General Medicine

Volume - 3

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//ME801SS-SAP

Volume - 3

Infectious Diseases

Cardiovascular Disorders

Hematology

----- Active space -----

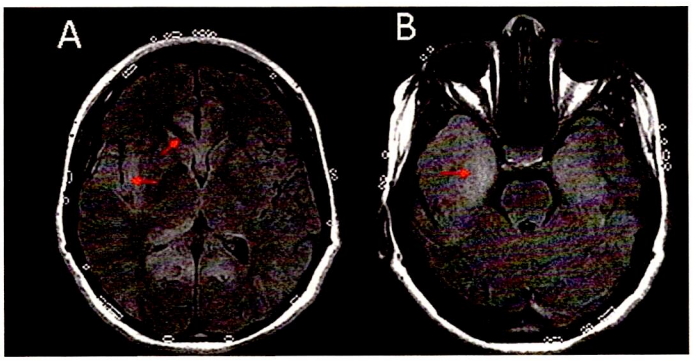
Viral encephalitis

00:09:33

- m/c cause of encephalitis : Infectious. HSV-1 > Arboviruses.
- 2nd m/c : Autoimmune.
- 3rd m/c : Paraneoplastic.

Clinical features :

- Acute onset
- Behavorial changes and seizures within 24 hrs of febrile illness.
- Reduction of consciousness, confusion, disorientation, lethargy, drowsiness.
- Hallucination, anosmia, aphasia, frank psychosis, focal neurological deficit



MRI : T2 weighted hyperintensities.

- Hemorrhagic necrosis of b/l inferior medial temporal lobe and medio orbital part of frontal lobe is very suggestive of HSV
- Japanese encephalitis : non specific hyperintensities.

CSF shows :

- Lymphocytic pleocytosis. (<500 u/L)
- Mild elevation of proteins.
- Normal glucose levels.
- CSF PCR to be done for HSV & japanese encephalitis

EEG :

PLED (Periodic Lateralised Epileptiform Discharge) is very suggestive.

Management : IV acyclovir 10 mg/kg TDS to be given.

----- Active space -----

CNS INFECTION : ACUTE BACTERIAL MENINGITIS

Meningitis

00:01:36

- Acute bacterial meningitis (m/c).

Subarachnoid space :

- Contains CSF :
  a. < 5cells/mL.
  b. No neutrophils.
  c. No globulins, complements.
- It is located between pia mater & arachnoid mater.
- If purulent infection (+) → No protective mechanism in CSF normally → → multiplication of organism → Reaches sufficient number → Triggers severe inflammatory response → Inflammation of meninges & subarachnoid space called as meningitis.
- The inflammation can extend to brain parenchyma : meningo-encephalitis.
- Products of organism triggers mediators for inflammatory response.

Organisms :

- Strep pneumoniae (m/c).
- Neisseria meningitides (2nd m/c).
- Group B Streptococci.
- Listeria monocytogenes.
- H influenza type B.

Patient group	Bacterial pathogen
< 1 month	(Gram negative) Enterobacteriaceae > Strep agalactiae > Listeria.
1-23 months	Strep agalactiae, E.coli, H. influenza, Strep. pneumoniae, N. meningitidis.
2-50 yrs	Strep. pneumoniae, N. meningitidis
Patient group	Bacterial Pathogen
> 50 yrs	L. monocytogenes, Strep. pneumoniae, N. meningitidis, Group B Streptococci.

----- Active space -----

Immuno compromised	Strep. pneumoniae (more common) > L. monocytogenes > P. aeruginosa
Post craniotomy, Head trauma, CSF rhinorrhea	Gram Negative Bacteria especially Pseudomonas.
Post shunting or post ommaya reservoir	S.aureus > Coagulase-negative staphylococci (CoNS)

Meningococci :

- Gram negative diplococci.
- Catalase & oxidase positive, ferments glucose & maltose.
- Half moon shaped, capsulated, no plasmid.
- Strict aerobes.
- Selective media : Modified Thayer Martin Media/Polyethanol sulfate.
- Epidemics : m/c strain in India : Group B streptococcus (no vaccine against it).
- Antigenicity :
  1. Capsular polysaccharide : Single most important pathogenic factors.
  2. Lipo oligosaccharide endotoxin causes endothelial Injury → increases vascular permeability → predispose to capillary leak syndrome.

