Virus

- Viral endocytosis, capsid dissolves, nucleic acid release into nucleus if DNA virus or cytoplasm if RNA virus, DNA is replicated or converted into mRNA and then protein while RNA is replicated or used to make protein or even converted into DNA via reverse transcriptase and then integrated into human genome via integrase
- Work-Up: Culture (Gold Standard as very specific but not sensitive as you need a very high VL, essentially the virus is inoculated onto fibroblasts and the specific CytoPathic Effects (CPEs) like inclusion bodies, etc suggest a type of virus), Direct Flourescent Ab aka DFA (IHC is done to determine the exact virus after Cx is done, this process takes a long time in the order of weeks), Serology (acute IgM and convalescent IgG titers eg. 1:8, good for determining vaccinations status only, it is also good to check levels in privileged sites specifically CNS as they can be higher or lower than in serum), PCR (copies/mL, there are no studies saying what the # of copies means, very sensitive even False +), EM (will be an emerging test), Tzank Smear (scrape lesion down to bottom layer, place material on slide, stain w/ Giemsa/Wright, not sensitive/specific, in HSV will show multinucleated giant cells)
- RNA Viruses aka Retroviruses: HIV, HTLV, HA/C/EV, Rubella, Hemorrhagic Fever Viruses, Encephalitis Viruses, Polio, Rhino, Coxsackie, Norwalk, Rotavirus, SARS, Influenza, RSV, Measles
 - Mumps (remerging)
 - RSV (interstitial pneumonia in adult transplant pts)
 - DNA Viruses: Herpes, HBV, Adenovirus, HPV, JCV, BKV, Parvovirus B19, Pox
 - Herpes Viruses
 - HHV-1/HSV-1 & HHV-2/HSV-2 (remember it can also cause Erythema Multiforme)
 - acyclovir (Zovirax) PO/IV/Top, famcyclovir (Famvir)/valacyclovir (Valtrex) PO (just like acyclovir but better bioavailability), pencyclovir (Denavir) Top (just like acyclovir but only topical b/c poor bioavailability), trifluridine (Viroptic) Eye Drop
 - Mechanism: guasine nucleoside analogue that is phosphorylated and competes with dTGP for DNA and when it does it acts a chain terminator
 - SEs: GI (N/V/D), headache, vertigo, arthralgia/myalgia, rash, fatigue, insomnia, drug fever, menstrual abnormalities, acne, sore throat, LAD, post-obstructive renal failure from crystallization, TTP/HUS
 - NB orolabial HSV (topical not that good so use systemic agents)
 - NB rare cases of drug resistance to acyclovir have occurred but virus is typically still susceptible to foscarnet
 - HHV-3/VZV (remember it can also cause pneumonia)
 - Chicken Pox (no Tx except if adult (PO acyclovir x7d) or immunocompromised/pregnant (IV acyclovir x5d))
 - Shingles (Tx with acyclovir/famciclovir/valacyclovir except if <50yo/mild pain/no eye/<3d)
 - Only Famvir/Valtrex have been shown to decrease the incidence of post-herpetic neuralgia (lancinating/burning pain that persists after rash has resolved),
 - neuropathic/topical analgesics (refer) esp TCAs/Capsaicin/Gabapentin/Oxycodone, it was once thought that prednisone would decrease incidence of neuralgia but it doesn't and in fact it prolongs the course of shingles
 - HHV-4/EBV (no Tx, in a normal pt infection causes a mono like illness, in an immunosuppressed pt infection causes various organ dz esp oral hairy leukoplakia, nasopharyngeal carcinoma, Burkitt's Lymphoma, etc)
 HHV 5 (CMV)
 - HHV-5/CMV

Virology Genome: double-stranded linear DNA INCIS MD PA

- Tegument: proteinaceous matrix
- Envelope: lipid bilayer w/ glycoproteins (gB and gH)
- Infection
 - Transmission: via urine, saliva, blood, semen, stool, milk, tissue
 NB risk w/ single unit of transfused blood is 0.38%
 - Primary Infection: typically occurs during the two decades of life
 - Latency: exists in non-replicating state w/in a variety of cells (PMNs, lymphocytes, endothelium, renal epithelium, salivary glands)
 - $\circ \qquad \text{Reactivation: seen uniquely in immunocompromised pts}$
- Epidemiology
 - Adult Seroprevalance of 50-80% in developed countries (higher in developing countries)
 - Diagnosis
 - Histology
 - H&E: large cells ("cyto-megalo-virus") w/ basophilic cytoplasmic inclusions and Cowdry Type A eosinophilic intranuclear inclusions ("owl's eyes" b/c of surrounding halo)
 - IHC Stain w/ Monoclonal Ab
 - Labs (these modalities lose their sensitivity in immunocompromised pts emphasizing the importance of tissue diagnosis)
 - Serology: only useful in assessing status in recipients/donor prior to
 - transplant and in determining post-transplant risk and duration of Px, otherwise not helpful especially

