HIV associated opportunistic infection

Mohammed Salameh Al Tarawneh,MD
Assistant professor of internal medicine and infectious disease
American Board of infectious diseases
American board of Internal Medicine
Consultant internal medicine and infectious diseases

HIV

- “Human Immunodeficiency Virus”
- A specific type of virus (a retrovirus)
- HIV invades the helper T cells to replicate itself.
- No Cure

AIDS

- Acquired Immunodeficiency Syndrome
- HIV is the virus that causes AIDS
- Disease limits the body's ability to fight infection
- A person with AIDS has a very weak immune system
- No Cure

Three Phases of HIV

Phase 1- Asymptomatic Stage

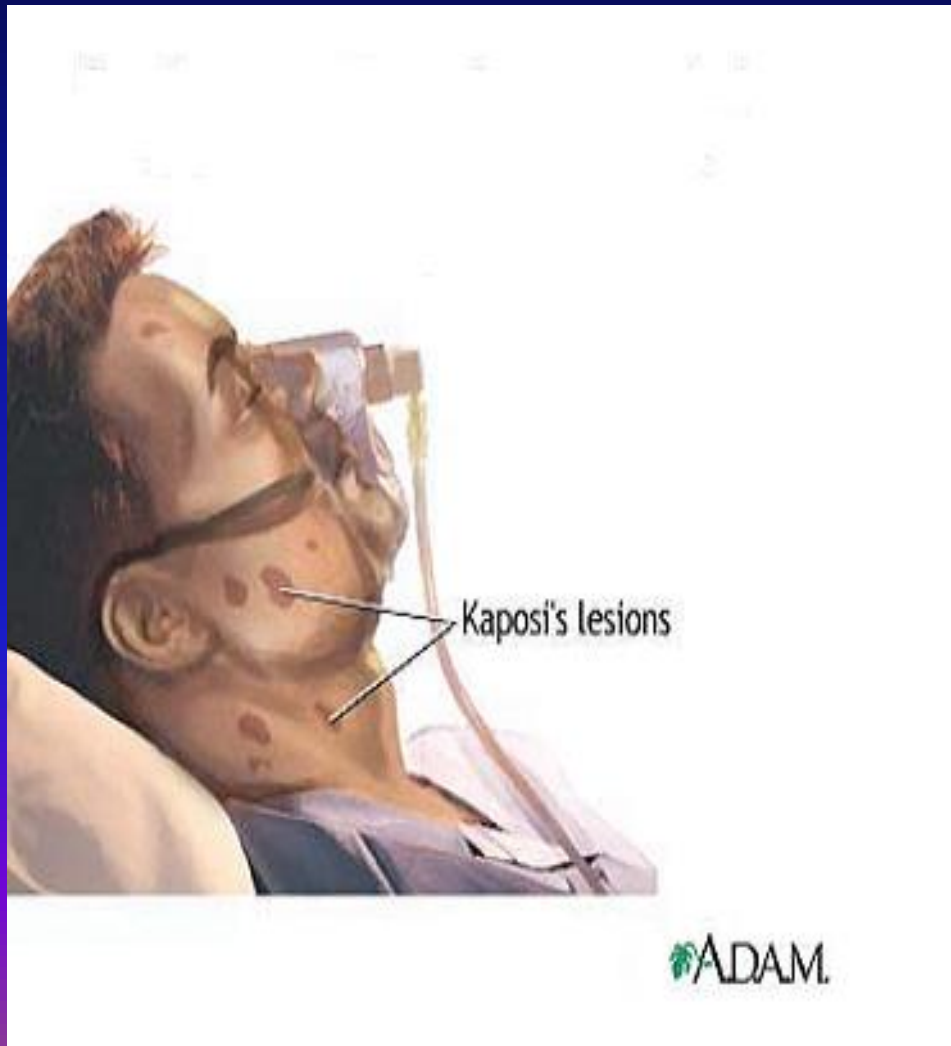
- Short, flu-like illness, swollen glands, fatigue, diarrhea, weight loss, or fevers - occurs one to six weeks after infection
- no symptoms at all
- Infected person can infect other people
- Lasts for an average of ten years
- HIV antibodies are detectable in the blood

Phase 2 - Symptomatic

- The symptoms worsen
- Mental changes, forgetfulness & abnormal thinking patterns

Phase 3 - HIV ⇨ AIDS

- Immune system weakens
- Emergence of opportunistic infections and cancers
- The illnesses become more severe leading to an AIDS diagnosis



What are Opprtunistic Infections (OI's) ?

OIs are those infections that are caused by organisms that do not ordinarily harm healthy people but occur in people with impaired defenses

(immunocompromised hosts).

Immunodeficiency may be:

1.Congenital

2.Secondary/Acquired,haematological,malignancies, splenectomy etc.

3.Therapeutic

CAUSE OF OIs

OI's are caused either by organisms of low or no virulence which are non pathogenic in individuals with an intact immune system or by known pathogens who present in a different way than usual in immunodeficient individuals in the form of increased virulence, recurrence, multi-drug resistant or atypical presentation.

TYPES OF OI's(Aetiological)

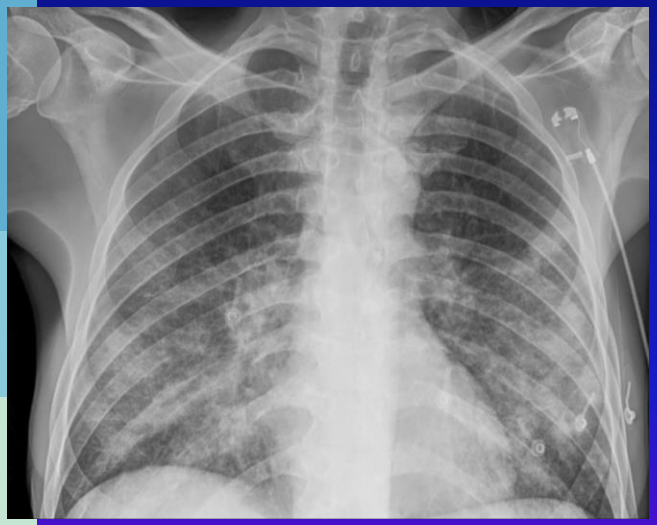
- Viral Opportunistic Infections
- Mycobacterial Opportunistic Infections
- Bacterial Opportunistic Infections
- Fungal Opportunistic Infections
- Parasitic Opportunistic Infections

First Documented OIs in US

MMWR™
Weekly
June 5, 1981 / 30(21);1-3

Pneumocystis Pneumonia --- Los Angeles

In the period October 1980-May 1981, 5 young men, all active homosexuals, were treated for biopsy-confirmed *Pneumocystis carinii* pneumonia at 3 different hospitals in Los Angeles, California. Two of the patients died. All 5 patients had laboratory-confirmed previous or current cytomegalovirus (CMV) infection and candidal mucosal infection. Case reports of these patients follow.



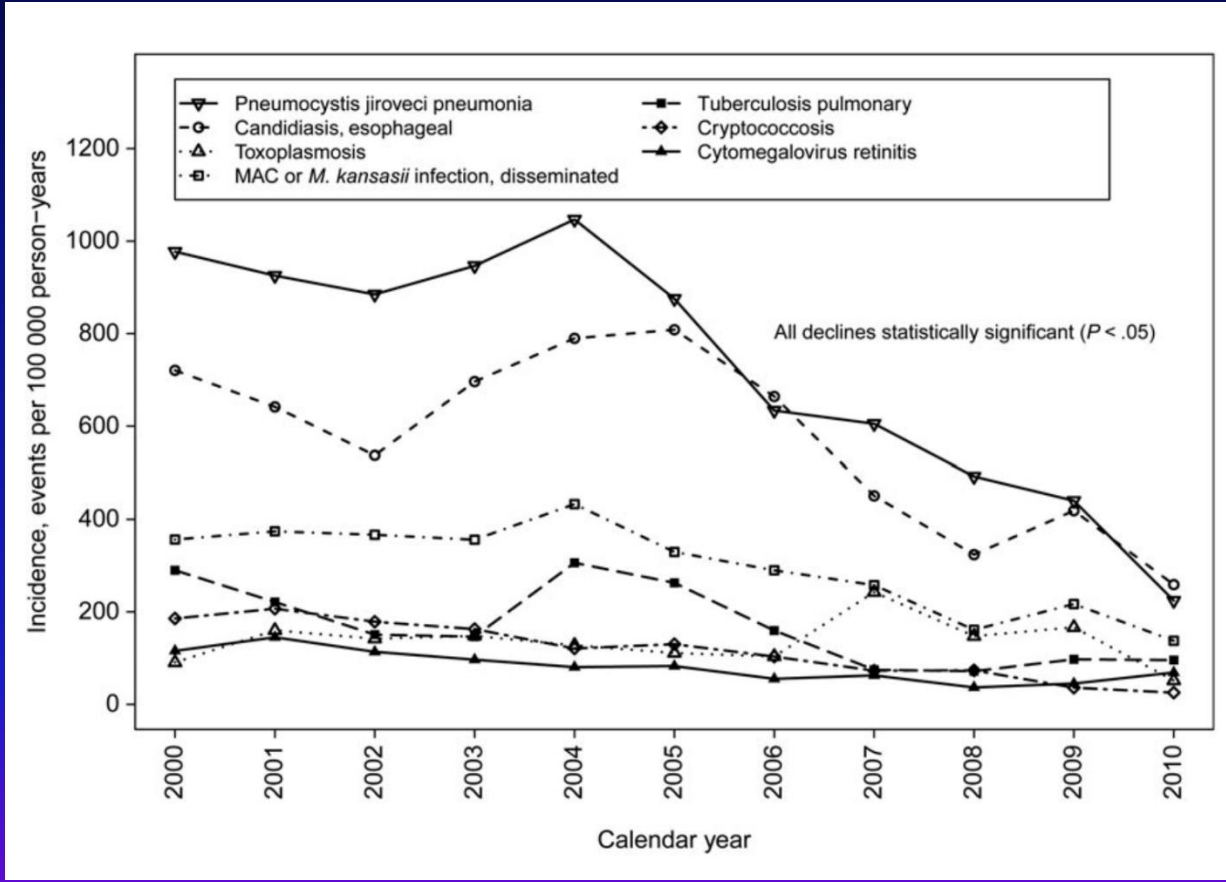
MMWR™
Weekly
June 18, 1982 / 31(23);305-7

A Cluster of Kaposi's Sarcoma and Pneumocystis carinii Pneumonia among Homosexual Male Residents of Los Angeles and range Counties, California

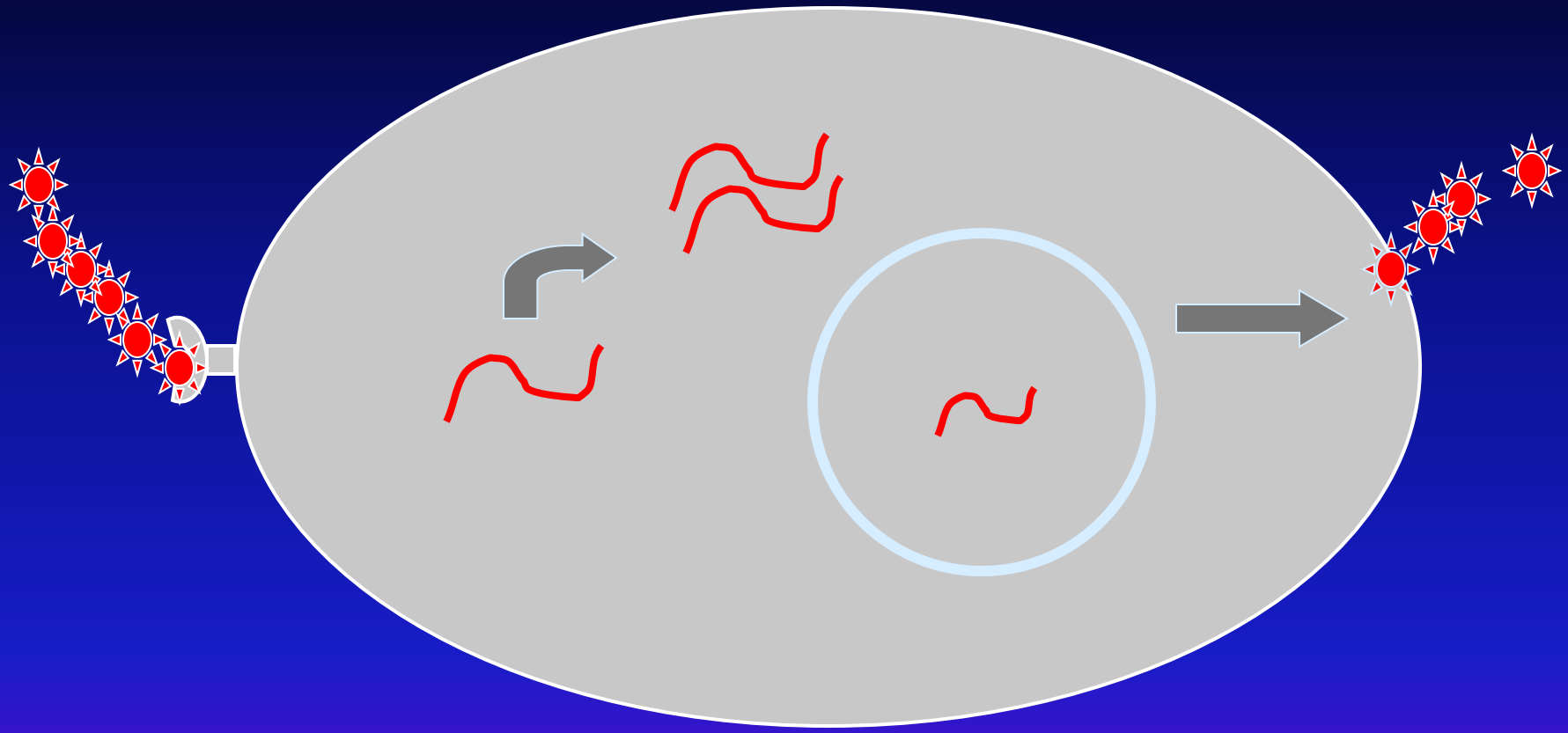
In the period June 1, 1981-April 12, 1982, CDC received reports of 19 cases of biopsy-confirmed Kaposi's sarcoma (KS) and/or Pneumocystis carinii pneumonia (PCP) among previously healthy homosexual male residents of Los Angeles and Orange counties, California. Following an unconfirmed report of possible associations among cases in southern California, interviews were conducted with all 8 of the patients still living and with the close friends of 7 of the other 11 patients who had died.

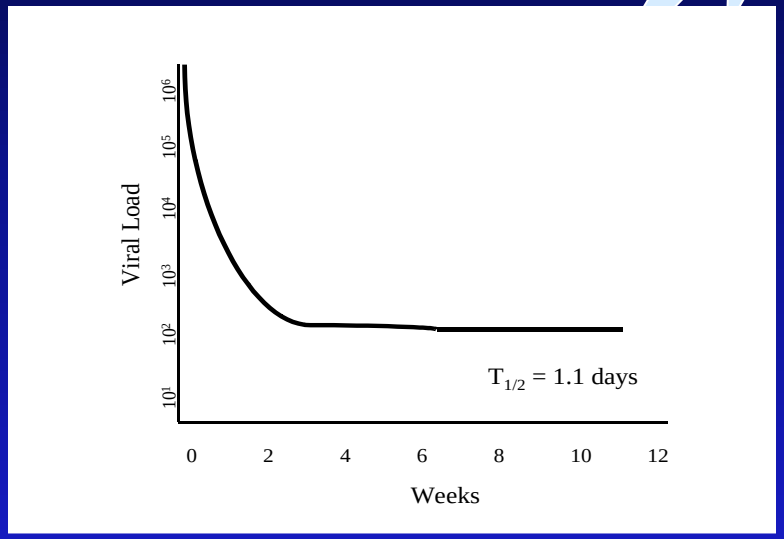
Decline in All OIs After ART

- Up to 40% of people with HIV developed disseminated MAC in the early 1990s
- Now < 2 cases of MAC as first OI per 1000 person-years



MMWR. June 1993. 42;14-20
Buchacz K et al. J Infect Dis 2016.





