

Urinary Tract Infections

Magdalena Sobieszczyk, MD, M.P.H.
Division of Infectious Diseases
Columbia University

Clinical Scenario #1

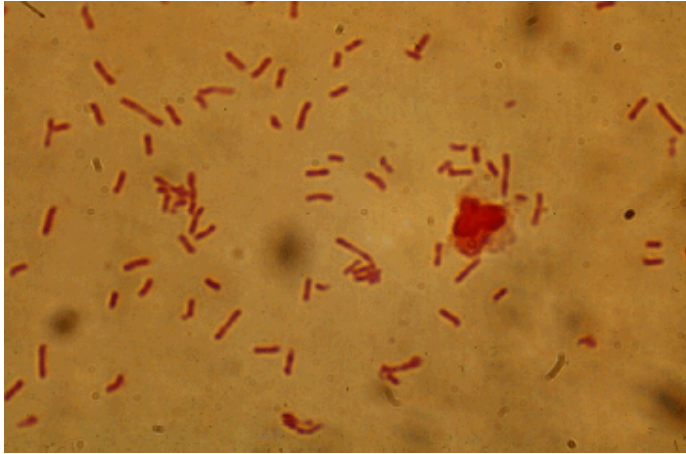
- 23 y.o woman presents to her doctor complaining of 1 day of increased urinary frequency, dysuria and sensation of incomplete voiding
- She is otherwise healthy, takes no medications, and is sexually active, using spermicide-coated condoms for contraception. She says she does not have fever, chills,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

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

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



Gram stain of urine shows numerous Gram-negative rods.
E.coli grew from this urine specimen

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 (e.g. indwelling catheters and renal calculi)
 - Cystitis of long duration or hemorrhagic cystitis.

UTI

Clinical Symptoms and Presentation in Adults

- **Lower tract: Cystitis**
 - 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
- **Upper tract: Pyelonephritis**
 - 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

- Younger than 2 years - enuresis, fever, poor weight gain
- Older than 3 years - dysuria, lower abdominal pain

Diagnosis of UTI

- U/A microscopic examination
 - WBC, RBC
 - Presence of bacteria
- Urine dipstick test: rapid screening test
 - leukocyte esterase test
 - Nitrate → nitrite test (+ in only 25%)
- Indications for urine culture
 - Pyelonephritis
 - Children, pregnant women
 - Patients with structural abnormalities of the urinary tract

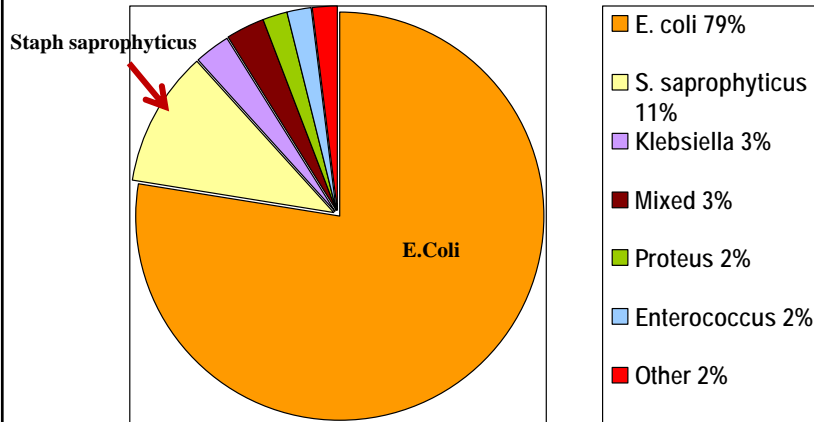
Indications for Evaluating the Urinary Tract

- 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

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Etiology of Uncomplicated UTI in Sexually Active Women



