The Physician Pharmacist: Virology/Antimicrobials/Antivirals

Virology:

Viral Genetics:

1. Recombination:
-exchange of genes btw 2 chromosomes by crossing over within regions of significant base sequence homology

2. Reassortment:
-viruses w/ segmented genomes (Influenza) exchange genetic material (H1N1 pandemic emerged via complex viral reassortment of genes)
-Has potential to cause Antigenic Shift

3. Complementation:
-when 1 of 2 viruses that infect the cell has a mutation that results in a nonfunctional protein → the non mutated virus "Complements" the mutated one by making a functional protein that serves both viruses
-ex.) HepD requires presence of replicating HepB virus to supply HBsAg (the envelope protein for HDV)

4. Phenotypic Mixing:
-occurs w/ simultaneous infxn of cell w/ 2 viruses
-for progeny 1, genome of virus A can be partially or completely coated (Forming Pseudovirion) w/ the Surface proteins of Virus B
-Type B protein coat determines the tropism (infectivity) of the hybrid virus
-aka Virus A progeny 1 has Type A genetic material but a hybrid coat of Virus B (the progeny the progeny will only make Virus A with no hybrid coat b/c a new cell will likely not be coinfected w/ Virus A and B

DNA Viral Genomes:
-All DNA viruses have dsDNA genomes (except Parvoviridae (ssDNA))
-All are Linear except Papilloma, Polyoma and Hepadnaviruses (Circular)

RNA Viral Genomes:
-All RNA viruses have ssRNA genomes except **Reoviridae (dsRNA) - Reovirus**
-(+) stranded RNA Viruses:
- Retrovirus, Togavirus, Flavivirus, Coronavirus, Hepevirus, Calicivirus, Picornavirus

Naked Viral Genome:
-Purified nucleic acids of most dsDNA (except Poxviruses + HBV) and (+) Strand ssRNA viruses are infectious
-Naked nucleic acids of (-) strand ssRNA and dsRNA viruses are NOT infectious (Require Polymerases contained in the complete virion)

Viral Envelopes:
-generally enveloped viruses acquire their envelopes from plasma membrane when they excite from cell
(Exception = Herpesviruses - which get membranes from Nuclear membrane)
-Enveloped DNA Viruses:
- Herpesvirus (Nuclear membrane)
- Hepadnavirus
- Poxvirus

-Naked (Nonenveloped)
- Papillomavirus
- Adenovirus
- Parvovirus
- Polyomavirus
- Calicivirus
- Picornavirus
- Reovirus
- Hepevirus

DNA Virus Characteristics:
-**H2AP4** = Hepadna, Herpes, Adeno, Pox, Parvo, Papilloma, Polyoma
-All double stranded (except Parvo - ssDNA)
-All have linear genomes (except Papilloma/Polyoma (Circular/supercoiled and Hepadema (Circular, incomplete)
-All are icosahedral (except Pox - complex)
-Replicate in Nucleus (except Pox - carries own DNA-dependent RNA Polymerase)

DNA Viruses:
-All replicate in the Nucleus (Except Pox)***
-"Pox is out of the box (nucleus)"

1. Herpesviruses:
-Enveloped
-dsDNA
-Linear

2. Poxvirus:
-enveloped
-dsDNA
-Linear (**Largest DNA Virus)**
- **Smallpox** = eradicated worldwide w/ Live attenuated vaccine (Sabin) or Salk (Inactivated Polysaccharide)
- **Cowpox** = "Milkmaid Blisters"
- **Molluscum Contagiosum** = Flesh-colored papule w/ central umbilication

3. Hepadnavirus:
-Enveloped
-dsDNA partially + **Circular*****
-**HBV =** acute or chronic hepatitis (not a retrovirus but has Reverse Transcriptase)

4. Adenovirus:
-**NOT enveloped*****
-dsDNA
-Linear
- **Febrile Pharyngitis** - sore throat
- **Acute Hemorrhagic Cystitis**
- **Pneumonia**
- **Conjunctivitis** - "Pink Eye"
- **Gastroenteritis**
- **Myocarditis**

5. Papillomavirus:
-No envelope
-dsDNA
-Circular
- **HPV -** warts, (1,2, 6, 11), Cancer (16, 18)

6. Polyomavirus:
-No envelope
-dsDNA
-Circular
- **JC Virus= PML** in HIV
- **BK Virus=** transplant pts (often Kidneys)

7. Parvovirus:
-No envelope
-**SS-DNA, Linear, Smallest DNA virus*****
- **B19** = aplastic crisis in Sickle Cell, "Slapped Cheek" in Children (Erythema Infectiosum/ Fifth Disease)...infects RBC precursors + endothelial cells → RBC destruction → Hydrops Fetalis + Death of Fetus, Pure RBC Aplasia, and Rheumatoid Arthritis

-Binds **P-antigen on RBCs** to gain entry

Herpesviruses:

-Enveloped
-dsDNA
-Linear

1. Herpes Simplex Virus-1 (HSV1):
-Respiratory secretions/saliva transmission
-dxs:
- **Gingivostomatitis** (mouth sores)
- **Keratoconjunctivitis**
- **Herpes Labialis (Cold Sores)**
- **Herpetic Whitlow on Finger**
- **Temporal Lobe Encephalitis**
- **Esophagitis**
- **Erythema Multiforme**

-Most commonly latent in Trigeminal Ganglia**
-Most common cause of **Sporadic encephalitis**, can present as altered mental status, seizures, and/or aphasia

2. Herpes Simplex Virus-2 (HSV2):
-Sexual contact, perinatal transmission
-dxs:
- **Herpes Genitalis**
- **Neonatal herpes**

-Most commonly latent in Sacral Ganglia***
-Viral meningitis more common w/ HSV2 than HSV1

3. Varicella-Zoster Virus (HHV-3):
-Respiratory secretions, contact w/ fluid from vesicles
-dxs:
- **Varicella-Zoster (Chickenpox, Shingles)**
  - Post-herpetic Neuralgia
- **Encephalitis**
- **Pneumonia**

-Latent in **dorsal root or trigeminal ganglia**
-CN V1 branch involvement can cause "Herpes Zoster Ophthalmicus" - shingles of the eye/face

4. Epstein-Barr Virus (HHV-4):
-Respiratory secretions, saliva "Kissing Disease" (common in teens, young adults)
-dxs:
- **Mononucleosis (Mono)** = fever, hepatosplenomegaly, pharyngitis, lymphadenopathy (posterior cervical nodes***)
  - No contact sports until resolution
  - risk of Splenic Rupture
- **Lymphomas** (Burkitt's Lymphoma, Nasopharyngeal Carcinoma - Asian Adults, Lymphoproliferative disease in Transplant)

-Infects **B-Cells via CD21**
-"Must be 21 to drink Beer in a Barr"
-Atypical Lymphocytes on peripheral smear (not B-cells, but reactive cytotoxic T-cells)
-**(+) Monospot Test** = heterophile antibodies detected by agglutination of sheep/horse RBCs
-Use of **Amoxicillin** (for presumed Strep Pharyngitis) causes **Maculopapular Rash**

5. Cytomegalovirus(CMV) (HHV-5):
-Congential CMV, Transfusion, sexual contact, saliva, urine, transplant, = binds to **Integrins** (Heparan Sulfate)
-dxs:
- **Mononucleosis (Mono)** but **(-) Monospot**
- Immunocompromised:
  - CMV Pneumonia
  - CMV Esophagitis
  - **CMV AIDS Retinitis** = Hemorrhage, cotton-wool exudates + vision loss
- **Congenital CMV**

-Infected cells have **"Owl Eye" Intranuclear Inclusions**
-Latent in Mononuclear Cells (bone marrow)

6/7. Human Herpes Viruses 6 and 7 (HHV6, HHV7):
-Saliva transmission
-dxs:
- **Roseola Infantum** = exanthem subitum
  - High fevers for several days causing **Seizures**
  - Followed w/ diffuse Macular Rash (starting on Trunk → spreading to extremities)
  - Children < 2 yo

-**"Roseola: Fever First, Rosy (Rash) Later**
-Self-limiting (often supportive care only - if seizures)
-HHV7 = less common cause of Roseola

8. Human Herpesvirus 8 (HHV8):
-Sexual contact spread
-dxs:
- **Kaposi Sarcoma**:
  - Neoplasm of endothelial cells
  - Seen in HIV/AIDS + Transplant
  - Dark/Violaceous Plaques/nodules demonstrating vascular proliferations

