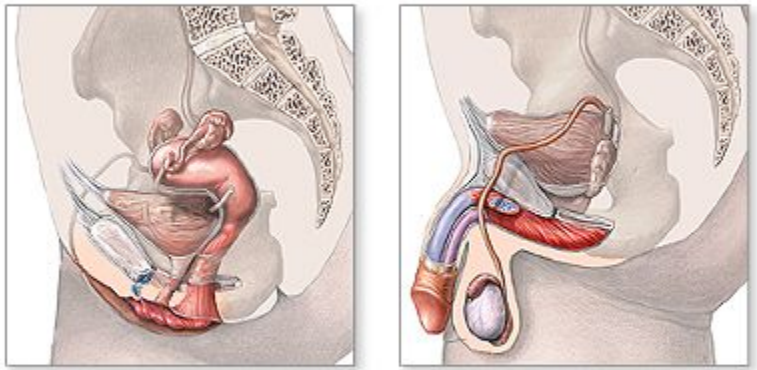
Extra Summaries

Microbiology 435's Teamwork
Reproductive Block



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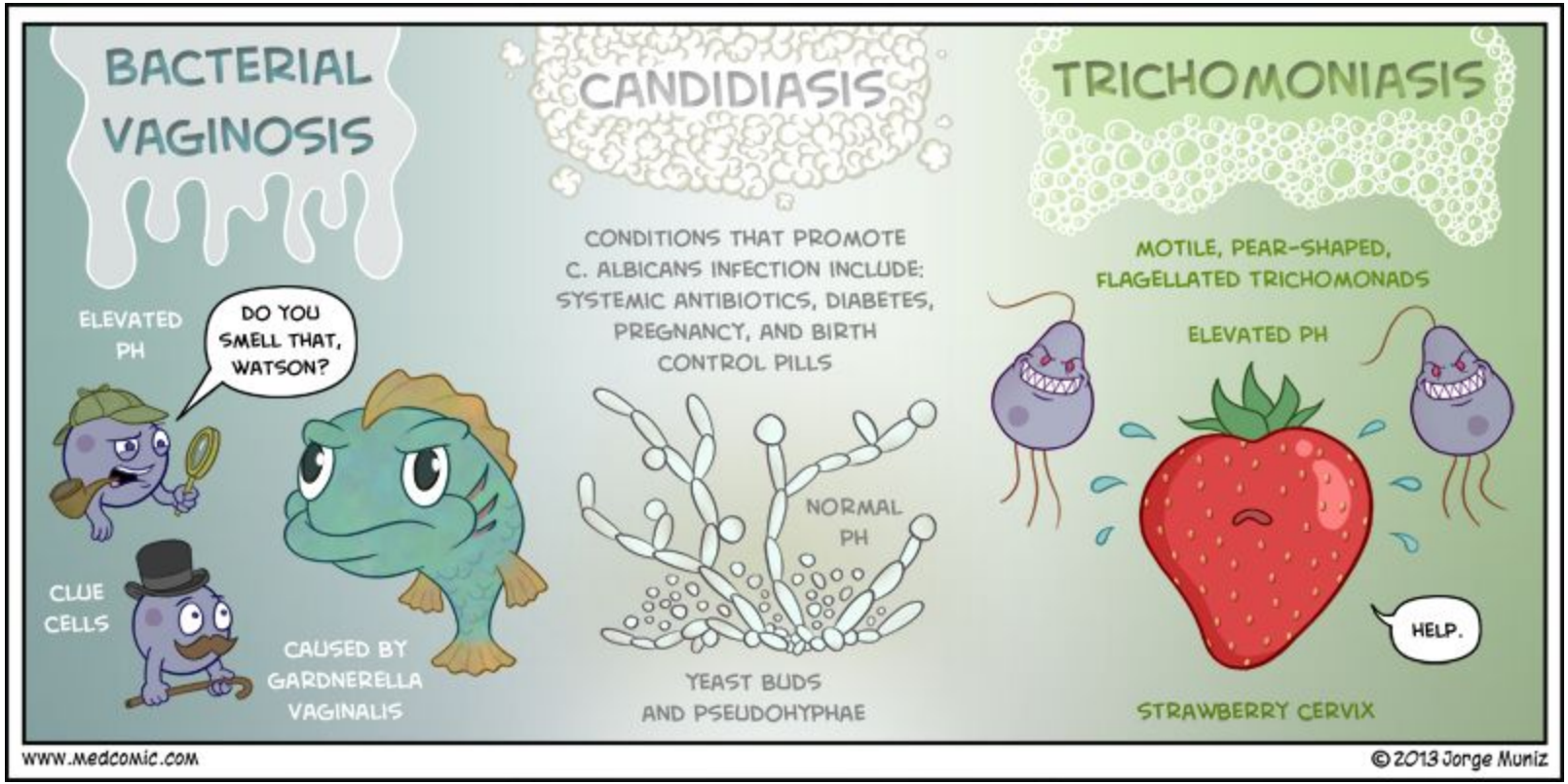
BACTERIAL VAGINOSIS
ELEVATED PH
DO YOU SMELL THAT, WATSON?
CLUE CELLS
CAUSED BY GARDNERELLA VAGINALIS
CANDIDIASIS
CONDITIONS THAT PROMOTE C. ALBICANS INFECTION INCLUDE: SYSTEMIC ANTIBIOTICS, DIABETES, PREGNANCY, AND BIRTH CONTROL PILLS
NORMAL PH
YEAST BUDS AND PSEUDOHYPHAE
TRICHOMONIASIS
MOTILE, PEAR-SHAPED, FLAGELLATED TRICHOMONADS
ELEVATED PH
HELP.
STRAWBERRY CERVIX
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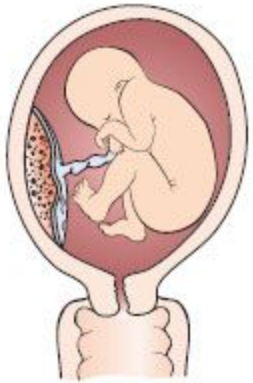
CONGENITAL INFECTION

Manifestations

- Growth retardation
- Congenital malformation
- Fetal loss



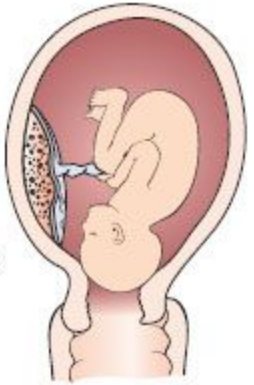
Rubella
CMV
HIV
Toxoplasma
T. pallidum
Parvovirus
VZV

PERINATAL INFECTION

Manifestations

- Meningitis
- Septicaemia
- Pneumonia
- Preterm labour

Gonococcus
Chlamydia
HSV
VZV
Group B strep
E. coli
Listeria



POSTNATAL INFECTION

Manifestations

- Meningitis
- Septicaemia
- Conjunctivitis
- Pneumonitis

N. gonorrhoeae
Chlamydia
Breast milk
HIV
CMV
Umbilicus
Staphylococci
Tetanus
Person-to-person
Group B strep
Listeria
E. coli

TOXOPLASMOSIS

Transmission

- Cysts in raw meat
- Oocytes in animal feces
- Transplacental

Classic triad

- ❑ Highest transmission rate → 3rd trimester
- ❑ Highest fetal death rate → 1st trimester

Syphilis

(Treponema pallidum)

STD

Penicillin G

Congenital classification:

- **Late abortion**
- **Infantile** (rash & funisitis, osteochondritis, periostitis, liver & lung fibrosis)
- **Childhood** (interstitial keratitis, Hutchinson teeth, 8th nerve deafness, saddle nose,..)

OTHERS

Varicella

Available vaccine

- Chickenpox
- Shingles
- Limbs hypoplasia
- CNS & eye defects

1ry infection → greater risk of severe disease

Acyclovir for varicella pneumonia

Parvovirus P19

5th disease — **Erythema infectiosum**

Transmission

Highest fetal death → 2nd trimester
Minimal risk → 3rd trimester
Hydrops fetalis, severe anemia, CHF generalized edema

digoxin

TORCH

Transplacental Infections..

RUBELLA

RNA enveloped virus
Spread by:
Respiratory droplets & transplacentally
- Available vaccine

Clinical features

- **Sensorineural hearing loss** (most common)
- "Salt & pepper" retinopathy
- Cataracts, glaucoma
- Patent ductus arteriosis
- HSM, thrombocytopenia
- "Blueberry muffin" lesions

CYTOMEGALOVIRUS

Most common congenital viral infection!

- ❑ Highest transmission rate → later in pregnancy
- ❑ Severe sequalae → earlier exposure

(like toxoplasmosis)

ganciclovir

Clinical features

90% are asymptomatic

Microcephaly (not hydro-)
Periventricular calcification (not intracranial)
Neurological deficits
HSM, petichiae, jaundice, chorioretinitis

Complications: hearing loss, vision impairment

HERPES

Herpes simplex 1 or 2

Transmission

Maternal genital tract
1ry infection → greater risk of transmission than reactivation

Remember!

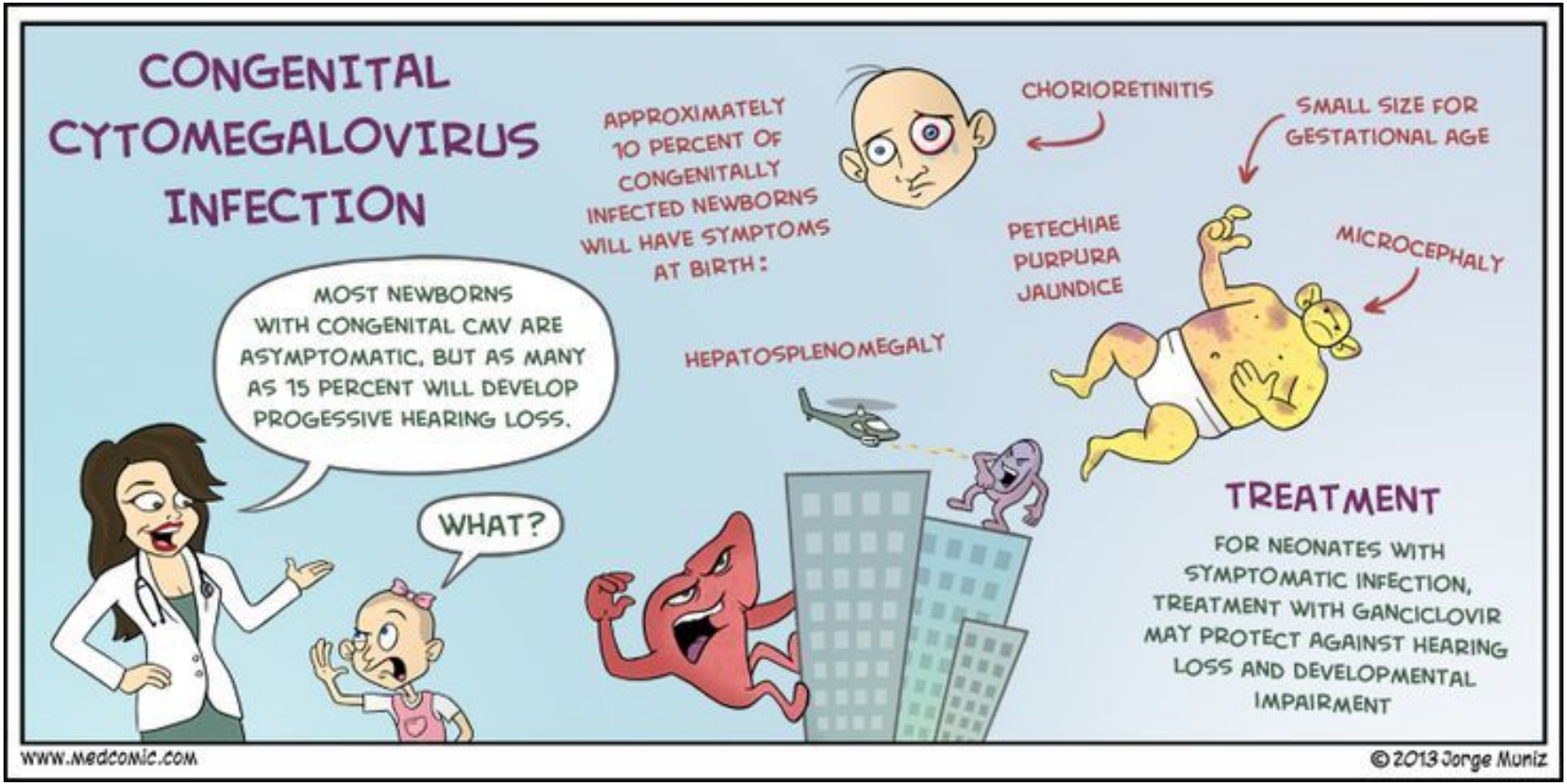
C-SECTION

Clinical features

Most are asymptomatic at birth
Symptoms between birth and 4wks: skin, eyes, mouth, CNS disease, disseminated disease (earlier)

