# Pneumonia Facts and UTI Myths

#### Nathan Shively, MD

Medical Director, Antimicrobial Stewardship Program
Allegheny Valley Hospital

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# **Learning Objectives**

- Identify appropriate workup and empiric treatment for patients with pneumonia.
- Distinguish asymptomatic bacteriuria from urinary tract infection (UTI), and identify first-line treatments for UTI.



#### **Outline**

- · Pneumonia classification and diagnostics
- · CAP/HAP/VAP, and the death of HCAP
  - Which of these does my nursing home patient have and how do I treat it?
- Asymptomatic bacteriuria
  - When to treat
  - More importantly, when not to treat
- Urinary tract infection
  - First line therapy



Pneumonia Fact #1:
Not all patients with pneumonia need antibiotics.



# **Microbiology of CAP**

- More than 100 microbes can cause CAP
- Bacteria
  - Streptococcus pneumoniae (generally the most common)
    - Preantibioitic era 95%
  - Now 10-15%
  - Staphylococcus aureus
  - Haemophilus influenzae Moraxella catarrhalis

  - Legionella pneumophila
  - Mycoplasma pneumoniae
  - Chlamydophila pneumoniae
  - Pseudomonas aeruginosa
  - Risk factors: Structural lung disease, bronchiectasis
    Gram-negative enteric bacilli

  - Klebsiella pneumoniae
    - Alcoholics



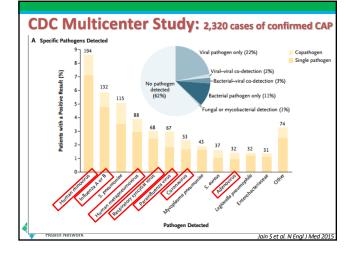
Restrepo, Chest 2008 Jain et al. N Engl J Med 2015

# **Microbiology of CAP**

- Viruses are common
  - Influenza
  - Rhinovirus, RSV, parainfluenza, adenovirus, human metapneumovirus, coronavirus



Restrepo, Chest 2008 Jain S et al. N Engl J Med 2015



# **Specific Populations**

- ICU vs non-ICU
  - S. pneumoniae
    - (8% vs. 4%)
  - S. aureus
    - (5% vs. 1%)
  - Enterobacteriaceae • (3% vs. 1%)
- > 65 years old:
  - 5 x incidence of influenza and S. pneumoniae
  - 10x incidence of rhinovirus



# Pneumonia Fact #2: HCAP is dead.



#### **Definitions** Hospital-acquired pneumonia (HAP) - Occurs within 48 hours or more after admission - Not incubating at the time of admission Ventilator-associated pneumonia (VAP) - Occurs within 48-72 hours after endotracheal intubation Health re-associated pneumonia (HCAP) 2 d or more in the – Ré Receipt of in merapy (even outpatient), and wound care ia VAP Inc Concept of HCAP removed from 2016 IDSA/ATS HAP/VAP Guidelines of HCAP removed from 2016 IDSA/ATS CAP Guidelines and abandoned in 2019 IDSA/ATS CAP Guidelines Kalil AC et al. CID 2016 Allegheny

#### **Definitions**

- Community-acquired pneumonia (CAP)
  - Acquired outside of the hospital
  - $-\,$  Essentially, now everything that is not HAP or VAP
  - Does not include patients with immunocompromising conditions
    - · HIV/AIDs with low CD4 count
    - · Neutropenic patients
    - Transplant patients



Metlay IP et al. Am I Respir Crit Care Med 201

# What Happened to HCAP?

- Premise of "HCAP"
  - Exposure to the healthcare environment increases likelihood of infection with resistant organisms
    - MRSA and Pseudomonas
  - We should cover "HCAP" like HAP/VAP
- Reality
  - Pathogens in "HCAP" actually resemble CAP
  - After creation of "HCAP," patients received more broad-spectrum antibiotic therapy
  - Broader therapy did not improve patient outcomes
  - Conclusion: "HCAP" is not a helpful classification has been retired

Metiay IP et al. Am J Respir Crit Care Med 2015
Allegheny Chalmers ID et al. (In Infect bis 2011
Gross et al. AAC 2016

