.

(b) Acute osteomyelitis, acute abscess formation, acute phlegmonous cellulitis and so on, 10,000-15,000 units every four hours intramuscularly. Seven days' treatment or less usually sufficient.

(c) Minor infections of the genitourinary tract (provided the infecting strain is sensitive), 10,000-15,000 units every four hours intramuscularly. If there is no clinical response in four or five days, continuation of therapy is probably not indicated.

(d) Empyema, meningitis or supplicative arthritis. 20,000 units locally daily or every two days for three or four injections. Systemic therapy as indicated by the nature of the primary infection.

2. Pneumococcic Infections.—(a) Pneumococcic pneumonia, 10,000 units every four hours intramuscularly. Ten injections frequently are sufficient, but continuation of therapy for two or three days may be necessary.

(b) Empyema, 20,000 units intrapleurally in 30 or 40 cc. of saline solution every two days for three or four injections. Systemic therapy as indicated.

(c) Meningitis, 20,000 units intrathecally daily. Two or three injections usually are sufficient. Systemic therapy as indicated.
Little quiz

• Identify this series of numbers:
• 7, 10, 14, 21, 4, 6, 3, 6, 12, 18, ∞
Little quiz

• Identify this series of numbers:
• 7, 10, 14, 21, 4, 6, 3, 6, 12, 18, ∞

These are:
A) football scores
B) A very confused toddler counting
C) More worrisome: a very confused accountant, counting
D) Bingo!
E) Antibiotic prescription duration in days, weeks, months
Agenda

- Principles of intelligent prescription
- Why duration is important
- Syndromes of interest
  - Sepsis/Bacteremia
  - HAP and VAP
  - Pneumonia
  - UTI
  - SSTI
  - Intra-abdominal infection
- Recommendations
- Discussion
Why this slide theme?

My KARMA Just Ran Over Your DOGMA!
The Microbiome is Important

The Human Microbiome Project says the human body has 100 trillion microscopic life forms living in it.

You call this living?
Why Shorter is Better than Longer

- Shorter LOS
- Less cost
- Less toxicity
- Less “Collateral Damage”

- In most cases shorter treatment is equally effective as longer treatment*

*Havey, Crit Care Med, 15:R267
Agenda

• Syndromes of interest
  – Sepsis/Bacteremia
  – HAP and VAP
  – Pneumonia
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• Recommendations

• Discussion
Bacteremia – What we do

Fig. 1. Distribution of recommended treatment durations for the five most common bacteraemic infections in critically ill patients.
Seven Versus 14 Days of Antibiotic Therapy for Uncomplicated Gram-negative Bacteremia: A Noninferiority Randomized Controlled Trial

- Randomized if stable for ≥ 48 hours at day 7
- Open label comparison stop day 7 v 14 days total
- 604 patients – 94% enterics, 68% UTI
- Failure, death, readmit: 46% 7d group, 50% 14d group
- Mortality rate same 11.8% v. 10.7%
- Faster return to baseline in 7 day group
- Substantial reduction in antibiotic use
Systematic Review of Duration for Bacteremia: Outcomes Essentially the Same

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Short Duration</th>
<th>Long Duration</th>
<th>Weight</th>
<th>Risk Ratio M-H, Fixed, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chowdhary</td>
<td>28</td>
<td>32</td>
<td>64.5%</td>
<td>0.88 [0.75, 1.02]</td>
</tr>
<tr>
<td>Jernelius</td>
<td>5</td>
<td>4</td>
<td>9.9%</td>
<td>1.00 [0.68, 1.46]</td>
</tr>
<tr>
<td>Siegel</td>
<td>0</td>
<td>3</td>
<td>5.3%</td>
<td>0.24 [0.02, 3.19]</td>
</tr>
<tr>
<td>Teller</td>
<td>12</td>
<td>8</td>
<td>20.3%</td>
<td>1.00 [0.83, 1.21]</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>45</td>
<td>47</td>
<td>100.0%</td>
<td>0.88 [0.77, 1.01]</td>
</tr>
</tbody>
</table>

