

CNS Infection In Advanced HIV Disease

Diagnosis and Management in Limited Resource Settings

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Disclosures/Conflicts

- ViiV Advisory Board
- No Conflicts

Approach to CNS Infections in HIV

- Presenting Signs/Symptoms

- Constitutional
 - Fever
 - Night sweats
 - Weight loss
- Headache
- Seizures-new onset
- Visual changes
- Focal Weakness
- Confusion

- Physical Exam

- Nuchal rigidity
- Photophobia
- Diminished visual acuity
- Abnormal reflexes
- Papilledema
- Cranial nerve palsies
- Skin lesions

Approach to CNS Infections in HIV

- Helpful Exposure History

- Travel
- Work exposure
 - Plants
 - Soil
- Animals
 - Cats
 - Reptiles
 - Fish
- Sick Exposures
 - Seasonal virus
 - Other viruses

- Lab Testing

- CD4
- HIV VL
- Prior Serostatus?
 - CMV
 - TOXO
 - EBV
 - RPR
- Blood Cultures
 - Bacterial
 - Fungal
 - Mycobacterial-if available
- POC/RAPID Testing
 - Gene/Xpert MTB/RIF*
 - Cryptococcal AG
 - Other

*Cepheid, Sunnyvale CA.

Approach to CNS Infections in HIV

- Imaging
 - CT with contrast (*DDD-CT)
 - MRI with gadolinium
- Lumbar Puncture
 - Helpful if can be done safely
 - Routine Testing
 - Cell count
 - Protein
 - Glucose
 - Bacterial smear & culture
 - Fungal smear & culture
 - AFB smear (if volume sufficient)
 - Mucicarmine stain
 - Gomori Methenamine Silver
 - VDRL
 - Cytology/Flow Cytometry
- Brain Imaging Patterns
 - Space-Occupying Lesions
 - Typically enhance with contrast
 - Non Space-Occupying Lesions
 - Typically DO NOT enhance
 - Solitary
 - Brains abscess/Tumor
 - Multiple lesions
 - Consider multiple etiologies
 - Hemorrhages
 - Location
 - Cortical
 - Periventricular
 - Subcortical white matter
 - Laterality

*Double dose, delayed

Approach to CNS Infections in HIV-Differential

- Solitary Lesions
 - Brain Abscess
 - Common
 - Bacterial
 - *S. aureus*
 - *Streptococcus* sp
 - *Salmonella* sp
 - Uncommon
 - Aspergillus
 - Nocardia sp
 - Listeria spp
 - Cryptococcomas
 - Tuberculomas
 - Multiple Lesions
 - Toxoplasma encephalitis
- Hemorrhagic
 - Secondary Syphilis
 - Viral
 - Varicella
 - Primary CNS lymphoma
 - Vasculitis
 - Location
 - Cortical
 - Toxoplasmosis
 - Brain abscess
 - CMV
 - Neurocysticercosis
 - Periventricular
 - Primary CNS lymphoma
 - PML

Approach to CNS Infections in HIV-Clinical Pearls

- Epidemiology
 - Known or suspected TB exposure
- Constitutional Symptoms
 - Fever, weight loss, night sweats
 - Tuberculosis
 - Primary CNS lymphoma (PCNSL)
- Progressive Dementia
 - HIV encephalopathy (HIVE)
 - Progressive Multifocal Leukoencephalopathy (PML)

Approach to CNS Infections in HIV-Clinical Pearls

- Seizures (new onset)
 - Common in space-occupying lesions
 - Toxoplasma encephalitis (TE)
 - PCNSL
 - abscesses
- Antiretroviral Adherence
 - Opportunistic infections (OIs) rare in adherence, even with **CD4 < 200** cells/μL
- Antimicrobial Prophylaxis
 - TE unlikely in setting of prophylaxis (TMP/SMX, atovaquone)
- Thrush/Skin Lesions
 - Molluscum contagiosum or Kaposi's Sarcoma
 - Indicators of low immune status

Causes of HIV-related CNS infection in Cameroon, Malawi, and Tanzania: epidemiological findings from the DREAMM HIV-related CNS implementation study.

Kayanama, Kounfack, Nyrenda et al

- Conducted in respective countries, Jan 9, 2018 and March 25, 2021
 - Funding: European and Developing Countries Clinical Trials Partnership
 - French Agency for Research on AIDS and Viral Hepatitis
 - 5 public hospitals
- Study Inclusion Criteria
 - Adults ≥ 18 living with HIV presenting to participating hospitals
 - Willing to have HIV test
 - First episode of suspected CNS infection
 - Willing to participate in the study

Causes of HIV-related CNS infection in Cameroon, Malawi, and Tanzania: epidemiological findings from the DREAMM HIV-related CNS implementation study.