Acyclovir

Done by: Lina Aljurf


CONGENITAL CYTOMEGALOVIRUS INFECTION
APPROXIMATELY 10 PERCENT OF CONGENITALLY INFECTED NEWBORNS WILL HAVE SYMPTOMS AT BIRTH:
CHORIORETINITIS
SMALL SIZE FOR GESTATIONAL AGE
PETECHIAE
PURPURA
JAUNDICE
MICROCEPHALY
HEPATOSPLENOMEGALY
MOST NEWBORNS WITH CONGENITAL CMV ARE ASYMPTOMATIC, BUT AS MANY AS 15 PERCENT WILL DEVELOP PROGESSIVE HEARING LOSS.
WHAT?
TREATMENT
FOR NEONATES WITH SYMPTOMATIC INFECTION, TREATMENT WITH GANCICLOVIR MAY PROTECT AGAINST HEARING LOSS AND DEVELOPMENTAL IMPAIRMENT
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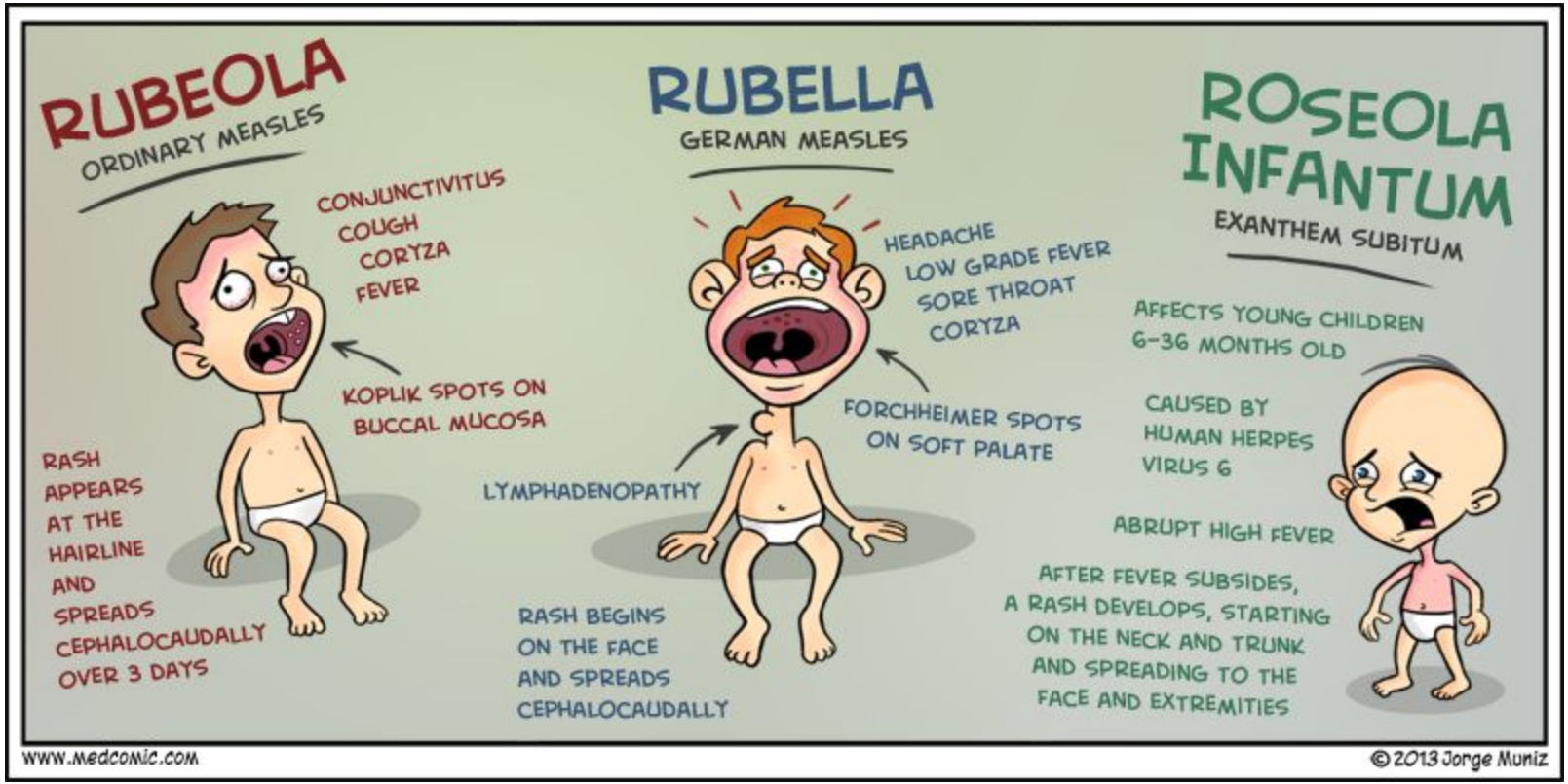
RUBEOLA
ORDINARY MEASLES
CONJUNCTIVITUS
COUGH
CORYZA
FEVER
KOPLIK SPOTS ON BUCCAL MUCOSA
RASH APPEARS AT THE HAIRLINE AND SPREADS CEPHALOCAUDALLY OVER 3 DAYS
RUBELLA
GERMAN MEASLES
HEADACHE
LOW GRADE FEVER
SORE THROAT
CORYZA
FORCHHEIMER SPOTS ON SOFT PALATE
LYMPHADENOPATHY
RASH BEGINS ON THE FACE AND SPREADS CEPHALOCAUDALLY
ROSEOLA INFANTUM
EXANTHEM SUBITUM
AFFECTS YOUNG CHILDREN 6-36 MONTHS OLD
CAUSED BY HUMAN HERPES VIRUS 6
ABRUPT HIGH FEVER
AFTER FEVER SUBSIDES, A RASH DEVELOPS, STARTING ON THE NECK AND TRUNK AND SPREADING TO THE FACE AND EXTREMITIES
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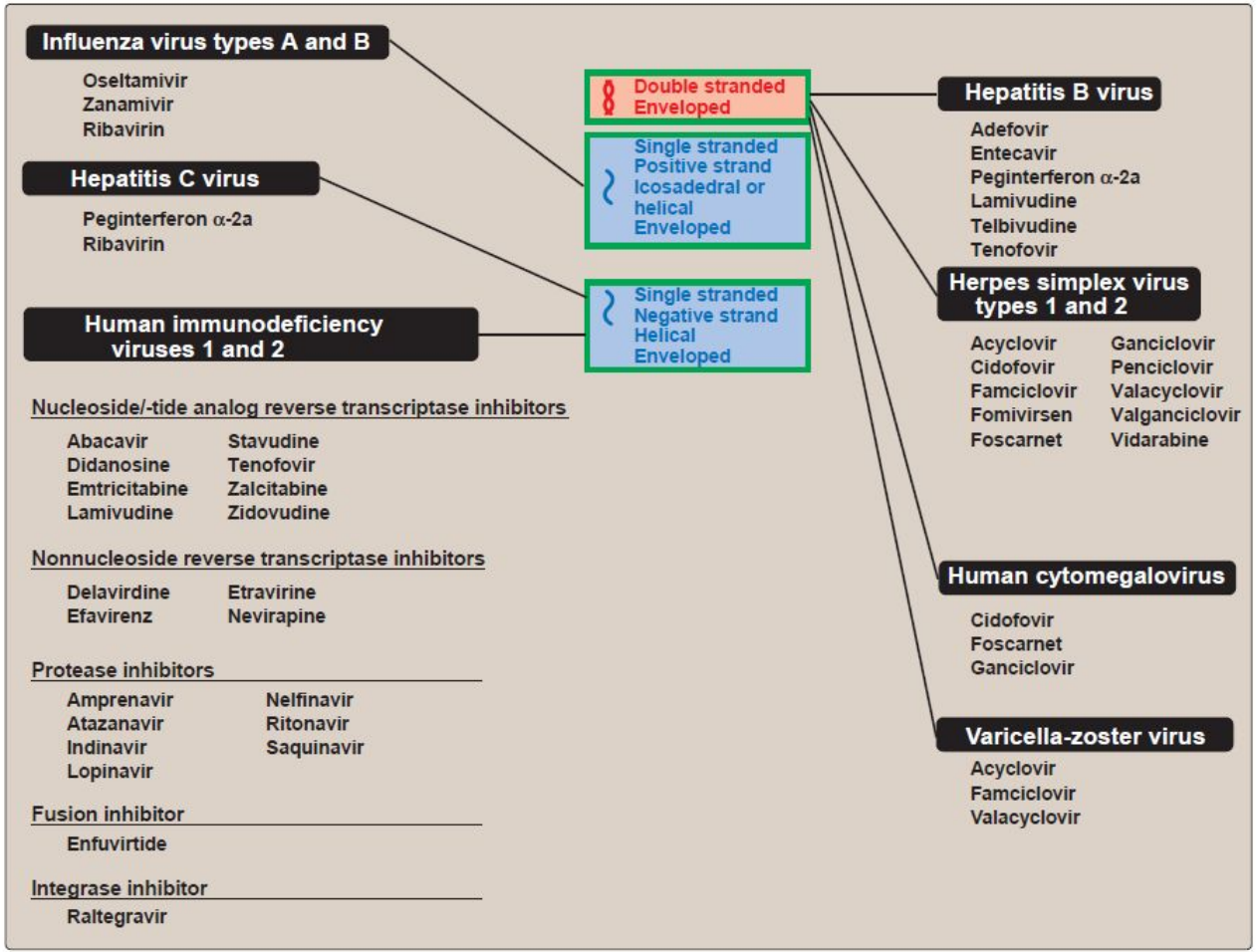


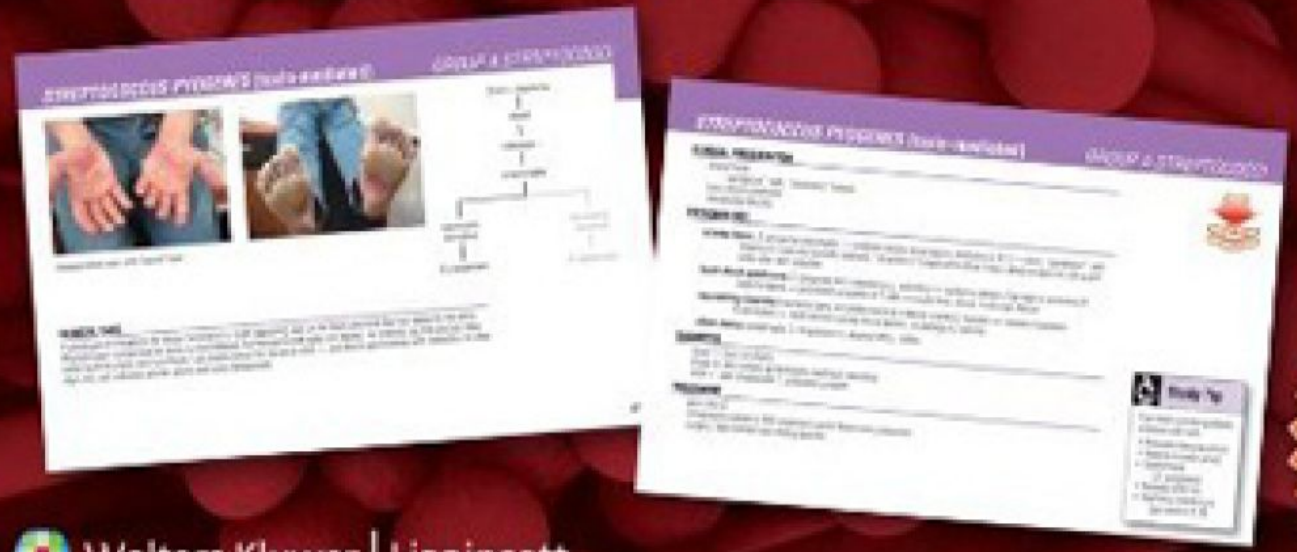
Figure 5.20
Summary of therapeutic applications of selected antiviral agents.

LIPPINCOTT'S MICROCARDS

MICROBIOLOGY FLASH CARDS

THIRD EDITION

SANJIV HARPAVAT SAHAR NISSIM



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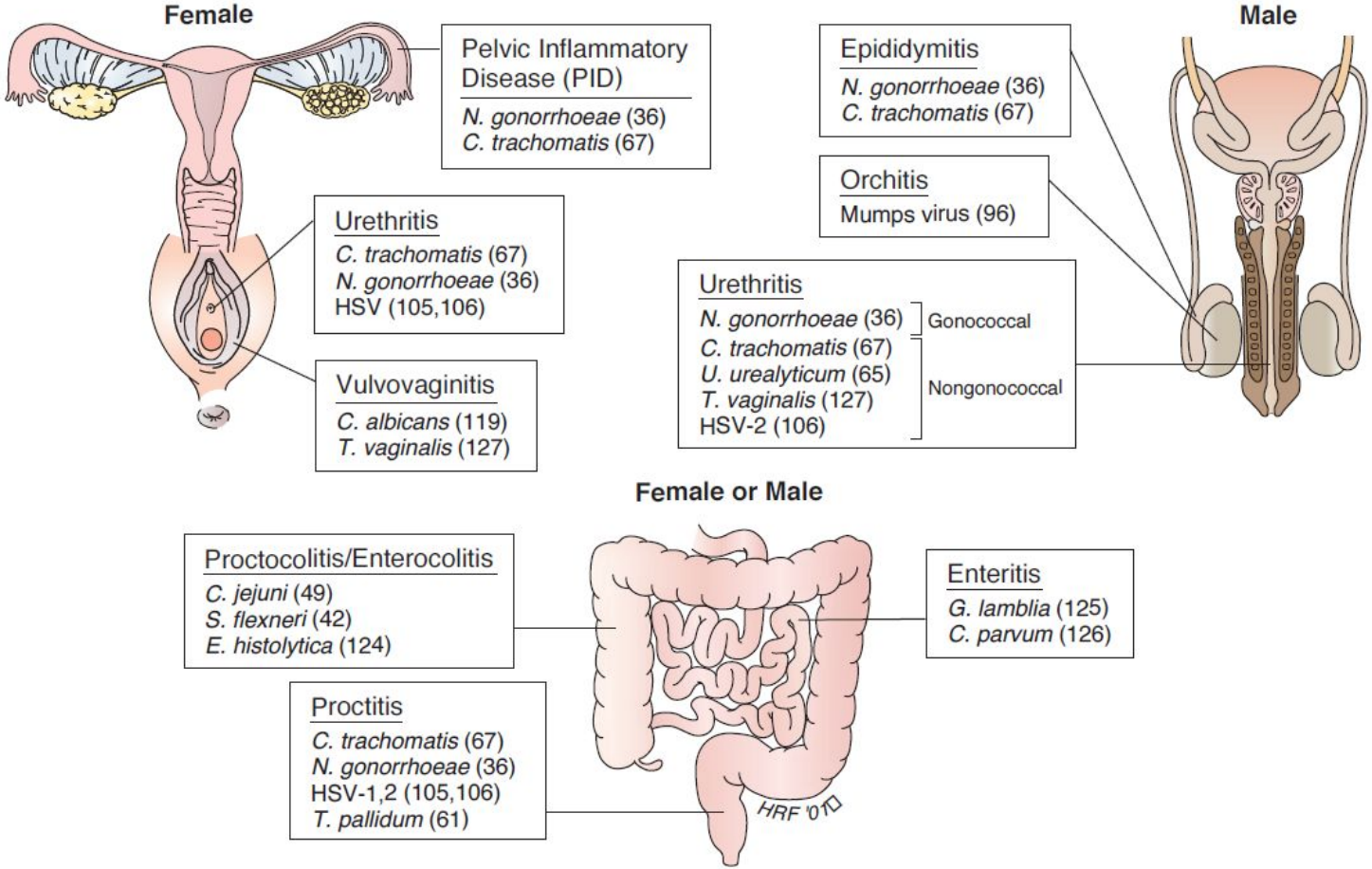
Wolters Kluwer Health | Lippincott Williams & Wilkins

Genital System Infections



Genital System Infections

CUTANEOUS LESIONS OF THE GENITALIA:

Ulcerative lesions:	Painful?	Type of Lesion
HSV-1, HSV-2 (105, 106) – Herpes	✓	vesicles
T. pallidum (61) – Syphilis		indurated
H. ducreyi – Chancroid	✓	
C. trachomatis (67) – Lymphogranuloma venereum		solitary, nonindurated

Wart lesions:

HPV (102)
Molluscum contagiosum (112)

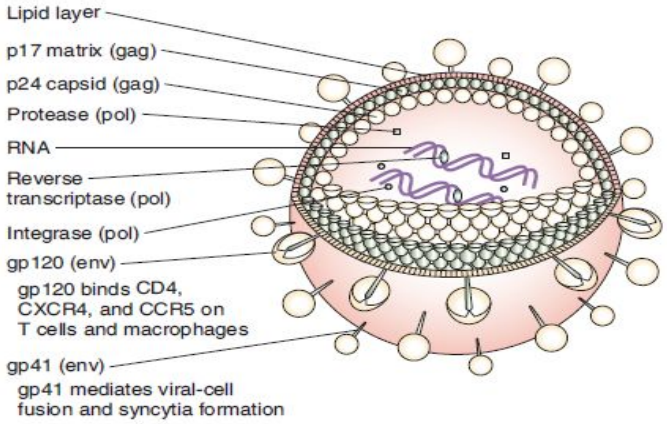
SEXUALLY TRANSMITTED PATHOGENS WITH SYSTEMIC EFFECTS:

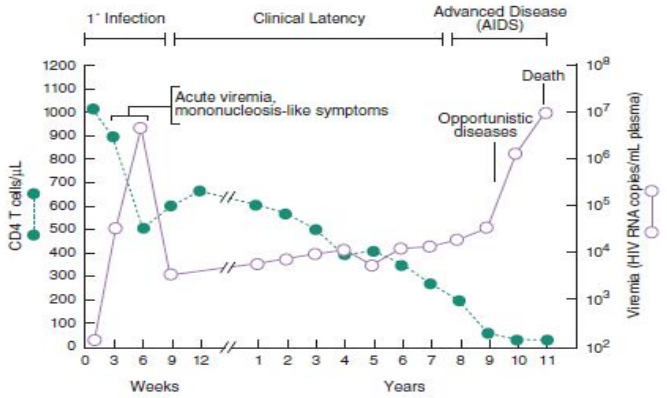
HIV (86)
HTLV (87)
HBV (110)
CMV (108)
T. pallidum (61)

