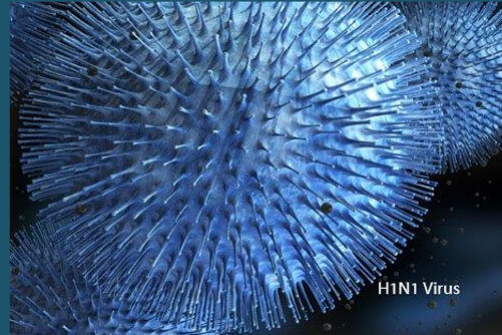
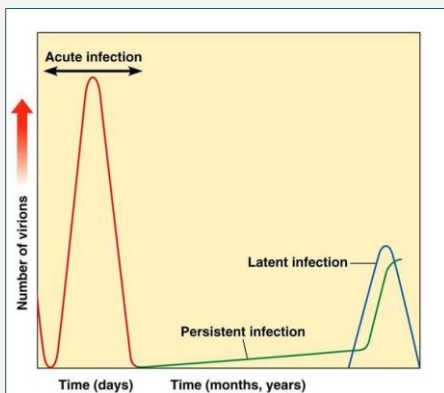


2020 VIRAL INFECTIONS AND CANCER RISK

FCDS Virtual Annual Conference
Steven Peace, CTR
August 27, 2020

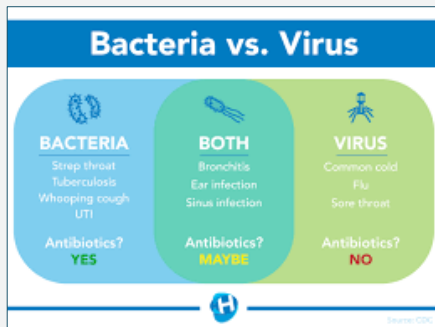


Presentation



- What is an Infection?
- What causes Infection?
- Can all Infections be Cured?
- Do you always know when you have an Infection?
- What Occurs Over Time When You Have Chronic Infection?
- Can Infections Increase Risk of Developing Cancer?
- Can Infections Actually Cause Cancer?
- Can You Prevent or Reduce Risk of Virus-Related Cancers?
- What Types of Infections are Related to Which Cancers?
- How Long Does It Take To Grow Virus-Related Cancer?
- Are Virus-Related Cancers Aggressive?
- Are Virus-Related Cancers Easy to Treat?
- Can Viruses Be Used to Treat Other Cancers?
- Questions?

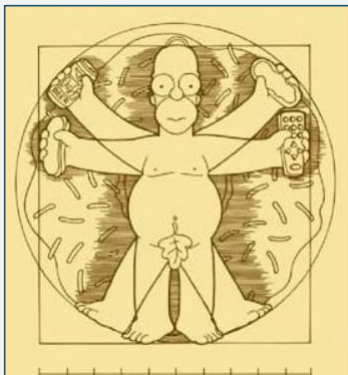
What is Infection



- An infection occurs when another organism enters your body and causes disease. The organisms that cause infections are very diverse and can include things like viruses, bacteria, fungi, and parasites.
 - Virus
 - Bacteria
 - Fungi
 - Parasites
- Infection occurs when viruses, bacteria, or other microbes enter your body and begin to multiply.
- Disease, which typically happens in a small proportion of infected people, occurs when the cells in your body are damaged as a result of infection, and signs and symptoms of an illness appear.
- Some infections are highly virulent and contagious and can be passed on to others and some will remain in the host for life slowly multiplying waiting for their chance.

What Causes Infection

What Spreads Infection



- Man is often the primary source for sharing infection with man
- Animals can spread some viruses, bacteria and fungi
- Biting Insects like mosquitoes, fleas, lice, ticks – malaria, plague
- Dirt – spores from other bacteria, etc.
- Viruses like Influenza, H1N1, HIV, HPV, COVID-19
- Bacteria like Helicobacteri Pylori, chlamydia,
- Parasites – blood flukes (schistosoma haematobium and two different species of Asian liver flukes
- Touching Infected Surfaces – or Infected Persons
 - Then Touching Yourself on Any Mucosal Surface
 - Mouth
 - Eyes
 - Nose
 - Open Wounds
- Found in Water – Washing, Drinking, Bathing
- Found in Food – Eating, Touching, Preparing and Sharing
- Contaminated Air – Sneezing, Coughing, Clearing Throat
- Contaminated Dirt – under fingernails, dirty hands

Other Infectious Agents

Approximately 20% of all cancers are associated with infectious agents, and at least 15% of all cancers are caused by oncoviruses.