Latently Infected
CD4+ Lymphocytes

HIV Infected
Cells

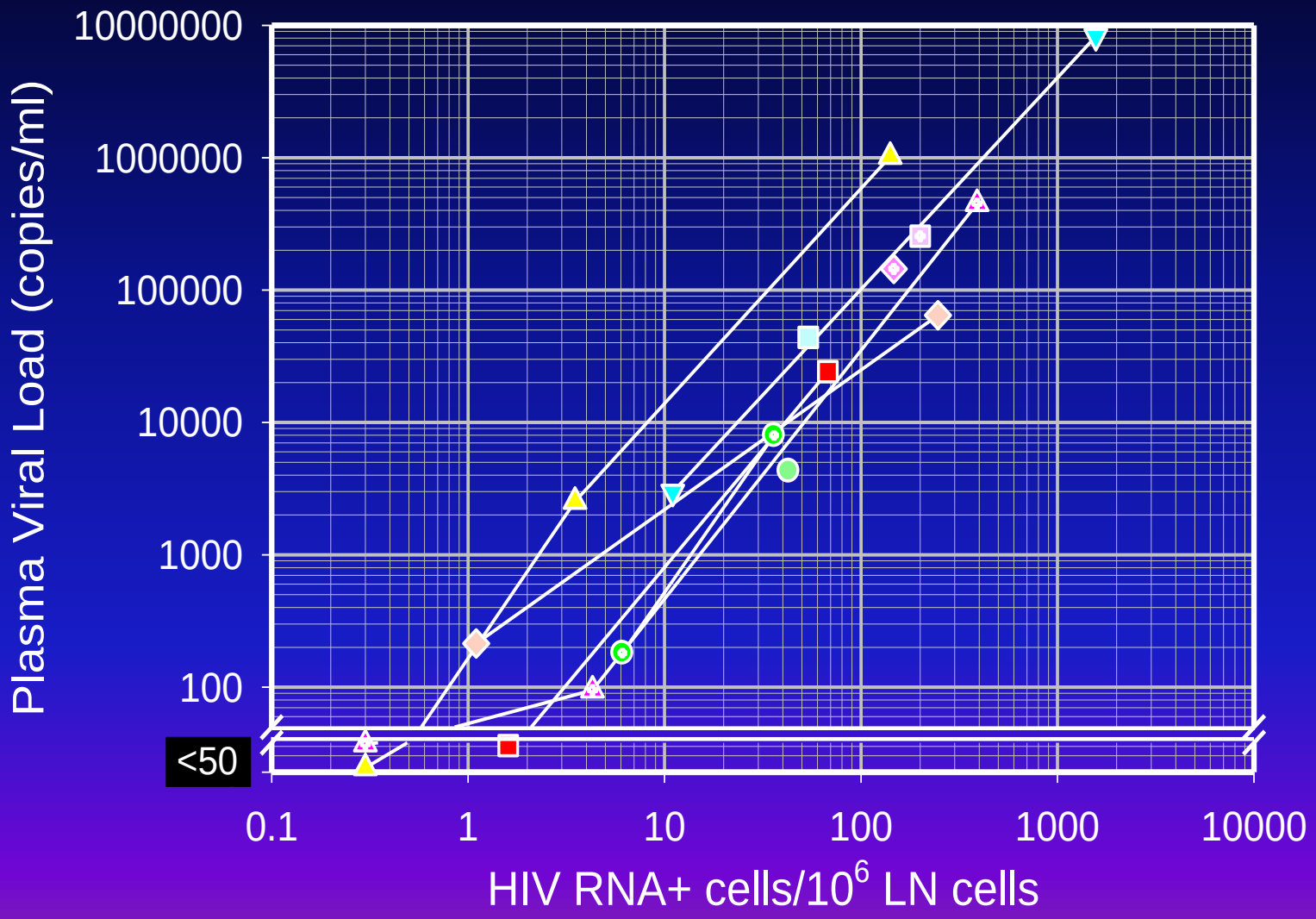
HIV virions

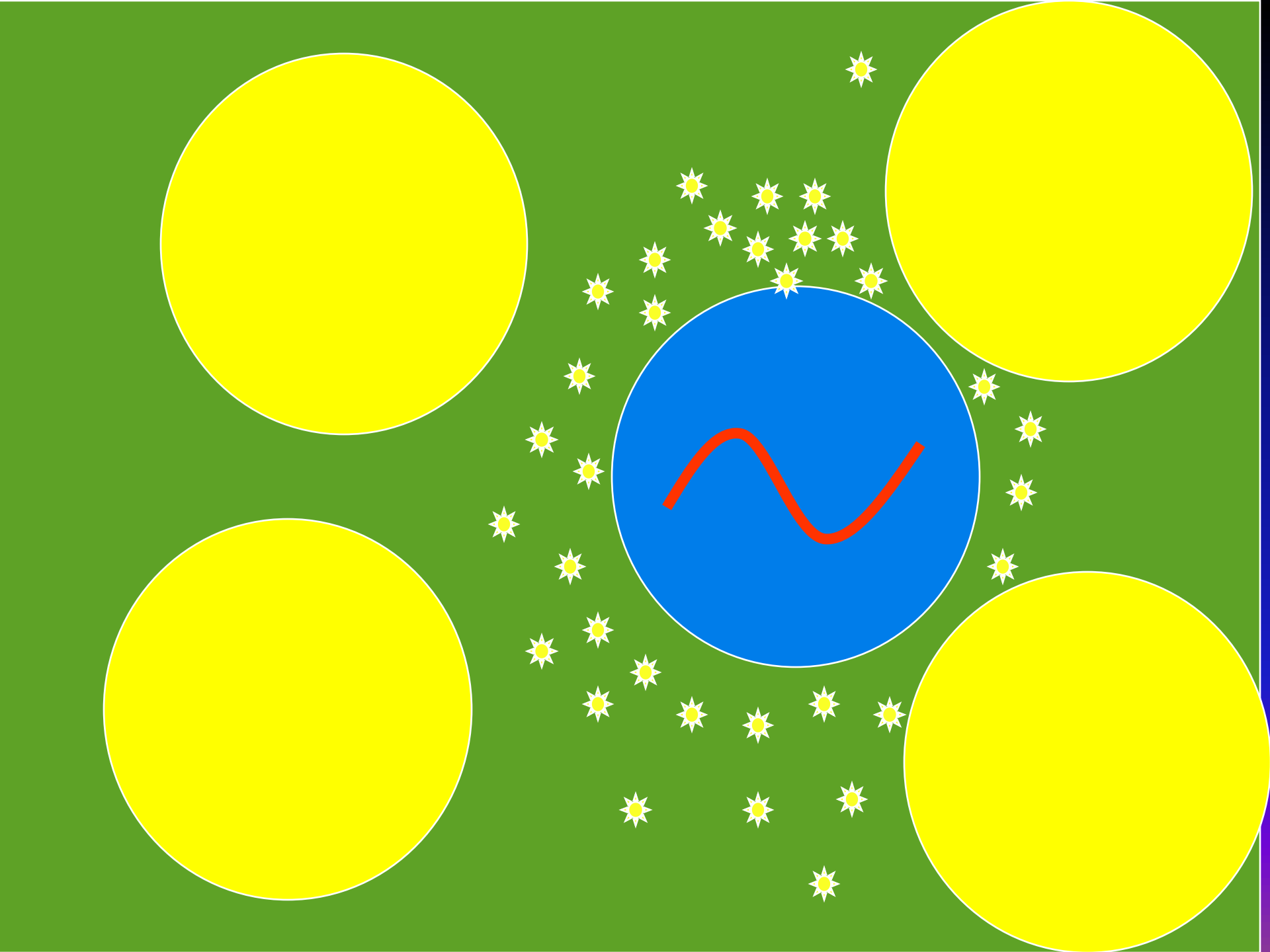
Antiretroviral Rx

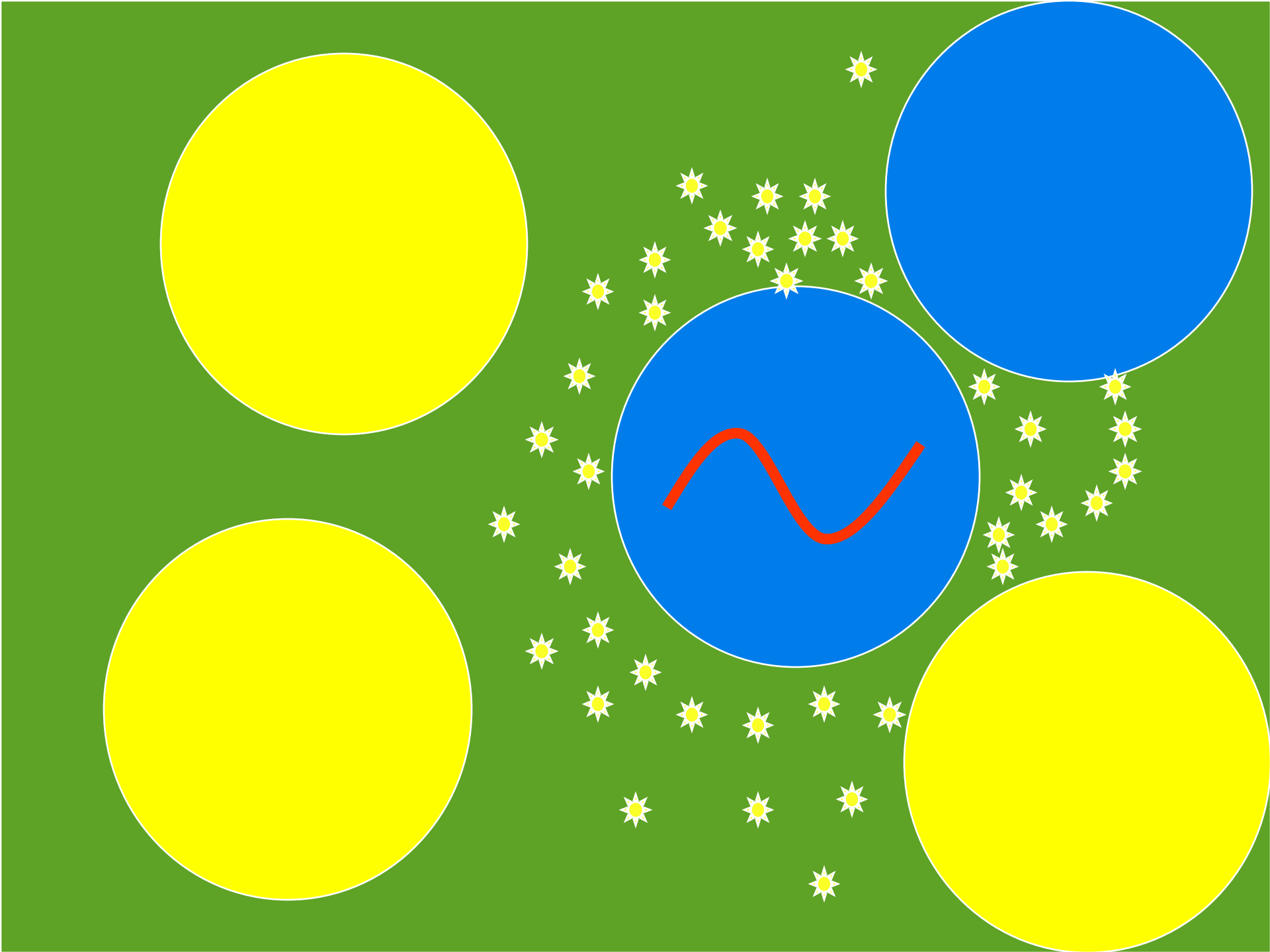
Uninfected Activated
CD4+ Lymphocytes

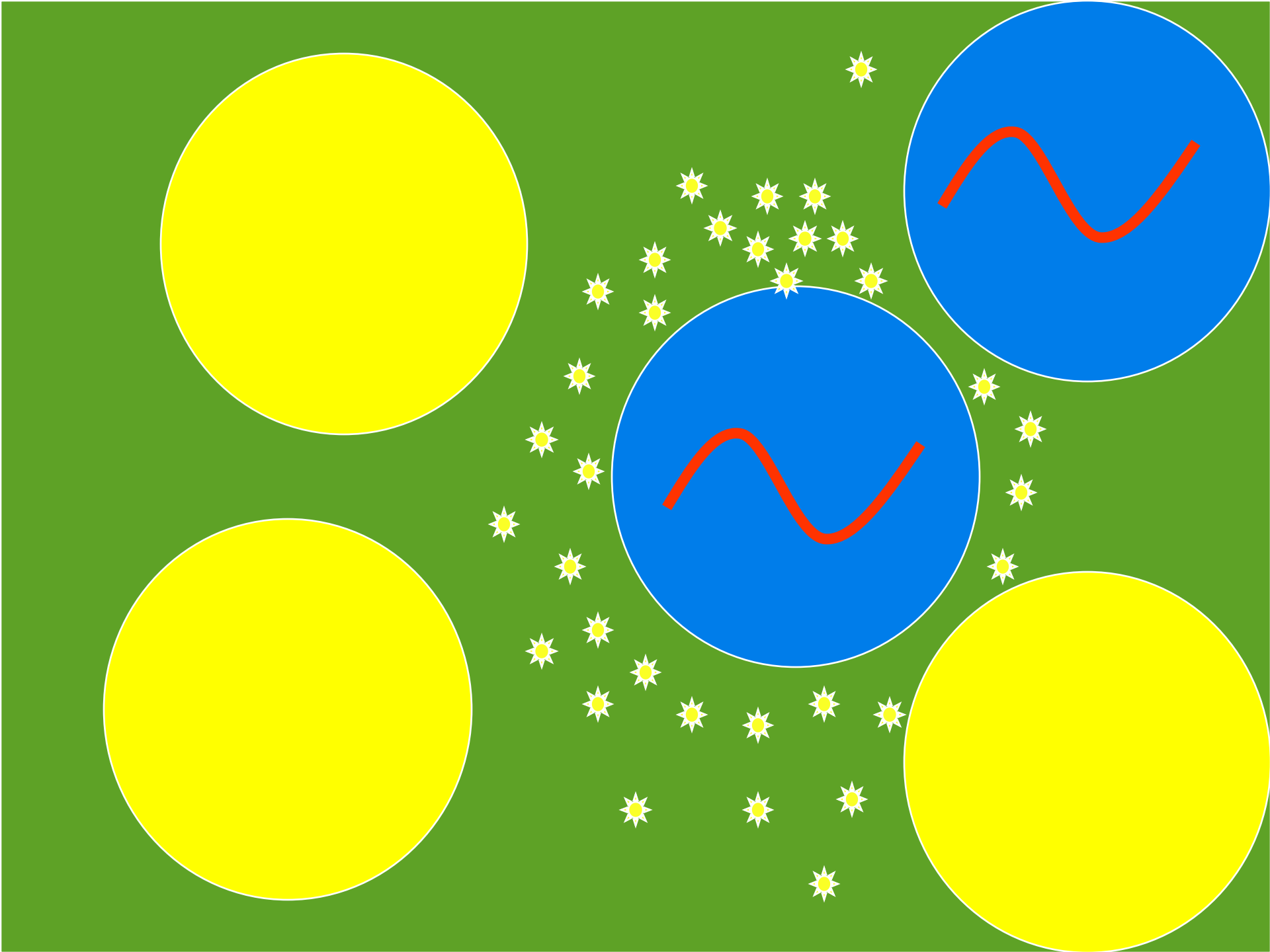
Uninfected Resting
CD4+ Lymphocytes

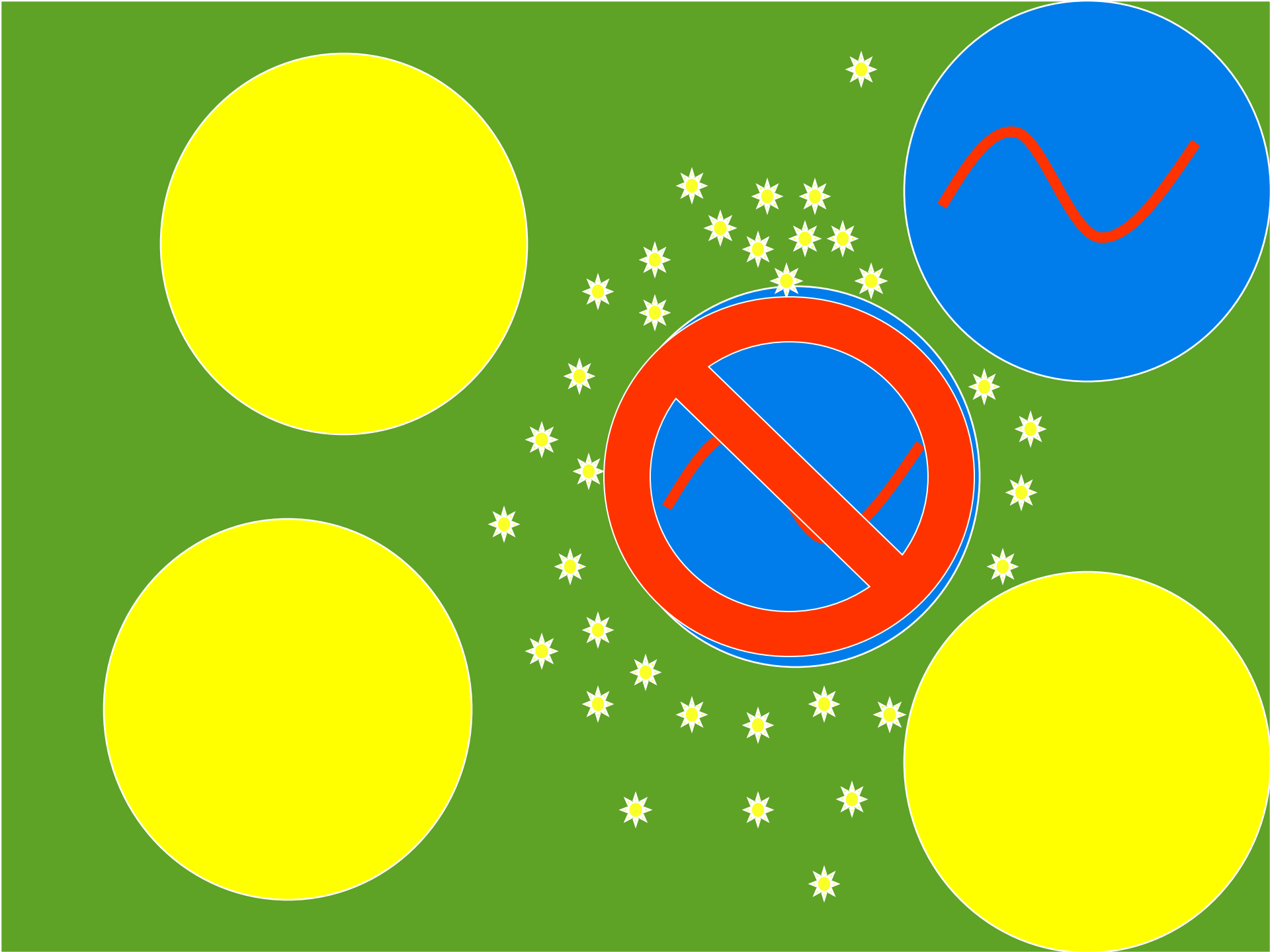
RNA+ cells in Lymph node *vs* RNA in Plasma

