AIDS - Pathology

Q) pathogenesis? etiopath?
Q) pathology of organ involved
Q) four investigations to be done?
Q) definition.
Q) lab diagnosis.
Q) opportunistic infection in AIDS.
Q) HIV associated change in immune function.
Q) pathogenesis of CNS lesion in HIV. — CNS - CF in Question → 2nd AIDS Question is kinda complicated... read it once and find answer
Neck stiffness + Kernig (+)
Q) prob. Cause of death?

! in chapter Q. P

definition

AIDS is a disease caused by the retrovirus - Human Immunodeficiency virus (HIV)
Characterized by profound immunosuppression and to that leads to opportunistic infections, secondary neoplasms and neurological manifestations.

- Infection and depletion of CD4+ T cells

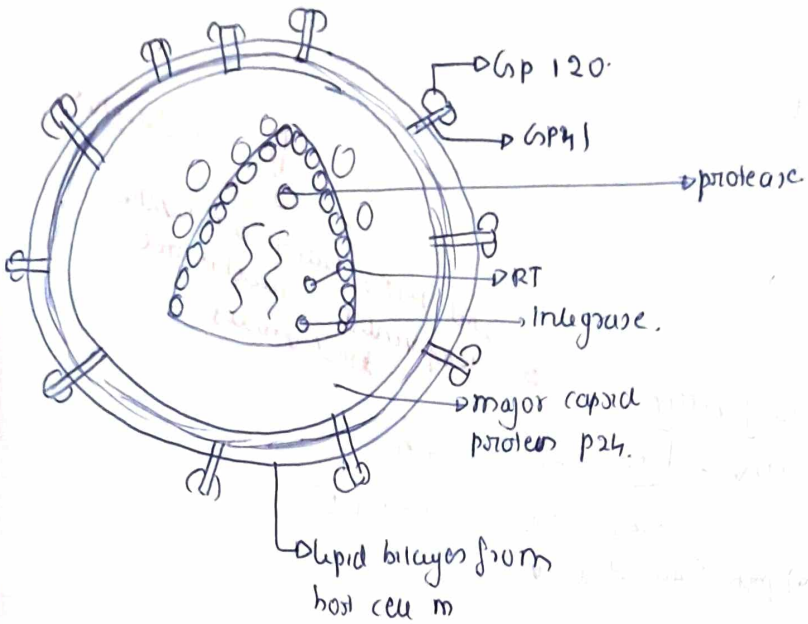
Etiopathogenesis → also includes modes of transmission

- HIV is a non-transforming human retrovirus belonging to the Lentivirus family.
- Retroviruses (RNA virus) —reverse transcriptase→ DNA copy of RNA genome.

{HIV-1 & 2 - 2 genetically different but related.}

Transmission → sexual ✓, parenteral ✓, vertical. ✓ } Expand it ok?

Structure.



viral genomics

GAG, POL, ENV genese → encode mature proteins.

GAG → P17, P24, P7, P6.

POL → Enzymes - P, I, RT

ENV → gp 160 → gp120, gp41

Pathogenesis

- Major target of HIV → Immune System
- Next most Imp target → CNS

* profound Immunodeficiency primarily affecting (CMI) is hallmark of AIDS.

↓ ↓ ↓

- due to infection and loss of CD4+ 'T' cells & impairment of function of surviving CD4+ 'T' cells.

✓ other cells involved in HIV.

✓ macrophage
✓ dendritic cells.

