Choosing Antibiotics Wisely

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November 30, 2020

DISCLOSURE OF CONFLICT OF INTEREST

	Nature of relationship(s) (over previous 2-years)	Y/N	Company/ Organization	Description of relationship(s)
A	Member of an Advisory Board or equivalent with a commercial organization.	NO		
B	Member of a Speakers bureau.	NO		
C	Received payment from a commercial organization. (including gifts or other consideration or 'in kind' compensation)	NO		
D	Received a grant(s) or an honorarium from a commercial organization.	NO		
E	Hold a patent for a product referred to in the CME/CPD program or that is marketed by a commercial organization.	YES	MedSafer	Copyright Holder, Marketed Product
F	Hold investments in a pharmaceutical organization, medical devices company or communications firm.	??	Mutual Funds / ETFs	I may hold these investments – don't know
G	Currently participating in or have participated in a clinical trial within the past two years.	YES	CIHR, Canadian Frailty Network, Centre for Aging and Brain Health Innovation	Principal Investigator, Co-Investigator

Note

- Despite the title of the talk and the highlighting of some of their free materials, I have little ongoing relationship with Choosing Wisely Canada and do not represent them.
- I was a co-author of the AMMI Canada Choosing Wisely declarative statements for infectious diseases

As a result of attending this session, participants will be able to:

1) Recognize opportunities to avoid the use of antibiotics for non-bacterial diseases
2) Feel empowered to use narrower spectrum therapy
3) Know drugs which maximize use of the oral route
4) Be aware of the evidence in favor or short(er) course therapies

The Use of Antibiotics

Indicated and beneficial antibiotics

ANTIBIOTIC OVERLOAD

- Antibiotics given for diseases which are not due to bacteria
- Antibiotics which are unnecessarily broad for the condition being treated
- Antibiotics by the vein when mouth will do
- Antibiotics given for too long

Why does it matter?

- Antibiotics can have consequences
  - *CDI*
  - *Interactions*
  - *Adverse Drug Events*
- Antibiotics cost money
- Antibiotic resistant organisms are a modern reality
  - *Their societal and individual prevalence is a function of exposure*

What can be done about Antibiotic Overload?

- Enter the concept of the "Antibiotic Stewardship"
- Optimizing:
  - *Selection of spectrum*
  - *Dose*
  - *Route*
  - *Duration*
- To MAXIMIZE clinical cure or prevention of infection

Case 1

- 40M presents with 3 days of stuffy nose and bothersome sinus pain with yellow phlegm. No fever.
- “Antibiotics worked last time”

Case 1

A) Amoxicillin

B) Saline rinses and supportive care

C) Ciprofloxacin

D) Doxycycline

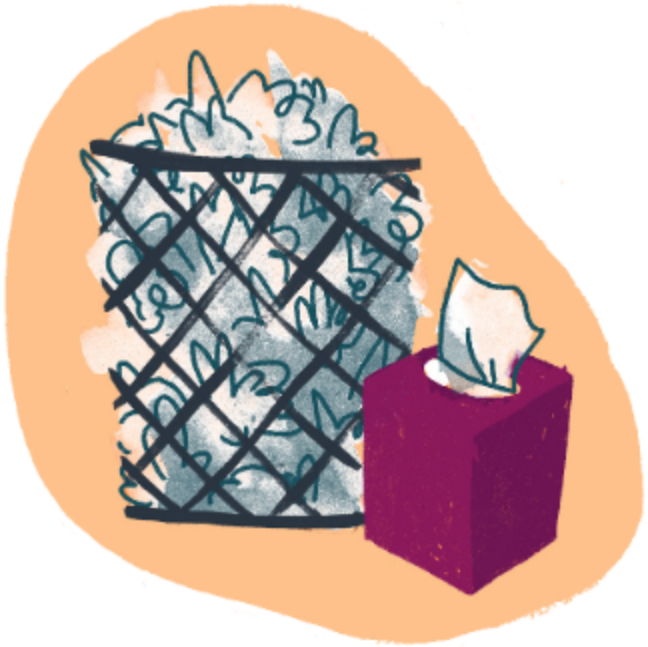
Section 1: Antibiotics given for diseases which are not due to bacteria

- Most sinusitis is not bacterial
- Respiratory symptoms in the era of virus detection – is there a role for additional testing?
- "Pyuria" or "Bacteriuria"

Treating Sinus Infections: Don't rush to antibiotics

Choosing Wisely Canada

Millions of people are prescribed antibiotics each year for sinus infections, a frequent complication of the common cold, hay fever, and other respiratory allergies. In fact, 15 to 21 percent of all antibiotic prescriptions for adults in outpatient care are for treating sinus infections. Unfortunately, most of those people don't need the drugs. Here's why:



The drugs usually don't help

Sinus infections can be painful. People with the condition usually have a stuffy nose combined with yellow, green, or gray nasal discharge plus pain or pressure around the eyes, cheeks, forehead, or teeth that worsens

So when are antibiotics necessary?

They're usually required only when symptoms last longer than a week, start to improve but then worsen again, or are very severe. Worrisome symptoms that can warrant immediate antibiotic treatment include a fever over 38.6 °C, extreme pain and tenderness over your sinuses, or signs of a skin infection, such as a hot, red rash that spreads quickly.

When you do need antibiotics, the best choice in many cases is amoxicillin, which typically costs about $4 and is just as effective as more expensive brand-name antibiotics. Note that some health care providers recommend CT scans when they suspect sinus infections. But those tests are usually necessary only if you have frequent or chronic sinus infections or you're going to have sinus surgery.

How should you treat sinus infections?

Most people recover from sinus infections caused by colds in about a week, but several self-help steps may bring some relief sooner:

Rest. That's especially important in the first few days when your body needs to channel its energy into fighting the virus. It also helps to elevate your head when lying down to ease postnasal drip.

Drink. Warm fluids can help thin nasal secretions and loosen phlegm.

Boost humidity. Warm, moist air from a bath, shower, or a pan of recently boiled water can loosen phlegm and soothe the throat.

Gargle. Use half a teaspoon of salt dissolved in a glass of warm water.

Rinse your nose. Saltwater sprays or nasal irrigation kits (such as Neti Pot) might make you feel better.

Use over-the-counter remedies with caution.

- Nasal drops or sprays containing oxymetazoline (such as Otrivin®, Drixoral® and generic) can cause rebound congestion if used for longer than three days.
- The benefits of oral decongestants (such as Sudafed) rarely outweigh the risks or side effects.
- Unless significant allergies are present, it's best to skip antihistamines since they don't ease cold symptoms very much and can cause bad side effects.

3 **Uncomplicated sinusitis** ▲

Don't prescribe antibiotics unless symptoms have persisted for greater than 7-10 days without improvement.

Differentiating viral rhinosinusitis (VRS) from acute bacterial rhinosinusitis (ABRS) can be challenging. Patients not meeting the below criteria are best managed with a viral prescription. Antibiotics should only be considered if the patient has at least 2 of the below **PODS** symptoms, one of those being O or D, AND the patient meets one of the following criteria:

1. The symptoms are severe
2. The symptoms are mild to moderate symptoms if there is no response after a 72 hours trial with nasal corticosteroids.

