Divine Intervention Episode 218
Q&A Comprehensive Microbiology
Review 3 (Viruses)

Divine-Favour Anene
Viral Basics

-Viruses can be classified in multiple ways-some as DNA and some as RNA Viruses.

-They could also be classified as being double or single stranded viruses.

-The +ve sense viruses have the ability to infect the host cell as they are essentially mRNA (this is really important!). The -ve sense RNA viruses require an RNA dependent RNA Polymerase to make the + strand that can infect the cell.

-All RNA viruses are single stranded (except Rotavirus that is double stranded).

-All DNA viruses are double stranded (except Parvovirus B19-transmitted via respiratory aerosols).

-All GI/arthropod borne viruses are +ve sense RNA viruses.

-Icosahedral viruses may be naked (no capsule). All helical viruses are encapsulated.
Viral Basics contd.

- There are a few enveloped viruses that utilize the strategy of simply moving from 1 cell to the other through fusion proteins to avoid immune system detection. This is the potential mechanism behind certain viruses leading to the formation of multinucleated giant cells which is actually helpful in detection (e.g. Herpes).

- Non-enveloped viruses are often sturdier than enveloped viruses and hence are often transmitted through the fecal oral route (e.g. Hep A and E).
Viral Hooks for The Boards

- All DNA viruses are double stranded except Parvo B19.

- All RNA Viruses are single stranded except Rotavirus.

- Any DNA virus ending with the letter A has a circular genome. The others have linear genomes.

- The only DNA Virus that replicates in the cytoplasm is the Poxvirus (carries its own DNA Dependent RNA Polymerase).

- All DNA viruses are enveloped with the key exceptions being Parvovirus, Adenovirus, and Papovaviruses (Polyoma and Papillomaviruses).

- Most DNA viruses get their envelope from the plasma membrane with the exception of Herpes (gets its envelope from the nucleus) and Hep B (gets its envelope from the endoplasmic reticulum).
RNA Viruses - Introduction

RNA Virus (icosahedral)

- Enveloped
  - SS + non-segmented
    - Picornaviruses
      - Enteroviruses
        - Poliovirus
      - Rhinoviruses
    - Caliciviruses
      - Norwalk Virus
  - DS segmenter
    - Rotaviruses

- Non-Enveloped
  - SS + non-segmented
    - Togaviruses
      - Alpha Vims
      - Rubivirus
    - Flaviviruses
      - Hepatitis C
    - Lenti virus
      - HTLV-1
      - HTLV-2
RNA Viruses

Capsid → Icosahedral

Enveloped

SS-Non-segmented

Non-Enveloped

SS-+ Diploid

Hepatitis C

Blood transmission

Hepatocellular Carcinoma

Enzyme

Flaviviruses

West Nile V.

Aedes mosquito

Yellow Fever

"Break back fever"

Ross River virus

"DS segmented"

Hep E (- Hepaviridae)

Reovirus (Core virus)

Reoviridae → Rotavirus

Non-segmented

Norwalk

"Cruise Ship Gastroenteritis", close quarters

"Really bad in pregnant women"

Entero viruses

Ventral horn destruction (Paralysis)

Fecal-Oral transmission; Sabin (live), oral V

Salk (Killed Inoculable V)

Shortest Hep incubation time

Asymptomatic, Killed vaccine available

- 3 day rash
- Polyarthritis
- "3 day rash"

"Horses"

"Horses"

"Horses"

Enteroviruses

Meningits

Hand, foot, mouth disease

AIDS

Most common cause of viral myocarditis

Virus damages the heart

Most common cause of viral gastroenteritis in kids

Genomic reassortment

Colorado Tick Fever
HY Factoids on the RNA Viruses

- Coronavirus is a SS +ve sense RNA virus that causes SARS.

- The Mumps virus is a common cause of Orchitis and Parotitis (and could also cause meningitis-LY).

- The Measles virus has the constellation of symptoms including cough, coryza (annoying medical term for runny nose), conjunctivitis, and a rash. There’s also Koplik spots on the buccal mucosa. It can reactivate later in life and cause the highly fatal Subacute Sclerosing Panencephalitis (SSPE). Vit A helps.