COMMON VAGINAL INFECTIONS:

		DISCHARGE		
	Itchiness?	Color	Amount	Other Features
C. albicans (119)	✓	white	small	clumped discharge
T. vaginalis (127)	✓	yellow	copious	
Gardnerella vaginalis		white/gray	moderate	malodorous

HIV and AIDS





VIRAL LIFE CYCLE:

viral gp120 binds CD4 on cell surface → viral gp120 conformational change → altered viral gp120 binds coreceptor CXCR4 (for T cell infection only) or CCR5 (for T cell or macrophage infection) → viral gp41 brought close to cell membrane → viral gp41 mediates virus–cell fusion

viral genome uncoated → reverse transcriptase converts viral RNA genome to dsDNA → integrase inserts randomly several copies of dsDNA into host genome → integrated provirus remains latent

when host cell activated (e.g., via chemokines), provirus genes expressed:

- *gag* encodes polyprotein of virion core
- *pol* encodes polyprotein of reverse transcriptase, integrase, and protease
- *env* encodes envelope glycoproteins
- six other genes encode for regulators of gene expression

viral protease cleaves polyproteins → infectious particles assemble at cell membrane and bud off cell membrane

COURSE OF CD4+ T CELL COUNT AND VIREMIA:

1° Infection Stage (first months): acute viremia → contained by vigorous host immune response → mononucleosis-like symptoms → equilibrium established between viral production and host containment

Clinical Latency Stage (7–10 years): virus replicates, especially in lymphoid organs → host responds to contain infection, mutations allow virus to evade → no or low-level symptoms

viral load gradually increases, CD4+ count gradually drops

CD4+ cells depleted by various mechanisms, including:

- —immune attack on infected cells by CTLs
- —cell lysis from extensive viral budding
- —syncytium formation between infected and uninfected cells (via gp120–CD4 interactions)

Advanced Disease (AIDS): CD4+ T cell count, <200 cells/μL → common opportunistic infections/neoplasms causing death (see card 86 for more details)

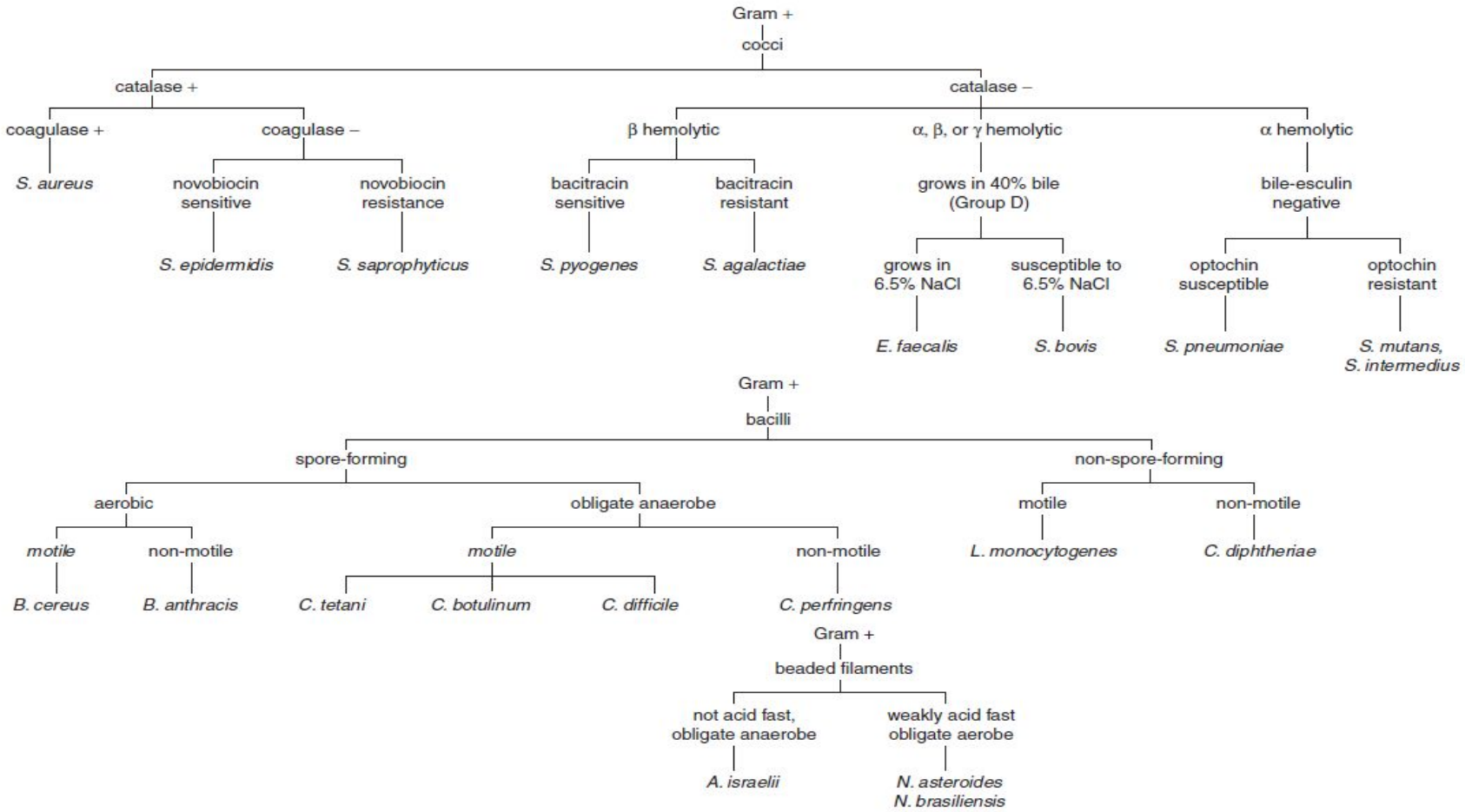
HIV and AIDS

COMMON OPPORTUNISTIC INFECTIONS IN HIV+ PATIENTS

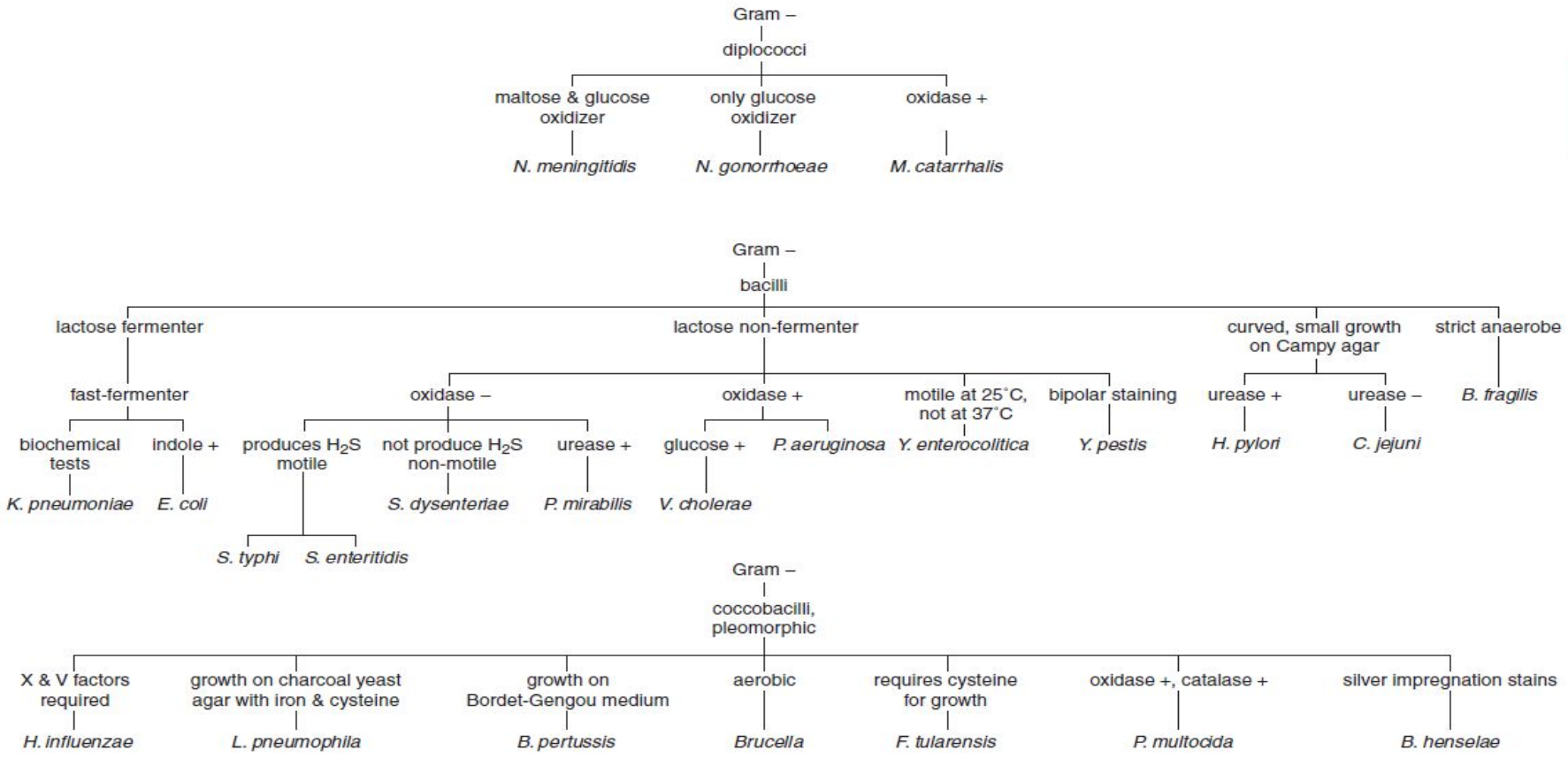
450–200 CD4+ T_h cells/μL		200–50 CD4+ T_h cells/μL		50–0 CD4+ T_h cells/μL	
H. influenzae (51)	pneumonia, sinusitis	*C. neoformans* (120)	meningitis	*M. avium-intracellulare* (59)	lung, liver, bone infection
S. pneumoniae (22)	pneumonia, sinusitis	*C. immitis* (116)	pneumonia, systemic infection		
S. aureus (13)	catheter-related sepsis			CMV (108)	retinitis, esophagitis, colitis
S. epidermidis (14)	catheter-related sepsis				
Salmonella species (40)	dysentery				
Shigella species (42)	dysentery	*P. jirovecii* (121)	pneumonia		
Campylobacter species (49)	dysentery	*C. parvum* (126)	diarrhea	*H. capsulatum* (117)	pneumonia, systemic infection
		T. gondii (128)	encephalitis		
M. tuberculosis (59)	tuberculosis				
EBV (109)	oral hairy leukoplakia				
VZV (107)	shingles				
HSV-1, HSV-2 (105, 106)	recurring oral and/or genital ulcers				
C. albicans (119)	thrush, vaginitis				
Tinea infections (114)	athlete's foot and other common fungal infections				

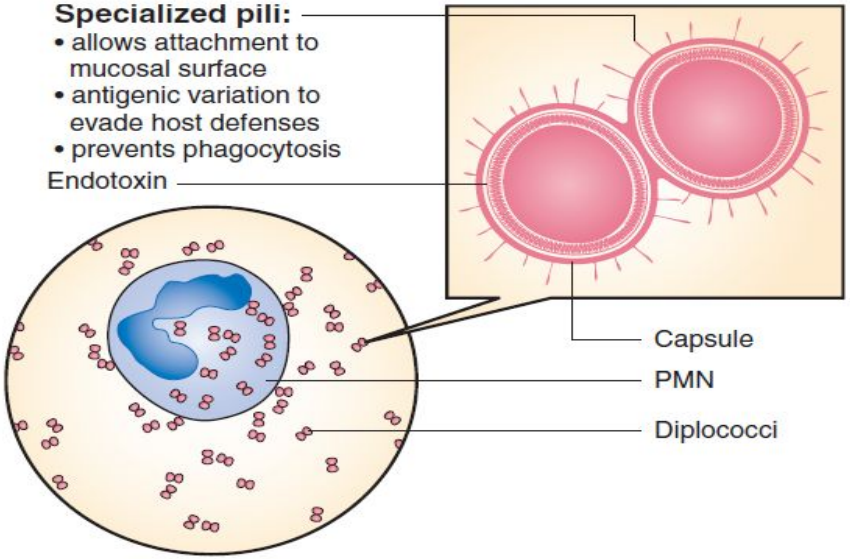
AIDS: <200 CD4+ cells/μL in an HIV+ individual

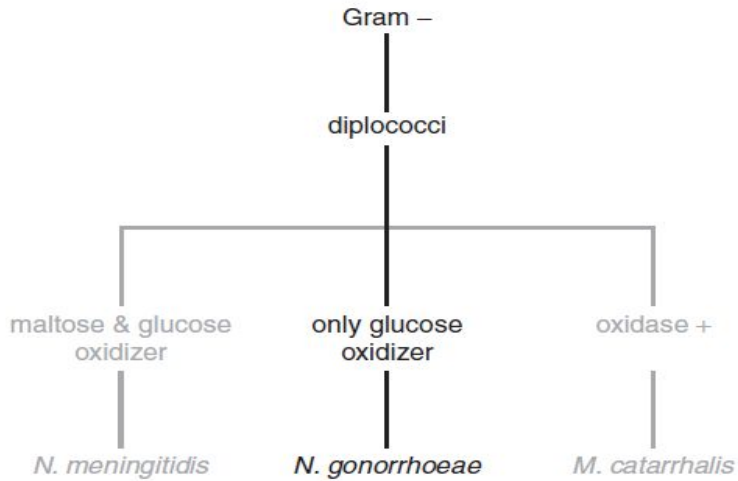
Gram + Bacteria



Gram – Bacteria







CLINICAL CASE

A teenager complains of pain during sexual intercourse and irregular intermenstrual bleeding. She has also begun to experience lower abdominal pain. A pelvic exam reveals a yellow mucopurulent discharge; during the exam, the cervix begins to bleed. Gram stain of discharge reveals Gram – intracellular diplococci. The teenager reports that she has been sexually active with several partners over the last year. One of her partners, a male, comes to the same clinic complaining of dysuria and profuse yellow urethral discharge.

