This virus review is written to help you keep track of the viruses and their most relevant facts. If there is a question in lecture, know the answer. If you want to get some free points on the exam, read Murray’s question book.

What you will find is a tree of different types of viruses. You should memorize the tree in the order it is presented. The tables that follow organize the content by structure. You will notice similar structures are lumped together. It helped me a lot to think of the viruses this way. If it doesn’t help you, reorganize as you see fit.

What follows is a small paragraph/blurb about each one. I pretty much memorized those paragraphs for each one, and regurgitated it here for you. It’s mostly Lange review cards spotted with details from lecture and Kaplan. You must know the details of the organisms in ridiculous detail, as shown in lecture, but this can get you by for the questions they don’t already give you.

![DNA viruses]

<table>
<thead>
<tr>
<th>Family</th>
<th>“NA”</th>
<th>Linear</th>
<th>Segmented</th>
<th>Shape</th>
<th>Envelope</th>
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<td>Icosahedral</td>
<td>Yes</td>
<td>Nucleus</td>
</tr>
</tbody>
</table>

**B19.** B19 is a parovirus and is a single stranded, linear, nonenveloped icosahedral DNA virus. It is implicated in **slap-cheek disease** which results in a high fever that breaks, followed by a bilateral red rash on a child’s cheeks, looking like it was slapped. It is ingested **fecal-oral** and then spreads via viremia to the **bone marrow** where it infects erythropoietic stem cells. This may result in **aplastic anemia** in a patient with hemolytic anemia, or the fatal condition in pregnant mothers called **hydrops fetalis.**

**JC Virus.** JC virus is the human polyomavirus and is a double stranded, circular, nonenveloped, icosahedral DNA virus. It is transmitted via respiratory droplets. JCV is acquired in respiratory droplets and spreads via viremia to multiple organs. When immunocompromised, it makes an opportunistic infection on the **oligodendrocytes** of the brain, leading to **demyelination.** This starts off with diplopia (blurry vision) and dysphonia (trouble speaking). Within 6 months the patient is dead of respiratory failure. It is an AIDS defining illness.
**HPV.** Human papilloma virus is a **double stranded, circular, nonenveloped, icosahedral DNA virus.** It is responsible for warts. Different serotypes cause different symptoms. 1, 2, and 4 cause plantar warts. 6 and 11 are the most common STD genital warts. 16 and 18 are the highest risk for cancer. There is a vaccine (Gardisil) against 16 and 18. There is no treatment for warts other than to burn, freeze, or cut them off. It targets the **basal epithelial cells** and gains entry through cracks, tears, or abrasions in mucosal surfaces. It is detected with a **pap smear.** Hybrid Capture II methods are much more sensitive (not Board Relevant). Protein E7 binds to **retinoblastoma** (Rb) while E6 inhibits p53 leading to tumorigenesis.

**Adenovirus.** Adenovirus is a **double stranded, linear nonenveloped icosahedral DNA virus.** It is implicated in conjunctivitis and pharyngitis (sore throats) without purulent discharge and with negative strep results. Adenoviruses are **rarely fatal** except in some isolated cases in army barracks. There are many serotypes; **acute gastroenteritis** is 40 and 41, **pharyngitis/pharyngoconjunctival fever** is 3 and 7, with **hemorrhagic cystitis** caused by 11. **Adenovirus 5** has been used to develop vaccines and attempted in **gene replacement therapy.** It is transmitted either by the **respiratory route** or the **oral-to-fecal route.** It colonizes the epithelium of the upper respiratory and GI tracts, causing direct Cytotoxic damage, being cleared by cell mediated immunity with antibodies conferring immunity. There is no treatment and there is no vaccine.

**Herpes Virus Family.** There are a lot. They do a lot of the same things in similar ways. For example, they all carry a **viral DNA polymerase** so they can replicate even in the absence of host cell division. They carry a **thymidine kinase** that makes nucleosides into nucleotides for DNA synthesis. They all use **host DNA-Dependent-RNA-Polymerase** to make the RNA for their protein. They are EBV, CMV, HH6/7, HH8, and VZV.