-may hit GI tract or lungs

HSV Identification:
-PCR of skin lesions is Test of Choice
-CSF PCR for Herpes Encephalitis
-Tzanck Test (outdated) - looking for multinucleated giant cells (commonly w/ HSV1, HSV2, VZV
-Intranuclear Eosinophilic Cowdry A Inclusions also seen (HSV1, HSV2, VZV)

Receptors Used by Viruses:
- **5. CMV = Integrins (Heparan Sulfate)**
- **4. EBV = CD21**
- **HIV = CD4, CXCR4, CCR5**
- **Parvovirus B19 = P antigen on RBCs**
- **Rabies = Nicotinic AChR**
- **Rhinovirus = ICAM-1**
  - "ICAM to see Rhino"

RNA Viruses	Envelope	RNA Structure	Capsid Symmetry	Dx/Notes
Reoviruses	no	**dsRNA** Linear Multisegmented	Icosahedral (Double)	• **Coltivirus** = Colorado Tick Fever • **Rotavirus** = fatal diarrhea in children
Picornaviruses "Small RNA Virus"	no	ssRNA (+) Linear RNA is translated into 1 large polypeptide that is cleaved by virus-encoded proteases into functional viral proteins	Icosahedral	**PERCH** • **Poliovirus** = Salk/Sabin Vaccines, Aseptic Meningitis* • **Echovirus** = Aseptic Meningitis* • **Rhinovirus** = "Common Cold" • **Coxsackievirus** = Aseptic Meningitis*, Herpangina (Mouth blisters, Fever), Myocarditis, Pericarditis ○ **Hand Foot Mouth Disease** • **HAV** = acute viral hepatitis
Hepevirus	no	ssRNA (+) Linear	Icosahedral	• **HEV** = Hepatitis E
Caliciviruses	no	ssRNA (+) Linear	Icosahedral	• **Norovirus** = Viral Gastroenteritis
Flaviviruses	YES	ssRNA (+) Linear	Icosahedral	• **HCV** • **Yellow Fever** • **Dengue** • **St. Louis Encephalitis** • **West Nile Virus** = meningoencephalitis, flaccid paralysis • **Zika Virus**
Togaviruses	YES	ssRNA (+) Linear	Icosahedral	**Toga CREW:** • **Chikungunya Virus** = coinfection w/ Dengue Virus can occur • **Rubella** • **Eastern Equine Encephalitis** • **Western Equine Encephalitis**
Retroviruses	YES	ssRNA (+) Linear 2 Copies	-Icosahedral (HTLV) -Complex and Conical (HIV)	**Reverse Transcriptase Present** • **HTLV** = T-cell Leukemia • **HIV** = AIDS
Coronaviruses	YES	ssRNA (+) Linear	**Helical**	• **"Common Cold"** • **SARS** • **MERS** • **COVID-19**

Orthomyxoviruses	YES	**ssRNA (-) Linear 8 segments**	Helical	• **Influenza Virus**
Paramyxoviruses	YES	ssRNA (-) Linear	Helical	**PRMM:** • **Parainfluenza** = Croup • **RSV** = Bronchiolitis in Babies • **Measles** • **Mumps**
Rhabdoviruses	YES	ssRNA (-) Linear	Helical	• **Rabies**
Filoviruses	YES	ssRNA (-) Linear	Helical	• **Ebola** • **Marburg Hemorrhagic Fever** = often fatal
Arenaviruses	YES	**SS (+) and (-) Circular** RNA w/ **2 segments**	Helical	• **LCMV** = Lymphocytic Choriomeningitis Virus • **Lassa Fever Encephalitis** = Spread by rodents
Bunyaviruses	YES	ssRNA (-) **Circular 3 segments**	Helical	• **California Encephalitis** • **Sandfly/Rift Valley Fevers** • **Crimean-Congo Hemorrhagic Fever** • **Hantavirus** = hemorrhagic fever, pneumonia
Delta Virus	YES	ssRNA (-) **Circular**	Unknown	• **HDV** = defective virus that requires presence of HBV (dsDNA virus) to replicate

Negative (-)-Stranded Viruses:
-Must transcribe (-) RNA strand to (+) RNA
-Virion brings its own RNA-Dependent RNA Polymerase (**OPRFAB**)

- Orthomyxoviruses
- Paramyxoviruses
- Rhabdoviruses
- Filoviruses
- Arenaviruses
- Bunyaviruses

Segmented Viruses:
-All are RNA viruses

- **Bunyaviruses (3 segments)**
- **Orthomyxoviruses (Influenza, 8 segments)**
- **Arenaviruses (2 segments)**
- **Reoviruses (10-12)**

-"BOARding flight 382 in 10-12 minutes"

Rhinovirus:
-Picornavirus
-Nonenveloped RNA virus
-cause of "Common Cold"
- > 100 serologic types (No vaccine possible)
-Acid Labile → destroyed by stomach acid; so no GI tract sxs (unlike other Picornaviruses)

Rotavirus:
-segmented dsRNA virus (Reovirus - #1 in chart)
-most important global cause of infantile gastroenteritis
-major cause of infantile gastroenteritis
-major cause of acute diarrhea in US during winter (especially w/ Day Care Centers, Kindergartens)
-Mech = Villous Destruction w/ Atrophy leads to absorption of Na+ and loss of K+
-Routine Vaccination of ALL infants (except those w/ SCID or hx of **Intussusception** (rare Rotavirus Vaccine Side effect))

Influenza Viruses:
-Orthomyxoviruses
-enveloped, (-) ssRNA w/ Segmented Genome
-**Hemagglutinin** (Binds Sialic acid and Promotes viral entry) + **Neuraminidase** (Promoting Progeny Virion Release) Antigens
-Pts at risk for fatal bacterial superinfection = S. aureus, Strep pneumo, H. influenzae
-Tx = Supportive +/- Neuraminidase Inhibitors (Oseltamivir, Zanamivir)
-Prevention = "Flu Shot" containing viral strains likely to appear during flu season (often Killed Viral Vaccine)
-Live attenuated vaccine (Intranasal) = contains temperature sensitive mutant that can only replicate in nose but NOT the lung
-**Sudden Shift is more deadly than GraDual Drift**

Genetic/antigenic Shift:
-Infection of 1 cell by 2 different segmented viruses (Swine flu + Human flu viruses) → RNA segment reassortment → dramatically different virus (Genetic Shift) → Major global outbreaks (Pandemic)

Genetic/Antigenic Drift:
-Random mutation in Hemagglutinin (HA) or Neuraminidase (NA) genes → minor changes in HA or NA protein (Drift) occur frequently → major global outbreaks (Pandemics)

Rubella Virus:
-Togavirus
-also known as **German (3-day) Measles**
-sxs = Fever, Postauricular lymphadenopathy, Arthralgias, Fine, Maculopapular rash starting on face + spreading **Centrifugally to involve trunk/extremities**
-TORCH Infxn = Congenital Rubella
1. **Sensorineural Deafness**
2. **Cataracts**
3. **Patent Ductus Arteriosus (PDA)**
4. **"Blueberry Muffin" Rash** from dermal extramedullary hematopoiesis*

Paramyxoviruses:
-cause dx in children
-**PRMM:**
- **Parainfluenza (Croup)**
- **RSV**
- **Measles**
- **Mumps**
- Human Metapneumovirus

-All subtypes cause Respiratory Tract Infection (Bronchiolitis, Pneumonia) in Infants
-All contain **Surface F (fusion) Protein** = causes respiratory epithelial cells to fuse + form multinucleated cells
-Palivizumab = monoclonal Ab against **F-protein** (Prevents pneumonia caused by RSV infxn in premature infants)
-"**Palivizumab for Paramyxovirus (RSV) Ppx in Preemies"**

1. Acute Laryngotracheobronchitis: "Croup"
-caused by parainfluenza (paramyxovirus)
-virus membrane contains Hemagglutinin (Binds Sialic Acid and Promotes viral entry) + Neuraminidase (progeny release)
-"Seal-like" barking cough + Inspiratory Stridor
-Narrowing of upper trachea + subglottis leads to **Steeple Sign** on X-ray

2. Measles (Rubeola):
-prodromal fever w/ cough, coryza, conjunctivitis → **Koplik Spots** (Bright red spots w/ blue-white center on buccal mucosa) → 1-2 days later w/ Maculopapular Rash (starts on head/neck and spreads downward)
-Lymphadenitis w/ **Warthin-Finkeldey Giant Cells** (Fused Lymphocytes) in a background **paracortical hyperplasia**
-Sequelae:
- Subacute sclerosing panencephalitis (SSPE) = personality changes, Dementia, Autonomic Dysfunction, Death (occurring years later)
- Encephalitis = within a few days of rash
- Giant Cell Pneumonia = rare unless immunosuppressed