Neisseria gonorrhoeae — Gonococci, Gonorrhea

CLINICAL PRESENTATION

Local (genital tract or anorectal infections)
- *asymptomatic, urethritis, dysuria (in men), cervicitis (in women), ophthalmia neonatorum*

Systemic
- *septic arthritis*

Complications
- *Pelvic Inflammatory Disease, ectopic pregnancy, sterility, Fitz-Hugh-Curtis Syndrome*

PATHOBIOLOGY

bacteria survive only in humans → attach via pili to mucosal cells of urethra and vagina → evades IgA antibodies with IgA protease → endocytosed by cells → kill ciliated cells → inflammatory response leading to urethritis (in men), cervicitis (in women)

in women, infection may progress to uterus, fallopian tubes, ovaries (PID) → increased risk for ectopic pregnancies → from fallopian tubes, bacteria may spill into peritoneal cavity (peritonitis) → may infect liver capsule (Fitz-Hugh-Curtis Syndrome)

can invade submucosa and enter bloodstream → may collect in synovial fluid → septic arthritis

in neonates, inoculates conjunctiva during passage through birth canal → ophthalmia neonatorum → risk for blindness

DIAGNOSIS

Gram − diplococci within PMNs
metabolizes glucose but not maltose (gonorrhea) vs. *N. meningitidis*
selectively grows on Thayer-Martin media

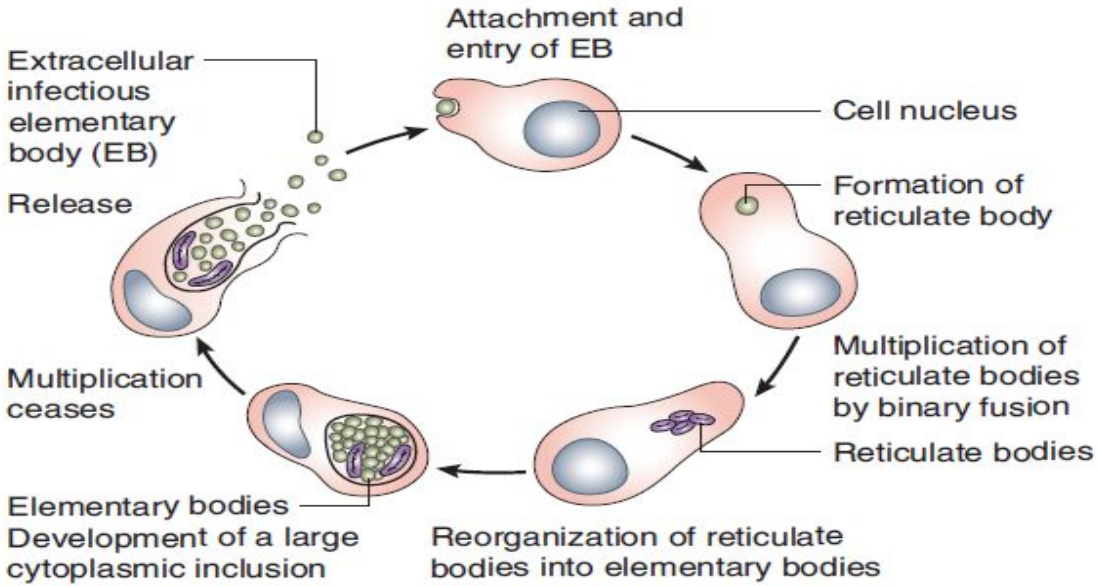
TREATMENT

ceftriaxone (+ doxycycline for probable concurrent *Chlamydia* infection)
prophylactic erythromycin eye drops for neonates
vaccine development difficult because of pili antigen variations

QUICK FACTS

Higher incidence of infection with menstruation or IUD.
Most common cause of septic arthritis in sexually active people.
Antigenic variation prevents immunity allowing recurrent infections.

Chlamydia trachomatis

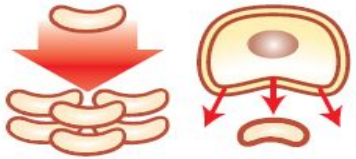


CLINICAL CASE

A woman is brought to the EW complaining of vaginal discharge and RUQ abdominal pain. On history, the patient reports having many sexual partners. Pelvic exam reveals cervical motion tenderness, and labs of vaginal discharge detect numerous PMNs but no organisms on Gram stain. The doctor makes a diagnosis based on these findings and administers doxycycline and ceftriaxone. Later, surgeons, concerned about the patient's abdominal pain, rule out cholecystitis by imaging, but laparoscopy reveals adhesions around the patient's liver capsule.

Chlamydia trachomatis

CLINICAL PRESENTATION



serovars D–K: urethritis, PID; neonatal pneumonia, neonatal conjunctivitis
serovars A–C: trachoma (chronic conjunctivitis)
serovars L1–L3: lymphogranuloma venereum (LGV)
complications: *Fitz-Hugh-Curtis syndrome;* Reiter's syndrome

PATHOBIOLOGY

different serovars have different manifestations:
serovars D–K: infects columnar epithelium ⟶ generates inflammation ⟶ damages GU tract ⟶
- in females: can spread to fallopian tubes and cause PID ⟶ increased risk for ectopic pregnancy ⟶ bacteria may spill into peritoneal cavity (peritonitis) ⟶ may infect liver capsule (Fitz-Hugh-Curtis syndrome)
- in males: can spread to synovial joints and other organs ⟶ arthritis, conjunctivitis ⟶ Reiter's syndrome (especially in HLA-B27 patients)

neonatal infection occurs as child passes through birth canal of infected mother ⟶ pneumonia, conjunctivitis
serovars A–C (trachoma): transmission by hand–eye contact ⟶ infect conjunctiva ⟶ inflammation promotes corneal vascularization and scarring ⟶ corneal damage ⟶ blindness
serovars L1, L2, L3 (lymphogranuloma venereum): sexually transmitted ⟶ painless ulceration at site of infection ⟶ ulcers heal spontaneously but bacteria spread to regional lymph nodes ⟶ lymphadenopathy (buboes) weeks later ⟶ buboes fuse, soften, and suppurate ⟶ creates multiple draining sinuses ⟶ may lead to proctitis, rectal stricture
Chlamydia life cycle has two forms: extracellular elementary body (EB) and intracellular reticular body (RB)—see side 1 for details

DIAGNOSIS

nucleic acid amplification (PCR, transcription-mediated amplification)
visualize intracytoplasmic inclusions: iodine stain + (inclusions contain glycogen), Giemsa stain +
serology
cultured in cell lines (intracellular growth)

TREATMENT

azithromycin
tetracyclines (+ ceftriaxone for concurrent *N. gonorrhea*)
oral erythromycin for neonates of infected mothers
prophylactic erythromycin eye drops for neonates

QUICK FACTS

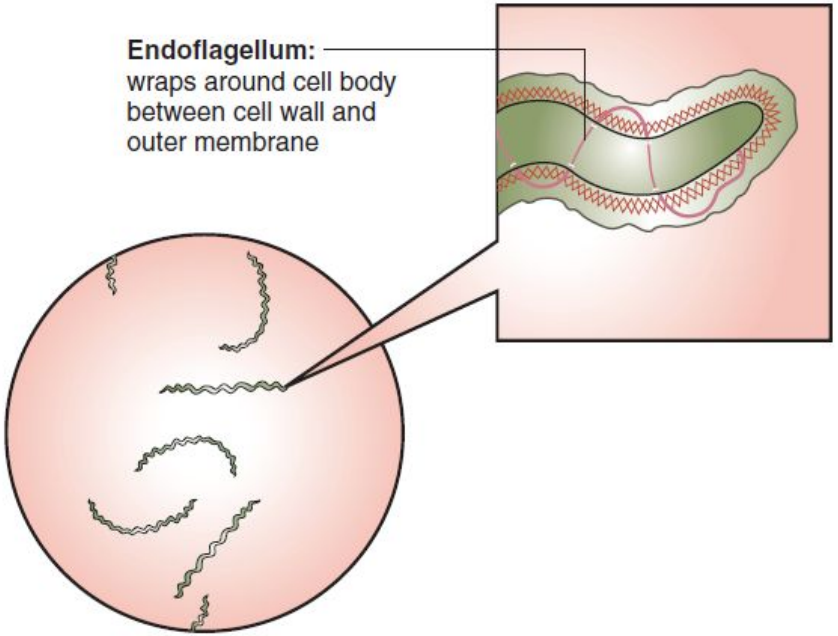
Most frequent cause of bacterial STD in the U.S. and most frequent cause of blindness worldwide
Chlamydiae infections in men are usually silent, so that infected individuals oftentimes unknowingly spread the organism to their partners.

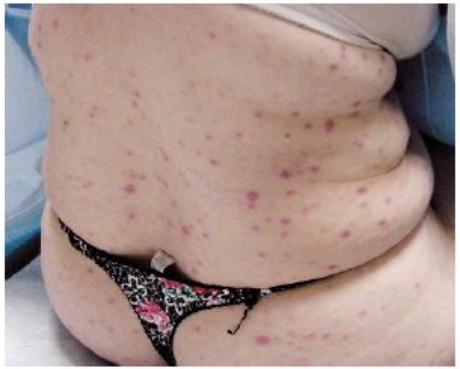
Study Tip

Two obligate intracellular (require host ATP for energy):
- Chlamydiae
- Rickettsiae

Chlamydiae replicate within inclusion bodies, Rickettsiae replicate freely in cytoplasm.
Common causes of non-gonococcal urethritis (NGU):
- *Chlamydia trachomatis*
- *Ureaplasma urealyticum*

Treponema pallidum — Syphilis





Secondary syphilis

Spirochetes

microaerophilic,
sensitive to high temperatures

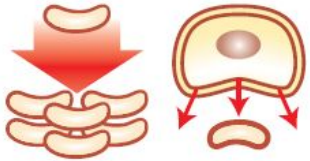
T. pallidum

CLINICAL CASE

A sexually active man seeks medical attention for a wart-like lesion developing on his genitals. He recalls a painless ulcer on his genitals over a month ago, but now is concerned because papules are appearing in his armpits and palms as well. Recently, he has also suffered fever and chills, and the doctor notices a nontender, generalized lymphadenopathy. The doctor questions the man about the health of his sexual partners. A dark-field analysis confirms the doctor's suspicion of the etiology and the patient is prescribed penicillin G.

Treponema pallidum — Syphilis

CLINICAL PRESENTATION



1° syphilis: painless chancre
2° syphilis: condyloma lata; maculopapular rash on palms and soles; meningitis, hepatitis, arthritis, and others
3° syphilis: gummas (granulomas of soft tissue, bone)
- CV: *aortitis, ascending aortic aneurysm*
- CNS: *tabes dorsalis, general paralysis, meningitis, Argyll Robertson pupil* (accommodates to near objects but does not react to light)

congenital syphilis: CN VIII deafness, mulberry molars, saber shins, saddle nose, Hutchinson's incisors

PATHOBIOLOGY

human is only host → transmitted from skin lesions containing spirochete (sexual or casual contact) → spirochete penetrates mucous membranes → systemic spread within hours of inoculation →

- 1° syphilis (visible 6 weeks after exposure): organism multiplies at inoculation site → painless chancre (ulcerated lesion shedding spirochetes) → lesion heals spontaneously over 6 weeks
- 2° syphilis (visible 6 weeks after chancre heals): disseminated spirochetes proliferate → form lesions throughout body including condyloma lata (wart-like painless lesions in moist areas, e.g., genitals) → lesions may heal spontaneously or may become latent syphilis (no symptoms but serologically +) → cycle of 2° syphilis can repeat multiple times
- 3° syphilis (many years later): chronic inflammation against remaining spirochetes → damage to soft tissue and bone (gummas), CV system (aortitis), CNS

transplacental transmission → congenital syphilis: stillbirth, fetal abnormalities

DIAGNOSIS

dark-field microscopy (spirochetes not visible on Gram stain) serological tests:
- VDRL (nonspecific): detects reagin antibodies against cardiolipin
- FTA-ABS (specific): detects anti-treponemal antibodies

TREATMENT

penicillin G

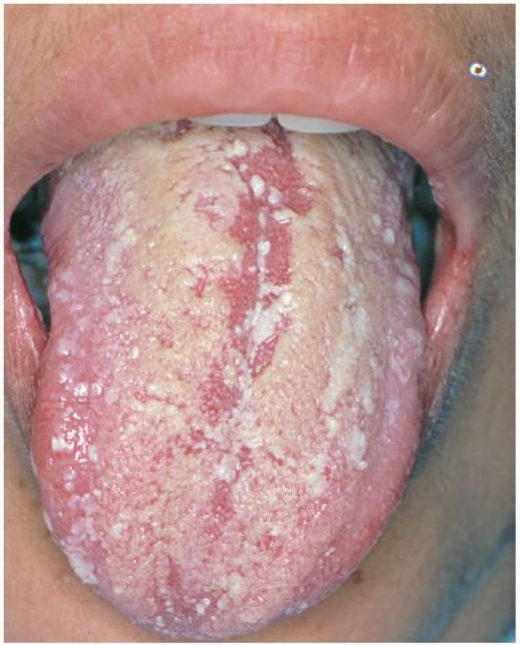
QUICK FACTS

Treatment may lead to Jarisch-Herxheimer reaction: lysis of treponeme → release of endotoxin-like factors → fever, chills, myalgias.
SLE and infectious mononucleosis patients can have false-positive VDRL tests due to anti-cardiolipin antibodies. Clarify with more specific FTA-ABS test.
Syphilis meningitis presents with ↑ lymphs, normal PMNs in CSF.
Treponema pallidum subspecies cause nonvenereal skin ulcers and skin/bone gummas: *T. pallidum endemicum* → endemic syphilis (common in Africa, Middle East); *T. pallidum pertenue* → Yaws (gummas disfigure face); *T. pallidum carateum* → Pinta (red → blue → white lesions, limited to Latin America).

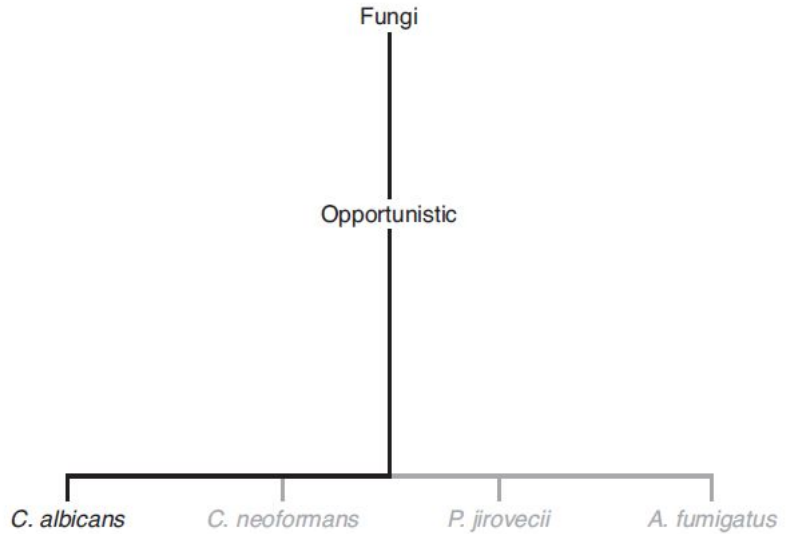
Study Tip

Palm & sole rash:
- Syphilis
- Rocky Mountain spotted fever
- coxsackievirus

Organisms that cross placenta and therefore allow infection to pass from pregnant mother to fetus (TORCHES):
- TOxoplasma gondii
- Rubella
- Cytomegalovirus
- HErpes, HIV
- Syphilis



Oral candidiasis



CLINICAL CASE

Several months ago, a patient presented to a free clinic with a thick, white membrane covering the roof of his mouth. After a thorough social history, the doctor suspected a possible HIV infection. However, at the time, the patient refused testing and never returned for follow-ups. Now, the patient revisits the clinic complaining of painful swallowing and severe chest pains. The doctor immediately places the patient on fluconazole and makes arrangements for future treatments and tests.

