Urinary Tract Infections

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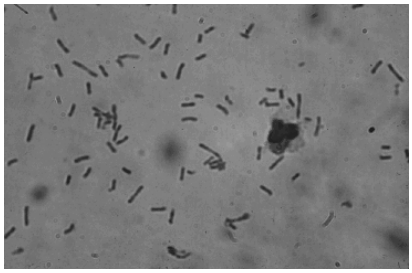
Clinical Scenario #1 : Labs

- Urinalysis: pyuria (WBC too numerous to count), RBC and bacteria present
- Urine dipstick: positive leukocyte esterase and nitrite
- Urine culture: not done
- Patient receives 3 days of TMP/SMX for UTI

Clinical Scenario #1

- 23 y.o woman presents to her doctor complaining of 1 day of increased urinary frequency, dysuria and sensation of incomplete voiding
- She is otherwise healthy, takes no medications, and is sexually active, using spermicide-coated condoms for contraception. She says she does not have fever, chills, vaginal discharge, or flank pain
- Sexually active with one partner, no hx/o sexually transmitted diseases



Gram stain of urine shows numerous Gram-negative rods.

E.coli grew from this urine specimen

Clinical Scenario #1

- She looks a little uncomfortable but is afebrile, with a normal blood pressure
- Her abdominal exam is notable for mild suprapubic tenderness, no RUQ tenderness, no costovertebral tenderness
- Pelvic exam is deferred

Urinary Tract Infections

- Definitions
- Clinical Symptoms and Diagnosis
- Microbiology and Epidemiology
- Pathogenesis
  - Host Factors
  - Bacterial Factors
- Clinical Scenario
- Treatment and Prevention

UTI: Definitions

- **Lower UTI**: cystitis, urethritis, prostatitis
- **Upper UTI**: pyelonephritis, intra-renal abscess, perinephric abscess (usually late complications of pyelonephritis)
- **Uncomplicated UTI** – Infection in a structurally and neurologically normal urinary tract. Simple cystitis of short (1-5 day) duration
- **Complicated UTI** – Infection in a urinary tract with functional or structural abnormalities (ex. indwelling catheters and renal calculi). Cystitis of long duration or hemorrhagic cystitis.

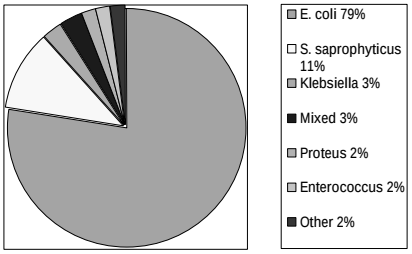
Indications for Evaluating the Urinary Tract

- Children
  - ultrasound, IVP, CT scan
- Bacteremic pyelonephritis not responding to therapy
  - ultrasound, IVP, CT scan
- Nephrolithiasis or Neurogenic Bladder
  - Ultrasound, CT, or IVP with post-voiding films
- Men with 1st or 2nd infection
  - Careful prostate examination
  - Ultrasound or IVP with post-voiding films

UTI: Clinical Symptoms and Presentation

- Cystitis in the adult:
  - Dysuria, urinary urgency and frequency, bladder fullness/discomfort
  - Hemorrhagic cystitis (bloody urine) reported in as many as 10% of cases of UTI in otherwise healthy women
- Pyelonephritis (upper UTI) in the adult:
  - Fever, sweating
  - Nausea, vomiting, flank pain, dysuria
  - Signs and symptoms of dehydration, hypotension
- A history of vaginal discharge suggests that vaginitis, cervicitis, or pelvic inflammatory disease is responsible for symptoms of dysuria (pelvic examination)
  - Important additional information includes a history of prior sexually transmitted disease (STD) and multiple current sexual partners.
- UTI in children:
  - < 2 years - enuresis, fever, poor weight gain
  - > 3 years - dysuria, lower abdominal pain

Etiology of Uncomplicated UTI in Sexually Active Women



Diagnosis of UTI

- U/A microscopic examination
  - WBC, RBC
  - Presence of bacteria
- Urine dipstick test: rapid screening test
  - leukocyte esterase test
  - Nitrate → nitrite test
- Indications for urine culture
  - Pyelonephritis
  - Children, pregnant women
  - Patients with structural abnormalities of the urinary tract