-**4 C's:**
- **Cough**
- **Coryza**
- **Conjunctivitis**
- **"C"oplik Spots**

-Vitamin A supplementation can Morbidity/Mortality
-Pneumonia is most common cause of measles-associated death in children

3. Mumps:
-uncommon due to effectiveness of MMR vaccine
-sxs =
- **Parotitis**
- **Orchitis (Inflam of Testes) → Sterility**
- **Aseptic Meningitis**
- **Pancreatitis**

Chikungunya Virus:
-Alphavirus member of Togavirus
-**Aedes Mosquito**
-sxs = Inflammatory Polyarthritis (can become chronic), High fever, maculopapular rash, HA, Lymphadenopathy
-Hemorrhagic manifestations uncommon (vs. Dengue)
-ddx = RT-PCR or serology
-No Tx available and no vaccine

Dengue Virus:
-Flavivirus
-**Aedes Mosquito**
-most common mosquito-borne viral dx in world
-**Dengue Fever**:
- Fever, Rash, HA, Myalgias, Arthralgias, Neutropenia
- Similar sxs to Chikungunya virus (transmitted by same mosquito) but Dengue is more pathologic (progressing to Neutropenia, Thrombocytopenia, Hemorrhage, shock, death)

-Dengue Hemorrhagic Fever:
- Dengue Fever + Bleeding/Plasma Leakage due to thrombocytopenia + extremely high/low Hematocrit
- Seen in pts infected with a different Dengue serotype compared to a previous dengue infection (leading to Antibody-Dependent Enhancement of Dx)

-Dengue Shock Syndrome:
- Plasma Leakage leading to circulatory collapse

-**vaccine = Live Recombinant** (using Yellow Fever virus backbone)

Rabies Virus:
-Rhabdovirus
-**Bullet-Shaped Virus**
-**Negri bodies** (Cytoplasmic Inclusions) found in **Purkinje Cells** of Cerebellum and Hippocampal Neurons
-Long incubation period (Weeks/Months) before sxs onset
-Postexposure PPx is wound cleaning + Immunization w/ Killed Vaccine + Rabies Immunoglobulin (Passive-Active Immunity)
-mech = travels to CNS via **Retrograde movement** (Dynein Motors) up nerve axons after binding to ACh receptors
-Progression = Fever, Malaise → Agitation, Photophobia, Hydrophobia, Hypersalivation → Paralysis, Coma → Death
-Infxn commonly from bat, Raccoon, Skunk Bites > Dogs

Yellow Fever:
-Flavivirus (Arbovirus) transmitted by **Aedes Mosquito** (monkey/human reservoir)
-Sxs = High Fever, Black Vomitus, Jaundice, Hemorrhage, Backache
-**Councilman Bodies (Eosinophilic Apoptotic Globules) on Liver biopsy**
-Flavi = "Yellow, Jaundice"

Ebola Virus:
-Filovirus
-incubation period of up to **21 days** → abrupt onset flu-like sxs, diarrhea, vomiting, high fever, myalgias → **DIC, Diffuse Hemorrhage, Shock**
-ddx = RT-PCR within 48 hrs of sxs onset
-High mortality rate
-Transmission requires direct contact w/ bodily fluids, fomites (dead bodies), infected bats/primates
-high incidence of Nosocomial infxn
-Supportive care, no definitive tx
-Vaccination of contacts

Zika Virus:
-Flavivirus (**Aedes Mosquito**)
-sxs = conjunctivitis, low-grade pyrexia, itchy rash
-DDx w/ RT-PCR or serology
-more common in tropical/subtropical climates
-Sexual + Vertical Transmission
-**Miscarriage**
-Congenital Zika Syndrome:
- **Ventriculomegaly**
- **Subcortical Calcifications**

-Characteristic Features:
1. **Microcephaly**
2. **Ocular Anomalies**
3. **Spasticity/Seizures**

Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2):
-Novel (+) ssRNA coronavirus causing Covid-19 pandemic
-Respiratory droplet + aerosol transmission
-Mech = **host cell entry via Viral Spike Protein to Angiotensin-Converting Enzyme-2 (ACE2) Receptor on cell membranes**
-Clinical course varies (often asymptomatic)
- Common = Fever, dry cough, SOB, Fatigue
- Anosmia (loss of smell), Dysgeusia (Altered taste)
- Severe = Respiratory failure, Hypercoagulability, shock, organ failure, death

-RF for poor outcomes = age, obesity, DM, HTN, CKD, Cardiopulmonary illness
-ddx = RT-PCR (most common); Antigen + Antibody tests are available
-Tx for Hospitalized pts = Remdesivir (Nucleoside Analog), Convalescent Plasma, Dexamethasone (for Cytokine storm)

Hepatitis Viruses:
-ALL = fever, jaundice, ALT/AST
-Naked Virus = HAV, HEV (both hit the gut) "The vowels hit the bowels" (b/c not destroyed by Gut b/c no envelope)
-HBV DNA Polymerase has DNA and RNA dependent activities;
- Entry into cell Nucleus → polymerase completes partial dsDNA
- Host RNA Polymerase transcribes mRNA from viral DNA to make Viral proteins
- DNA Polymerase then Reverse transcribes viral RNA to DNA

-HCV lacks 3'-5' exonuclease activity → no Proofreading ability → antigenic variation of HCV envelope proteins (Host antibody production lags behind production of new mutant strains of HCV)

1. HAV:
-RNA Picornavirus
-Fecal/oral (Shellfish, travelers, day care)
-Short incubation (weeks)
-Acute / Self-Limiting (Adults), Asymptomatic (Children)
-Good prognosis
-No HCC risk
-Biopsy = Hepatocyte Swelling, Monocyte infiltration, councilman bodies
-no carrier state

2. HBV:
-**DNA** Hepadnavirus
-Parenteral (Blood), Sexual (Bed), Perinatal (Birth) transmission
-Incubation = Months
-Initially like serum sickness (fever, arthralgias, rash) but can progress to carcinoma
-Adults → mostly full resolution; neonates have worse prognosis
-HCC Risk
-Biopsy = Granular eosinophilic "ground glass" appearance due to accumulation of surface antigen within infected hepatocytes (cytotoxic T cells Mediate Damage)
-Carrier State is common

3. HCV:
-RNA Flavivirus
-Primarily blood ((IV drugs, posttransfusion) transmission
-may progress to Cirrhosis + Carcinoma
-Most develop stable, chronic Hepatitis C
-HCC risk
-Biopsy = Lymphoid aggregates w/ focal areas of macrovesicular steatosis
-Carrier State very common

4. HDV:
-RnA Deltavirus
-parentreral, sexual perinatal transmission
-Superinfection (HDV after HBV) = short; Coinfection (HDV w/ HBV at same time) = Long
-Similar to HBV sxs
-Superinfection → Worse prognosis
-HCC risk
-Biopsy similar to HBV
-Defective virus depends on **HBV HBsAg coat for entry into hepatocytes**

5. HEV:
-RNA Hep Virus
-Feal/oral (waterborne) transmission
-Short incubation (weeks)
-sxs = Fulminant Hepatitis w/ Expectant (Pregnant) pts
-High mortality in pregnant pts
-no HCC risk (also HAV)
-Biopsy = Patchy necrosis
-Enteric, Epidemic, no carrier state, Endemic Regions

Extrahepatic Manifestations of HBV, HCV:
-HBV = Aplastic Anemia, Membranous GN > MPGN, Polarteritis Nodosa
-HBC:
- Essential mixed Cryoglobulinemia
- risk of B-cell NHL
- ITP
- AUtoimmune Hemolytic anemia
- MPGN > Membranous GN
- Leukocytoclastic vasculitis
- Sporadic porphyria cutanea tarda, lichen planus
- risk of DM, Autoimmune Hypothyroidism

Hepatitis Serologic Markers:

-Anti-HAV (IgM) = (+) acute HAV
-Anti-HAV (IgG) = (+) indicates prior HAV infxn/vaccination
-HbsAg = (+) HepB infection (found on surface of HBV)
-Anti-HBs = antibody to HbsAg ((+) indicates immunity to HBV due to vaccination or recovery from infxn)
-HBcAg = antigen associated w/ cord of HBV
-Anti-HBc = antibody to HBcAg
- IgM = acute/recent infxn (may be the only (+) marker during the window period)
- IgG = prior exposure or chronic infection