- Acute: (1) +IgM and –IgM (2) +IgM and +IgG that increases 4x in titer over a 4wk period
 - NB IgM becomes + during the first 2wks of acute
 - infection and can remain + for 4mos Recovered: -IgM and +IgG
- PCR: good for monitoring Tx, correlates w/ risk of symptomatic disease during reactivation
- pp65 Ag: rarely done
- Culture: rarely done b/c cytopathic changes are slow taking up to 6wks

Infection Types o Pediatric

- Trans-placental Transmission: significant irreversible neurologic deficits (microcephaly, encephalitis, retinitis → psychomotor retardation, seizures, deafness) along w/ IUGR, hepatitis, petechia w/ death in 20%
- Peri-natal Transmission: 70% asymptomatic vs 30% self-limiting hepatomegaly, hepatitis, pneumonitis
- o Immunocompetent (infection induces primary immune response and subsequent
 - establishment of lifelong immunity)
 - Asymptomatic (most pts)
 - Mononucleosis-Like Syndrome (indistinguishable from EBV except that pharyngitis and splenomegaly is rare)
 - Serious Illnesses (rare)
 - Pneumonitis
 - Retinitis
 - Hepatitis
 - Peri/myocarditis
 - Guillain-Barre Syndrome
 - Encephalitis
 - Immunocompromised (reactivation of latent infection, after the era of

immunosuppressants and HIV CMV has emerged a cause of multiple serious conditions) Transplantation

- CMV initially localizes in the transplanted organ <u>+</u> rejection (eg. OLTx pts = CMV hepatitis) which can subsequently spread systemically
- Lowest risk in kidney transplants while highest risk in pancreas/heart/lung transplants
 - Highest risk in seronegative recipients receiving seropositive donor organ
 - High risk groups who receive 1-3mo Px decrease their risk of symptomatic infection from 85% to 10%
 - RFs for reactivation: organ rejection, bacterial/fungal infection,

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- Since the advent of HAART in 1995 there has been a marked decline in CMV infection w/ most cases attributed to newly diagnosed HIB or non-adherence to HAART
- b/f HAART and anti-CMV CMV infection was generally fatal w/in a few months
- Currently the r/o CMV in HAART compliant HIV pts is ~1%/12month period vs 15% in HAART non-compliant pts
- Generally occurs when CD4<50 cells/mcL
- Malignancy
 - Usually seen in hematologic malignancies
 - Types of Infection
 - Systemic Sx (fever, malaise, etc)
 - Heme (leucopenia, thrombocytopenia)
 - Liver (hepatitis, seen as microabscesses w/ a characteristic increase in AP)
 - Eye (iritis)
 - Lung (Pneumonitis)
 - GI (anywhere from mouth to anus)
 - 1° Colitis: chronic watery non-bloody diarrhea w/ ab pain, weight loss, fever, Colonoscopy (colitis w/ subepithelial hemorrhage 15%, ulcers 35%, colitis+ulcers 35%, normal 25% hence random biopsy

important), L-sided Bx ~75% sensitivity vs pan-colon Bx ~95% sensitivity, can also occur in IBD on immunosuppressive therapy however difficult to determine if inflammation is from underlying IBD or CMV as inclusion bodies are hard to see in active inflammation

- 2° Esophagitis: multiple, large shallow distal ulcers w/ dysphagia/odynophagia
- 3° Gastritis:
- Other: Cholangiopathy, Focal Enteritis, Oropharyngeal Ulcers

Тx

HHV-7 (?)

