

VIROLOGY REVIEW

- I. Viruses – General info.
 - A. Filterable agent
 - B. Non-living
 1. Considered energy parasites
 - C. Building a Virus
 1. Genome – **EITHER DNA OR RNA; NEVER BOTH** – Gives us the main division point for grouping the viruses for study
 2. Capsid - holds the genome
 - a. Without an envelope – “Naked”
 1. Icosahedral Structure – Conveys largest internal area with the most stable structure.
 2. VAP’s are on the capsid surface
 3. Capsids give the virus the ability to survive for long periods outside the body.
 - b. Envelopes come from the infected cell
 1. Most viruses don’t have information to make lipid bilayer, POX BEING THE EXCEPTION
 2. VAP’s are on the envelope surface. If you disrupt the membrane on enveloped viruses this effectively inactivates them as they will have no VAP’s on the capsid.
 - D. A simple Virus can encode as little material as the capsid protein only
 - E. More complex viruses encode more information
 1. Polymerase
 2. Integrase
 3. Nuclear Proteins – to help hold the genome together
 4. Immune Evasion Proteins
 5. Enveloped Viruses encode a Matrix Protein that provides a base for the envelope
 - a. Don’t have to memorize which viruses have a Matrix Protein unless it has been implicated in some major immunological function, identification purpose, etc.
 - II. The DNA Viruses – 6 total
 - A. Some generalities
 1. The more complex the virus the more likely it is to carry its own DNAPolymerase with it.
 - a. The more complex virus will not have to wait on the cell to replicate.
 - b. It will carry specific viral replication origins that the DNAP will use for more efficient replication.
 2. A virus that does not carry its own DNAP will perish if it infects a cell that is near the end of its life, whereas a cell that carries its own DNAP can still scavenge dNTP’s and then make more of itself before the cell dies.
 3. The more complex the virus the more likely it will be to have immune evasion proteins.
 4. If a virus infects an internal organ it gets there by one of three routes:
 - i. Viremia
 - ii. Lymphoreticular System
 - iii. Nerves
 - B. Naked Viruses – Parvo, Adeno, Papova
 1. Parvoviridae
 - a. Only one with **SINGLE-STRANDED DNA** – doesn’t matter which strand is packaged.
 - i. In order to replicate – must be made double-stranded first, therefore must go to the nucleus first.
 - b. Prefers to infect erythroid precursor cells – does not carry its own DNAP so it needs cells that are still replicating, can’t do “anything by itself”.
 - c. Spread by respiratory route, replicates in respiratory tree somewhat giving a “prodrome” event – flu-like symptoms, caused by **CYTOKINES** ; then disseminates via viremia to the bone marrow.
 - d. The virus lyses the infected cells, causing anemia, which will not bother a healthy pt. However, a pt. with Sickle Cell will develop **APLASTIC CRISIS**.