-HBeAg = secreted by infected hepatocyte into circulation (Not part of mature HBV virion) → indicating active Viral Replication + therefore high transmissibility + poorer prognosis
-Anti-HBe = Antibody to HBeAg (indicates low transmissibility)

-Acute HBV = (+) HBsAg, (+) HBeAg, Anti-HBc (IgM)
-Window = (+) Anti-HBe, Anti-HBc (IgM)
-Chronic HBV (High infectivity) = (+) HBsAg, (+) HBeAg, Anti-HBc **(IgG)**
-Chronic HBV (Low infectivity) = (+) HBsAg, (+) Anti-HBe, Anti-HBc (IgG)
-Recovery = (+) Anti-HBs, (+) Anti-HBe, Anti-HBc (IgG)
-Immunized = (+) Anti-HBs

HIV:
-Diploid genome (2 molecules of RNA)
-3 Structural genes;
- **Env (gp120 and gp41)**
  - Formed from cleavage of gp160 to Form envelope glycoproteins
  - **gp120 = attachment to host CD4+ T-cells**
  - **gp41 = fusion + entry**
- **Gag (p24, p17):**
  - P24 = Capsid proteins
  - P17 = matrix proteins
- **Pol:**
  - **Reverse transcriptase**
  - **Integrase**
  - **Protease**

-RT synthesizes dsDNA from genomic RNA; dsDNA integrates into host genome
-Virus binds CD4 and coreceptor (CCR5 on macrophages during early infection, or CXCR4 on T cells during late infection)
-**Homozygous CCR5 Mutation = Immunity**
-Heterozygous CCR5 mutation = slower course

HIV Diagnosis:
-HIV-1 or HIV-2 Ag/Ab immunoassays
-detects viral p24 Ag capsid protein and IgG Abs to HIV-1/2
-AIDS = occurs when CD4+ count ≤ 200 or HIV (+) w/ AIDS defining condition (Pneumocystis pneumonia)

Time Course:
-4 Stages of Untreated Infection;
1. **Flu-like (Acute)**
2. **Feeling Fine (Latent)** - Virus replicating in Lymph nodes*** (HIV Viral Load decreases considerably but begins to rise as CD4+ counts falls)
3. **Falling Count**
4. **Final Crisis**

Common-Diseases of HIV-Positive Adults:
- CD4+ cell count → reactivation of past infections (TB, HSV, Shingles), dissemination of bacterial infections, and fungal infections (Coccidioidomycosis), and Non-Hodgkin Lymphomas (PCNSL)

CD4+ < 500:
1. Candida Albicans = **Oral thrush** (scrapable white plaque, pseudohyphae)

2. EBV = **Oral Hairy Leukoplakia** (Unscrapable white plaque on Lateral Tongue

3. HHV-8 = **Kaposi Sarcoma** (perivascular spindle cells invading + forming vascular tumors on histology)

4. HPV = Squamous Cell Carcinoma (SCC) at sites of sexual contact (most commonly Anal, Cervix, Oropharynx)

CD4+ < 200:
1. Histoplasma Capsulatum = fever, weight loss, fatigue, cough, SOB, N/V/D (Oval yeast cells within macrophages)

2. HIV Dementia = cerebral atrophy

3. JC Virus (Reactivation) = **Progressive Multifocal Leukoencephalopathy (PML)** (Nonenhancing Areas of Demyelination on MRI)

4. Pneumocystis Jiroveci = Pneumocystis Pneumonia (PCP) (Ground-Glass opacities)

CD4+ < 100:
1. Aspergillus Fumigatus = Hemoptysis, pleuritic pain, cavitation and infiltrates on imaging

2. Bartonella spp = Bacillary Angiomatosis (multiple red to purple papules or nodules), Biopsy w/ Neutrophilic predominance

3. Candida Albicans (Esophagitis)

4. CMV = **CREEP**, Intranuclear "Owl-Eye" Inclusion Bodies
- **Colitis**
- **Retinitis** (Cotton-Wool Spots)
- **Esophagitis** (Linear Ulcers)
- **Encephalitis**
- **Pneumonitis**

5. Cryptococcus Neoformans (Meningitis) = encapsulated yeast on India Ink Stain or (+) Capsular antigen

6. Cryptosporidium spp = chronic watery diarrhea, acid-fast oocysts in stool

7. EBV = B-cell Lymphoma (Non-Hodgkin Lymphoma, CNS Lymphoma), CNS Lymphoma (Singular Ring-enhancing Lesion - vs. Toxo(multiple))

8. Mycobacterium Avium Complex (MAC) = nonspecific systemic sxs (Fever, Night sweats, weight loss) or Focal Lymphadenitis
- Most commonly seen CD4+ < 50

9. Toxoplasma Gondii = Brain abscesses (Multiple Ring-enhancing lesions on MRI)

Prions;
-conversion of normal (predominantly a-helical) protein (PrPc) to B-pleated form (PrPsc) → resisting protease degradation + facilitates conversion of more PrPc to PrPsc
-Causes Spongiform Encephalopathy, Dementia, Ataxia, Startle myoclonus, death
-Creutzfeldt-Jakob Disease = rapidly progressive dementia, typically sporadic
-Bovine Spongiform Encephalopathy = "Mad Cow Disease"
-Kuru = acquired prion disease from human cannibalism

Microbiology Systems:

Normal Flora Dominant:
-Skin = S. epidermidis
-Nose = S. epidermidis; colonized by S aureus
-Oropharynx = Viridans group streptococci
-Dental Plaque = S mutans
-Colon = B fragilis > E.coli
-Vagina = Lactobacillus (colonized by E Coli and Group B strep- Agalactinae)

Bugs causing Food-Borne Illness:
-B cereus = reheated rice
-C botulinum = canned foods (toxins), raw honey (spores)
-C perfringens = reheated meat
-E coli (O157:H7) = undercooked meat
-Listeria Monocytogenes = Deli meats, soft cheeses
-Salmonella = Poultry, meat, eggs
-Staph Aureus = meats, mayonnaise, custard, preformed toxin

Bloody Diarrhea:
-Campylobacter = comma/S-shaped organisms (growth at 42C)
-Entamoeba. Histolytica = Protozoa, Amebic Dysentery, liver abscesses (eats RBCs)
-Enterohemorrhagic E. coli (EHEC) = O157:H7 causing HUS (Shiga Toxin)
-Enteroinvasive E coli (EIEC) = invades colonic mucosa
-Salmonella (non-typhoidal) = lactose (-) Flagellar motility; has animal reservoir, especially poultry/eggs
-Shigella = Lactose (-), very low ID50, produces Shiga Toxin; Human Reservoir only; bacillary dysentery

Watery Diarrhea:
-C. Diff = Pseudomembranous colitis (Abx - Clinda/PPIs)
-C. Perfringens = gas gangrene
-Enterotoxigenic E coli (**ETEC**) = "**Traveler's Diarrhea**" producing Heat-Labile (LT) and Heat Stable (ST) toxins
-Protozoa (Giardia, Cryptosporidium)
-V. Cholerae = Comma shaped, rice-water diarrhea (infected seafood)
-Viruses = Norovirus (most common in developed world), Rotavirus, Enteric Adenovirus

Pneumonia Groups:
1. Neonates (< 4 wks)
-Group B Strep (Agalactiae)
-E. Coli

2. Children (4wk-18 yo):
-Viruses (RSV)
-Mycoplasma
-Chlamydia Trachomatis (Infants-3 yo)
-Chlamydia Pneumoniae (School aged children)
-Strep Pneumoniae

3. Adults (18-40yo)
-Mycoplasma
-C pneumoniae
-S pneumo
-Influenza

4. Adults (40-65yo):
-Strep pneumo
-H influ
-Anaerobes
-Viruses
-Mycoplasma

5. Elderly:
-strep pneumo
-Influenza
-Anaerobes
-H influenzae
-Gm (-) Rods

-Alcohol Overuse = Klebsiella
-IV drug use = Strep pneumo, Staph Aureus
-Aspiration = Anaerobes
-Atypicals = Mycoplasma, Chlamydophila, Legionella, Viruses (RSV, CMV, Influenza, Adenovirus)
-CF = Burkholderia cepacia
-Postviral = Strep pneumo, Staph aureus, H. Influ
-COPD = strep pneumo, staph aureus, M. Cat, Pseudomonas

Meningitis:
-Ceftriaxone + Vanc empirically (add Ampicillin if Listeria suspected)
-Viral = Coxsackievirus, HSV-2 (HSV-1 = Encephalitis), HIV, West Nile Virus (also Encephalitis), VZV
-HIV? Cryptococcus Spp