Figure 2 Forest plot for outcome of clinical cure among bacteremic subgroups of randomized trials of shorter versus longer antibiotic treatment. CI, confidence interval; df, degrees of freedom; M-H, Mantel-Haenszel.
7 versus 14 days of antibiotic treatment for critically ill patients with bloodstream infection: a pilot randomized clinical trial

Nick Daneman¹, Asgar H. Rishu², Ruxandra Pinto², Pierre Aslanian³, Sean M. Bagshaw⁴, Alex Carignan⁵,

- Pilot study in ICU patients in Canada
- Pathogenic bacteremia in normal host
- No immune compromise or need for longer Rx
- 115 patients (358 eligible), 77% adherence
- 31 lung, 29 abdominal, 9 UTI, 12 unknown, 8 other
- Outcome (clinical success and adverse events) by treatment group awaits further enrollment.
Balance Trial:

Canadian Critical Care Trials Group

The CCCTG has more than 30 research programs underway and over 100 peer-reviewed publications to its credit, with direct impact on clinical practice in critical care.

Learn More

PROGRAMS

Principal Investigator(s)
Nick Daneman & Rob Fowler

Coordinator(s)
A Rishu

Status
Completed

BALANCE — Bacteremia Antibiotic Length Actually Needed for Clinical Effectiveness

The BALANCE research program focuses on optimizing antibiotic treatment duration in critically ill patients with bloodstream infections. The aim of this research program is to determine whether shorter duration antimicrobial therapy is associated with non-inferior mortality compared with longer duration antimicrobial therapy. Thus far we have completed:

- a systematic review of the literature
- a national survey of infectious diseases and critical care physicians
- a single centre observational study on duration of antibiotic therapy
- a multi-centre observational study on duration of antibiotic therapy
- a pilot RCT of 7 vs. 14 days of adequate antibiotics for bacteremia to determine (publication of results pending).
7 vs 14 days vs CRP (PIRATE Trial) for Gram Negative Bacteremia

von Dach E et al. JAMA 2020;323(21):2160-69
Sepsis and Bacteremia

Exceptions to the bacteremia literature discussed:

• **Staphylococcus aureus**
  – Known to colonize privileged sites,
  – Higher failure/relapse rate with shorter course therapy†
  – Minimum therapy 14 days (IV)* if quick blood clearance
  – Goes to 4 weeks (IV) if blood clearance slow

• **Candida**
  – Also goes to bad places
  – Minimum therapy 14 days (IV or PO)

• **Neutropenic hosts**
  – At least 14 days, and usually to recovery of counts

*= if clearly from a easily controlled source (e.g. skin), IV (mainstay) PO only with expert guidance.
†= Havey, Crit Care Med, 15:R267, Chong, AAC 57(3):1150
Sepsis and Bacteremia

• Exceptions to the rules:

• **Bacterial Endocarditis:**
  – Depends on organism and sensitivities
  – This is an *entirely separate topic*

• **Osteomyelitis/joint infections and bacteremia**
  – Usually 4-6 weeks IV Usually large joints
  – *or* can be longer

• **Hardware infections and bacteremia**
  – Depends on location and ability to remove hardware
## Bacteremia – What we should do

<table>
<thead>
<tr>
<th>Organism/condition</th>
<th>Duration</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>S. aureus</em></td>
<td>14 days</td>
<td>Uncomplicated</td>
</tr>
<tr>
<td><em>S. aureus, complicated</em></td>
<td>4-6 weeks</td>
<td>Endocarditis etc.</td>
</tr>
<tr>
<td>Central line infection (excludes S aureus)</td>
<td>5-7 days</td>
<td>Removal of line required</td>
</tr>
<tr>
<td></td>
<td>May be shorter if coagulase negative Staphylococcus species</td>
<td></td>
</tr>
<tr>
<td><em>S. pneumoniae with pneumonia</em></td>
<td>5 days</td>
<td>If clinical improvement</td>
</tr>
<tr>
<td><em>Enterobacterales</em></td>
<td>7 days</td>
<td>Source control achieved.</td>
</tr>
</tbody>
</table>
Principles of intelligent prescription
Why duration is important
Syndromes of interest
  – Sepsis/Bacteremia
  – HAP and VAP
  – Pneumonia
  – UTI
  – SSTI
  – Intra-abdominal infection
Recommendations
Discussion
Ventilator Acquired Pneumonia