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

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

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

UTI: Epidemiology and Risk Factors by Age Group

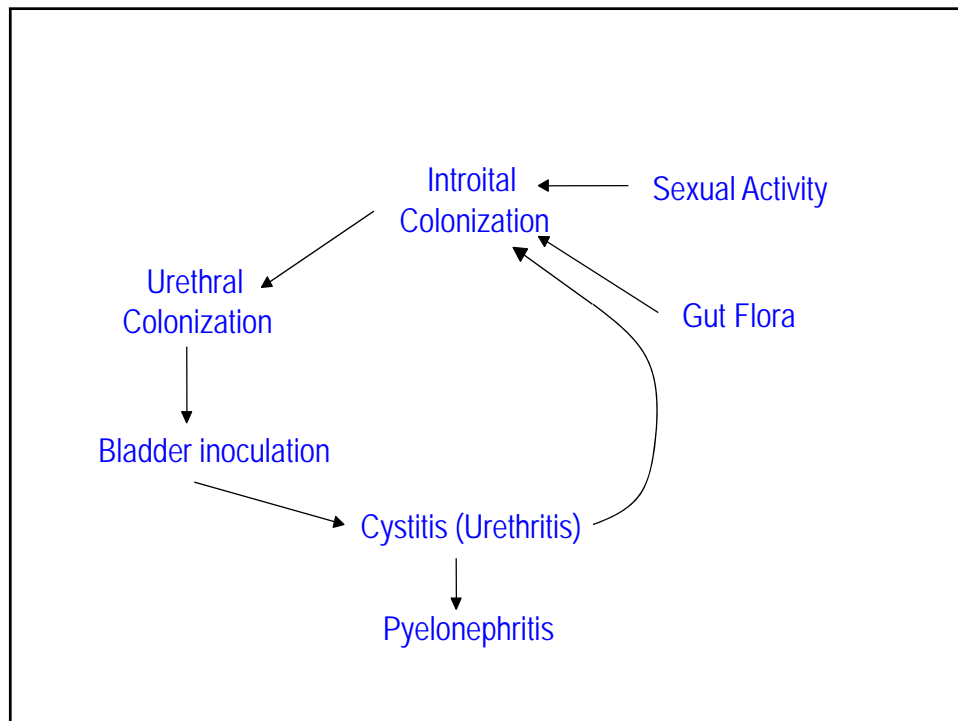
Age in years	Females (% Prevalence)	Males (% Prevalence)
< 1	Anatomic/functional abnormalities (1%)	Anatomic/functional abnormalities (1%)
1-5	Congenital abnormalities, Vesicoureteral reflux (4.5%)	Congenital abnormalities, uncircumcised penis (0.5%)
6-15	Vesicoureteral reflux (4.5%)	Vesicoureteral reflux (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, catheterization (20%)
>65	Estrogen deficiency and loss of lactobacilli (40%)	All of the above; urinary catheters (35%)

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Pathogenesis of UTI

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



UTI in Women: Factors Predisposing to Infection

- Short urethra
- Sexual intercourse & lack of post coital voiding
- Diaphragm, spermicide use
- Estrogen deficiency
- P₁ blood group - upper UTI

Host Factors Predisposing to Infection

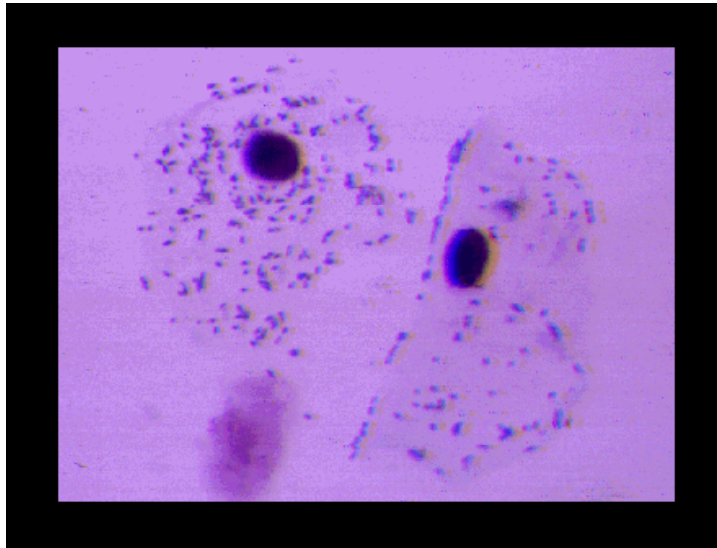
- Extra-renal obstruction
 - Posterior urethral valves
 - Urethral strictures
- Renal calculi
- Incomplete bladder emptying
- Neurogenic bladder
- Immunocompromised individuals (e.g. DM, transplant recipients)