Kayanama, Kounfack, Nyrenda et al

● Diagnostic Procedures

- All patients unless contraindicated had:
 - bedside Cryptococcal Antigen Lateral Flow Assay (CrAg LFA) of blood and CSF
 - urinary lipoarabinomannan
- If CrAg LPA was negative
 - *Streptococcus pneumoniae* Rapid Diagnostic Test (RDT) performed on CSF
- Neuroimaging: if altered consciousness, focal neurologic deficits or other clinical suspicion of space-occupying lesions

Causes of HIV-related CNS infection in Cameroon, Malawi, and Tanzania: epidemiological findings from the DREAMM HIV-related CNS implementation study.

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- Criteria for confirmed tuberculous meningitis
 - One or more
 - AFB seen in CSF
 - MTB cultured from CSF
 - CSF commercial Nucleic Acid Amplification Test (NAAT) positive
 - *GeneXpert MTB/RIF
 - *GeneXpert MTB/RIF Ultra
- Criteria for Cerebral Toxoplasmosis
 - Clinical history
 - focal neurological exam
 - seizures

Causes of HIV-related CNS infection in Cameroon, Malawi, and Tanzania: epidemiological findings from the DREAMM HIV-related CNS implementation study.

Kayanama, Kounfack, Nyrenda et al

- Diagnostic uncertainty after initial testing
 - 2nd LP performed
 - Cell count, glucose, protein,
 - large volume CSF TB culture and MTB NAAT
- Neurosyphilis
 - RDT on blood (DPP Syphilis Screen and Confirm)
 - Positive DPP RDT confirmed with VDRL -where available

Causes of HIV-related CNS infection in Cameroon, Malawi, and Tanzania: epidemiological findings from the DREAMM HIV-related CNS implementation study.

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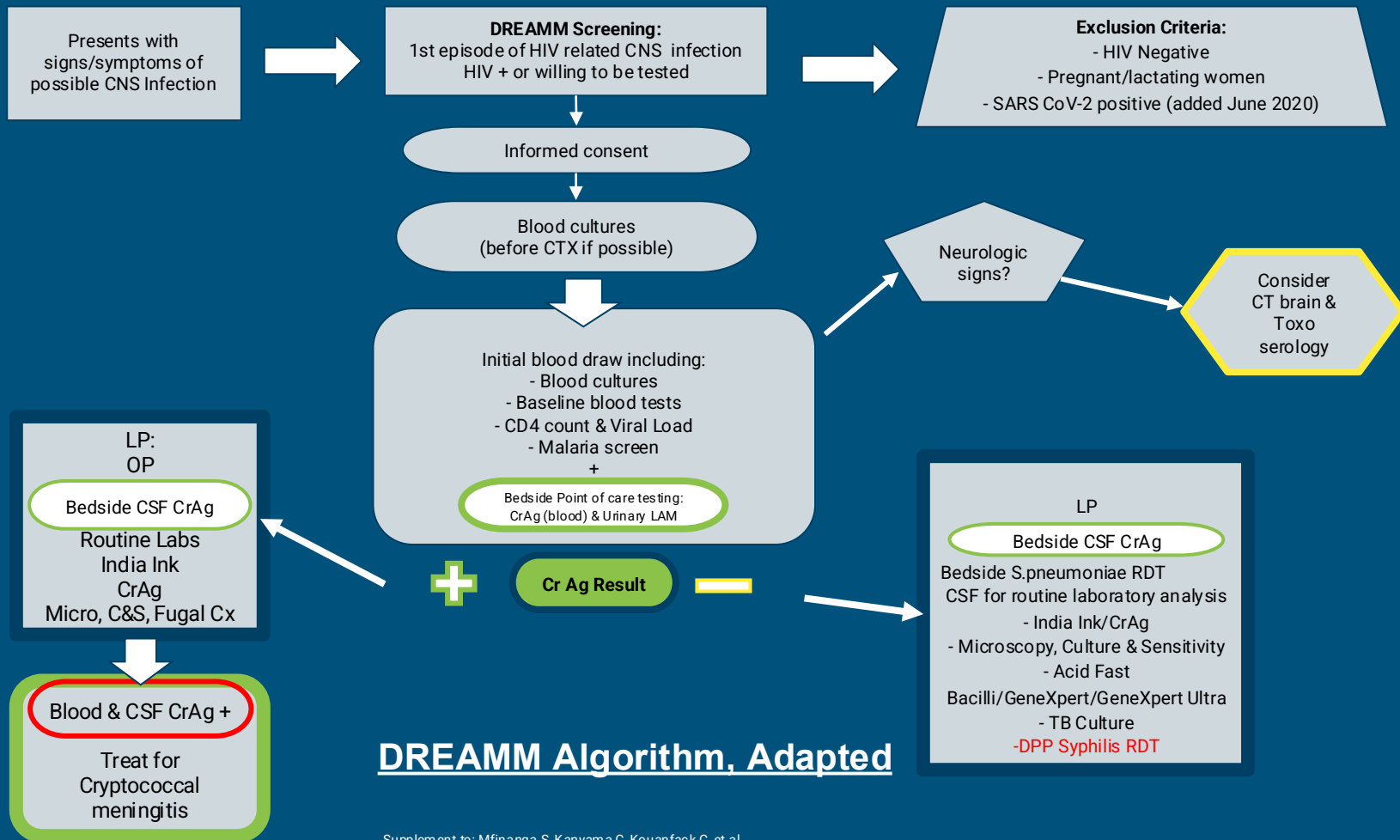
● Results

