# Hematology

## Microbiology

☑ Sheet ☐ Slide ☐ Handout

Number: **2**

Subject: **Parvo virus,HHV8 &HTLV**

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Date:

Price:

Topics discussed in this sheet:

- Parvo virus
- Human herpes virus 8
- Human T-lymphotropic virus

***Remember, DNA Viruses:***
***the HHHAPPPy viruses:***
***Herpes***
***Hepatitis B***
***Human papilloma***
***Adeno***
***Polioma***
***Parvo***
***Pox***

## Parvovirus B19

- Remember we studied this virus with childhood exanthems in the MSS. Exanthem means superficial rash on the skin vs enantheme: internal rash on the mucosa.Example: in measles the child presents with fever, sore throat, lesions in the bucccal musoca(enanthems).
- Parvovirus is a DNA virus. It is among the smallest DNA viruses.
- Has an **icosahedral** caspid (**naked** virus) and a **single strand of DNA**. The capsid is made of more than one protein; **VP1**, VP2 and VP3.
- Viral uncoating, DNA replication, RNA transcription, protein translation, and virus capsid assembly **all occur in the cell's nucleus**. (Uncoating: opening of the capsid and release of viral DNA into the cell).
- **Tissue tropism for parvovirus**: cells of the erythroid lineage -immature (nucleated) RBCs, megakaryocytes and endothelial cells.
- Can be cultured **in bone marrow cells and in liver cells** (in the lab)- (sites of erythropoiesis).

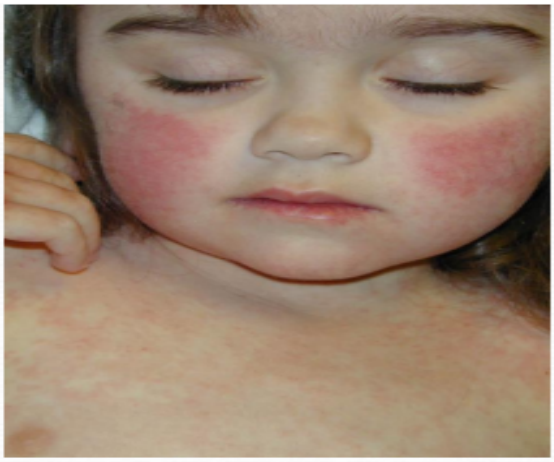
## Clinical consequences:

- minimal unless compromised with chronic hemolytic process.
- **Children** are the most susceptible age group 6-10 years though younger children may become Infected, they are symptomatic while adults are mostly not . If they get infected with this virus they get erythema infectiosum (fifth disease or slapped check disease) which is indicated by the characteristic rash of parvovirus infection- **facial rash** that spreads over

the cheeks and the forehead, spares the nosolabial folds, the circum-oral region and the forehead. One to two days later it **spreads into the trunk and extremities**. This rash is called indurated rash (rounded light pink spots with lacy look).

- Even in immunocompetent patients the infection might pass asymptomatically.

- By adulthood,50% of the population has seroconversion. When it infects adults: it might go unnoticed. Or it might be symptomatic if not previously infected in the past. In this case the patient will have, **arthralgia** and arthritis (arthralgia and arthritis do not take place in children as a consequence of this infection), they might or might not have rash.



Fifth Disease (parvovirus B19)

-In patients with **preexisting hemolytic disorder** (like sickle cell anemia and thalassemia); the body is already struggling for the RBCs and the oxygen and they are depending on the newly formed cells to compensate for the destructed cells . If parvovirus infects these patients, it will lead to lysis and destruction of RBCs and they will have severe anemia.

-These patients might present with fever only and you will find out that they have anemia and an **aplastic crisis**. (Aplastic crisis is precipitous worsening of anemia in patients with a shortened RBC life span and reduced erythropoiesis that can be life threatening).

-A patient may present with fever only, but he/she is then found to have anemia and aplastic crisis.

**Treatment:** Blood transfusion.

-In the immunosuppressed, especially **AIDS** patient, present with **anemia** you should suspect being infected with parvovirus B19.