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 disaccharide on the surface of uroepithelial cells and to P1 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
 - In strains that cause upper-tract infections: Type 1 down-regulated, Type P upregulated (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



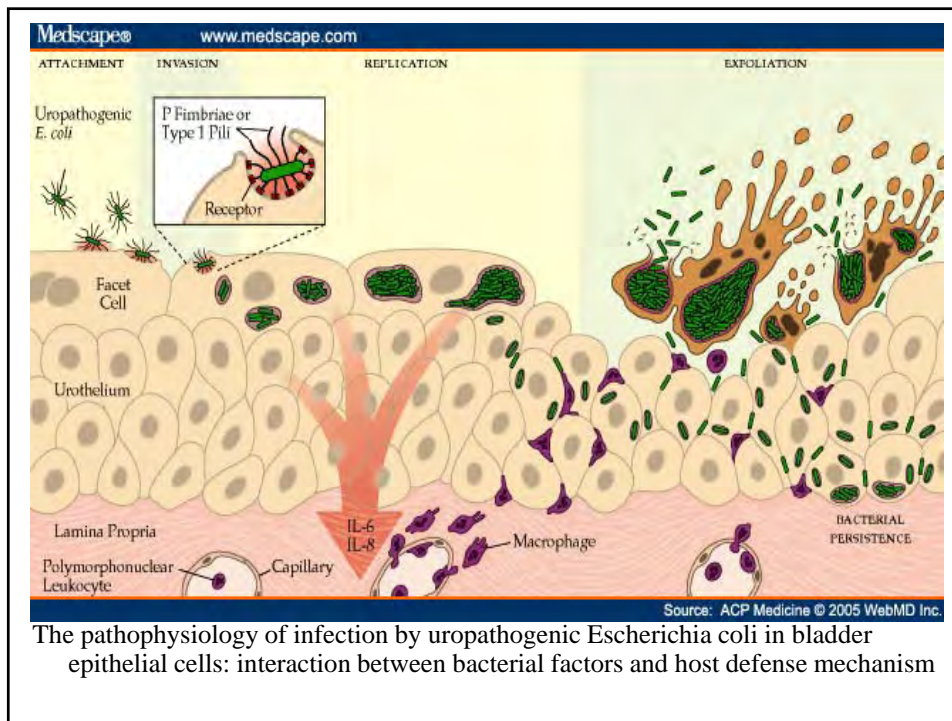
Increased adhesion with uropathogenic E. coli Adherence of uropathogenic Escherichia coli onto uroepithelial cells. Courtesy of Agnès Labigne, MD, Institut Pasteur, Paris.

Bacterial Virulence Factors-II

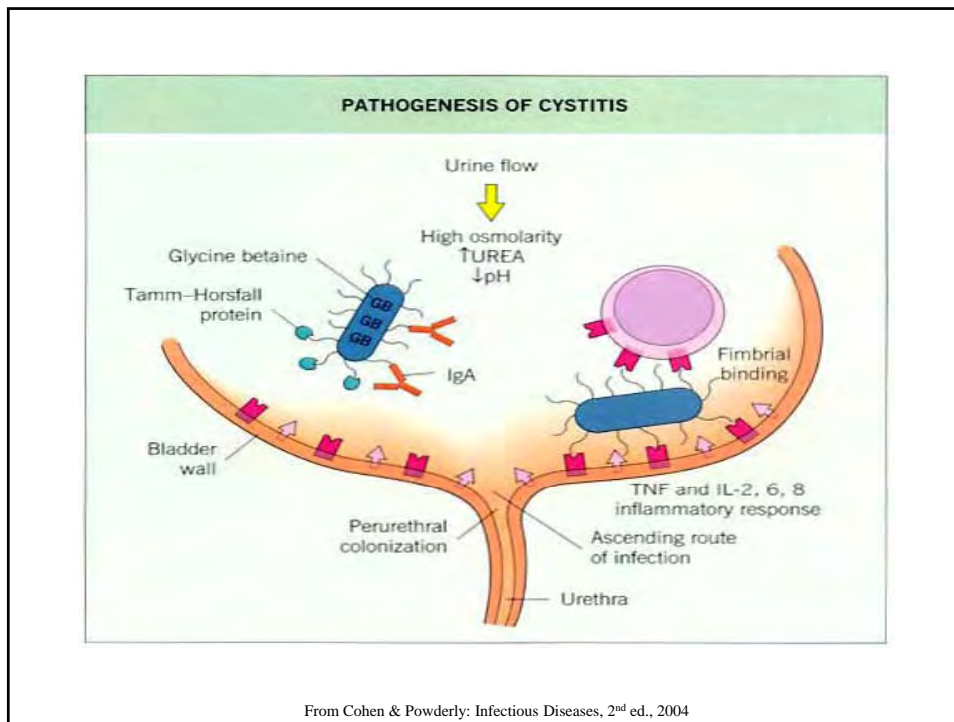
- Flagella- enhanced motility
- Production of hemolysin → induces pore formation in cell membrane → cell lysis (nutrient release)
- Production of aerobactin (a siderophore) iron → acquisition in the iron-poor environment of the urinary tract