- The Rabies Virus (which belongs to the Rhabdovirus family) is contracted through exposure to animals like bats, raccoons, and wild dogs. It has a super long incubation period and ascends via motor neurons to the CNS. Is treated with the administration of IVIG (for immediate immunity) with subsequent killed vaccine immunization (for active, long term immunity). Once Rabies hits the CNS, it is typically 100% fatal.

- All RNA Viruses replicate in the cytoplasm with the exception of the Retroviruses and the Influenza Virus.
RNA Viruses-The Influenza Virus

-The Influenza virus causes the flu (NOT Haemophilus Influenzae).

-It is highly segmented and REASSORTMENT of viral segments with segments of other animal viruses leads to an antigenic SHIFT (which is more severe and causes pandemics).

-Point mutations in the genes coding for Hemagglutinin and Neuraminidase leads to an antigenic DRIFT (which is less severe and causes epidemics).

-Hemagglutinin is the molecule that enables the attachment of the influenza virus to the host and permits entry. This is what is targeted by the Influenza Vaccine.

-Neuraminidase is the enzyme that cleaves viral particles (from sialic acid) and allows the virus to leave the cell and infect others. This is the target of the drugs Zanamivir and Oseltamivir.
RNA Viruses-The Parainfluenza Virus/RSV Virus

- Belongs to the group known as the Paramyxoviruses.

- Causes Laryngotracheobronchitis (also known as CROUP).

- If you see the words “seal like barking cough” on your exam, stop thinking and pick Parainfluenza/Paramyxovirus (if they want to make it more difficult). They’ll have stridor. It’s a “subglottic” problem.

- The RSV (Respiratory Syncytial Virus) is the most common cause of Bronchiolitis in infants. If you see an exam question talking about viral Pneumonia in an infant, pick RSV. They’ll have interstitial infiltrates and typically present with wheezing.
Common Exam Mistake—Rubella vs. Rubeola vs. Roseola

- The Rubella virus is a member of the Togavirus family and causes “German Measles” (also known as the “3 day measles”).

- The Rubeola Virus is the cause of “Regular Measles” (rash that starts on the head and then moves to the toes).

- The Roseola Virus refers to HHV-6 (Human Herpesvirus 6) which causes fever and a subsequent rash in infants.

- Please do not mix these up on an exam!
HY DNA Virus Factoids

- Adenovirus is commonly implicated as the offending organism in infantile cases of conjunctivitis and hemorrhagic cystitis (classic Q stem involving a child at a daycare who has red urine).

- The Poxvirus causes Smallpox (a little obvious but just making sure). Replicates in the cytosol.
HY DNA Viruses-Parvovirus B19

- Is a single stranded DNA Virus that causes 5th Disease.

- The classic clinical presentation is a child with a “slapped cheek appearance” in the setting of a rash and arthralgias (joint pains). The “buzzword” here is Erythema Infectiosum. Can also affect elementary school teachers. They classically have migratory joint pain.

- Parvo B19 has a predilection for Erythroid Stem Cells in bone marrow and hence causes a pure red cell aplasia. Other non-RBC lines are intact!

- The method of transmission is via respiratory inoculation.

- In normal hosts, the “transient aplastic crisis” from Parvo B19 is tolerable. In patients with Sickle Cell Disease/Thalassemia, the aplastic crisis from Parvo B19 could be fatal.

- The contraction of Parvo B19 infection in utero is associated with Hydrops Fetalis (more on the next slide).
Clinical Correlate-The Mechanism Behind Hydrops Fetalis

-Anemia secondary to Parvo B19 infection of erythroid precursors leads to tissue hypoxia.

-Tissue hypoxia places a larger demand on the fragile heart of the fetus (heart does its best to pump more blood).

-As time goes on, the pumping ability of the heart is compromised.

-When the heart gives up, all proximal organs begin to accumulate fluid (hydrops).

-Since this phenomenon occurs in utero, it is called “Hydrops Fetalis”.

-Good example of high output heart failure.
HY DNA Viruses-HPV

- Is a DNA Virus that causes most of the cervical cancer cases in women.

- There are low and high risk HPV’s.