Microbial Species Most Often Associated with Specific Types of UTI's

Organism	*Acute uncomplicated cystitis*	*Acute uncomplicated pyelonephritis*	*Complicated UTI*	*Catheter-associated UTI*
E.coli	79%	89%	32%	24%
S. saprophyticus	11%	0%	1%	0%
P. mirabilis	2%	4%	4%	6%
Klebsiella spp.	3%	4%	5%	8%
Enterococcus spp.	2%	0%	22%	7%
Ps. aeruginosa	0%	0%	20%	9%
Mixed	3%	5%	10%	11%
Other*	0%	2%	5%	10%
Candida spp.	0%	0%	1%	28%
S. epidermidis	0%	0%	15%	8%

**Serratia, Providencia, Enterobacter, Acinetobacter, Citrobacter*

UTI: Epidemiology and Risk Factors by Age Group

Age in years	Females (% Prevalence)	Males (% Prevalence)
< 1	Anatomic/functional abnormalities (1%)	Anatomic/functional abnormalities (1%)
1-5	Congenital abnormalities, Vesicoureteral reflux (4.5%)	Congenital abnormalities, uncircumcised penis (0.5%)
6-15	Vesicoureteral reflux (4.5%)	Vesicoureteral reflux (0.5%)
16-35	Sexual intercourse, spermicide use, previous UTI (20%)	Anatomic, insertive anal intercourse (0.5%)
36-65	Gynecologic surgery, bladder prolapse (35%)	Prostate hypertrophy, obstruction, catherization (20%)
>65	Estrogen deficiency and loss of lactobacilli (40%)	All of the above; urinary catheters (35%)

UTI in Women: Factors Predisposing to Infection

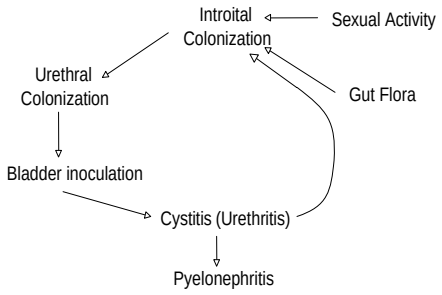
- Short urethra
- Sexual intercourse & lack of post coital voiding
- Diaphragm, spermicide use
- Estrogen deficiency
- P_1 blood group - upper UTI

Pathogenesis of UTI

- Hematogenous Route
- Ascending Route
  - Colonization of the vaginal introitus
  - Colonization of the urethra
  - Entry into the bladder
  - Infection

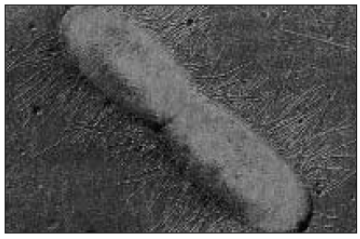
Host Factors Predisposing to Infection

- Extra-renal obstruction
  - Posterior urethral valves
  - Urethral strictures
- Renal calculi
- Incomplete bladder emptying
- Neurogenic bladder
- Immunocompromised individuals (e.g. DM, transplant recipients)



Bacterial Virulence Factors-I

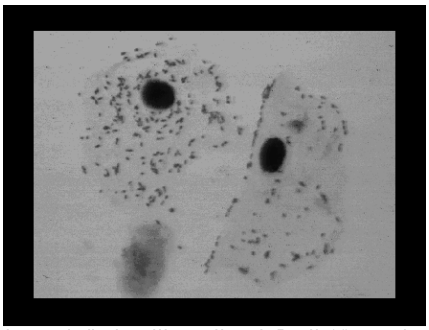
- Enhanced adherence to receptors on uroepithelial cells
  - **Type 1 fimbriae:** mediate binding to uroplakins, mannosylated glycoproteins on the surface of bladder uroepithelial cells
  - **P fimbriae:** bind to galactose dissaccharide on the surface of uroepithelial cells and to P blood group antigen (D-galactose-D-galactose residue) on RBCs
    - 97% of women with recurrent pyelo are P1 blood group (+)
    - Higher prevalence of P-fimbriated *E.coli* in cystitis-causing strains than in strains from asymptomatic persons (60% vs. 10%)
- Phase variation:
  - Type 1 fimbriae increase susceptibility to phagocytosis, P-fimbriae block phagocytosis
  - Type 1 down-regulated, Type P upregulated in strains that cause upper-tract infections (PAP gene expression triggered by temperature, [glucose], concentration of certain amino acids)



