

Lecture 10: HIV Pathology

wiseGEEK

▣ Important

▣ Notes

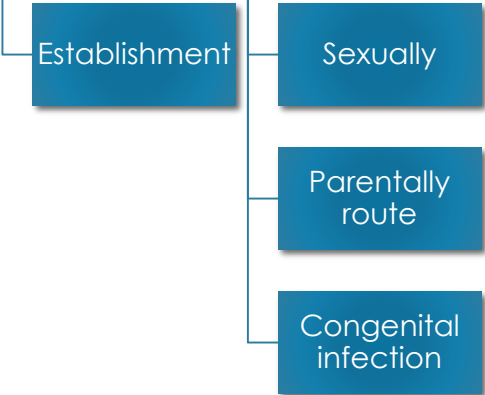
▣ Explanation

Objectives

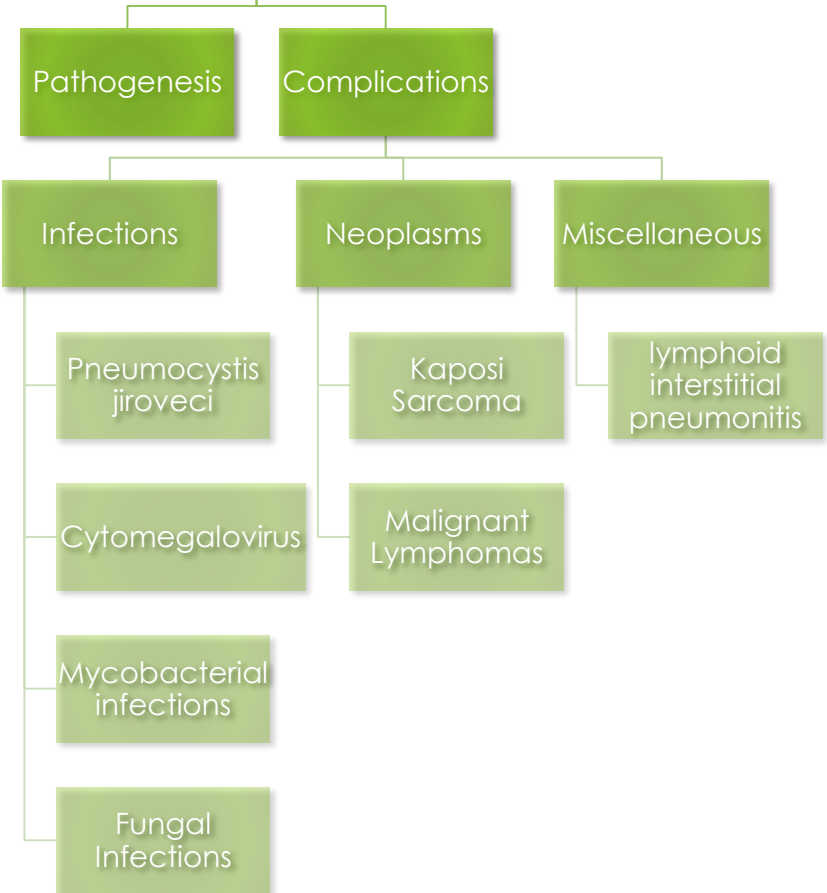
The student should know :

- Understand the aetiology and pathogenesis of AIDS.
- Opportunistic infections and its relation to AIDS.
- Clinicopathological features of the major systemic manifestations of AIDS, with special emphasis on *Pneumocystis carinii*, fungal infections, viral infections and some tumors like Kaposi sarcoma and lymphoma.

HIV



AIDS

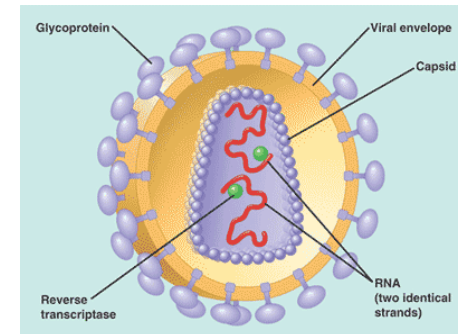


Introduction :

- The most common type of HIV infections is known as HIV-1 and is the type that has led to the worldwide AIDS epidemic.
- There is also an HIV-2 that is much less common.
- The result of HIV infection is the **destruction of the immune system**.
- All HIV infected persons are **at risk for illness and death from development of opportunistic infections** and tumors and the inevitable manifestations of AIDS.