- **Dogma:**
  - 10-21 days

  - CPIS score <6 less likely pneumonia

- **Singh** (*Am J Respir Crit Care Med Vol 162:505–511, 2000*)
  - 3 d if CPIS score <6 (days 0 and 3)

- **Chastre** (*JAMA, 290(19):2588-98*)
  - 8 days as good as 15 days (except for non-fermentors)

- **Multiple subsequent studies show decreased adverse events, cost, LOS and days of intubation with less Rx**
  - with or without CPIS score (*Cochrane review, 10(2), 2011*)

* = excludes non-fermenting GNR and S. aureus bacteremia
Guidelines for HAP and VAP

- Duration 7-8 days, irrespective of organism
  - Based on Response
  - Excludes
    - Immune compromised
    - Structural lung disease

- Duration 7 days, irrespective of organism
  - Based on response
  - Use of biomarkers
  - No exclusions
Agenda

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Community Acquired Pneumonia

• Most common cause of death world-wide (11.3%)*
• Ranges from mild, self limiting to fulminate sepsis
• Extremes of age associated with worse outcome
• Reasonably predictable microbiology except:
  – Immunocompromised
  – Unusual exposures

* WHO data 2010
Scores – predict mortality

• CRB-65
  – **C** onfusion of new onset
  – **R** espiratory rate of 30 breaths per minute or greater
  – **B** lood pressure less than 90 mmHg systolic or diastolic blood pressure 60 mmHg or less
  – **65** years of age or older

• PSI (“fine” score)
  – Too complicated to put here score (clinical, comorbid, laboratory, physical exam findings . . .

• Others . . .
Summary of data CAP- Duration of therapy

- Broncosopies show bacterial eradication with 3d Rx
- Studies in children with mild disease 2-3 = 5d Rx days†
- Meta-analysis shows <7 days similar or better than >7d (Li, Am J Med, 120:783, 2007)
- Meta-analysis shows <5 days similar to ≥7d (Dimopoulos, Drugs 68(13):1841, 2008)
- Ontario Systematic Review 2013 concludes: “high quality evidence indicates there is no significant difference in mortality for patients who received therapy ≥7d compared to ...<7d”
- IDSA CAP guidelines: min 5d Rx ➔ afebrile >48 h, and ≤ 1 vital sign abnormality. (minimum 5 days but could be slightly longer) If MRSA, minimum 7 days.


Confirmatory Trial of IDSA guidelines

- Randomized controlled trial 312 patients
  - 150 control, 162 intervention
- Either physician discretion or IDSA guidelines

<table>
<thead>
<tr>
<th>Table 4. Results for Secondary Study Outcomes in the Per-Protocol Analysisa</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Outcome</strong></td>
</tr>
<tr>
<td>----------------------------</td>
</tr>
<tr>
<td>Time, median (IQR), d</td>
</tr>
<tr>
<td>Taking antibiotics</td>
</tr>
<tr>
<td>Not taking antibiotics</td>
</tr>
<tr>
<td>Taking intravenous antibiotics</td>
</tr>
<tr>
<td>Until clinical improvement</td>
</tr>
<tr>
<td>Radiographic resolution at day 30</td>
</tr>
<tr>
<td>In-hospital mortality</td>
</tr>
<tr>
<td>30-d Mortality</td>
</tr>
<tr>
<td>Recurrence by day 30</td>
</tr>
<tr>
<td>Readmission by day 30</td>
</tr>
</tbody>
</table>