- e. This viral infection in children results in **ERYTHEMA INFECTIOSUM**, aka “**Slapped Cheeks Disease**” aka “**Fifth Disease**”. This is the result of a hypersensitive reaction involving immune complexes.
 - f. This viral infection in adults will cause **ARTHRITIS**.
 - g. This viral infection in pregnancy can cause **HYDROPS FETALIS**, the virus can infect any of the embryo’s cells since they are rapidly dividing.
2. Papovaviridae – the two genera that infect humans are the papilloma and polyoma
- a. Papilloma
 - i. Cellular infection can have two outcomes:
 - 1) Permissive cell – Wart formation
 - 2) Non-permissive cell – Papilloma has a circular genome which can integrate into host genome and possibly cause immortalization. Immortalized cells lose contact inhibition, and can grow in suspension(they no longer require affixation to a solid surface for growth)
 - ii. Has proteins that bind the growth repressor proteins p53 and RB, causing cellular proliferation. **E6 & E7**
 - iii. Causes genital, skin, & laryngeal warts. Usually not life threatening although may be removed for cosmetic reasons. The laryngeal warts can cause obstruction of the airway.
 - iv. The genital warts are caused by **serotypes 16 & 18**, which are responsible for causing **cervical cancer**; serotypes 6 & 11 are non-cancer causing.
 - b. Polyoma
 - i. BK and JC viruses, don’t routinely make us sick but we all probably have them.
 - ii. BK ends up in the kidneys and lies dormant until an immunocompromised state is encountered, then it can reactivate and cause UTI., Ex. in pregnancy.
 - iii. JC also lies dormant in kidney, but upon reactivation it goes viremic and ends up in the brain, causing **PROGRESSIVE MULTIFOCAL LEUKOENCEPHALOPATHY**, eventually causing death.
3. Adenoviridae
- h. Has a fibril sticking out that it uses as its VAP. The protein can cause damage to the cell that it infects.
 - ii. Has wide tropism – doesn’t require actively dividing cells
 - 1) respiratory
 - 2) GI – can be fatal for infants
 - 3) eyes
 - 4) kidney – rejection of transplants
 - 5) liver – fulminant hepatitis
 - iii. Carries proteins designated **E1A**(binds to RB) and **E1B**(binds to p53)
 - iv. Pharyngoconjunctival Fever
 - 1) Can get from swimming – withstands chlorine.
 - v. Serotypes **4 & 7**, cause **Acute Respiratory Disease** in military barracks. A vaccine is available.
- C. The enveloped viruses – Herpes, Hepadna, Pox
- 1. Herpes – 3 subfamilies
 - i. Generalities
 - 1) Enveloped icosahedral
 - 2) Unique replicatory cycle - Transcription organized in 3 stages
 - a) alpha stage – transcription of the proteins necessary to turn the host cell’s machinery to making virus particles
 - b) beta stage – replication of the virus genome
 - c) gamma stage – another round of transcription, this time of the structural proteins to make the capsid
 - 3) Replication in the nucleus, then translation using the cell’s machinery in the cytoplasm(She made a point that no viruses bring their own translation machinery with them).

- 4) The proteins made by an enveloped virus needs to be glycosylated, so they must enter the Golgi and ER to be processed.
 - 5) The Herpes viruses bud off from the nuclear membrane, so the newly glycosylated proteins are recycled from the ER back to the nucleus.
- ii. Alpha Family – HSV1, HSV2, VZV
- 1) Cause vesicular lesions – get into mucous membranes and skin
 - a) HSV1 – oral herpes; encephalitis
 - b) HSV2 – genital; meningitis
 - c) VZV – chicken-pox 1st, then shingles as an adult. Spread via respiratory route, most contagious, has a vaccine.
 - 2) Remain latent in NEURONS
 - 3) Reactivated by stress, immunosuppression, UV light, trauma, etc.
- ii. Beta Family – HHV6, HHV7, CMV
- 1) Have tropism for T cells, Macrophages, Pharyngeal cells(CMV)
 - 2) Remain latent in Monocytes & Lymphocytes – circulating in body
 - 3) Usually do not cause much disease, the exception being CMV reactivation in infants - causing congenital defects. Cause other problems in AIDS pts. CMV can also cause **HETEROPHILE NEGATIVE MONONUCLEOSIS**
 - 4) HHV6 associated with **ROSEOLA** in children
- iii. Gamma Viruses – EBV, HHV8
- 1) Tropism for B cells, Oral Pharyngeal cells(EBV)
 - 2) Latent in B cells
 - 3) Associated with **BURKITT'S LYMPHOMAS, KAPOSI'S SARCOMA, NASOPHARYNGEAL CARCINOMA.**
 - 4) EBV in children is usually subclinical, in young adults causes **HETEROPHILE POSITIVE MONONUCLEOSIS** – swollen glands, pharyngitis, and **REACTIVE LYMPHOCYTES**(Tcells) found in blood.
 - 5) Vaccines against either of these viruses is not feasible. A live attenuated virus could easily revert. A killed virus would only give humoral immunity, which would be useless against virus-infected cells. Wouldn't want to put a piece of the genome in a vector either due to integration into the host genome.
 - 6) EBV makes an antigen called Membrane Antigen, which is being studied as a possible way to induce antibodies that might be able recognize an infected cell.

This ends the first hour.