Meningococci is the causative organism in :

- C5b-C9 deficiency.
- Hypogammaglobulinemia.
- Hyposplenism.
- Water-House Friedrichsen Syndrome : Large purpuric rash/shock /adrenal hemorrhage.
- Carrier state is seen in 70 to 90 %.
- m/c mode of spread : via Nasopharynx.
- Penicillin : DOC for treatment/prophylaxis.

Pneumococci

00:15:11

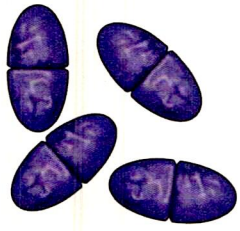
- Gram positive.
- Catalase negative (Alpha hemolytic).
- Fastidious.
- Flame shaped or lanceolate (chains).
- Draughtsman's /Carrom Coin appearance : Greenish coloured on blood agar due to partial hemolysis.

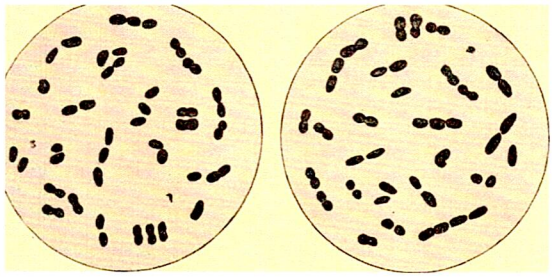
----- Active space -----

- 3 factors to differentiate pneumococci & S.viridans :
  - Bile soluble.
  - Optochin susceptible.
  - Inulin susceptible.

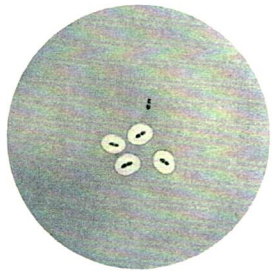
Antigenicity :

- Capsular polysaccharide.
- Pneumolysin.
- IgA1.
- Abnormal protein which precipitates with somatic C antigen of pneumococci : C Reactive Protein.





Lanceolate diplococci



Quellung's reaction

- Rapid identification is by Quellung reaction.
- Invasion of nasopharynx is seen only with serotype 3.
- Pneumolysin is a cytolytic toxin which forms pores in cell membrane.

Risk factors for pneumococci :

- Elderly.
- Diabetes mellitus.
- Alcohol.
- Ear infection/sinusitis.
- Sickle cell disease.
- Celiac disease.
- HIV.
- Cochlear implants.
- CSF leak.

Note :

- CSF leak with rhinorrhea : Gram negative organism is more common.
- Listeria (seen in extremes of age) → route of spread : Contaminated food ingestion.
- Pneumococci & meningococci are sensitive to penicillin.

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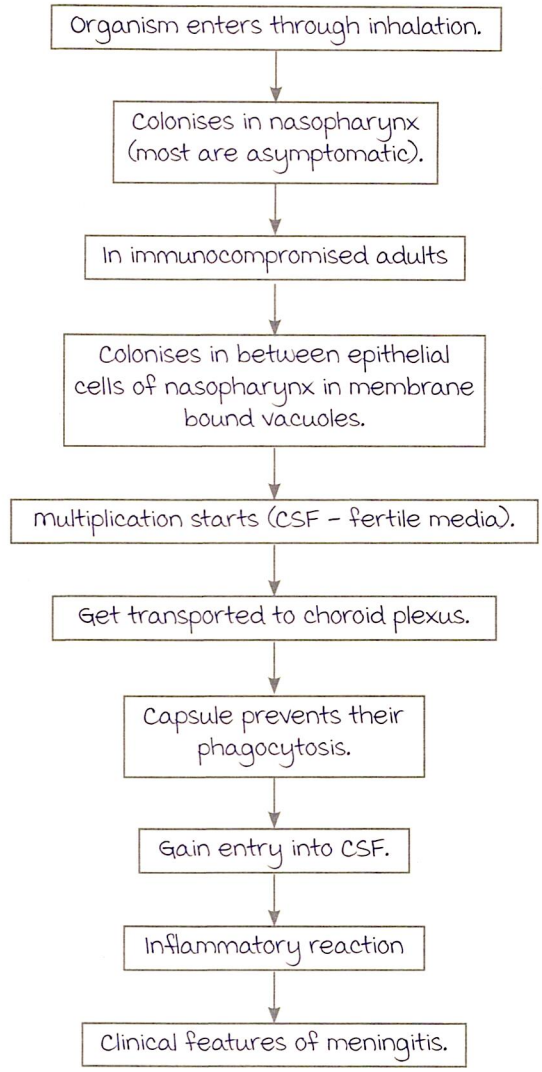
Pathophysiology :



Combination of interstitial, cytotoxic and vasogenic edema.