Antibacterial Host Defenses

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



The pathophysiology of infection by uropathogenic *Escherichia coli* in bladder epithelial cells: interaction between bacterial factors and host defense mechanism



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

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 microscopic 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

Clinical Scenario #2

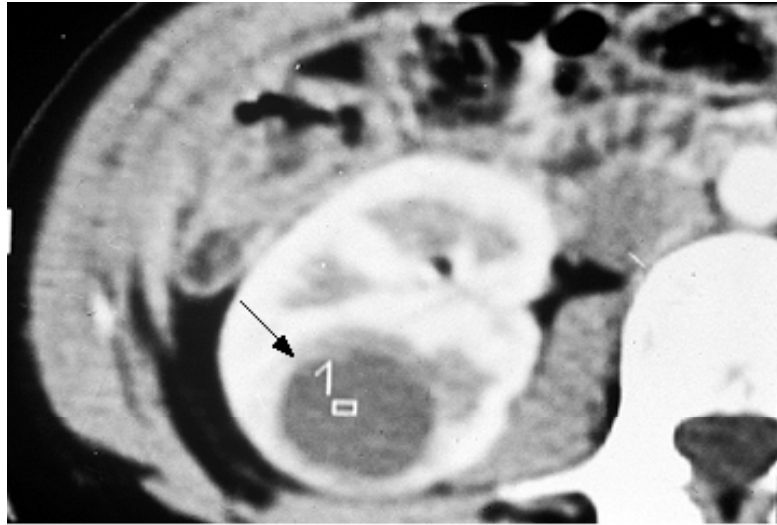
- The next day, urine and blood cultures show Gram-negative rods
- After 72 hours of hydration and intravenous antibiotics your patient is still febrile and repeat urine examination is still notable for pyuria and bacteriuria
- You are concerned about
 - urinary obstruction
 - intrarenal/perinephric abscess
 - infection with resistant organism

Clinical Scenario #2

- 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:** pyelonephritis complicated by a renal abscess in a diabetic patient



