CHAPTER 23
INFECTIONS OF THE
GENITOURINARY SYSTEM

WHY IS THIS IMPORTANT?

◆ The genitourinary tract is a body system that is open to the outside world
◆ Many pathogens use this portal of entry and as a health care professional you will see many infections here

OVERVIEW

◆ Many infections occur in the urinary and reproductive systems
  ◆ Open to the outside environment
  ◆ Some urinary system infections begin in the urethra
    ◆ Travel up to the bladder
    ◆ Can reach the kidneys
    ◆ Outcome can be severe and even life-threatening
  ◆ Variety of reproductive system infections
    ◆ Many are sexually transmitted (STDs)
OVERVIEW

Infections of the Genitourinary System

URINARY TRACT INFECTIONS

Urine is essentially sterile
- Presence of pathogens or inflammatory cells indicates a urinary tract infection (UTI)

UTIs are more common in women
- Pathogen is usually bacterial or yeast

URINARY TRACT INFECTIONS

- UTIs are serious problems in hospitals
- Usually associated with indwelling catheters
- Bacteria or yeast ascend the outside of the catheter and reach the bladder
- Antibiotics should be given following removal of the catheter

URINARY TRACT INFECTIONS

- Urine ideally flows in one direction
- Can be a reflux action
- Pathogens can use this to infect the urinary tract
- UTIs are named according to the place of infection
  - Urethritis – in the urethra
  - Cystitis – in the bladder
  - Nephritis – in the kidneys
  - Prostatitis – in the prostate (males only)

ANATOMY OF URINARY SYSTEM

BACTERIAL UTIs

- A few bacteria routinely enter the bladder
  - From external environment
  - From blood passing through the renal artery
  - Normally flushed out during urination
- Prevalence of bacterial UTIs varies with age
  - First three months of life – more common in males
  - Preschool age – more common in females
BACTERIAL UTIs

- Anatomical changes associated with aging predispose to chronic bacteria in urine
  - Often asymptomatic
  - Enlargement of the prostate (in males) increases the incidence of UTIs
  - Gynecological or prostatic surgery, incontinence, and chronic catheterization increase the rates of bacterial UTIs 30-40%

- Problem of nosocomial bacterial UTIs is complicated by antibiotic-resistant bacteria found in hospitals
  - 7 million cases of cystitis in the US
  - 250,000 cases of nephritis in the US
  - *E. coli.* accounts for 90% of both

<table>
<thead>
<tr>
<th>Organism</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Escherichia coli</em></td>
<td>trimethoprim, cephalaxin, gentamicin</td>
</tr>
<tr>
<td><em>Proteus</em> spp.</td>
<td>trimethoprim, cephalaxin, gentamicin</td>
</tr>
<tr>
<td><em>Klebsiella</em> spp.</td>
<td>trimethoprim, cephalaxin, gentamicin</td>
</tr>
<tr>
<td><em>Pseudomonas aeruginosa</em></td>
<td>ciprofloxacin, gentamicin</td>
</tr>
<tr>
<td><em>Enterococcus</em> spp.</td>
<td>amoxilillin, vancomycin</td>
</tr>
<tr>
<td><em>Staphylococcus aureus</em></td>
<td>trimethoprim, cephalaxin, gentamicin</td>
</tr>
<tr>
<td><em>Staphylococcus</em> negative</td>
<td>trimethoprim, cephalaxin, gentamicin</td>
</tr>
</tbody>
</table>
BACTERIAL UTIs: Pathogenesis

- Infection occurs when bacteria get into the urine and remain
- All portions of the urinary tract connected to one another
  - Infection is spread easily

- Pathogenesis in these infections is a result of anatomy
  - Males have some protection from a longer urethra
  - Shorter female urethra means a shorter route to bladder for bacteria
  - Female urethra ends in the vaginal area
    - Colonized by a variety of bacteria as part of normal flora
    - Many can initiate a UTI

- Uropathogenic *E. coli* is responsible for most bladder infections
  - Most potent of all the pathogens that cause UTIs
  - Pathogenicity is associated with virulence factors
    - α hemolysins
    - Specialized pili – P pili
      - Bind to receptor cells of urinary tract
      - Causes successful colonization
BACTERIAL UTIs: Pathogenesis

Clinical sequelae vary
- More than 50% do not produce recognizable illness
- Those that cause symptoms are grouped by the area they affect