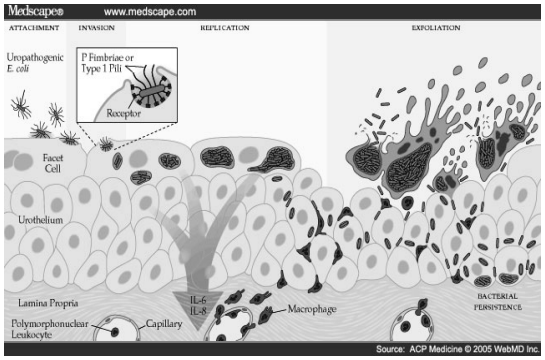
Electron microscopic view of an *E.coli* showing the fimbriae (pili) bristling from the bacterial cell wall

Antibacterial Host Defenses

- Urine flow and micturition
- Urine osmolality and pH
- Inflammatory response (PMNs, cytokines)
- Inhibitors of bacterial adherence
  - Bladder mucopolysaccharides
  - Secretory immunoglobulin A



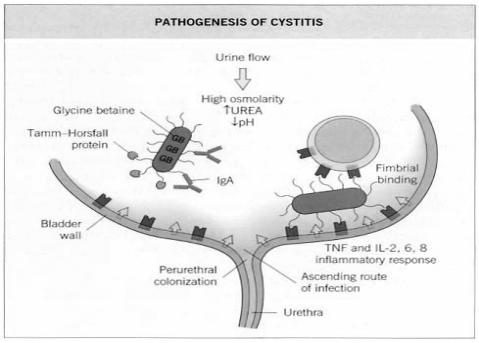
Increased adhesion with uropathogenic E. coli Adherence of uropathogenic Escherichia coli onto uroepithelial cells. Courtesy of Agnès Labigne, MD, Institut Pasteur, Paris.



The pathophysiology of infection by uropathogenic Escherichia coli in bladder epithelial cells

Bacterial Virulence Factors-II

- Flagella- enhanced motility
- Production of hemolysin ⟶ induces pore formation in cell membrane
- Production of aerobactin (a siderophore) ⟶ iron acquisition in the iron-poor environment of the urinary tract



From Cohen & Powderly: Infectious Diseases, 2nd ed., 2004

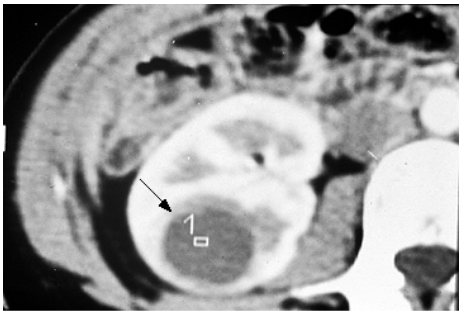
Clinical Scenario #2

- 43 y.o woman with DM presents to the ER complaining of chills, nausea and low back pain for the past 2 days. Earlier in the week she developed increased urinary frequency and dysuria.
- Recognizing the symptoms of UTI she took two days of TMP/SMX but was unable to finish treatment because of nausea and vomiting
- Past medical history is notable for frequent UTIs treated with TMP/SMX and a history of Diabetes Mellitus
- No hx/o STDs, no vaginal discharge

Renal abscess on ultrasonography Ultrasonic examination of the kidney showing an abscess cavity (arrow). The internal echoes within the lesion can also be seen with a malignancy but not with a simple cyst. Courtesy of Alain Meyrier, MD.