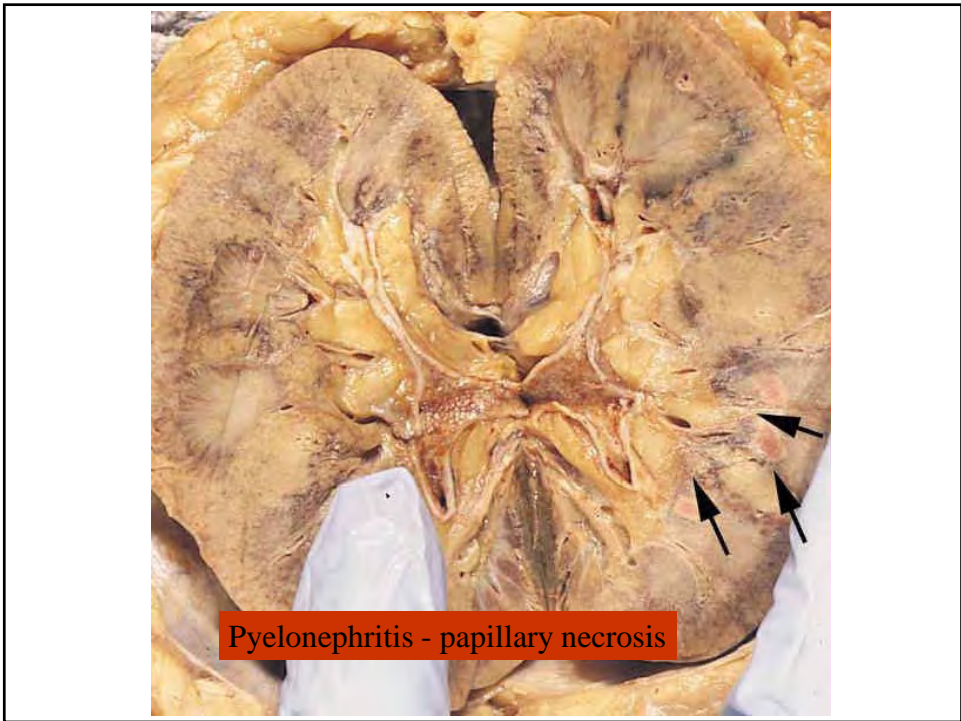
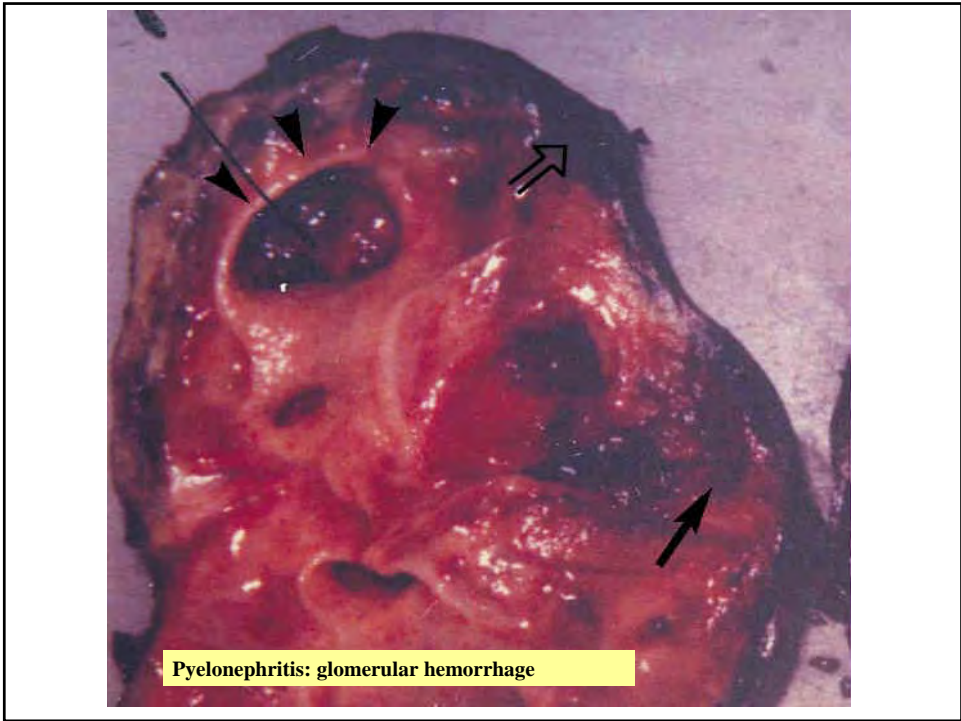
Renal abscess on ultrasonography Ultrasonic examination of the kidney showing an abscess cavity (arrow). The internal echoes within the lesion can also be seen with a malignancy but not with a simple cyst. Courtesy of Alain Meyrier, MD.