Candida albicans

CLINICAL PRESENTATION

normal host:
- *thrush*
- *vaginitis* (yeast infection)

immunocompromised host:
- *esophagitis*
- *systemic infection*

PATHOBIOLOGY

normal flora in mucous membranes of respiratory, GI, and female genital tracts → overgrowth may occur in warm, moist areas:
- mouth: oral thrush (white exudate on mucous membrane)
- female genitals: vaginitis (itching, copious secretion, "cottage cheese"-appearing clumps)
- cutaneous: skin under breasts, nails

if immunocompromised, infection persists chronically → infection may spread:
- from mouth to esophagus: esophagitis
- from local to systemic sites: disseminated candidiasis

DIAGNOSIS

pseudohyphae and budding yeast observed in tissue scrapings
disseminated infection: + blood cultures (not normally found in blood)

TREATMENT

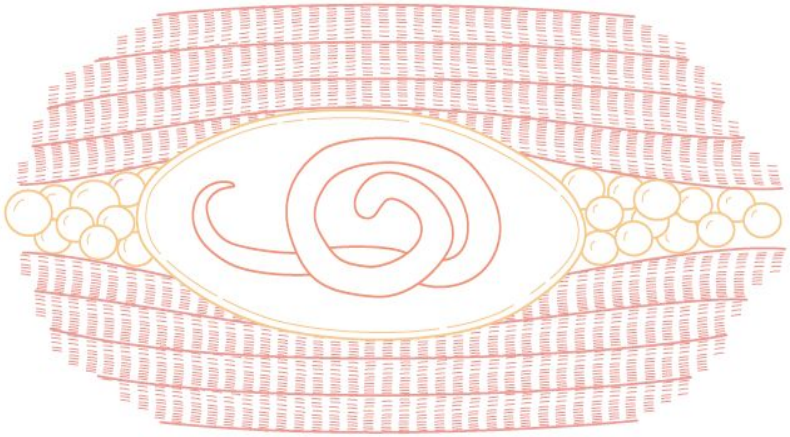
thrush/esophagitis: nystatin mouthwash, fluconazole
vaginitis: fluconazole, topical antifungal
systemic: antifungals (e.g., amphotericin B)

QUICK FACTS

Candidiasis is one of several causes of diaper rash in young children.
Esophagitis and disseminated candidiasis are major opportunistic infections in AIDS patients.

Trichomonas vaginalis — Trichomoniasis

T. vaginalis is transmitted between humans by sexual contact. Lacking a cyst, it does not survive well in the external environment.



Cysts with larvae in skeletal muscle

Trophozoite resides in vagina or orifice of urethra and is spread in vaginal or prostatic secretions as well as in urine.

Protozoa

Urogenital infection

T. vaginalis

CLINICAL CASE

A teenage girl complains of vaginal itching and burning. Sexual history reveals numerous sexual partners. Her gynecologist performs a pelvic exam and finds a greenish, foul-smelling thin discharge from the vagina. A wet mount of the discharge reveals motile amoeba, each with 1 nucleus and 5 flagella. The patient is started on metronidazole.

Trichomonas vaginalis — Trichomoniasis

CLINICAL PRESENTATION

vaginitis
urethritis (mainly in males)

PATHOBIOLOGY

sexual transmission → trophozoite colonizes:
- vagina in females → greenish, watery, & foul-smelling vaginal discharge; itching
- urethra in males → mostly asymptomatic

DIAGNOSIS

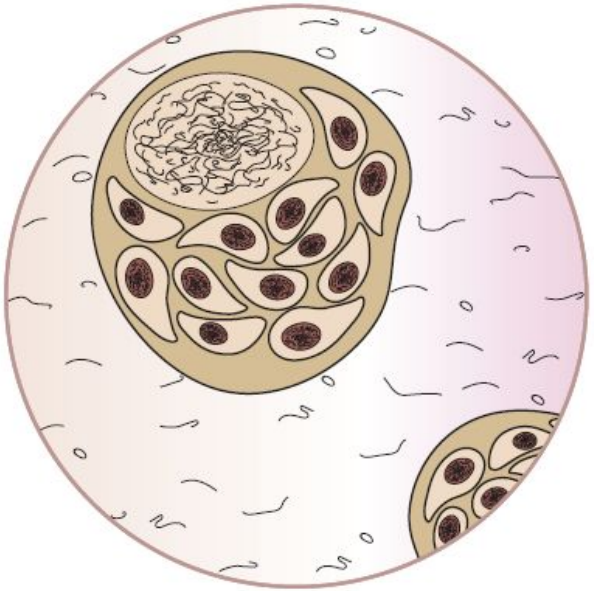
wet mount of vaginal or urethral discharge: tear-drop shaped trophozoites; 5 flagella, 1 nucleus

TREATMENT

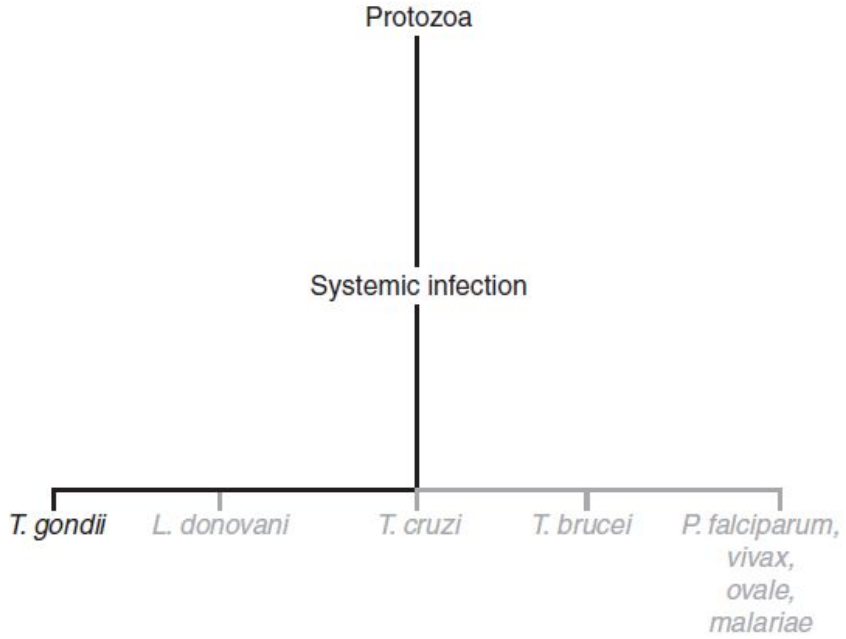
metronidazole to the patient and patient's sexual partner(s)

QUICK FACTS

Trichomonas can be distinguished from other flagellate protozoa in that it lacks a cyst form (by sexual transmission, the organism never leaves a host).



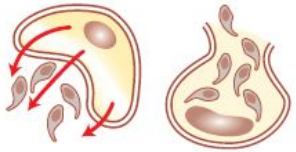
Crescent-shaped trophozoites within macrophage



CLINICAL CASE

An AIDS patient is brought to the EW after suffering a grand mal seizure. The man informs the EW physician that he has suffered a persistent headache in the past few weeks but denies any sensory problems or weakness. Fearing a brain tumor, the EW physician orders a CT scan of the patient. However, the scan, instead, reveals several ring-enhancing masses in the patient's brain. The physician confirms his suspicions when he learns the patient has many cats at home. He expects that a brain biopsy would show crescent-shaped trophozoites.

Toxoplasma gondii — Toxoplasmosis



CLINICAL PRESENTATION

in immunocompetent patients: *asymptomatic, mononucleosis-like illness*
in immunocompromised patients: *encephalitis, chorioretinitis*
congenital infection: *mental retardation, chorioretinitis*

PATHOBIOLOGY

cysts ingested from undercooked meat or cat feces → in small intestine, cysts release invasive form → penetrate intestinal wall → phagocytosed and disseminated by macrophages → infects, damages cells at distant sites → host response contains infections (with mononucleosis-like symptoms) → in tissue, invasive forms become dormant → contained within cyst
if host becomes immunocompromised → cyst ruptures and releases invasive form → encephalitis, chorioretinitis, other infections
if active infection in pregnant mother → invasive form crosses placenta to fetus → congenital toxoplasmosis → mental retardation, chorioretinitis, other birth defects → invasive form becomes dormant and may reactivate later in life

DIAGNOSIS

serology (IgM in infants)
tissue biopsy: trophozoites (active), cysts (dormant)
CT, MRI of head

TREATMENT

sulfonamide + pyrimethamine

QUICK FACTS

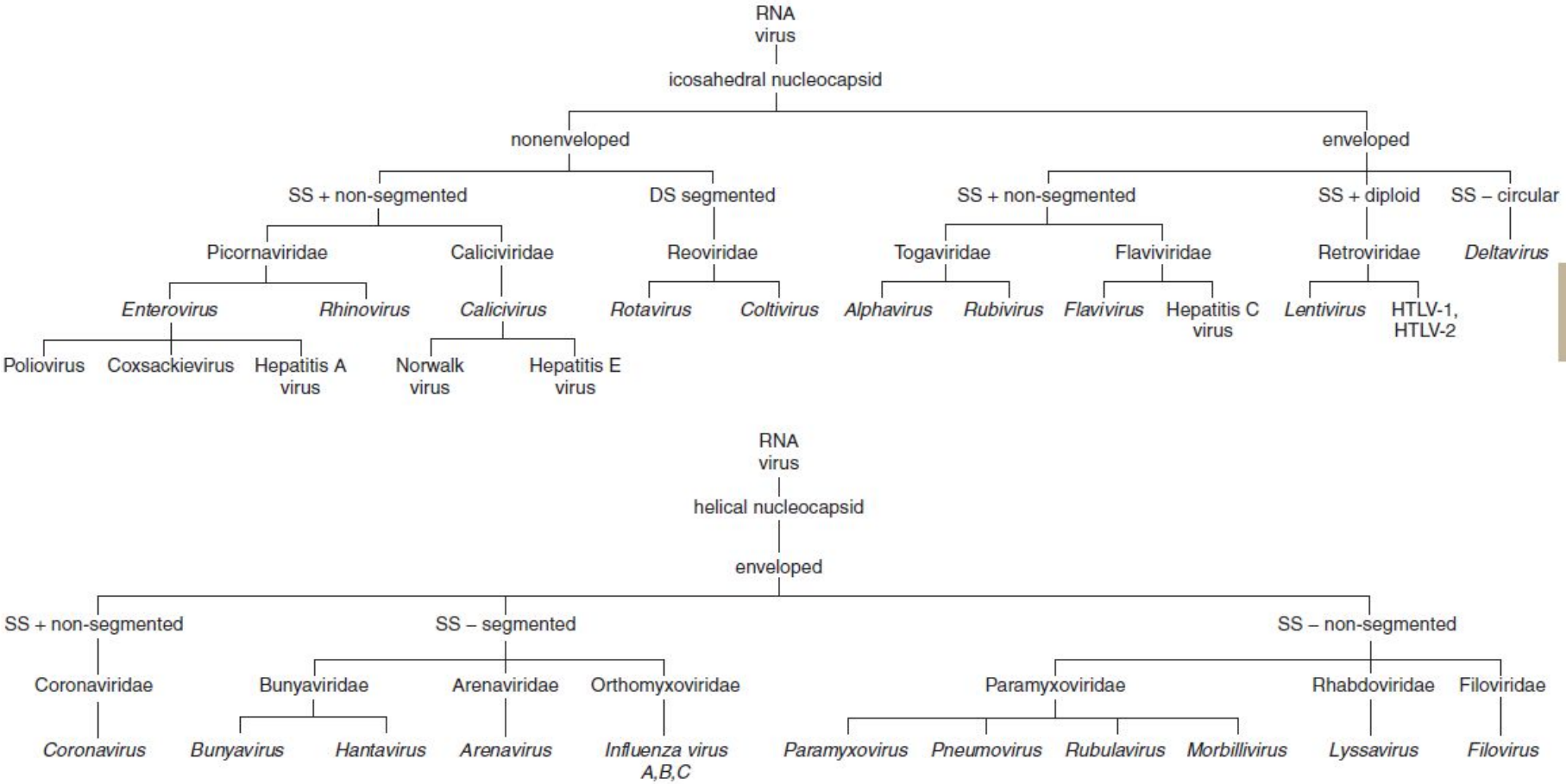
Toxoplasma is the most common cause of encephalitis in HIV patients.
Only pregnant mothers with an active primary infection can result in congenital toxoplasmosis; mothers with previous infections mount an immune response that protects the fetus.
Pregnant mothers, especially those without previous exposure, are encouraged to avoid cats to prevent congenital toxoplasmosis.

Study Tip

Organisms that cross placenta and therefore allow infection to pass from pregnant mother to fetus (TORCHES):

Toxoplasma gondii
Rubella
Cytomegalovirus
Herpes, HIV
Syphilis

RNA Viruses


RNA virus
icosahedral nucleocapsid
nonenveloped
enveloped
SS + non-segmented
DS segmented
SS + non-segmented
SS + diploid
SS – circular
Picornaviridae
Caliciviridae
Reoviridae
Togaviridae
Flaviviridae
Retroviridae
Deltavirus
Enterovirus
Rhinovirus
Calicivirus
Rotavirus
Coltivirus
Alphavirus
Rubivirus
Flavivirus
Hepatitis C virus
Lentivirus
HTLV-1, HTLV-2
Poliovirus
Coxsackievirus
Hepatitis A virus
Norwalk virus
Hepatitis E virus
RNA virus
helical nucleocapsid
enveloped
SS + non-segmented
SS – segmented
SS – non-segmented
Coronaviridae
Bunyaviridae
Arenaviridae
Orthomyxoviridae
Paramyxoviridae
Rhabdoviridae
Filoviridae
Coronavirus
Bunyavirus
Hantavirus
Arenavirus
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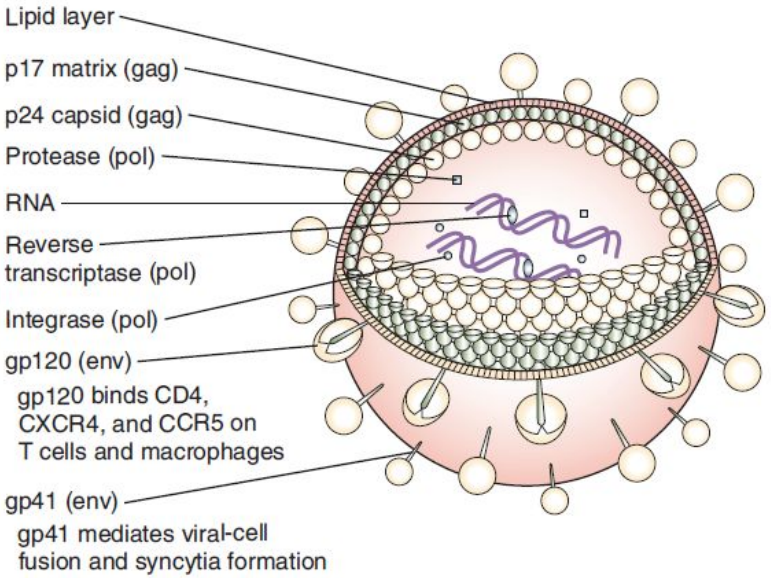
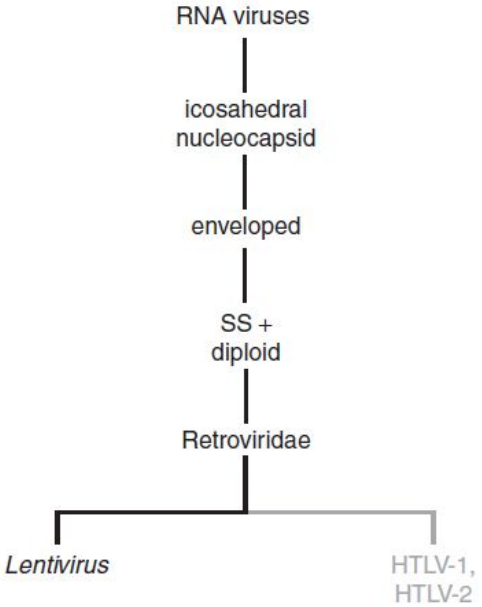
Paramyxovirus
Pneumovirus
Rubulavirus
Morbillivirus
Lyssavirus
Filovirus



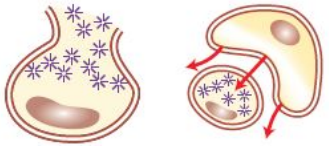


CLINICAL CASE

A 45-year-old homeless man complains to an EW doctor of fever, cough, and a burning pain in his chest. These symptoms have "lingered on and off" for several weeks, and weight loss forces him to resolve the vague illness once and for all.
The physician notes no chest sounds, and chest X-ray reveals only a faint interstitial infiltrate. Suspecting some sort of pneumonia, the physician requests a sputum analysis. Lab results reveal the presence of *Pneumocystis jirovecii* confirmed by PCR. Concerned about this fungal infection, the physician administers trimethoprim/sulfamethoxazole and requests a blood count. The results—a white blood cell value of 2,000 cells/μL and CD4+ T-cell count of 500 cells/μL—confirm a grave suspicion. The physician tells the patient the likely diagnosis and asks if he would like a social worker's help.