HHV-8 (Kaposi Sarcoma)

0

- Px: Valgancyclovir
 - Routine in high-risk pts after solid-organ transplant
- Tx: Induction w/ gancyclovir (Cytovene) 5mg/kg IV Q12hr x2-6wks or until document clearance of viremia then Maintenance w/ valgancyclovir (Valcyte) 900mg PO QD x?d
 - NB acyclovir/valaciclovir (inhibits thymidine kinase which is NOT expressed in CMV)
 - NB Tx underlying cause of immunosuppression (eg. HAART for HIV, Tx of malignancy, etc)
 - Gancyclovir/Valgancyclovir
 - Mechanism: like other "-cyclovirs"
 - SEs: pancytopenia, headache, N/D, edema, peripheral neuropathy
 - NB valine ester of gancyclovir that is converted by hepatocytes to gancyclovir such that 900mg PO valganciclovir ~5mg/kg IV gancyclovir
 - NB in cases of severe enteritis oral valgancyclovir is avoided b/c of theoretic decreased risk of absorption which subsequent potential risk of developing resistance

NB if gancyclovir resistant cases then 1° foscarnet (Foscavir) 2° cidofovir (Vistide)

- Mechanism: guanine nucleotide (therefore no need to be phosphorylated by kinase) that competes with dTGP for DNA and when it does it acts a chain terminator
- SEs: nephrotoxicity (very important, seen in 1/3 of all pts), hypocalcemia/magnesemia and hyperphosphatemia/kalemia, CNS (headache, seizure, neuropathy), iritis, penile ulcers

- Viral Hemorrhagic Fevers
 Common World Wide: (Dengue Fever & Yellow Fever Virus) Geography: world-wide, Reservoir: monkeys Vector: Aedes mosquito Location: tropical environments (Americas, Africa, Asia, etc) thus like malaria except that Dengue is also found in tropical urban cities unlike malaria which is only found in tropical rural areas, Incubation: ~1wk, S/S: (below), Dx: serology/PCR, Tx: supportive
 - Dengue S/S: asymptomatic to dengue fever (F, retro-orbital HA w/ conjuctival injection, bone/muscle pain, rash, resp Sx, GI Sx w/ HM, LAD) to dengue hemorrhagic fever (" " + skin bleeding aka petechia, mucosal bleeding, 3rd spacing, thrombocytopenia, increased LFTs) to dengue shock syndrome (" " + shock) w/ 1-10% mortality, Px: mosquito prevention
 - Yellow S/S: asymptomatic to non-specific constitutional Sx w/ multi-organ insufficiency especially liver failure (hence called "yellow fever"), renal failure, and hemorrhage followed by several months of fatigue for those who don't die, NB no human-to-human transmission unlike other viral hemorrhagic fevers, w/ 5-50% mortality Px: vaccination
 - Rare South American/African: (Junin, Machupo, Guanarito, Sabia Virus, Crimean, Rift River, Hanta, Lassa, Ebola, Marburg, Amsk, Kyasanur Virus) S/S: fever/chills, myalgia/arthralgia, N/V, bradycardia/hypotension, meningismus/AM, Hemorrhage 2/2 Thrombocytopenia: petechia/purpura and mucosal bleeding, NB each specific virus has also other unique features, Tx: supportive, ribavirin, immune serum (very difficult to obtain), Px: none

Severe Acute Respiratory Syndrome (SARS) Corona Virus	 Reservoir: Small Asian Mammals Vector: aerosolized mammal feces Geography: Asia NB emerged in fall 2002 in Guangdong Province in South China and spread from there on where the virus transmitted to humans from cats caged in restaurants Unique problem: not contagious early on but very contagious 10d later when pt has 	 S/S: atypical PNA that looks like influenza early on but then easily progress to resp failure Complications: ARDS, shock death 	 Dx: Cx Tx: Supportive Care, some evidence of lopinavir/ritonavir, Steroids more harm than good, Infusion of convalescent serum from recovered persons, Vaccine under development
	already been admitted		
Hantavirus Pulmonary	Reservoir: Rodent	S/S: severe atypical hemorrhagic PNA	• Dx: Serology
Synarome (HPS)	Vector: aerosolized rodent urine/feces	W/ GI SX	Ix: Supportive Care
Hanta / Sin Nombre Virus	Geography: Desert SE	Complications: polycythemia, thrombocytopenia ARDS, shock, death (50% die!!!)	