Clinical Scenario #2

- She looks unwell and appears uncomfortable
- She is febrile to 101.2, tachycardic to 100 with a BP 100/60
- On exam her mucous membranes are dry; there is suprapubic tenderness, and severe right flank and right costovertebral tenderness
- Urinalysis, Urine microspic examination and urine culture are performed: pyuria, hematuria, bacteriuria
- Blood cultures are drawn
- Patient is admitted to the hospital for IV antibiotics and pain management



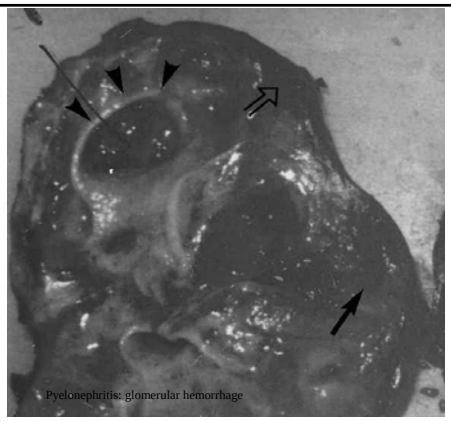
Renal abscesss on CT scan CT scan showing a large renal abscess with internal echoes in the right kidney (arrow). Courtesy of Alain Meyrier, MD.

Clinical Scenario #2

- The next day, urine and blood cultures show Gram-negative rods
- After 72 hours of hydration and intravenous antibiotics your patient is still febrile and repeat urine examination is still notable for pyuria and bacteriuria
- You are concerned about
  - urinary obstruction
  - intrarenal/perinephric abscess
  - infection with resistant organism
- Microbiology lab informs you that the the pathogen is an *E.coli* sensitive to fluoroquinolones, resistant to TMP/SMX
- Renal CT is notable for a large renal abscess
- Diagnosis: pyelenephritis complicated by a renal abscess in a diabetic patient

UTI: Upper Tract Disease

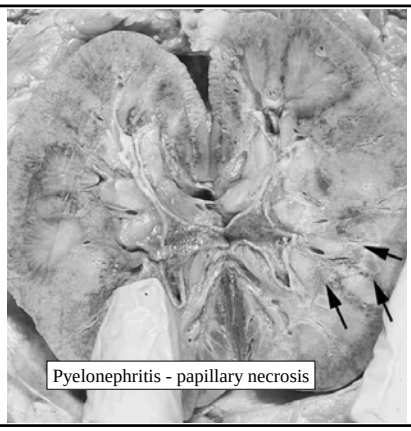
- Symptoms suggestive of upper tract disease (pyelonephritis):
  - Fever (usually greater than 101º F.),
  - Nausea, vomiting, and
  - Pain in the costovertebral areas
  - Urinary frequency, urgency and dysuria
  - Renal abscess: patients with urnary tract abnormalities, diabetic patients
- Evaluation: urine culture, +/- blood cultures,
  - Imaging if no improvement
- Microbiology: *E.coli*, and *Citrobacter*, *Pseudomonas aeruginosa*, *Enterococci*, *Staphylococcus* spp.
- Initial therapy: intravenous antibiotics for 10-14 days (perinephric abscess treat longer, +/- drainage)



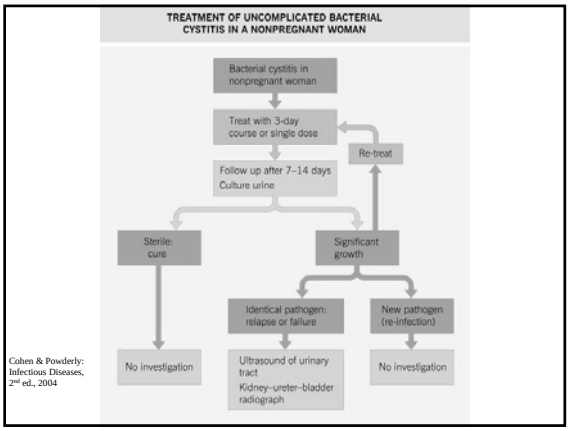
Pyelonephritis: glomerular hemorrhage

Empiric Antimicrobials

- Choice of antimicrobial agents
  - Primary excretion routes through the urinary tract
  - Achieve high concentration in urine and vaginal secretions
  - Inhibit *E.coli*, the primary pathogen
- Short course (3-day) therapy for uncomplicated infections
- Longer duration (10-14 days) for complicated infection (e.g. pyelonephritis)
- Oral vs. intravenous agents (TMP/SMX, Fluoroquinolones)