- The low risk ones include HPV 6 and 11 which cause genital warts (also known as Condyloma Acuminata—please do not confuse with Condyloma Lata that is found in what stage of what disease?). HPV 1 and 6 cause plantar warts.
HY DNA Viruses-HPV

-The high risk HPV’s include HPV 16 and 18 which cause Cervical Cancer. The proteins implicated in this process are E6 (which inhibits p53) and E7 (which inhibits Rb).

-Rb and p53 are involved in the transition from the G1-S phase.

-In the presence of E6/E7 there is unchecked continuation through the cell cycle even in the presence of DNA damage with an increased risk of malignancy. E6 is a ubiquitin ligase!
HY DNA/RNA Viruses-The Hepatitis Virus (only DNA Virus is Hep B)

- Hep A (Picornavirus) is associated with fecal oral transmission but does not progress to chronic hepatitis.

- Hep B (Hepadnavirus-A DNA virus) is transmitted via sexual contact/IVDU. It can become chronic and presents an increased risk of hepatocellular carcinoma. It is vaccine preventable. Highest risk of chronicity is contraction by a fetus in utero. If at risk, give Hep B vaccine/IgG at delivery (mom/baby).

- Hep C (Flavivirus) is transmitted sexually and most commonly via IVDU/blood transfusions. It presents the highest risk of progression to a chronic infection (can also progress to Hepatocellular Carcinoma) and is treated with super expensive drugs like Sofosbuvir (about 80k dollars).
HY DNA/RNA Viruses-The Hepatitis Virus (only DNA Virus is Hep B)

-Hep D is dependent on Hep B for infectivity (super HY!)

-Hep E is transmitted via the fecal-oral route and is associated with high mortality in pregnant women.

-A/E are the first/last letters of the Hepatitis alphabet so translate that to mean fecal-oral transmission (i.e. the first and last orifices of your body).
HY DNA Virus-Human Herpes Viruses 1

-HHV1 (or HSV 1) is typically associated with Herpes Labialis which is oral. It could be associated with genital herpes as well.

-HHV2 (or HSV 2) is typically associated with Genital Herpes but could also be associated with oral herpes.

-HHV3 or (VZV) is associated with chickenpox for the primary childhood infection and shingles for the reactivation later in life. A Super, Super HY Buzzword here is the presence of “pain and vesicles in a dermatomal distribution”.
-HHV4 (EBV) is associated with Infectious Mononucleosis. HY history here is a sexually active teenager with cervical lymphadenopathy and splenomegaly. The virus infects/remains latent in B cells. EBV causes a Monospot +ve mononucleosis syndrome. For Step 1, there’s atypical T cells (Downey cells, CD8+) on blood smear. CD21 is the “entry” receptor.

-HHV5 (CMV) is typically spread via renal transplantation or blood transfusions. The clinical presentation in an infant with disease is the presence of an enlarged liver (hepatomegaly) and a “blueberry muffin” rash (with periventricular intracranial calcifications). CMV can also cause Colitis and Retinitis in HIV/Immunocompromised patients. The virus remains latent in mononuclear cells. CMV causes a Monospot -ve mononucleosis syndrome.
HY DNA Virus-Human Herpes Viruses 3

- HHV6 (Roseola) is associated with a high fever followed days later by a rash (in an infant). This sequence of events is almost pathognomonic for Roseola (also known as 6th disease).

- HHV8 is associated with Kaposi’s Sarcoma in AIDS patients (classically described as violaceous nodules on the skin).

- Most viruses get their envelopes from the CELL MEMBRANE, not so for Herpes (nuclear membrane).
Viral Disease Presentation Triggers

- Rash with slapped cheek appearance
- Cough, Coryza, Conjunctivitis (3C’s) + Koplik Spots
- Descending maculopapular rash
- Gastroenteritis + Eventual Paralysis
- Cervical Cancer in the Sexually Active
- Parotitis, Orchitis, Male Sterility
- Cataracts/Blindness in a Newborn
- Painful skin lesions in a dermatomal pattern
- Virus remains dormant in Dorsal Root Ganglion
- Retinitis in an AIDS patient
- Genital Warts
- Painful vesicles on the genitals
- Hepatitis in a Pregnant Woman with high mortality
- Gastroenteritis on a cruise ship
- Fatigue + Splenomegaly + Atypical Lymphocytes on Blood Smear in a young person
- Childhood Gastroenteritis
- 2 common causes of the Common Cold
- Bronchiolitis in an infant
- Segmented Genome + Epidemic Shift Pneumonia
- Animal Bite + Fatal Encephalitis
- Encephalitis in a Neonate
Viral Disease Presentation Triggers-Key