BACTERIAL UTIs: Pathogenesis

Urethritis and cystitis
- Dysuria, frequency, and urgency
- Low back pain, abdominal pain, and tenderness over bladder
- Urine may be cloudy

Cystitis has more acute onset and more severe symptoms
- Presence of bacteria and blood in urine

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BACTERIAL UTIs: Pathogenesis

- **Nephritis**
  - Pain in the flanks
  - Fever above 38.3°C
  - Severe cases can cause septic shock
  - Usually no damage to kidney function

- **Prostatitis**
  - Pain in the lower back, perirectal area, and testicles
  - Can be high fever, chills, and symptoms similar to bacterial cystitis
  - Inflammatory swelling can lead to obstruction of the urethra
  - Retention of urine can cause abscess formation, epididymitis, and seminal vesiculitis
  - Acute prostatitis usually seen in young men
  - Chronic form in the elderly and usually with catheterization

- **Diagnosis of a bacterial UTI based on examination of urine**
  - Requires collection of a clean voided midstream sample
  - In 90% of patients UTIs are identified as pyuria
  - More than 10 white blood cells per cubic millimeter of urine
  - Presence of white blood cell casts in the urine
  - Most positive way to confirm is a Gram-stain of a urine sample
  - One bacterium per oil-immersion field indicates infection
BACTERIAL UTIs: Treatment

- Trimethoprim is most commonly used
  - Alone or in combination with sulfamethoxazole or a fluoroquinolone
  - Treatment is best guided based on antimicrobial susceptibility tests
  - Duration of treatment depends on severity of bacterial infection
  - Success of treatment is determined by a culture of urine two weeks after therapy

BACTERIAL INFECTIONS OF THE REPRODUCTIVE SYSTEM

- Most infections in the reproductive system are sexually transmitted
  - Most often affect women
  - More sexual promiscuity = more likely to contract an STD
- Many infected individuals will not seek medical help
  - Because they are asymptomatic
- Infections are caused by a wide range of organisms

BACTERIAL INFECTIONS OF THE REPRODUCTIVE SYSTEM

- STDs can cause:
  - Urethritis
  - Cervicitis
  - Prostatitis
  - Pharyngitis
  - Pelvic Inflammatory Disease (PID)
BACTERIAL INFECTIONS OF THE REPRODUCTIVE SYSTEM

- PID can also result from gonococcal or chlamydial infection
  - Can lead to infertility and ectopic pregnancy
- Infections can infect fetus and newborn
  - Expectant mothers routinely screened for STD

SEXUALLY TRANSMITTED INFECTIONS CAN BE LOCALIZED OR SYSTEMIC
- Localized: most common
- Localized infections cause inflammatory symptoms
  - May not be noticed by patient
- Deeper tissues and structures can be affected
  - Epididymitis and salpingitis
  - These can become systemic
COMMON CLINICAL CONDITIONS ASSOCIATION WITH STDs

- Genital ulcers
- Sexually transmitted urethritis
- Epididymis
- Cervicitis
- Vaginitis
- Lymphadenitis

GENITAL ULCERS

- Lesions on the genitalia
  - Pustules evolve into ulcers
  - Different infections cause different types of ulcer

GENITAL ULCERS

<table>
<thead>
<tr>
<th>Infection</th>
<th>Type of ulcer</th>
<th>Treatment of normal length ulcers</th>
<th>Duration and normalisation</th>
<th>Healing consistency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Genital herpes</td>
<td>Ulcer</td>
<td>Amoxicillin</td>
<td>Less than 5 days</td>
<td>Poor</td>
</tr>
<tr>
<td>Lupus</td>
<td>Ulcer</td>
<td>Doxycycline</td>
<td>7-10 days</td>
<td>Good</td>
</tr>
</tbody>
</table>
SEXUALLY TRANSMITTED URETHRITIS

- Presents as dysuria or urethral discharge or both
- Caused by *N. gonorrhoeae* and *C. trachomatis*
  - Many cases involve both
- Diagnosis of gonococcal urethritis usually requires culture
  - Can be done by direct microscopic examination
  - DNA analysis also used

SEXUALLY TRANSMITTED URETHRITIS

- Detection of *C. trachomatis* requires DNA amplification analysis
- Successful treatment depends on:
  - Agent causing infection
  - Whether the infection has spread