**-Incubation period** : 6 to 7 days up to 3 weeks, in average 10-12 days.

-Illness Is characterized by fever, malaise, headache, myalgia and itching. Indurating rash from the face might spread to the arms and neck, it can mostly involve lymph nodes and liver and spleen leading to hepatosplenomegaly.

-The rash stays for one to two weeks but after that recurrence of the rash is possible during the next 4-8 weeks upon exercise, heat, if the person is out in the sun or is under emotional stress.

-It is sometimes associated with vasculitis and arthritis(more commonly seen in adults).

**-Very rare complications:** encephalitis, nephritis, hepatitis and thrombocytopenia.

-Primary rout of **transmission: Upper respiratory tract**, usually during the spring. Virus stays in the blood causing viremia for one to 2 weeks.

**-Diagnosis**: **PCR**, **serology.**

**-Treatment**: **no specific antiviral** drugs nor vaccine, treatment is symptomatic patients given **Ig** against the virus show improvement which is not routinely done as it is expensive.
Patients who have a preexisting hemolytic diseases are given blood transfusion as an emergency treatment.

## Human Herpes virus 8 (HHV8) or Kaposi sarcoma associated virus

-From the herpes virdea family. Originally isolated from the cells of kaposi sarcoma.

-Isolated from 100% of the lesions of kaposi sarcoma with Kaposi and associated with other malignancies with castleman's disease (a very rare malignancy of the lymphatic system) and primary effusion lymphoma. (Remember the difference between AIDS and HIV infection; HIV infection is having HIV in your

body, but AIDS develops when HIV has caused serious damage to the immune system that your T-cell count has gone below 200 and you are now sick!)

- Kaposi sarcoma is a cancer that can occurs in the skin or even in the internal organs, it can infect vacscular or lymphoid cells. Most patients of kaposi sarcoma have antibodies against HHV8, the seroconversion is low among the general population but is high in susceptible individuals such as homosexual men in most cases.

-The mechanisms by which the virus is contracted are not well understood though its mostly through sex and it could be transmitted via saliva so if the individual is infected it can be transmitted via oral sex. Transmission can be prevented by protected sex.

- **Prevention**: protected sex.

-Infection can go asymptomatic. Patients that usually show symptoms are cancer patients, patients on chemotherapy, AIDS patients, organ transplantation patients. So any drop of the immune system will lead to activation of the virus.

- **Treatment**: Ganciclovir; a theoretical treatment because most of the time we know about being HHV 8 infected after the Kaposi sarcoma appearance and most of infections are asymptomatic but once the cancer has developed there's no point of using Ganciclovir.

-HAART (Highly active anti-retroviral therapy); we usually use three drugs in this therapy, each works at a different level of viral replication to drop the viral load and restore T cells.

## Human T-cell lymphotropic virus (HTLV)

- From retroviridea (this family includes HIV, HTLV-1(associated with T–cell leukemia), and HTLV-2,, associated with hairy cell leukemia)

- **Retroviruses**:
  1. have reverse transcriptase enzyme and replication occurs the nucleus.(Remember that the general rule for RNA vruses is that they

replicate in the cytoplasm, influenza and retroviruses are the exeptions).
2. Enveloped RNA viruses,Single stranded RNA, +ve sense (+ve sense serves as a messenger RNA, while the complemntary strand of a -ve sense serves as a template).

3.Genome is integrated non-segmented.(segmented viruses are Reo family and influenza virus, segmented means that each segment codes for one gene and therfore produces one protein)

4.Diploid genome (in each virus there are 2 copies of positive sense single stranded RNA).

- Remember there is another class that is DNA virus with reverse transcriptase enzyme is Hepatitis B virus.

- For the virus to enter the cell we need a receptor and a coreceptor on the virus that would interact with glycoproteins (or spikes on the virus).For HIV virus the glycoproteins **gp120**, and **gp 41** interact with **CD 4** receptor on T cell and this requires a coreceptor which would be **TCR5** or **CXCR4** to facilitate viral entry to the T cell.