Rash with slapped cheek appearance-Parvovirus B19
Cough, Coryza, Conjunctivitis (3C’s) + Koplik Spots-Measles (Rubeola)
Descending maculopapular rash-Measles (Rubeola)
Gastroenteritis + Eventual Paralysis-Poliovirus (an Enterovirus)
Cervical Cancer in the Sexually Active-HPV 16 and 18
Parotitis, Orchitis, Male Sterility-Mumps Virus
Cataracts/Blindness in a Newborn-Rubella (also cardiac problems like PDA, together called the congenital rubella syndrome).
Painful skin lesions in a dermatomal pattern-Varicella Zoster Virus (HHV3)
Virus remains dormant in Dorsal Root Ganglion-Varicella Zoster Virus (HHV3)
Retinitis in an AIDS patient-Cytomegalovirus (CMV)
Genital Warts-HPV 6 and 11 (read your exam Q’s carefully, DO NOT PICK 16/18)
Painful vesicles on the genitals (HSV2, occasionally HSV1)
Hepatitis in a Pregnant Woman with high mortality-Hepatitis E
Gastroenteritis on a cruise ship-Norovirus/Norwalk Virus
Fatigue + Splenomegaly + Atypical Lymphocytes on Blood Smear in a young person-EBV
Childhood Gastroenteritis-Rotavirus (for Step 1, it is ultra HY to know that this is involved in reassortment)
2 common causes of the Common Cold-Coronavirus and Rhinovirus (Rhinovirus is the most common cause)
Bronchiolitis in an infant-Respiratory Syncytial Virus (RSV-prophylaxis is with Palivizumab)
Segmented Genome + Epidemic Shift Pneumonia-Influenza Virus
Animal Bite + Fatal Encephalitis-Rabies Virus (a Rhabdovirus)
Encephalitis in a Neonate (HSV-especially in the temporal lobes/bloody CSF)

As an aside, viruses that lack an envelope almost always have an icosahedral capsid. These viruses tend to survive really well in the environment since the icosahedral capsid is extra stable.
A 75 yo. man is being evaluated for a 3 day history of productive cough, fever, and chills. The medical student on service collects some of the patients’ rust colored phlegm for evaluation prior to beginning empiric treatment. PE reveals a febrile patient with a temperature of 103 degrees F and crackles in the right lower posterior lung field. Which of the following best explains a key virulence factor associated with the offending organism?

a. Makes a glycopeptide that allows attachment to the Upper Respiratory Tract
b. Crosslinks IgE on the surface of mast cells leading to nonspecific degranulation
c. Binds to the constant region of monomeric immunoglobulins
d. Cleaves a dimeric immunoglobulin
e. Inhibits protein synthesis by binding to the 60S ribosomal subunit
- The best answer here is D.

- The offending organism is S. Pneumoniae which has an IgA protease.

- The rust-colored sputum is pathognomonic for S. Pneumo (which is a catalase negative, alpha hemolytic, gram positive diplococcus that grows in chains).

- Not sure how HY this is but Salmon colored Sputum is associated with S. Aureus pneumonia.

- Treatment with Pneumonia caused by S. Pneumo is typically Penicillin but increasing resistance has tilted the balance towards Ceftriaxone (which belongs to what generation of Cephalosporins??)
Q HY Clinical Presentations-Triggers

