Microm 301
Genitourinary Infections
Nov. 28, 2012

Urinary tract infections
   Cystitis, pyelonephritis, bacteremia, sepsis,
   E. coli in community acquired, variety in nosocomial

Pathogenesis
   Selection of uropathogenic strains from normal fecal flora
   Specific fimbrial adhesins
   membrane damaging toxin
   iron acquisition
   intracellular persistence

Diagnosis
   clinical, urine dipstick, microscopic analysis and culture
   Importance in pregnancy

Therapy – antibiotics
   recurring infections a problem

Epidemiology
   Adult women – association with sexual activity
   Nosocomial – association with bacteremia, sepsis

Bacterial Vaginosis
   abnormal vaginal discharge and odor

Epidemiology
   very common
   risk factors – Black race, number of sex partners, WSW

Pathogenesis
   alteration of normal vaginal flora
   absence of Lactobacillus spp, presence of Gardnerella vaginalis and obligate anaerobes

Diagnosis
   clue cell, discharge, odor of amines, vaginal pH

Therapy
   antibiotics active against obligate anaerobes
   frequent recurrence a problem
*Chlamydia trachomatis* urethritis/cervicitis
- obligate intracellular pathogen
- no peptidoglycan, cross-linked proteins instead
- EB – extracellular form, RB – intracellular replicative form

**Disease**
- Men – urethritis, epididymitis
- Women – frequently asymptomatic
  - persistent cervicitis with discharge, pelvic inflammatory disease
- Neonatal eye infections, neonatal pneumonia

**Pathogenesis**
- bacterial induction of phagocytosis by epithelial cell
- replication in vacuole becomes “inclusion”
- inflammation, cell mediated immune response

**Diagnosis**
- Nucleic acid amplification from urine specimen
- Annual screening of women ≤ 25 years old

**Epidemiology**
- Most commonly reported infectious disease in US
- High incidence in sexually active 15-19 year old women
Genitourinary Tract Infections

Urinary Tract Infections

Bacterial Vaginosis

Chlamydia Urethritis/Cervicitis

Urinary tract infections

- Cystitis – inflammation of the bladder
- Dysuria, frequency, urgency
- Pyelonephritis - inflammation of the kidney
- Fever, flank pain, nausea, vomiting, malaise

Complications

- Bacteremia, sepsis
- Hospital-acquired infections
- Renal scarring
- Infants
- Recurring infections
- UTI in pregnancy
  - Premature delivery, low birth weight
  - Premature labor, spontaneous abortion

Urinary tract infections

Etiology

- Community acquired
  - *E. coli* (> 80%)
  - *Staphylococcus saprophyticus* (10 – 15%)
- Nosocomial (hospital acquired)
  - Above plus:
    - Other Enterobacteriaceae
    - *Proteus, Klebsiella, Enterobacter*
    - *Enterococcus sp.*
    - *Pseudomonas aeruginosa*
    - *Candida albicans* (yeast)

Pathogenesis

- Selection of uropathogenic strains from normal flora of the colon
- *E. coli*
  - Specific fimbrial adhesins
    - Binding to epithelial receptors in bladder and kidney
  - *Hemolysin*
  - *Aerobactin* (iron siderophore)
  - Intracellular persistence

Diagnosis

- Uncomplicated cystitis
  - Clinical observation
  - Urine “dipstick” tests for neutrophils (leukocyte esterase) and bacteria (nitrites)
  - Microscopic analysis
- Acute pyelonephritis
- Culture and susceptibility testing important
- Pregnancy
  - Quantitative culture regardless of presence or absence of symptoms
    - Important during early prenatal care

Therapy

- Antibiotics – emerging resistance is a problem
  - Community acquired cystitis
    - Empiric therapy usually adequate, 3-5 days
  - Acute pyelonephritis
    - Longer course, hospitalization may be required
    - Recurring infections (>3 infections per year)
    - 6 month, low dose therapy
- Asymptomatic bacteriuria in pregnancy should be treated
Urinary tract infections

- Epidemiology, risk factors
  - Pediatric
    - Common in uncircumcised neonatal boys
    - Problematic in infant girls 3 months – 1 year
  - Urinary reflux
  - Adult women – majority of cases, very common
    - Sexual activity
    - Spermicide use
    - Bacterial vaginosis
    - Pregnancy
    - Recurring infections common
    - Complications uncommon in community-acquired infections in non-pregnant women

Bacterial Vaginosis (BV)

- The disease: abnormal vaginal odor and discharge
  - Complications: salpingitis, endometritis, pelvic inflammatory disease, premature labor and delivery, low birth weight, increased susceptibility to HIV infection

- Epidemiology:
  - Common (most common vaginal infection)
    - ~30% of women show microbiological evidence of BV, ~50% of these are symptomatic
    - Risk correlates with number of sex partners, Black race
    - High prevalence (35-50%) in WSW (women who have sex with women) with concordance between partners

Bacterial Vaginosis

- Diagnosis
  - Any 3 of the following
    - observation of "clue cell" on microscopic examination of vaginal smear wet mount
    - adherent grayish discharge
    - production of volatile malodorous amines (like rotten fish) on addition of KOH (whiff test)
    - vaginal pH > 4.5

- Therapy
  - Therapy: oral or topical antibiotics active against anaerobes
  - Recurrence is frequent