We do not yet know what short or long-term effects the novel SARS-CoV2 Infection or the Coronavirus Diseases this virus causes in some patients will have on cancer or other health issues in the future.

We expect people will have heart, blood vessel, lung, kidney, brain and other related illnesses - but, do not yet know of what kind or duration or severity for recovered patients.

- Virus – ebola, influenza, zika, west nile virus, dengue
- Bacteria – cholera, typhoid fever, smallpox, plague
- Parasite – schistosomiasis flatworm, giardiasis, pinworms
- FOCUS ON VIRUS TODAY – PREVENTABLE INFECTIONS.
- Viruses are causative agent of several type of human cancer .
- Tumor viruses established persistent infection in hosts, with long latent period before tumor appearance.
- Viral infections tend to be more chronic than bacterial infections, thus viruses have a more prominent role in the development of cancer.
- Multiple tools to fight infections, barriers to infection sources like masks and gloves, vaccination, safe injection practices, screening of blood transfusion, safe sex practices, antimicrobial treatments can have beneficial effects on the future burden of cancer related-infections

Do You Always Know When You Have Infection?

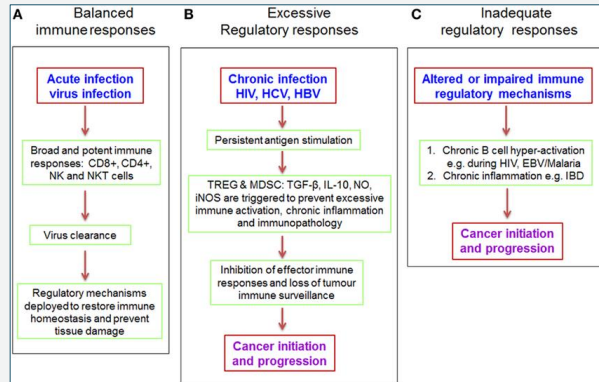


- It Depends on the Infection Location (internal or external), level of infection, and ferocity of the virus
- It also may depend upon your personal immunity or whether or not you were exposed to sufficient infectious agent to cause illness, disease or death
- Primary Infection – Initial Infection with Organism in Host
- Reinfection – Subsequent Infection by Same Organism in a Host Following Recovery
- Superinfection – Infection by same organism in a host before recovery
- Secondary infection – When in a host whose resistance is lowered by a pre-existing infectious disease, a new organism may set up infection in the same host
- Focal Infection – Localized Site of Infection
- Cross-Infection – Two different infections in same host

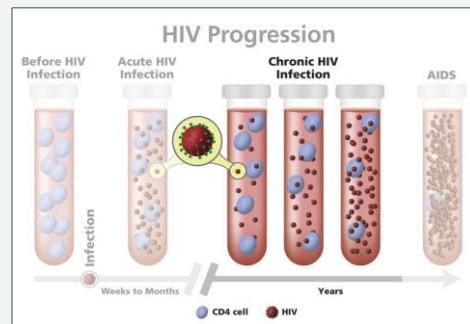
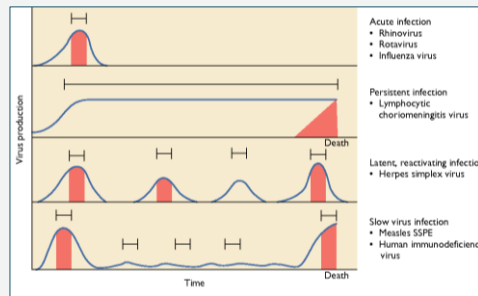
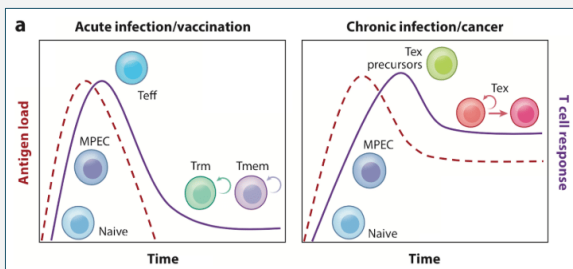
Can Viral Infections Be Cured/Treated?



