Urinary Tract Infections

(an emerging evidence of a Urinary Microbiome…Is urine sterile?)

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Overview

- Defining infection
- UTI diagnosis, treatment and emerging research
- The discovery of the urinary microbiome
- Conclusions
Defining Infection
Urinary Tract Infection

- Microbial pathogens in the urinary tract

- Classified by
  - Site
    - Bacteriuria (urine)
    - Cystitis (bladder)
    - Pyelonephritis (kidney)
  - Severity
    - Uncomplicated
    - Complicated
      - Pregnancy, diabetes, symptoms >7d, hospital acquired, renal disease, obstruction, catheter/instrumentation, anatomic abnormality, childhood UTI, transplant/immunosuppression

Risk Factors

- Genetic
  - ABO blood group

- Biologic
  - Congenital abnormality, urinary tract obstruction, estrogen deficiency, recent antimicrobial exposure

- Behavioral
  - Diaphragm, spermicide, recent intercourse

- Prior UTI

Diagnosis

- 28 year old woman presents to clinic with chief complaint: “I have a UTI”
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What is the probability that she has a UTI?

- A. 5%
- B. 20%
- C. 50%
- D. 80%
- E. 95%
Diagnosis

- Pretest probability
Diagnosis

- Pretest probability = incidence in population
Diagnosis

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Diagnosis

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  - Pretest P(UTI) in adult woman = 5%
  - Pretest P(UTI) in woman presenting to clinic with complaint of UTI = 50%

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- Pretest \( P(\text{UTI}) = 50\% \)

*What is the most important diagnostic tool in determining her probability of having a UTI?*

- A. History
- B. Physical exam
- C. Urinalysis
- D. Pain score
Diagnosis

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- Pretest P(UTI) = 50%
  - History – evaluation of her symptoms
Diagnosis

- Pretest $P(\text{UTI}) = 50\%$
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Which of the following is the most important symptom to consider in diagnosing a UTI?

- A. Dysuria
- B. Hematuria
- C. Frequency
- D. Vaginal discharge
- E. Vaginal bleeding
Diagnosis

- Pretest P(UTI) = 50%
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<th>95% CI</th>
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<td>50% - 53%</td>
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Adapted from Giesen LG, et al. BMC Fam Pract 2010.
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Does the evidence support empirically treating this patient for a UTI?

- Yes
- No

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<td>77%</td>
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<td>Discharge without dysuria</td>
<td>4%</td>
</tr>
<tr>
<td>Dysuria or frequency with vaginal discharge/irritation</td>
<td>9%</td>
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- No

Diagnosis

- Urine testing
  - Urinalysis
    - Nitrites
    - Leukocyte esterase
    - Negative UA does NOT exclude UTI
  - Urine culture
    - **GOLD STANDARD**
    - >10^5 or 10^3 CFU

Diagnosis

We should almost always send a urine culture

• True
• False
Diagnosis

*We should almost always send a urine culture*

- True
- False

Diagnosis

**Back Pain or Fever?**
- Yes: Probability of UTI Moderate (~60%) and Probability of Pyelonephritis Unknown
  - Consider Urine Culture to Establish Diagnosis
  - Consider Empirical Treatment
- No: Low to Intermediate Probability of UTI (~20%)
  - Pelvic Examination (Including Cervical Cultures When Appropriate) and Urine Culture to Establish Diagnosis

**Vaginal Discharge?**
- Yes: High Probability of UTI (~90%)
  - Consider Empirical Treatment Without Urine Culture
- No: Low to Intermediate Probability of UTI (~20%)
  - Consider Urine Culture or Close Clinical Follow-up and Pelvic Examination (Including Cervical Cultures When Appropriate)

**Most Elements of the History (and Physical Examination†) Positive?**
- Yes: High Probability of UTI (~80%)
  - Consider Empirical Treatment Without Urine Culture
- No: Perform Dipstick Urinalysis

**Dipstick Results Positive?**
- Yes: High Probability of UTI (~80%)
  - Consider Empirical Treatment Without Urine Culture
- No: Low to Intermediate Probability of UTI (~20%)