Appropriate Durations for CAP/HCAP-No Increase in Morbidity

• 6481 patients

<p>| Table 3. Association of Excess Antibiotic Treatment Duration With 30-Day Adverse Outcomes (n = 6481)* |
|---------------------------------|---------------------------------|---------------------------------|---------------------------------|---------------------------------|---------------------------------|---------------------------------|</p>
<table>
<thead>
<tr>
<th>Outcomes at 30 Days</th>
<th>Appropriate Duration (n = 2090), n (%)†</th>
<th>Excess Duration (n = 4391), n (%)‡</th>
<th>Unadjusted OR per Excess Day (95% CI)§</th>
<th>Unadjusted P Value$</th>
<th>Adjusted OR per Excess Day (95% CI)§</th>
<th>Adjusted P Value$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality§</td>
<td>40 (1.9)</td>
<td>88 (2.0)</td>
<td>0.99 (0.94-1.03)</td>
<td>0.52</td>
<td>1.01 (0.97-1.05)</td>
<td>0.60</td>
</tr>
<tr>
<td>Readmission§</td>
<td>294 (14.1)</td>
<td>497 (11.3)</td>
<td>0.99 (0.96-1.02)</td>
<td>0.48</td>
<td>1.00 (0.98-1.03)</td>
<td>0.92</td>
</tr>
<tr>
<td>Emergency department visit§</td>
<td>238 (11.4)</td>
<td>480 (10.9)</td>
<td>0.97 (0.94-1.00)</td>
<td>0.021</td>
<td>0.98 (0.95-1.01)</td>
<td>0.166</td>
</tr>
<tr>
<td>Antibiotic-associated adverse event§</td>
<td>72 (3.4)</td>
<td>210 (4.8)</td>
<td>1.04 (1.01-1.07)</td>
<td>0.012</td>
<td>1.03 (1.00-1.06)</td>
<td>0.038</td>
</tr>
<tr>
<td><em>Clostridioides difficile infection</em>*</td>
<td>11 (0.5)</td>
<td>22 (0.5)</td>
<td>0.92 (0.81-1.05)</td>
<td>0.21</td>
<td>0.93 (0.81-1.07)</td>
<td>0.30</td>
</tr>
<tr>
<td>Provider-documented† † † † † † † †</td>
<td>43 (2.1)</td>
<td>87 (2.0)</td>
<td>1.00 (0.94-1.05)</td>
<td>0.86</td>
<td>0.99 (0.94-1.05)</td>
<td>0.85</td>
</tr>
<tr>
<td>Patient-reported† † † † † † † † † † †</td>
<td>26/1132 (2.3)</td>
<td>114/2460 (4.6)</td>
<td>1.05 (1.02-1.08)</td>
<td>&lt;0.001</td>
<td>1.05 (1.02-1.08)</td>
<td>0.001</td>
</tr>
<tr>
<td>Composite adverse outcome§</td>
<td>499 (23.9)</td>
<td>897 (20.4)</td>
<td>0.98 (0.96-1.00)</td>
<td>0.078</td>
<td>0.99 (0.97-1.01)</td>
<td>0.40</td>
</tr>
</tbody>
</table>

OR = odds ratio.
* Outcomes were collected via the medical record and a follow-up telephone call at 30 d, and their associations with number of excess days of antibiotic treatment are shown. Outcomes were adjusted for hospital clustering, were inverse probability of treatment weighted, and were adjusted for known predictors of the outcome of interest (see footnotes below).
† Actual duration was within 1 d of expected duration.
‡ Actual duration was >1 d longer than expected.