- Typically viral symptoms and some viral replication can be reduced with medications – few are curable – many stay in your body for the rest of your life and cause problems later in life like cancer from constant inflammation as your body constantly reacts to the intruder causing inflammation but not curing disease.



Infections Over Time (Acute to Chronic)

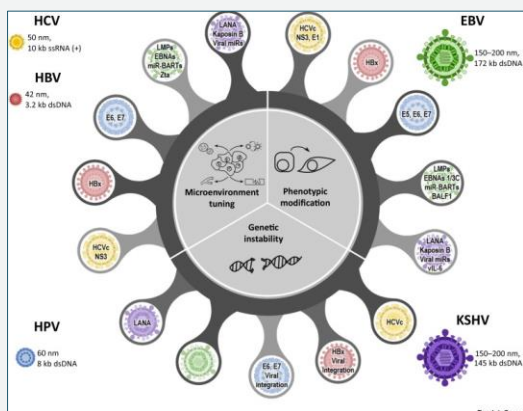


Reducing Your Chances of Infection



- PREVENTION – STAY AWAY FROM INFECTED PEOPLE
- Cleanliness and Sanitation – home, office, car, persons
- Don't Touch Your Face (eyes, nose, mouth)
- Wash Hands Frequently
- Wash Hands Thoroughly – Sing Happy Birthday – TWICE!
- Wear a Mask – Wear Mask CORRECTLY – over nose/mouth
- Wear Eye Protection as Needed – high risk activities/environment
- Wear the Right Mask
 - 3 layers or more of thickness – does not have to be N95
 - What is difference between N95 and KN95 Mask?
 - Not just a bandana – it isn't fashion
- Hand Sanitizers and Sanitizing Wipes – temporary
 - Do not substitute for washing hands – it is just a type of cover-up protection and the infections still sits on the surface until you wash

Oncoviruses



- An oncovirus is a virus that can cause cancer and which induce malignant transformation of cells.
- Most oncogenic viruses often contribute to cancer development in similar ways
 1. These viruses have the ability to infect, but not kill their host cells.
 2. They establish persistent and long-term infections.
 3. They have evolved strategies that enable them to evade mechanisms of viral clearance by the host immune system
- Tumor viruses usually act as a cofactor, providing only some of the steps required to generate malignant cells.
- Viruses are necessary - but not sufficient for development of tumors with viral etiology.
- Viruses often acts as initiators of neoplastic process and may do so by different mechanisms.
- There are currently only 7 known/confirmed oncoviruses

