Lecture 5: 06 November 2022

Retroviridae (retroviruses) Malik Sallam, MD, PhD

The virus family *Retroviridae* has four members that can cause human disease:

1. Human immunodeficiency virus type 1 (HIV-1)
2. Human immunodeficiency virus type 2 (HIV-2)
3. Human T cell lymphotropic virus type 1 (HTLV-1)
4. Human T cell lymphotropic virus type 2 (HTLV-2)

General features of retroviruses:

A. The genome is two copies (diploid) of positive-sense single stranded RNA
B. The three major gene regions are:
    1. Gag (Group antigen): codes the capsid proteins
    2. Pol: Polymerase gene region that codes reverse transcriptase, integrase and protease
    3. Env: Envelope gene region that codes the envelope glycoproteins
C. Reverse transcriptase converts viral RNA into DNA which will be integrated in the host cell chromosomes by the viral enzyme called integrase. The integrated viral DNA is called "provirus"
D. An envelope is present
E. They infect cells of the immune system (mainly CD4+ T helper cells, monocytes)
F. They remain in the body forever in the form of provirus

HTLVs will be discussed briefly because these two viruses will be covered in details in the third year (hematolymphatic system).

The most important points:

1. More than 95% of all HTLV infections remain asymptomatic (will NOT cause any known disease)
2. Transmission through mother-to-child route, injection drug use (استخدام الحُقن الملوثة عند مدمني المخدرات), sexual route and blood transfusion
3. A recent estimate about HTLV-1 prevalence: 5–10 million had the virus
4. A recent estimate about HTLV-2 prevalence: Less than 1 million had the virus
5. In less than 5% of the infected persons, adult T-cell leukemia/lymphoma can occur

This is the only material required for the exam. No other source is needed
For any questions you can contact me through the following email: malik.sallam@ju.edu.jo

HIV/AIDS (acquired immune deficiency syndrome)

1. **Tropism:** CD4+ T cells, monocytes/macrophages, dendritic cells
2. **Receptors:** CD4 (present on CD4+ T cells, monocytes/macrophages and dendritic cells) and a coreceptor (CCR5 on monocytes/macrophages, dendritic cells) or (CXCR4 on CD4+ T cells). So, HIV strains that infect CD4+ T cells are called X4 viruses. HIV strains that infect monocytes/macrophages and dendritic cells are called R5 viruses. HIV strains that infect all these cells are called R5X4 viruses.
3. **Epidemiology:** In 2021, 40 million people were living with HIV infection. Mostly in Africa.
4. **Transmission:**
    A. Heterosexual and homosexual practices.
    B. Mother-to-child.
    C. Injection drug use by contaminated needles.
    D. Needle stick injuries (إصابات الوخز بالإبر في المستشفيات والعيادات بشكل رئيسي)
    E. Blood transfusion.

Not every exposure will result in infection. For example, of all needle stick injuries only 0.3% will result in HIV infection.

5. After transmission, the incubation period is variable (few weeks to few months). This is followed by acute infection. Acute HIV infection can be symptomatic (influenza-like illness or sore throat, fever and lymphadenopathy). Acute infection can be totally asymptomatic. In acute HIV, the CD4+ T cells are killed and their numbers decrease significantly. About 6 months after exposure, the immune system controls the viral load (number of viruses) in blood to a low level. This low level of viral load is different from person to person based mainly on the genetics of the patient. CD4+ T cells increase when the immune system controls the virus. Viral load after 6 months is called **HIV set point**. After 6 months, the patient will be mostly asymptomatic but the virus remains in the body. This is called the **clinical latency** period. HIV escapes from immunity. During clinical latency, immunity tries to control HIV again. HIV escapes from immunity. Immunity tries to control HIV again and again. HIV escapes from immunity. Immunity tries to control HIV again, again and again. Finally, the immune

system becomes exhausted (مُنهك ومُستنزف). So, the virus takes over and the number of CD4+ T cells will be lower than 200 cells/mm^3 (normal level is 500–1500 cells/mm^3). **When the CD4+ T cells is lower than 200 cells/mm^3, the diagnosis of AIDS is reached.** In AIDS patients, cellular immunity is deficient (نقص في المناعة بسبب موت الخلايا التائية المُساعدة). So, the patients will develop severe virus and fungal infections and cancers. Time from acute infection to AIDS is called progression to AIDS. Rapid progressors will have AIDS in 2–3 years. Long-term non-progressors can live for more than 20 years without AIDS. A majority of patients will have AIDS in 8-12 years. Higher HIV set point is associated with shorter time of progression to AIDS. Lower HIV viral set point is associated with longer time of progression to AIDS.

6. **Diagnosis:**
   A. Nucleic acid amplification to measure the viral load.
   B. Serology (antibody testing).
   C. Antigen detection.
7. **Treatment:** is based on combination of two or three drugs to prevent emergence of resistance. This is called **h**ighly **a**ctive **a**nti-**r**etroviral **t**herapy (**HAART**). Early treatment can slow progression to AIDS. **Treat as early as possible**. Drugs:
   A. Reverse transcriptase inhibitor drugs.
   B. Protease inhibitor drugs.
   C. Integrase inhibitor drugs.
   D. CCR5 receptor antagonists.
8. **Prevention**
   A. Effective vaccines have not been developed so far.
   B. Drugs can be given before exposure in the high-risk groups (called pre-exposure prophylaxis الوقاية)
   C. Drugs can be given after exposure (called post-exposure prophylaxis)
   D. Behavioral (clean needles, condoms, or even better not engaging in high-risk sexual practices الحرام لذة ساعة، والعذاب دهر حرفياً في مرض نقص المناعة المُكتسبة لإن الفيروس سيبقى في الجسم مدى الحياة).

Please note that the previous lecture #4 was covered in handout #3

This is the only material required for the exam. No other source is needed
For any questions you can contact me through the following email: malik.sallam@ju.edu.jo