EPIDIDYMITIS

- Unilateral swelling of the epididymis
  - Usually quite painful
  - Presents with fever and swelling of the testicles
- Two bacteria implicated:
  - *N. gonorrhoeae*
  - *C. trachomatis*
CERVICITIS

- Etiology can vary
  - Usually caused by *N. gonorrhoeae* and *C. trachomatis*
- May involve mucopurulent vaginal discharge
  - Inflammation of the cervix
  - Phagocytic leukocytes found in discharge

VAGINITIS

- Bacterial is the most common type of vaginitis
  - Associated with overgrowth of *Gardnerella vaginalis*
- Can be homogeneous yellowish discharge
  - Stays adhered to vaginal wall
  - Clue cells found in discharge covered with bacteria
- Discharge can occur alone or in connection with salpingitis, endometritis, or cervicitis

PELVIC INFLAMMATORY DISEASE (PID)

- Usually presents with abdominal pain
- 50% of cases caused by *N. gonorrhoeae*
- Can be non-gonococcal and caused by a combination of bacteria
  - More complex than gonococcal
  - Usually milder
LYMPHADENITIS

- Inflammation of lymph nodes
- Seen in several sexually transmitted infections
  - Especially herpes and lymphogranuloma venereum
- Usually begins as a small genital ulcer that is frequently unnoticed
- First evidence is usually a tender swollen lymph node in groin

COMMON SEXUALLY TRANSMITTED INFECTIONS

- Three of the most common bacterial sexually transmitted infections:
  - Syphilis
  - Gonorrhea
  - Non-gonococcal urethritis

SYPHILIS

- Earliest recorded sexually transmitted infection
  - First described in 1600s
- Caused by *Treponema pallidum*
  - Slim spirochete
  - Slow rotating motility
  - Cannot be grown on bacterial media
  - Can be grown in mammalian cell cultures
SYPHILIS

- Treponema pallidum
  - Extremely susceptible to any changes in its environment
  - Dies rapidly if dehydrated or heated
  - Very sensitive to detergents and disinfectants
  - Transmission restricted to direct contact
  - Exclusively a human pathogen

SYPHILIS

- Infection is acquired by sexual contact
  - Possibility of transmission through the sharing of contaminated needles
  - Also transplacentally
- Still a major health problem
  - More than 12 million cases each year

SYPHILIS: Pathogenesis

- No animal model
  - Pathogenesis extrapolated from observations
- Spirochetes reach the subepithelial tissues by two means:
  - Through breaks in skin
  - Passing between epithelial cells of the mucous membranes
- Little or no inflammatory response during the initial stage

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SY Philis: Pathogenesis

- A lesion develops and small arterioles begin to swell
  - Endothelial cells proliferate
  - Reduces blood flow
  - Necrotic ulceration seen at the primary infection site
- Granulocytes, lymphocytes, monocytes, and plasma cells surround the affected blood vessels

SY Philis: Pathogenesis

- Primary lesion heals spontaneously
  - Bacteria have already spread to other locations through blood and lymph
- Syphilis then goes silent before the secondary stage develops
  - Also silent period before tertiary stage
- Treponema binds to immunoglobulins and complement proteins
  - Could be camouflage to protect the bacterium
- Treponema does not produce virulence factors as disease progresses

SY Philis: Pathogenesis

- Several clinically defined stages:
  - Primary
  - Secondary
  - Latent
  - Tertiary
  - Congenital
SYPHILIS:
Primary Syphilis

- Associated with appearance of primary syphilitic lesion
  - Starts as a papule and becomes an ulcer
- Ulcer usually located on external genitalia or cervix
  - Also found in the oral cavity or anus
- Ulcer remains painless – a chancre

SYPHILIS:
Primary Syphilis

- Incubation time to appearance of the chancre is 3 weeks
  - Chancre will disappear in 4-6 weeks
- Lymphadenopathy occurs within 1 week of the initial lesion
  - Can persist for months
- Primary syphilis can cause unilateral or bilateral enlargement of lymph nodes of the groin
SYMPHILIS: Secondary Syphilis

- Also known as disseminated syphilis
- Develops 2-8 weeks after the chancre disappears
- Characterized by:
  - Generalized lymphadenopathy
  - Symmetric mucocutaneous maculopapular rash
    - On the face, trunk, and extremities including the palms of the hands and soles of feet
  - Also fever, malaise, and lymphadenitis