December 2, 1999
Farukhi/Sebesta
4:00pm Micro Review
Hudec
Saved as: Panic.doc
Jay's Random Mac Disk
Hamood

Damsels in Distress:

Hannibal: Jay

B.A.: Spencer Su
Murdock: Dr. Colmer-

Virology Review II

A Conflict of Interest Production

I. Pox Virus

A. Specs

1. Big Size (almost visible under a light microscope)
2. Replicates in Cytoplasm, doesn't need its own ribosomes
3. Has own DNAP, RNAP
4. So complex it even has a second membrane
5. Almost bacterium except it doesn't have both RNA and DNA

B. Diseases

1. Variola (Small Pox) - got rid of by vaccination
2. Molluscum contagiosum - human virus
 - a. Warts - not fatal
3. Animal Pox
 - a. Can transmit to human handlers

C. Dx

1. Nodule where viruses produced (Guarnieri bodies) - makes huge pink blob in virus

D. Vaccine

1. Original vaccine for small pox has bad complications
2. Vaccina - Recombined Virus
 - a. Combination of Small Pox and Cow Pox (synthetic, not natural)
 - b. Use as Vaccine Vector still debated
 - c. Complications if not strongly attenuated, if attenuated too much, might not work
3. No vaccines for other poxes, they don't cause enough problems to merit a vaccine

13 Different RNA Viruses

II. + Sense RNA Viruses

A. mRNA goes to cytoplasm

1. Needs viral polymerase b/c eukariotic cells do not replicate RNA
2. Polymerase not needed initially
3. Immediate translation
4. 1st thing translated is RNAP - need device to replicate RNA
5. +/- Double Stranded (ds) intermediate produced next
 - a. Generates Antiviral State
6. Now virus must replicate genome back to + RNA
7. Produces lots of viruses in the cell very rapidly

C. Naked Viruses

1. Specs.

- a. Do not require as many types of proteins
- b. Fecal- Oral Spread except Rhinovirus (cannot withstand stomach pH)
 - i. teach children to wash hands
 - ii. use clean, treated water
 - iii. sewage breaks causes large outbreaks of Picornavirus
 - iv. Icosohedral capsid allows viruses to survive
- c. Cell translates mRNA into Polyprotein

- i. requires cleavage which requires protease
 - d. Once cleaved, have all necessary proteins and polymerase to continue replication
 - e. Lytic virus tend to have rapid aggressive infections that go fast and resolve
 - f. Starts in G.I. tract and respiratory, travels to lymph nodes to replicate, then spreads to blood
 - back to G.I. tract and respiratory tree
 - i. come back to eyes, skin, CNS, etc.
- 2. Picornaviridae
 - a. Rhinovirus
 - i. cause cold
 - ii. temperature sensitive
 - don't like to replicate at 37 degrees
 - iii. mutations
 - obtain ability to survive in body
 - cause more serious infections
 - very uncommon
 - iv. 113 types
 - v. bad for kids and babies
 - as age, can better withstand because stronger immune system
 - b. Enterovirus
 - i. Poliovirus
 - Poliomyelitis (disease name)
 - can cause Paralysis and death
 - most serious form was Bulbar
 - didn't happen very often
 - infection went to brain leading to withered limb and disability
 - Post Polio Syndrome
 - people over 50 who already had polio getting it again
 - probably immune system attacking cells from a long time ago
 - wild type polio gone in the US but rampant in the rest of the world (God Bless America)
 - may show up in patients who travel
 - 3 Polio Vaccines (according to her, but only 2 types listed in the notes)
 - oral, injectible versions
 - know advantages and disadvantages of each
 - ii. Coxsackievirus A
 - Herpangia - bright red throats
 - mostly stays in throat
 - hand, foot, and mouth disease
 - vesicles and rashes
 - occasionally cause meningitis but not often
 - iii. Coxsackievirus B
 - Myocarditis
 - Pleurodynia - can't breathe because muscles sore
 - causes muscles to be swollen and "itissed" (Cz note: Ph.D. word for swollen)
 - iv. Echovirus
 - pretty innocuous
 - Meningitis
 - v. Enterovirus
 - vi. All Enterovirus often occur in summer, only when Temperature above 100 degrees
 - 3. Caliciviridae and Astroviridae
 - a. Cause Gastroenteritis that lasts 24 to 60 hours
 - b. Not major cause of Gastroenteritis (that would be rotavirus)
- III. Reoviridae
 - A. Specs.
 - 1. +/- **dsRNA**
 - 2. **Double capsid**
 - 3. Must be tripson digested - not infectious if digested by cell