**Epstein Barr Virus.** EBV causes **infectious mononucleosis** (“Mono” or the “kissing Disease”). This is categorized by fatigue, fever, lymphadenopathy, and splenomegaly. It is spread via **respiratory droplets** and **mucosal contact.** 80% of people entering college are already seropositive for mono. The virus gets into **B cells** and can immortalize them. It is transported to the lymph nodes and spleen, where it replicates, causing the swollen lymph and spleen. Sequella include **burkitt’s lymphoma** and **Hodgkins Disease.** It is detected in serum by the **Heterophile-Ag** and histologically by the **Downey Cells.** There is no treatment nor vaccine for EBV.

**Cytomegalovirus.** While not often associated with mono, it can cause **mono-like symptoms in immunocompetent patients.** It is commonly associated with being an **opportunistic infection** of immunocompromised patients, such as AIDS or organ transplants. It causes **retinitis, encephalitis, and colitis.** CMV can cross the **placenta** causing hepatosplenomegaly, jaundice, growth retardation and neurologic complications. CMV starts in the oropharynx, spreads to lymphatic tissue and produces a viremia that leads to multiple tissues. It does not have Heterophile-Ag nor Downey cells. It is classically diagnosed histologically as cell with an **enlarged cytoplasm with a perinuclear halo with an eosinophilic inclusion body** (so called “Owl’s-Eye”). There is no vaccine, but you can use nucleoside analogs to try to fix it.
**Varicella-Zoster.** This is the virus of *chickenpox* and *shingles*. The primary infection is chickenpox. The virus is spread through *respiratory droplets* and colonizes the upper respiratory epithelium. After a 2 week incubation period, the typical macular-papular rash breaks out over the entire body. These contain virus and are contagious. The later in life you get the disease, the worse the symptoms. Varicella-Zoster then *hides in the dorsal root ganglion* of the associated dermatome. When immunocompromised, it returns, with a *prodrome of pain* and a *syndrome of a rash that covers one dermatome*. It is called retrograde transport to the neuron, and anterograde back to the skin. There is no treatment, but there is a *live attenuated vaccine* to vaccinate children and at risk adults. Shingles is a secondary infection meaning there must have been the primary infection of chickenpox.

**Human Herpes Virus 6 & 7.** Not a lot to know about these two. They cause *Rosela*. Usually effects kids, spread by *respiratory droplets*. Coinfection with 7 may be required for AIDS. 90% of adults are seropositive. There is a *rash that starts distally and works its way proximally*. More severe forms can result in seizure. No vaccine, no treatment.

**Human Herpes Virus 8, aka Kaposi Sarcoma.** This virus is an AIDS-defining virus. It is a spindle-cell tumor of endothelial origin characterized by *bluish-black lesions on trunk, neck and face*. It infects B cells (much like EBV) and sets up a permanent infection. B cell cancers are possible. It also causes primary effusion lymphoma. This is usually towards the end of the disease and the patient’s life.

**Hep B.** There is a lot to know for this one & is massively board relevant. Hep B is a hepatitis virus that can cause acute, chronic or carrier states. It is spread through *bodily secretions (STD)*, or *injected drug use*. The virus spreads through viremia and targets only the hepatocytes. Most of Hep B cases resolve spontaneously with clearing of the virus associated with an acute hepatitis. Acute hepatitis is described as *jaundice, dark urine, clay colored stools, hyperbilirubinemia*. The virus does not do anything to the liver. It is your own immune response (cell mediated Cytotoxicity) clearing the virus that causes hepatocellular damage. *If you suffer severe acute hepatitis you are likely to clear the virus, if you suffer mild symptoms, you will have a chronic infection*. The strength of the immune response is dependent on the status of your T cell immunity. Very young children are screwed. 5 or older have a developed immune system to prevent it. You must use *serology to determine state*. The *dane particle* is the virion itself (a 42nm particle with the DNA, core protein [HBC], surface antigen [HBS], and the envelope). There is another secreted protein (HBe) that tricks the immune system and is 22nm. The body forms antibodies to all 3 antigens (HBCAg, HBSAg, HBeAg). If you have *IgM* anti-anything, you are in the *acute stage*. If you have Anti-HBC but HBSAg you are chronically infected. *Anti-HBs means immunity*. There is a period called the *HBsAg Window* where there amount of antibodies = the amount of antigen, and neither is detected. This lasts about 2 months and follows the acute phase. There is a *recombinant vaccine* that can be coadministered with Hep A vaccine. Anti-HBs Ig is given to neonates of infected mothers and accidental needlesticks for prophylaxis. *Interferon*, *lamivudine* and *adefovir* are given to reduce the risk of hepatocellular carcinoma, but there is no cure.
Flavivirus
Coronavirus
Calicivirus
Astrovirus