- 356 patients analysed
 - 269 (76%) had confirmed CNS infection
 - Median CD4=61 cells
 - 87(24%) had no CNS infection
- HIV viral load was available in 143(40%)
- CD4 counts were available in 260 (73%)
 - Patients with CNS infection- median CD4=61 cells/μL
 - Patients with no CNS infection-median CD4=282 cells/μL

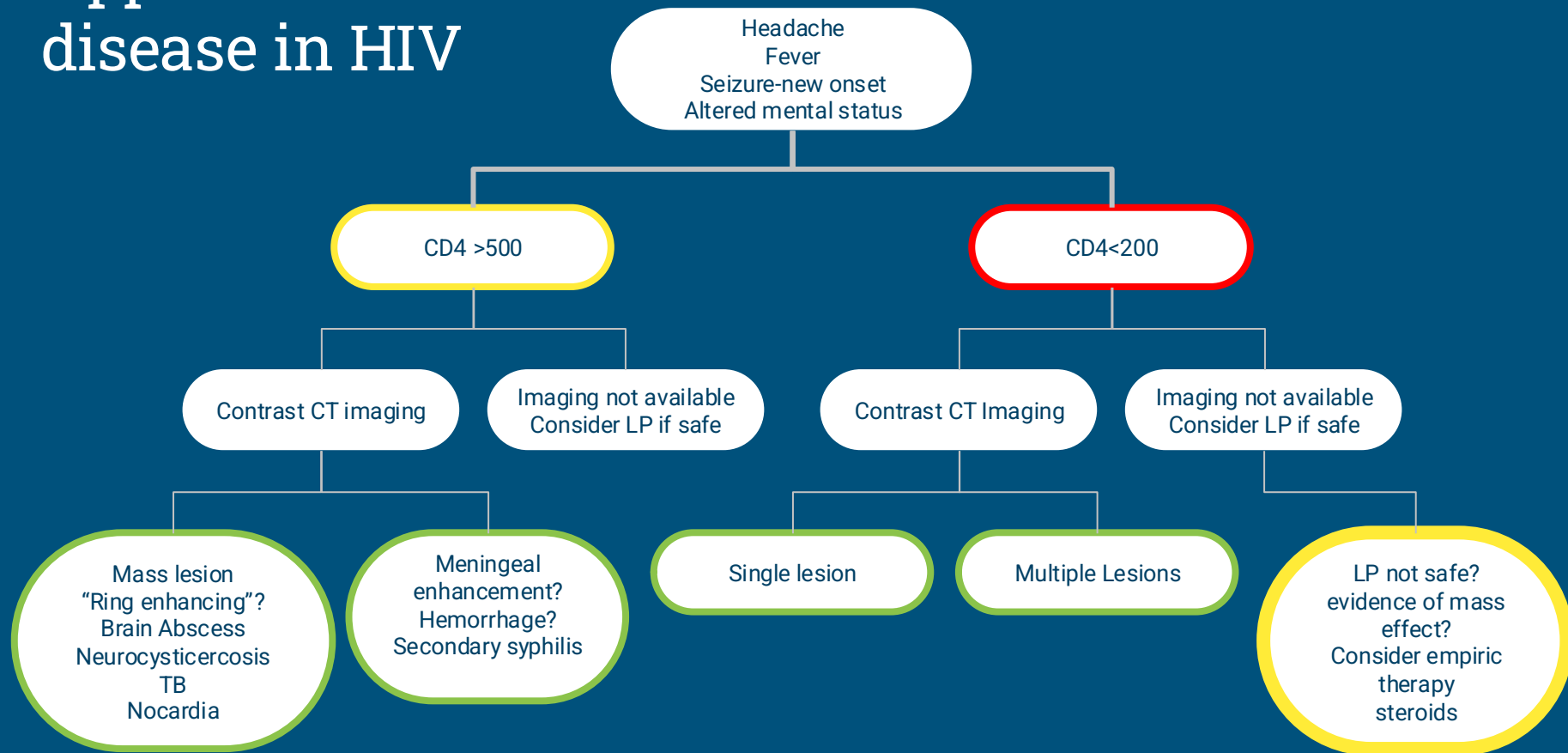
Causes of HIV-related CNS infection in Cameroon, Malawi, and Tanzania: epidemiological findings from the DREAMM HIV-related CNS implementation study.