4. Has RNAP and everything it needs to make proteins
5. RNA genome always stays in capsid to be transcribed, only mRNA leaves capsid
6. Replication of genome make many + and - strands which accumulate leading to big aggregates of parts that assemble into viruses
7. **Segmented** genome - each piece is a gene
8. Virus must go through **golgi apparatus** - unique

B. Rotavirus

1. Receives glycoproteins when envelope is added and then removed, leaving only the glycoproteins
 - a. Glycoproteins serve as anchors
 - b. Glycoproteins develop antibodies
2. Causes
 - a. Gastroenteritis
 - b. Diarrhea - lasts a week
 - c. Fever
 - d. Vomiting
 - e. Often leads to dehydration - especially in malnourished children
3. Vaccine unavailable
 - a. Original vaccine caused problems - intestinal obstructions led to dead children (bad)
 - b. Need vaccine to protect people around the world

C. Coltivirus (Colorado Tick Fever Virus)

1. Spread by ticks, hence the name
2. Travels in blood cells,
 - a. Unlike Parvovirus no lysis or anemia
 - b. Virus lasts in blood stream until blood cells die (RBC last 21 days)
3. Can be spread by transfusion
4. Long Viremia - months
5. No rash - "Spotless Fever"
6. Primarily in Pacific northwest and Rocky mountains
7. Rocky mountain spotted fever actually in southeast and not Rocky mountains (Cz: bright naming

job)

IV. Hepatitis A, B, C, D

- Skipped because "big globby viruses"
- Cause Hepatitis (gee, thanks)

V. -ssRNA

A. Specs

1. **Always enveloped**

B. Segmented

1. Orthomyxoviridae
 - a. Influenza A, B, and C
 - b. A and B affect people
 - c. A has shift which allows it to live
 - i. drift - point mutation change structure of 3 Hemagglutinin (HA) and 2 Neuraminidase (NA)
 - ii. shift - get new virus
 - segments produced separately and then combined
 - many different combinations
 - many are defective viruses which interfere with virus reducing severity of infection
 - thought to occur when human virus infiltrates animal and mixes with animal virus
 - virus gets back into human as new virus
 - not every animal virus HA or NA can function in human
 - chicken H7 virus did not run rampant in China because could not attach
 - c. In general an epidemic requires susceptible population, occur every 10 -30 years
 - d. All - sense RNA need their own RNAP - stuck on genome
 - d. Replicates in nucleus
 - e. ds intermediate - antiviral state - especially in (-)sense viruses
 - i. non-specific innate immune defense elicited to fight virus
 - ii. alpha and beta interferon chew up RNA and stop protein synthesis

- iii. cell becomes target for NK cell because not producing self proteins
- iv. increased response of immune system cause "flu" symptoms in prodrome state

C. Single

1. Paramyxoviridae

a. Mumps

- i. **Viremic**
- ii. Parotid Glands - do not need to get both sides to be immune
- iii. Orchitis, sterility
- iv. vaccine

b. Parainfluenza virus

- i. **Respiratory**
- ii. Croup - "seal bark cough"
- iii. no vaccine
- iv. can cause death

c. Morbillivirus (think morbid)

- i. **Viremic**
- ii. Measles
 - Rash (final stage) - immune mediated phenomenon
 - Prodrome: cough, coryza (really runny nose), photophobia, conjunctivitis (3C's + P)
 - Encephalitis - kills
 - Pneumonia - kills
 - Subacute sclerosing panencephalitis - very rare
 - Death

iii. vaccine

d. Pneumovirus

- i. **Respiratory**
- ii. Respiratory Syncytial Virus
 - Bronchiolitis - swelling and inflammation of bronchial tree
 - can lead to incr. in heart rate
 - can kill babies, but adults can with stand it b/c they are bigger with bigger lungs
- iii. no vaccine