ICT increase is fatal.

1. Vasogenic edema : Inflammatory response to bacterial products → cytokines released → Alter blood brain barrier permeability → leakage of plasma protein into CSF → vasogenic edema. Steroids given because of it.
2. Interstitial edema : Leakage of plasma protein into CSF → exudate in subarachnoid space → obstruction to outflow & resorption of CSF → interstitial edema.
3. Cytotoxic edema : Cytokines will also activate WBCs → migrate into CSF → cytotoxic edema. Mannitol is given.

Clinical presentation

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- Acute in onset.
- High grade fever of short history (1 day) with lethargy /drowsiness.
- Classical triad : Altered sensorium + fever+ neck stiffness (in 24 hours).
- Headache is m/c symptom, severe headache : Frontal tightness, feels like compression.
- In children, tiredness→irritable→lethargic →high grade fever with intermittent episodes of vomiting.

O/E :

Lethargic, drowsy.

Neck stiffness.

- Kernig's sign : Patient in supine position with their knee & hips flexed. This test is positive if there is pain on passive extension of the knee.
- Brudzinski's sign : Patient in supine position and passively flex their neck.This test is positive if this manoeuvre causes flexion of the hip and knee.
- Lymphadenopathy.
- Papilledema.
- Rash → meningitis usually Neisseria (petechiae).
- Focal neurological signs/focal seizures → encephalopathy.

Complicated vs uncomplicated meningitis :

Combination of interstitial, cytotoxic and vasogenic edema → raised ICT (Intra cranial Tension) → impending herniation → herniation → coning & death.

Uncomplicated meningitis :	Complicated meningitis :
• Raised ICT + no impending herniation. • Lumbar puncture is advised.	• Raised ICT + impending herniation present. • Lumbar puncture is contraindicated.

Analyze patient for :

1. Features of Cushing's reflex : HTN , bradycardia → s/o raised ICT.
2. Uncal herniation : 3rd nerve involved. Assess pupillary reflex → latent reaction → impending herniation.

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Before LP Imaging is needed in (C/I to lumbar puncture) :

- Focal neurological signs.
- Immunocompromised adult.
- Recent onset seizures.
- Impaired consciousness.
- Severe hypertension & bradycardia with signs of impending herniation.
- Papilledema :

  s/o raised ICT.

  But it is not an absolute contraindication unless very high ICT.

MRI :

- Confirms meningitis.
- Diffuse meningeal enhancement, T2 flair as blood brain barrier is lost.

In meningococcal infection :

- Petechiae and palpable purpura +.
- Concurrent arthritis +.

Listeria :

- Causes brainstem meningitis/meningoencephalitis.
- Seizures with ataxia/cranial nerve palsy.

Cerebral infarction :

- Can occur due to : End arteritis : s/o TB.
- Vasculitis : s/o pneumococci.

CSF abnormalities

00:41:44

CSF Values in a normal adult :

- Colourless.
- Specific gravity : 1.006-1.008.
- Pressure : 50-180mm H_2O.
- Glucose : 40-70mg/dl.
- CSF/serum glucose > 0.6 .
- Protein : 15-45mg/dl.
- LDH : 10 % OF serum levels.
- pH : 7.28 - 7.32.
- Cl^- : 115 - 130meq/L.

- Cell : < 5 WBCs.
- Even one Polymorphonuclear leukocytes : Abnormal.

----- Active space -----

CSF abnormalities in bacterial meningitis	
Opening pressure	180-350 mmH_2O
White blood cells	10/uL to 10,000/uL; neutrophils predominate
Red blood cells	Absent in non traumatic tap
CSF abnormalities in bacterial meningitis	
Glucose	< 2.2 mmol/L (< 40 mg/dL) (very low glucose)
CSF/serum glucose	< 0.4
Protein	> 0.45 g/L (> 45 mg/dL)
Gram's stain	Positive in > 60 %
Culture	Positive in > 80 %
Latex agglutination	No role.
Limulus lysate	No role.
PCR	Detects bacterial DNA

PCR : Polymerase chain reaction.
CSF : Cerebrospinal fluid.

Opening pressure :

>350 mmHg → Subacute meningitis → TB meningitis/ fungal meningitis.