SYMPHILIS: Secondary Syphilis

- Lesions of the rash are teeming with spirochetes
- Extremely infectious
- Lesions usually resolve in a few days
  - 1/3 of cases take many weeks
  - If lesions disappear in a few days, latent syphilis develops
SYMPHIS:
Latent syphilis

- Can last for years
  - No clinical signs or symptoms but infection is continuing
- Latency can be interrupted by less severe bouts of secondary syphilis
  - Sexual transmission only possible during relapses
- Transmission from mother to fetus is possible throughout latent period

SYMPHIS:
Tertiary syphilis

- Occurs in about 1/3 of untreated patients
- Takes years to develop
  - Can be 5 years after the initial infection
  - Usually 15-20 years
- Characterized by appearance of gummas
  - Localized granulomatous lesions in skin, bones, joints, and internal organs
- Clinical findings depend on where the infection spreads
  - Cardiovascular system – cardiovascular syphilis
  - Nervous system – neurosyphilis

SYMPHIS:
Tertiary Syphilis

- Cardiovascular syphilis
  - Bacteria move to the vaso vasorum of the aorta
  - Causes necrosis, destruction of elasticity
    - Development of aneurisms
    - Aortic valvular incompetency
SYPHILIS:
Tertiary Syphilis

- Neurosyphilis is characterized by:
  - Meningovasculitis
  - Degenerative changes in any area of the body
- Most common symptoms are:
  - Chronic meningitis, fever, and headache
  - Increased cells and protein in the cerebrospinal fluid
  - Can also be cortical degeneration
- Cortical degeneration causes mental changes
  - Decreased memory, hallucinations, and psychoses

SYPHILIS:
Tertiary Syphilis

- Passed from mother to fetus
  - Only after 4th month of gestation
- Can have devastating consequences
  - Miscarriage
  - Changes to entire skeletal structure
  - Anemia, thrombocytopenia, and liver failure
- Mother must be treated before 4th month
**SYPHILIS: Treatment**

- *Treponema pallidum* is very sensitive to penicillin
  - Treatment of choice
  - Patients allergic to penicillin are treated with tetracycline, azithromycin, or cephalosporin
- Safe sex is effective for prevention

**GONORRHEA**

- Caused by *Neisseria gonorrhoeae*
  - Gram-negative diplococcus
  - Numerous pili
  - Grows well on chocolate agar
    - Also requires CO₂
  - Can change antigens from generation to generation
    - Antigenic variability also in pili
- Extensive genetic changes that occur in *N. gonorrhoeae*:
  - Allow pathogen to escape host defenses
  - Make it able to bind to variety of receptors
  - Maximize the potential for infection

Safe sex is effective for prevention.
GONORRHEA

- Reported cases represent only 50% of the actual number
  - Still a major public health problem
- Highest rates seen in young adults
  - Women aged 15-19
  - Men aged 20-24
- Major reservoir is asymptomatic patients
  - 50% are infectious
  - Infection rate can be 20-50% for sexual intercourse with a carrier

GONORRHEA: Pathogenesis – Attachment and invasion

- Bacterium have pili and adherence proteins
  - Used to attach to urethral and vaginal epithelium
  - Also attaches to sperm and parts of fallopian tubes
- Pathogen invades host epithelial cells
  - Microvilli of the epithelial cells escort it into cytoplasm

GONORRHEA: Pathogenesis – Attachment and invasion

- Invasion process called parasite-directed endocytosis
  - Initiated by the bacterium
  - Entry involves nonphagocytic cells
- Once inside host cell:
  - Transcytoses through cytoplasm
  - Exits through the basal membrane
GONORRHEA: Pathogenesis – Survival in submucosa

- Enters the submucosa and immediately exposed to the host defenses
- *Neisseria* has a variety of evasion mechanisms.
  - Blocks the deposition of C3 and shuts down complement
  - Surface proteins bind to antibodies and inhibit their bacteriocidal response
    - Blocked antibodies are found in patients with repeated gonococcal infections
  - Produces excess catalase and neutralizes oxidative killing part of phagocytosis