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

UTI: Upper Tract Disease

- Symptoms suggestive of upper tract disease (pyelonephritis):
 - Fever (usually greater than 101° F.),
 - Nausea, vomiting, and
 - Pain in the costovertebral areas
 - Urinary frequency, urgency and dysuria
 - Renal abscess: patients with urinary 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)



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Treatment: General Principles

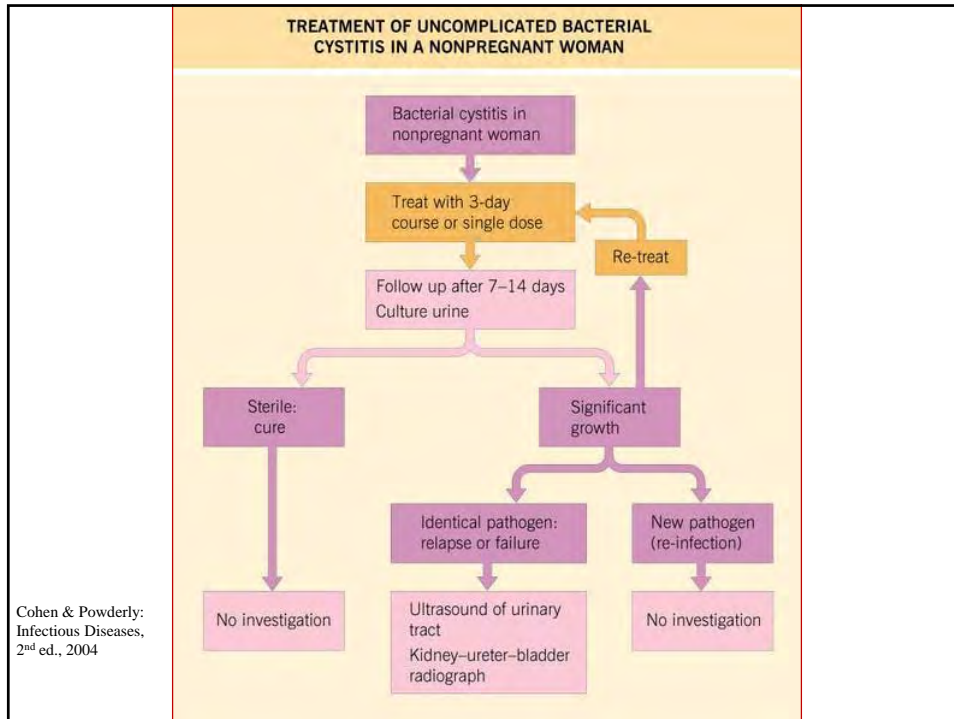
- Quantitative cultures may be unnecessary before treatment of typical cases of acute uncomplicated cystitis.
- Culture urine in patients with upper UTI, complicated UTI, or with treatment failure.
- Susceptibility testing is necessary in all recurrent or complicated infections, perhaps not for uncomplicated cases.
- Identify or correct factors predisposing to infection
 - Obstruction, calculi
 - Diabetic patients who are at risk for recurrent infections, pyelonephritis and perinephric abscesses

Treatment: General Principles

- 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.