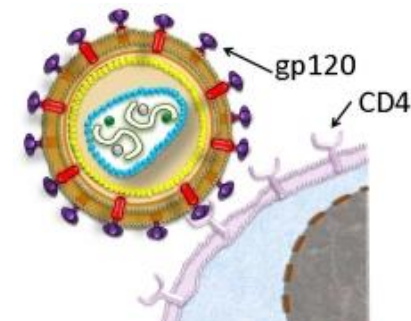
Structure of HIV :

The mature virus consists of an electron dense core containing the viral genome consisting of the 2 short strands of **RNA** (ribonucleic acid). In addition the enzymes **reverse transcriptase**, **protease**, **ribonuclease**, and **integrase** are present. **All are encased by an outer lipid envelope**.



Pathogenesis of HIV :

- The HIV virion expresses a cell surface protein/antigen **called gp120**, that aids in the binding of the virus to the target cells. Once the virus enters the human body it attaches itself to the target cell via the CD4 receptors on the surface of the target cell and therefore gains entry into the target cell.
- In addition gp120 also binds to two co-receptors **CXCR4** and **CCR5** on the host cell surface. They too assist in the entry of HIV into the host cell.
- HIV infects mainly CD4+ T cells, macrophages, and dendritic cells which express the surface receptor CD4. Destroying CD4+ T cells leads to severe immunologic impairment and eventually death.



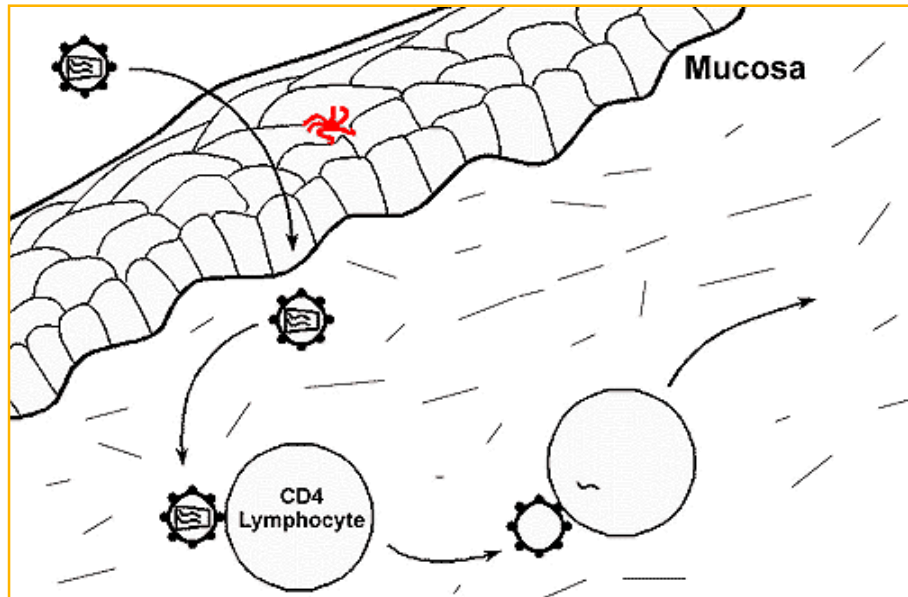
Gp120 is responsible for tropism/attraction to CD4+ receptors. This helps in entry of HIV into the host cell.

Pathogenesis of HIV (Cont):

- Retroviruses are **unable to replicate outside of living host** cells **because they contain only RNA** and do not contain DNA. Therefore once HIV infects a cell, it must use its **reverse transcriptase** enzyme to **convert its RNA to host cell proviral DNA for replication**.
- This HIV proviral **DNA is then inserted into host cell genomic DNA by the integrase enzyme**.
- Once the HIV proviral DNA is within the infected cell's genome, the HIV provirus is replicated by the host cell to produce additional HIV virions which are released by surface budding. Alternatively the infected cells can undergo lysis with release of new HIV virions which can then infect additional cells.