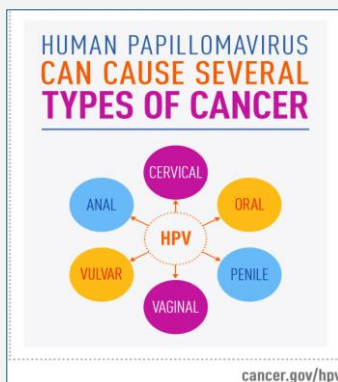
Oncoviruses

Oncoviruses

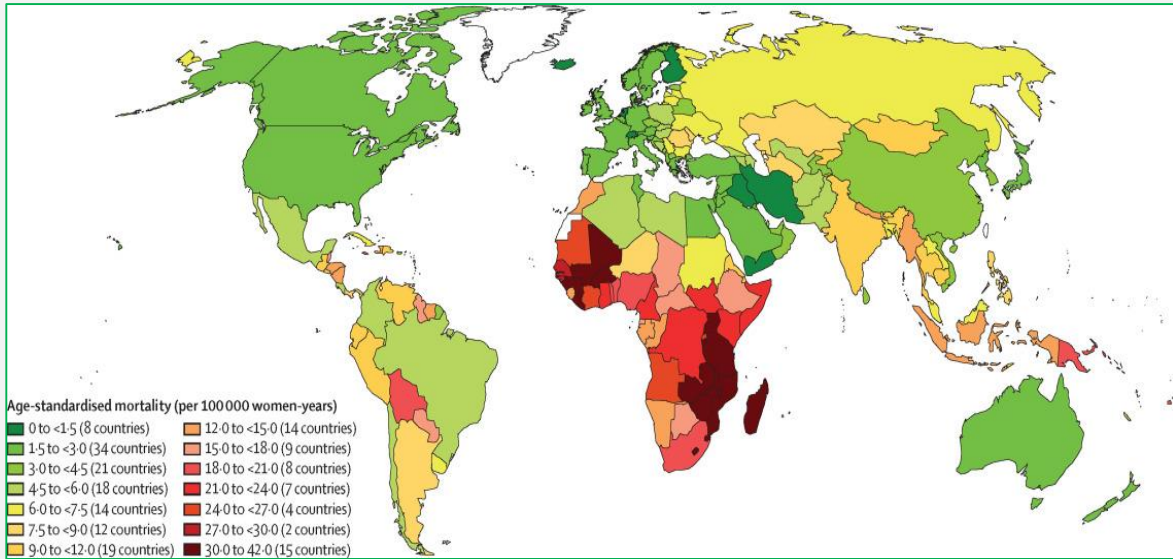
Virus	Genome	Cancer
Epstein-Barr virus (EBV)	DNA	<ul style="list-style-type: none"> • Endemic Burkitt's Lymphoma • Nasopharyngeal Carcinoma • Hodgkin's Disease
Hepatitis B (HBV)	DNA	<ul style="list-style-type: none"> • Hepatocellular Carcinoma
Hepatitis C (HCV)	RNA	<ul style="list-style-type: none"> • Hepatocellular Carcinoma
Human Herpes virus 8 (HHV8)	DNA	<ul style="list-style-type: none"> • Kaposi's Sarcoma
Human Papilloma virus (HPV)	DNA	<ul style="list-style-type: none"> • Cervical Cancer • Oropharyngeal Cancer • Anogenital Cancer
Human T-Lymphotropic virus-1 (HTLV-1)	RNA	<ul style="list-style-type: none"> • Adult T-Cell Leukemia

HPV and P16

Human Papilloma Virus

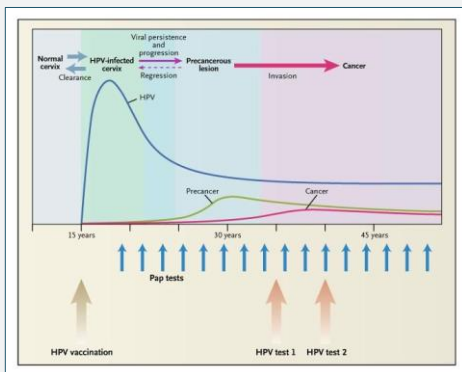


- HPV is a double-stranded DNA Virus and is very common even epidemic in many communities around the world.
- There are actually hundreds of HPV strains in circulation around the world
- Oncogenic strains are HPV16 and HPV18 which are usually associated with cervical carcinoma.
- HPV like other viruses degrade the pathway to natural cell death and keep cells alive long enough to become carcinogenic by way of p53 and pRb tumor suppressor genes which lead to cell and tissue proliferation