Treatment

- Considerations
  - Recent antimicrobial exposure
  - Collateral damage, drug interactions, side effects
  - Complicated versus uncomplicated
Asymptomatic Bacteriuria
Asymptomatic Bacteriuria

• Treatment is only indicated if:
  • Pregnant
  • Undergoing urologic procedure with anticipated mucosal bleeding
  • Catheter-acquired bacteriuria has persisted >48 hours after catheter removal

ACOG Practice Bulletin #91 2016.
Uncomplicated Cystitis

- 1st Line

ACOG Practice Bulletin #91 2016.
Uncomplicated Cystitis

1\textsuperscript{st} Line
- Nitrofurantoin 100mg bid x 5 days (CrCl > 40-60mL/min)
- TMP/SMX 160/800mg bid x 3 days

ACOG Practice Bulletin #91 2016.
Uncomplicated Cystitis

1st Line
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Alternatives
- Fosfomycin 3mg x 1 dose
- Cefuroxime 250mg bid x 3 days
- Ciprofloxacin 250mg po x 3 days (no coumadin)
- Trimethoprim 100mg bid x 3 days

NOT recommended for empiric therapy
- Amoxicillin or ampicillin due to poor efficacy and high prevalence of resistance

ACOG Practice Bulletin #91 2016.
Complicated Cystitis

- 1\textsuperscript{st} Line
  - Ciprofloxacin 500mg bid x 5-10 days
  - Levofloxacain 750mg daily x 5-10 days

- IV therapy
  - Levofloxacain 500mg, ceftriaxone 1g, ertapenem 1g, gentamycin/tobramycin daily x 5-10 days

- NOT recommended for empiric therapy
  - Nitrofurantoin, TMP/SMX, fosfomycin

- NOT recommended
  - Moxifloxacain (attains low urinary levels)

ACOG Practice Bulletin #91 2016.
Acute Pyelonephritis

- Must obtain **urine culture**

- **Outpatient**
  - Ciprofloxacin 500mg bid x 7 days
  - Levofloxacin 750mg bid x 7 days
    - Add 1g ceftriaxone if fluoroquinolone resistance >10%
  - TMP/SMX 160/800mg bid x 14 days
    - Add 1g ceftriaxone IV if susceptibility unknown

- **Inpatient**
  - IV ceftriaxone / ceftazidime / piperacillin+tazobactam

Special Considerations

- **ESBL**
  - Carbapenems (ertapenem, meropenem, imipenem, and doripenem)
  - May consider nitrofurantoin or fosfomycin if susceptibility is shown

- **Enterococcus**
  - Ampicillin 1g q6h or Amoxicillin 500mg q8h
Unusual Pathogens

- **Fungal UTI**
  - Most likely asymptomatic colonization
  - Consider second culture, change catheter
  - If healthy, no treatment and recheck in 2-3 months
  - If unhealthy/symptomatic
    - Fluconazole 200 - 400mg po x 14 days
    - Alternative = amphotericin B IV or via bladder irrigation

- **Viral UTI (CMV, adenovirus)**
  - Supportive therapy +/- cidofivir

Special Populations

- Pregnancy
  - Most common bacterial infection
  - Increased risk of pyelonephritis due to mechanical compression of ureters (hydroureter) and reduced ureteral tone
  - 30% risk of pyelonephritis with untreated asymptomatic bacteriuria
  - Associated with adverse outcomes

UTI in Pregnancy

- Check urine culture if UA positive or suspect infection
  - Remember: *streptococci infection is nitrite negative*
- If urine culture positive
  - Treat asymptomatic bacteriuria and do a test of cure
  - Mixed gram+ bacteria, lactobacilli and staphylococcus (except S saprophyticus) are presumed contaminants

ACOG Guidelines for Prenatal Care 2012.
ACOG Committee Opinion #494 2015.
UTI in Pregnancy

- Treatment options
  - Penicillins
  - Erythromycin
  - Cephalosporins
  - Nitrofurantoin or sulfonamides (only in 1st trimester if no suitable alternative available)

ACOG Committee Opinion #494 2015.
Recurrent UTI

- ≥ 3 UTIs in 12 months / ≥ 2 UTIs in 6 months
- Risk factors
  - Genetic, biologic, behavioral
- Treatment
  - Urine culture
  - Same as for acute cystitis