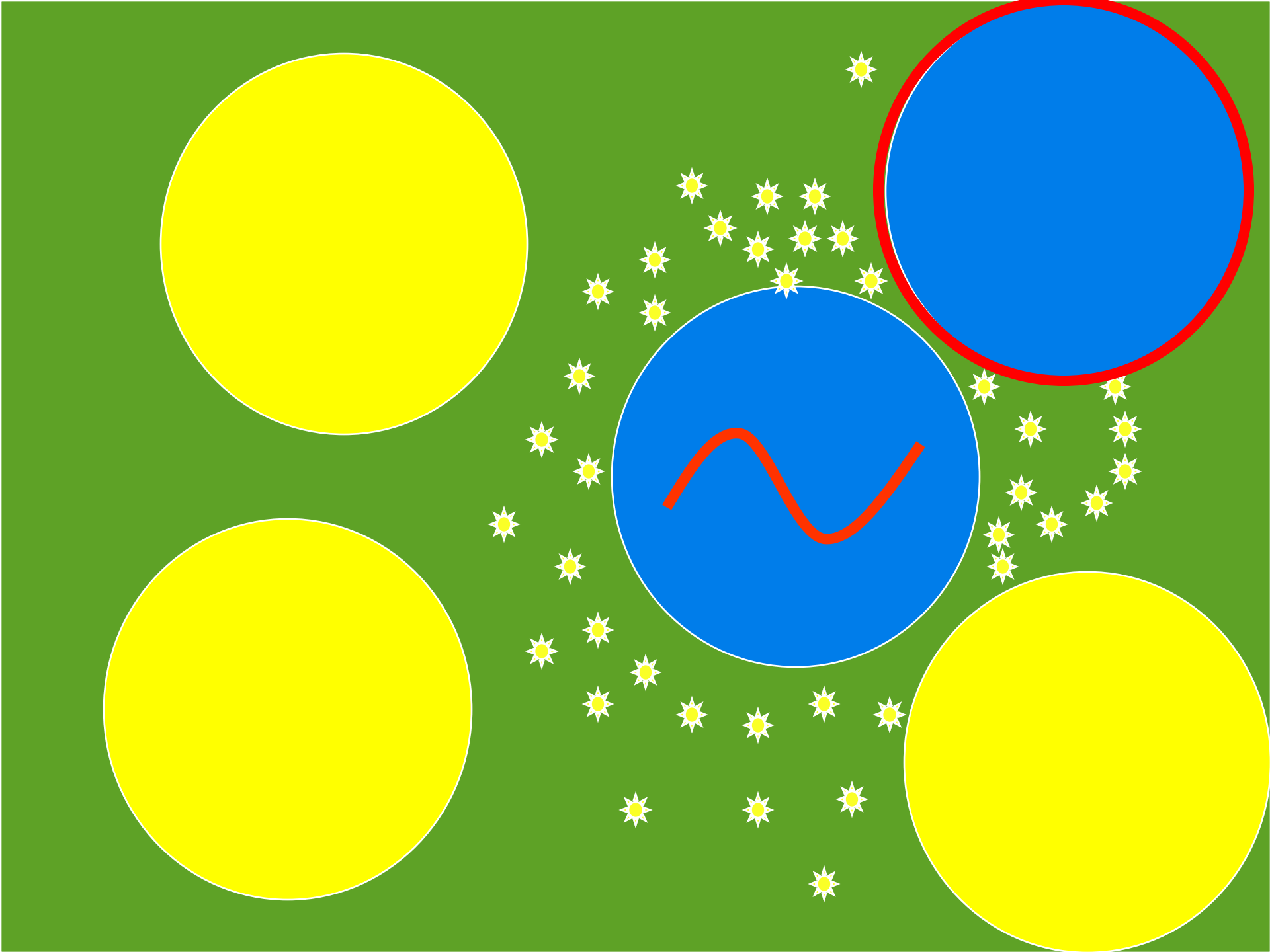


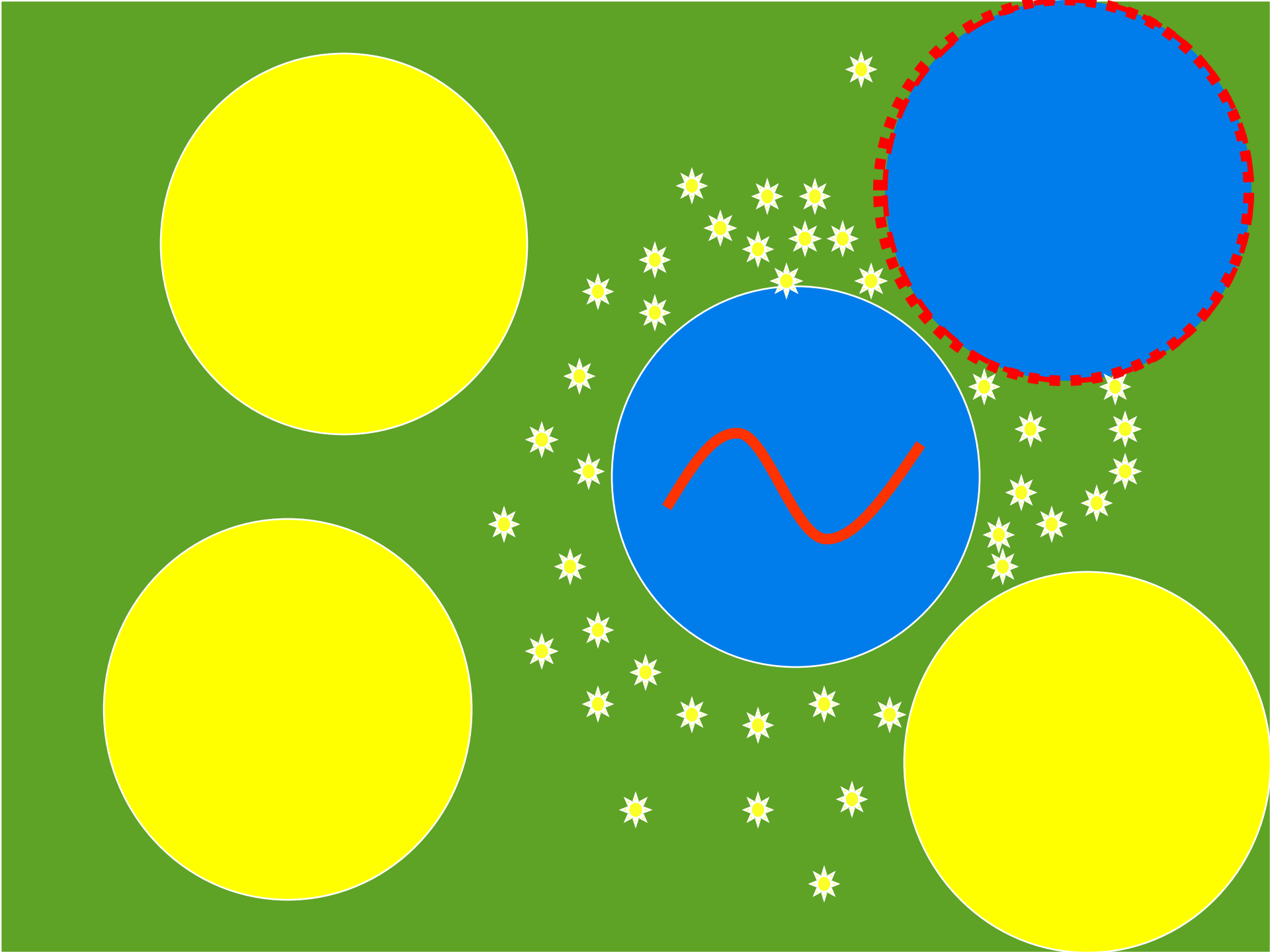


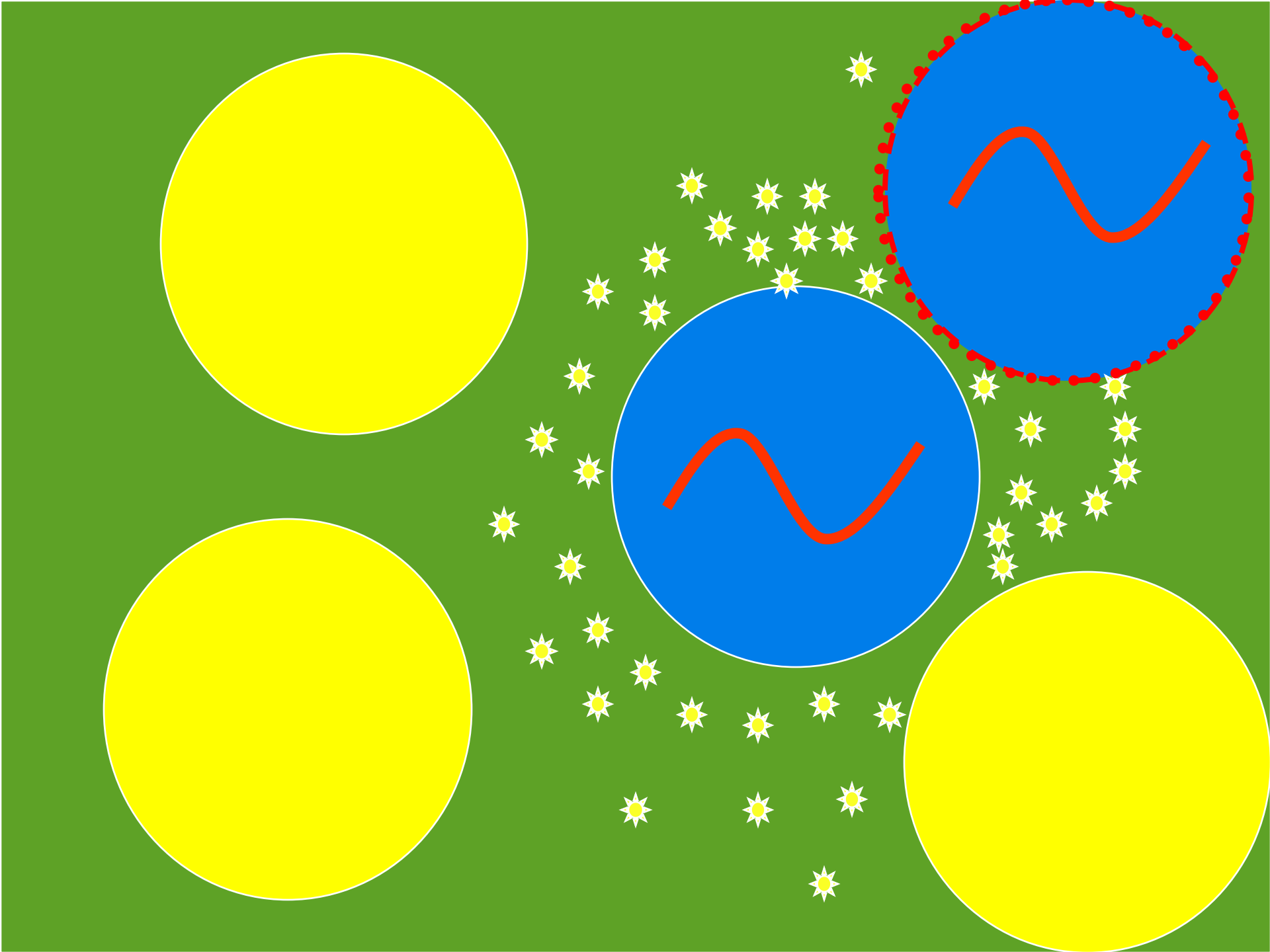




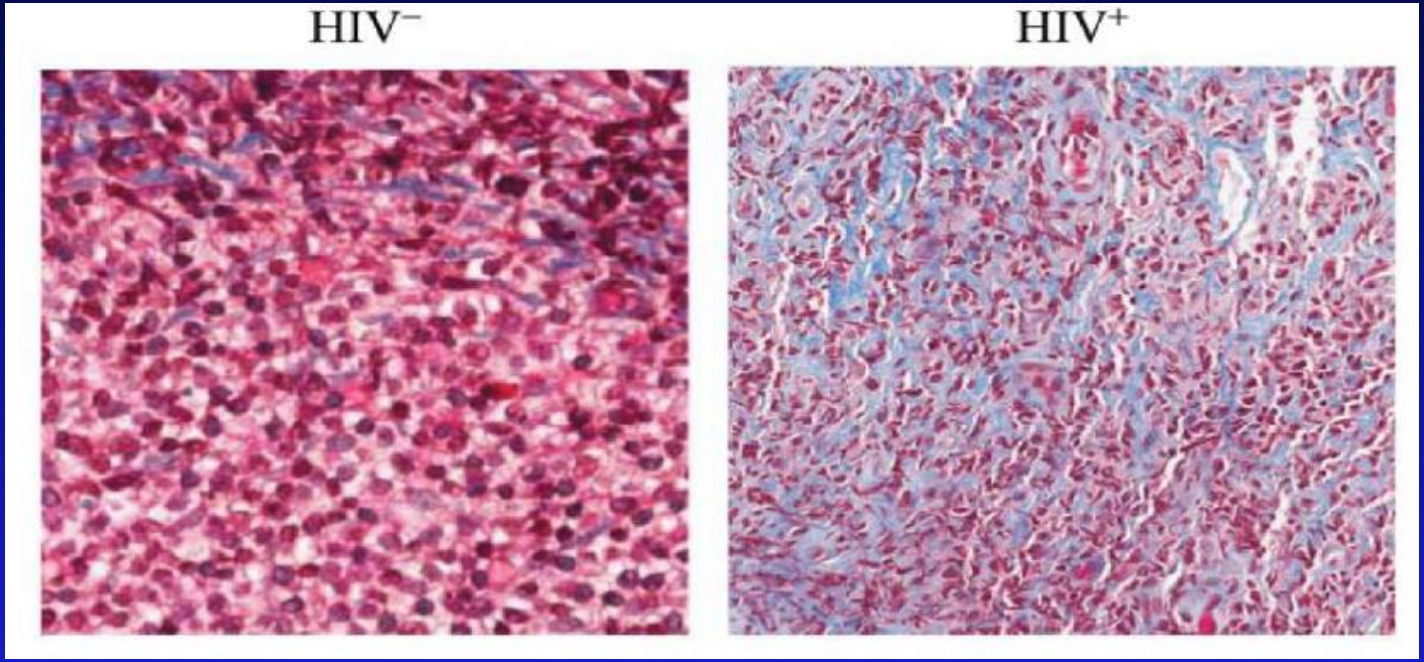








Inflammation Can Cause Lymphoid Tissue Fibrosis

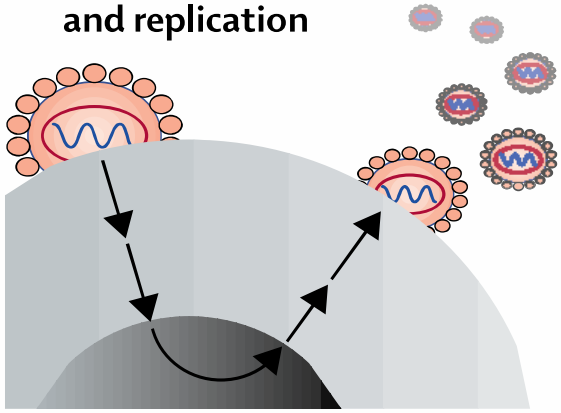


- Associated with low %naïve T cells and poor CD4+ T cell recovery
- May impair functional immune responses

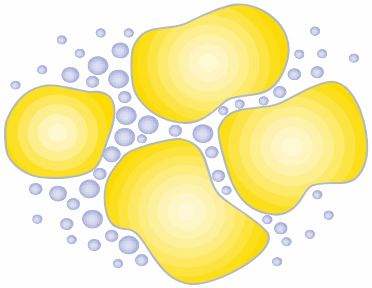
Estes, JID, 2008; Schacker, JCI, 2002; Zeng, JCI, 2011

Model of Inflammation

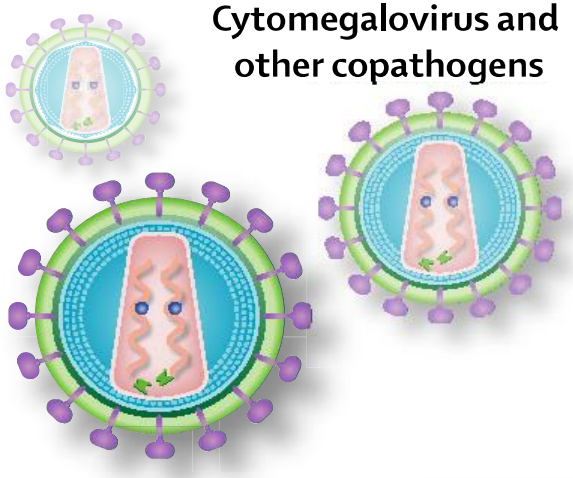
HIV production and replication



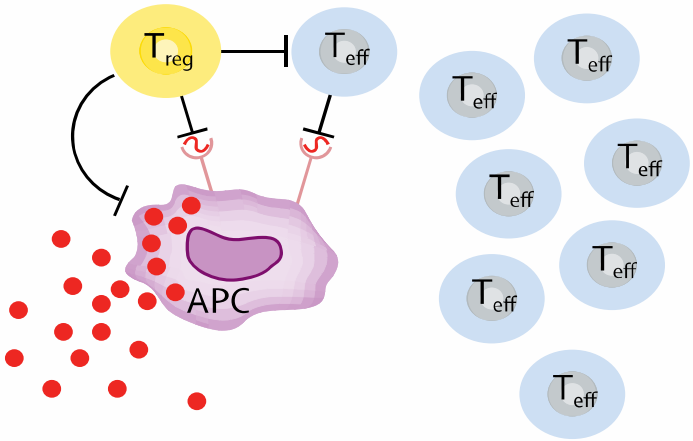
ART toxicity, lipodystrophy, and traditional risk factors



Cytomegalovirus and other copathogens

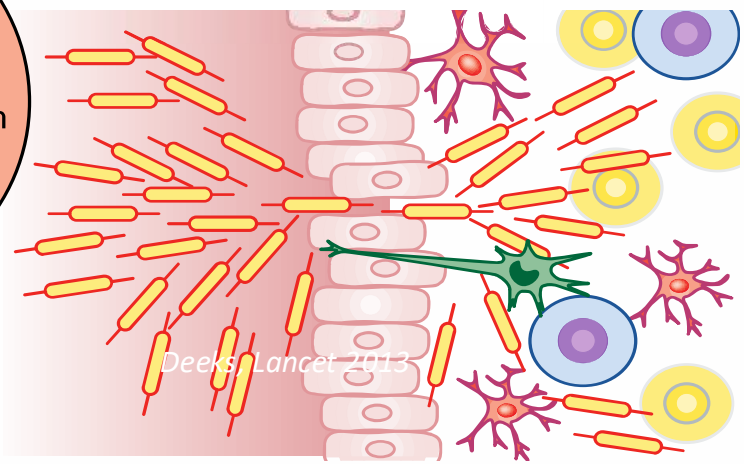


Loss of regulatory cells



Inflammation
↑Monocyte activation
↑T-cell activation
↑Endothelium adhesion
Dyslipidaemia
Hypercoagulation