Newborns (0-6 months): -Group B strep (Agalactiae) - decreased due to better awareness and ppx Abx -E coli **-Listeria**	**Children (6m-6 yo):** -Strep pneumo -N meningitidis -H influenzae Type B -Group B Strep -Enterovirus
6-60 yo: -Strep pneumo -N meningitidis -Enteroviruses -HSV	**60+:** -Strep pneumo -N meningitidis -H influenzae Type B -Group B Strep **-Listeria**

	Bacterial	**Fungal/TB**	**Viral**
Opening pressure			-/
Cell Type	PMNs	Lympho	Lympho
Protein			-/
Glc			Normal

Osteomyelitis:
-Assume **Staph Aureus** (most common overall)
-Sexually active = neisseria gonorrhoeae
-Sickle Cell = salmonella, staph aureus
-Vertebral Involvement = Staph, M tuberculosis (Pott Disease)

UTIs:
-Cystitis = dysuria, frequency, urgency, suprapubic pain, WBCs in urine (not casts); often due to ascension of microbes from urethra to bladder (ascension to kidneys causes Pyelonephritis - fever, chills, flank pain, CVA tenderness, hematuria, WBC Casts)
-RF = Obstruction(stones, BPH), Female, kidney surgery, catheterization, congenital GU malformation (Vesicoureteral Reflux), DM, Pregnancy
-(+) Leukocyte Esterase = WBC activity in urine
-(+) Nitrite Test = Reduction of Urinary Nitrates by Gm(-) bacterial species (E Coli)
-Bugs:
- **E Coli** = MOST COMMON (Pink-lactose fermenting colonies on MacConkey Agar)
- **Staphylococcus Saprophyticus** = #2 most common (esp Young sexually active females)
- **Kleb Pneumo** = #3 most common (large mucoid capsule)
- **Serratia marcescens** (red pigments - often nosocomial and drug resistant)
- **Enterococcus**
- **Proteus Mirabilis** = “swarming” on agar; struvite stones (pH) from Urease Production
- **Pseudomonas Aeruginosa** = blue-green fruity odor

Common Vaginal Infections:
1. Bacterial Vaginosis:
-no inflammation, thin, white discharge w/ Fishy odor
-Clue Cells, (+) KOH whiff test, pH > 4.5
-Tx = Metronidazole or Clinda

2. Candida Vulvovaginitis:
-Inflammation, Thick, white, “Cottage Cheese” discharge
-Pseudohyphae, NORMAL pH (<4.5)
-Tx = Fluconazole

3. Trichomans Vaginitis:
-Inflammation (**Strawberry Cervix**), Frothy, Yellow-Green foul-smelling discharge
-Motile pear-shaped trichomonads
-pH > 4.5
-Tx = Metronidazole + **Tx Partners too** (STI)

TORCHHS Infections:
-pass from mother to fetus (either transplacentally or vaginal delivery (especially HSV-2)
-Nonspecific Findings = Hepatosplenomegaly, Jaundice, Thrombocytopenia, Growth Restriction
-Important “non-TORCH” infections that cause Meningitis in Neonates:
- **Streptococcus Agalactiae (Group B Strep)**
- **E. coli**
- **Listeria Monocytogenes**

-**Parvovirus B19 = Hydrops Fetalis**

Toxoplasmosis Gondii:
-cat feces /ingestion of undercooked meat (avoid cats in pregnancy)
-Usually asymptomatic in mother
-Neonate Triad:
- **Chorioretinitis**
- **Hydrocephalus**
- **Intracranial Calcifications**
- **+/- Blueberry Muffin rash**

Rubella:
-Respiratory droplet transmission
-Maternal = Rash, Lymphadenopathy, Polyarthritis
-Neonatal Triad:
- **Cataracts**
- **Deafness**
- **Patent Ductus Arteriosus (PDA)**
- **+/- Blueberry Muffin rash**

Cytomegalovirus (CMV):
-Sexual contact, organ transplant transmission
-Maternal = asymptomatic (or Mono-Like Sxs)
-Neonate:
- **Hearing Loss (Deafness)**
- **Seizures**
- **Petechial Rash**
- **Blueberry Muffin Rash**
- **Chorioretinitis**
- **Periventricular Calcifications****

HIV:
-Sexual contact, needlestick
-Mother = presentation depends on CD4+ count
-Neonate = Recurrent Infections, Chronic Diarrhea

Herpes Simplex Virus-2 (HSV-2):
-Skin or mucous membrane contact
-Maternal = usually asymptomatic (Herpetic Vesicles)
-Neonate = **Meningoencephalitis, Herpetic Lesions**

Syphilis:
-Sexual contact transmission
-Maternal = Chancre (Primary), Disseminated Rash (Secondary) - 2 stages that likely results in fetal infection
-Neonate:
- Often Stillbirth → Hydrops Fetalis
- If Child Survives = facial abnormalities (Notched Teeth, Saddle Nose, Short Maxilla), Saber Shins, CN VIII Deafness

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Nosocomial Infections:

-Antibiotic use = C. diff

-Aspiration (AMS, Old Age = Polymicrobial (Anaerobes or Grm (-))

-Decubitus Ulcers/Surgical Wounds = Staph aureus, Grm (-) Anaerobes (Bacteroides, Prevotella, Fusobacterium)

-Urinary Catheterization = Proteus, E coli, Kleb (PEcK)

-Water Aerosols = Legionella

Pelvic Inflammatory Disease (PID):
-Bugs = **Chlamydia Trachomatis + Neisseria Gonorrhoeae**
-Chlamydia Trachomatis = most common bacterial STI in USA
-sxs = Cervical Motion tenderness, Adnexal Tenderness, Purulent Cervical Discharge
-PID may include **Salpingitis (risk for Ectopic Pregnancy, Infertility, Chronic Pelvic Pain, Adhesions)**, Endometritis, Hydrosalpinx, Tubo-ovarian Abscess
-**Fitz-Hugh-Curtis Syndrome =** Infection + inflammation of Liver Capsule and **"Violin String"** Adhesions of Peritoneum to Liver

Red Rashes of Childhood:

1. Hand-Foot-Mouth Disease:
-Coxsackievirus Type A
-Oval-shaped vesicles on Palms/Soles + Vesicles/ulcers in oral mucosa (Herpangina)

2. Roseola (Exanthem Subitum):
-HHV6
-Asymptomatic rose-colored macules appear on body after several days of High fever (Febrile Seizures - usually affecting infants)

3. Measles (Rubeola):
-Measles Virus
-Confluent rash beginning at head + moving down; preceded by cough, coryza, conjunctivitis, blue-white (**Koplik**) Spots on Buccal Mucosa

4. Rubella:
-Rubella Virus
-Pink macules + papules; Start at head, move down but remain discrete → Fine desquamating truncal rash
-Postauricular lymphadenopathy

5. Erythema Infectiosum "Slapped Cheek Dx" (Fifth Disease)
-Rash on face
-Parvovirus B19 (ssDNA)
-Hydrops Fetalis in Pregnant Pts

6. Chicken-Pox:
-Varicella-Zoster Virus
-Vesicular rash begins on Trunk → spreads to face + extremities w/ lesions of different stages

7. Scarlet Fever:
-Streptococcus Pyogenes
-SCARLET:
- Sore throat
- Circumoral Pallor
- group A strep
- Rash (sandpaper-like from neck to trunk and extremities)
- Lymphadenopathy
- Erythrogenic Toxin
- Strawberry Tongue (also Kawasaki Vasculitis)

Sexually Transmitted Infections:

1. Chancroid
-painful genital ulcer w/ exudate, inguinal adenopathy
-**Haemophilus Ducreyi**
-"It's so painful you DO CRY"

2. Chlamydia
-Chlamydia Trachomatis (D-K)
-Urethritis, Cervicitis, Epididymitis, Conjunctivitis, Reactive Arthritis, PID

3. Condylomata Acuminata:
-Genital Warts
-Koilocytes
-HPV-6 + 11

4. Genital Herpes:
-Painful penile, vulvar, cervical vesicles and ulcers (can cause systemic sxs such as Fever, HA, Myalgia)
-HSV-2 > HSV-1

5. Gonorrhea:
-urethritis, cervicitis PID, Prostatitis, Epididymitis, Arthritis, Creamy purulent discharge
-Neisseria Gonorrhoeae

6. Granuloma Inguinale (Donovanosis):
-Klebsiella (Calymmatobacterium) Granulomatis
-Cytoplasmic "Donovan Bodies" (Bipolar Staining)
-Painless, BEEFY red ulcer that bleeds readily on contact