Recurrent UTI

- Prevention
  - Daily or postcoital antibiotics (NNT = 1.85)
  - Other therapies
    - Vaginal estrogen
    - Cranberry tablets
    - Methenamine
    - Probiotics

Hospital Acquired

- 40% of hospital-acquired infections
- 80% indwelling urethral catheter
- Mandatory reporting with zero tolerance

Hospital Acquired

- Prevent UTI by
  - Avoiding catheters
  - Limiting catheters
  - Being aware of catheters
    - 28% of time team (MDs, medical students) were not aware patient had a catheter
    - As training level increased, awareness of catheterization decreased

Perioperative UTI

- Significant risk in patients undergoing pelvic surgery
- Risk of UTI between 5% to 35%
  - Significant risk factor = postoperative catheterization
  - Retention occurs in up to 58% of women undergoing pelvic surgery

Perioperative UTI

- Are prophylactic antibiotics effective?
  - 2004 RCT nitrofurantoin vs placebo daily with suprapubic catheterization for a median of 10-11 days
    - Antibiotic reduced UTI at 6-8 weeks after surgery
  - 2014 RCT nitrofurantoin vs placebo daily while using transurethral catheterization or CISC for a median of 1-2 days
    - Antibiotics did not reduce UTI within 3 weeks after surgery

Overview

- Defining infection
- UTI diagnosis, treatment and emerging research
- The discovery of the urinary microbiome
- Conclusion
So... back to the definition of infection
Human Microbiome Project

- “Urogenital” samples:
  - Mid vagina
  - Posterior fornix
  - Vaginal introitus
The Next Food Fad Is Coming: Feed Your Microbiome

Get to know your microbes

Change Your Microbiome, Change Yourself

Explore Your Microbiome
GET SEQUENCED

New research finds that people emit their own personal microbial cloud

How Your Gut Microbiome Influences Your Mental and Physical Health

Microbe Mix May Play Role In Preterm Birth Risk

Updated September 14, 2015 · 9:15 AM ET
Published August 17, 2015 · 3:03 PM ET
• 2012 study assessing urinary bacteria in women without known UTI by bacterial culture, light microscopy and 16S rRNA gene sequencing
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Bacterial bladder communities of different types do exist in women
2013 study examining urinary microbiota in healthy men and women ages 26 to 90 years by 16S rRNA amplification
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- A “core” microbiome could potentially exist
- The bacterial genera in women are more heterogeneous
- Bacterial genera changes with age
- Conventional microbiological methods are inadequate to fully identify ~2/3rds of the bacteria identified in this study
Urinary Microbiome

- Since 2013 research has emerged showing that...
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  - Bacteria are associated with a range of LUTS including nocturia, urgency and bladder pain

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Urinary Microbiome

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  - Bacteria are associated with a range of LUTS including nocturia, urgency and bladder pain
  - A urinary microbiome with living bacterial species exists in the adult female bladder
  - Clinical response to solifenacin (Vesicare) is related to baseline microbiome/microbiota

Comparison of average bacterial sequence abundance in urine by treatment group and urinary tract infection outcome.

The average amount of bacterial sequences that were detected in the sequence positive urine of each randomized treatment cohort (anticholinergic vs botox) and urinary tract infection outcome cohort (positive vs negative) was calculated. The average bacterial sequence abundance profiles were similar between treatment cohorts, whereas the profiles differed between urinary tract infection outcome cohorts.

UTI, urinary tract infection.

The next step…

- Further characterize the microbiome
  - How does it change with age?
  - How does it affect LUTS and urologic diseases?
  - How can we use the microbiome to treat and improve these conditions?
Conclusions

- UTI is a common condition often diagnosable with history and symptoms alone
- Consider how your intervention/evaluation will affect your diagnostic work-up
- First line therapy for uncomplicated UTI is nitrofurantoin or TMP/SMX
- Always treat asymptomatic bacteriuria in pregnant women, otherwise do not need to treat
Conclusions

- A urinary microbiome exists
- The bacterial microbiota appears to change with age and affect LUTS and other urologic diseases
- Lots to be discovered!!!
Thank you