CLINICAL PRESENTATION

AIDS and opportunistic infections



PATHOBIOLOGY

1° infection stage (first months): transmission by bodily fluids: sexual contact, blood transfer, maternal transfer (transplacental, during birth, via breast milk)⟶ infects CD4+ cells, including T_h lymphocytes in blood and macrophages in epidermis ⟶ replicates in spleen and lymphoid organs ⟶ viremia ⟶ contained by vigorous host immune response ⟶ mononucleosis-like symptoms ⟶ equilibrium established between viral production and host containment

Clinical Latency Stage (7–10 years): mutations in antigens help virus evade host response ⟶ virus replicates, especially in lymphoid organs ⟶ host responds with (1) increased T_h cell production and (2) CTL response against infected cells ⟶ no or low-level symptoms

continued viral evasion by mutations ⟶ viral load gradually increases, CD4+ count gradually drops

CD4+ cells depleted by various mechanisms, including:

- immune attack on infected cells by CTLs
- cell lysis from extensive viral budding
- syncytia formation between infected and uninfected cells (via gp120-CD4 interactions)

Advanced Disease (AIDS): CD4+ T-cell count <200 cells/μL ⟶ common opportunistic infections/neoplasms causing death: *Pneumocystis jirovecii* pneumonia, *Candida albicans* thrush, disseminated HSV, CMV, histoplasmosis, toxoplasmosis, cryptococcal meningitis, *Mycobacterium tuberculosis*, *Mycobacterium avium-intracellulare*, Kaposi's sarcoma

infection of brain microglia, oligodendrocytes, astrocytes ⟶ neuropathy, encephalopathy, dementia

(see HIV life cycle card for information on viral and host protein interactions, e.g., gp120-CD4 interactions)

DIAGNOSIS

detection of virus by ELISA, Western, PCR

TREATMENT

NRTI = nucleoside reverse transcriptase inhibitors (nucleoside analogs) (e.g., AZT, ddI, lamivudine, abacavir, tenofovir, emtricitabine)
NNRTI = nonnucleoside reverse transcriptase inhibitors (bind outside active site) (e.g., efavirenz, nevirapine, delavirdine)
PI = protease inhibitors (e.g., indinavir, nelfinavir)
FI = fusion inhibitors (e.g., enfurvitide)
HAART = Highly Active AntiRetroviral Therapy is a drug cocktail (e.g., NNRTI + 2 NRTI, PI + 2 NRTI) initiated for symptomatic HIV or low CD4 count
Prevention: protected sex, screening of blood, AZT to infected pregnant mothers

QUICK FACTS

HIV-1 and HIV-2 have similar clinical presentations and share common antigens. HIV-1 is found throughout the world, whereas HIV-2 is found mainly in West Africa.

Monocytes and macrophages advance HIV infection in two ways: (1) they transport HIV to the CNS and (2) they are a reservoir for HIV, especially when T-cell counts are low.

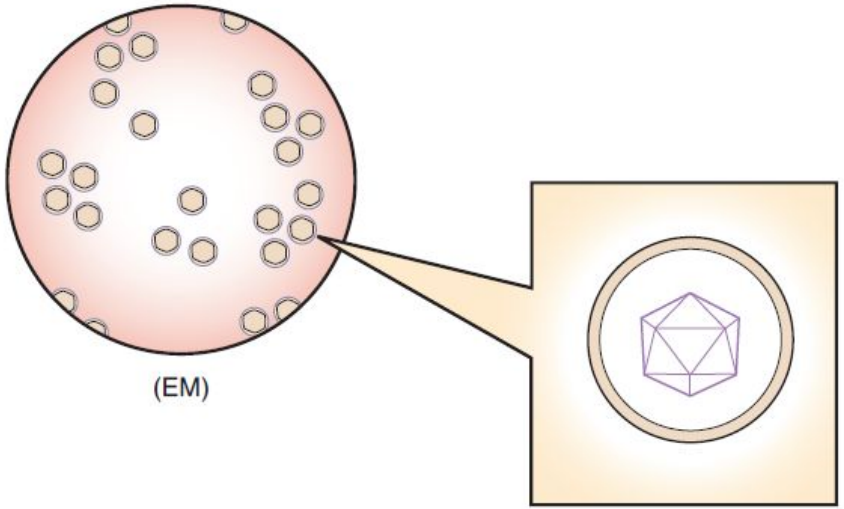
Kaposi's sarcoma has been associated with human herpesvirus 8 (HHV 8) infection.

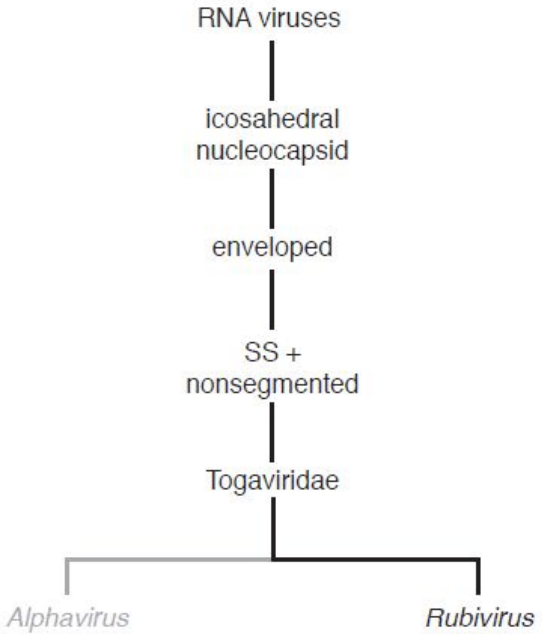
HHV 8 can be transmitted sexually.

Study Tip

Organisms that cross placenta and therefore allow infection to pass from pregnant mother to fetus (TORCHES):

TOxoplasma gondii
Rubella
Cytomegalovirus
HErpes, HIV
Syphilis





CLINICAL CASE

A woman goes to her doctor complaining of a red rash on her face. She reports having a fever that resolved just before the rash appeared. During a physical exam, the doctor notes that the rash has spread to the arms. Swollen lymph nodes are felt in the cervical region and behind the ears. The doctor inquires about the woman's vaccination record and makes a diagnosis to be confirmed by serological studies. The doctor also makes sure that the woman is not pregnant. The woman is relieved to know the rash will go away in several days, although she may experience arthritis for some time thereafter.

Togaviridae Rubivirus — Rubella Virus, German Measles

CLINICAL PRESENTATION

rubella: fever followed by descending rash
congenital rubella: congenital malformations (deafness, patent ductus arteriosus, pulmonary artery stenosis, cataracts, microcephaly)

PATHOBIOLOGY

transmitted by aerosol → virus infects nasopharynx and replicates in local lymph nodes → systemic spread via blood (viremia) → antibody-mediated reaction leads to maculopapular rash beginning in face and spreading to extremities → antibody complexes may result in arthritis in women
if it infects pregnant woman in first trimester → may cross placenta to fetus → infects fetal cells and promotes mitotic arrest, necrosis, or chromosomal damage → congenital defects in brain, heart, or eyes
lifelong immunity following infection

DIAGNOSIS

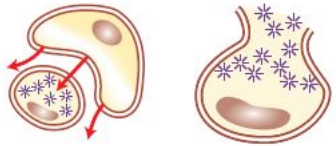
detection of anti-rubella antibodies:
IgM if recent infection
IgG if immune
blocks CPE of ECHO virus in culture
virus in amniocentesis indicates congenital rubella

TREATMENT

self-limiting (no antiviral treatment available)
vaccine: live-attenuated rubella virus in measles–mumps–rubella (MMR) vaccine

QUICK FACTS

Pregnant women are screened for rubella immunity. However, the rubella vaccine is not administered until after delivery for fear of fetal infection.
An infant with congenital rubella may transmit the virus up to the age of 2, complicating control of infection from such patients.
Unlike other *Togaviridae*, rubella is not an arbovirus because it is not transmitted by an arthropod.
MMR is the only live viral vaccine that can be given in HIV-positive individuals.



Study Tip

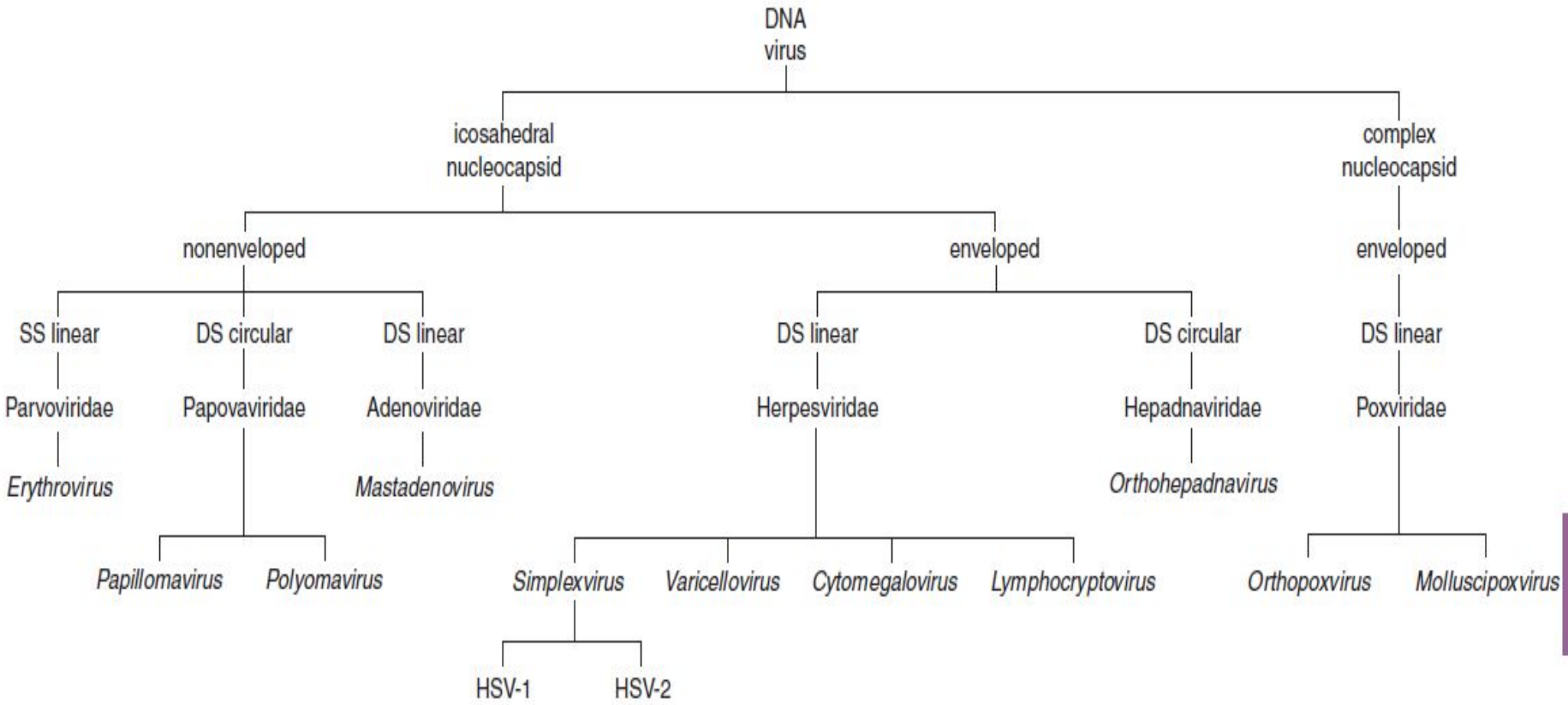
Five most common pediatric diseases with rash:

- Measles (measles virus)
- Rubella (rubella virus)
- Scarlet fever (*S. pyogenes*)
- Roseola (HHV 6)
- Erythema infectiosum (Parvovirus B19)

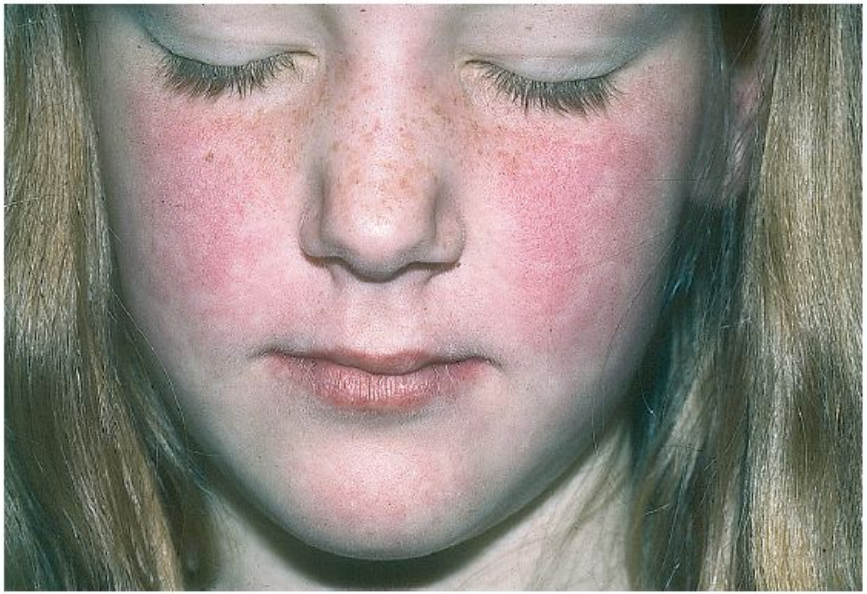
Organisms that cross placenta and therefore allow infection to pass from pregnant mother to fetus (TORCHES):

TOxoplasma gondii
Rubella
Cytomegalovirus
HErpes, HIV
Syphilis

DNA Viruses


DNA virus
icosahedral nucleocapsid
complex nucleocapsid
nonenveloped
enveloped
enveloped
SS linear
DS circular
DS linear
DS linear
DS circular
DS linear
Parvoviridae
Papovaviridae
Adenoviridae
Herpesviridae
Hepadnaviridae
Poxviridae
Erythrovirus
Mastadenovirus
Orthohepadnavirus
Papillomavirus
Polyomavirus
Simplexvirus
Varicellovirus
Cytomegalovirus
Lymphocryptovirus
Orthopoxvirus
Molluscipoxvirus
HSV-1
HSV-2

Parvoviridae Erythrovirus — Parvovirus B19



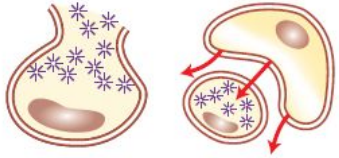
Erythema infectiosum: "slapped-cheek" rash

DNA viruses
↓
icosahedral nucleocapsid
↓
nonenveloped
↓
SS linear
↓
Parvoviridae
↓
Erythrovirus

CLINICAL CASE

An African American girl with sickle cell anemia visits the doctor after developing weakness, fatigue, and pallor. She tells her physician that several days before, she felt a fever, headache, and muscle aching. She also began to feel joint pain and developed a rash that had a "slapped-face" appearance on her face. A blood test reveals severe anemia, as well as a decline in neutrophils and lymphocytes. The myeloid lineage seems normal. Serology confirms the diagnosis, and the doctor orders a transfusion of erythrocytes to prevent life-threatening anemia.