GONORRHEA: Spread and Dissemination

- Pathogens tend to stay localized in the genital structures
  - Facilitates transmission
  - Causes increased inflammation and localized tissue injury
- Purulent exudates are the infectious units
- Infection may spread to adjacent cells by progressive extension
  - Prostate, cervical glands, and fallopian tubes
  - Bacteria adhering to sperm can facilitate spread
- *Neisseria* can reach the blood and cause systemic infection

GONORRHEA: Clinical Manifestations

- Genital gonorrhea
  - Primarily in the urethra
  - Symptoms 2-7 days after infection
    - Purulent urethral discharge and dysuria
    - In men infection can spread to epididymis and prostate
    - In women can be abdominal pain and menstrual abnormalities
  - Symptoms can be mild or completely absent
GONORRHEA: Clinical Manifestations

- Pelvic inflammatory disease (PID)
  - Seen in 10-20% of women infected with Neisseria
  - Symptoms are caused by pathogen spreading along the fallopian tubes and into the pelvic cavity
    - Fever, bilateral abdominal tenderness, and leukocytosis
    - Salpingitis
    - Pelvic peritonitis and abscess formation
  - PID can have serious complications
    - Infertility and ectopic pregnancy

- Disseminated gonococcal infection can be caused by localized gonorrhea or PID
  - Clinical features
    - Fever, polyarthralgia, petechial maculopapular, or pustular rash
  - Some symptoms caused by the host response to bacteremia
  - Spread can lead to endocarditis or meningitis
  - Most commonly purulent arthritis

GONORRHEA: Treatment

- Patients who discontinue treatment early:
  - Continue to transmit the disease
  - Increase development of antibiotic resistance
- Resistance to penicillin has rendered this drug useless
- Third-generation cephalosporins are the best option
  - Fluoroquinolones, azithromycin, doxycycline are also effective
NON-GONOCCAL URETHRITIS  
(CHLAMYDIA TRACHOMATIS)

- NGU is the most common sexually transmitted disease
- Caused by Chlamydia – a unique form of bacteria
  - Obligate intracellular
  - Round cell surrounded by an envelope
  - Do not contain peptidoglycan
  - One of the smallest genomes of all the prokaryotes
  - C. trachomatis most common species

NGU: Replication of Chlamydia

- Unique replication cycle involving two forms
  - Small, hardy, infectious form
    - Elementary body (EB)
  - Larger, more fragile, replicative form
    - Reticulate body (RB)

- EB attaches to unknown receptors
  - Enters the cell through endocytosis
- In the endocytic vesicle, EB converts to RB
- Endocytic vesicles do not fuse with lysosomes
  - Fuse with other endocytic vesicles carrying the pathogen
  - Number of Chlamydia in vacuole increases
- Endosome membrane expands by fusing with the lipids of the Golgi apparatus
**NGU: Replication of Chlamydia**

- Forms a large inclusion body
- Process reverses after 24-72 hours
  - RB form re-organizes and condenses to the EB form
  - Endosome membrane disintegrates or fuses with host cell membrane
    - Releases the EBs which infect new targets
- Forms a large inclusion body

<table>
<thead>
<tr>
<th>NGU: Pathogenesis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Humans are the only reservoir</td>
</tr>
<tr>
<td>Many infected men show no symptoms of the disease</td>
</tr>
<tr>
<td>Re-infection is a common occurrence</td>
</tr>
</tbody>
</table>
NGU: Pathogenesis

- *Chlamydia* has an affinity for:
  - Epithelial cells of the endocervix
  - Upper genital tract of women
  - Urethra and rectum of both men and women
- After infection, epithelial cells release pro-inflammatory cytokines
  - Tissue infiltration by polymorphonuclear leukocytes
  - Further infiltration by lymphocytes, macrophages, plasma cells, and eosinophils

NGU: Pathogenesis

- If infection not treated or failure in the immune response:
  - Aggregates of lymphocytes and macrophages form in the submucosa
  - Causes necrosis, fibrosis, and scarring
- NGU can become chronic

NGU: Pathogenesis

- Similar clinical sequelae to gonorrhea
  - Urethritis and epididymitis in men
  - Cervicitis, salpingitis, and urethritis in women
- Usually presents with dysuria and thin urethral discharge
- Infection of the cervix is usually asymptomatic
NGU: Treatment

- *Chlamydia* are sensitive to doxycycline, azithromycin, and some fluoroquinolones
- No vaccine against NGU