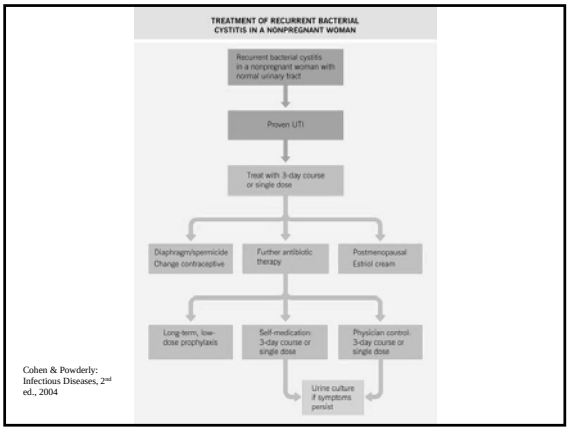
Pyelonephritis - papillary necrosis



Cohen & Powderly: Infectious Diseases, 2nd ed., 2004

Treatment: General Principles

- Quantitative cultures may be unnecessary before treatment of typical cases of acute uncomplicated cystitis.
- Culture urine in patients with upper UTI, complicated UTI, or with treatment failure.
- Susceptibility testing is necessary in all recurrent or complicated infections, perhaps not for uncomplicated cases.
- Identify or correct factors predisposing to infection
  - Obstruction, calculi
  - Diabetic patients who are at risk for recurrent infections, pyelonephritis and perinephric abscesses
- Recurrent infections common in young women (20% by 6 months).
  - Majority are exogenous infections rather than failure to cure initial infection
- Duration of therapy depends on the site and duration of the infection.



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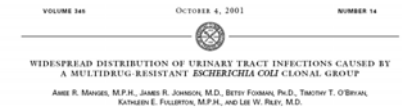
Treatment of Asymptomatic Bacteriuria

- Pregnant women
- Patients with neurological or structural abnormality of the urinary tract
- Patients undergoing urologic surgery

Antimicrobial Resistance



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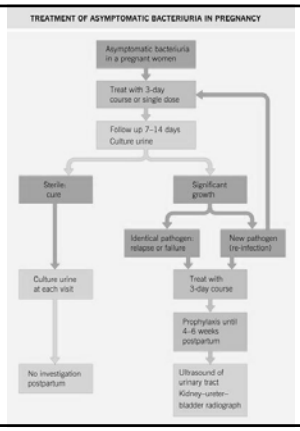
WIDESPREAD DISTRIBUTION OF URINARY TRACT INFECTIONS CAUSED BY A MULTIDRUG-RESISTANT *ESCHERICHIA COLI* CLONAL GROUP

AMEE R. MANGES, M.P.H., JAMES R. JOHNSON, M.D., BETSY FOXMAN, PH.D., TIMOTHY T. O'BRYAN, KATHLEEN E. FULLERTON, M.P.H., AND LEE W. RILEY, M.D.

- Reports of increased resistance to TMP/SMX
- Regional variation
- Rates between 18-40%



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Prevention of Recurrent UTI

- Risk factors for recurrent uncomplicated UTI
  - P1 blood group positive; postmenopausal status; diabetes
  - Recent antimicrobial use
  - Behavioral risk factors (spermicide use, new partner, first UTI <15 y.o.)
- Prevention Strategies
  - Contraception
  - Postcoital voiding and increased fluid intake
  - Cranberry juice (sexually active women with previous UTI)
  - Antibiotic prophylaxis
    - >2 symptomatic UTIs within six months or >3 over 12 months
    - Postcoital prophylaxis vs. continuous prophylaxis vs. self-treatment