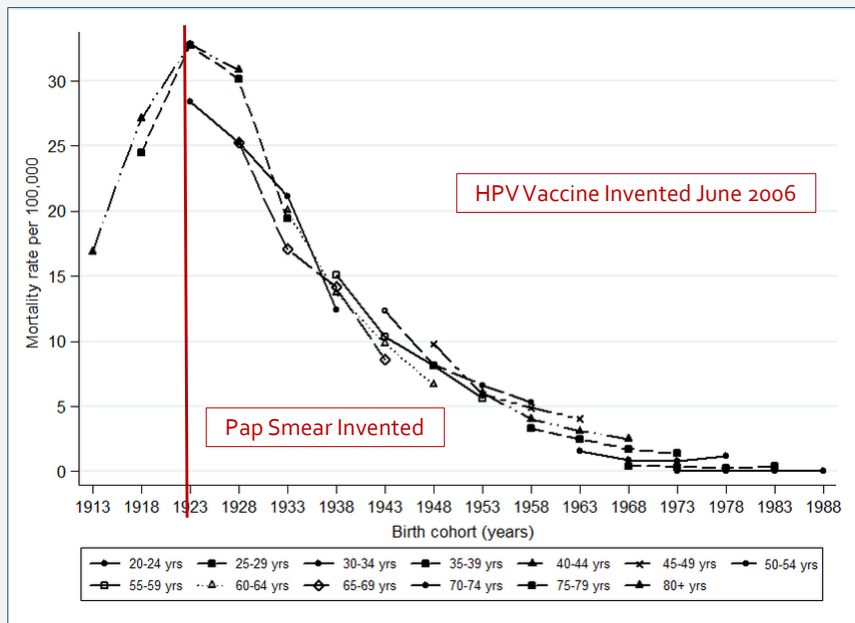
HPV and P16

- Human papillomavirus types (HPV) 16, 18
 - Genital tumors
 - Oropharyngeal cancer



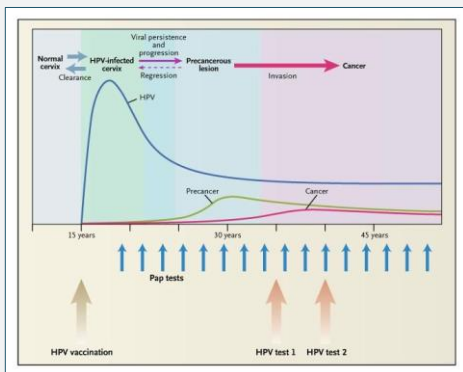
HPV Infection and P16 Testing

- CoC swears they want to keep these separate. However, they have provided ZERO clear guidelines to distinguish between p16+ or p16- and HPV+/- disease or the use of the new ICD-O-3 Histology codes 8085/8086
- A mention of HPV Infection is NOT sufficient for coding a case as being p16+ or p16- or for using 8085/8086.
- Documentation is sorely lacking in this area.
- There are as many as 100 different HPV DNA subtypes identified and associated with genital and oropharyngeal HPV infections.
- Most Types 6, 11, 16 and 18 are associated with high-risk cancers of genital areas
- HPV types 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, 68, 73, and 82 may also be present in oral and/or anogenital mucosal cancers
- p16, is a protein that slows cell division by slowing the progression of the cell cycle by acting as a tumor suppressor. Detection of a tumor suppressor protein, known as p16, is commonly used to diagnose an HPV associated oropharyngeal cancers.
- However, p16+ does not exclude any other type of HPV from being positive from that site, whether oropharynx or cervix or anus or wherever...so, it is exclusive to the HPV16 subtype.
- People can have HPV-related cancers that are not HPV16 type or p16+...
- So, it can be very, very confusing determining if the patient has p16 or HPV+



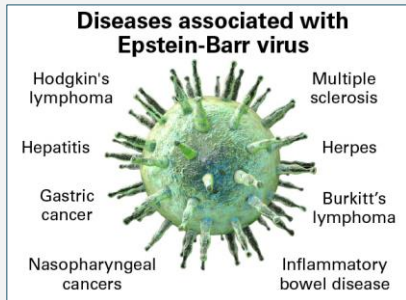
HPV and P16

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- 1928 Georgios Papanicolaou developed the Papanicolaou technique
- 1941 First 'Pap smear' screening technique developed
- 1949 First mass 'Pap smear' screening
- 1949 HPV seen on an electron microscope
- 1963 HPV DNA identified
- 1976 Harald Zur Hausen found HPV DNA in cervical cancer and warts
- 1983 Harald Zur Hausen identifies HPV type 16 in cervical cancer
- 1984 Harald Zur Hausen identifies HPV type 18 in cervical cancer
- 1988 Bethesda System for reporting 'Pap smear' results developed
- 2003 First HPV-based cervical cancer screening test FDA approved
- 2006 First HPV vaccine, Gardasil (Merck), approved by the FDA
- 2007 Second HPV vaccine, Cervarix (GSK), approved by the FDA
- 2008 Gardasil and Cervarix approved by the MCC in South Africa