P: Facial **P**ain/pressure/fullness; **O:** Nasal **O**bstruction;

D: Purulent/discolored nasal or postnasal **D**ischarge; **S:** Hyposmia/anosmia (**S**mell)

Tools to Support Practice:

1. Viral prescription pad
2. General information for kids

Rx Patient Name : _____ Date : _____

The symptoms you presented with today suggest a VIRAL infection.

- ☐ Upper Respiratory Tract Infection (Common Cold) : Lasts 7-14 days
- ☐ Flu : Lasts 7-14 days
- ☐ Acute Pharyngitis ("Sore Throat") : Lasts 3-7 days, up to ≤10 days
- ☐ Acute Bronchitis/"Chest Cold" (Cough) : Lasts 7-21 days
- ☐ Acute Sinusitis ("Sinus Infection") : Lasts 7-14 days

You have not been prescribed antibiotics because
antibiotics are not effective in treating viral infections.
Antibiotics can cause side effects (e.g. diarrhea, yeast infections) and may cause serious harms such as severe diarrhea, allergic reactions, kidney or liver injury.

When you have a viral infection, it is very important to get plenty of rest and give your body time to fight off the virus.

If you follow these instructions, you should feel better soon :

- ➳ Rest as much as possible
- ➳ Drink plenty of fluids
- ➳ Wash your hands frequently
- ➳ Take over-the-counter medication, as advised :

- ☐ Acetaminophen (e.g. Tylenol®) for fever and aches
- ☐ Ibuprofen (e.g. Advil®) for fever and aches
- ☐ Naproxen (e.g. Aleve®) for fever and aches
- ☐ Lozenge (cough candy) for sore throat
- ☐ Nasal Saline (e.g. Salinex®) for nasal congestion
- ☐ Other : _____

(e.g. Nasal decongestant if Salinex® does not work, for short-term use only!)

Please return to your provider if :

- ➳ Symptoms do not improve in _____ day(s), or worsen at any time
- ➳ You develop persistent fever (above 38°C, or _____ as directed)
- ➳ Other : _____

Prescriber _____

This "Viral Prescription Pad" has been adapted from the RQHR Antimicrobial Stewardship Program
www.rqhealth.ca/antimicrobialstewardship, and is **available in other languages.**
http://www.rxfiles.ca/rxfiles/uploads/documents/ABX-Viral-Prescription-Pad-Languages.pdf

Multiplex Respiratory Virus Testing for Antimicrobial Stewardship: A Prospective Assessment of Antimicrobial Use and Clinical Outcomes Among Hospitalized Adults

Makeda Semret,[1] Ian Schiller,[2] Barbara Ann Jardin,[2] Charles Frenette,[1] Vivian G. Loo,[1] Jesse Papenburg,[1] Shelly A. McNeil,[4] and Nandini Dendukuri[3]

[1]Division of Infectious diseases and Medical Microbiology, Department of Medicine and Laboratories, [2]Research Institute, and [3]Technology Assessment Unit, McGill University Health Centre, Montreal, Québec, and [4]Canadian Center for Vaccinology, IWK Health Centre and Nova Scotia Health Authority, Dalhousie University, Halifax, Canada

JID 2017:216 (15 October)

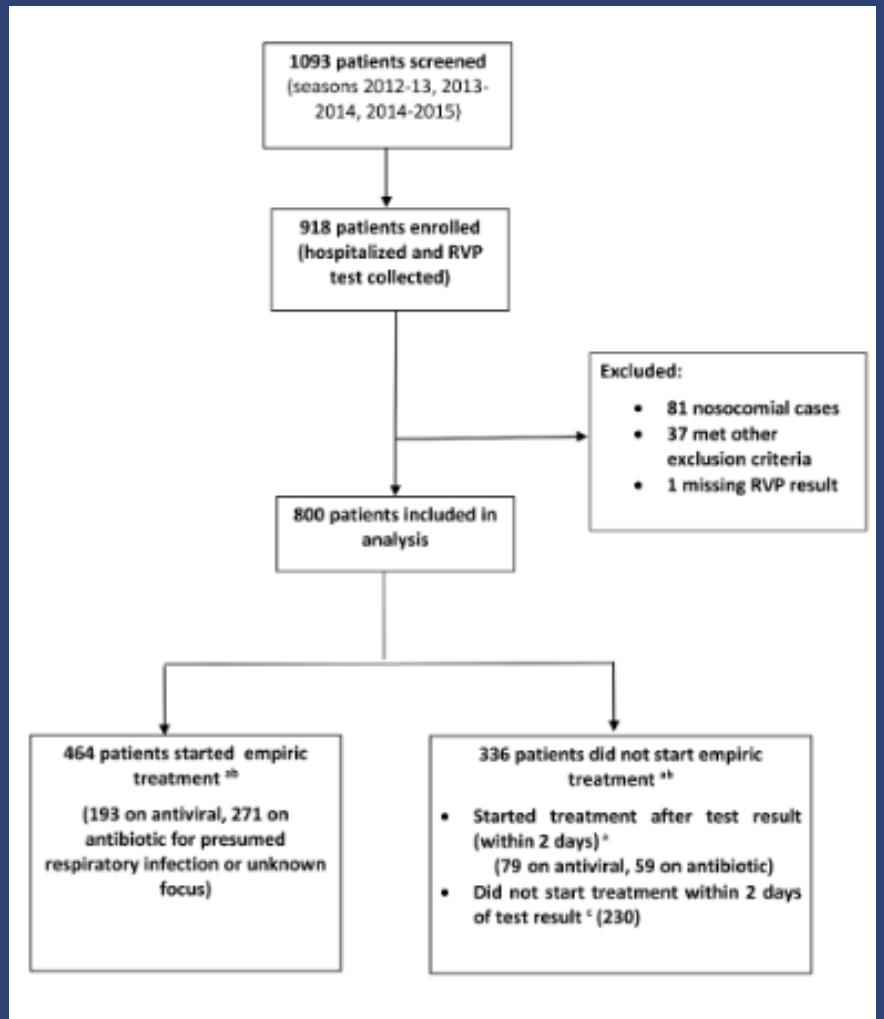


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Table 1. Respiratory Virus Panel Findings

Virus	Positive Test Results, Patients, No. (%)
Influenza A and B virus	425 (53)
RSV A and B	24 (3)
Parainfluenza virus 1–3	4 (0.5)
Rhinovirus/enterovirus	6 (0.8)
Adenovirus	29 (3.6)
CoV OC43 and 229E	11 (1.4)
Human metapneumovirus	13 (1.6)

Abbreviations: CoV, coronavirus; RSV, respiratory syncytial virus.