VIRAL INFECTIONS OF THE GENITOURINARY SYSTEM

- Most important viral infection is HIV
- Two other prominent viruses:
  - Herpes simplex type 2
  - Human papillomavirus

HERPES SIMPLEX VIRUS TYPE 2

- Two distinct epidemiological and antigenic types of herpes simplex virus
  - Herpes simplex virus type 1 (HSV-1)
  - Herpes simplex virus type 2 (HSV-2)
- DNA viruses linear double-stranded DNA
- Two types share many of the same antigens
  - 50% homology in genomes
HSV-2

- HSV-1 – above-the-waist
  - Causes cold sores
- HSV-2 – below-the-waist
  - Causes genital herpes
- HSV-2 distributed throughout the world
  - Humans are the only reservoir

 HSV-2

- Transmission is through direct contact with infected secretions
- Antibodies against HSV-1 found in large portion of the population
- Antibodies against HSV-2 are rarely seen before puberty

 HSV-2

- Many patients infected with HSV-2:
  - Are asymptomatic
  - Have small lesions that go unnoticed
- Shedding of virus occurs in asymptomatic patients
  - They can transmit the infection
- Estimated 1 million new cases each year in the US
HSV-2: Pathogenesis

- Two types of infection:
  - Acute
  - Latent

HSV-2: Pathogenesis

- Acute infection
  - Appearance of multinucleate giant cells
  - Ballooning degeneration of epithelial cells
  - Focal necrosis
  - Eosinophilic intraneural inclusion bodies
  - Inflammatory response

HSV-2: Pathogenesis

- Virus in an acute infection can spread:
  - Intraneuronally
  - Interneuronally
  - Through networks of axons or nerves
  - By cell-to-cell transfer
    - Inhibits the effects of circulating antibody
HSV-2: Pathogenesis

- Latent infection
  - Virus has been found in the sacral region (S2-S3)
  - Infection does not result in the death of neuron
    - Effects on host cell not understood
  - No synthesis of viral proteins
    - Most antiviral drugs do not eradicate latent infection

HSV-2: Pathogenesis

- Reactivation of latent virus accounts for most recurrent genital infections
- Mechanisms not yet known, but there are several precipitating factors:
  - Exposure to ultraviolet radiation
  - Fever
  - Trauma
- Genital herpes infections can be primary, recurrent, or neonatal

HSV-2: Primary Genital Herpes

- Relatively few people develop clinical symptoms
- Incubation time from sexual contact to onset of lesions is about 5 days
  - Lesions begin as small erythematous papules
  - Develop into vesicles
  - Then pustules on mucosal tissue
HSV-2: Primary Genital Herpes

- Within 3-5 days, lesions break to form painful coalesced ulcers
  - Some crust over before healing
  - All lesions crust over eventually
- Primary genital herpes lesions are usually multiple, bilateral, and extensive
  - Urethra and cervix can also be involved

Bilateral enlarged and tender lymph nodes in groin persist for weeks or even months
- One-third of patients show systemic symptoms
  - Fever, malaise, and myalgia
  - Some cases of aseptic meningitis
- First episodes last average of 12 days
HSV-2: Recurrent Genital Herpes

- Shorter duration than primary infection
  - Usually localized in genital region
  - Usual symptoms burning or prickly sensation in the pelvic area
    - Occur 12-24 hours before appearance of grouped vesicular lesions
    - Last 4-5 days
    - Lesions usually disappear in 2-5 days

HSV-2: Recurrent Genital Herpes

- 80% patients develop recurrent episodes
  - Median number of recurrences 4-5 per year
  - Recurrent viral shedding may occur without evidence of disease

HSV-2: Neonatal herpes infection

- Infections in newborn infants results from transmission during delivery
- Most cases associated with maternal primary infection at or near the time of delivery
  - Intense viral exposure to infant
- Very serious infection
  - Mortality rate of approximately 60%
HSV-2: Neonatal herpes infection

- Those infants that survive have severe difficulties
  - Abnormal nervous system function
  - Disseminated vesicular lesions
  - Necrosis of the liver, adrenal glands, listlessness, and seizures