Features	Viral	Bacterial	Tuber-culous	Fungal	Normal
Opening Pressure	N/High (150 -200)	High	High	Very high	50-150
Colour	Clear	Cloudy	Cloudy/Yellow	Clear/Cloudy	Clear
Cells/mm3	N-High (100-300)	Very high (1000-50,000)	Slight increase (25-500)	< 50	< 5
Type of cells	Lymp-hocytes	Neutro-phils	Lymp-hocytes	Lymp-hocytes	Lymp-hocytes
CSF/Plasma Glucose Ratio	Normal	Low (<0.4)	Very low (<30%)	N-Low	66 %
Protein (g/dl)	N-High (0.5-1)	High (>1) (100mg/dl)	High-Very High (1-5)	N-High	< 0.5

Treatment :

- Empirical treatment within 60 minutes of hospitalisation.
- Empirical therapy :

----- Active space -----

In adults :

- Penicillin is sensitive to pneumococci & meningococci.
- 2g IV BD of Ceftriaxone.

In Penicillin resistant Streptococcus pneumoniae (PRSP) :

- Ceftriaxone + Vancomycin 15mg/kg IV BD.
- PRSP not reported in India.

> 50yrs :

- Ceftriaxone + Vancomycin 15mg/kg IV BD +
- Ampicillin (for Listeria) 2g IV Q4h, for 14 days.
- IF ENT source → Metrogyl can be added.
- Best possible outcome : 2 to 4 days improves.

Monitor (daily) :

- Pulse rate, blood pressure, Pupillary reaction, fundus examination.
- After 2-3 days → altered sensorium → r/o SIADH (Syndrome of Inappropriate Secretion of AntiDiuretic Hormone) → Hyponatremia.

Steroids :

- Beneficial in vasogenic edema (In pneumococcal & meningococcal meningitis).
- Dexamethasone 10mg IV Q6h for 4 days.
- Given 20 minutes before antibiotics administration.

ACUTE VS SUBACUTE MENINGITIS

----- Active space -----

Subacute meningitis :

Intracranial involvement :

1. TB meningo-enchephalitis with necrotizing vascular endarteritis (obliterative vasculitis).
2. Tuberculoma : Space occupying lesion (SOL).

Spinal involvement :

1. Spinal myelitis (acute transverse myelitis).
2. Compressive myelopathy (extramedullary)

Tubercular meningitis 00:02:30

- Subacute meningoencephalitis.
- Prodrome : Fever, lethargy, weight loss, myalgia (2 weeks).
- Transition period after 2 weeks : Headache is a prominent feature, along with neck stiffness.
- Maybe associated with seizures and personality changes by 3 weeks.
- By 4TH week : Compressive myelopathy.

Pathogenesis :

- Subependymal tubercles progression and rupture into subarachnoid space
- Inflammatory changes at base of brain : Basal fibrous exudates encase cranial nerves and penetrating vessels leading to CN palsies and proliferative basal arachnoiditis.
- In 17 -40% cases, cranial nerve involvement is seen, most commonly affecting the 2nd, 3rd, 4th & 6th cranial nerves.

Diagnostic triad :

1. Presence of basal exudates.
2. Infarcts (necrotizing arteritis).
3. Hydrocephalus

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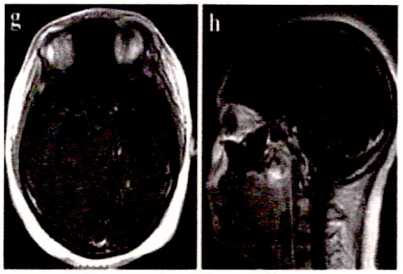
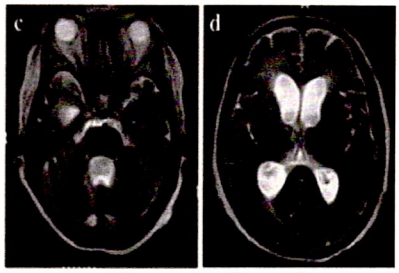
Stroke with meningitis D/D :

- Brainstem issues with Listeria.
- Endarteritis with TB
- Vasculitis issues with pneumococci.



TB meningitis with meningeal enhancement



TB meningitis with hydrocephalus

Subacute febrile illness :

- Prodromal phase : Malaise /headache/low grade fever/personality change
- Meningitic phase : Meningism/headache
- Paralytic phase.

CSF analysis :

- Opening pressure : Very high (350-500 mm H_2O).
- CSF protein : 100-500mg/dl.
- CSF/ s. glucose : 0.4-0.6
- Cells : 100 to 500 cells/micro liter, lymphocytes.