7. HBV = jaundice

8. Lymphogranuloma Venereum (LGV):
-Chlamydia Trachomatis (L1-L3)
-Infection of lymphatics; painless genital ulcers, painful lymphadenopathy (Buboes)

9. Syphilis = Treponema Pallidum
- Primary = painless chancre
- Secondary = Fever, Lymphadenopathy, skin rashes, condylomata lata
- Tertiary = Gummas, Tabes Dorsalis General Paresis, Aortitis, Argyll Robertson Pupil

10. Trichomoniasis:
-Trichomaonas Vaginalis
-Vaginitis, strawberry cervix, Motile in Wet prep

Antibiotics:

PCN G, V:
-PCN G (IV/IM), PCN VK (Oral),
-mech = D-ala-D-ala structural analog (Binds PBPs = Transpeptidases)
- Blocking transpeptidase cross-linking of peptidoglycan in cell wall
- Activates autolytic enzymes

-Spirochetes (T. Pallidum) = DOC for Syphilis
-Bactericidal
-sxs = Hypersensitivity rxns, (+) Coombs Hemolytic Anemia, Drug-induced Interstitial Nephritis
- R= B-lactamase cleaves B-lactam ring, changes in PBP

Penicillinase-Sensitive PCNs: "AminoPCNs"
-**Amoxicillin, Ampicillin**
-mech = same but wider spectrum of action (combine w/ clavulanic acid to protect against destruction by B-lactamases)
-Use = H influ, H pylori, E coli, Enterococci, Listeria, Proteus, Salmonella (kills enterococcus)
-ADRs = HSR, rash, pseudomembranous colitis
-R = penicillinase cleaving ring

Dicloxacinillin, Nafcillin, Oxacillin:
-Penicillinase-resistant PCNs
-Narrower spectrum; but bulky R-group blocks access of B-lactamase to B-lactam ring
-use = Staph aureus (no MRSA)
-sxs = HSR, Interstitial Nephritis
-R = MRSA has altered PBP protein target site

Piperacillin, Ticarcillin:
-"Antipseudomonal PCNs"
-Extended spectrum, penicillinase sensitive, use w/ B-lactamase inhibitors
-HSR rxns

B-Lactamase Inhibitors:
-Clavulanic Acid, Avibactam, Sulbactam, Tazobactim
-added to PCN antibiotics to protect from B-lactamases
-**Amox-Clav (Augmentin), Ceftaz-Avibactam (Avycaz), Amp-Sulb (Unasyn), Pip-Taz (Zosyn)**

Cephalosporins:
-Mech = B-lactam drugs inhibits cell wall synthesis but are less susceptible to penicillinases
-Bactericidal
-Not covered = Listeria, Atypicals (Chlamydia, Mycoplasma), Enterococci***
-Sxs = HSR, autoimmune hemolytic anemia, disulfiram-like rxns, Vitamin K def
-**Low rate of cross-reactivity even in PCN-allergic pts**
- nephrotoxicity of aminoglycosides

1. Cefazolin, Cephalexin:
-Grm (+) Cocci, Proteus, E. coli, Kleb
-Cefazolin used prior to surgery to prevent Staph aureus wound infections

2. Cefaclor, Cefoxitin, Cefuroxime, Cefotetan:
-Grm (+), H flu, Enterbacter, Neisseria, Serratia, Proteus, E coli, Kleb

3. Ceftriaxone, Cefotaxime, Cefpodoxime, Ceftazidime, Cefixime:
-serious Grm (-) infections resistant to other B-lactams
-cross BBB
-Ceftriaxone = great for meningitis, gonorrhea, disseminated lyme disease
-Ceftazidime = Pseudomonas

4. Cefepime;
-Grm (-) organisms, w/ activity against pseudomonas + grm (+) organisms

5. Ceftaroline:
-broad grm (+) and grm (-) coverage
-Added MRSA and Enterococcus Coverage***
-Loses Pseudomonas Coverage

Carbapenems: Doripenem, Imipenem, Meropenem, Ertapenem
-Mech = Imipenem is broad spectrum, B-lactamase resistant carbapenem (Always given w/ **Cilastatin** - Inhibitor of **Renal Dehydropeptidase I**) to inactivation of drug in renal tubules
-sxs = **Seizures (Least w/ Meropenem)**, GI distress, rash
-R = inactivated by Carapenemases produced by Kleb pneumo (KPC), E Coli, E aerogenes

Aztreonam:
-less susceptible to B-lactamases
-prevents peptidoglycan cross-linking by binding to **PBP-3**
-Synergistic w/ Aminoglycosides
-No cross-allergenicity w/ PCNs
-Grm (-) rods ONLY = no activity against grm (+) rods or anaerobes

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Vancomycin:
-mech = inhibits cell wall peptidoglycan formation by binding D-Ala-D-ala portion of Cell wall precursors
-Bactericidal (static against C diff)
-Not susceptible to B-lactamases
-use = Grm (+) bugs only (MRSA, Strep epidermidis, Enterococcus, C diff)
-**Red man Syndrome** = diffuse flushing rxn (histamine mediated) nonimmunogenic response to infusion rate
-**Nephrotoxicity, Ototoxicity, Thrombophlebitis, DRESS Syndromes**
-R = amino acid modification of D-ala-D-ala to D-ala-**D-Lac** (Enterococcus - VRE)

Protein Synthesis Inhibitors:
-targeting small bacterial ribosome (70S = 30S + 50S)
-All are Bacteriostatic (except Aminoglycosides + Linezolid)

30S Inhibitors = Aminoglycs + TCNs
50S Inhibitors = Chloramphenicol, Clinda, Erythromycin (Macrolides), Linezolid

"buy AT 30, CCEL at 50"

Aminoglycosides:
-Gentamicin, Neomycin, Amikacin, Tobramycin, Streptomycin
-Bactericidal (Irreversible inhibition of initiation complex through binding of 30S → misreading of mRNA + blockage of translocation)
-Requires O2 for uptake*** (NOT effective against Anaerobes)
-Severe grm (-) rod infections, Synergistic w/ B-lactam Antibiotics
-Neomycin for Bowel Surgery
-ADR = **Nephrotoxicity, Neuromuscular Blockade** (Contraindicated in Myasthenia Gravis)**, Ototoxicity** (esp. w/ Loops), **Teratogenicity**
-R = bacterial transferase enzymes inactivate

Tetracyclines: Doxycycline, TCN, Minocycline
-30S = prevent attachment of aminoacyl-tRNA
-limited CNS penetration
-Doxycycline is fecally eliminated can used in pts w/ Renal failure
-Chelation = antacids, milk, iron-preps (blocking absorption of drug)
-Borrelia Burgdorferi, Mycoplasma pneumonia (drugs ability to accumulate intracellularly makes them very effective against Rickettsia/Chlamydia)
-Doxy = CA-MRSA
-sxs = GI distress, Teratogenic (Discoloration of teeth, bone growth restrictions), Photosensitivity
-R = uptake, efflux (Plasmid-encoded transport pumps)

Tigecycline:
-TCN derivative = binds 30S inhibiting protein synthesis
-Bacteriostatic
-Broad-spectrum anaerobic, grm (-) and (+) coverage
-MRSA, VRE coverage

Chloramphenicol:
-Blocks Peptidyl Transferase at 50S ribosomal subunit
-Bacteriostatic
-Use = rickettsial diseases + Meningitis (H flu, Neisseria mening, strep pneumo)
-sxs = Anemia (dose dependent), aplastic anemia, Gray Baby Syndrome (if Lacking UDP-Glycuronosyltransferase)

Clinda:
-blocks peptide transfer (Translocation) of 50S ribosome
-Bacteriostatic
-Anaerobic infxns (Bacteroides, clostridium, strep pyogenes - Group A strep)
-"**Tx anaerobic infections above diaphragm, vs. Metronidazole treating anaerobic below"**
- risk of Pseudomembranous Colitis (C. diff)

Linezolid:
-Binding of 50S, preventing formation of initiation complex
-grm (+) species including MRSA, VRE
-Bone marrow suppression (Thrombocytopenia), Peripheral neuropathy, Serotonin Syndrome (MAOI activity)

Macrolides: Azithro, Clarithro, Erythro
-inhibit protein synth via blockade of Translocation ; bind to 23S rRNA of 50S ribosomal subunit
-Bacteriostatic
-Atypical coverage (Mycoplasma, Chlamydia, Legionella)
-sxs:
- GI motility issues (Constipation)
- Arrhythmias (prolonged QT interval)
- Acute Cholestatic Hepatitis
- Rash
- Eosinophilia