# Pneumonia Fact #3: **Nursing home patients** have community-acquired pneumonia.



# **CAP Empiric Therapy: Outpatient**

- In patients without coexisting illnesses or recent use of antibiotics

#### EXCEPT: if > 25% of pneumococci in the community exhibit macrolide resistance

- If coexisting illness, recent use of antibiotics, or > 25% resistance:
  - Amoxicillin-clavulanate + Azithromycin
  - Mild PCN allergy: Cefdinir + Azithromycin
  - IgE-mediated PCN allergy: Levofloxacin or Moxifloxacin
  - Contraindication to macrolide: Substitute doxycycline



Metlay JP et al. Am J Respir Crit Care Med 2019

# **CAP Empiric Therapy: Inpatient**

- - Ampicillin-sulbactam (Unasyn) 3G IV Q6hrs + Azithromycin 500mg IV/PO Q24hrs
- Mild PCN allergy

   Ceftriaxone 1-2G IV Q24hrs + Azithromycin 500mg IV/PO Q24hrs
- - Levofloxacin 750mg IV/PO q24h monotherapy
- Contraindication to macrolides: substitute doxycycline
- Influenza active in the community:
  - Empiric Oseltamivir even if > 48h elapsed since onset of symptoms
  - If PCR (-), discontinue antiviral
    - Note rapid antigen test has poor (40-70%) sensitivity



Metlay JP et al. Am J Respir Crit Care Med 2019 Uyeki TM et al. CID 2019

# Why Unasyn, not Ceftriaxone? Same efficacy Excellent coverage for CAP bacterial pathogens Preservation of Ceftriaxone for intra-abdominal infections

#### Why Unasyn, not Ceftriaxone?

- More collateral damage with Ceftriaxone
  - Risk factor for C. diff infection
  - Risk factor for ESBL colonization / infection
  - Risk factor for VRE colonization / infection

# Unasyn should be the beta-lactam of choice for CAP

Muto CA et al. Infect Control Hosp Epidemiol 2005 Wilcox MH et al. Journal of Antimicrobial Chemotherapy 2004 Settle CD et al. Aliment Pharmacol Ther 1998

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Asensio A et al. Clin Infect Dis 2000

Du BY et al. Intensive Care Med 2002

Eveillard MJ et al. Infect. Control Hosp Epidemiol 2002

Vin BN et al. I. Hosp Infect 2002

2002
Kim BN et al. J. Hosp. Infect 2002
Lautenbach E et al. Clin Infect Dis 2001
Lee SO et al. Infect Control Hosp Epidemiol 2004
Pesson-Silva Cl et al. J Hosp Infect 2003
Schiappa DA et al. J Infect Dis 1996

Tornieporth NG et al. Clin Infect Dis 1996 McKinnell JA et al. Infect Control Hosp Epidemiol 2012 Loeb M et al. Infect Contro. Hosp Epidemiol 1995 Fridkin SK et al. Ann Intern

Med 2001 Ostrowsky BE et al. Arch Intern

# When do patients need MRSA and Pseudomonas coverage?

- Strongest risk factors:
  - Prior isolation from the respiratory tract
  - Recent hospitalization AND parenteral antibiotics (last 90 days)
- Coverage suggestions:
  - Prior isolation of MRSA
    - Add Vancomycin or Linezolid
  - Prior isolation of Pseudomonas
  - Add Cefepime or Piperacillin-tazobactam
     Recent hospitalization AND parenteral antibiotics
    - · Nonsevere pneumonia:
      - Standard CAP therapy with diagnostics (sputum culture, MRSA nasal swab)
    - <u>Severe</u> pneumonia
  - Vancomycin and Cefepime (and Azithromycin)

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    De-escalate based on culture data

**Table 1.** 2007 Infectious Diseases Society of America/American Thoracic Society Criteria for Defining Severe

Validated definition includes either one

major criterion or three or mor minor criteria

Respiratory rate ≥ 30 breaths. Pa<sub>O2</sub>/Fi<sub>O2</sub> ratio ≤ 250 Multilobar infiltrates Confusion/disorientation Uremia (blood urea nitrogen

Leukopenia\* (white blood cell count < 4,000 cells/µl) Thrombocytopenia (platelet count < 100,000/µl) Hypothermia (core temperature < 36°C)

Hypothermia (core temperature < 36° Hypotension requiring aggressive flui resuscitation

Major criteria

Septic shock with need for vasopressors Respiratory failure requiring mechanica ventilation

