

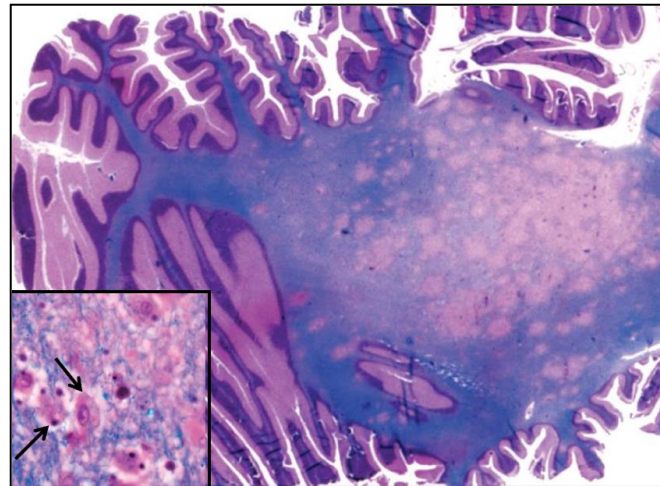


- Opportunistic infections occur in HIV-positive patients and can be lethal when the CD4 count falls below 200 cells/mm³ and the CD4/CD8 ration is less than 1 (severe immunosuppression).
- If the CD4 count is >500 cells/mm³, patients will be asymptomatic but might have persistent generalized lymphadenopathy.

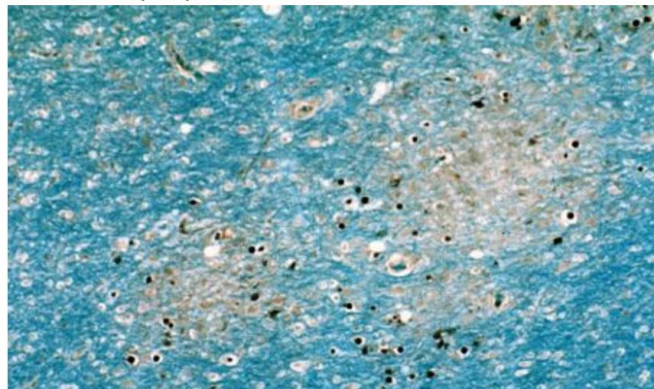
HIV-related CNS manifestations

- CNS dysfunction is seen in 1/3 of HIV-positive patients while CNS pathology is observed in ¾ of cases during autopsy (التشريح).
- HIV virus enters the CNS via macrophages (which possess CCR5 chemokine receptor that will bind to gp120 present on the surface of the viral particle and mediating fusion of the virus with the host cell) → microglial cells.
- **Aseptic HIV-1 meningitis (not caused by an infection):**
 - Appearing 1-2 weeks after seroconversion (appearance of antibodies in patient's blood). This occurs only in 10% of HIV-positive patients.
 - **Clinical manifestations:** mild lymphocytic meningitis, perivascular infiltration, mild myelin loss in hemispheres.
- **HIV-1 meningoencephalitis:**
 - AIDS dementia complex (dementia is marked by: memory disorders, personality changes and impaired reasoning).
 - This is caused by cytokines which are released from infected microglial cells resulting in neuronal injury.
- **Vacuolar myelopathy (اعتلال النخاع الشوكي):**
 - Lesions involving the spinal cord tracts (resembling subacute combined degeneration of vitamin B12 deficiency).
- **The three conditions described above are HIV-related CNS manifestations caused by HIV virus itself. There other viruses which can cause CNS manifestations:**

- **Encephalitis:** caused by cytomegalovirus (CMV), herpes simplex virus (HSV) and varicella.
- **Progressive Multifocal leukoencephalopathy (PML):** this condition results from infection with JC virus (reactivation of this latent virus in immunosuppressed patients).
 - ✓ Insidious onset (على نحو تدريجي) and steady progression of symptoms which include: behavioral, speech, cognitive, motor and visual impairment.
 - ✓ **Morphology:** irregular, poorly defined areas of demyelination in hemispheres and cerebellar white matter, which become confluent in places (figure). There are viral inclusions in the nuclei of oligodendrocytes (arrows in the figure).