Neonatal encephalitis from a mom that handles cats
Bloody diarrhea from undercooked chicken
Hyaluronic acid capsule with M protein
Ataxia and loss of sensation in a sexually active female
Encephalitis weeks after consuming undercooked pork
CT scan shows “ring enhancing” lesions in the brain of a HIV patient
Bloody diarrhea and hepatomegaly (liver abscess)
AFB staining in the stool sample of an AIDS patient
Sexually active male with arthritis and skin petechiae
Inflammation of the testicles/parotid gland
Sickle Cell patient with super low hemoglobin
Permanent flaccid paralysis in an unvaccinated child
Nuchal rigidity in a 2 week old child
Most common bacterial cause of STDs in the US
Most common cause of UTI’s in the US
Elevated liver enzymes in a pregnant woman that subsequently dies
Genetic property associated with a worldwide Influenza Epidemic/Pandemic
Viral Conjunctivitis
Black eschar in a diabetic
Viral Myocarditis
Flu Like Symptoms after visiting Hawaii
Neonatal encephalitis from a mom that handles cats-Toxoplasma Gondii
Bloody diarrhea from undercooked chicken-Campylobacter Jejuni
Hyaluronic acid capsule with M protein-Streptococcus Pyogenes
Ataxia and loss of sensation in a sexually active female-Tabes Dorsalis of Tertiary Syphilis
Encephalitis weeks after consuming undercooked pork-Taenia Solium (Neurocysticercosis)
CT scan shows “ring enhancing” lesions in the brain of a HIV patient-T. Gondii reactivation.
Bloody diarrhea and hepatomegaly (liver abscess)-Entamoeba Histolytica
AFB staining in the stool sample of an AIDS patient-Cryptosporidium Parvum
Sexually active male with arthritis and skin petechiae-Neisseria Gonorrhoeae
Inflammation of the testicles/parotid gland-Mumps Virus
Sickle Cell patient with super low hemoglobin-Parvovirus B19
Permanent flaccid paralysis in an unvaccinated child-Poliomyelitis (Polio-an Enterovirus)
Nuchal rigidity in a 2 week old child-Group B Strep (S. Agalactiae)
Most common bacterial cause of STDs in the US-Chlamydia Trachomatis (D-K Serovars)
Most common cause of UTIs in the US-Escherichia Coli
Elevated liver enzymes in a pregnant woman that subsequently dies-Hepatitis E
Genetic property associated with a worldwide Influenza Epidemic/Pandemic-A Segmented Genome.
Viral Conjunctivitis-Adenovirus
Black eschar in a diabetic-Pseudomonas Aeruginosa (Ecthyma Gangrenosum)
Viral Myocarditis-Coxsackie B Virus
Flu Like Symptoms after visiting Hawaii-Leptospirosis
Q HY Clinical Presentation Triggers

Cellulitis in a burn patient
Bull’s eye rash
Strawberry Tongue
Strawberry Cervix
Diarrhea after returning from Mexico and drinking water
Maculopapular rash a few weeks after returning from Spring Break
Fever, Nuchal Rigidity, Altered Mental Status
Meningitis in a college student
Next best step in the management of a patient with nuchal rigidity
Meningitis in an older individual (60’s)
Meningitis in an unimmunized infant
DOC in the treatment of N. Meningitidis
Meningitis in a neonate
Q HY Clinical Presentation Triggers-Key

Cellulitis in a burn patient-Pseudomonas Aeruginosa
Bull’s eye rash-Lyme Disease
Strawberry Tongue-Scarlet Fever (S.Pyogenes)
Strawberry Cervix-Trichomonas Vaginalis.
Diarrhea after returning from Mexico and drinking water-Enterotoxigenic E. Coli.
Maculopapular rash a few weeks after returning from Spring Break-Secondary Syphilis.
Fever, Nuchal Rigidity, Altered Mental Status-Meningitis
Meningitis in a college student-Neisseria Meningitidis
Next best step in the management of a patient with nuchal rigidity-Lumbar Puncture (although give **Ceftriaxone**/Vancomycin/maybe steroids empirically).
Meningitis in an older individual (60’s)-S. Pneumoniae
Meningitis in an unimmunized infant-N. Meningitidis OR H. Influenzae.
DOC in the treatment of N. Meningitidis-Ceftriaxone (3rd Gen Cephalosporin).
Meningitis in a neonate-Group B Strep or E. Coli.

As an aside, pay attention to “triads” that pop up in micro. They usually mention every part of the “triad” in an exam Q. 2 classic ones include the cough/conjunctivitis/coryza of measles (rubeola) AND the chorioretinitis, hydrocephalus, and intracranial calcifications that are characteristic of toxoplasmosis.

In the future, pay attention to “triads” that pop up in other systems (maybe keep a working list???). They are good pimp fodder.