Table 4. Change in Management of Antivirals and Antibiotics After Respiratory Virus Panel (RVP) Testing Among Patients Treated Empirically (Before Testing), by RVP Result

Treatment, Pneumonia Suspicion	Influenza Virus Positive	Other Virus Positive	Virus Negative
Antivirals			
Suspicion			
Patients	47[a]	4	18
Antiviral continued[b]	37 (79)	0 (0)	1 (6)
No suspicion			
Patients	100[a]	5	12
Antiviral continued[c]	81 (81)	1 (20)	6 (50)
Antibiotics			
Suspicion			
Patients[d]	57	15	90
Antibiotic continued[e]	35 (61)	12 (80)	63 (70)
No suspicion			
Patients[d]	53	7	42
Antibiotic continued[f]	21 (40)	1 (14)	26 (62)


Sorry,
but no
amount of
antibiotics
will get
rid of your
cold.

ORIGINAL ARTICLE

Procalcitonin-Guided Use of Antibiotics for Lower Respiratory Tract Infection

D.T. Huang, D.M. Yealy, M.R. Filbin, A.M. Brown, C.-C.H. Chang, Y. Doi, M.W. Donnino, J. Fine, M.J. Fine, M.A. Fischer, J.M. Holst, P.C. Hou, J.A. Kellum, F. Khan, M.C. Kurz, S. Lotfipour, F. LoVecchio, O.M. Peck-Palmer, F. Pike, H. Prunty, R.L. Sherwin, L. Southerland, T. Terndrup, L.A. Weissfeld, J. Yabes, and D.C. Angus, for the ProACT Investigators*

N ENGL J MED 379;3

- Randomized patients who presented with suspected lower resp tract infection where physician was "unsure" of need of antibiotics to procalcitonin testing with interpretation (n=826) vs. usual care (n=830)
- Primary outcome was antibiotic use

Table 2. Antibiotic Exposure.*

Outcome	Procalcitonin (N=826)	Usual Care (N=830)	Difference (95% or 99.86% CI)†
Intention-to-treat population‡			
Antibiotic-days by day 30§	4.2±5.8	4.3±5.6	−0.05 (−0.6 to 0.5)
Received any antibiotics by day 30 — estimated no. (%)¶	471 (57.0)	513 (61.8)	−4.8 (−12.7 to 3.0)
Antibiotic prescription in ED — estimated no. (%)¶‖	282 (34.1)	321 (38.7)	−4.6 (−12.2 to 3.0)
Antibiotic-days during hospital stay	2.6±3.3	2.7±3.0	−0.1 (−0.8 to 0.6)
Hospital length of stay — days	5.0±4.4	4.7±3.5	0.3 (−0.2 to 0.9)

Case 2

- 75 man awakens from sleep with crushing retrosternal chest pain, dyspnea, nausea, and a sense of impending doom
- He calls an ambulance and is taken to the emergency department of a tertiary care hospital
- On arrival he is hypertensive, afebrile and has evidence of diffuse horizontal ST segment depression in the anterior leads and his initial cardiac enzymes are positive

Case 2 – Continued

- His urinalysis (dipstick) is positive for leukocytes
- Which antibiotics should be started to treat his "urosepsis"?
  - *A) Ciprofloxacin*
  - *B) Ceftriaxone*
  - *C) Piperacillin-Tazobactam*
  - *D) Trimethoprim-Sulfamethoxazole*
  - *E) Other*

Pyuria is sensitive but not specific for bacteriuria and UTI

- Function of pre-test probability
- Positive predictive value as low as 10% (meaning 90% false positives)
- This is a rule out test (e.g. if negative much less likely to be UTI; the converse is not true)


UTI

“If you [culture] it, he will [probably] come…”

Downstream Impact of Urine Cultures Ordered without Indication at Two Acute Care Teaching Hospitals

Author(s): Jerome A. Leis, MD; Wayne L. Gold, MD; Nick Daneman, MD, MSc; Kaveh Shojania, MD; Allison McGeer, MD

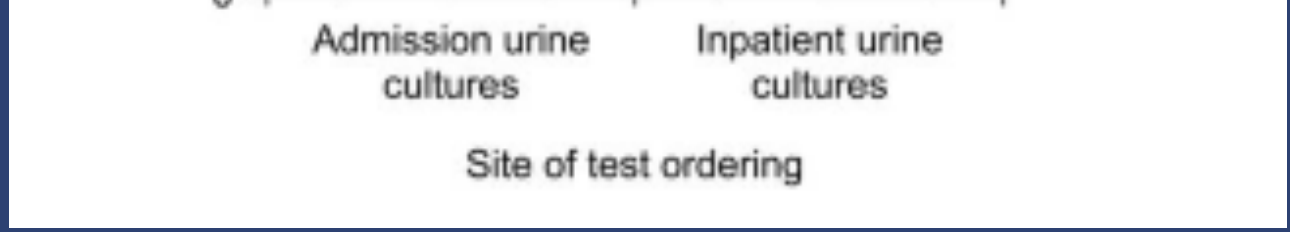
Source: *Infection Control and Hospital Epidemiology*, Vol. 34, No. 10 (October 2013), pp. 1113-1114

CULTURES WITHOUT INDICATION VERY COMMON

INPATIENT CLINICAL YIELD EXTREMELY LOW (<2%)

UNNECESSARY ANTIBIOTICS IN UP TO 50%

RAISES THE QUESTION: DO THESE CULTURES DO MORE HARM THAN GOOD?



Symptom-Free Pee: LET IT BE

A national initiative to stop inappropriate antibiotic use for asymptomatic bacteriuria in long-term care residents.

For more direction and guidance:

www.ammi.ca

#SymptomFreeLetItBe

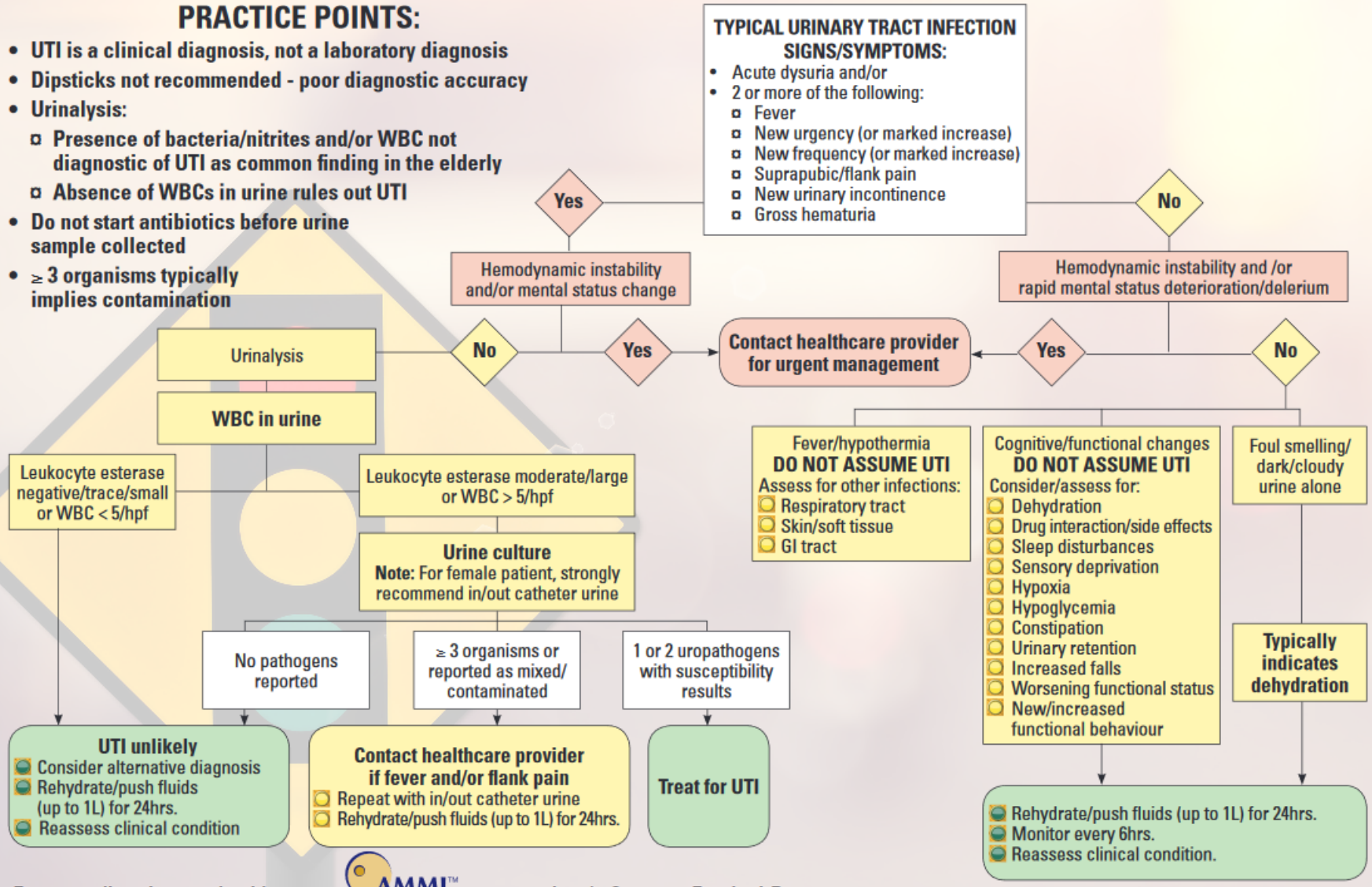
AMMI™ Canada

Symptom-Free Pee: LET IT BE

Diagnosis of Suspected Urinary tract Infection (UTI) in Non-Catheterized Elderly Patients in Acute Care Setting

PRACTICE POINTS:

- UTI is a clinical diagnosis, not a laboratory diagnosis
- Dipsticks not recommended - poor diagnostic accuracy
- Urinalysis:
  - Presence of bacteria/nitrites and/or WBC not diagnostic of UTI as common finding in the elderly
  - Absence of WBCs in urine rules out UTI
- Do not start antibiotics before urine sample collected
- ≥ 3 organisms typically implies contamination



For more directions and guidance: AMMI Canada www.ammi.ca | #SymptomFreeLetItBe

Discussion for “Antibiotics given for diseases which are not due to bacteria”

Case 3:

- 65F diabetic who presents with what appears to be community acquired pneumonia
- CRB-65 = 1; No oxygen
- Choice of antibiotics:
- A) Amoxicillin-clavulanate
- B) Amoxicillin with doxycycline
- C) Levofloxacin or moxifloxacin
- D) Azithromycin or Clarithromycin

Section 2: Antibiotics which are unnecessarily broad for the condition being treated

Antibiotics which are unnecessarily broad for the condition being treated

- CAP being treated with piperacillin-tazobactam, or carbapenems
  - *See INESS guidelines → amoxicillin + doxycycline should suffice for majority of patients*
  - *https://www.inesss.qc.ca/fileadmin/doc/INESSS/Outils/GUO/Anglo/Guide_Pneumo_Adulte_EN_Web.pdf*
- Most COPDE being treated with respiratory quinolines
  - *FDA has removed indication for acute bronchitis due to belief harm>benefits*
  - *Evidence supporting antibiotics for COPD in outpatients is "low"*
    - Doxycycline, macrolide, amoxicillin, TMP/SMX probably all equal "evidence"
- Piperacillin-tazobactam or carbapenem for cellulitis
- IV vancomycin in patients with "low risk" of MRSA

Case 4:

- 35F presents with fever, rigors, chills, right sided flank pain, and dysuria. Had been having burning in the urine for about 5 days prior but thought it would get better on its own. Blood pressure is 110 systolic, heart rate 90
- Scenario 1: No prior information
- Assuming oral therapy, which would you choose?
- A) Amoxicillin-clavulanate
- B) TMP-SMX
- C) Ciprofloxacin
- D) Cefixime (or ceftriaxone if in ER)

Case 4:

- 35F presents with fever, rigors, chills, right sided flank pain, and dysuria. Had been having burning in the urine for about 5 days prior but thought it would get better on its own. Blood pressure is 110 systolic, heart rate 90
- Scenario 2: 3 months ago had an *E. coli* in her urine which was **ciprofloxacin resistant**
- Assuming oral therapy, which would you choose?
- A) Amoxicillin-clavulanate
- B) TMP-SMX
- C) Ciprofloxacin
- D) Cefixime (or ceftriaxone if in ER)

What is the risk of resistance?

Utility of prior cultures in predicting antibiotic resistance of bloodstream infections due to Gram-negative pathogens: a multicentre observational cohort study

D.R. MacFadden [1,*], B. Coburn [1], N. Shah [3], A. Robicsek [4], R. Savage [2], M. Elligsen [5], N. Daneman [1,6]

Clinical Microbiology and Infection 24 (2018) 493–499

- Patient level
  - Previous resistance in clinical cultures (by drug)

Characteristic	Test characteristic			
	Sensitivity	NPV	Specificity	PPV
Overall	0.50 (0.47–0.54)	0.86 (0.85–0.88)	0.92 (0.91–0.93)	0.66 (0.61–0.70)
Antibiotic-specific resistance				
Ceftazidime	0.44 (0.34–0.53)	0.86 (0.83–0.89)	0.92 (0.89–0.95)	0.59 (0.48–0.70)
Ceftriaxone	0.60 (0.53–0.68)	0.81 (0.77–0.85)	0.87 (0.84–0.91)	0.71 (0.63–0.78)
Ciprofloxacin	0.59 (0.51–0.66)	0.82 (0.78–0.86)	0.89 (0.85–0.92)	0.71 (0.63–0.79)
Meropenem	0.37 (0.22–0.51)	0.94 (0.92–0.96)	0.96 (0.94–0.97)	0.43 (0.26–0.59)
Piperacillin/tazobactam	0.40 (0.30–0.50)	0.87 (0.84–0.90)	0.94 (0.92–0.96)	0.61 (0.49–0.73)
Tobramycin/gentamicin	0.39 (0.27–0.50)	0.86 (0.82–0.90)	0.96 (0.93–0.98)	0.68 (0.54–0.83)