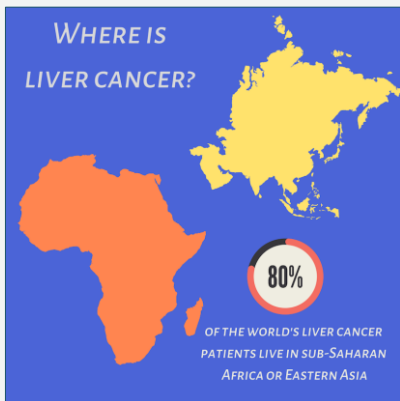
Epstein-Barr Virus



Epstein Barr Virus

- Double-Stranded DNA Virus that reproduces in epithelial cells or B-cells of the oropharynx and then to escape the immune system finding the virus, the virus turns off most of its genes and enters a state of latency, with resting memory B-cells as primary reservoir for storing active EPV cells for future use.
- EBV demonstrates strategies to evade the immune response to protect virally infected cells from immune clearance.
- Epstein-Barr virus (EBV)
 - Burkitt lymphoma
 - Hodgkin lymphoma
 - Nasopharyngeal carcinoma

Hepatitis (HBV/HCV)



Hepatitis B Virus and Hepatitis C Virus

- Both can cause acute and chronic hepatic infections
- The typical natural history of viral carcinogenesis in hepatocellular carcinoma involves many years of chronic viral infection leading to development of cirrhosis in about 20-30% of patients, which subsequently leads to HCC
- The virus promotes dysplasia and cancer via several routes including deregulation of p53 and the retinoblastoma pRb genes which promote development of cancers after years of chronic infection
- Hepatitis B virus (HBV) Hepatocellular carcinoma
- Hepatitis C virus (HCV) Hepatocellular carcinoma



Human Herpes Virus 8 (HHV-8)

- Kaposi sarcoma herpesvirus (KSHV)
- Human herpesvirus 8 (HHV 8)
 - Kaposi sarcoma



Human Herpes Virus 8 (HHV-8)

- HHV-8 is a double stranded DNA Virus
- It is also referred to as the Kaposi Sarcoma-Associated Herpes Virus or KSHV
- This virus establishes a latent infection in its host
- It encodes many potential oncogenes and can even transform human endothelial cells into cancer cells
- This in turn can actually turn off the natural cell death viral b-cell lymphoma-2 oncoprotein that gives these cells a lifecycle, so they can stay alive for many years
- There has been recent discovery that even 25 years after HAART Therapy with No Evidence of Active HIV or AIDS, some patients are now developing Kaposi Sarcoma Associated with this virus decades after exposure and unrelated to current personal health conditions – HIV neg

HTLV-1-4 and HIV-2

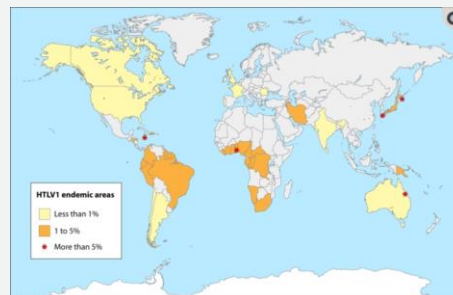
Summary of the global HIV epidemic (2019)

	People living with HIV in 2019	People newly infected with HIV in 2019	HIV-related deaths in 2019
World	38.0 million [31.6 million – 44.5 million]	1.7 million [1.2 million – 2.2 million]	690 000 [500 000 – 970 000 million]
Men	30.2 million [30.2 million – 42.5 million]	1.5 million [1.1 million – 2.0 million]	600 000 [430 000 – 840 000]
Women	19.2 million [16.4 million – 22.2 million]	790 000 500 000 – 1.1 million]	300 000 [220 000 – 420 000]
Children (15 years)	17.6 million [13.8 million – 20.4 million]	870 000 630 000 – 1.2 million]	300 000 [280 000 – 560 000]
Children (5 years)	1.8 million [1.3 million – 2.2 million]	150 000 [94 000 – 240 000]	65 000 [61 000 – 150 000]