- **Ways of entry:** either by receptor mediated endocytosis or by fusion (fusion only works for enveloped viruses. HIV enters by fusion(there are some studies saying that recptor-mediated endocytosis may be a way of its entry in addition to fusion). This means fusion of the viral envelop with the cellular membrane.
  This leads to one of the pathogenic marks of this virus which is **syncytia formation** (multinucleated giant cell)-because the each cell now has on its membrane its own proteins (receptors) as well as glycoproteins that were on the viral envelop. This will make infected cells able to bind to other cells, and the two merge in the same way that the HIV particle originally merged into the cell: the membranes fuse and become one. This repeats, and eventually you have one large multinucleated cell.

- After that uncoating occurs, and two copies of ssRNA are released to the cytoplasm. Reverse transcriptase makes DNA out of ssRNA positive sense and here we have DNA-RNA intermediate. Then RNA dissociates and is

destroyed by RNaseH. Another component of this reverse transcriptase is going to make dsDNA out of this ssDNA. This double stranded DNA will go to the nucleus and integrate to the cell genome through the activity of the enzyme integrase through making sticky ends(at this stage the virus is called a provirus).

- Cellular machinery then transcripts the viral genome over with the cell genome, This will lead to the production of a mRNA that will leave the nucleus to the cytoplasm to (1) be assembled as a genome of a new virion. (2) go to the ribosomes to make proteins. The mRNA is translated into a polyprotein that will be cleaved by proteases to produce individual functional proteins.

Back to HTLV;

## HTLV-1:

- It is endemic in parts of Japan and south America, it is asymptomatic in majority of individuals, approximately 2-5% of individuals carrying HTLV-1 develop disease 10-40 years after infection, so infection doesn't necessarily means developing cancer.

- It infects CD4 cells, transmission by close contact, sexual transmission, blood products, IV drug abusers, vertical transmission during pregnancy and breast feeding which is a primary route.

- HTLV-1 is isolated from 100% of those who have T-cell leukemia.

However, it is Asymptomatic in majority of cases. Most carries develop disease 20 to 40 years after infection. It has a long clinical latency (should not be confused with viral latency; clinical latency is when the virus is replicating, but it is asymptomatic, this is another word for the term incubation period. However, viral latency is when the virus is not fully replicating. It is staying dormant in the cells as an episome and produces just a very small percentage of the viral genome that are the immediate early proteins only which are important to maintain latency)

- Drop in immunity shortens the incubation period.

It is associated with:

1. **Adult T-cell leukemia:**

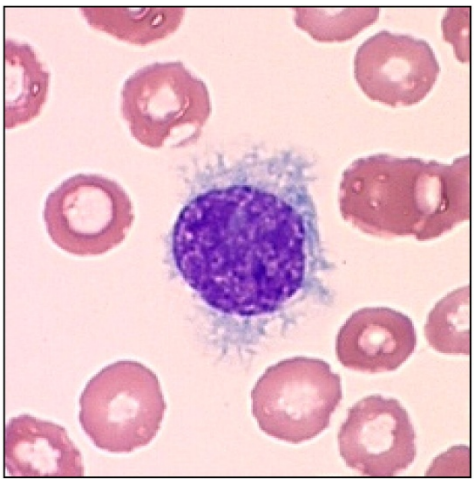
-Exact mechanism of transformation is not fully known. Part of the answer is in the viral protein *tax oncoprotein* that induces proliferation promote cellular survival so we will have more faults in the DNA and impairs cellular DNA repair mechanisms. There could be other factors that play a role in transformation.

2. **Tropical spastic parparesis:**

- a neurodegenerative disease of the central nervous system that is endemic in parts of south America. Associated with progressive demyelination muscle/neurons disease. Characterized by sensory and motor defecets particularly in the lower extremities, incotinence and impotence.

**-Diagnosis**: ELISA, western blotting, PCR (most definitive)

## HTLV-2:



**-Hairy cell leukemia:**
- characterized by malignant cells that are multinucleated.

**Treatment**: treat opportunistic infections if drop of the immune system takes place.
Chemotherapy and retroviral drugs in case of leukemia and lymphoma. Symptomatic treatment with interferon and corticosteroids.