HSV-2: Treatment

- Most effective and most commonly used is the nucleoside analog acyclovir
  - Decreases the duration of a primary infection
  - Can also suppress recurrent infections
- Foscarnet is effective for resistant HSV virions
- Can be prevented by avoiding contact with infected individuals expressing lesions
  - Important to remember virus still being shed in asymptomatic individuals
  - Can also be transmitted via saliva

HUMAN PAPILLOMAVIRUS (HPV)

- Papillomaviruses are small, non-enveloped, with double-stranded DNA and icosahedral symmetry
- Cause papillomas (benign tumors) or warts
  - Infections are species specific
  - Tumors can be malignant
**HPV**

- Wide genetic diversity among human papillomaviruses
  - Indicated by using numbers to identify different genotypes
  - More than 70 genotypes of HPV have been identified
  - Some are associated with specific lesions
- HPV genotypes identified cause genital hyperplastic epithelial lesions
  - Cervical, vulvar, and penile warts
- HPV genotypes are also associated with premalignant and malignant cervical cancer

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**HPV**

- 12 HPV genotypes identified in human genital lesions
  - Many other genotypes cause silent infections
  - Possible to be infected with more than one genotype of HPV
  - Incidence of HPV infection is rising
    - 20-60% of women in the US are infected with one HPV genotype
  - Types 6 and 11 associated with benign genital warts in males and females
  - Types 16, 18, 31, and 45 cause warty lesions of vulva, cervix, and penis
    - Infections with any of these may progress to malignancy

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**HPV: Pathogenesis**

- Papillomaviruses have a predilection for the junction of squamous and columnar epithelium
- Mechanism of malignant transformation not understood
  - Difficult to study because HPV is difficult to grow
HPV: Pathogenesis

- Viral genome can be found integrated into the host cell chromosome
  - Integration does not seem to be site-specific
- Host cells normally produce protein that inhibits expression of papillomavirus – transforming genes
  - HPV seems to inactivate that protein

HPV - Pathogenesis

- External genital HPV infection presents as genital warts
  - Often caused by genotypes 6 or 11
  - Lesions may grow to a cauliflower-like appearance during pregnancy or immunosuppression
- HPV infections usually benign
  - Many lesions reverse spontaneously
  - May become dysplastic
    - Proceed to severe dysplasia or carcinoma

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- HPV infections are usually benign
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HPV: 
Treatment

- Only treatments are surgical, cytotoxic drugs, and cryotherapy
- Recurrence is common after cessation of treatment
- A vaccine has recently become available

FUNGAL INFECTIONS OF THE GENITOURINARY SYSTEM

- Genitourinary system is exposed to many fungal organisms
- Infections are usually opportunistic
- Most prominent fungal infection is vaginal candidiasis
- Caused by Candida albicans

VAGINAL CANDIDIASIS (CANDIDA ALBICANS)

- Candida albicans part of the normal microbial flora
- In oropharyngeal and gastrointestinal regions in males and females, genital tract of females
- Can grow in multiple morphological forms
- Mainly seen as yeast
- Infection can be local or systemic
VAGINAL CANDIDIASIS (CANDIDA ALBICANS)

- Main symptoms are itching and a thick white discharge
- Infections are normally endogenous
  - Except in direct mucosal contact e.g. sexual intercourse
- Indwelling catheters and over-use of antibiotics
  - Additional opportunities to become opportunistically pathogenic

C. ALBICANS: Pathogenesis

- Part of the normal flora
  - Must undergo change to become pathogenic
  - One of the changes is appearance of hyphae
- Hyphae are seen when Candida invades tissues
  - Accompanied by production of several factors permitting strong attachment to host cells
  - Attachment involves usurping of host cell enzymes

C. ALBICANS: Pathogenesis

- Hyphae excrete proteases and phospholipases
  - Digest epithelial cells
  - Facilitate tissue invasion
- Candida binds to the C3 fragment of complement
  - Inhibits opsonization
C. ALBICANS: Pathogenesis

- *Candida* infection of the vagina produces a thick discharge
- Consistency of cottage cheese
- Accompanied by itching
- Small percentage of women become chronically infected
- Experience recurrent symptoms
- *Candida* can also infect urinary tract causing:
  - Cystitis, nephritis, abscesses, and expanding fungus ball lesions in the renal pelvis

C. ALBICANS: Treatment

- Usually susceptible to azole drugs, Amphotericin B, nystatin, and flucytosine
- In many cases lesions resolve spontaneously after elimination of predisposing conditions