Polio
Coxsackie A and B
Echovirus
Rhinovirus
Hep A

norovirus

Family | “NA” | Linear | Segmented | Shape | Envelope | Site of Replication
--- | --- | --- | --- | --- | --- | ---
Picornovirus | ss+RNA | Linear | Non | Icosahedral | No | Cytoplasm
Calicivirus | ss+RNA | Linear | Non | Icosahedral | No | Cytoplasm
Astroviridae | ss+RNA | Linear | Non | Icosahedral | No | Cytoplasm
Togavirus | ss+RNA | Linear | Non | Icosahedral | Yes | Cytoplasm
Flavivirus | ss+RNA | Linear | Non | Icosahedral | Yes | Cytoplasm
Coronavirus | ss+RNA | Linear | Non | Icosahedral | Yes | Cytoplasm

**Polio.** Polio is mostly eradicated from the western world. It is spread by **fecal-oral route.** It invades the upper respiratory epithelium and the gastric mucosa. There it enters the blood stream via the lymph, spreading by viremia, with **preference for the CNS, motor neurons.** Invasion causes motor neuron death, resulting in a **flaccid paralysis with retention of sensation,** usually affecting the legs. Only a small fraction of people infected with polio will get flaccid paralysis; most get flu-like symptoms. Antibody mediated Cytotoxicity clears the virus, but the damage is permanent. There are **two vaccines.** The **Sabin Vaccine** is introduced orally, is a **live attenuated virus,** develops the strongest IgA and IgG immunity, but may result in flaccid paralysis. The **Salk vaccine** is injected, is a **killed vaccine,** require multiple doses, but achieves similar efficacy.

**Coxsackie A &B, Echovirus.** Coxsackie virus is similar to polio, only targeting the meninges instead of the motor neurons. It is transmitted **fecal-oral,** invading the upper respiratory epithelium and the gastric mucosa. It enters the blood via the lymph and spreads to the CNS via viremia. This causes a **meningitis like symptoms** with stiff neck, fever, headache and photophobia. There will be **no neutrophils but instead lymphocytes in the CSF.** Damage is caused by the virus itself. There is no vaccine and there is no cure. Coxsackie A is associated with **hand-foot-and-mouth disease** (blistering of soles, palms and mouth) while Coxsackie B is associated with Pericarditis and Myocarditis.

**Rhinovirus** causes the common cold. It is spread by **respiratory droplets** or **direct inoculation** by hands. It affects the nasal epithelium resulting in rhinitis, congestion, sneezing, headache and a minor pharyngitis. Rhinovirus binds to cells using **Intercellular Cell Adhesion molecule 1 (ICAM-1),** a big board point (as big as it can get for viruses). It is usually self-diagnosed, self-limiting, and has no vaccine nor cure, though growth at hot temperatures is difficult (so hot-chicken noodle soup actually works).
**Hep A.** Hepatitis A causes **only acute hepatitis.** It lasts about 3–4 weeks, causes dark urine, jaundice, clay-colored stools, elevated liver enzymes, etc. but has no real long term effects. Hepatic injury is by T cell mediated **Cytotoxicity** clearing the virus. There is no risk of carrier or chronic state, though **acute hepatic failure** has resulted. You get this **fecal-oral**. There is no treatment, but there is an **inactivated vaccine** and Hep A Immunoglobulins can be administered if caught at exposure.

**Norovirus.** This calicivirus is also known as **Norwalk virus.** It is a **single stranded, non segmented, linear, non enveloped RNA virus** that has plagued the cruise line industry. If you see “cruise ship” in question stem, it’s probably calicivirus. It is a **self-limiting gastroenteritis** that results in watery diarrhea. It is transmitted by sick workers who continue to work; causes a “walking diarrhea” that ruins your vacation, may warrant fluid replacement, but is not fatal. You can identify it by running PCR in the stool. Any city that has a port of entry (like New Orleans) has the ability to do PCR to find Norwalk Virus.