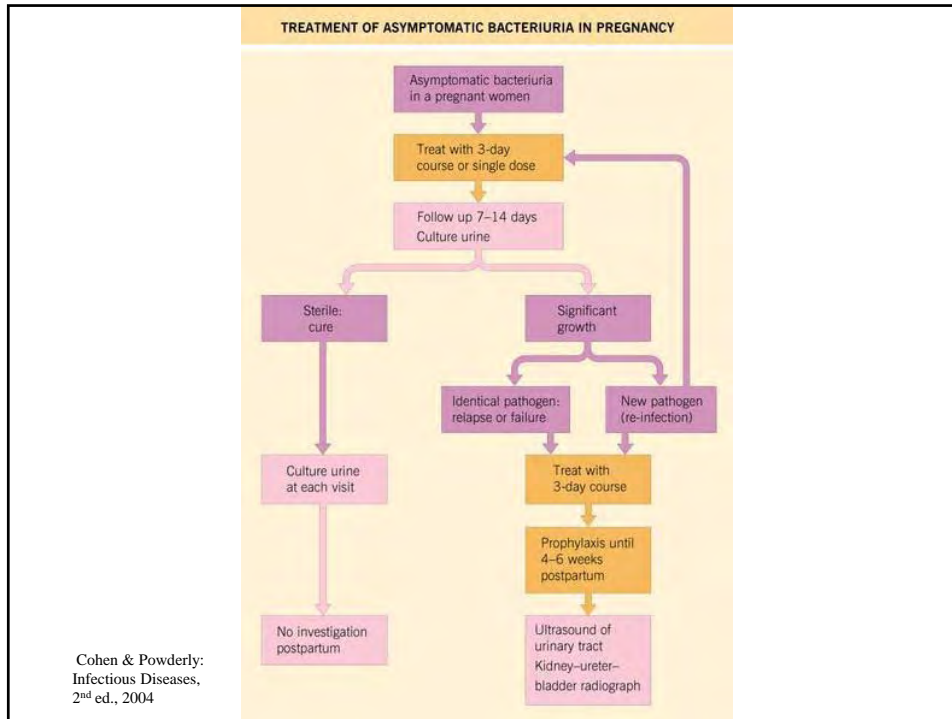
Empiric Antimicrobials

- 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 in cystitis
- 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)



Treatment of Asymptomatic Bacteriuria

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

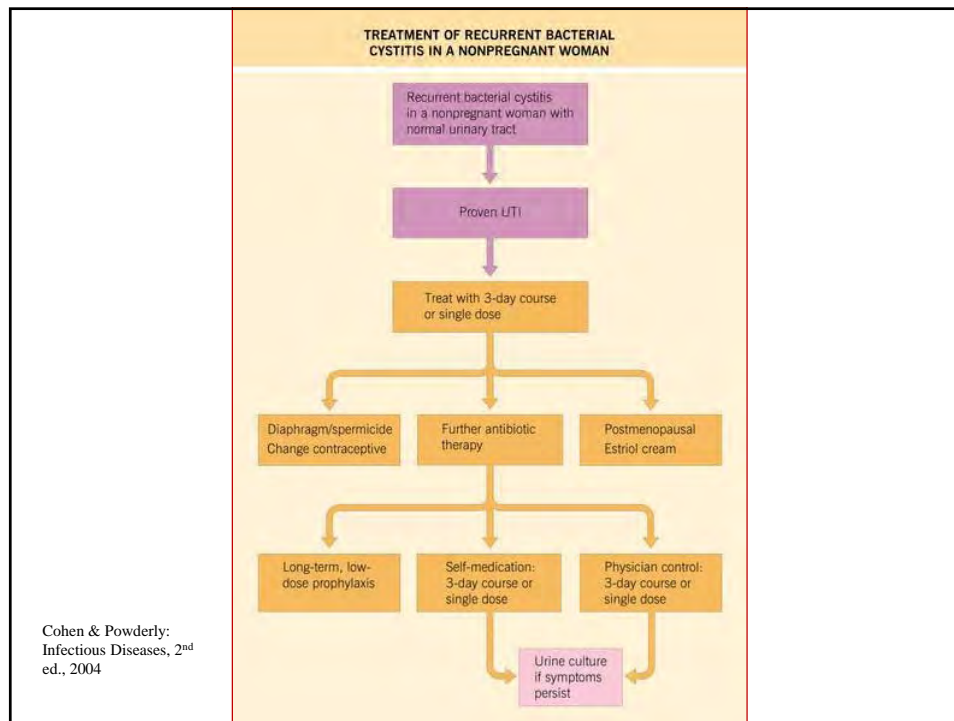


Recurrent UTI

- Risk factors for recurrent uncomplicated UTI
 - Postmenopausal status; diabetes
 - Recent antimicrobial use
 - Behavioral risk factors
 - Frequency of sexual intercourse
 - spermicide use, oral contraceptive use
 - new partner
 - first UTI <15 y.o.

Prevention Strategies

- Prevention Strategies
 - Alternative methods of contraception (avoid spermicide, diaphragms)
 - 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



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'BRYEN,
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%

Selected References

- Svanborg S., Godaly G. Bacterial virulence in urinary tract infection. *Infect Dis Clin North Am* 1997; 11:513-29
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- Raz R., Chazan B., Dan M., Cranberry juice and urinary tract infection. *Clinical Infectious Diseases* 2004; 38:1413-9