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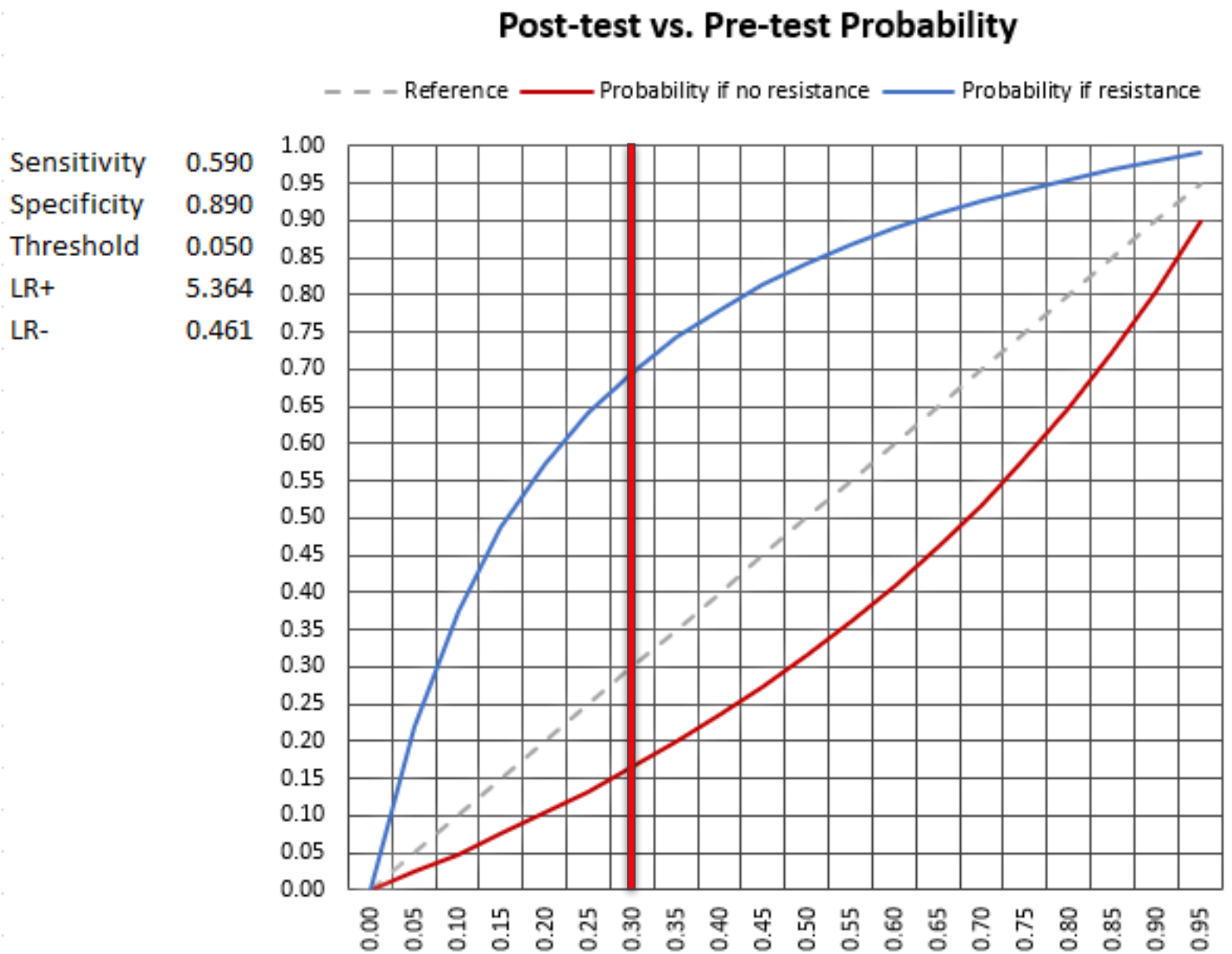
- NPV/PPV depend on your local prevalence!
- Example for ciprofloxacin


Post-test vs. Pre-test Probability
Reference
Probability if no resistance
Probability if resistance
Sensitivity 0.590
Specificity 0.890
Threshold 0.050
LR+ 5.364
LR- 0.461
1.00
0.95
0.90
0.85
0.80
0.75
0.70
0.65
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0.55
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0.00 0.05 0.10 0.15 0.20 0.25 0.30 0.35 0.40 0.45 0.50 0.55 0.60 0.65 0.70 0.75 0.80 0.85 0.90 0.95

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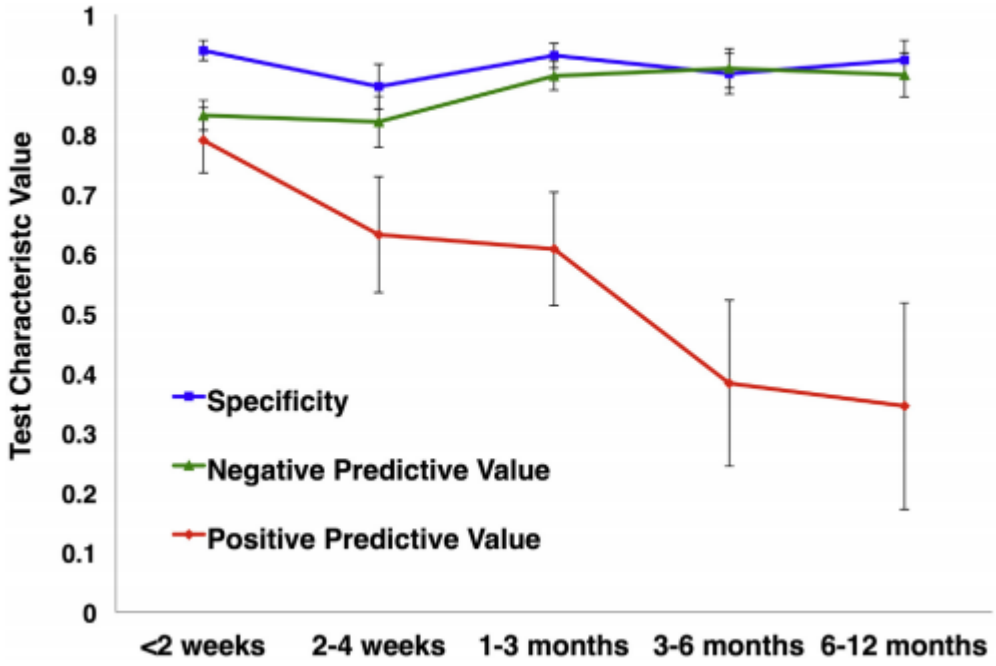
- Patient level
  - Previous resistance as a function of time



M[i]4 Interdisciplinary Initiative in Infection and Immunity

Increasing Evidence of the Nephrotoxicity of Piperacillin/Tazobactam and Vancomycin Combination Therapy—What Is the Clinician to Do? FREE

Richard R Watkins ✉, Stan Deresinski

Clinical Infectious Diseases, Volume 65, Issue 12, 15 December 2017, Pages 2137–2143, https://doi.org/10.1093/cid/cix675

Published: 29 July 2017 **Article history** ▾

- Vancomycin has a risk of nephrotoxicity which is probably augmented when combined with certain beta-lactams (e.g. piperacillin-tazobactam)
- The goal of empiric vancomycin is mainly to cover MRSA
  - *MRSA remains "rare" in Canada*
  - *Prevalence depends on ID syndrome*
  - *Therefore need to cover empirically will depend on clinical presentation, any known patient epidemiology, and severity of illness*

Can I avoid vancomycin?