\*Due to infection alone (i.e., not chemotherapy

Metlay JP et al. Am J Respir Crit Care Med 2019

# **Switch to Oral Therapy**

- Clinically stable and improving
  - Temperature ≤ 37.8
  - Heart rate ≤ 100 bpm
  - Respiratory rate ≤ 24 bpmSystolic blood pressure ≥ 90
  - Not hypoxic (defined by the guidelines as arterial oxygen
  - saturation ≥ 90% or pO2 ≥ 60 mm Hg on room air)
  - Tolerating PO
  - Normally-functioning GI tract



Mandell LA et al. Clin Infect Dis 2007

Pneumonia Fact #4: 5 days of therapy is enough for most patients.



#### **Duration for CAP**

- Multiple RCTs and meta-analyses have consistently demonstrated short-course therapy equally efficacious as compared to long-course therapy
- Guidelines suggest 5 days of therapy as long as patients achieve clinical stability at 48-72 hours
  - If MRSA or Pseudomonas pneumonia, 7 days

Allegheny Health Network Mandell LA et al. Clin Infect Dis 2007 Metlay JP et al. Am J Respir Crit Care Med 2019 https://www.bradspellberg.com/shorter-is-better Li JZ et al. Am J Med 2007

Dimopoulos G et al. Drugs 2008

Research

IAMA Internal Medicine | Original Investigation | LESS IS MOR

#### Duration of Antibiotic Treatment in Community-Acquired Pneumonia A Multicenter Randomized Clinical Trial

Ane Uranga, MD; Pedro P, España, MD; Amaia Bilbao, MSc, PhD; Jose María Quintana, MD, PhD; Ignacio Arriaga, MD; Maider Intxausti, MD; Jose Luis Lobo, MD, PhD; Laura Tomás, MD; Jesus Camino, MD Juan Nuñez, MD; Alberto Capelastegui, MD, PhD

- Validation of IDSA/ATS guideline recommendations
- 312 patients
- 5 days antibiotics (if afebrile x 48hrs and no clinical instability) vs physician-guided
- No difference in clinical success at 10 days or 30 days
- Less antibiotics in intervention group (10 days vs 5 days, p<0.001)</li>
- More readmissions in the control group (6.6% vs 1.4%, p=0.02)



Uranga A et al. JAMA Int. Med. 2016

### Summary so far...

- A lot of pneumonia is caused by viruses
- · Many patients with pneumonia don't need antibiotics
- Nursing home patients have community-acquired pneumonia
  - If they need antibiotics, most don't need Vancomycin and Cefepime



Pneumonia Fact #5: Diagnostics can help.



# **Pneumonia Diagnostics**

- CXR
- Sputum induction panel -> Sputum cultures
- Blood cultures
- Strep pneumo urine antigen
- Legionella urine antigen
- Influenza PCR / Respiratory Viral Panel
- Procalcitonin
- MRSA nasal swab



# **Pneumonia Diagnostics**

#### • Blood cultures:

- --Positive in 20-25% of inpatients with pneumococcal CAP
- --Far fewer in cases of *H. influenzae* and very rare in *M. catarrhalis*

#### Pneumococcal urinary antigen:

- --Sensitivity: 50%–80%; Specificity of > 90%
- --Positive in in 77% of patients with bacteremic pneumococcal pneumonia, 64% without bacteremia

#### Legionella urinary antigen:

- --Several urinary antigens available, all detect L. pneumophila serogroup 1
- --80-95% of community-acquired cases of legionnaires
- --Sensitivity of 70%–90% and Specificity of nearly 99% in culture-proven legionnaires
- --Positive on day one on disease, remains positive for weeks



Mandell LA et al. CID 2007; 44:S27–72

# **Pneumonia Diagnostics**

#### • Sputum gram stain and culture:

- --The earlier, the better
- --Positive in 80% of cases of pneumococcal CAP with high quality specimen (>10 WBCs/epithelial cell) if obtained within 6 hours of Abx administration
- --Legionella culture