Even Shorter Rx May Work

- RCT placebo controlled
- 119 (63 3d v 56 8d)
- 3d v 8d amoxicillin
- IV 3 days, if better:
  - Placebo 5d
  - Amoxicillin PO
- Outcomes similar
- Adverse events
  - 11% v 21% in longer Rx

El Moussaoui et al., BMJ, 2006; 332:13555
Moderately severe disease requiring hospitalization
Needed to make stability criteria of IDSA
310 patients, Non-inferiority demonstrated
Final data to be published?
• Recommendations:

• Treat 5 days (3 for Azithro) . . . But may decrease soon
• Step down to PO as soon as improving (day 2-3)
• Stop antibiotics after 5 days, once:
  – Patient improving
  – WBC declining
  – Afebrile 48 hours*
  – No more than one clinical sign of instability (e.g. tachycardia, need for O2 etc)

* = some studies and guidelines go as low as 8 hours
COPD exacerbations

• Supportive management
  – Bronchodilators
  – Steroids
  – Anti-inflammatory agents
  – Oxygen

• NICE guidelines
  – 5 days

• ATS guidelines
  – No comment on duration

Treatment with Antibiotics only if:
New or purulent sputum, bacterial disease suspected, moderate to severe disease
Does antibiotic treatment duration affect the outcomes of exacerbations of asthma and COPD? A systematic review

- Systematic review of RCT of COPD exacerbations
- Same antibiotic, different duration
Agenda

• Syndromes of interest
  – Sepsis/Bacteremia
  – HAP and VAP
  – Pneumonia/sinusitis
  – UTI
  – SSTI
  – Intra-abdominal infection

• Recommendations

• Discussion
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UTI- or what should not be a UTI

• Most commonly Over-diagnosed clinical entity
• *Sine Qua Non* of UTI: SYMPTOMS!
• Positive culture is not sufficient for diagnosis
  – Up to 50% of elderly females have positive cultures
  – Up to 30% of elderly males have positive cultures
  – Almost all catheterized patients will eventually have positive cultures
• Prevention is the best strategy
  – Remove catheters as soon as not necessary
  – Good perineal hygiene
UTI the “many headed” beast

• **Cystitis**
  – Local irritation, very annoying, but never fatal
  – DDx vaginosis, foley irritation, HSV, urethritis etc.
  – Since common, the collateral damage of ‘over-treating’ is high (e.g. fluoroquinolones)

• **Pyelonephritis**
  – Infection in upper tract
  – Associated with systemic symptoms
  – Can develop into Urosepsis

• **Urosepsis**
  – SIRS reaction in the presence of a UTI can be fatal
Cystitis-Data for duration

• **Women**
  – robust data for 1-5 days depending on antibiotic*
  – Extensive studies of uncomplicated cystitis/UTI

• **Men**, far few studies – “complicated cystitis” Prostate enlargement or cancer, voiding issues
  – No RCTs
  – VA cohort study of 39149 UTIs out patient setting (very heterogenous, using administrative data)
  – Rx ≤7d same or lower recurrence rate,
  – less *C. difficile* if ≤7 days compared to >7d#

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Cystitis

• Uncomplicated Cystitis (young, healthy women)
  – 1 or 2 doses Fosfomycin
  – 3 days – Septra, β-lactams
  – 5 days – Macrobid, β-lactams

• “Complicated” Cystitis (older women)
  – No data, based on expert opinion
  – 2 doses Fosfomycin
  – 5 days septra, β-lactams
  – 7 days macrobid, β-lactams
Pyelonephritis and Urosepsis

- Comparison >7 v ≤ 7 days Rx
- Meta-analysis 10 RCTs
  - ≤7d vs >7d (includes bacteremia)
  - Same results, short vs. long Rx
  - Short Rx failed with urologic abnormalities
- Regardless of ABic class
- Adverse events balanced

Eliakim-Raz J Antimicro Chemo 2013;68:2183-2191
Double-blind RCT febrile UTI, Netherlands, Primary care centers and ED departments
- 200 patients (No Pseudomonas), 55% initially hospitalized, 23% and 15% bacteremic (7 vs 14 days)
- "Clinical cure" -10-18 days and 70-84 days post therapy
- No difference between Abic class
- Follow-up in Women equivalent (93% vs 94%)
- Follow-up in Men (not equivalent)
  - Immediate clinical cure worse for 7 day group (86% vs 98%)
  - No difference in the 70-84 day follow-up
  - Authors recommended 14 day course for men if over age 50 yo