- Clinical presentation with MRSA unlikely cause?
- Patient not in septic shock?
- Patient not known to have MRSA?

MRSA colonization status as a predictor of clinical infection: A systematic review and meta-analysis

Guillaume Butler-Laporte[a,*], Samuel De L'Étoile-Morel[b], Matthew P. Cheng[a], Emily G. McDonald[b,c], Todd C. Lee[a,b,c,**]

[a] Division of Infectious Diseases, Department of Medicine, McGill University Health Center, Montréal, Canada
[b] Division of Internal Medicine, Department of Medicine, McGill University Health Center, Montréal, Canada
[c] Clinical Practice Assessment Unit, McGill University Health Centre, Montréal, Canada

Journal of Infection 77 (2018) 489–495

Table 2
LRTI: lower respiratory tract infection, MRSA: methicillin resistant *Staphylococcus aureus*, SSI: surgical site infection, SSTI: skin and soft tissue infection. Graphs of post-test probability as a function of prevalence are included in the supplement.

Including all organisms or when the organism is unknown, what does a MRSA colonization swab say about				
Infectious syndrome	MRSA prevalence (%) below which the negative predictive value exceeds 90% (95% CI)	MRSA prevalence (%) below which the negative predictive value exceeds 95% (95% CI)	MRSA prevalence (%) above which the positive predictive value exceeds 50% (95% CI)	Median and range of MRSA prevalences in included studies (%)
The risk of MRSA infection?[4,21,22,32,44,46]	22.9 (19.8–26.8)	12.4 (10.5–14.8)	18.6 (12.2–24.4)	6.1 (4.4–10.3)
The risk of MRSA bacteremia?[22,46]	27.1 (21.2–36.8)	15.1 (11.3–21.6)	12.5 (6.4–19.6)	3.4 (2.6–4.1)
The risk of MRSA LRTI?[22–27,29,37,43,46]	31.3 (23.6–40.5)	17.8 (12.8–24.4)	11.3 (9.0–13.7)	7.7 (3.1–10.9)
The risk of MRSA SSI?[31,33,34]	17.0 (7.0–28.9)	9.0 (3.5–16.2)	31.2 (9.9–61.6)	16.4 (10.1–28.6)
The risk of MRSA SSTI?[22,30,35,36,38–40,46,47]	18.7 (14.1–25.3)	9.8 (7.2–13.8)	11.9 (9.4–15.2)	33.3 (13.2–73.1)
Knowing that *S. aureus* is the pathogen, what does a MRSA colonization swab say about				
Infectious syndrome	MRSA prevalence (%) below which the negative predictive value exceeds 90%	MRSA prevalence (%) below which the negative predictive value exceeds 95%	MRSA prevalence (%) above which the positive predictive value exceeds 50%	Range of MRSA prevalences in included studies (%)
The risk of MRSA bacteremia?[13,19,41,42]	20.7 (14.6–28.7)	11.1 (7.5–16.0)	8.1 (2.5–18.4)	21.1 (8.1–28.9)
The risk of MRSA SSTI?[28,36,38,40]	19.4 (10.9–35.7)	10.4 (5.5–20.8)	17.1 (8.8–36.0)	57.4 (45.3–77.1)

Discussion – Section 2

Section 3 - Antibiotics by the vein when mouth will do

Antibiotics by the vein when mouth will do

1 **Don't routinely prescribe intravenous forms of highly bioavailable antimicrobial agents for patients who can reliably take and absorb oral medications.**

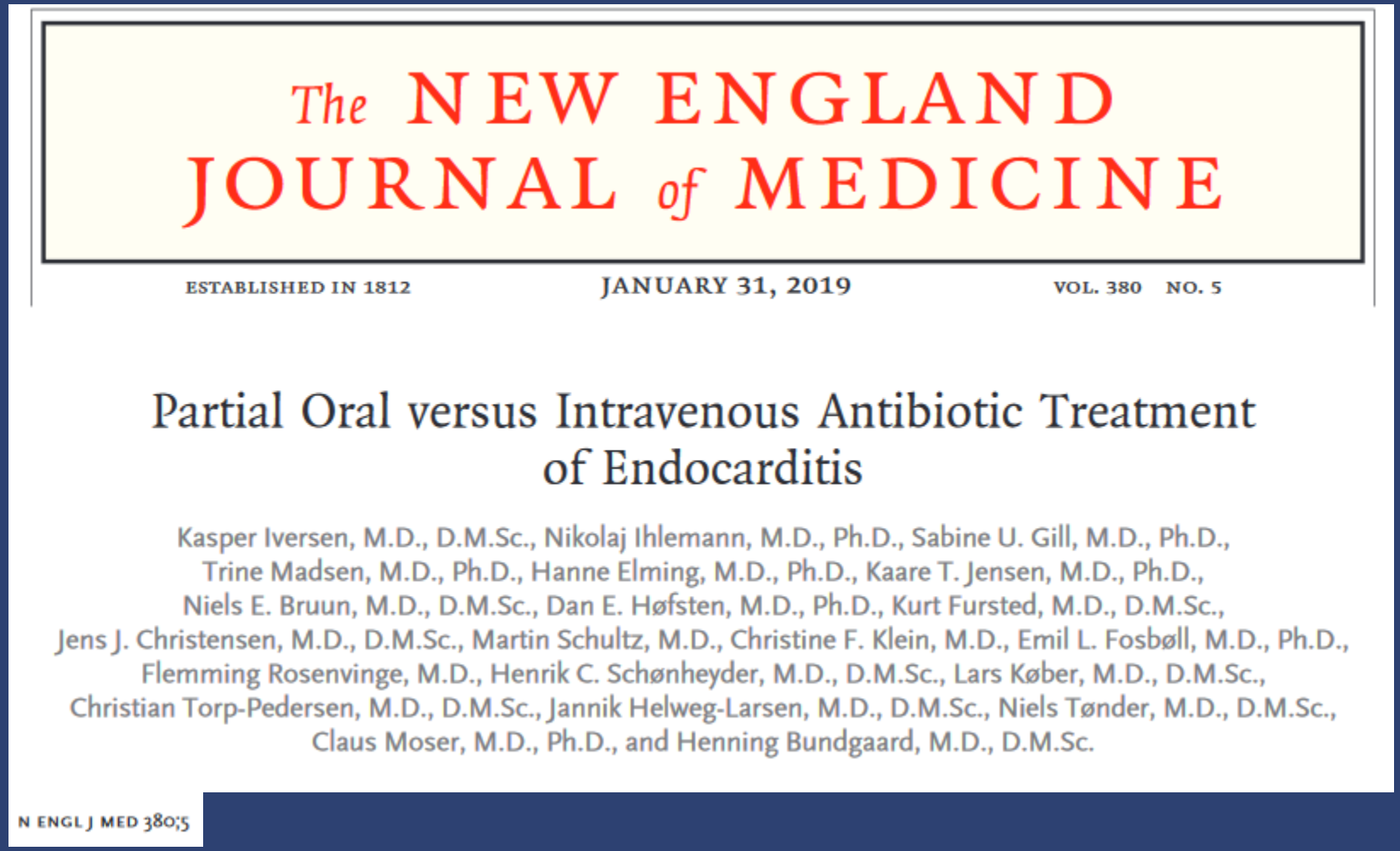
Antimicrobials such as fluoroquinolones, trimethoprim-sulfamethoxazole, clindamycin, linezolid, metronidazole and fluconazole have excellent bioavailability and only rarely need to be administered intravenously. Use of oral formulations of these medications reduces the need for placement and maintenance of venous access devices and their associated complications.