Parvoviridae Erythrovirus — Parvovirus B19



CLINICAL PRESENTATION

erythema infectiosum ("fifth disease")
transient aplastic anemia crisis

PATHOBIOLOGY

inoculates nasal cavity → 6-day incubation → viremia and fever → virus infects and lyses erythroid precursor cells in the bone marrow → mildly reduced reticulocytes, lymphocytes, neutrophils, platelets (normal hosts can tolerate lack of erythropoiesis for 1 week)
immune complexes form and deposit → erythema infectiosum: rash with "slapped-cheek" appearance, arthralgias for several days
in patients requiring increased erythropoiesis (e.g., sickle cell anemia, thalassemias) → transient aplastic crisis: severe reticulocytopenia, normal myeloid lineage

DIAGNOSIS

detect viral DNA
serology

TREATMENT

supportive: RBC transfusion
in immunodeficient patients: Ig transfer

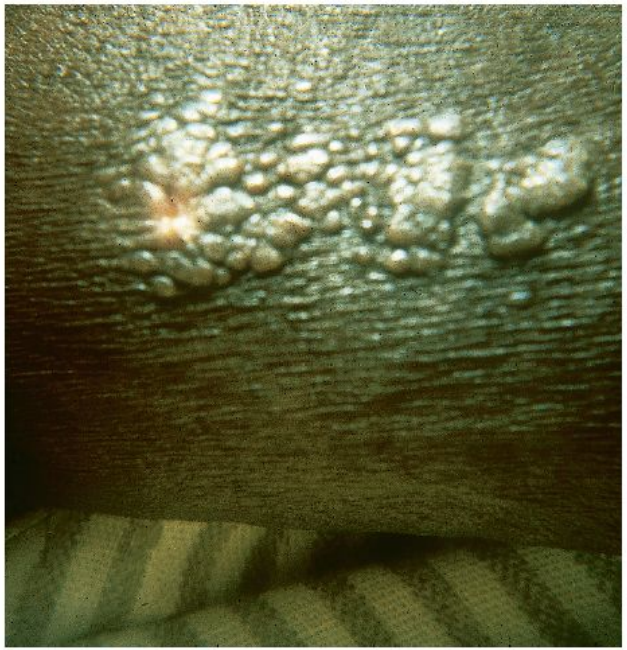
QUICK FACTS

In immunodeficient patients, parvovirus infection can lead to chronic severe anemia.
Fetuses, who require higher RBC production and are immunodeficient, are especially vulnerable to parvovirus infections. Infected fetuses may develop severe anemia and hydrops fetalis.
Erythema infectiosum is called "fifth disease" because it is one of the five most common pediatric diseases with rash.

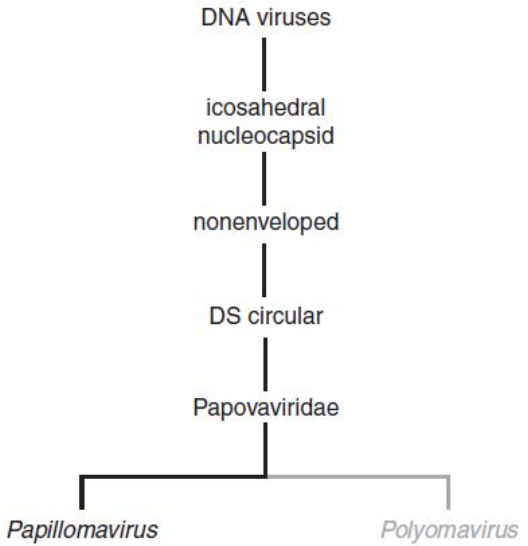
Study Tip

Five most common pediatric diseases with rash:

- Measles (measles virus)
- Rubella (rubella virus)
- Scarlet fever (*S. pyogenes*)
- Roseola (HHV 6)
- Erythema infectiosum (parvovirus B19)



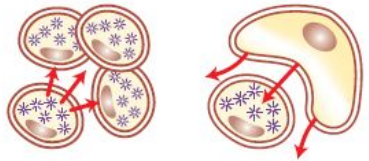
Condyloma acuminatum warts



CLINICAL CASE

A 22-year-old sexually active man complains of warts on his penis. He does not report pain, but he is concerned that he might be spreading them to his female sexual partner. The doctor, diagnosing the warts as condyloma acuminata, treats the patient by ablating the warts. He also decides to test the sexual partner, fearing that if she contracted the patient's illness, she would be at increased risk for cervical cancer.

Papovaviridae Papillomavirus — Human Papilloma Viruses (HPV)



CLINICAL PRESENTATION

Acute: *warts* (on penis, vulva, cervix, fingers, hands, soles, knees, elbows, oropharynx, larynx)
Chronic: *asymptomatic; carcinomas (cervical carcinoma, squamous cell carcinoma, laryngeal carcinoma)*

PATHOBIOLOGY

transmitted by close contact → virus infects squamous epithelial cells in epidermis or mucous membranes →

- Lysogenic cycle: infects basal cells → attempts to replicate → basal cell environment disfavors viral replication → virus can transform basal cells via E6 (blocks p53) and E7 (blocks Rb) viral proteins → benign cell growth and vacuolization (warts)
- Lytic cycle: infects upper keratinized epithelium or progresses with basal cell as it rises/differentiates → keratinized cell environment favors viral replication → replicates DNA, assembles → vacuolizes cytoplasm → lyses cell, viral particles released for further infection

infection controlled by cell-mediated immunity

DIAGNOSIS

1% acetic acid turns lesions white
colposcopy + biopsy of white lesions
PCR using viral specific primers

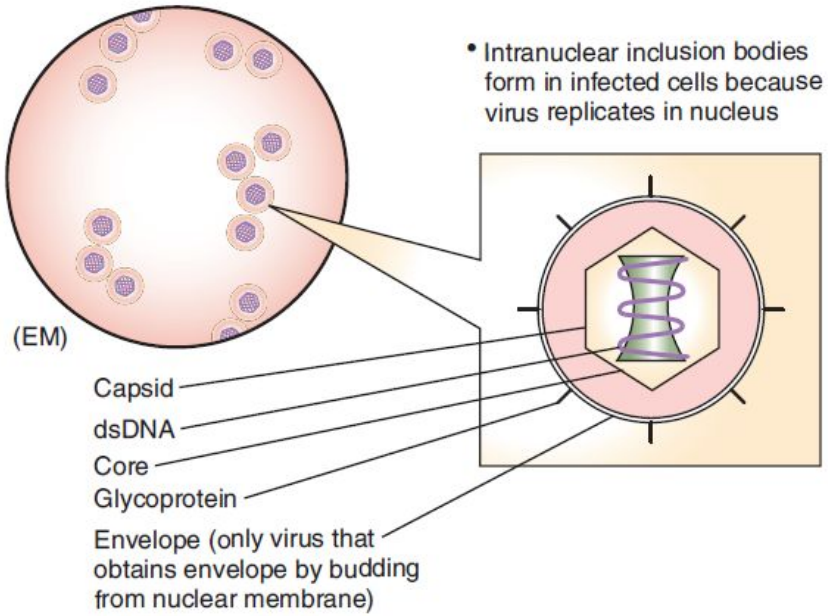
TREATMENT

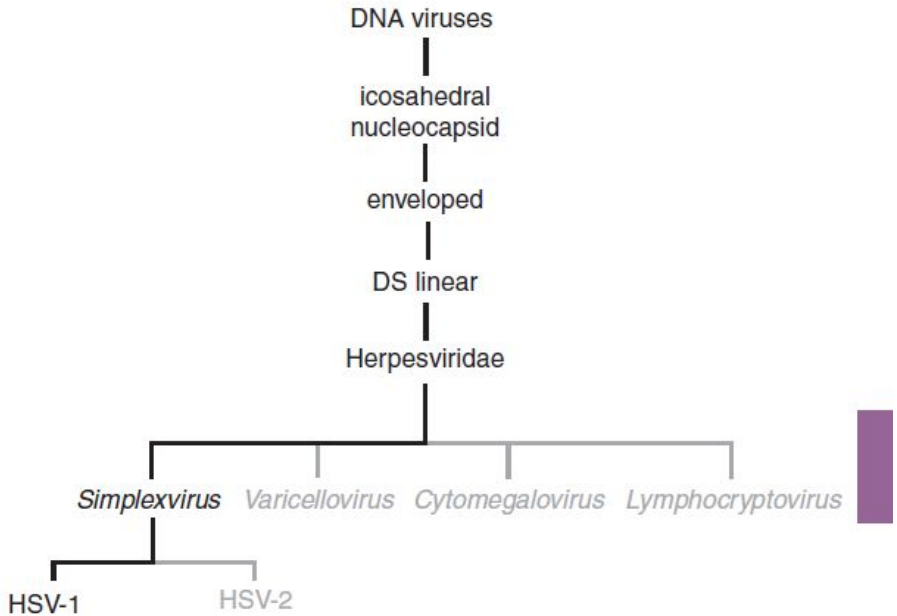
50% of warts spontaneously regress in 1–2 years
ablation
HPV vaccine available to prevent cervical cancer. Gardasil protects against HPV 6, 11, 16, and 18. Cervarix protects against HPV 16 and 18.

QUICK FACTS

HPV virus 16 and 18 cause genital warts that can progress to cervical carcinoma.
Warts in the larynx (which can be acquired by infants vaginally borne to mothers with genital warts) cause airway swelling, hoarseness, and secondary bacterial pneumonia.
Epidermodysplasia verruciformis presents as many flat warts on the skin, which may progress to squamous cell carcinomas.
HPV is a very parsimonious virus, using host machinery for most of its replicative functions. It also codes for proteins in all three reading frames of a single DNA strand.
Papanicolaou testing ("Pap smears") has been effective in detecting dysplastic HPV-infected cells before they transform into neoplastic cells.
Papovaviridae is derived from *PA*pillomaviruses, *PO*lyomaviruses, and *VA*cuolating viruses.

Herpesviridae Simplexvirus — *Herpes Simplex Virus 1 (HSV-1) or Herpesvirus 1*





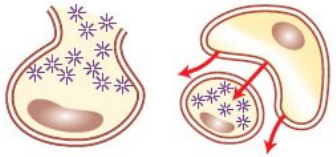
CLINICAL CASE

A 55-year-old man is hospitalized for a recent onset of high fever, headaches, and sporadic sensations of smelling sausages. Physical exam reveals neck stiffness, prompting the physician to perform a lumbar puncture. CSF values indicate elevated lymphocytes, elevated protein, and normal glucose. A CT image confirms encephalitis localized to the temporal lobes. A diagnosis is confirmed by PCR of the CSF. The physician begins treatment with acyclovir and informs the patient that he may suffer permanent neurological abnormalities from the infection.

Herpesviridae Simplexvirus — *Herpes Simplex Virus 1 (HSV-1) or Herpesvirus 1*

CLINICAL PRESENTATION

gingivostomatitis
keratoconjunctivitis
herpes labialis (cold sores)
temporal lobe encephalitis



PATHOBIOLOGY

only human reservoir → transmitted via saliva → virus invades mucous membranes → local primary infection → typically asymptomatic but can cause vesicular lesions that ulcerate in:
- mouth → gingivostomatitis
- eye → keratoconjunctivitis (on cornea, typically presents as branching "dendritic ulcer")

primary infection resolves after 2–3 weeks → virus enters local sensory nerve endings → axonal transport proximally to sensory ganglion cell bodies → latent infection of trigeminal ganglion or other sensory ganglia

stress (fever, menstruation, sunlight) → viral reactivation → axonal transport of virus from ganglia to nerve endings → recurrent local infection → may result in herpetic labialis (cold sores around mouth), gingivostomatitis, or keratoconjunctivitis

rarely, virus may spread via cranial nerves to brain → focal necrotic lesions in temporal lobe → inflammation → encephalitis → permanent neurological abnormalities or death

DIAGNOSIS

detection of virus (PCR, especially for early detection in encephalitis)
multinucleate giant cells on Tzanck smear of skin lesions
eosinophilic Cowdry intranuclear inclusion bodies on skin biopsy

TREATMENT

acyclovir
trifluridine (topical, for eye infections)

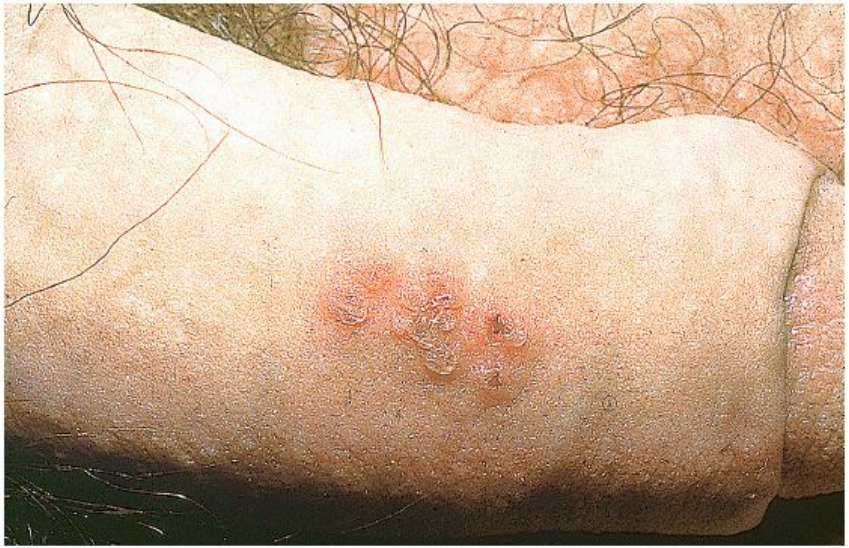
QUICK FACTS

Herpesviruses are the most common cause of sporadic encephalitis in the U.S.: HSV-1 in adults, HSV-2 in neonates.
Most adults have been infected by HSV-1 or -2, but very few infections are symptomatic and only 25% of latent infections exhibit recurrent infections.
Herpetic whitlow is a painful hand vesicle that can occur in health care workers who come in contact with herpetic lesions.
Recurrent keratoconjunctivitis is a common cause of blindness in the U.S.