	Acute		Sub-acute	
	Bacteria	Viral	TB	Fungal
	Acute onset	Theory of fever returns → meningitis	Prodrome phase, meningeal phase, paralytic phase	Immuno-compromised host
CSF pressure	High (350 mm H2O)	High (< 350 mm H2O)	Very high	very high (> 500 mm H2O)
Protein (mg/dl)	High (> 100)	< 100	Very high (100 - 500)	High.
CSF/ Serum glucose	< 0.4	Normal	0.4 - 0.6	Normal/ low
Cells /mm3	1000-50,000 neutrophils	< 500 lymphocytes	100 - 500 lymphocytes	< 50 lymphocytes
MRI findings	-	meningeal enhancement	• Basal arachnoiditis. • Hydrocephalus • Infarcts.	-

----- Active space -----

- Slowly progressive dementia
- Early paradox and therapeutic paradox in CSF analysis: Lymphocytes are predominant in TB meningitis, but In first 10 days : Neutrophils(early paradox). 10 days after starting Rx : Neutrophils(therapeutic paradox). Elderly : Acellular can also be there
- ADA levels >10
- CSF GeneXpert can be done

Subacute presentation (2 -3 weeks) of nerve root and cord compression signs.
Exudative adhesions cause hydrocephalus.

Tuberculoma

00:12:32

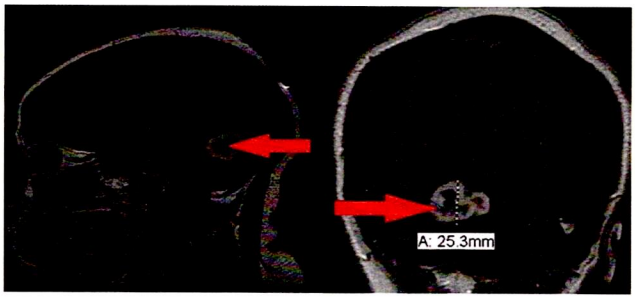
Tuberculoma : SOL.
Clinical features of SOL :

- No fever.
- Headache
- Focal seizures
- Papilledema

D/D for SOL :

- Tuberculoma
- Neurocysticercosis.
- Brain tumors

	Neurocysticercosis	Tuberculoma
Margin	Regular	Irregular
Size	Smaller (<20 mm)	Larger (>20 mm)
Signal intensity	T1W hypointense, T2W hyperintense.	T1W & T2W hypointense, often with hyperintense rim
Midline shift	No	Yes
MR spectroscopy	• Elevated succinate. • Choline/ creatinine ratio < 1.	• Elevated lipid. • Choline/ creatinine ratio > 1.



MRI Brain : Bigger lesion, hypointense lesion with hyperintense rim → Tuberculoma

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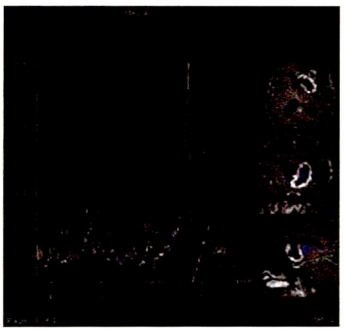
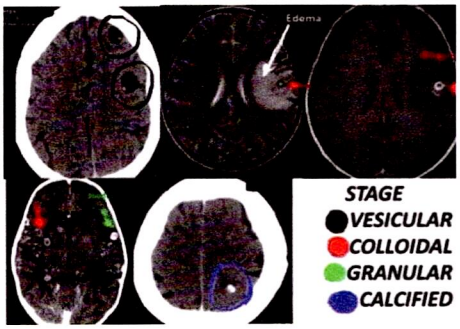
Neurocysticercosis :



- Most common presentation : Seizures.
- Brain parenchyma > IV > Spinal cyst > Meningeal lesion
- Nonimmune/eggs from fecally contaminated host.
- Rx : Praziquantel 2 weeks + Steroids



Causes of Eosinophilic Meningitis :

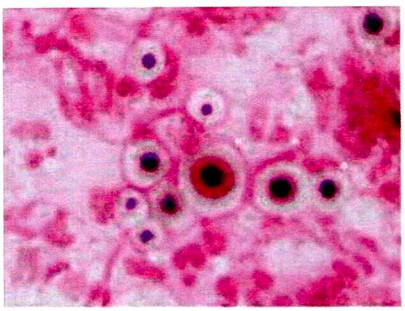
Parasitic diseases

1. Angiostrongyliasis
2. Gnathostomiasis
3. Schistosomiasis
4. Cysticercosis
5. Toxoplasmosis
6. Toxocariasis
7. Paragonimiasis