Kayanama, Kounfack, Nyrenda et al

	Tanzania (n=99)	Malawi (n=80)	Cameroon (n=90)	TOTAL (n=269)	Proven DX (n=202)
Cryptococcal meningitis	59 (60%)	53 (66%)	36 (40%)	148 (55%)	144/148 (97%)
CNS TB	29 (29%)	7 (9%)	11 (12%)	47 (17%)	17/47 (36%)
Bacterial meningitis	5 (5%)	15 (19%)	6 (7%)	26 (10%)	11/26 (42%)
Cerebral Toxo	0	0	39 (43%)	39 (14%)	38/39 (97%)
CNS toxo/CNS TB	4 (4%)	0	1 (1%)	5 (2%)	NA
Neurosyphilis	3 (3%)	5 (6%)	0	8 (3%)	7/8 (88%)
Other	5 (5%)	3 (4%)	3 (3%)	11 (4%)	0



Approach to CNS disease in HIV



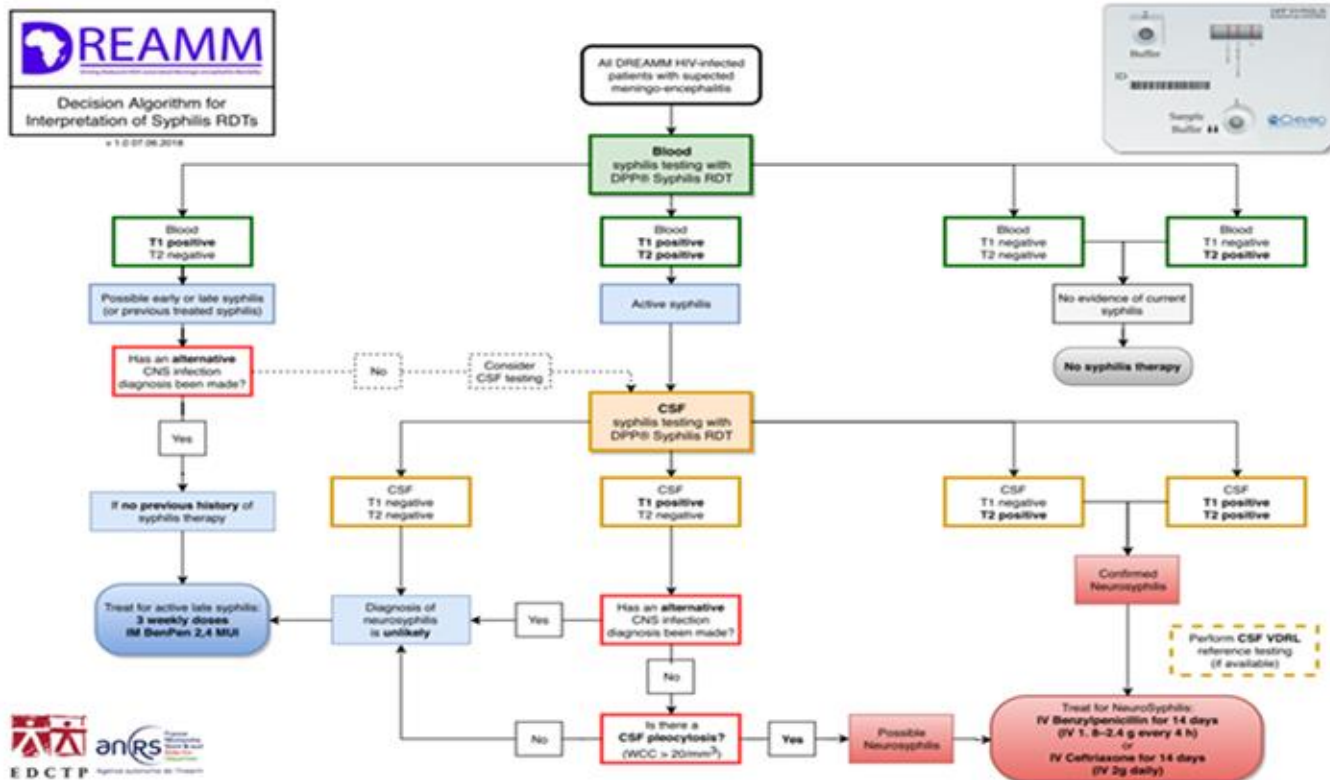
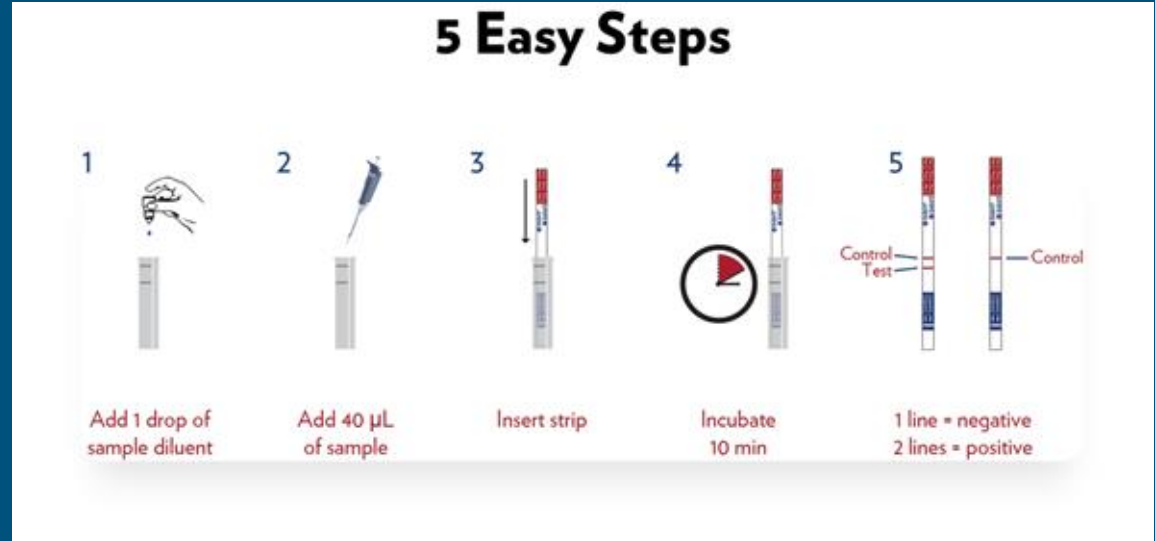


Figure S1: Syphilis algorithm from the DREAMM Educational Module on neurosyphilis.

Quick Show and Tell

CrAg® LFA— Cryptococcal Antigen Lateral Flow Assay



GeneXpert



Cepheid

Xpert® MTB/RIF

Accurate Detection of MTB and Rifampin Resistance Mutations

Easy as 1, 2, 3

with less than one minute hands-on time

1

Obtain swab specimen

1

2

Transfer sample to cartridge



3

Insert cartridge and start test



Urine Lipoarabinomannan



Abbott Laboratories

Test Procedure- Urine TB LAM

1. Prepare Test
Tear one strip from the right and remove cover.

2. Add Sample
Apply 60µL of urine to sample pad.

3. Read Results
Wait 25 minutes and read the results.

Reference scale card

Line	Positive	Negative	Invalid
Control	[Blue line]	[Blue line]	[Blue line]
Patient	[Blue line]	[Blue line]	[Blue line]

25 min.

Abbott Determine® TB LAM Ag Reference Scale Card

Hold the card alongside the patient window and read the result.
• If the result line is faint or blurry, repeat the test.
• If the result line is faint or blurry, repeat the test.
• If the result line is faint or blurry, repeat the test.