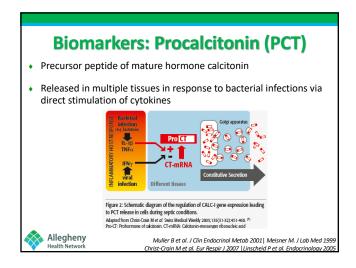
#### • Negative cultures do have value

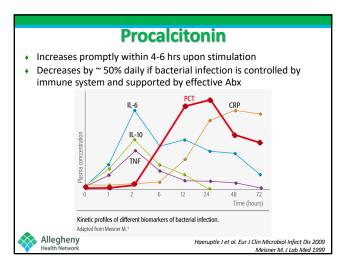
- No isolation of S. aureus or GNR means these pathogens are unlikely to be present
- Growth inhibition by antibiotics is lower with these pathogens than S. pnuemoniae

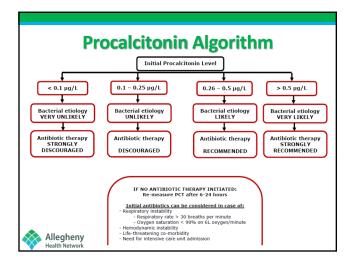


Mandell LA et al. CID 2007; 44:S27–72 Musher DM et al. N Engl J Med 2014 Musher DM et al. Clin Infect Dis 2004

Pathogens	Sensitivity		Specificity
	Prospective	Retrospective	Prospective
Adenovirus	88.9%	100%	98.3%
Coronavirus HKU1	95.8%	n/a	99.8%
Coronavirus NL63	95.8%	n/a	100%
Coronavirus 229E	100%	100%	99.80%
Coronavirus OC43	100%	100%	99.60%
Human Metapneumovirus	94.6%	n/a	99.2%
Human Rhinovirus/Enterovirus	92.7%	95.7%	94.6%
Influenza A	90.0%	n/a	99.8%
Influenza A/H1	n/a	100%	100%
Influenza A/H3	n/a	100%	100%
Influenza A/H1-2009	88.9%"	100%	99.6%
Influenza B	n/a	100%	100%
Parainfluenza Virus 1	100%*	97.1%	99.9%
Parainfluenza Virus 2	87.4%*	100%	99.8%
Parainfluenza Virus 3	95.8%	100%	98.8%
Parainfluenza Virus 4	100%"	100%	99.9%
Respiratory Syncytial Virus	100%	n/a	89.1%
Bordetella pertussis	100%*	94.6%	99.90%
Chlamydophila pneumoniae	100%*	100% <sup>†</sup>	100%
Mycoplasma pneumoniae	100%"	84.4%	100%







Effect of procalcitonin-guided antibiotic treatment on mortality in acute respiratory infections: a patient level meta-analysis

Philips Schuetz', Yannick Wez', Rumon Soge', Miljom Christ-Crain, Daiana Stok, Michael Tamm, Lila Boodma, Charles Euse, Michael Wolff, Juna Chaste, Florenz Tobach, Kintine B Kristoffera, Olif Burkhauft, Tobas Web, Seefan Schweder, Vandack Hobe, Long Wei, Hener C Bucher, Djullad Annae, Kornad Rehndar, Am Seleky, Angels Brunch, Ferre Dumas, Maternik Misser, Define We Lange, Rodos Dockberdon, Carolina F Olivera, Vern Marusk-Stayloud, Alesis Verdruft, Bianca Begle, Bian Cao, Yolyu Shehad, Jern-Uilki S Jerner, Caspar Corti, Jos AH van Den, Albertus Besirbuira, Armand RJ Girbes, Evellen de Jong, Matthias Brief', Best Moeiler

6708 patients, 26 eligible trials, 12 countries

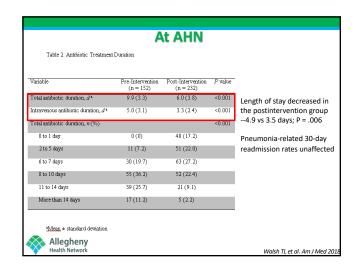
First meta-analysis to show a mortality benefit

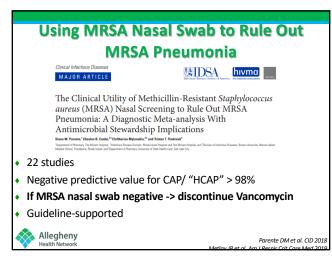
286 deaths (9%) in PCT-guided patients, 336 (10%) in controls, p=0.037