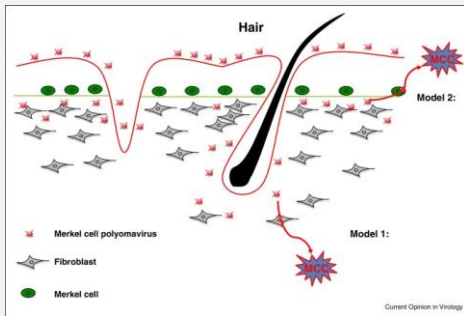
Source: UNAIDS/WHO estimates

People living with HIV/AIDS	Mortality	Prevention
38 million	690 000	90
people living with HIV/AIDS worldwide in 2019	people died of HIV-related illnesses worldwide in 2019	low- and middle-income countries reported a total of 190 million people tested and received results in 2018
Number of people (all ages) living with HIV	Number of deaths due to HIV	Number of tests performed

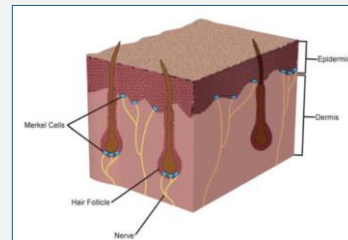
- Human T-cell lymphotropic virus 1 (HTLV1) – 4 types
 - Adult T-cell leukemia
 - Cutaneous T-cell Lymphoma
 - HTLV-associated myelopathy/tropical spastic paraparesis
- Human immunodeficiency virus 1 (HIV 1)
 - This is HTLV3
 - AIDS-related neoplasms – lymphoma, KS, Hodgkin, cervical cancer, H&N, Anal, Liver, other



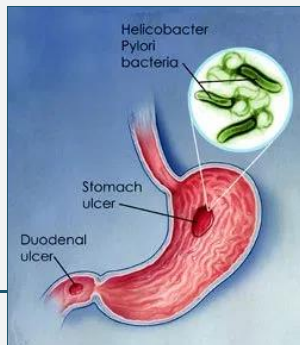
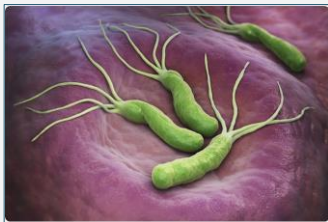
Merkel Cell Polyomavirus



- Merkel cell polyomavirus (MCPyV or MCV)
 - Merkel cell carcinoma
- First described in January 2008 in Pittsburgh, PA
- First example of a human viral pathogen discovered using unbiased metagenomic next-generation sequencing with a technique called digital transcriptome subtraction.
- MCV is one of seven currently known human oncoviruses.

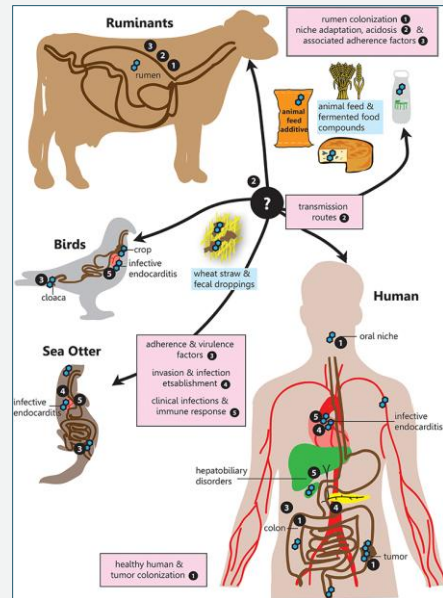
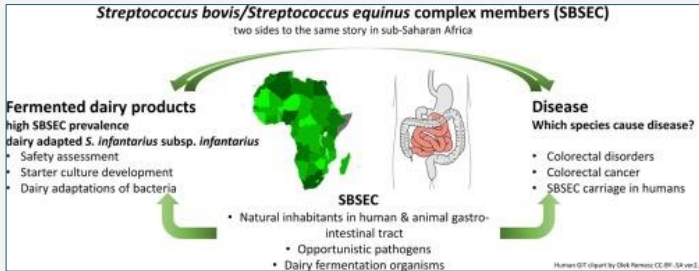


Helicobacter Pylori



- The exact way *H. pylori* infects someone is still unknown.
- *H. pylori* bacteria may be passed from person to person through direct contact with saliva, vomit or fecal matter.
- *H. pylori* may also be spread through contaminated food or water.
- Risk factors
 - Living in crowded conditions. You have a greater risk of *H. pylori* infection if you live in a home with many other people.
 - Living without a reliable supply of clean water. Having a reliable supply of clean, running water helps reduce the risk of *H. pylori*.
 - Living in a developing country. People living in developing countries, where crowded and unsanitary living conditions may be more common, have a higher risk of *H. pylori* infection.
 - Living with someone who has an *H. pylori* infection. If someone you live with has *H. pylori* infection, you're more likely to also have *H. pylori* infection.