- conc of Theophylline + oral anticoagulants (Erythro/Clarithro inhibit CYPS)
-R = methylation of 23S rRNA-binding site prevents drug binding

Polymyxins:Colistin (Polymyxin E), Polymyxin B
-Cation polypeptides that bind to phospholipids on cell membrane of Grm (-) Bacteria → disrupt cell membrane integrity → leakage of cellular components → cell death
-Salvage therapy for MDR grm (-) bacteria (pseudomonas, E coli, KPC)
-**Nephrotoxicity, Neurotoxicity** (slurred speech, weakness, paresthesias), respiratory Failure

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Sulfonamides: Sulfamethoxazole (SMX), SUlfisoxazole, Sulfadiazine
-mech = inhibit **Dihydropteroate Synthase** (inhibiting folate synthesis)
- Accumulation of PABA + Pteridine

-Bacteriostatic alone (bactericidal w/ Trimethoprim)
-use = Grm (+), (-), nocardia
-sxs = HSR rxns, Hemolysis if G6PD deficient, Nephrotoxic (Tubulointerstitial Nephritis), Photosensitivity, SJS, Kernicterus in infants, Displace other drugs from albumin (Warfarin)

Dapsone:
-similar to Sulfonamides, structurally distinct agent
-Leprosy + Pneumocystis jirovecii ppx
-Hemolysis if G6PD deficient, Methemoglobinemia, Agranulocytosis

Trimethoprim:
-inhibits bacterial **dihydrofolate reductase**
-Bacteriostatic
-used w/ SMX to also block folate synthesis
-sxs = **Hyperkalemia,** Megaloblastic anemia, leukopenia, granulocytopenia (Marrow Toxic)

Fluoroquinolones: Cipro, Resp = Moxi, Levo
-inhibit prokaryotic enzyme Topoisomerase II (DNA Gyrase) adn Topoisomerase IV
-Bactericidal
-Avoid Antacids
-Grm (-) rods of urinary and GI tracts (including pseudomonas) + grm (+) organism (otitis externa)
-Sxs = GI upset, Superinfections, Skin rashes, HA, dizziness (Leg cramps/Myalgias)
-**Tendon Rupture** (esp > 60 yo, taking prednisone)
-Contraindicated during Pregnancy or Breastfeeding and children < 18 y due to possible damage to cartilage (QTc prolongation)
-R = mutation in DNA gyrase, plasmid-mediated resistance, Efflux pumps

Daptomycin:
-Lipopeptide that disrupts cell membranes of Grm (+) Cocci by creating transmembrane channels
-MRSA, VRE
-NO Pneumonia b/c inactivated by Lung Surfactant
-sxs = Myopathy, Rhabdomyolysis (CK)

Metronidazole:
-Forms toxic free radical metabolites in bacterial cell that damage DNA (Bactericidal, Antiprotozoal)
-Giardia, Entamoeba, Trichomonas, Gardnerella Vaginalis, Anaerobes (Bacteroides, C diff), Triple Therapy for H pylori if PCN allergy
-**Tx anaerobic infxn below the diaphragm vs. Clinda which is above the diaphragm**
-ADRs = Disulfiram-Rxns (Severe flushing, Tachycardia, Hypotension) w/ Alcohol, HA, Metallic Taste

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AntiMycobacterial:
-TB = ppx w/ Isoniazid, tx w/ RIPE
-M avium-intracellulare = ppx w/ Azithro, Rifabutin, Tx w/ Azithro/clarithro + ethambutol
-M Leprae = Tx w/ Dapsone, Rifampin, Clofazimine

-Isoniazid = blocks mycolic acid synthesis

-Ethambutol = arabinogalactan synthesis (Arabinosyl Transferase inhibition)

-Rifabutin/Rifampin = mRNA synthesis (DNA-dependent RNA polymerase inhib)

-Pyrazinamide = Intracellular (unknown)

Rlfamycins:
-Inhibit DNA-dependent RNA Polymerase
-4 Rs'
- RNA Polymerase inhibitor
- Ramps up Microsomal CYPs (Inducer)
- Red/Orange Body Fluids
- Rapid Resistance if used alone

-Hepatotoxicity

Isoniazid:
- synth of mycolic acids (bacterial Catalase-peroxidase (KatG gene) needed to convert INH to active form
-sxs = **Hepatotoxicity,** CYP Inhibition, DILE (SLE), Anion gap metabolic acidosis, Vitamin **B6 Deficiency** (**peripheral neuropathy, sideroblastic anemia**), Seizures
-Give w/ B6 (Pyridoxine)

Pyrazinamide:
-works best at acidic pH (in host phagolysosomes)
-Hyperuricemia + Hepatotoxic

Ethambutol:
- Carbohydrate Polymerization of mycobacterium cell wall by blocking Arabinosyltransferase
-Optic Neuropathy (red-green color blindness, irreversible)

Antifungals:

1. Terbinafine = Lanosterol Synthesis
2. Azoles = Ergosterol Synthesis
3. Echinocandins = Cell wall synthesis
4. Polyenes (Ampho/Nystatin) = Cell Membrane Integrity
5. Flucytosine = Nucleic Acid Synthesis

Amphotericin B:
-mech = binds Ergosterol + forms membrane pores that allow leakage of electrolytes
-Cryptococcus, blastomyces, coccidioides, Histoplasma, Candida, Mucor
-Fevers/chills (Shake and Bake), Hypotension, Nephrotoxicity, Arrhythmias, anemia, IV phlebitis
-"Amphoterrible"
-Liposomal Ampho Toxicity (hydration nephro)

Flucytosine:
-inhibits DNA and RNA biosynthesis by conversion to 5-FU by cytosine deaminase
-Cryptococcus = in combo w/ Ampho
-Bone Marrow Suppression

Azoles: Clotrimazole, Fluconazole, Isavuconazole, Itraconazole, Ketoconazole, Miconazole, Voriconazole
-mech = inhibit fungal sterol (Ergosterol) synthesis via inhibition of CYP450 enzymes that convert lanosterol to ergosterol
-sxs = Testosterone synthesis inhibition (Gynecomastia - Ketoconazole), Liver Dysfunction, Drug Intxns

Terbinafine:
-inhibits fungal enzyme **Squalene Epoxidase** (preventing synthesis of Lanosterol)

Echinocandins: **Anidulafungin, Caspofungin, Micafungin**
-mech = inhibit cell wall synthesis via blocking Synthesis of **B-glucan**
-DOC for Invasive Aspergillosis, Candida infxns

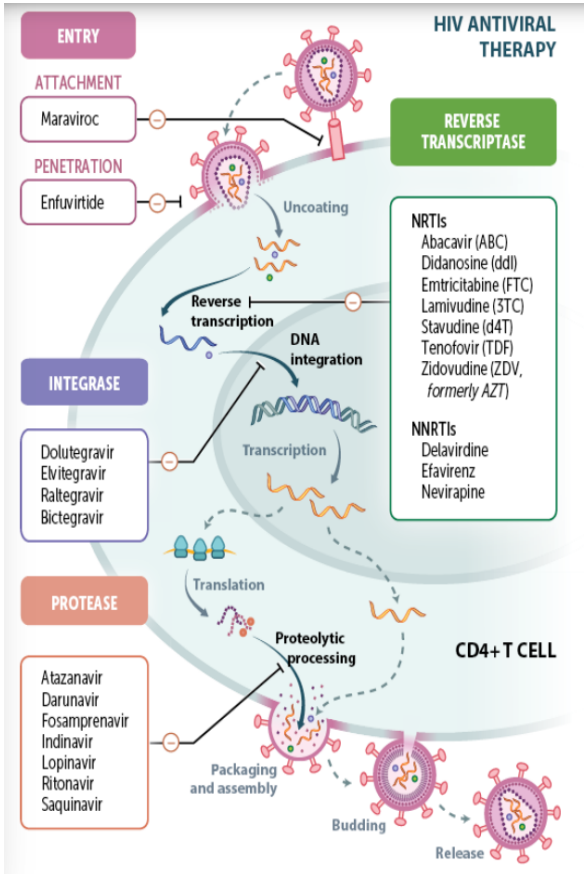
Griseofulvin = interferes w/ microtubule function; disrupts mitosis (Deposits in Keratin-containing tissues)
-Teratogenic, Carcinogenic, Confusion, HA, Disulfiram-Rxns, Warfarin metabolism