VI. Arboviruses (+ssRNA)

A. Flaviviridae

- 1. Humans can be reservoirs
- 2. Encephalitis
 - a. St. Louis
 - b. West Nile
 - c. Powassan
 - d. Carried by mosquitoes - urban cycle between mosquitoes and humans
- 3. Hemorrhagic Fever
 - a. Yellow Fever
 - b. Dengue - Often occurs in Lubbock (Cz note: yet another reason to get out of this crazy town)
- 4. Hepatitis C and G are not Arboviruses, rest of Flaviviruses are

B. Togaviridae

- 1. **Humans cannot be reservoirs** - only in mosquitoes
- 2. Encephalitis
 - a. Eastern Equine
 - b. Western Equine
 - c. Venezuelan Equine
 - d. Enzootic (endemic disease) in live animals - only transferred to humans who work with animals
 - e. Epizootic - more animals get it, animals die - more transmission to humans (Zoonosis)
- 3. Rubivirus (not Arbovirus)
 - a. Rubella
 - i. cause bad birth defects in pregnant mothers (heart defects, organomegaly, cataracts, etc.)
 - ii. vaccine (must be live) - don't give to pregnant women, give after or before pregnancy
 - iii. can cause serious defect in any cell type in baby

D. Bunyaviridae

1. Encephalitis
 - a. California Encephalitis (LaCrosse)
2. Hemorrhagic fever
 - a. Hemolytic Uremic Syndrome
 - b. Hanta virus
 - i. Sin Nombre - transmitted by deer mice
 - ii. Convict Creek - in Colorado (Cz: name that really brings in the tourists each year)
 - iii. Black Canal virus? - cotton rats in Florida
3. Unusual vector reservoir cycle
 - a. **Transmit Vertically** - mosquitoes pass it to their eggs
 - i. allows virus to survive harsh climate like Russian winters
 - b. Vectors specific

VII. Rabies

(She said she covered this enough in class, so she wanted to skip it.....but we didn't, #!@* gunners)

- A. Transmitted **mostly by bats** now as opposed to domestic and wild animals
 1. Vaccinate dogs (reservoirs for rabies worldwide)
 2. Round up strays (in hick towns they get together in a posse and shoot em' for fun on Friday nights)
 3. Know when bitten/chased by anything but bats - so go get vaccinated
 - a. Bat bites don't hurt (she knows from her nature center days)
 - b. Dog bites do hurt
- B. Once you get symptoms its too late and you die
- C. Can prevent rabies by immunizing because incubation period is so long
- D. Rabies gets to brain by retrograde transport up the neuron to the brain and then out and down

(ascending and descending infection).

VIII. Retrovirus

A. She didn't want to cover this today because she was "exhausted" (as I am now). She offered a review for anytime next week just on retroviruses..... Of course by the time you read this, it'll probably be the night before the test, so it really doesn't matter does it.

To relieve tension, here are questions that would be on the test if your friendly neighborhood scribe czar wrote it.

1. Pox Virus has been known to cause
should
 - A. AIDS
 - B. Strep Throat
 - C. Small Pox
 - D. Colorado Spotted Leopard Fever
2. Patient presents with rabies symptoms, you
 - A. Give them a vaccine
 - B. Treat them with antibiotics
 - C. Refer them to a veterinarian
 - D. Make sure their bill is paid in full
3. M. Tuberculosis causes:
 - A. Tuberculosis
 - B. Shingles
 - C. Boredom
 - D. Antidisestablishmentarianism
4. Who's the black private (eye) that's a sex machine with all the chics?
 - A. Sam Spade
 - B. Shaft!!
 - C. Matt Stringer
 - D. Ravi
5. A Grandmother with Shingles would give what to her 8 year old grandson?
 - A. Varicella (Chicken Pox)
 - B. Shingles
 - C. A roof
 - D. Procrastinationitis
6. Hepatitis A, B, C, D
 - A. Cause Hepatitis
 - B. Are big globby viruses
 - C. Are fun for the whole family
 - D. Any two of the above

Answer Key: 1:C, 2:D, 3:A, 4:B (can you dig it?), 5:A, 6:D