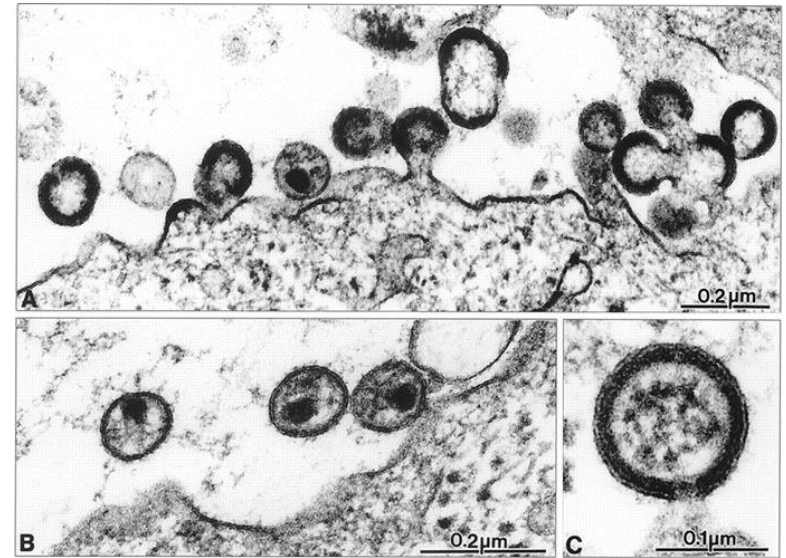
Establishment of HIV Infection :

- Macrophages and Langerhans cells are important both as **reservoirs and vectors** for the spread of HIV in the body including the CNS. Both macrophages and Langerhans cells can be HIV-infected but aren't destroyed. HIV can then be carried elsewhere in the body.
- Once the infection extends to the lymph nodes, the HIV virions are trapped in the processes of follicular dendritic cells (**FDC's**), where they provide a reservoir and infect CD4+ T lymphocytes that are passing through the lymph node. The FDC's themselves become infected, but are not destroyed.
- The target cells are: blood monocytes and tissue macrophages, T lymphocytes, B lymphocytes, natural killer (NK) lymphocytes, dendritic cells (*i.e. the Langerhans cells of epithelia and follicular dendritic cells in lymph nodes*), hematopoietic stem cells, endothelial cells, microglial cells in brain, and gastrointestinal epithelial cells.
- In addition HIV has the ability to **mutate easily**. This high mutation rate leads to the emergence of HIV variants within the infected person's cells that are more toxic and can resist drug therapy. Over time, different tissues of the body may harbor differing HIV variants.

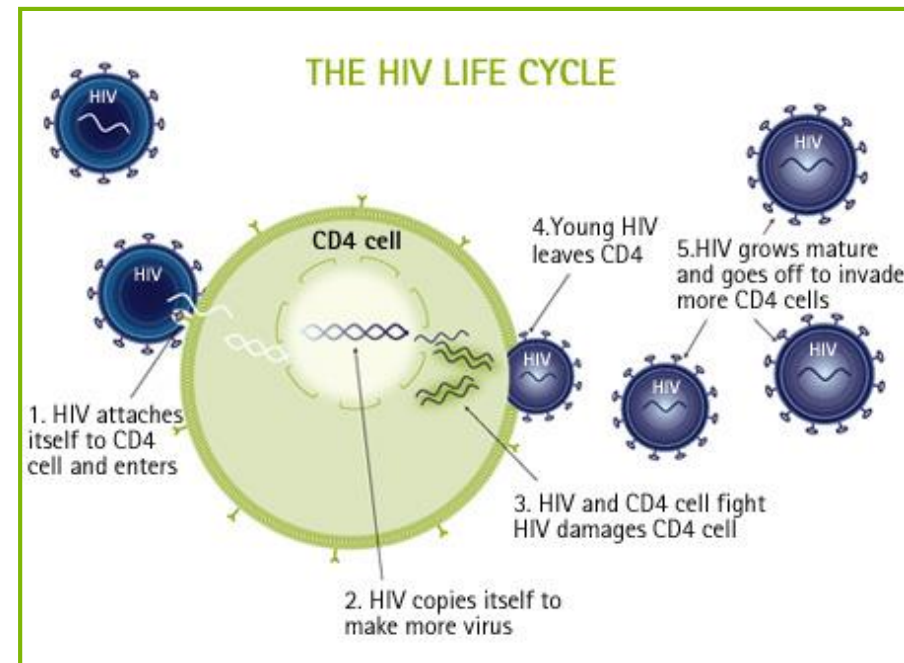


Human immunodeficiency virus is shown crossing the mucosa of the genital tract to infect CD4+ T-lymphocytes. A langerhans cell in the epithelium is shown in red in this diagram.