Microbial translocation

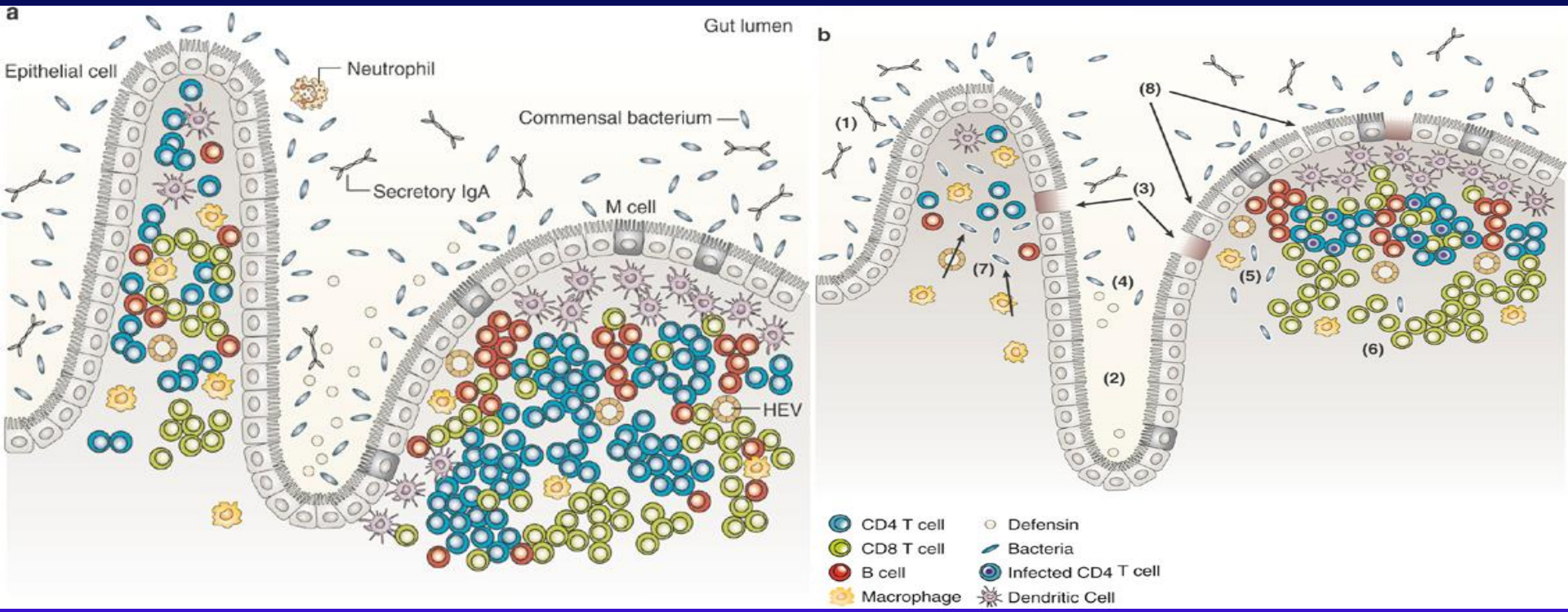


Comorbidities
(cardiovascular disease, cancer, kidney disease,
liver disease, osteopenia/osteoporosis, neurocognitive disease)

Microbial Translocation

Healthy GI tract

Damaged GI tract during HIV infection



J. Brenchley and D. Douek

Natural History of HIV Infection

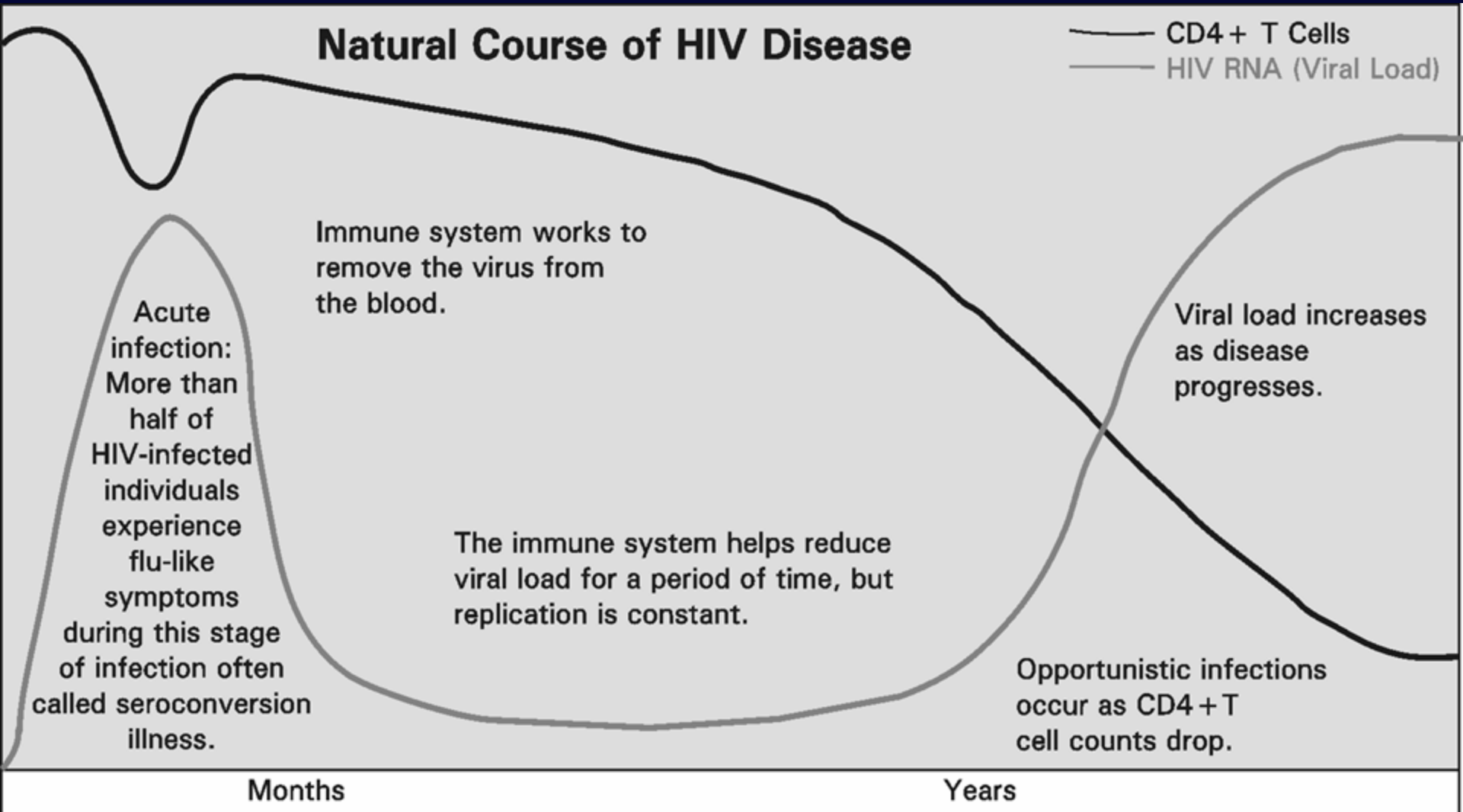
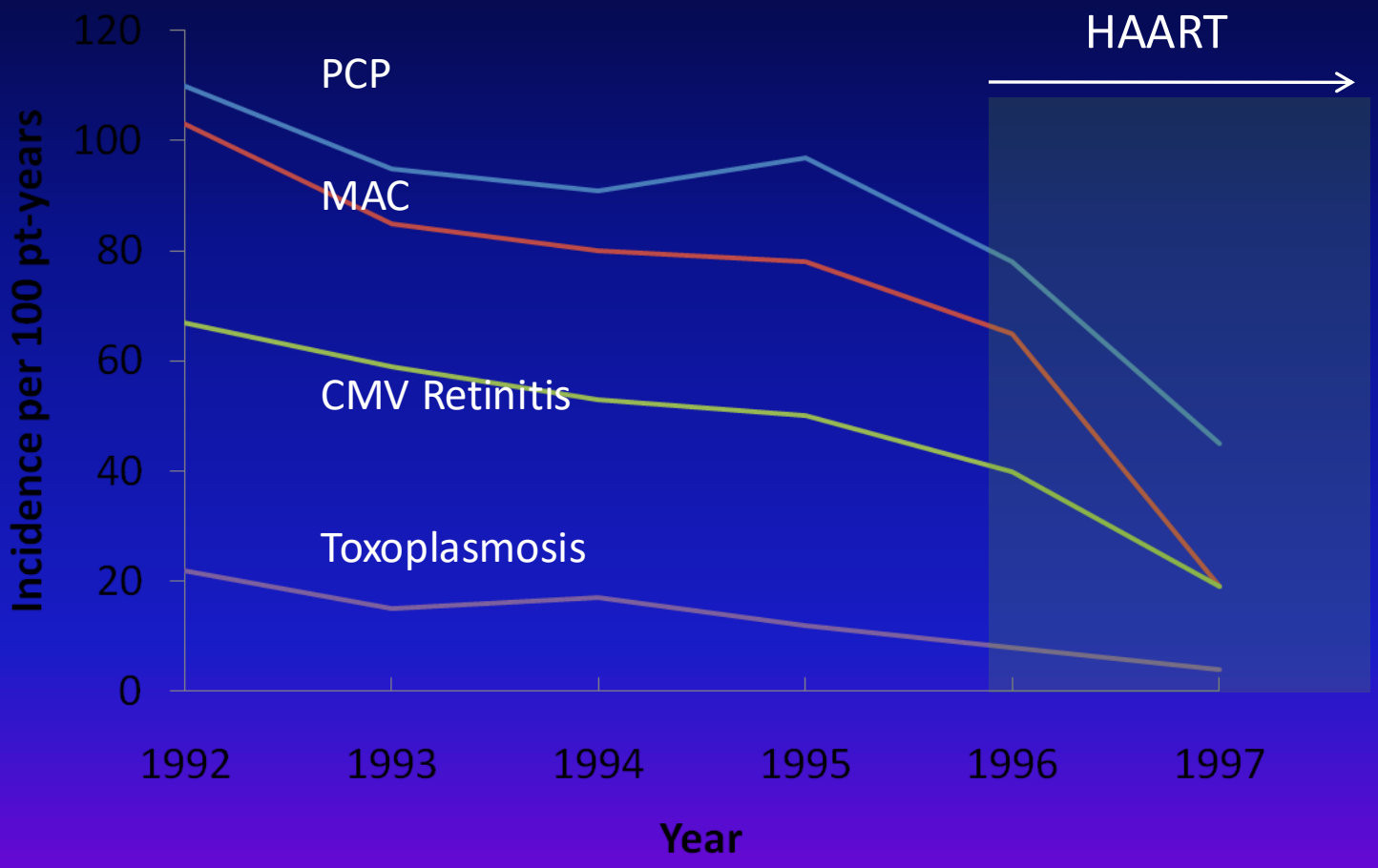
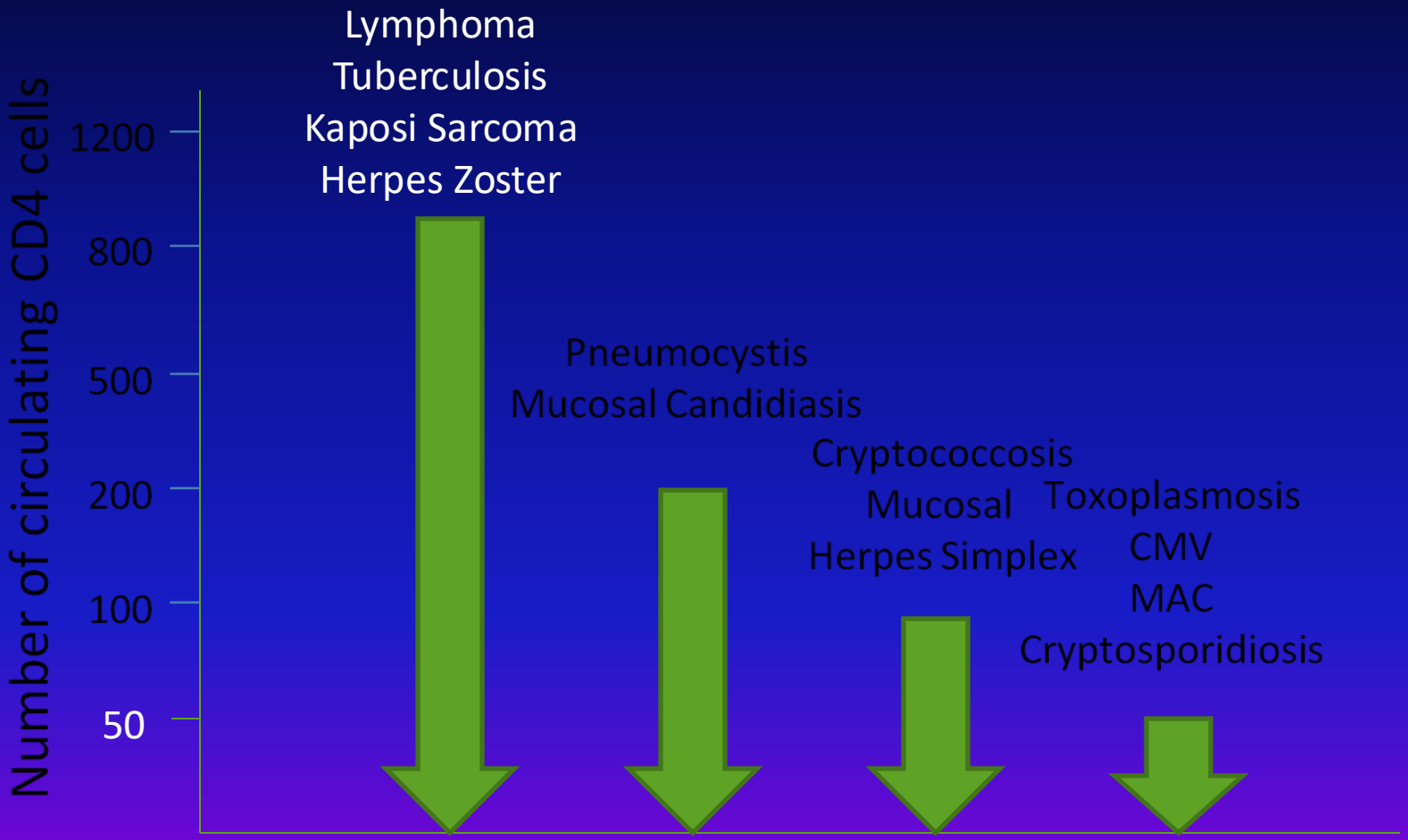


Figure1. The natural progression of HIV disease. Without intervention, viral load will continue to increase as CD4+T cell counts decline.

Impact of HAART on the Incidence of Opportunistic Infections



Typical Relationship of Clinical Manifestations to CD4 Count in HIV Infected Patients



CD4 Count	Organisms to Consider	Clinical Clues
>500	Community acquired organisms	More likely to acquire bacterial pneumonia, more likely to have HSV and zoster reactivation
200 – 500	Tuberculosis	Hemoptysis, night sweats, weight loss
<200	Pneumocystis jiroveci	Hypoxia induced by activity, interstitial infiltrates, ↑ LDH
	Cryptosporidium	Profuse watery diarrhea
	Candida	Oral thrush, oral lesions
	Fungal pneumonia	Cavitary lesions or diffuse infiltrates on X-ray
<100	Toxoplasmosis	Ring enhancing lesions on CT brain
	Candidal, HSV or CMV esophagitis	Odynophagia, dysphagia
<50	Cytomegalovirus	Visual changes, esophagitis, enteritis, encephalitis
	Cryptococcus	Headache, altered mentation, +India ink
	Mycobacterium avium complex	Night sweats, weight loss, diarrhea, malaise
	Primary CNS lymphoma (EBV assoc.)	Focal neuro deficits, seizures, weight loss, confusion

Criteria for Starting, Discontinuing, and Restarting Opportunistic Infection Prophylaxis for Adults with HIV

OI	Criteria for Initiating Primary Prophylaxis	Criteria for Discontinuing Primary Prophylaxis	Criteria for Restarting Primary Prophylaxis	Criteria for Initiating Secondary Prophylaxis	Criteria for Discontinuing Secondary Prophylaxis	Criteria for Restarting Secondary Prophylaxis
PCP	CD4 < 200 or oral candidasis	CD4 > 200 for 3 mos	CD4 < 200	Prior PCP	CD4 > 200 for 3 mos	CD4 < 200
Toxoplasmosis	+ serum IgG CD4 < 100	CD4 > 200 for 3 mos	CD4 < 100 – 200	Prior toxoplasmic encephalitis	CD4 > 200 sustained and completed initial therapy and is asymptomatic	CD4 < 200
MAC	CD4 < 50	CD4 > 100 for 3 mos	CD < 50 – 100	Documented disseminated disease	CD4 > 100 sustained and completed 12 mos of MAC tx and asymptomatic	CD4 < 100
Cryptococcosis	none	n/a	n/a	Documented disease	CD4 > 100 – 200 sustained and completed initial therapy and asymptomatic	CD4 < 100 - 200
Histoplasmosis	none	n/a	n/a	Documented disease	No criteria recommended for stopping	n/a
CMV	none	n/a	n/a	Documented end-organ disease	CD4 > 100 – 150 sustained and no evidence of active disease and regular exams	CD4 < 100 - 150

33 y/o man w/no PMH presents with shortness of breath x 5 days. Initially it was only on exertion but has progressed now to be at rest. He has a dry cough and progressive chest pain over his sternum that started after the cough.