**Fig. 2** Difference in clinical cure rates (10- to 18-days post-treatment) of febrile UTI treated for 7 days versus 14 days in specific subgroups. Step-down treatment implies initial empiric intravenous antibiotic treatment. UTI: urinary tract infection; CI: confidence interval. P values represent test for interaction. Data presented from intention to treat analysis.
Treatment Recommendations - UTI

• Positive urine culture (asymptomatic bacteruria):
  – Please, please, please, do not send nor treat the culture!!!
  – Except: pregnant women, pre-urologic surgery (Nicolle, CID2019;68(10):e83-75)

• Cystitis:
  – Consider waiting for sensitivities (if symptoms mild)
  – 3-5 days sufficient, Nitrofurantoin 5-7 days

• Pyelonephritis/Urosepsis
  – 7 days is usually sufficient (esp. healthy females)
  – Up to 14 days if slow response or urologic abnormalities
  – Men, any patient with diabetes, or recurrences may require >7 days of therapy and individualized durations.
CAUTI (Catheter associated UTI)

• Data summarized in IDSA guidelines
• Applies to men and women, low risk (< 1%) of bacteremia
• Culture only through new catheter if symptomatic
  – Or better yet, remove catheter and do clean catch
• For mild symptoms consider not treating
  – Removal of catheter may be sufficient
  – Especially low CFU or weak pathogens (yeast, enterococcus)
• For more severe symptoms
  – 7 days if symptoms resolve quickly
  – Up to 14 days for slow resolution

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Skin and Soft Tissue Infections

- Double-blind RCT 2014-2017 (Netherlands)
  - 6 vs 12 days for severe cellulitis (hospitalized)
  - 151 patients randomized
  - More relapse in 6d group at 90 days
  - Confidence intervals wide for symptom scores
- 2 other RCTs for outpatient cellulitis found no differences
- Trial in 2004, 87 patients, levofloxacin
  - Uncomplicated cellulitis had similar cure rates with 5 vs 10 days
  - Hospitalized pts more relapse in 5 day group compared to 10 days

Cranendonk Clin Microbiol Infect. 2020 May;26(5):606–12
Recommendations - SSTI

• Purulent SSTI should have drainage of abscesses as it usually helps clinical symptoms and shortens course of antibiotic, allows for culture of material
• Treat until better +1 day, then stop
  – 5-6 days, possibly longer if slow to resolve
• Exceptions: deeper infections
  – Need drainage / imaging
• Excludes Bone/Joint infections (exclude *N. gonorrhea*)
  – Usually 4-6 weeks for large joints
  – 2-3 weeks for small joints
• Excludes immunocompromised hosts, rarer infections
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Intra abdominal infections

• Type of intrabdominal infections (IAI)
  – Spontaneous Bacterial Peritonitis
  – Community Acquired (e.g. appendicitis with IAI)
  – Complicated- (e.g. post surgical, underlying bowel disease)
  – Nosocomial (e.g. prolonged open abdomen)

• Primary treatment modality
  – Source control

• Antimicrobials are supportive
# Intra-abdominal infections

<table>
<thead>
<tr>
<th>Study</th>
<th>Details</th>
<th>Duration favoured</th>
</tr>
</thead>
<tbody>
<tr>
<td>RCT of 90 patients with SBP (Runyon et al Gastroenterology 1991;100(6):173-42.)</td>
<td>Similar rates of cure for 5 vs. 10 d Rx with cefotaxime</td>
<td>5d</td>
</tr>
<tr>
<td>RCT of 111 patients with CA-IAI (Basoli A. J Gastrointest Surg 2008;12(3):592-600)</td>
<td>Source control - similar cure for 3d vs. prolonged duration of ertapenem</td>
<td>3d</td>
</tr>
<tr>
<td>RCT 518 pts with source control: duration 4 days vs 2 days after resolution of fever, WBC ileus. (Sawyer R NEJM 2015;372:1996-2005)</td>
<td>No difference in recurrence or death (21.8% vs 22.3%) Control group had median of 8 days of antibiotics</td>
<td>4 d</td>
</tr>
</tbody>
</table>
Recommendations - post Source control