HIV enters via mucosal Tissue and blood

↓

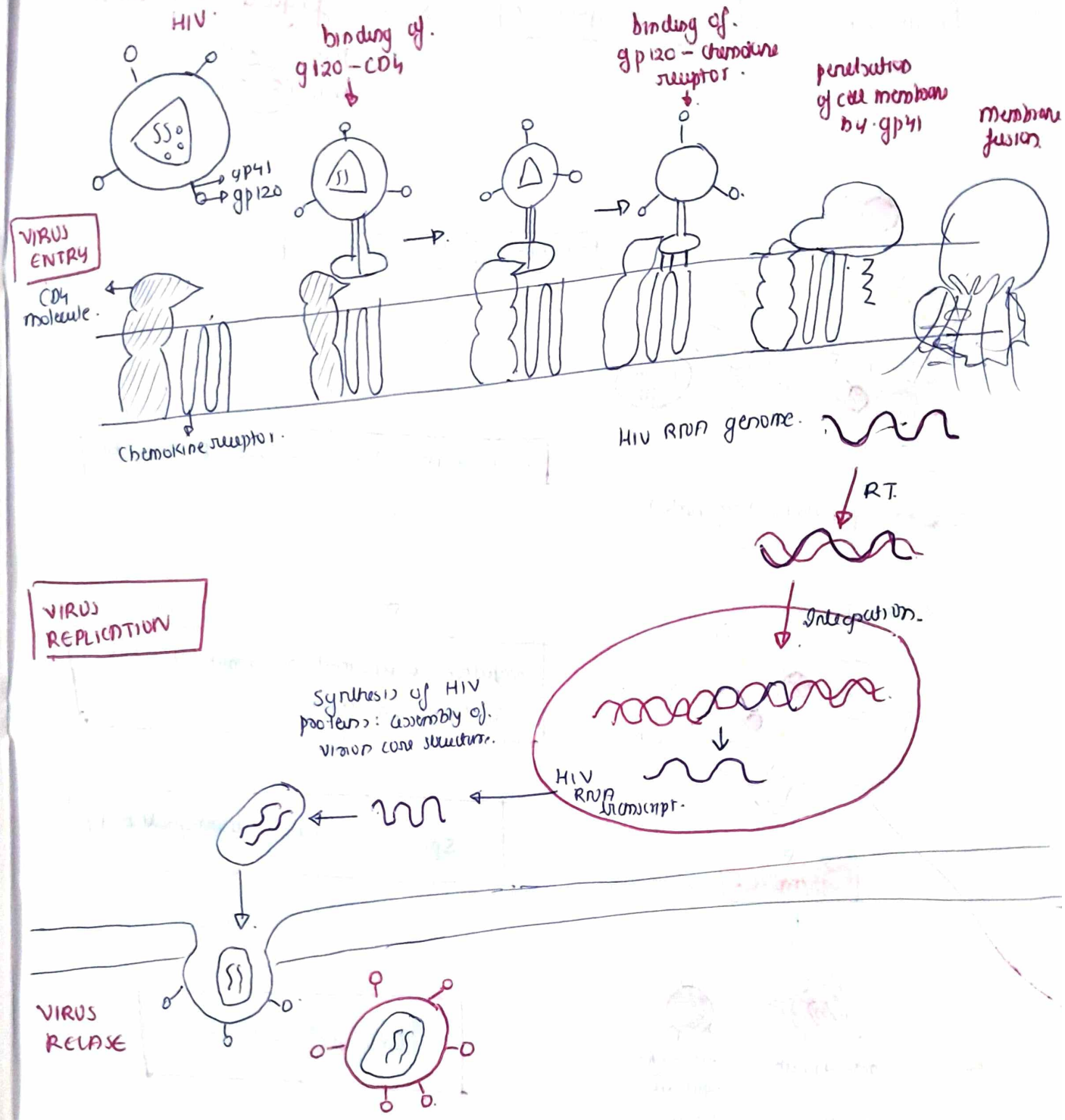
1st Infects T cells as well as DC's & macrophages

↓

Infection established in lymphoid tissue where virus remains latent for long periods.

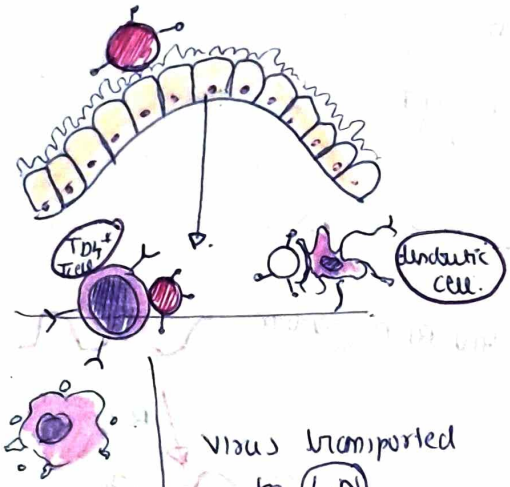
↓ ↓

active viral replication is associated with more infection of cells and progression to AIDS.


HIV
binding of gp120 – CD4
binding of gp120 – chemokine receptor
penetration of cell membrane by gp41
membrane fusion
gp41
gp120
VIRUS ENTRY
CD4 molecule
Chemokine receptor
HIV RNA genome
RT
VIRUS REPLICATION
integration
Synthesis of HIV proteins: assembly of virion core structure
HIV RNA transcript
VIRUS RELEASE

Pathogenesis & Disease progression

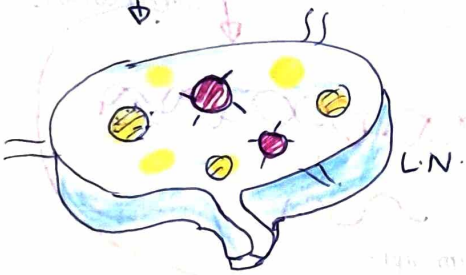
✓ figure in Robbins. page - 250 also (S·G)



Injection of mucosal tissues.

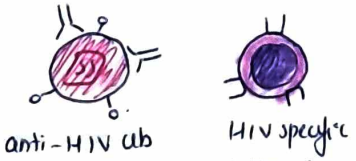
death of mucosal memory CD4+ T cells

Infection established in lymphoid tissue. eg: lymph node.



