RETROVIRAL PATHOGENESIS & IMMUNOLOGY BRIEF

Human Immunodeficiency Virus (HIV): Pathogenesis, Latency & Support

How HIV targets CD4+ T-cells, rewrites host DNA, establishes dormant reservoirs, and responds to antiretroviral therapy.

> **Core Framework Summary:** HIV is an enveloped retrovirus that specifically infects the immune system's master coordinators—**CD4+ T-helper cells**. By converting its RNA into DNA and stitching itself directly into human chromosomes, HIV creates permanent viral factories and dormant reservoirs that require targeted antiretroviral therapy (ART) to suppress completely.

1. How HIV Hijacks Immune Cells

HIV targets cells displaying the **CD4 receptor** and coreceptors (CCR5 or CXCR4) on their surface:

- **Step 1 — Docking & Fusion:** Viral **gp120** spikes lock onto CD4 and coreceptors, allowing **gp41** to fuse the viral envelope into the host cell membrane.
- **Step 2 — Reverse Transcription:** The viral enzyme *reverse transcriptase* converts HIV RNA into DNA. Because this enzyme lacks proofreading, it mutates rapidly, generating diverse viral quasispecies.
- **Step 3 — Integration & Latency:** The viral *integrase* enzyme splices HIV DNA into host chromosomes. If the T-cell returns to a resting state, the virus becomes dormant—forming a **latent reservoir** hidden from immune surveillance.
- **Step 4 — Assembly & Budding:** Active host cells manufacture viral proteins, which are cut to size by the *protease* enzyme before budding out to infect neighboring cells.

2. The Three Clinical Stages of Untreated HIV

Stage	Biological Activity & Mechanism	Clinical Profile & Symptoms
1. Acute Infection (2–4 weeks post-exposure)	Explosive viral replication; massive depletion of CD4+ T-cells in gut-associated lymphoid tissue (GALT).	Flu- or mono-like illness (fever, fatigue, swollen lymph nodes, rash); viral load peaks to millions of copies/mL.
2. Clinical Latency (Years to decades)	Immune system establishes a viral set point; persistent low-level replication slowly erodes CD4+ reserves.	Often asymptomatic for years while viral activity quietly degrades immune architecture.
3. AIDS Stage (Advanced depletion)	CD4+ T-cell count drops below 200 cells/mm^3; profound immune failure allows opportunistic infections.	Vulnerability to opportunistic pathogens (Pneumocystis, Candida, Toxoplasma, CMV) and malignancies.

3. Modern Treatment (ART) & Cellular Support

While **antiretroviral therapy (ART)** is strictly required to suppress viral replication to undetectable levels (U=U: Undetectable = Untransmittable), targeted nutritional support aids recovery:

- **Antiretroviral Combinations:** Daily pills or long-acting injections combining reverse transcriptase inhibitors, integrase inhibitors, and protease inhibitors.
- **Gut Barrier & Microbiome Repair:** L-glutamine, zinc carnosine, and probiotics to restore gut mucosal integrity where early CD4+ depletion occurs.
- **Mitochondrial & Glutathione Support:** N-acetylcysteine (NAC) and selenium to replenish glutathione, alongside CoQ10 and magnesium to support cellular energy.