1 st Disease Measles (Rubeola Virus)	3 rd Disease German Measles 3-Day Measles	5 th Disease Erythema Infectiosum (Parvovirus B19)	6 th Disease Exanthema Subitum Roseola Infantum	Chicken Pox (young) Shingles (old) (Varicella-Zoster Virus)
	(Rubella Virus)		(HHV-6)	
Incubation 10d	 Incubation 17d 	 Incubation 12d 	 Incubation 9d 	Chicken Pox
\downarrow	\downarrow	\downarrow	\downarrow	 Incubation 15d
Prodrome 3d	Prodrome 1d (often	Prodrome 2d	Prodrome 5d	\downarrow
"3 C's" Cough, Coryza (mucus	no prodrome in	Low F	• High F (can cause	Prodrome 0d
rhinorrhea), Conjunctivitis	children)		Febrile Seizures)	Low F
High F	Malaise	 Slapped Cheek Rash 	\downarrow ,	Malaise
Malaise	• Fever		Mobilliform Rash	Anorexia
Photophobia	Anorexia		(begins on trunk	Rapid Progression (7hrs) from
			and spreads	Pruritic Crops of Macules to
Koplik's Spots on Buccal	 Generalized LAD 		peripherally)	Papules to Vesicles on an
Mucosa (bluish-white lesions	• Forchheimer's Sign		High Leukocytosis	Erythematous Base to Ruptured
on an erythematous base)	(palatal petechiae)		followed by Low	Lesions ("dew drops on rose
	Morbilliorm Rash		Leukopenia	petals")
A DECEMBER OF THE OWNER.	(lasts 3d) that begins	Lacy/Poticular Pash		various stages vs Small Pox
	on face and spreads	Lacy/Reticular Rasin (bogins on trunk	Complications:	(last case in 1977, very
and the second se	to trunk	and sproads	encephalitis	contagious, 30% mortality
	↓ ↓	norinhorally)		vaccine available to soldie
	Complications: 1.5		Mantas MI	PA - begins on trunk and
	transient noly		///////////////////////////////////////	spreads peripherally
4	arthritis/arthralgia.	C P COMP		
Morbilliform Rash (begins on	encenhalitis	11 1 . N 18 W		
head and moves caudally)	thrombocytopenia	and the second		
includ and moves caudality)	anomooyapena			
A STATISTICS	Congenital Rubella			· · · · · · · · · · · · · · · · · · ·
	Syndrome: heart			
a the second second second	defects			
and the second second	microcenhaly MR	 Rashes Eluctuate 		
and some and	deafness cataracts			\downarrow
A COMPANY OF	glaucoma	Hot or Cold		Complications: bacterial
\downarrow	• b/f vaccination it was			superinfection, necrotizing fasci
Complications: Pneumonia,	the primary cause of	Complications:		thrombocytopenia. arthritis
Encephalitis, Subacute	congenital infection	Transient Anlastic		pneumonia, encephalitis
Sclerosing Panencephalitis,	consentar infection	Anemia Crisis in nts		meningitis, ataxia. Guillain-Barr
Pericarditis, Hepatitis, 10%		who have chronic		Syndrome, hepatitis, TTP. purpu
Death if Malnourished		hemolysis		fulminans, GABHS skin infection
		nemorysis		(very common), Reve Syndrome
		Congenital 5 th		(very common if associated w/
		Disease Syndrome		aspirin use), Ramsav-Hunt
		hydrons fotalis fotal		Syndrome (pain + vesicles on
		anomia		external auditory meatus + loss
	1	anenna		

				 ipisilater facial palsy) 2/2 geniculate nucleus infection Variable Presentation from few crops and low fever to many crops, high fever, and death Infectious from 1d before rash to when entire rash is crusted Shingles
				 reactivation of infection in adult who had chicken pox in past Painful Dermatomal Rash Similar to Chicken Pox but lasts longer and is painful especially in elderly
				Dx: (1) Tzank Test for Multinucleated Giant Cells (2) Varicella Fluorescent Ab Test for Actual Virus (3) Culture
No True Tx	• No True Tx (but	No True Tx	No True Tx	Normal Child
 vitamin A (for some reason vit A deficiency increases r/o 	b/c postnatal			 Antipurities (Calamine Lotion, Caladrin Lotion)
complications)	infection is			Oatmeal Baths
 IG if given w/in 6d of 	innocuous)			Cool Compresses
exposure				Adult or Immunocompromised Child
Vaccine if given w/in 72hrs of exposure				 Antivirals w/ max benefit if started w/in 24brs of symptoms
UI EXPOSUIE				 VZIG w/ max benefit if started w/in
				72-96hrs of exposure
				 Vaccine w/ max benefit if started w/in 72-120hrs of exposure
N	\anu	al		

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