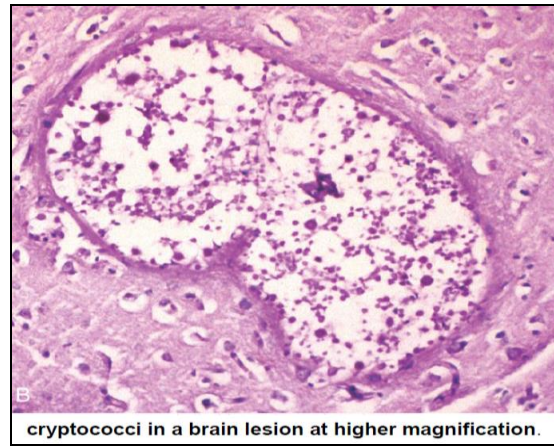
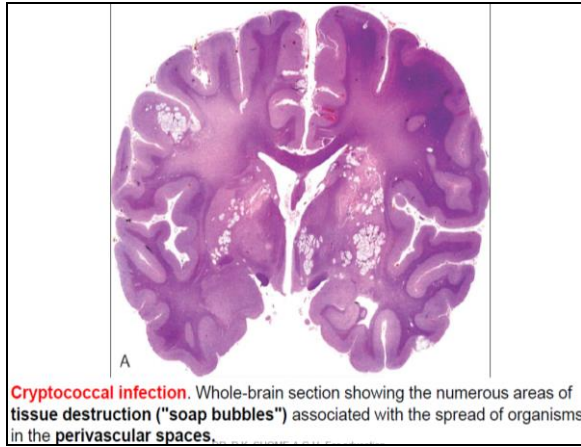
Enlarged oligodendrocyte nuclei stained by immunohistochemistry for viral antigens surround an area of early myelin loss.



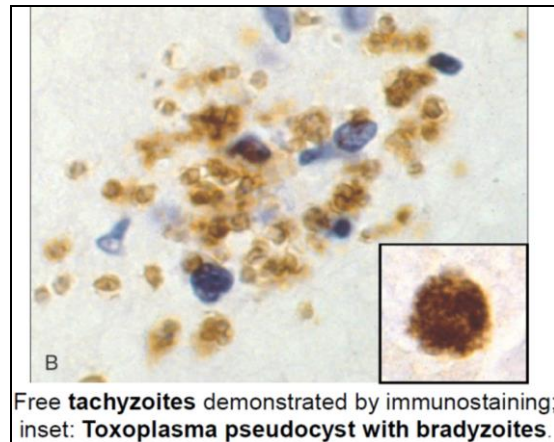
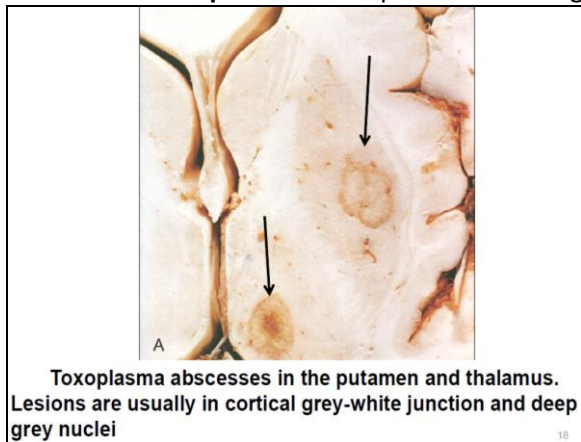


- **CNS manifestations caused by fungal infections and protozoa:**

- **Cryptococcal meningitis (5-8% of all infections):** it is a fungal infection.



- **Toxoplasma:** it is a protozoa causing brain abscess.

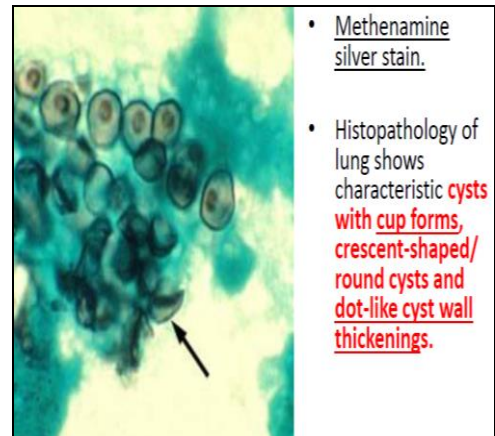
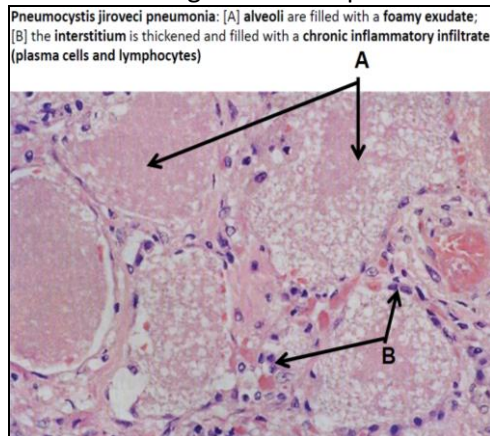