- Treat 4-7 days, Unless

Adequate source control cannot be achieved . . .
Agenda

• Syndromes of interest
  – Sepsis/Bacteremia
  – HAP and VAP
  – Pneumonia
  – UTI
  – SSTI
  – Intra-abdominal infection

• Recommendations

• Discussion
Other conditions not discussed

• See AMMI practice point
  – Acute bacterial Sinusitis
  – Acute otitis media (children)
  – Streptococcal pharyngitis
  – Vertebral osteomyelitis
  – Acute hematogenous osteomyelitis (children)
Summary of Key Recommendations

• Sepsis and bacteremia
  – Assess source and bacterial isolate, remove catheters, IV lines
  – Gram negatives (7 days) and central line infections usually ≤ 7 days if uncomplicated
  – Minimum 14 days for Staph aureus and yeast that is uncomplicated
  – ID consult for S. aureus sepsis

• Ventilator associated pneumonia (VAP)
  – Generally ≤ 7 days
  – Maybe longer if MRSA

• Community acquired Pneumonia (CAP)
  – at least 5 days and until afebrile X 48 hrs and stable

• UTI
  – 3 days cystitis, 5-7 days complicated, 7-14 days pyelonephritis (even bacteremic)

• SSTI (cellulitis)
  – Until it’s better (5-10 days)

• Abdominal infections
  – Source control is key to decreasing durations
  – Less than 7 days is fine, as few as 3 is fine if drained and pt not systemically unwell
### Table. Infections for Which Short-Course Therapy Has Been Shown to Be Equivalent in Efficacy to Longer Therapy

<table>
<thead>
<tr>
<th>Disease</th>
<th>Treatment, Days</th>
</tr>
</thead>
<tbody>
<tr>
<td>Community-acquired pneumonia&lt;sup&gt;1-3&lt;/sup&gt;</td>
<td>3-5</td>
</tr>
<tr>
<td>Nosocomial pneumonia&lt;sup&gt;6,7&lt;/sup&gt;</td>
<td>≤8</td>
</tr>
<tr>
<td>Pyelonephritis&lt;sup&gt;10&lt;/sup&gt;</td>
<td>5-7</td>
</tr>
<tr>
<td>Intraabdominal infection&lt;sup&gt;11&lt;/sup&gt;</td>
<td>4</td>
</tr>
<tr>
<td>Acute exacerbation of chronic bronchitis and COPD&lt;sup&gt;12&lt;/sup&gt;</td>
<td>≤5</td>
</tr>
<tr>
<td>Acute bacterial sinusitis&lt;sup&gt;13&lt;/sup&gt;</td>
<td>5</td>
</tr>
<tr>
<td>Cellulitis&lt;sup&gt;14&lt;/sup&gt;</td>
<td>5-6</td>
</tr>
<tr>
<td>Chronic osteomyelitis&lt;sup&gt;15&lt;/sup&gt;</td>
<td>42</td>
</tr>
</tbody>
</table>

|                | 7-10 | 10-15 | 10-14 | 10    | ≥7    |

Abbreviation: COPD, chronic obstructive pulmonary disease.
Important Concepts to Apply in Practice to Decrease Durations

1. Durations are often influenced more so by cultural norms rather than good science. Be cognizant of this impact on your practice. ("Slow thinking" moment, should not be reflexive unless clear guidelines such as IE)

2. Always be prepared to discontinue antibiotics if infection is not the correct diagnosis for the clinical presentation. (antibiotic time-out 24 -72 hours)

3. Discuss durations with patients. We know for sure shorter durations decreases C. difficile. Talk about risk versus benefit. Refrain from putting durations in orders early in admission. For out-patients, follow-up is key.