Sources:

Centers for Disease Control and Prevention. Core elements of antimicrobial stewardship programs [Internet]. Atlanta, GA: US Department of Health and Human Resources, CDA; 2014 [cited 2015 Jul 10].

Dellit TH, et al. Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America guidelines for developing an institutional program to enhance antimicrobial stewardship. Clin Infect Dis. 2007 Jan 15;44(2):159-77. PMID: 17173212.

Antibiotics by the vein when mouth will do



The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JANUARY 31, 2019 VOL. 380 NO. 5

Partial Oral versus Intravenous Antibiotic Treatment of Endocarditis

Kasper Iversen, M.D., D.M.Sc., Nikolaj Ihlemann, M.D., Ph.D., Sabine U. Gill, M.D., Ph.D., Trine Madsen, M.D., Ph.D., Hanne Elming, M.D., Ph.D., Kaare T. Jensen, M.D., Ph.D., Niels E. Bruun, M.D., D.M.Sc., Dan E. Høfsten, M.D., Ph.D., Kurt Fursted, M.D., D.M.Sc., Jens J. Christensen, M.D., D.M.Sc., Martin Schultz, M.D., Christine F. Klein, M.D., Emil L. Fosbøll, M.D., Ph.D., Flemming Rosenvinge, M.D., Henrik C. Schønheyder, M.D., D.M.Sc., Lars Køber, M.D., D.M.Sc., Christian Torp-Pedersen, M.D., D.M.Sc., Jannik Helweg-Larsen, M.D., D.M.Sc., Niels Tønder, M.D., D.M.Sc., Claus Moser, M.D., Ph.D., and Henning Bundgaard, M.D., D.M.Sc.

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Antibiotics by the vein when mouth will do

ORIGINAL ARTICLE

Oral versus Intravenous Antibiotics for Bone and Joint Infection

H.-K. Li, I. Rombach, R. Zambellas, A.S. Walker, M.A. McNally, B.L. Atkins, B.A. Lipsky, H.C. Hughes, D. Bose, M. Kümin, C. Scarborough, P.C. Matthews, A.J. Brent, J. Lomas, R. Gundle, M. Rogers, A. Taylor, B. Angus, I. Byren, A.R. Berendt, S. Warren, F.E. Fitzgerald, D.J.F. Mack, S. Hopkins, J. Folb, H.E. Reynolds, E. Moore, J. Marshall, N. Jenkins, C.E. Moran, A.F. Woodhouse, S. Stafford, R.A. Seaton, C. Vallance, C.J. Hemsley, K. Bisnauthsing, J.A.T. Sandoe, I. Aggarwal, S.C. Ellis, D.J. Bunn, R.K. Sutherland, G. Barlow, C. Cooper, C. Geue, N. McMeekin, A.H. Briggs, P. Sendi, E. Khatamzas, T. Wangrangsimakul, T.H.N. Wong, L.K. Barrett, A. Alvand, C.F. Old, J. Bostock, J. Paul, G. Cooke, G.E. Thwaites, P. Bejon, and M. Scarborough, for the OVIVA Trial Collaborators*

N ENGL J MED 380;5

Section 4: Antibiotic duration

Case 4:

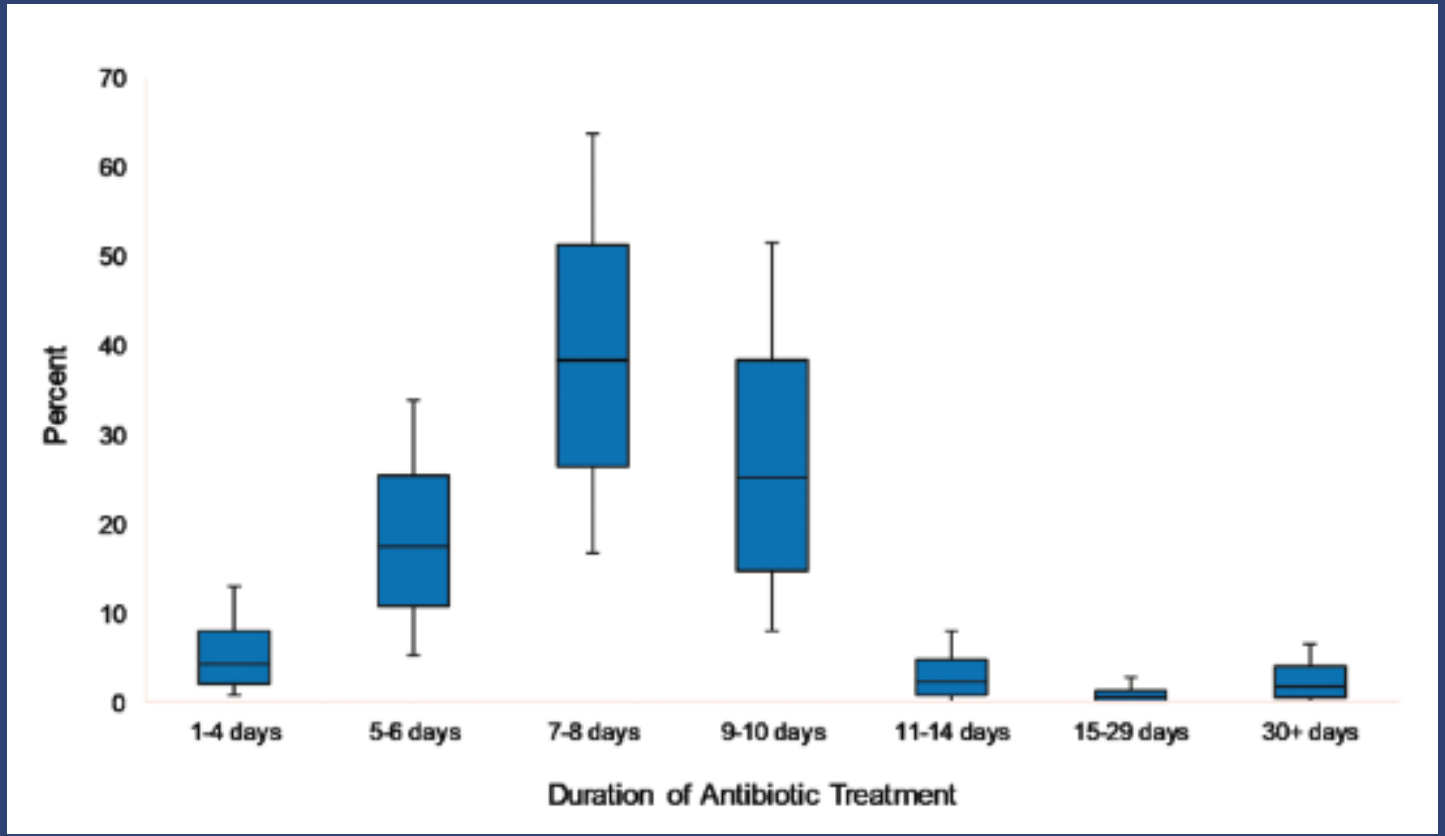
- 35F presents with fever, rigors, chills, right sided flank pain, and dysuria. Had been having burning in the urine for about 5 days prior but thought it would get better on its own. Blood pressure is 110 systolic, heart rate 90
- You start antibiotics and she feels better in about 48 hours
- What duration of total therapy should the patient receive?
- A) 5 days
- B) 7 days
- C) 10 days
- D) 14 days