Respiratory system

- **Opportunistic infections:**

- **Pneumocystis jiroveci (carinii) pneumonia:**

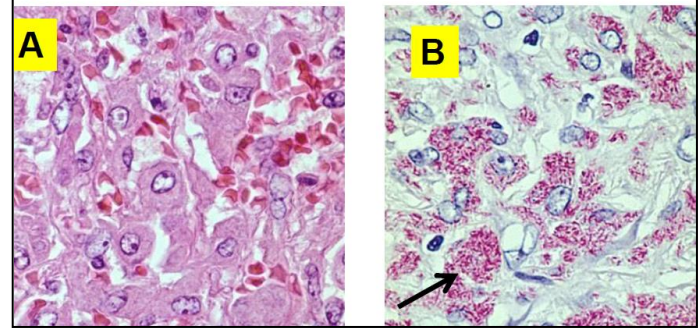
- ✓ It is a fungal infection.
- ✓ Seen in immune-compromised patients.
- ✓ Variable presentation: minimal respiratory symptoms to progressive respiratory failure.
- ✓ Diagnosis: sputum taken by bronchioalveolar lavage (BAL) and examined under the microscope (using Giemsa or silver stain) or by direct antigen detection immunofluorescence.
- ✓ Histology: alveoli are filled with a foamy exudates (figure: A) and there is interstitial infiltrate of plasma cells and lymphocytes (figure: B). The organisms are seen as bubbles in a proteinaceous background (in H&E stain). With silver stain (figure), the organisms are seen as:
 - * Indented (مسنن أو ممزق), crescent-shaped, cup-shaped, round cysts (size: 5µm).
 - * Focal thick region in the capsule.





- **Cytomegalovirus (CMV).**
- **Mycobacterium avium complex.**
 - ✓ Presented with disseminated disease and systemic symptoms (fever, night sweats & weight loss).
 - ✓ There is hepatosplenomegaly and lymphadenopathy indicating the involvement of mononuclear phagocyte system.
 - ✓ GI symptoms include: diarrhea and malabsorption.
 - ✓ Pulmonary involvement: indistinguishable from tuberculosis in AIDS patients.
 - ✓ Infection with this organism occurs late in the course of the disease, when CD4 counts are very low (below 50 cells/mm³), hence tissue examination usually does not reveal granulomas.
 - ✓ Foamy histiocytes stuffed with atypical mycobacteria are typically seen.

M. avium complex disease: [A] Histiocytes in *Mycobacterium avium-intracellulare* infection in an AIDS patient (HE). Note lack of typical granuloma. [B] Acid-fast staining of numerous bacilli within macrophages



- **Polymicrobial pneumonia.**

Gastrointestinal tract

- Diarrhea in >75% with > 1 organism.
- **Protozoa:** *Giardia lamblia*, *Cryptosporidium parvum*, *Isospora belli*.
- **Bacteria:** *Mycobacterium avium* complex & *Salmonella typhi*.
- **Virus:** cytomegalovirus (occurring when CD4 is less than 50 cells/mm³ and causing watery diarrhea).

Hepatitis C virus infection

- Found in more than 25% of deaths and seen especially among IV drug abusers.
- HIV and HCV may accelerate the course of the disease with each other.

Skin manifestations (infections)

- **Bacterial:** *S.aureus*: bullous impetigo, ecthyma, folliculitis.
- **Viral:** *Molluscum contagiosum*, HPV; chronic mucocutaneous herpes simplex; *Varicella zoster*.
- **Parasitic:** scabies.
- **Fungal:** candidiasis

AIDS-defining neoplasms

- **Kaposi sarcoma (HHV-8):**
 - A malignant tumor of the vascular endothelial cells.
 - Caused by Human Herpes Virus-8 (HHV-8).
 - Seen in Africans and people in Mediterranean region.
 - More common in homosexuals compared to drug abusers.
 - This tumor has multicentric origin.
 - Evolve through 3 stages: patch → plaque → nodule (cutaneous and visceral).
 - **Morphology (figure):** formation of endothelium-lined channels and vascular spaces admixed with bundle of spindle cells. There is extravasated red cells, hemosiderin pigment and light inflammatory infiltrate of lymphocytes and plasma cells.

Kaposi sarcoma. A. The dermis is expanded by a solid tumor nodule (H&E stain). B. Fascicles of relatively monomorphic spindled cells, with slit-like vascular channels containing erythrocytes (H&E stain). C. The nuclei of the tumor cells demonstrate immunoreactivity for HHV-8 (immunohistochemical stain).