RoS: otherwise negative

PMHx: gonorrhea x 1

PSHx: +tobacco, occasional MJ, no recreational drugs, sex with women, last several months ago

Physical examination and labs

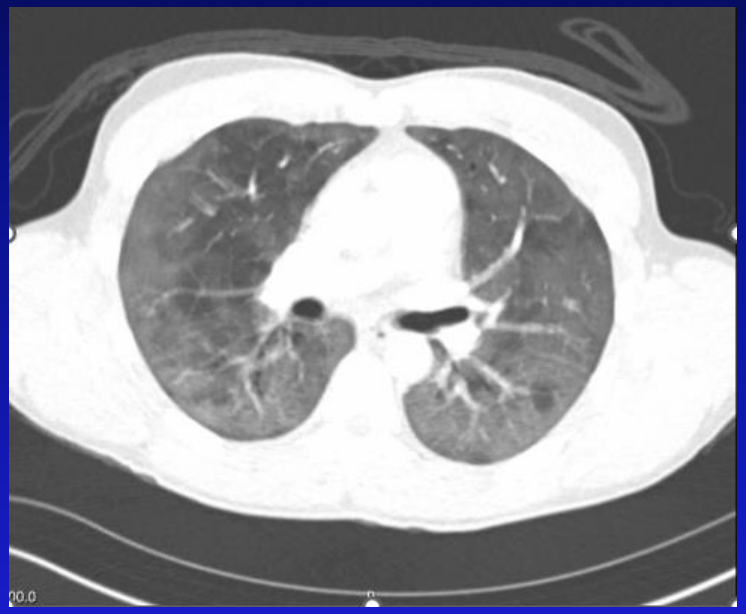
VS: T 37°C, hr 113, rr 34, bp 116/79, O2 sat 86% on RA, 90% on 2L, BMI 21
Gen: thin man, non-toxic, increased work of breathing
HEENT: thrush, no cervical or supraclavicular adenopathy
CV: tachycardic, regular rhythm, no murmurs
Pulm: increased work of breathing, clear to auscultation

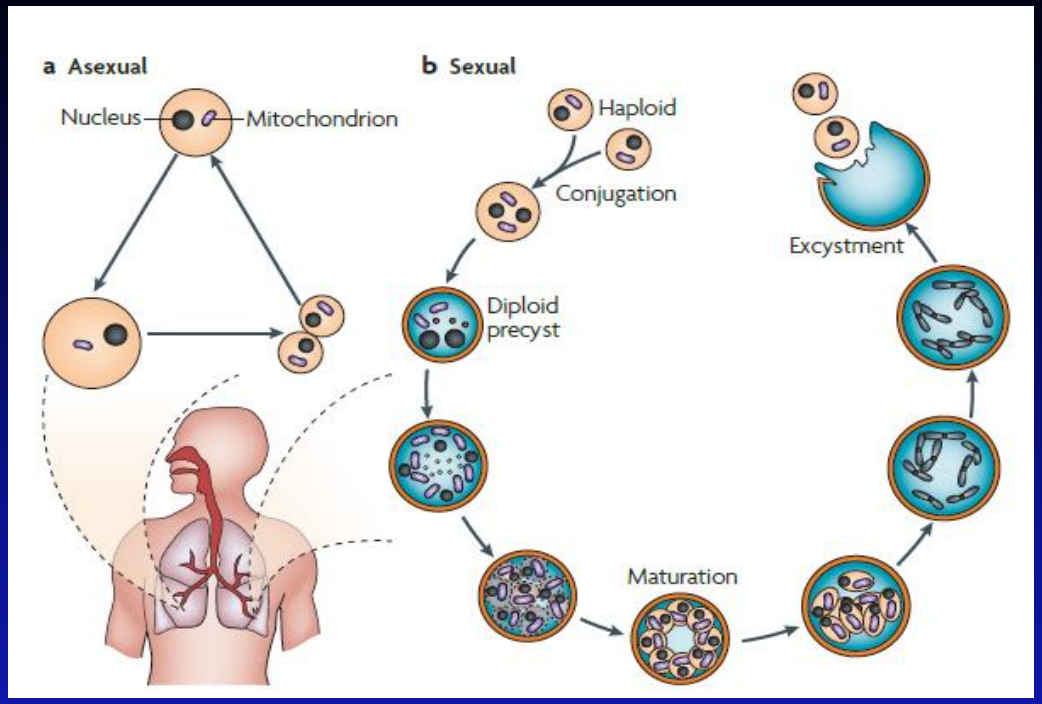
Routine labs: WBC 7.4. nl CBC, nl complete metabolic panel

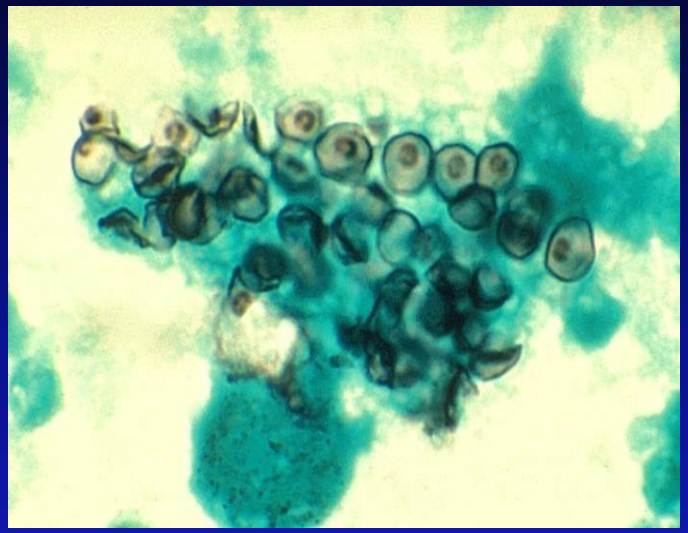
LDH 625
COVID, RSV and Influenza A/B were negative
HIV testing was +
Further respiratory studies were pending
CXR was normal

Further studies

- **PJP PCR positive**
- Urine legionella Ag negative
- Urine histo Ag negative
- Crypto Ag negative
- Respiratory multiplex PCR panel negative
- CD4 51 cell/ml^3
- HIV VL 3,700,000 copies/cc







CDC Public Health Image Library

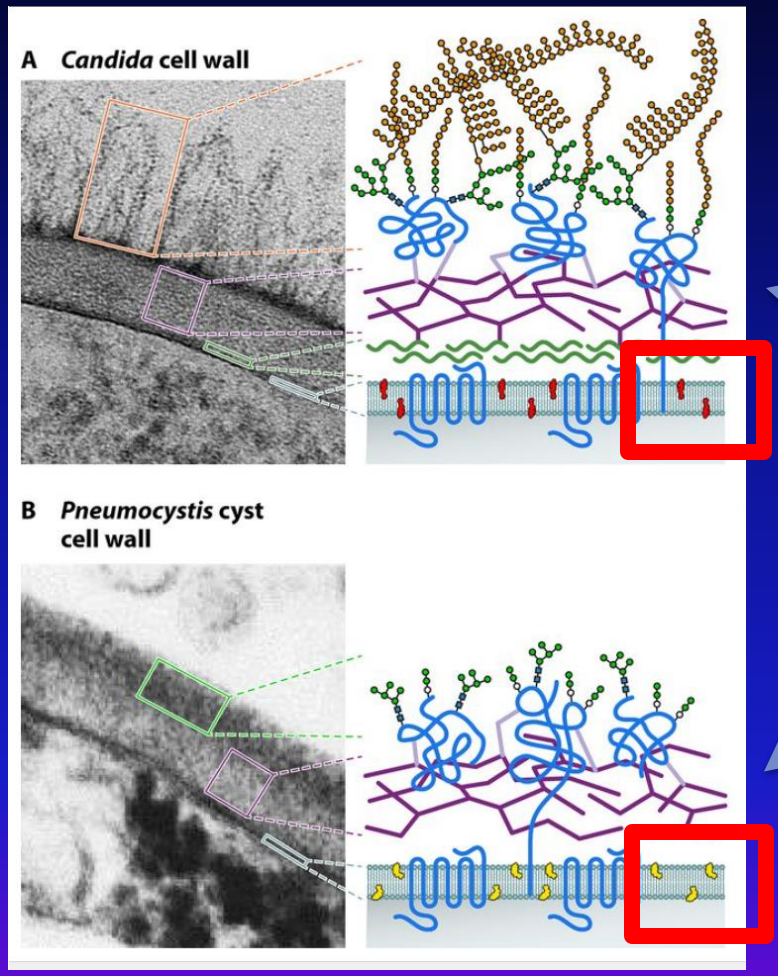
Trophozoite

- Primary form in infection (10:1 trophs: cysts)
- More difficult to detect with staining and small (1-4 microns)

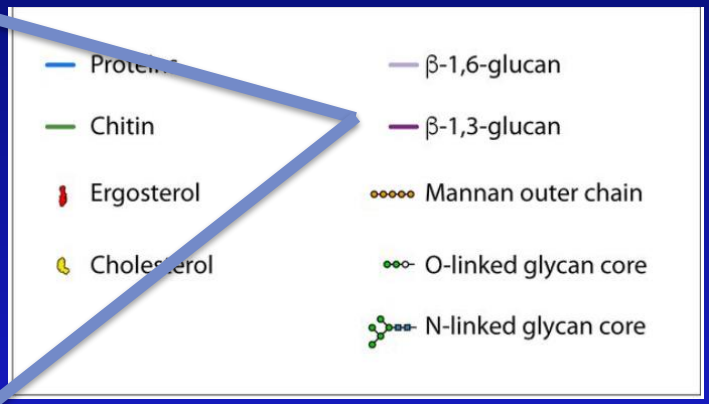
Cyst

- Responsible for transmission (airborne)
- Thick cell wall with beta D glucan (implications for diagnosis and treatment)
- Easily stains and is large (8-10 microns)

Nature Rev Micro, Thomas et al, 2007:5;298



Ergosterol- target of azoles and terbinafine



Cholesterol, not ergosterol

Ma et al, Clin Microbiol Rev 2018; 31:e00009-19

Risk Factors

- CD4+ T cell mediated activation of host macrophages is critical for protection from *Pneumocystis*
- B cells are also critical – the susceptibility to *Pneumocystis* of B cell-deficient mice is similar to that of T cell-deficient mice
- Innate and adaptive immune responses important

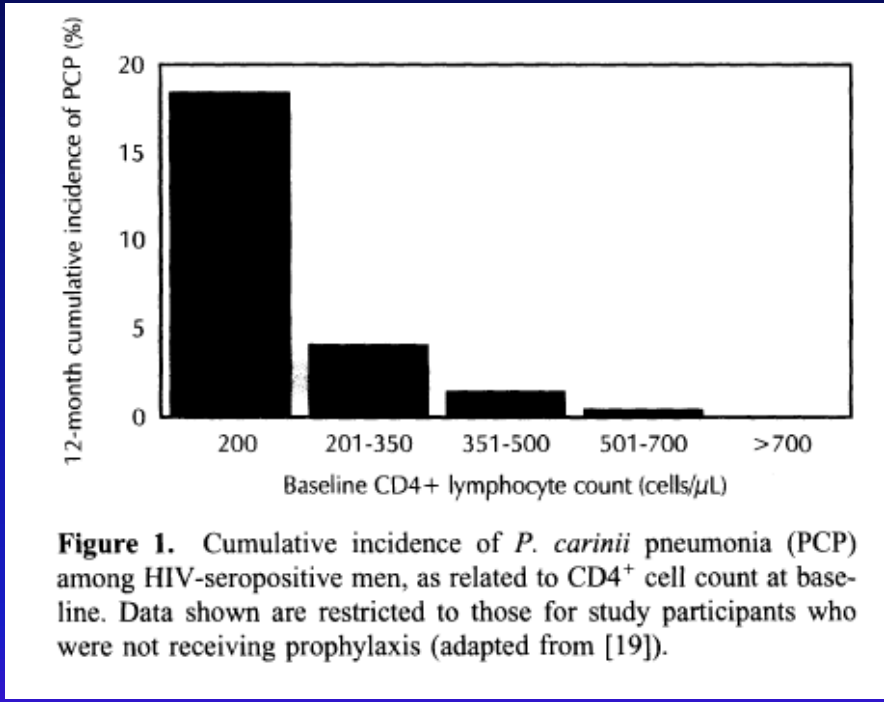


Figure 1. Cumulative incidence of *P. carinii* pneumonia (PCP) among HIV-seropositive men, as related to $CD4^+$ cell count at baseline. Data shown are restricted to those for study participants who were not receiving prophylaxis (adapted from [19]).

Simonds et al, CID 1995:S44-48

Transmission

- Ubiquitous organism
  - Nearly everyone exposed by age 4
  - Cause of childhood PNA
  - Colonization
- Reactivation versus new infection
  - Person to person spread plays a definite role
  - No recommendation for infection control procedures in hospitalized patients with *Pneumocystis*

Clinical Presentation

- Systemic
  - Fever, fatigue
- Pulmonary
  - Subacute onset of progressive SOB with DOE
  - Non-productive cough
- Extra-pulmonary disease can occur but is very rare

Physical Examination

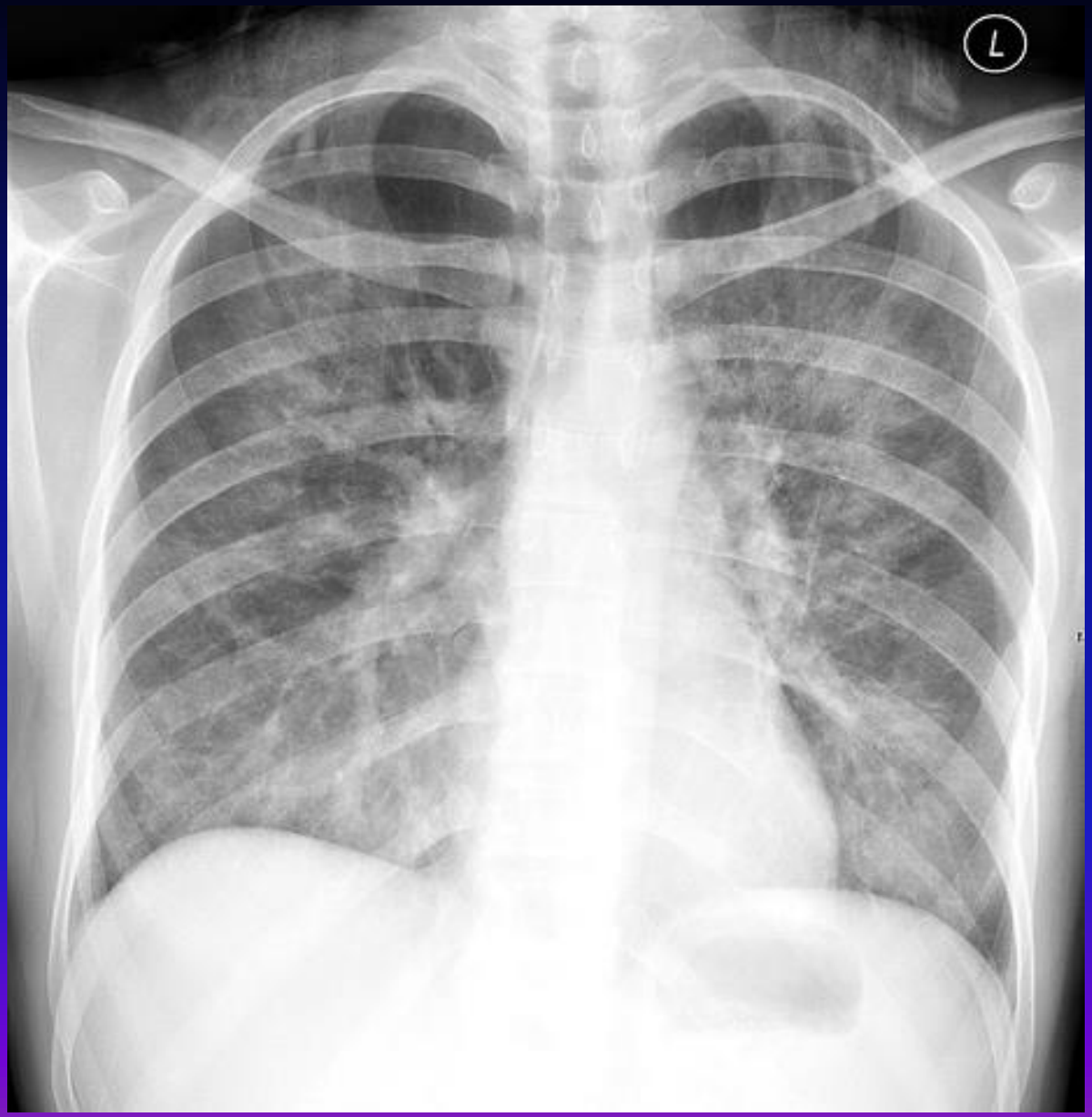
Other signs that suggest late-stage HIV
- thrush, seb derm, wasting

Crackles on examination (may be absent)