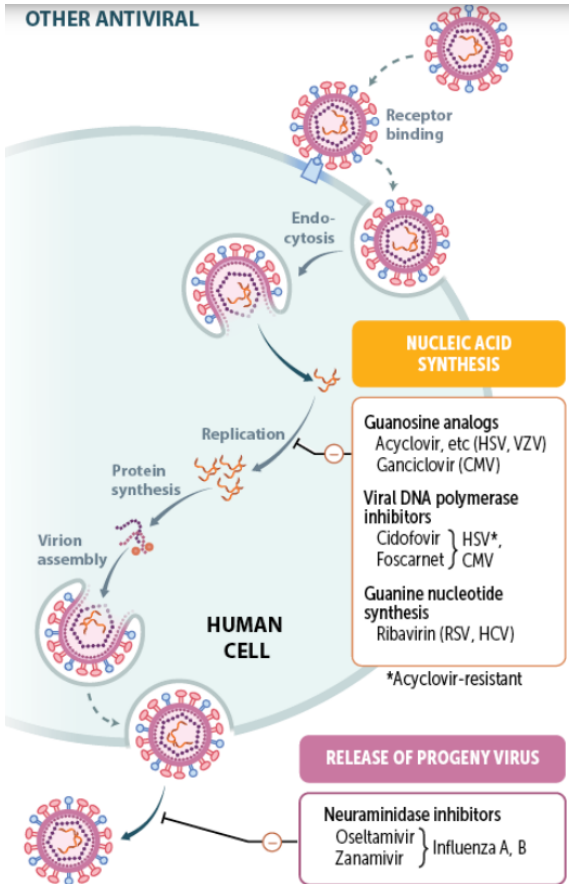
Permethrin/Malathion = AChE Inhibitors

Chloroquine:
-blocks detoxification of heme into hemozoin (Heme accumulates and is toxic to plasmodia)
-Tx Malaria (Plasmodium Falciparum)
-Retinopathy, Pruritus

Pyrantel, Ivermectin, Mebendazole = Microtubule inhibitor to treat "bendy worms")
Praziquantel = ca2+ permeability → vaculozation

Antivirals:





Oseltamivir, Zanamivir:
-Neuraminidase Inhibitors (preventing Influenza Viral progeny release from host)
-begin therapy within 48 hrs of sxs onset to shorten illness duration

Baloxavir:
-mech = Inhibits "Cap Snatching" endonuclease activity of influenza virus RNA polymerase → viral replication
-Tx within 48 hrs

Remdesivir:
-Prodrug of an ATP analog → active metabolite inhibits viral **RNA**-dependent **RNA** polymerase and evades proofreading by viral exoribonuclease (ExoN) → viral RNA production

Acyclovir, Famciclovir, Valacyclovir:
-**Guanosine Analogs** = monophosphorylated by HSV/VZV Thymidine Kinase (NOT phosphorylated in infected cells) → few adverse effects
-Triphosphate formed by cellular enzymes (preferentially inhibit viral DNA polymerase by chain termination)
-use = HSV, VZV (no EBV, CMV)
-sxs = Obstructive Crystalline Nephropathy + AKI

Ganciclovir:
-Guanosine Analog (5'-monophosphate formed by CMV viral Kinase), Triphosphate formed by cellular kinases (preferentially inhibits viral DNA polymerase)
-use = CMV (esp. If immunocompromised)
-Valganciclovir (prodrug) w/ better oral Bioavail
-sxs = Bone marrow suppression (leukopenia, neutropenia, thrombocytopenia), renal toxicity

Foscarnet:
-Viral DNA/RNA Polymerase inhibitor + HIV RT inhibitor (Binds to **Pyrophosphate-binding** site of enzymes) (Does not require any kinase activity)
-Pyrophosphate analog
-CMV retinitis in immunocompromised pts when Ganciclovri fails
-sxs = Nephrotoxicity, electrolyte abnormalities (hyperphos, hypoK+, / Ca2+, hypomag), seizures

Cidofovir:
-inhibits viral DNA polymerase (Does not require phosphorylation by viral kinase)
-CMV retinitis in immunocompromised pts (acyclovir-resistant HSV)
-Long t1/2
-Sxs = Nephrotoxicity (give w/ Probenecid/ IV saline to tox)

HIV Therapy:
-regiments consist of 3 drugs to prevent resistance; 2 NRTIs + Integrase Inhibitor
-Most ARTs are active against both HIV-1 and HIV-2 (NNRTIs and Enfurvirtide is NOT active w/ HIV-2)

1. Entry Inhibitors:

Enfuvirtide = gp41 (inhibiting viral entry - Fusion inhib)

Maraviroc = CCR5 binding on T-cells/Macrophages inhibiting interaction w/ gp120 (inhibits Docking)

2. NRTIs:
-Competitively block nucleotide binding to RT and Terminate the DNA chain (lack a 3'-OH group)
-Tenofovir is a NucleoTide, others are NucleoSides
-All need to be phosphorylated to become active
-**Zidovudine** = useful in pregnancy to fetal transmission
-sxs = Bone Marrow Suppression (give G-CSF/Epo), Peripheral Neuropathy, Lactic Acidosis (nucleosides), Anemia (Zidovudine)

- **Abacavir (HLA-B*5701 - Fatal Rash)**
- **Emtricitabine**
- **Lamivudine**
- **Tenofovir (TAF, TDF)**
- **Zidovudine**

2. NNRTIs:
-mech = bind to RT at site different from NRTIs
-DO NOT require phosphorylation to be active or complete w/ other natural Nucleotides
-sxs = Rash, Hepatotoxicity, Vivid Dreams/CNS sxs (Efavirenz)

- **Delavirdine**
- **Efavirenz**
- **Nevirapine**

3. Integrase Inhibitors: "-gravir"
-Inhibits HIV genome integration into host cell chromosomes (inhibiting HIV Integrase)
-sxs = Creatine Kinase

- **Bictegravir**
- **Dolutegravir**
- **Elvitegravir**
- **Raltegravir**

4. Protease Inhibitors: "-navir"
-Assembly of virions depends on HIV-1 protease (pol gene), which cleaves polypeptide products of HIV mRNA into their functional parts
-Protease inhibitors prevent Maturation of new Viruses
-**Ritonavir** = Boosts other drugs by inhibiting CYPs
-sxs = Hyperglycemia, GI intolerance (N/D), Lipodystrophy (Cushing-Like Sxs)
-Rifampin (potent CYP inducer) reduces protease inhibitor concentrations

- **Atazanavir**
- **Darunavir**
- **Lopinavir**
- **Ritonavir**

Hepatitis C Therapy:
-Chronic HCV infection treated w/ Multidrug therapy

NS5A Inhibitors: "**-asvir"**
-blocks NS5A (viral phosphoprotein needed for RNA replication)

- **Ledipasvir**
- **Ombitasvir**
- **Velpatasvir**

NS5B Inhibitors: "**-buvir"**
-Inhibits NS5B (RNA-dependent RNA polymerase; by acting as a chain terminator) → preventing viral replication

- **Sofosbuvir**
- **Dasabuvir**

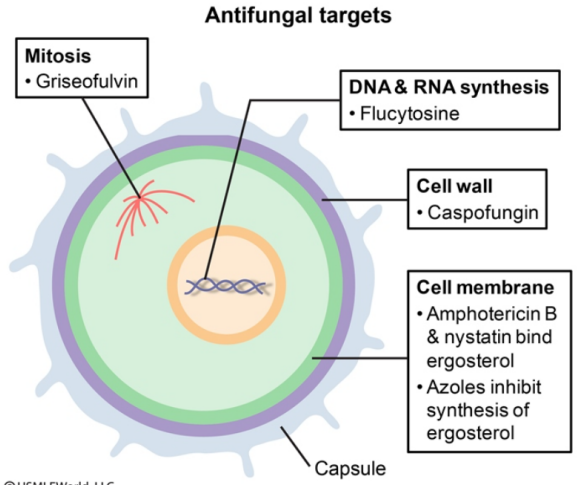
NS3/4A Inhibitors: "**-previr"**
-Inhibits NS3/4A (viral protease) preventing viral replication

- **Grazoprevir**
- **Simeprevir**

Ribavirin:
-inhibits synthesis of guanine nucleotides by competitively inhibiting IMP dehydrogenase
-sxs = Hemolytic anemia + Severe Teratogen

Pregnancy ABx to avoid:

- Sulfonamides = Kernicterus
- Aminoglycosides = Ototoxicity
- Fluoroquinolones = Cartilage damage
- Clarithromycin = embryotoxicity
- TCNs = Discolored teeth, bone growth issues
- Ribavirin = Teratogenic
- Griseofulvin = teratogenic
- Chloramphenicol = Gray Baby Syndrome



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