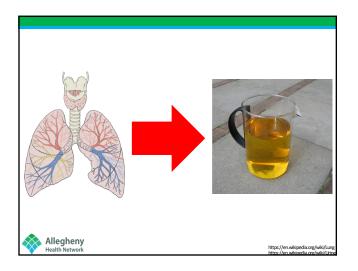
Reduction in antibiotic exposure (5.7 vs 8.1 days)

Reduction in antibiotic-related side-effects (16% vs 22%)

Schuetz P et al. Lancet Infect Dis 2018; 18: 95–







# UTI Myth #1: A positive urine culture or abnormal urinalysis (UA) always indicates a UTI and requires antibiotics.

# FACT: Symptoms are needed to diagnose a UTI

- Asymptomatic Bacteriuria (ASB)
  - Isolation of a specified quantitative count of bacteria in an appropriately collected urine specimen obtained from a person WITHOUT symptoms or signs referable to urinary infection
- Simply stated:
  - Bacteria in the urine
  - $10^2$  vs  $10^3$  vs  $10^5 \rightarrow$  does not matter
  - NO urinary symptoms or signs of systemic infection



Rubin RH et al. Clin Infect Dis 1992 Nicolle LE et al. Clin Infect Dis 200:

# **Definition of UTI**

- Acute uncomplicated UTI
  - **SYMPTOMATIC** bladder infection characterized by frequency, urgency, dysuria, or suprapubic pain in a nonpregnant woman with normal GU tract
- **Complicated UTI** 
  - **SYMPTOMATIC** urinary infection involving either the bladder or the kidneys in individuals with functional or structural GU tract abnormalities
- UTI is a CLINICAL diagnosis
  - Cannot diagnose a UTI by looking at a UA/culture
  - Need history and objective data to differentiate colonization from infection



Hooton TM et al. Infect Dis Clin North Am 1997 Nicolle LE. Drugs Aging 2001

# How common is asymptomatic bacteriuria?

Healthy Women	1-5%	32%
Dungmont Monton		34/0
Pregnant Women	2-10%	30-70%
Diabetic Women	9-27%	70%
Diabetic Men	1-11%	
Elderly Women (community)	11-16%	
Elderly Men (community)	4-19%	
Elderly Women (long-term care)	25-50%	90%
Elderly Men (long-term care)	15-40%	
Hemodialysis	28%	90%
Long-term indwelling catheter	100%	50-100%

Allegheny

# Who to Screen/Treat for ASB

- Pregnant women (A-I)
  - 20 30x increased risk of developing pyelonephritis during pregnancy
  - Antibiotic therapy for ASB during pregnancy decreases risk of subsequent pyelonephritis from 20 - 30% to 1 - 4%
  - Higher rates of premature delivery and low birth weight infants
- Before transurethral resection of the prostate (TURP) (A-I)
- Other urologic procedures for which mucosal bleeding is anticipated (A-III)
  - High rates of post-procedure bacteremia and sepsis
  - Bacteremia occurs in up to 60% of ASB patients who undergo TURP



Nicolle LE at al. Clin Infect Dis 2005

Smaill F. Cochrane Database Syst Rev 2001 Situation: Continue Education Syst Rev 2001 Elder HA et al. Am J Obstet Gynecol 1971 Grabe M. J IVal 1987 Grabe Met al. Eur J Clin Microbiol 1987 Allan WR et al. Brit J Urol 1985

#### Whom NOT to Screen/Treat for ASB

- Everyone else
- Prospective, randomized controlled trials of treating ASB have been done in:
  - Diabetics
  - Long-term care facility patients
  - Outpatient elderly
  - Long-term catheter use
  - Spinal cord injury patients
  - Renal transplant patients (> 1 month from transplant)
- Treating <u>DOES NOT</u> decrease the rate of symptomatic infection or alter long term outcomes
- Treating <u>DOES</u> increase cost, adverse effects, and resistance

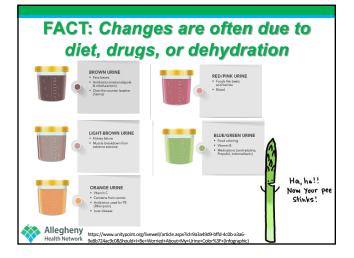


Clin Infect Dis. 2005:40(5):643-54

# UTI Myth #2:

Cloudy or malodorous urine is always diagnostic of a UTI.