Chest pain

Desaturation on ambulatory pulse oximeter testing

PEARL: NP cough plus thrush = PCP until proven otherwise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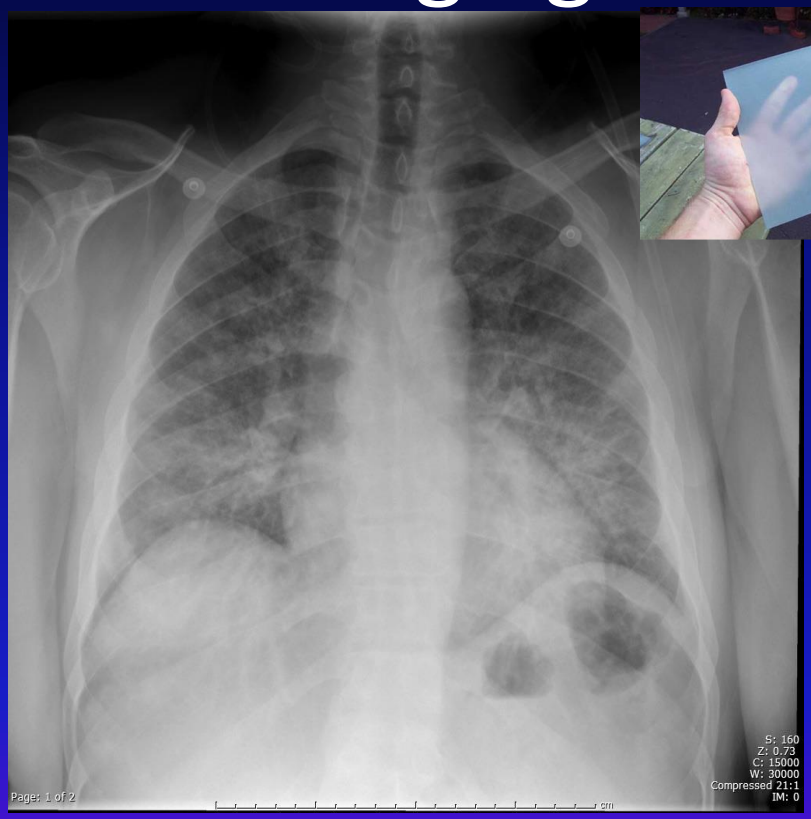
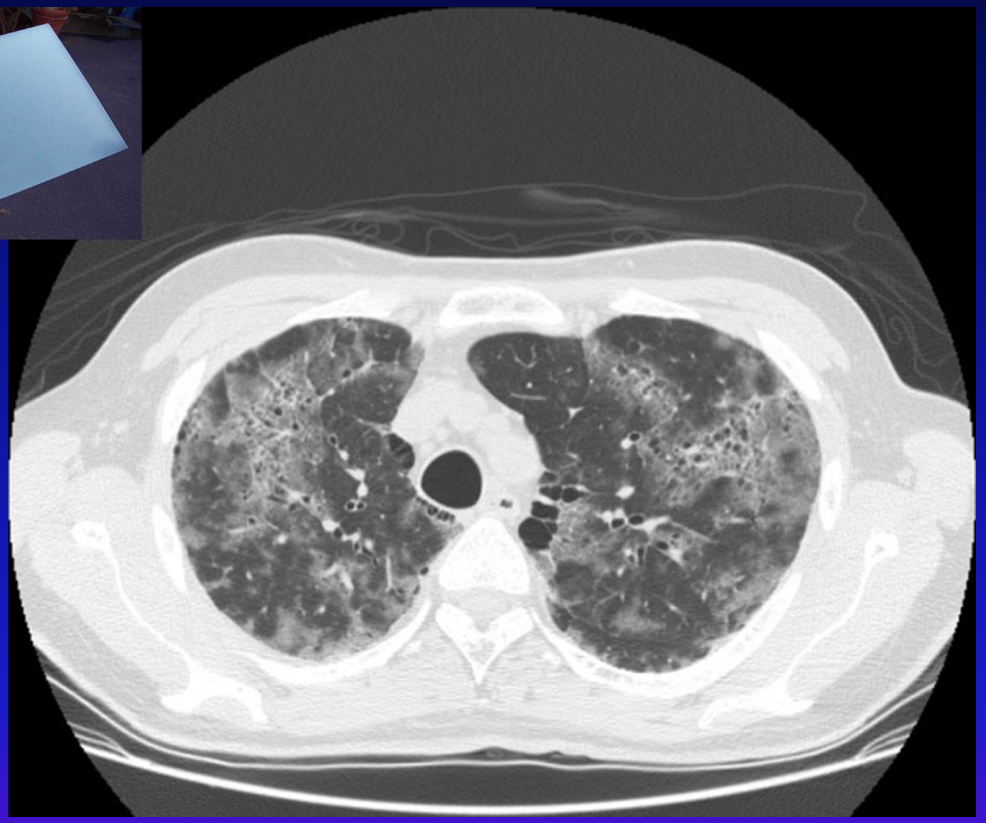
Imaging: Plain XR and Chest CT





Bilateral interstitial infiltrates is classic
Normal, cystic, nodular, spontaneous PTX

Ground glass infiltrates

Serologic tests

- Lactate Dehydrogenase
  - Poor sensitivity and specificity
  - Reflects lung disease
  - I do not put much stock in this
- Beta-d-glucan testing
  - Great for ruling OUT Pneumocystis pneumonia
  - Many things lead to positive results
  - VERY HIGH in PCP
  - Turn around time is a factor

High sensitivity, lower specificity

Approach to Respiratory Disease in HIV Infection: Diagnostic Clues

Parameter	**Example**
Rapidity of onset	> 3 days: PCP, Tb < 3 days: bacteria
Temperature	Afebrile: neoplasm
Character of sputum	Purulent: bacteria Scant: PCP, Tb, virus
Laboratory Tests ↓O2 post exercise	WBC, LDH
X-ray atypical	**Pattern : Beware!**

Diagnosis of Pneumocystis Pneumonia

A 30 year-old male with HIV infection and fever, cough, and diffuse infiltrates has a bronchoscopy performed.

Which of the following is the most sensitive and specific test to perform to establish whether or not pneumocystis is the causative pathogen?

a. PCR of the bronchalveolar lavage (BAL)
b. Culture of the BAL
c. Immunoflourescent stain of the BAL
d. ELISA of the BAL
e. Serum PCR

A patient with HIV infection presents with PCP (room air pO2=82mHg). He has a history of a severe exfoliative rash to TMP-SMX.

Which of the following therapies would you recommend:

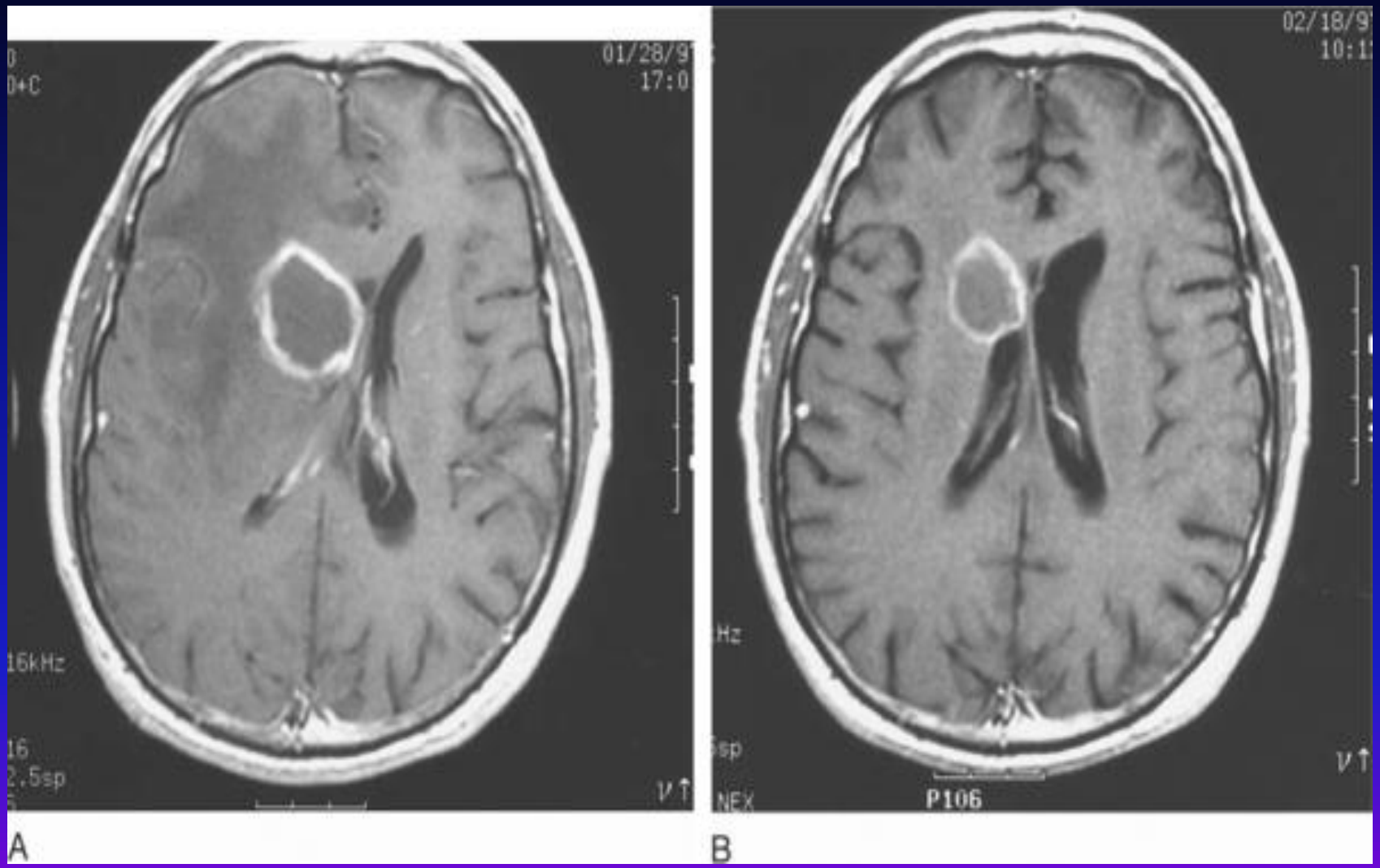
a. TMP-SMX + Prednisone
b. TMP + Dapsone
c. Parenteral Pentamidine
d. Clindamycin plus pyremethamine
e. Atovaquone

Toxicity Regarding Antipneumocystis Therapy

Drug	Issues
TMP-SMX	**Toxicities**: ↓WBC, ↓Plat, ↑LFT ↑Creat, ↑Amylase, rash, fever Cross reactivity: dapsone (+/- 50%)
Pentamidine	Hypotension, ↑Crea, ↑Amylase, ↓WBC ↓Glucose: related to ↑Crea occurs days-wks post-rx Torsade de Pointes
Atovaquone	Absorption
Clindamycin + Primaquin	Rash, LFT, diarrhea Methemoglobinemia Hemolytic anemia (G-6-PD)
Dapsone	Rash, fever, ↑LFT, Hemolytic anemia (G-6-PD), peripheral neuropathy

A 34 y/o man who has been HIV pos for ~ 10 years is brought to the ER after a witnessed seizure. He had been receiving HAART until ~ 5 years ago when he dropped out of care. Family members report that he has had some memory loss and unusual behavior for the past 2 weeks.

On PE is he is confused and disoriented.


A
B
P106

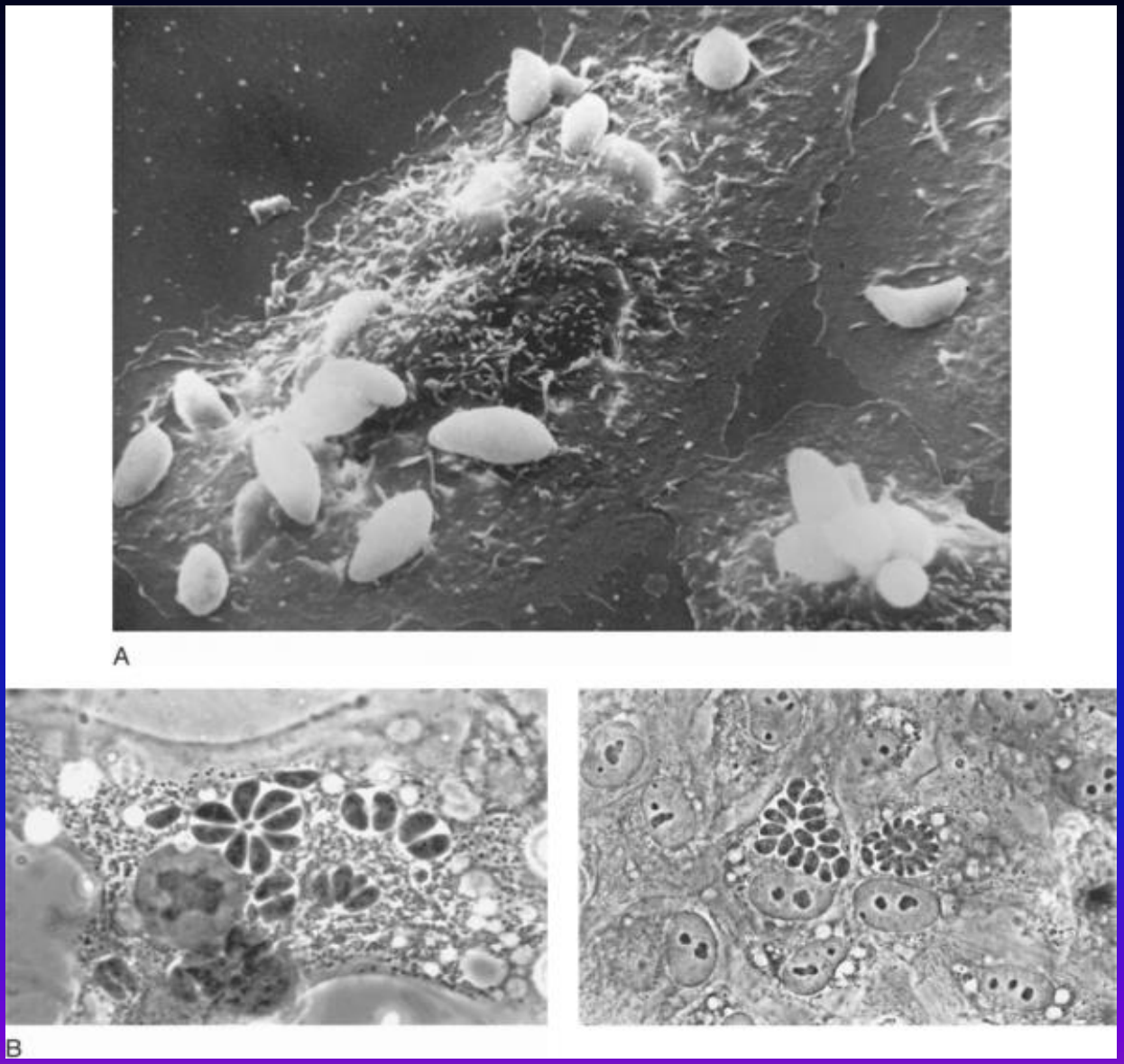
Evaluation of CNS Mass Lesions in Patients with AIDS

Toxoplasmosis
Lymphoma
PML
Tuberculosis
Fungus
Nocardia
Bacterial
Syphilis
Kaposi Sarcoma
Glioblastoma

Radiologic
non specific
extra CNS lesions

Laboratory
Serology – Toxo IgG, crypt Ag
Blood culture – AFB, fungus
CSF – Crypt Ag, CMV PCR, EBV PCR
Urine – Histo Ag

Empiric Therapy


A
B

How is toxoplasmosis most often transmitted ?

Toxoplasmosis - Diagnosis

- Definite diagnosis: Biopsy with demonstration of tachyzoites
- Presumptive diagnosis acceptable when
  - CD4 < 200
  - Compatible neurologic disease
  - No prophylaxis
  - Serology: positive toxo IgG

Therapy for Cerebral Toxoplasmosis

- Preferred Regimen
  - Sulfadiazine + **pyremethamine**
- Alternative Regimen
  - Clindamycin + **pyremethamine**
- Less studied regimens
  - TMP-SMX
  - Atovaquone + sulfadiazine
  - Azithromycin + **pyremethamine**
  - Dapsone + **pyremethamine**

A 35 year-old male with HIV (CD4 = 30, VL 100k copies) not on HAART, is brought to the emergency room with several weeks of declining cognitive function, ataxia, and aphasia. CT scan shows multiple hypodense, non enhancing cerebral white matter lesions. The gray matter is spared. CSF analysis shows: WBC 25 (100% lymphs), protein 110 mg/dl; glucose 90 mg/dl; VDRL neg, Crypt Ag neg, PCR for JC virus positive

What therapy is effective for this condition:

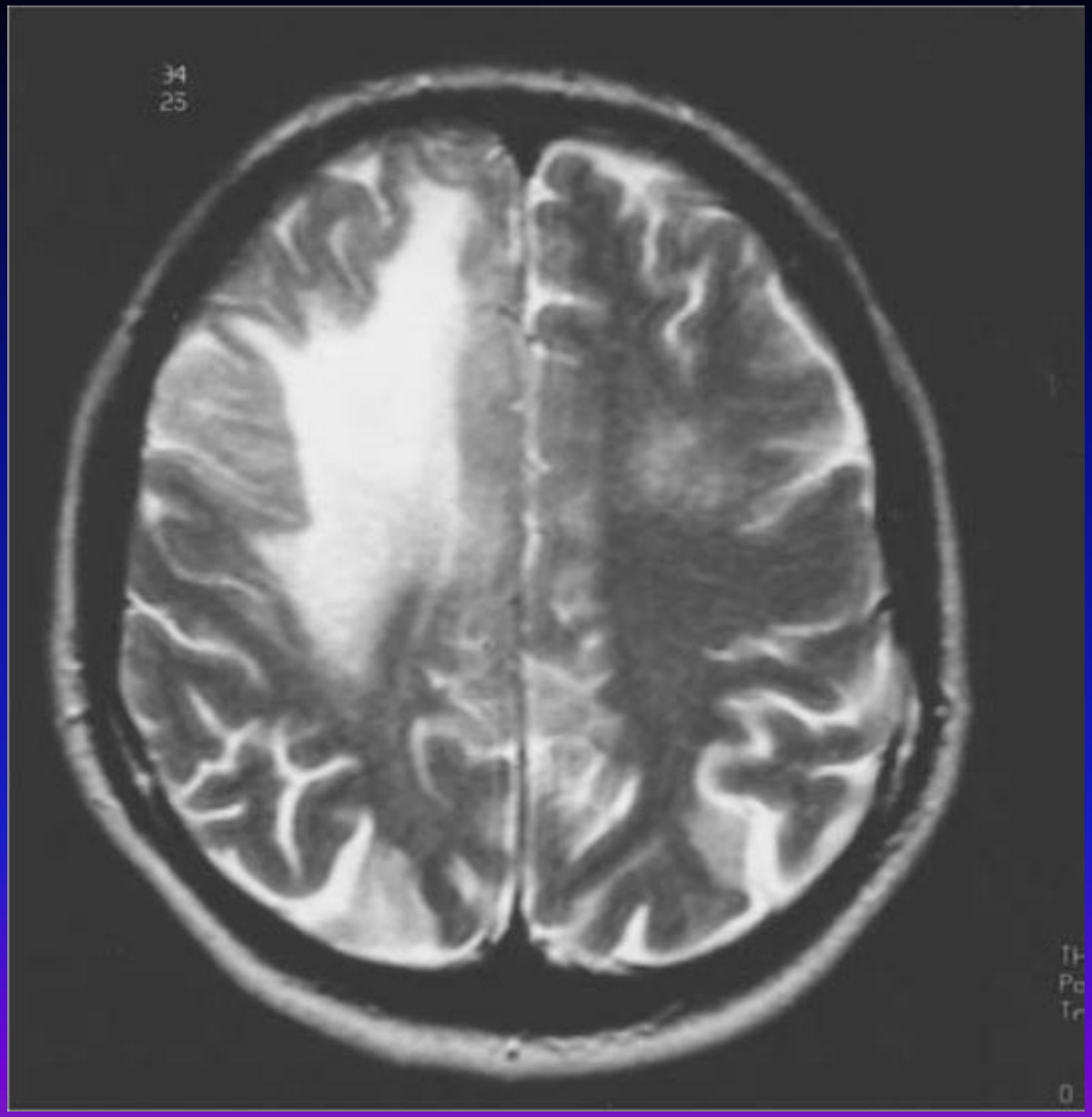
a. high dose acyclovir

b. Cidofovir

c. Vidarabine

d. Foscarnet

e. None of the above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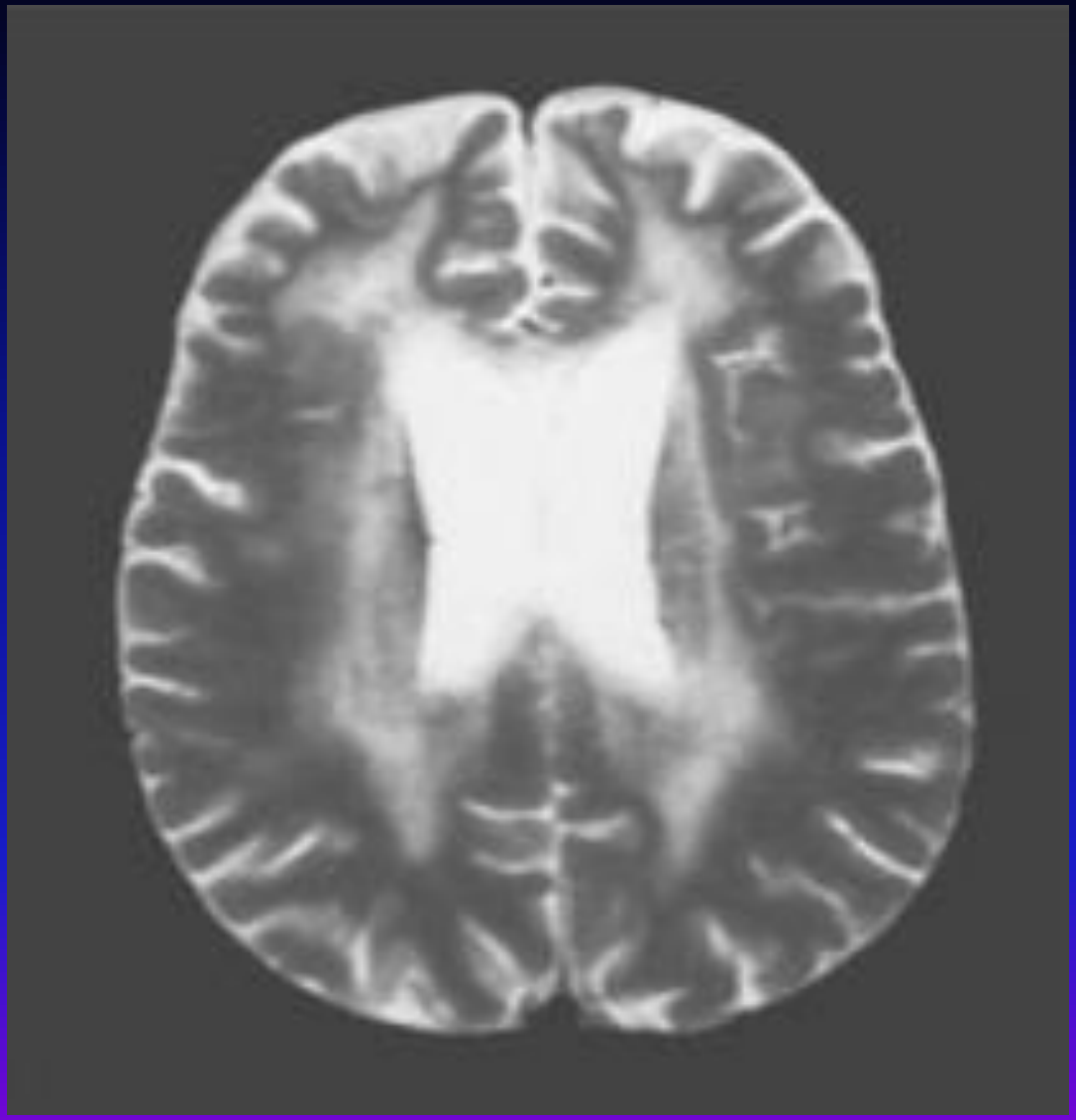
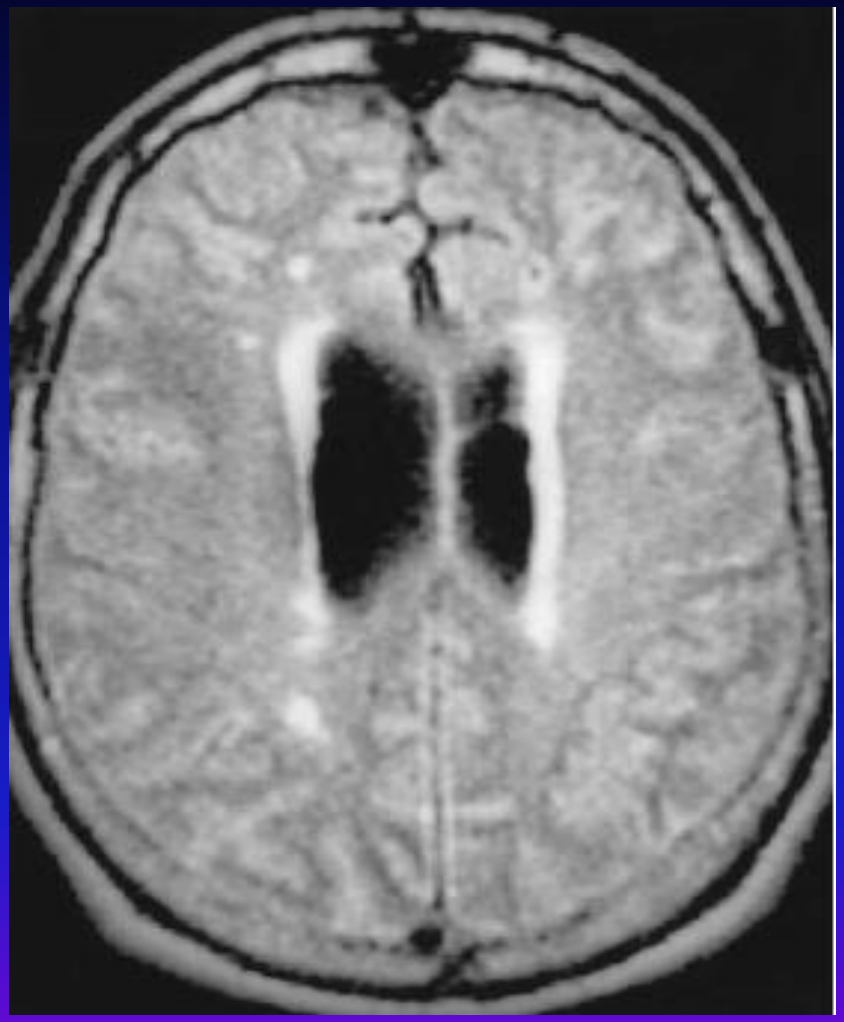




HIV associated CMV Disease

Pre-HAART, 30% of patients developed:

- Retinitis
- Colitis
- Others:
  - Pneumonitis
  - Ventriculoencephalitis
  - Myelitis
  - Radiculomyelopathy
  - Adrenalitis

Diagnosis of CMV Disease

- Serology (IgG, IgM)
- Viremia common in asymptomatic persons with low CD4
- Histology required for diagnosis of colitis and pneumonitis
    - ‘owl’s eye ‘ intranuclear inclusion bodies pathognomonic
    - Rare cells in the absence of clinical disease insignificant
- Retinitis clinical diagnoses
    - Fluffy exudate
- CNS – CMV PCR

CMV Detection in Specific Anatomic Sites

Site	Significance
BAL	None
Blood (cells, plasma)	maybe
CSF	Qualitative: probably

Mycobacterium Avium Intracellulare Complex

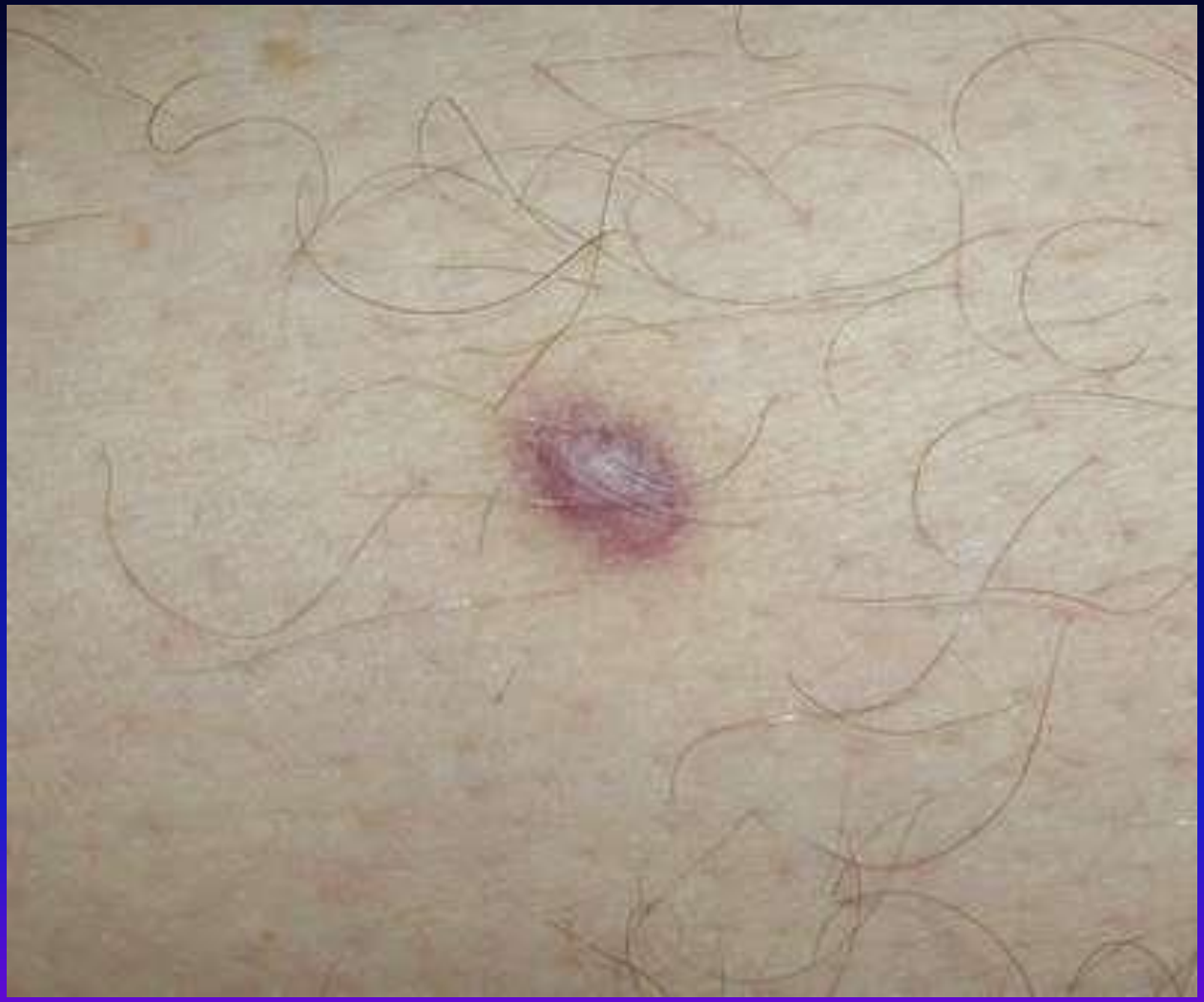
- Epidemiology: Ubiquitous in dirt, animals etc
- Avium: 95% isolates
- Transmission
  - Respiratory and GI, environmental source undetermined
  - Person-to-person NOT likely
- Clinical manifestations
  - Fever, wasting, ↑nodes, ↑liver, ↑spleen
  - Rare as cause of lung disease
  - Labs: ↑alk pho, ↓Hb (severe), ↓albumin

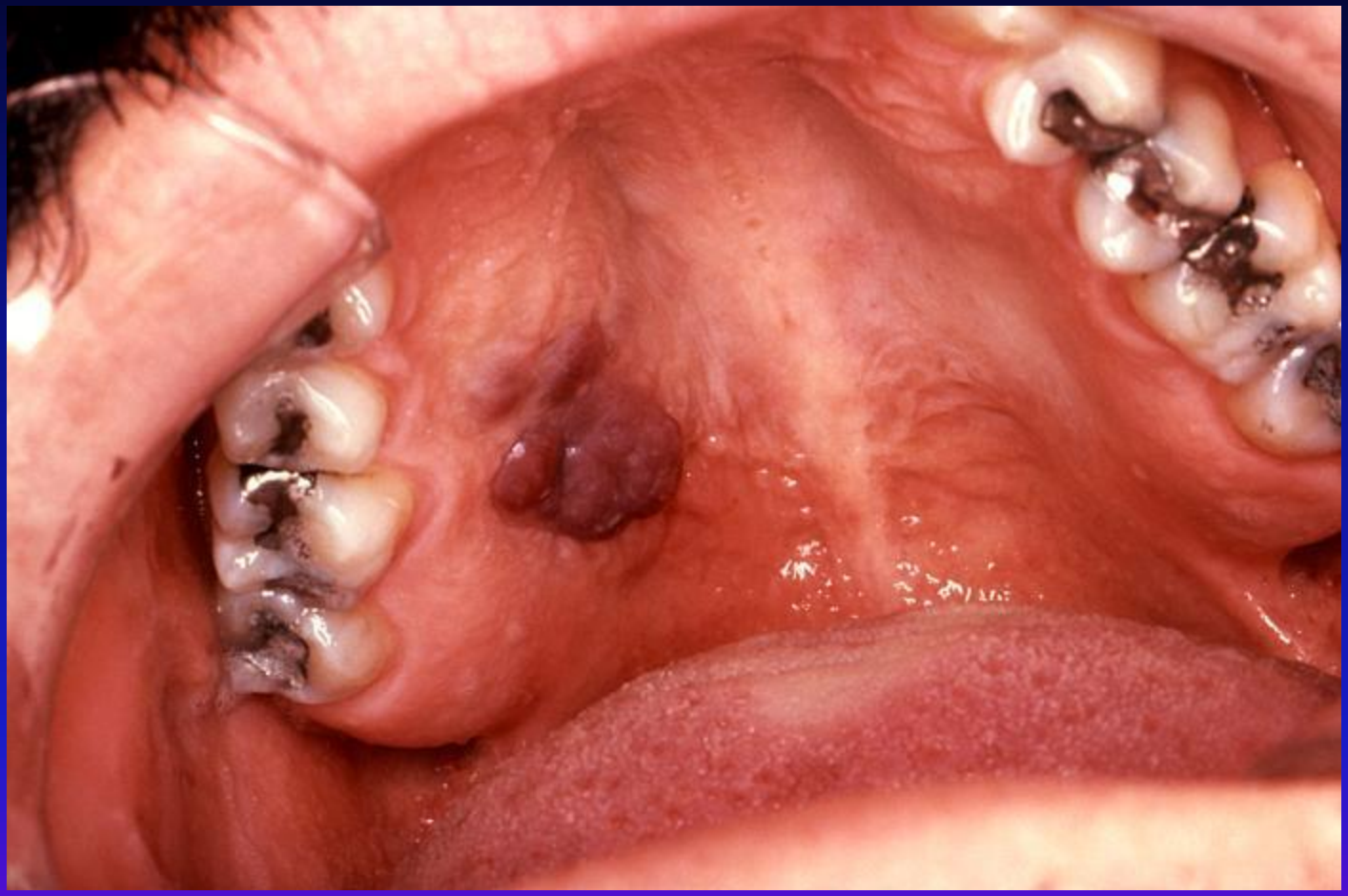
Mycobacterium Avium Intracellulare: Diagnosis and Treatment