Spread of infection throughout body.

viremia.



Immune response.

partial control of viral replication.

Establishment of chronic infection; virus concentrated in lymphoid tissues; low level.

Clinical latency.

other microbial infections if, cytokines.

Increased viral replication

AIDS

destruction of lymphoid tissues: depletion of CD4+ T cells.

Explanation

Primary Infection (0-2 w)

- HIV enters via mucosal surfaces,
  ↓
  infect memory CD4+ T cells. (CCR5+)
  in mucosal lymphoid tissue (esp-GALT)
  ↓
  massive CD4+ T cell death,
  mucosal barrier damage,
  ↓
  microbes cross into blood → microbial translocation.

Viral dissemination & Acute Retroviral Syndrome within days.

- Virus captured by dendritic cells, are carried to L.N.
  ↓
  infects CD4+ T cells, Macrophages, dendritic cells present in L.N.
  → it replicates inside all these cells
- Results in viremia → systemic spread.
- Host mounts immune response:
  CD8+ cytotoxic T cells, antibodies, seroconversion
  ↓
  viral load reduces (but not eradicated)
- Acute retroviral sx - flu like sx (fever, sore throat, malaise, myalgia, weightloss, fatigue)
  occurs 3-6 w after infection

Chronic Phase (Clinical latency)

- Virus hides in LN.
- Continuous replication of virus in Lymphoid tissue
  ↓
  gradual CD4+ T cell depletion
- Initial Compensation via new T cell production.
  → But slow decline in CD4+ count over years.
  → Asymptomatic but yet opportunistic infections,

Progressive Immune decline

- CD4+ count drops, viral load increases.
- Increased susceptibility to opportunistic infections.
  (eg: thrush, TB)
- ~~Minor infections occur even in asymptomatic phase.~~

AIDS

- CD4+ < 200 cell / uL.
  severe immunosuppression.
  Chronic diarrhea, weight loss, fever > 1M., gen. lymphadenopathy
- Risk of opportunistic infections, neoplasm, neurologic disease

① p° infection
② Acute retroviral sx.
③ Clinical latency
④ AIDS.

Gen lymphadenopathy

SP

- IN generalized Lymphadenopathy, pathology of organ involved. Question.

Stages

Gen. Lymphadenopathy

① follicular hyperplasia. - overstimulated B cells proliferate in germinal centres.

- prominent follicular hyperplasia.
- enlarge, confluent germinal centres
- Attenuated mantle zone.
- Germinal centre impinging on interfollicular T cell areas.
- Tingible body macrophages, Warthin–Finkeldey giant cell may be present

② Follicular Involution - (in chronic phase)

- fragmentation and regression of germinal centres.
- reduction in follicle no. & size.
- ↑ plasma cells - interfollicular infiltration
- fibrosis.

in AIDS.

③ Lymphoid depletion - Burnt out nodes.

- marked lymphocyte depletion.
- follicles absent or hyalinized.
- disruption of follicular dendritic cell network.
- fibrosis.
- atrophic, small lymph nodes with effaced architecture

List Investigations

Lab diagnosis

① ELISA → screening ✓
anti-gp 120 detection ✗

② western blot → specific ✓ confirmatory ✓

③ Direct detection of virus:
→ p24 ag capture assay ✓
→ RT-PCR
→ DNA-PCR.

④ CD4+ T cell count.
< 200 ⇒ AIDS ✓

⑤ Lymph node biopsy.

⑥ detect opportunistic infections.

db
In AIDS, do we see hyperplasia/ lymphadenopathy
Burnt out nodes?

dB

Opportunistic Infections in AIDS.

AIDS defining opportunistic infections and neoplasms

protozoal & Helminthic infections:

- Cryptosporidiosis
- pneumocystosis. {pneumonia}.
- Toxoplasmosis {pneum or CNS infection}.

Fungal.

- Candidiasis. - esoph, tracheal, pulmonary
- Cryptococcosis
- Coccidiodomycosis.
- Histoplasmosis.

Bacterial.

mycobacteriosis. - atypical - M. avium.

TB.

.Nocardiosis - pneum, menin,

- salmonella.

Viral

CMV - pulm, Gast, retinitis, CNS inf.

HSV →

Varicella zoster

↓

Neoplasms

Kaposi sarcoma. (Kaposi sarcoma herpes virus) (m/c).

primary lymphoma of brain. - NHB cell Lymphoma. (m/c).
(EBV)

Invasive cancer of uterine cervix. (HPV).

anal carcinoma (HPV).

m/c opportunistic infection in HIV.

- Globally → M. TB
- India → M. TB
- AIDS pneumonia → pneumocystic pneumonia.

- m/c fungal infection in AIDS – Candidiasis
- m/c cancer – NHL.
- m/c lymphoma affecting organ: Brain.