# UTI Myth #3:

UTI with no symptoms except for a change in mental status or delirium.



#### FACT: Change in mental status or delirium is a non-specific syndrome and requires an exploration of alternative causes

- Dehydration
- Metabolic derangements
- Constipation
- Head trauma
- Polypharmacy
- Sensory deprivation
- Urinary retention
- Environmental changes

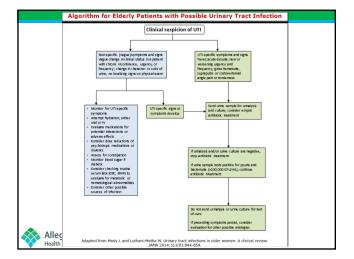


## What to do when the patient can't give a history?

- Updated McGeer Criteria (2012)
- Both 1 & 2 must be met:
- At least 1 of following signs and symptoms:
  - a) Dysuria OR acute pain, swelling, tenderness of testes/epididymis/prostate
  - b) Fever or leukocytosis AND at least 1 of following:
  - i. <u>CVAT</u>, <u>suprapubic pain</u>, gross hematuria, new/increased incontinence, urgency, frequency
     c) If no fever/leukocytosis, then 2 or more of following:
  - - Suprapubic pain, gross hematuria, new/increased incontinence, urgency, frequency
- One of the following:
  - a) ≥ 10<sup>5</sup> CFU/mL of no more than 2 organisms in a voided urine
  - b) ≥ 10<sup>2</sup> CFU/mL of any number of organisms in an in/out cath sample



Stone ND et al, Infect Control Hosp Epidemiol, 201

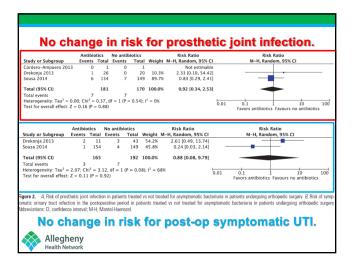


# UTI Myth #4: My patient needs a screening UA / urine culture before hip replacement. Allegheny

#### FACT: Only patients undergoing <u>UROLOGIC</u> surgery should be screened and treated for ASB.

 IDSA guidelines recommend AGAINST screening for or treating ASB in patients undergoing elective nonurologic surgery





# UTI Myth #5:

Better safe than sorry - we should treat for UTI when we aren't sure. A few days of an antibiotic will not hurt.



# ASB Treatment Harm Number Collateral damage Clostridium difficile infection (CDI) Drug-drug interactions Adverse drug events Worsening antimicrobial resistance Increased healthcare costs

Stone ND et al, Infect Control Hosp Epidemiol, 2012. https://www.sign.ac.uk/assets/sign88.pdj

# If they really, truly, have a UTI

- UA + Urine culture
- Empiric treatment for the most likely pathogens
  - E. coli in 75-95%

E. coli Susceptibilities Across AHN				
Sensitive to Ciprofloxacin	Sensitive to TMP/SMX	Sensitive to Nitrofurantoin		
64-79%	69-80%	91-97%		

- If concerned for pyelonephritis / sepsis with urinary source
  - Ceftriaxone 2G IV Q24hrs
- If uncomplicated cystitis

1 <sup>st</sup> Line Empiric Therapy Recommendations				
Regimen	Duration			
Nitrofurantoin (monohydrate/macrocrystals) 100mg PO BID  Not recommended for CrCl <40mL/minute	5 Days			
Cephalexin 500mg PO BID	3-7 Days			
Allegheny Health Network				

# **Take Home**

#### <u>Pneumonia</u>

- Viral > bacterial
- Procalcitonin can help
- HCAP is dead

Allegheny Health Network

- If antibacterials needed:
  - Amp-sulbactam / Azithro for most
  - Duration = 5 daysCover MRSA/pseudomonas:
    - If isolated previously
    - If severe pneumonia and recent admission with IV antibiotics

#### UTI

- +UA / Urine culture ≠ UTI
- Need SYMPTOMS to diagnose UTI
- Only treat asymptomatic bacteriuria in pregnancy and before UROLOGIC surgeries
- ASB very common in elderly
  - Confusion in elderly with +UA / Urine culture ≠ UTI
  - Treatment risks >> benefits (NNTH = 3)
- If true UTI, treat empirically with Nitrofurantoin or Keflex