Negative
Positive

FINGERSTICK WHOLE BLOOD

1 Prepare

Collect sample

Transfer sample

VENOUS WHOLE BLOOD/SERUM/PLASMA

Collect sample

Transfer sample

2 Run

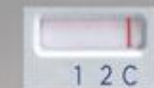
2 drops
Buffer
into Well 1

5 drops
Buffer
into Well 2

WAIT
5
MINS

WAIT
15
MINS

3 Read



NON-REACTIVE



REACTIVE TREP
REACTIVE NON-TREP



REACTIVE TREP
NON-REACTIVE NON-TREP



NON-REACTIVE TREP
REACTIVE NON-TREP

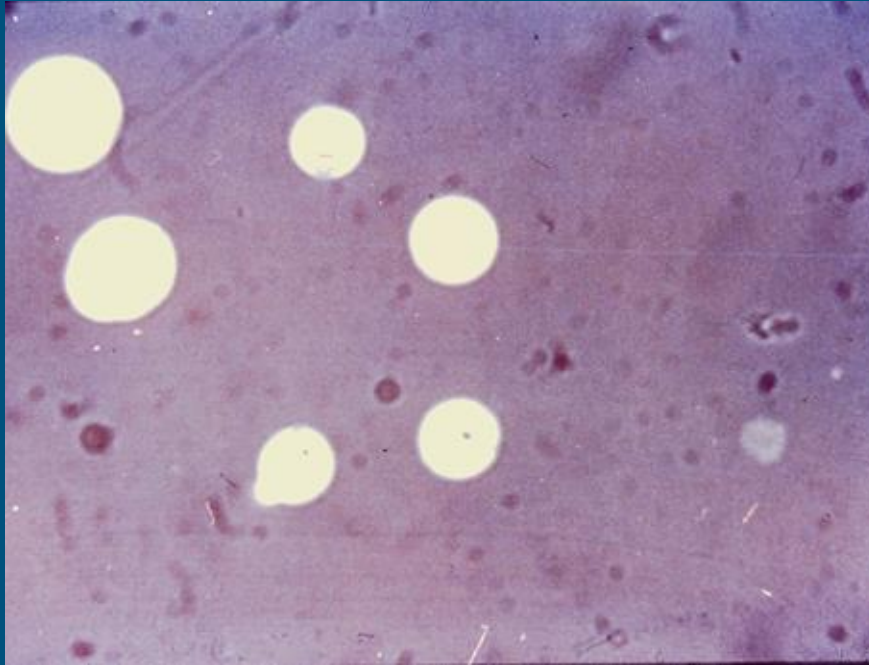


INVALID

Chembio DPP Syphilis Screen & Confirm Assay

Chembio Blosynex

Microscopic
appearance of
Cryptococcus
neoformans cells
in CSF



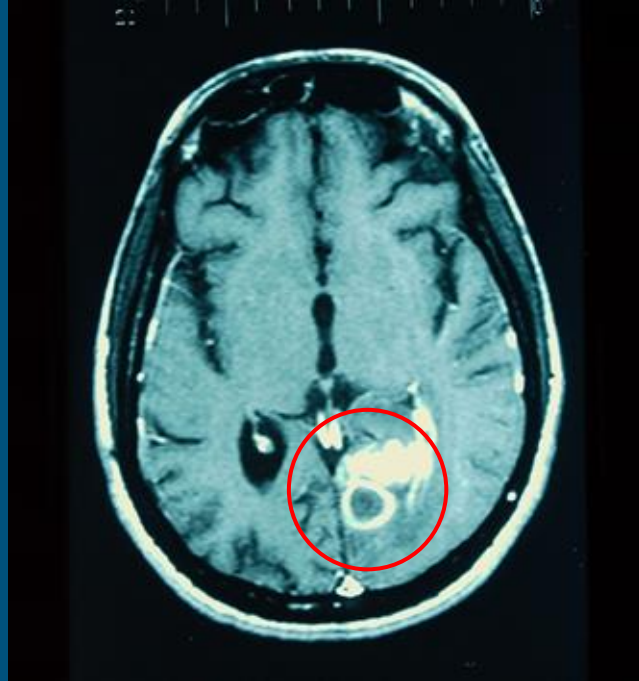
Credit: Richardson, Warnock Campbell. Blackwell
Science. Slide Atlas of Fungal Infection, 1995