Fungal Meningitis

00:17:54

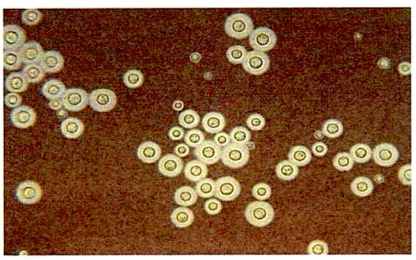
- Subacute or chronic meningitis in immunocompromised host.
- m/c cause : Cryptococcus neoformans.
- Route : Inhalation of spores
- High predilection for CNS/cross Blood Brain Barrier.
- Subacute presentation : Fever, headache and myalgia.
- Invasion of blood vessels (angioinvasion).



Gram stain showing Cryptococcus

Investigations :

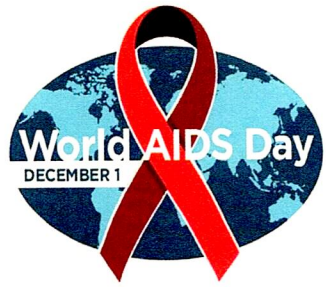
1. CSF analysis :
   - Cells : < 50 cells/mcL.
   - Protein increased <100mg/dL.
   - Glucose normal or slightly low
   - Pressures are very high.
2. India ink staining : Cryptococcus showing prominent clear zone representing capsule.
3. Latex agglutination



India ink stain showing Cryptococcus

Treatment : Amphotericin B + flucytosine.

HIV 2022



ENDING THE HIV EPIDEMIC
Equitable Access, Everyone's Voice

History

00:07:08

First reported case : 1981.
CDC coined the term Acquired Immunodeficiency Syndrome (AIDS) : 1982.
First isolation of LAV : 1983 ; By Luc Montagnier & colleagues from an African patient (lymphadenopathy associated).

If a patient has an AIDS defining illness, they become stage 3 irrespective of CD4+ count.

Stage	CD4 count	CD4 %	Clinical evidence
0	Early HIV infection		
1	≥ 500 cells/mm^3	≥ 26	No AIDS defining condition.
2	200–499 cells/mm^3	14–25	No AIDS defining condition.
3	< 200 cells/mm^3	< 14	Or documentation of AIDS defining condition.
unknown	No data	No data	And no information on presence of AIDS defining conditions.

CDC classification system for HIV infected :

	Clinical categories		
CD4 cell count categories	A – Asymptomatic, acute HIV	B – Symptomatic conditions, not A/C	C – AIDS indicator conditions
≥ 500 cells/μL	A1	B1	C1
200–499 cells/μL	A2	B2	C2
<200 cells/μL	A3	B3	C3

----- Active space -----

CDC stage 3 AIDS defining opportunistic illnesses in HIV Infection :

1. Malignancies :
   - Kaposi's sarcoma.
   - Invasive cervical cancer.
   - Lymphoma :
     - Burkitt's lymphoma
     - Immunoblastic lymphoma
     - Primary CNS lymphoma

     } EBV mediated.

2. Viruses :
   - Cytomegalovirus disease (other than liver, spleen, or nodes), onset at age > 1 month.
   - Cytomegalovirus retinitis (with loss of vision).
   - Herpes simplex : chronic ulcers (> 1 month's duration) or bronchitis, pneumonitis, or esophagitis (onset at age > 1 month). Zoster is not involved.
   - Progressive multifocal leukoencephalopathy (JC virus).

3. Fungi :
   - Candidiasis of bronchi, trachea, lungs & esophagus.
   - Cryptococcosis (extrapulmonary).
   - Coccidioidomycosis, disseminated or extrapulmonary.
   - Histoplasmosis, disseminated or extrapulmonary.
   - Pneumocystis jirovecii (previously known as Pneumocystis carinii) pneumonia.

4. Parasites :
   - Cryptosporidiosis, chronic intestinal (> 1 month's duration).
   - Isosporiasis, chronic intestinal (> 1 month's duration).
   - Toxoplasmosis of brain, onset at age > 1 month.

5. Bacteria :
   - mycobacterium avium complex or mycobacterium kansasii, disseminated or extrapulmonary.
   - mycobacterium tuberculosis of any site, pulmonary, disseminated, or extrapulmonary.
   - mycobacterium, other species or unidentified species, disseminated or extrapulmonary.
   - Salmonella septicemia, recurrent.