Urinary tract infections

- Elderly
  - Associated with lack of estrogenic hormones in women, loss of bladder tone, incontinence, prostatic hypertrophy in men, catheterization

- Hospitalized
  - Associated with instrumentation
  - Greater risk of bacteremia, sepsis
  - Greater variety of bacteria
  - Antibiotic resistance is a greater problem

- Other predisposing conditions
  - Diabetes, spinal chord injuries, HIV infection, multiple sclerosis

Bacterial Vaginosis

- Pathogenesis: abnormal vaginal microflora
  - association with absence of H2O2-producing Lactobacillus species (L. crispatus and others)
  - elevated vaginal pH
  - predominance of Gardnerella vaginalis
    - Gram-variable facultative coccobacilli (Gram positive structure)
  - Increased numbers of anaerobic bacteria
    - production of amines (trimethylamine) induces transudation and exfoliation of epithelial cells, produces odor
  - degradation of mucins producing thin homogenous discharge
  - Epidemiology suggests sexual transmission of a pathogen, but the component of BV microbiota capable of transmitting the disease remains a mystery

Chlamydia urethritis/cervicitis

- Chlamydia trachomatis
  - Obligate intracellular bacteria
  - No detectable peptidoglycan
  - but they do encode all necessary biosynthetic enzymes ???
  - Cellular integrity maintained by extensively crosslinked outer membrane proteins

Cross-linked proteins

LPS

Outer membrane

Extensively crosslinked cysteine-rich proteins

Cytoplasmic membrane
**Chlamydia urethritis/cervicitis**

- **Forms**
  - Elementary body (EB)
  - Extracellular spore-like form
  - Metabolically inert, non-replicating, infectious form
  - Stabilized by extensive disulfide crosslinking of outer membrane proteins
  - Reticulate body (RB)
  - Intracellular replicating form
  - Divide within membrane-bound inclusion
  - Osmotically unstable, cannot survive extracellularly

- **Chlamydia life cycle**

**Chlamydia urethritis/cervicitis**

- **Urethritis**
  - Men: dysuria with urethral discharge
  - 7-14 day incubation period (longer than gonorrhea)
  - Asymptomatic infections common
  - Epididymitis is common complication
  - Frequently unilateral, not associated with infertility

- **Women**
  - Dysuria, frequency, absence of hematuria (blood in urine) (in contrast to E. coli UTI)

**Chlamydia urethritis/cervicitis**

- **Cervicitis**
  - Inflammation of the uterine cervix
  - Most (~70%) infected women are asymptomatic
  - Mucopurulent cervical discharge
  - Untreated infections persist for months
  - Pelvic inflammatory disease most important complication

**Chlamydia trachomatis**

- **Neonatal infections**
  - Inclusion conjunctivitis
  - Occurs in ~30% of infants born to infected mothers
  - Untreated disease ultimately resolves without damage
  - Pneumonia
  - Occurs in ~15% of infants born to infected mothers
  - Apparent 1-8 weeks after birth
  - Untreated disease can persist for weeks to month
  - Associated with long term respiratory sequelae
  - Obstructive airway disease, asthma
**Chlamydia trachomatis**

- Pathogenesis – intracellular replication in urogenital epithelial cells
  - EB induces epithelial cell internalization
  - Inclusion associates with Golgi secretion apparatus
  - RBs obtain host nucleotides, amino acids, and lipids from host cell
  - Chlamydial proteases degrade host proteins
  - Anti-apoptotic factors secreted by Chlamydia
  - keeps host cell alive until RBs mature into EBs

- Epidemiology
  - Most commonly reported infectious disease in U.S.
  - Incidence in women 3X > men
  - Highest incidence in sexually active 15-19 y.o. women, 20-24 y.o. men
  - Cervical ectopy (exposure of columnar epithelial cells) is more common in younger women, and is risk factor for acquisition of Chlamydia infection

- Diagnosis
  - Nucleic acid amplification techniques
    - High sensitivity and specificity
  - Urine and vaginal swabs can be used
  - Screening
    - CDC recommend annual screening
    - All sexually active women ≤ 25 years
    - MSM (men who have sex with men) for urethral and rectal gonorrhea and chlamydia, and pharyngeal gonorrhea

- Therapy
  - Antibiotics

- Other sexually-transmitted infections
  - Neisseria gonorrhoea – gonorrhea
    - Gram-negative diplococci
    - Urethritis/cervicitis, pelvic inflammatory disease, neonatal eye infections, proctitis, pharyngitis
    - Facultative intracellular pathogen
    - Invasion and intracellular replication in epithelial cells and neutrophils
  - Treponema pallidum
    - Spirochete
    - Genital ulceration, systemic infection, latency, late chronic infections
    - Congenital syphilis
    - neonatal and late (teenage years) development of systemic infection
  - Herpes simplex virus type 2
    - Genital ulceration, recurrent lesions with latent infection
    - Neonatal infections can be fatal

- Other diseases caused by Chlamydia trachomatis (different serotypes than urethritis/cervicitis strains)
  - Lymphogranuloma venereum
    - genital ulceration and chronic lymphadenitis
    - rare in U.S.
  - Trachoma
    - blindness due to inflammation and scarring of cornea
    - significant morbidity in sub-Saharan Africa

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