NOTE: The probability of infection depends on both the number of infective HIV virions in the body fluid which contacts the host as well as the number of cells with CD4 receptors available at the site of contact.



HIV viral particles are seen adjacent to the cell surface in this electron micrograph



The Major Modes of Transmission of HIV (the high risk population):

- HIV can be present in a variety of body fluids and secretions. They include genital secretions, blood, breast milk, saliva, urine, tears, and sweat.
 - **NOTE: saliva, urine, tears, and sweat is of no major clinical importance, as transmission of HIV through these fluids does not routinely occur because of the low concentration of HIV in these fluids.**
1. HIV is primarily spread as a **sexually transmissible** disease. Transmission of HIV can occur from male to male, male to female, and female to male. Female to female transmission remains extremely rare.
 2. HIV can be transmitted through **parenteral route**, e.g.
 - **Intravenous drug users sharing infected needles**. Less common practices like use of instruments such as tattoo needles not properly disinfected also carries a potential risk.
 - Health care workers with **percutaneous exposures** (needle puncture) to HIV-containing blood.
 - Persons receiving **multiple blood transfusions** e.g hemophiliacs. Screening of blood products for HIV has significantly reduced HIV transmission by this means.
 3. HIV infection can also be acquired as a **congenital infection** either perinatally or in infancy. Mothers with HIV infection can pass the virus
 - transplacentally i.e. in utero.
 - at the time of delivery through the birth canal.
 - through breast milk.
- **NOTE: HIV infection is not spread by casual contact in public places, households, or in the workplace. HIV is not spread by insect vectors. There is no vaccine to prevent HIV infection.**

Diagnosis of HIV :

- Test for HIV antibodies is done with a rapid test using an enzyme-linked immunosorbent assay (ELISA) technique.
- If rapid test is positive, then the next step is to:
 - Confirm HIV infection with Western blot or immunofluorescence assay (IFA)
- **NOTE: The average HIV-infected person may take up to several weeks to become seropositive, and then may live up to 8 or 10 years, on average, before development of the clinical signs and symptoms of AIDS.**

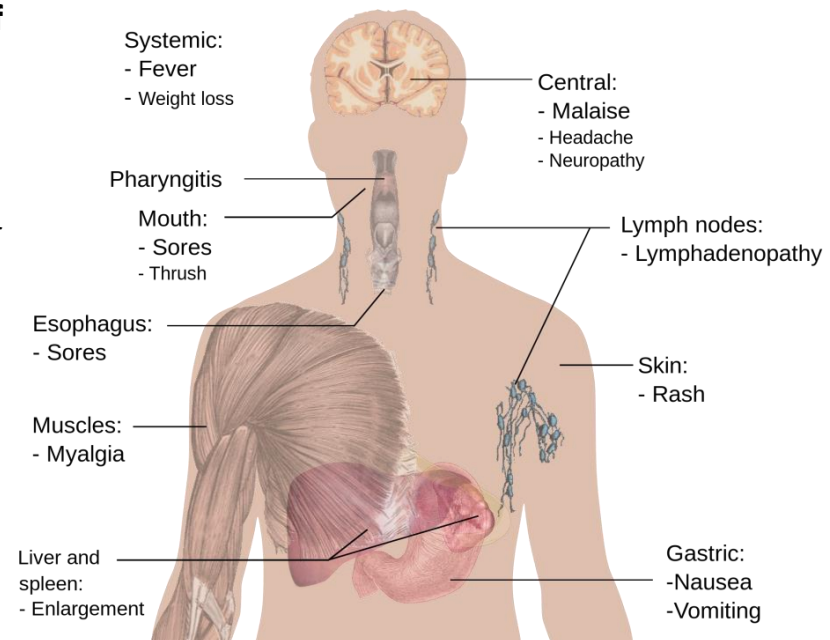
Primary HIV Infection :

- **Primary HIV infection may go unnoticed in at least half of cases or produce a mild disease which quickly subsides, or produce acute HIV infection.**
- Primary acute HIV infections may include **fever, generalized lymphadenopathy, pharyngitis, rash, arthralgia and diarrhea**. These symptoms diminish over 1 to 2 months.