Late-career Physicians Prescribe Longer Courses of Antibiotics

Cesar I. Fernandez-Lazaro,[1,2] Kevin A. Brown,[1,3] Bradley J. Langford,[1] Nick Daneman,[1,4,5] Gary Garber,[1,6] and Kevin L. Schwartz[1,3,7]

[1]Infection Prevention and Control, Public Health Ontario, Toronto, Canada; [2]Department of Biomedical and Diagnostic Sciences, University of Salamanca, Spain; and [3]Dalla Lana School of Public Health, University of Toronto, and [4]Division of Infectious Diseases, Department of Medicine, Sunnybrook Health Sciences Centre, University of Toronto, Canada; [5]Institute of Health Policy, Management and Evaluation, University of Toronto, Canada [6]Department of Medicine, Ottawa Hospital Research Institute, Canada; and [7]Department of Medicine, St. Joseph's Health Centre, Toronto, Canada

Predictors of Prolonged Antibiotic Courses • CID 2019:XX (XX XXXX)



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Predictors of Prolonged Antibiotic Courses • CID 2019:XX (XX XXXX)

Table 2. Bivariate and Multivariable Logistic Regression Models Using Generalized Estimating Equation Evaluating Predictors of Prolonged Antibiotic Courses

		Bivariate Analyses		Multivariate Logistic Regression	
Variables	Proportion of Prolonged Antibiotic Courses (Mean ± Standard Deviation)	Crude OR	95% CI	Adjusted OR	95% CI
Physician variables (N = 10 616)					
Gender					
Male	36.7% ± 19.3%	**1.13**	(1.09–1.16)	1.02	(0.96–1.08)
Female	34.0% ± 16.5%	Ref.	Ref.	Ref.	Ref.
Career stage					
Late career (>24 years)	38.6% ± 19.8%	**1.44**	(1.39–1.49)	**1.48**	(1.38–1.58)
Mid-career (11–24 years)	34.4% ± 17.2%	**1.19**	(1.15–1.24)	**1.25**	(1.16–1.34)
Early career (<11 years)	30.5% ± 13.9%	Ref.	Ref.	Ref.	Ref.

Section 4: Antibiotics given for too long

- Treating for only "as long as necessary" strikes the best balance between safety and efficacy
- But what is "necessary"?
- The reliance on multiples of 7 and 14 have more to do with ancient Roman calendar decisions than scientific evidence
- Clear evolving evidence from RCTs that "less is more" than we used to think
  - *At least 40 RCTs in various disease states*

Antibiotics are given for too long

- Adapted from Noah Wald-Dickler and Brad Spellberg, Short Course Antibiotic Therapy—Replacing Constantine Units with "Shorter Is Better", Clinical Infectious Diseases January 2019

Diagnosis	Short (d)	Long (d)	Result
Community Acquired Pneumonia	3 or 5	7, 8, or 10	Equal
Hospital Acquired/Ventilator Associated Pneumonia	7-8	14-15	Equal
Complicated Urinary Tract Infections/Pyelonephritis	5 or 7	10 or 14	Equal
Complicated/Post-Operative Intra- Abdominal Infections	4 or 8	10 or 15	Equal
Gram Negative Bacteremia	7	14	Equal
Acute Exacerbation of Chronic Bronchitis/Chronic Obstructive Pulmonary Disease (meta-analysis of 21 trials)	≤5	≥7	Equal
Acute Bacterial Skin and Skin Structure Infections (Cellulitis/Major Abscess)	5-6	10	Equal
Chronic Osteomyelitis	42	84	Equal
Empiric Neutropenic Fever	Afebrile and stable x 72h	Afebrile and stable x 72 h and with absolute neutrophil count > 500 cells/uL	Equal

Stewardship: Shorter = Better

A

Diagnosis	Short (d)	Long (d)	Result	#RCTs
CAP	3-5	5-14	Equal	10
VAP	8	15	Equal	2
Pyelo	5 or 7	10 or 14	Equal	7
Intra-abd	4	10	Equal	2
GNB Bacteremia	7	14	Equal	2*
AECB	≤5	≥7	Equal	>20
Cellulitis	5-6	10	Equal	4**
Chronic Osteomyelitis	42	84	Equal	2
Septic Arthritis	14	28	Equal	1
Ortho Implant w/removal	28	42	Equal	1
Neutropenic Fever	AFx72 h	+ANC>500	Equal	1
P. vivax Malaria	7	14	Equal	1

*GNB bacteremia also in UTI/cIAI RCTs; **3 cellulitis RCTs equal, 1 (low dose oral flucox) ↑relapses; refs at https://www.bradspellberg.com/shorter-is-better

What can we do to use antibiotics more wisely? Summary

- Stop giving antibiotics for diseases which are not due to bacteria
  - *Most sinusitis*
  - *Viral LRTI*
  - *Symptom-Free Pee – Let it be!*
- Antibiotics which are unnecessarily broad for the condition being treated
  - *Follow INESS guidelines (or develop your own)*
  - *Avoid knee-jerk escalation to broader beta-lactams or MRSA coverage*

What can we do to use antibiotics more wisely? Summary

- Antibiotics by the vein when mouth will do
  - *Avoid IV use of highly bioavailable*
  - *Evolving evidence for use of high dose oral stepdown from hospital to avoid complications (and costs) of IV*
- Antibiotics given for too long
  - *Why use 2 when 1 (week) will do?*
  - *Don't be a slave to Constantine!*

Open Discussion

Thank you

Questions and comments welcome

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