**Equine Encephalitis.** This is a member of the **Togavirus Family** and as such is a **single stranded, enveloped, linear, icosahedral RNA virus.** It is stored in horses and transmitted by mosquitoes. Causes fever, headache, myalgia, coma and death. Eastern Equine Encephalitis (EEE) is the worst, then Western and Venezuelan. Even though this is a mosquito associated disease, it is NOT a Flavivirus (even though other Flaviviruses cause encephalitis). There is no vaccine, and no cure. There is a vaccine for horses.

**Rubella.** Rubella is the more important of the two relevant togaviruses. This causes a **mild infection in children and adults** identified as a **maculopapular rash, low-grade fever and lymphadenopathy.** This causes “German Measles” with the rash starting on the forehead, working its way down. Adults who get it can develop arthralgia. Most importantly it can **cross the placenta** and cause **congenital rubella syndrome** characterized by **cataracts, heart defects, deafness,** and **mental retardation.** There is a vaccine that is the **live attenuated vaccine** given with measles and mumps.

**Flavivirus Family.** These are the viruses that are transmitted by injection by a mosquito directly into the blood stream. The virus then spreads to a preferential site. Where it happens to go will dictate its symptoms. For example, Yellow fever goes to the liver, Dengue Fever goes to the vasculature, and St Louis Encephalitis (and associated West Nile and Japanese Encephalitis) go to the brain. Hep C doesn’t fit the bill, but is still a Flavivirus.

**Yellow Fever.** Endemic to Africa and South America, this is a severely fatal disease. Transmitted by **injection by mosquito,** it spreads through the blood to the liver, entering the Kupfer cells. Yellow Fever screws up your liver and turns you yellow, no big deal. However, it can cause **hemorrhagic fever** which causes jaundice, fever, headache, black vomit (from the bleeding) hemorphages and shock. The mortality is 50%. There is no treatment but there is a **great live attenuated vaccine**.

**Dengue Fever.** Endemic to everywhere tropical, this is seen in the United States when people come back on vacation. This is rarely fatal, has no treatment, and has no vaccine. This is characterized by **fever, headache, retro-ocular pain,** and **deep bone pain.** Antibodies and cell mediated immunity work to fight off the infection. It is caused by an injection by a mosquito and binds to macrophages in the vasculature. Controlling the vector (DEET spray) is a preventative measure.
**Bunyavirus**

**Arenavirus**

**Filovirus**

**St Louis Encephalitis.** This follows identical patterns to Japanese Encephalitis (in Japan) and West Nile Encephalitis (somewhere west of the Nile). The mosquito injects the virus which preferentially is taken up in the brain via capillary endothelial cells of the choroid plexus. It causes encephalitis with non-specific flu-like symptoms. It can cause fever, headache, malaise, myalgia, neck stiffness, and disorientation. (Boards = travel + bite + disorientation)

**Hep C.** Abundant in homosexual males, transmitted via blood (transfusions), injectable drugs (usually Hep B) and via sexual contact. Unlike Hep A (which is always acute) and Hep B (which is usually acute) Hep C will always establish a chronic infection. Hepatitis is caused by inflammation and cell mediated Cytotoxicity and viral clearance. Hepatocellular carcinoma is acquainted with this Hepatitis as well. Mutations are abundant creating variability in the major envelope protein leading to immune system escape. There is no vaccine. Treatment is similar to Hep B chronic treatment (interferon and ribavirin).

**Coronavirus.** Up until about 4 years ago this was “rhinovirus.” Now, since the SARS outbreak, we learn about it. We don’t know a lot about it, but what we do know is that it is highly associated with travel to China and Hong Kong. SARS can rapidly deteriorate to death or require mechanical ventilation. It gives you fever, headache, diarrhea, dry cough, then death.