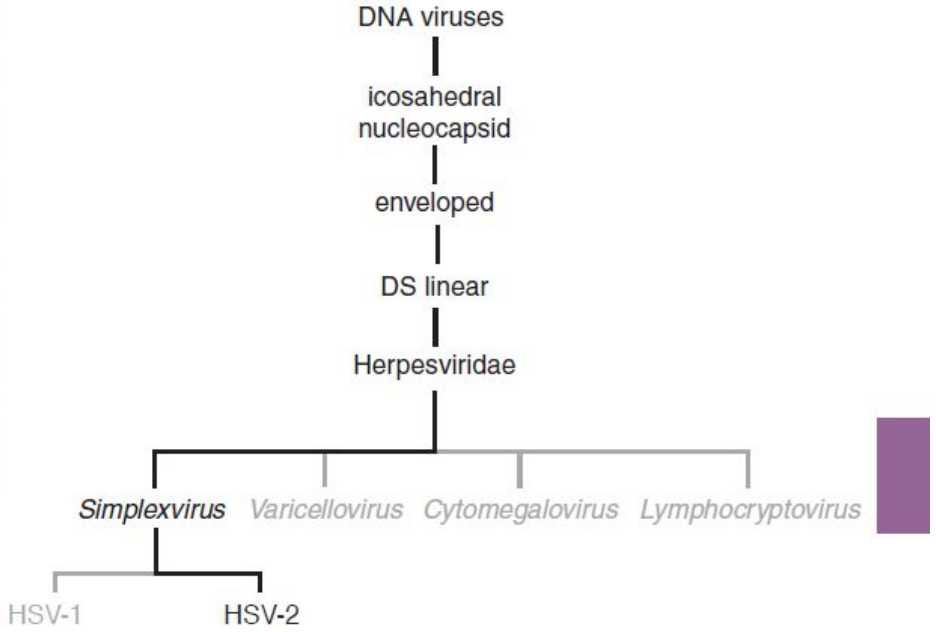
Study Tip

Typically,
HSV-1 infects ABOVE the waist: eye and mouth lesions
HSV-2 infects BELOW the waist: genital lesions
(oral-genital sex can lead to HSV-1 below and HSV-2 above)

Herpesviridae Simplexvirus — *Herpes Simplex Virus 2 (HSV-2) or Herpesvirus 2*



Herpes simplex genitalis



CLINICAL CASE

At a preterm evaluation, a 31-year-old pregnant mother reports pain on urination and a burning, itching sensation in the genital area. A careful exam of her vagina reveals a vesicular rash. The physician confirms a diagnosis with a Tzanck smear of the lesions showing multinucleate giant cells with intranuclear inclusion bodies. The mother is administered acyclovir with assurances that the infection will likely resolve, but she is informed that should the infection persist, her child will have to be delivered by cesarean section.

Herpesviridae Simplexvirus — *Herpes Simplex Virus 2 (HSV-2) or Herpesvirus 2*

CLINICAL PRESENTATION

genital herpes
neonatal herpes

PATHOBIOLOGY

only human reservoir → transmission by sexual contact → virus invades mucous membranes → local primary infection → typically asymptomatic but can cause vesicular lesions in genital/perianal area
primary infection resolves after 2–3 weeks → virus enters local sensory nerve endings → axonal transport proximally to sensory ganglion cell bodies → latent infection of lumbosacral ganglia
stress (fever, menstruation, sunlight) → viral reactivation → axonal transport of virus from ganglia to nerve endings → milder, recurrent vesicular infection at primary site
if pregnant mother is infected: virus may transfer to fetus through placenta or during delivery → child infected → congenital defects, abortion, or neonatal encephalitis

DIAGNOSIS

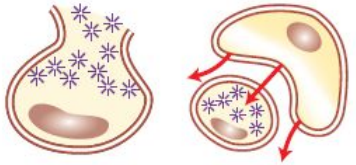
detection of virus
multinucleate giant cells on Tzanck smear of skin lesions
eosinophilic Cowdry intranuclear inclusion bodies on skin biopsy

TREATMENT

acyclovir
prevention: cesarean section in infected mothers

QUICK FACTS

Herpesviruses are the most common cause of sporadic encephalitis in the U.S.: HSV-1 in adults, HSV-2 in neonates.
Most adults have been infected by HSV-1 or -2 and reactivation is common, but not all infections are symptomatic.
Herpetic whitlow is a painful hand vesicle that can occur in health care workers who come in contact with herpetic lesions.



Study Tip

Typically,
HSV-1 infects ABOVE the waist: eye and mouth lesions
HSV-2 infects BELOW the waist: genital lesions
(oral-genital sex can lead to HSV-1 below and HSV-2 above)

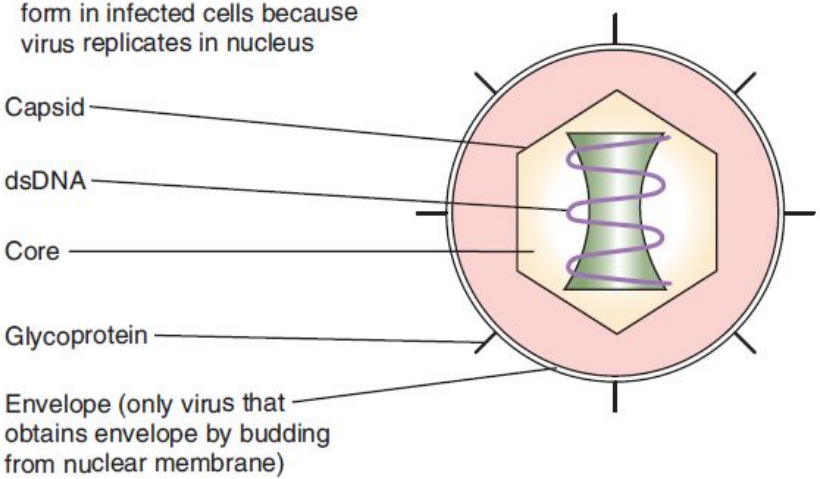
Organisms that cross placenta and therefore allow infection to pass from pregnant mother to fetus (TORCHES):

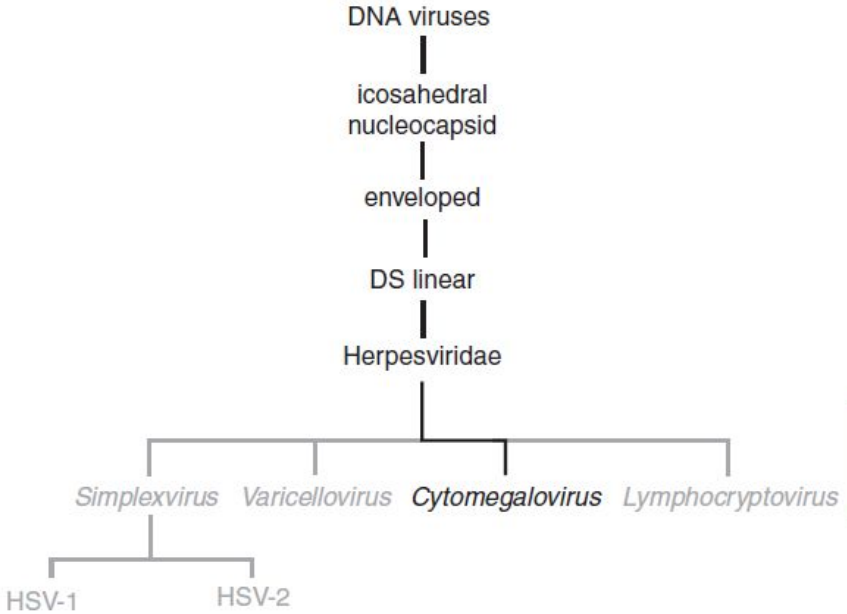
TOxoplasmosis
Rubella
Cytomegalovirus
HErpes, HIV
Syphilis

Herpesviridae Cytomegalovirus

Cytomegalovirus (CMV) or Herpesvirus 5

- Intranuclear inclusion bodies form in infected cells because virus replicates in nucleus





CLINICAL CASE

A 34-year-old kidney transplant patient currently on immunosuppressants complains of shortness of breath and coughing. Physical exam reveals fever and abnormal lung sounds while chest X-ray indicates interstitial infiltrates in the lungs. No cysts are detected on silver stain of bronchoalveolar lavage fluid, ruling out *Pneumocystis jirovecii* infection. The doctor makes a diagnosis after viewing a sample of the patient's lung tissue, which shows abnormal giant cells with "owl's eye" intranuclear inclusions.

Herpesviridae Cytomegalovirus — Cytomegalovirus (CMV) or Herpesvirus 5

CLINICAL PRESENTATION

cytomegalic inclusion disease (newborns)
heterophil-negative mononucleosis
immunocompromised: *retinitis, pneumonia, esophagitis*

PATHOBIOLOGY

transmitted by close contact (blood, breast milk, saliva, semen), organ transplantation, or transplacentally → can infect a diverse array of cells → replicates within cells and eventually kills them, causing:

- cytomegalic inclusion disease: deafness, hepatosplenomegaly, microencephaly in newborns
- mononucleosis: flu-like symptoms, abnormal lymphocytes

infection contained by host immune response → virus remains latent in leukocytes → reactivates when host becomes immunocompromised, causing:

- retinitis (especially in AIDS patients)
- pneumonia (especially in transplant patients)
- esophagitis

DIAGNOSIS

giant cells with "owl's eye" intranuclear inclusion bodies found in tissues/urine
serology (negative monospot test as compared to EBV mononucleosis)
detection in buffy coat culture (CMV infects WBCs)

TREATMENT

ganciclovir (NOT acyclovir, because no viral thymidine kinase is made)
foscarnet

QUICK FACTS

The giant cells, or "cytomegalo" cells, that form during infection give CMV its name.
Most adults have been infected but show few symptoms because their normal immune response limits the infection.
Other viruses that infect lymphocytes are human herpesvirus 6 and 7 (HHV 6, HHV 7). They infect B and T cells causing *roseola* (fever and rash on trunk) in infants.

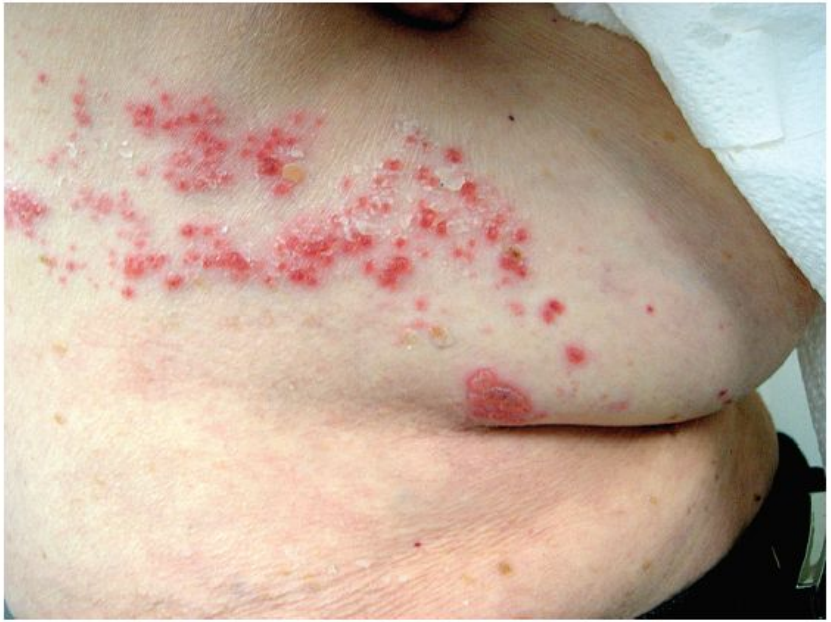
Study Tip

CMV is the most common viral cause of mental retardation in the U.S.

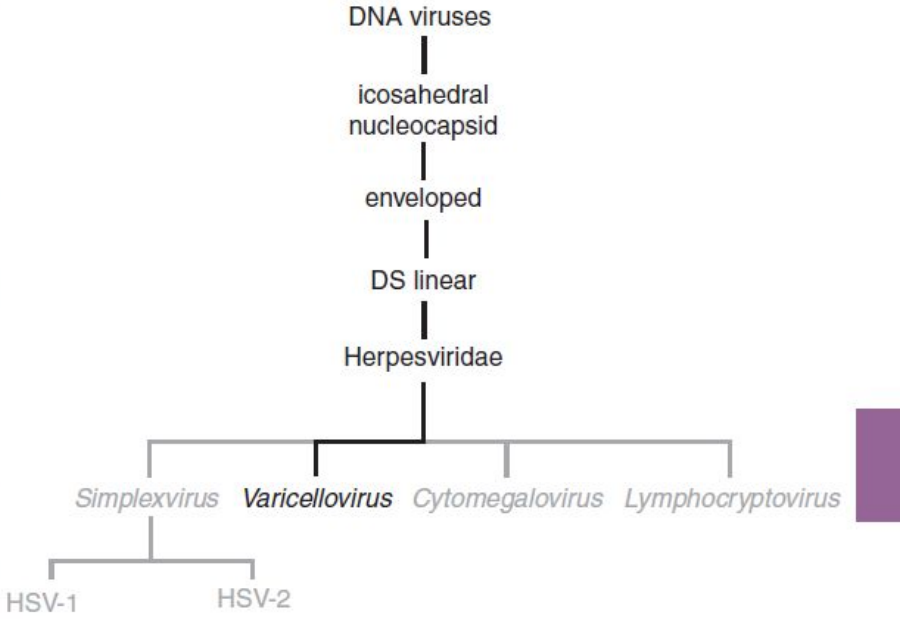
Organisms that cross placenta and therefore allow infection to pass from pregnant mother to fetus (TORCHES):

TOxoplasmosis
Rubella
Cytomegalovirus
HErpes, HIV
Syphilis

Herpesviridae Varicellovirus — *Varicella-Zoster Virus (VZV) or Herpesvirus 3*



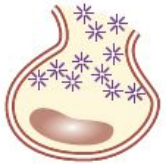
Herpes zoster



CLINICAL CASE

A 72-year-old woman complains to her doctor of a burning, painful rash on her chest. A physical exam reveals fever and a vesicular, erythematous rash limited to the right side of her chest and overlapping the dermatomal area of T7–T8. The physician confirms a diagnosis by a Tzanck smear of the lesions showing multinucleate giant cells with intranuclear inclusion bodies. The physician administers acyclovir and explains that though the rash will likely ameliorate, the regional pain might persist longer.

Herpesviridae Varicellovirus — *Varicella-Zoster Virus (VZV) or Herpesvirus 3*



CLINICAL PRESENTATION

varicella (chickenpox)
zoster (shingles)

PATHOBIOLOGY

highly contagious from respiratory secretions or ruptured varicella vesicles → virus infects respiratory tract → 2-week incubation period → viremia → flu-like symptoms and widespread vesicles with red base appearing as "dew on a rose petal" (varicella) → rash spreads centrifugally → mild in children, severe and may progress to pneumonia or encephalitis in adults

varicella resolves within 2 weeks → virus enters local sensory nerve endings → axonal transport proximally to sensory ganglion cell bodies → latent infection of dorsal root ganglion

stress or immune-compromise → viral reactivation → axonal transport of virus from ganglia to nerve endings → recurrent painful vesicular rash over sensory dermatome (zoster)

DIAGNOSIS

detection of virus
multinucleate giant cells on Tzanck smear of skin lesions
eosinophilic Cowdry intranuclear inclusion bodies on skin biopsy

TREATMENT

supportive
acyclovir, famciclovir (severe)
anti-VZV immunoglobulin (for immunocompromised)
vaccine: attenuated VZV

QUICK FACTS

The VZV vaccine is controversial for two reasons: (1) immunity may wane, allowing more serious adult varicella infections; (2) a latent state from prior infection is not eliminated, so zoster can still occur.

Reye's syndrome (liver damage, encephalomyelitis): associated with aspirin treatment for chickenpox in children.