4. It is unknown exactly how duration affects the microbiome however, logically, we need to advocate for “appropriate” durations.

5. This is emerging data, support trials that assess durations.

Questions?
Please enter one thing you have learned from today's presentation into the chat box
We Appreciate Your Feedback

Please take a few moments following the webinar to complete the evaluation form. An email will be sent to you with a survey link.

Accreditation

This activity is eligible for MOC section 1 credits as an unaccredited group learning activity. Please note that unaccredited group learning activities are only eligible for 0.5 credits for every hour of learning, with a maximum of 50 credits per cycle. If you have any questions about how to enter these credits into Mainport, please contact the Royal College Service Centre at cpd@royalcollege.ca
Thank you for joining us!

The Practice Point: Duration of Antibiotic Therapy for Common Infections document and a recording of the webinar will be available on the AMMI Canada website (ammi.ca).
IV to PO conversion

- Reduces IV complications
- Encourages early ambulation
- Results in 3d ↓ LOS*
- Preferred by patients . . .

- Approximately 40% of patients on IV are eligible for oral switch on day 2-3 of Rx†¶

* Rhew, Arch Int Med 161:722  † Mertz, JAC 64:188  ¶ Ramirez, Arch Int Med 159:2449
IV to PO switch – pneumonia

• Quinolones can be given orally initially
  – As can other bioequivalent drugs
• Decreases LOS by 2d, IV Rx by 3.4d (BMJ, doi:10.1136/bmj.38993.560984.BE)
• For up to 50% of patients can be done in 2-3 days (Rhew, Arch Int Med 161:722, Ramirez Arch Int Med 155:1273 & Arch int med 159:2449)
• Is part of national/international guidelines (CID, 44:s27)
• Irrespective of S. pneumoniae bacteremia (Arch Int Med 161:848)
IV to PO switch CAP

- Severe CAP
- RCT 7 d IV v rapid oral switch
- 302 patients
  - 150 control
  - 152 rapid switch (day 3)
- Adverse events lower in intervention group (NS)
- Includes 10% bacteremia

Table 3 Outcomes in multicentre randomised trial of early switch from intravenous to oral antibiotics in severe community acquired pneumonia. Intention to treat analysis. Values are number of patients (percentage) unless stated otherwise

<table>
<thead>
<tr>
<th>Clinical outcome</th>
<th>Treatment group</th>
<th>Mean difference (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Intervention (n=132)</td>
<td>Control (n=133)</td>
</tr>
<tr>
<td>Death after day 3</td>
<td>5 (4)</td>
<td>8 (6)</td>
</tr>
<tr>
<td>Clinical cure</td>
<td>110 (83)</td>
<td>113 (85)</td>
</tr>
<tr>
<td>Clinical failure</td>
<td>22 (17)</td>
<td>20 (15)</td>
</tr>
<tr>
<td>Clinical cure but still in hospital</td>
<td>9 (7)</td>
<td>6 (5)</td>
</tr>
<tr>
<td>Clinical deterioration</td>
<td>8 (6)</td>
<td>6 (5)</td>
</tr>
<tr>
<td>Death</td>
<td>5 (4)</td>
<td>8 (6)</td>
</tr>
<tr>
<td>Clinical deterioration and death</td>
<td>13 (10)</td>
<td>14 (11)</td>
</tr>
<tr>
<td>Mean (SD) length of hospital stay (days)</td>
<td>9.6 (5.0)</td>
<td>11.5 (4.9)</td>
</tr>
<tr>
<td>Mean (SD) duration of intravenous treatment (days)</td>
<td>3.6 (1.5)</td>
<td>7.0 (2.0)</td>
</tr>
</tbody>
</table>

Oosterheert, BMJ 7 Nov 2006
IV to PO conversion UTI

- Not necessary with bioequivalent drugs
  - Cipro, septra, fluconazole for UTI
- Can be done
  - Patient has a functional GI tract
  - Patient is improving
  - Afebrile for 24 hours
- Benefits as for CAP and other syndromes