CNS Tuberculosis

CNS Tuberculosis

Left: Pre treatment

Right: Post treatment



Courtesy: RB Uttamchandani, MD

Brain Abscess

Solitary space-occupying lesion.
Bacterial brain abscess



Credit: Case #04032: A woman with a headache, fever and neck stiffness. [Internet]. Partners Infectious Disease Images. Available from: <http://www.idimages.org/idreview/case/caseid=294>

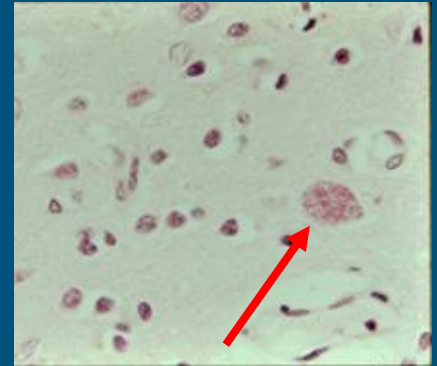
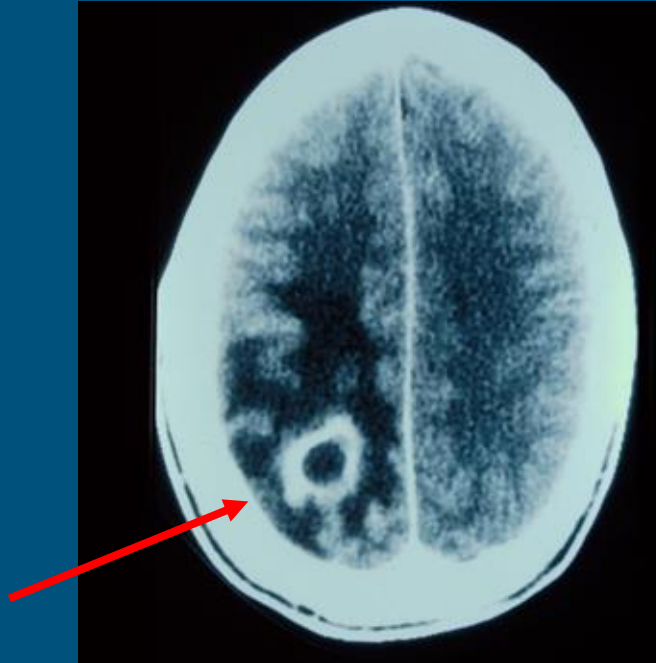
CNS Toxoplasmosis

Left:

Solitary lesion of parietal area caused
by *T. gondii*

Right:

Brain biopsy Hematoxylin and Eosin
Stain showing Toxoplasma cyst



Courtesy: RB Uttamchandani, MD

Progressive Multifocal Leukoencephalopathy

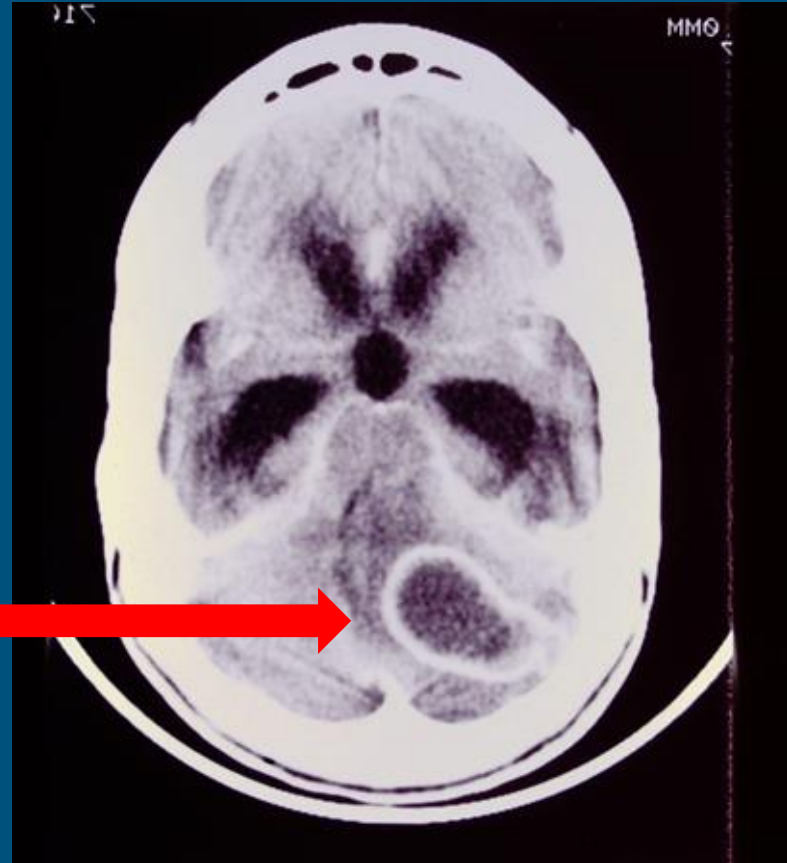
Enhancement with contrast due to PML.
(JC Virus)