Streptococcus Bovis



Schistosoma Haematobium

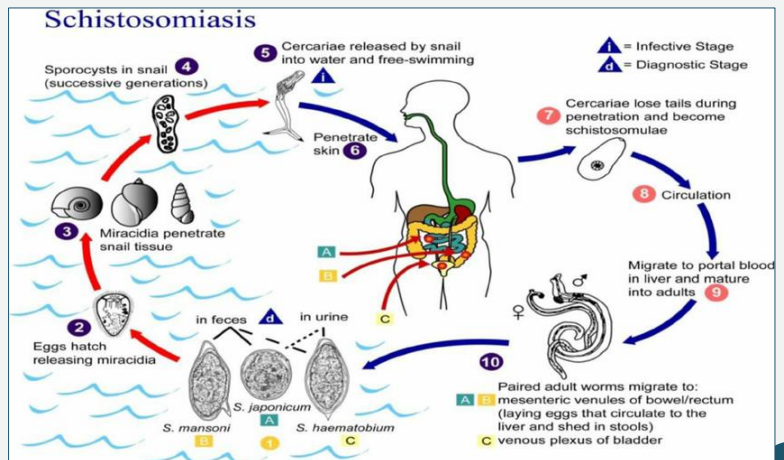


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Viruses Used in Treatment of Cancer (Oncolytic Virus)

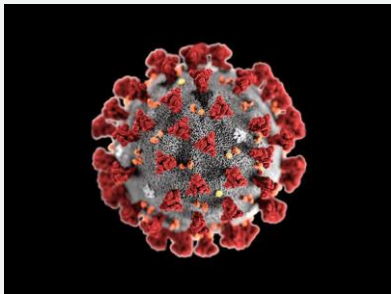
There is currently one oncolytic virus therapy approved by the FDA for the treatment of cancer:

T-VEC (Imlygic®): a modified herpes simplex virus (HSV) that infects tumor cells and promotes their destruction; approved for subsets of patients with melanoma

Oncolytic virus platforms under evaluation in clinical trials include:

- **Adenovirus:** a family of common viruses that can cause a wide range of typically mild effects including sore throat, fatigue, and cold-like symptoms
- **Herpes simplex virus:** a virus that can cause the formation of sores on or near the mouth
- **Maraba virus:** a virus found exclusively in insects
- **Measles:** a highly contagious virus that infects the respiratory tract and can cause measles
- **Newcastle Virus:** a virus primarily found in birds; can cause mild conjunctivitis and flu-like symptoms in humans
- **Picornavirus:** a family of viruses that can cause a range of diseases in mammals and birds; the coxsackie virus is an example from this family that is being clinically tested
- **Reovirus:** a family of viruses that can affect the gastrointestinal and respiratory tracts in a range of animal species
- **Vaccinia virus:** the virus that was used to help vaccinate against and eliminate smallpox; rarely causes illness in humans and is associated with a rash covering the body
- **Vesicular stomatitis virus:** a virus that belongs to the same family as the Maraba virus; can cause flu-like symptoms in humans
- **Rubeola virus:** a highly contagious virus that infects the respiratory tract and can cause measles

What About COVID-19?



- Acute Infection will effect ongoing treatment & F/U
- Acute Infection will effect new cases/late stage at dx
- Acute Infection in community raises fears to travel
- Acute Infection effects many organs and organ systems
- We have absolutely no idea what chronic infection will do
- We don't even know if there will be chronic infection
- Will there be Reinfection – Will it be different? In what way?
- What about Co-Infection with other viruses?
- How long will the virus stay in the body?
- Will there be a vaccine – annual, once in lifetime
- Will there be natural immunity?
- Will there be treatment?
- Will there be cure?

References & Resources



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Questions??