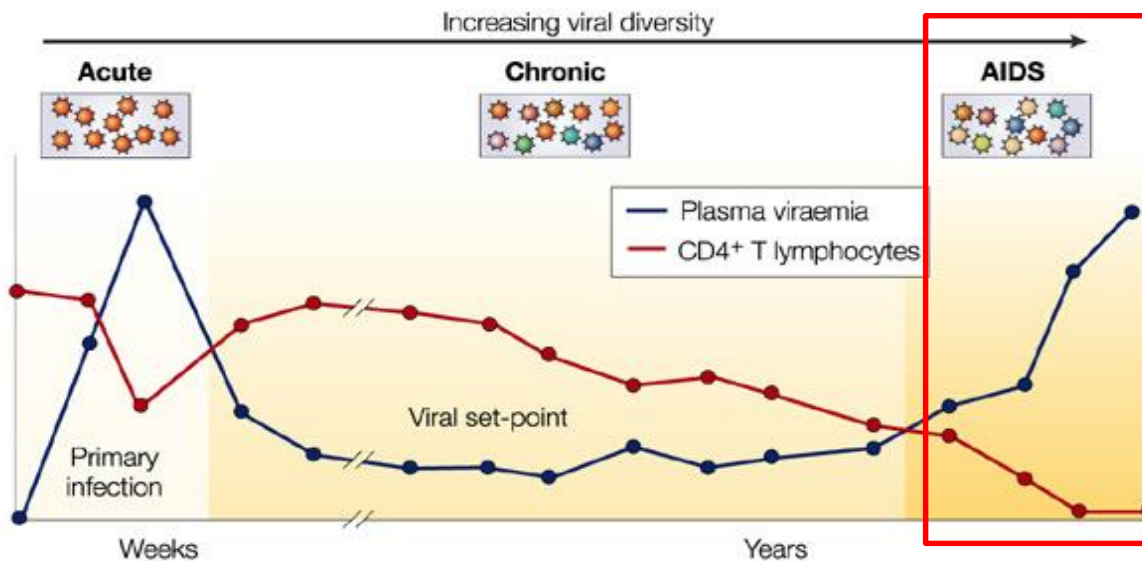
Primary HIV infection is followed by a long clinical **(latent)** period that lasts years, no symptoms occur.

Main symptoms of Acute HIV infection



Pathogenesis of AIDS/Clinical Aids :

- The primary target of HIV is the immune system, which is gradually destroyed.
- Clinically, HIV infection may appear "**latent**" for years. During this period there is ongoing immune system destruction but still enough of **the immune system remains intact** to provide immunity and prevent most infections.
- Eventually, when significant numbers of **CD4+ T lymphocytes have been destroyed** and **production of new CD4 cells cannot match destruction**, clinical AIDS will occur.
- The progression to clinical AIDS is also marked by the appearance of **syncytia-forming (SI)** variants of HIV in about half of HIV infected patients. These SI viral are associated with more rapid CD4+ cell decline.
- The development of signs and symptoms of AIDS typically parallels laboratory testing for CD4 lymphocytes. **When the CD4 lymphocyte count drops below 200/microliter, then the stage of clinical AIDS has been reached.** This is the point at which **the characteristic opportunistic infections and neoplasms of AIDS appear.** The CD4+T cells to CD8+T cells ratio is also greatly reduced, often to less than 1.0



Acquired Immunodeficiency Syndrome (AIDS)

- The stage of clinical AIDS is reached years after initial infection and is marked by the development of one or more of the typical opportunistic infections or neoplasms common to AIDS.
- Following are some of the more common complications seen with AIDS:
 - Infections e.g. pneumocystis jiroveci, CMV, mycobacteria, fungal etc.
 - Neoplasms
 - Miscellaneous e.g. lymphoid interstitial pneumonitis is a condition involving the lung that can be seen in AIDS in children.

AIDS related infections :

Pneumocystis jiroveci:

- Pneumocystis jiroveci (formerly carinii) **is the most frequent opportunistic infection seen with AIDS**. It commonly produces a **pulmonary infection**.
- Diagnosis is made histologically by finding the organisms in cytologic (bronchoalveolar lavage) or biopsy (transbronchial biopsy) material from lung.
- Add more info regarding soap bubble intra alveolar exudate, cyst like structures and silver stain.