CNS Nocardia

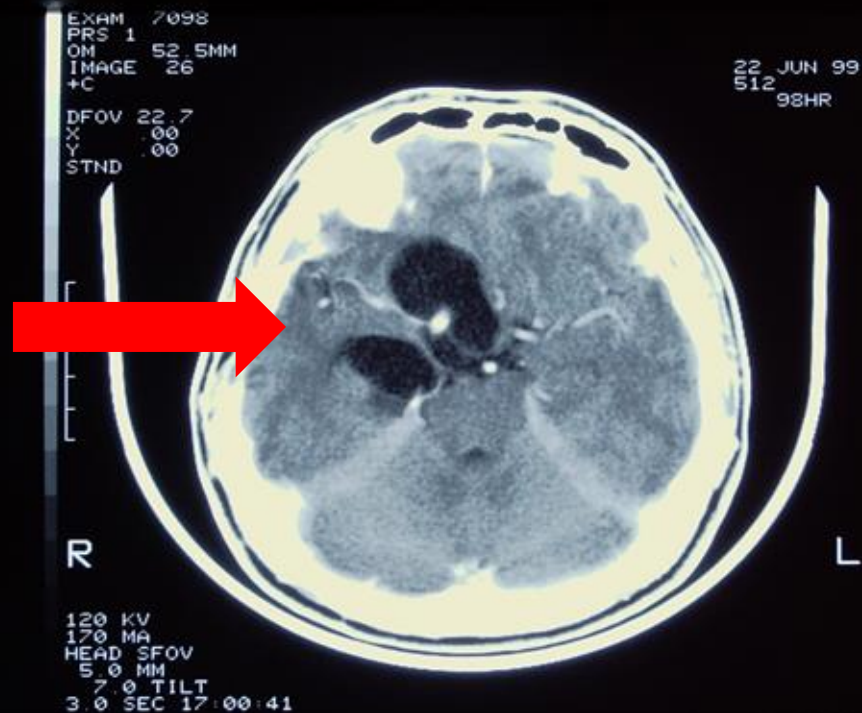
LeBlang SD, Whiteman ML, Post MJ, Uttamchandani RB, Bell MD, Smirniotopolous JG. CNS Nocardia in AIDS patients: CT and MRI with pathologic correlation. J Comput Assist Tomogr. 1995 Jan-Feb;19(1):15-22. doi: 10.1097/00004728-199501000-00003. PMID: 7822535.

Courtesy: RB Uttamchandani, MD



Racemose Neurocysticercosis

Example of unusual presentation of
Neurocysticercosis



CNS Aspergillosis



Selected References

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2. Samuels THA, Molloy SF, Lawrence DS, Loyse A, Kanyama C, Heyderman RS, Lai WS, Mfinanga S, Lesikari S, Chanda D, Kouanfack C, Temfack E, Lortholary O, Hosseini-pour MC, Chan AK, Meya DB, Boulware DR, Mwandumba HC, Meintjes G, Muzoora C, Mosepele M, Ndhlovu CE, Youssouf N, Harrison TS, Jarvis JN, Gupta RK. Personalised risk-prediction tools for cryptococcal meningitis mortality to guide treatment stratification in sub-Saharan Africa: a prognostic modelling study based on pooled analysis of two randomised controlled trials. *Lancet Glob Health*. 2025 May;13(5):e920-e930. doi: 10.1016/S2214-109X(25)00010-5. PMID: 40288401.
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4. Ramos LRD, Ninomiya DA, Sequeira MF, Leite OHM, Magri MMC. HIV-associated neurological infections in a Brazilian tertiary care center: clinical-epidemiological features and predictors of in-hospital mortality. *Rev Inst Med Trop Sao Paulo*. 2026 Jan 30;68:e8. doi: 10.1590/S1678-9946202668008. PMID: 41637347; PMCID: PMC12858172.

Thank You