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<th>Family</th>
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<th>Linear</th>
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**Measles.** The measles are highly infectious spread by respiratory droplets. There is a prodromal state of cough, coryza, and conjunctivitis. Following that, Koplik Spots (small white spots on the buccal mucosa) on the inside of the cheek, followed by a maculopapular rash starting behind the ears, working its way down onto trunks and extremities. A complication is subacute sclerosing panencephalitis, a rare, late, progressive neurological disease that occurs months to years after the measles. You never see it coming, until it does. There is a live, attenuated measles virus vaccine that is part of the MMR.
**Mumps.** There is a prodromal phase characterized by fever, malaise, headache followed by parotitis (the big “mumps” in the cheeks). Male adults can get orchitis (inflammation of the testis). There is a live attenuated mumps virus vaccine.

**Rabies.** Carried in animals (usually associated with bats, raccoons, skunks, and dogs) it is zoontic. It has a huge incubation period of 30-60 days, so repeated post-exposure vaccine is the only treatment. Once symptoms start, it’s too late, and rabies is fatal. The virus reproduced locally, at the site of bite/infection and climbs into the CNS via acetylcholine receptors. It replicated in the CNS, then descends to skin and salivary glands. You will find RNA in the saliva and urine. Fever, nausea, vomiting, hydrophobia and hallucinations are the clinical course. Rabies is confirmed on autopsy by the presence of Negri Bodies (eosinophilic inclusion granules in the cytoplasm) in neurons. You can get pre-exposure vaccines, but that is usually for high risk people like Vets. Bottom line: if you get bit, get a rabies shot.

**Filovirus (Ebola).** You don’t want this. Ebola is the star of the movie “outbreak” and is 90% fatal. Contamination occurs from direct contact of bodily fluids. It infects macrophages and spreads systemically via lymphatics. It results in dumping of cytokines all over the body resulting in the fatal hemorrhagic fever. This is way worse than Yellow or Dengue fever. There is no treatment, and there is no vaccine. Isolation is the only way to protect society; those infected are considered dead anyway. Marburg virus does the same thing.

**Influenza.** Orthomyxoviruses are unique in the –ssRNA in that they are the only relevant family that is segmented and linear. This virus has three types, A, B, and C. Influenza A is the worst, infecting multiple species, including humans, and has the most severe symptoms. Influenza B is limited to humans and causes not-as-severe-disease. Influenza C doesn’t really matter. Influenza is identified by the antigenic variation of envelope proteins H (hemagglutinin) and N (neuraminidase). H5N1 is the avian bird flu. Even though there are live attenuated vaccines, immunity doesn’t last long. This is because of antigenic drift (point mutations in antigens that change variability slightly) but more so from antigenic shift (reassortment of RNA gene segments between two influenza viruses). Many diseases are said to have “flu-like symptoms” which are fever, chills, prostration, myalgia, headache, nausea, and vomiting followed by respiratory symptoms including a dry cough. You can treat is with antivirals such as amantadine and rimantadine, or with neuraminidase inhibitors (zanamivir and oseltamivir).

**La Crosse/California Encephalitis.** These two Bunyaviruses are closely related. They are negative sense circular segmented RNA viruses with an envelope. They are spread by direct inoculation of the virus via mosquitoes, usually in the central Midwest. The encephalitis is characterized by fever, headache, malaise, nausea and vomiting. Seizures happens often (50%) and the history will be significant for camping in endemic areas. This disease can be fatal, but usually is not. Seizures may be a sequella of the disease. There is no vaccine and no cure. Children under the age of 16 are at severe risk.

**Hantavirus.** This Bunyavirus is also a negative sense circular segmented RNA virus with an envelope. It is spread by inhalation or inoculation of rodent excrement. This doesn’t mean eating rat feces, this means sweeping the barn where a mouse you didn’t even know was there happened to have been last week. It multiplies in the pulmonary capillary endothelial cells. X-ray will show bilateral infiltrates on a rapidly
deteriorating pulmonary system in a patient with fever, myalgia, headache, cough, N/V/D. There is no treatment and now vaccine. Mechanical Ventilation is common, mortality in healthy subjects is 50%. Nasty virus. It is also called Sin Nombre virus, because the Native Americans (yeah, apparently they speak Spanish) didn’t want the virus to be named after the sacred tribal lands it was originally named after. This is a board relevant point (just kidding).

Lassa Fever. This is an arenavirus which oddly has basically the same characteristics of bunyavirus. There are some details you can read in lecture, but aren’t high enough yield to matter. This is transmitted by a rodents in west Africa. The most common sequella is hearing loss. Treat it with ribavirin.