Cytomegalovirus:

- Cytomegalovirus (CMV) infection is seen with AIDS. It causes **pneumonia** and it can also cause serious diseases in the **brain** (the patient may come with **dementia** and **encephalitis**) and gastrointestinal tract.
- It is also a common cause for retinitis and blindness in persons with AIDS.
- **Histologically, the nucleus is big.**

AIDS related infections (Cont.):

Mycobacterial infections:

- **Mycobacterium tuberculosis.**
- Mycobacterium avium complex (MAC) infection.
- **Definitive diagnosis** of mycobacterial disease is made by **culture and PCR**.

Fungal Infections:

- **Candidiasis** of the esophagus, trachea, bronchi, or lungs.
- **Cryptococcus neoformans** (produces **pneumonia and meningitis**), Histoplasma capsulatum, and Coccidioides immitis.

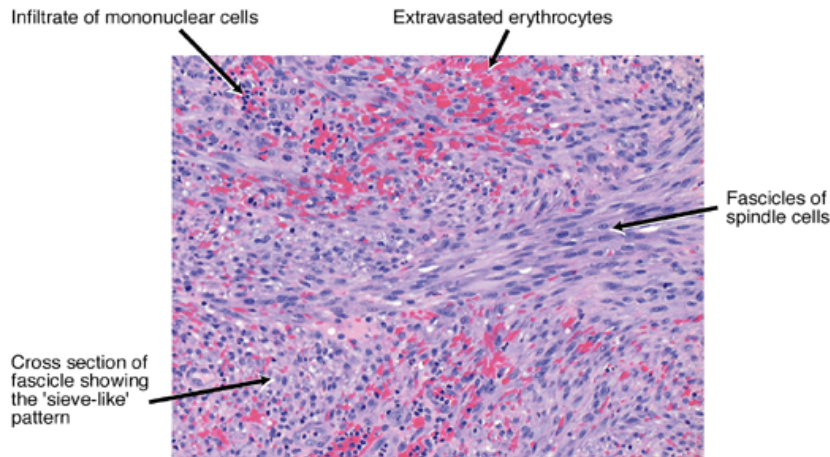
Other infections:

- Toxoplasmosis caused by Toxoplasma gondii is a protozoan parasite that most often leads to infection of the brain with AIDS.
- Herpes simplex infection in the mucosa.
- Aspergillosis especially in the lung.
- Cryptosporidium and Microsporidium produce voluminous watery diarrhea in patients with AIDS.
- Viral HIV encephalitis.
- Syphilis (primary, secondary and tertiary).

Malignant Neoplasms :

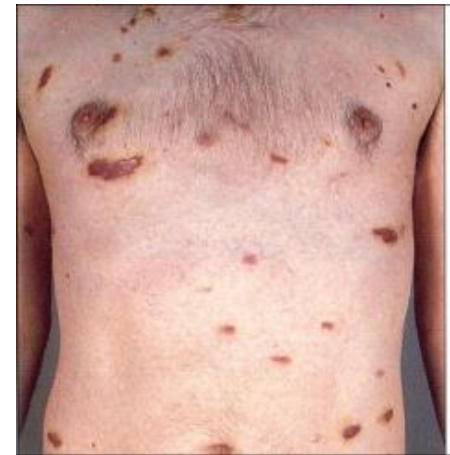
Kaposi Sarcoma:

- produces **reddish purple patches or nodules over the skin** and can be **diagnosed with skin biopsy**.
- Visceral organs can also be involved with Kaposi Sarcoma.
- It is a sarcoma of the **blood vessels**.
- **It is associated with HHV-8 (Human Herpes Virus 8)**. We have special markers, CD 31 and CD 34.
- **On histological examination** it shows **hyperplasia of pleomorphic spindle cells** and **areas of hemorrhage**.



Haematoxylin–Eosin stain of a Kaposi's sarcoma lesion

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Malignant Lymphomas:

- Are seen with AIDS. Commonly it is **B-cell Non Hodgkin Lymphoma**.
- They are typically of a high grade and often in the brain.
- They are very aggressive and respond **poorly** to therapy.

Thank You!

We hope you found this helpful and informative.

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