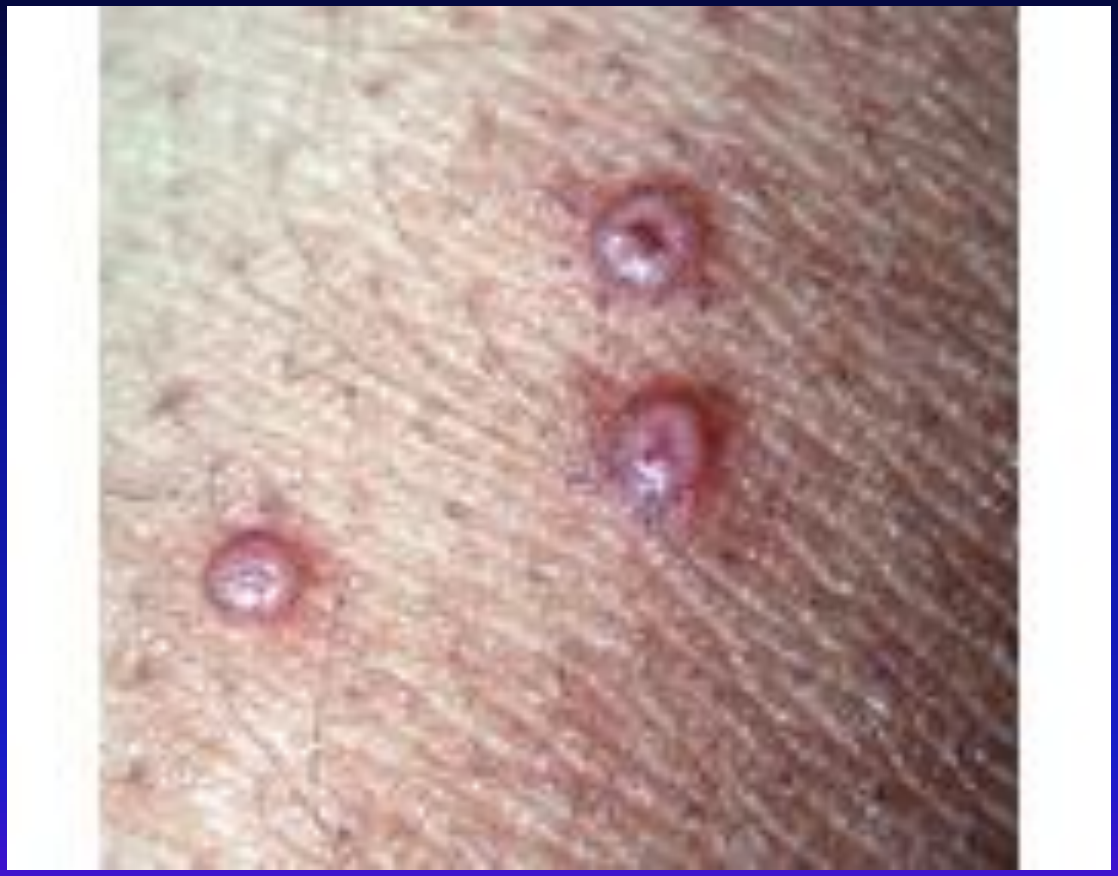
Compatible clinical syndrome
+
Isolation of *M. avium*

- Source of Isolates
  - Blood (if patient symptomatic)
    Pos culture 80 – 90 %: Bactec (7-14 days), solid (21 days)
  - Sputum/Stool/Urine
    - Low predictive value
- Treatment: Clarithro (or Azithro) + Ethambutol (+/- Rifabutin) x 1 year

Show and Tell



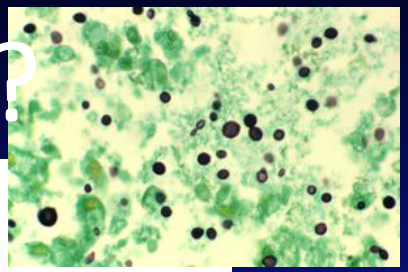


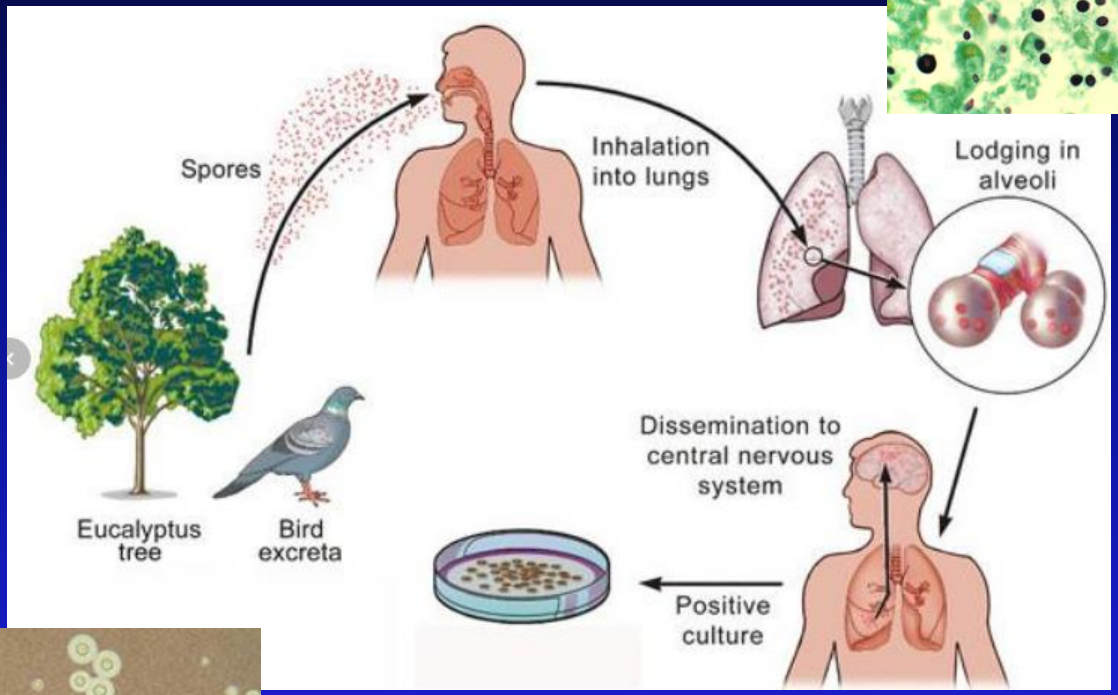


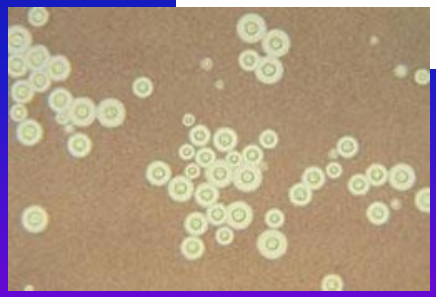
Cryptococcal Meningitis in Patients with HIV Infection

- Epidemiology: CD4 count < 50 cells/mm3 (75% cases)
- Diagnosis
  - CSF: Ag positive 95-100%
  - Serum: Crypto AG positive 95-99%,
  - Blood Culture: positive 75%
- Poor prognosis
  - Abnormal mental status
  - Low CSF WBC
- Beware unusual presentations
  - Skin (molluscum)
  - Lung (variable x-ray)
- Screening with CRAG: Titer > 1:8 should be treated

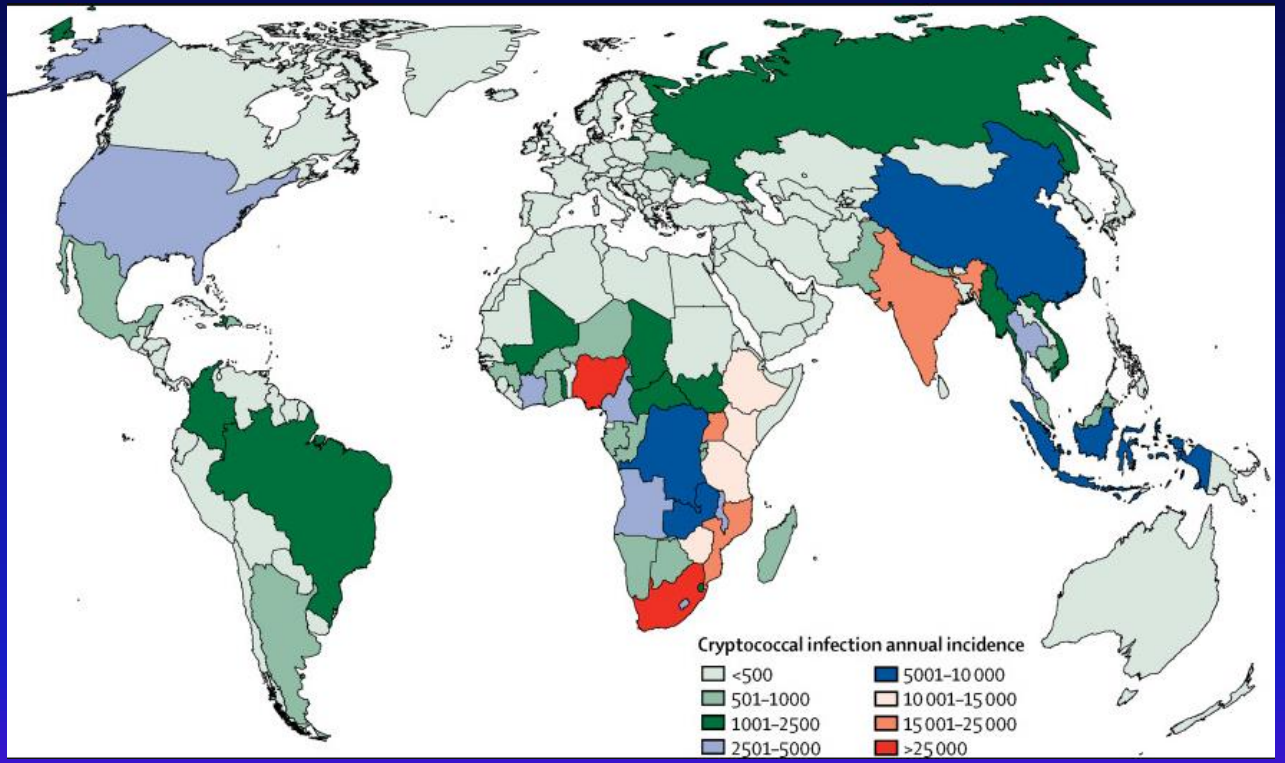
What is Cryptococcus?







Cryptococcal Disease causes 19% of AIDS-related deaths



Rajasingham et al. Lancet Infect Dis. 2022

Symptoms of cryptococcal meningitis

- Fever
- Headache
- Stiff neck
- Nausea/vomiting
- Sensitivity to light
- Altered mental status/confusion

2. CRYPTOCOCCAL DIAGNOSTICS

Question: Cryptococcal Diagnostics

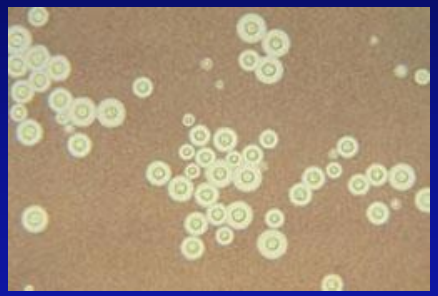
What test has the best diagnostic performance to exclude cryptococcal disease?

A. CSF India ink
B. CSF culture
C. CSF cryptococcal antigen by latex agglutination
D. CSF cryptococcal antigen lateral flow assay
E. Serum cryptococcal antigen lateral flow assay
F. CSF PCR

2. Cryptococcal Diagnostics

India ink

- 60-85% sensitivity
- Need microscope

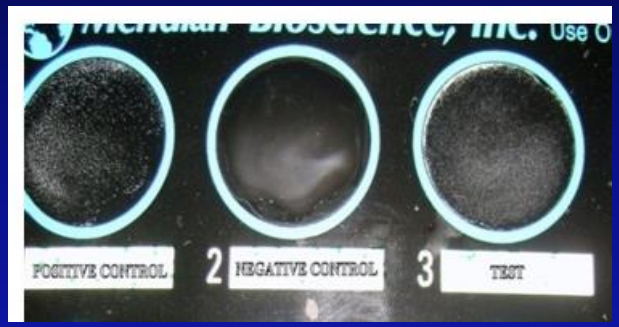


2. Cryptococcal Diagnostics

- India ink
- CSF Culture
  - Grows in 3 to 4 days for high burden, up to 7-10 days

2. Cryptococcal Diagnostics

- India ink
- CSF Culture
- Cryptococcal Antigen
  - Latex Agglutination
    - 97% sensitive, 99% specific
    - Expensive
    - Requires cold chain, shipping, storage
    - Labor intensive
    - Different manufacturers, different performance (↓*C. gattii*)



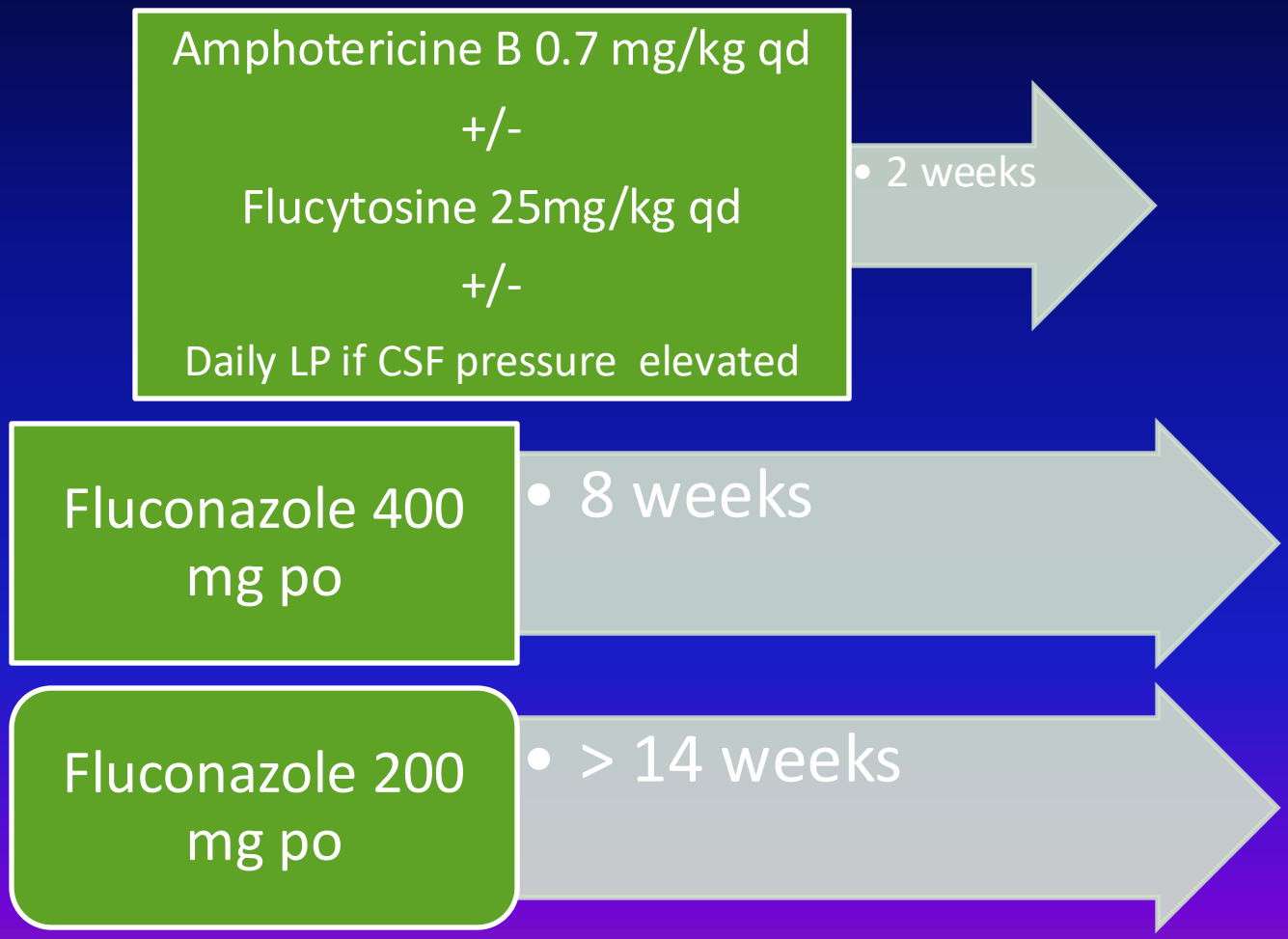
3.Principles of Antifungal Therapy

2010 IDSA Guidelines (OUTDATED)

Phase	Diagnosis	Week 2	Week 10	>12 months
Induction	Amphotericin x 14d			
	Flucytosine 100mg/kg x 14d			
Consolidation		Fluconazole 400 mg		
Maintenance			Fluconazole 200 mg*	

* and CD4 >200/μL x 6mo

Therapy of Cryptococcal Meningitis



What's wrong with amphotericin?

- Amphotericin B deoxycholate side effects include:
  - **Nephrotoxicity**
  - **Hypokalemia (100%) -low potassium**
  - **Hypomagnesemia (96%) –low magnesium**
  - Anemia
  - Nausea
  - Rigors, Phlebitis, Arthralgias

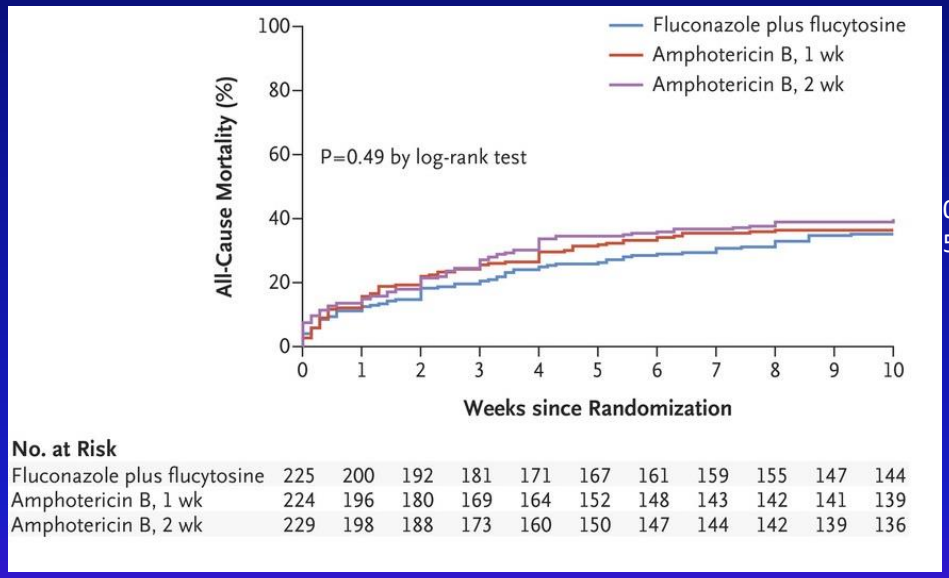
Liposomal formulation has fewer side effects.

Liposomal Amphotericin B does not have better survival than deoxycholate.[1]

[1] Kimuda S. Clin Infect Dis 2024

ACTA trial results

1 week of Amphotericin is as good as 2 weeks, less toxic.

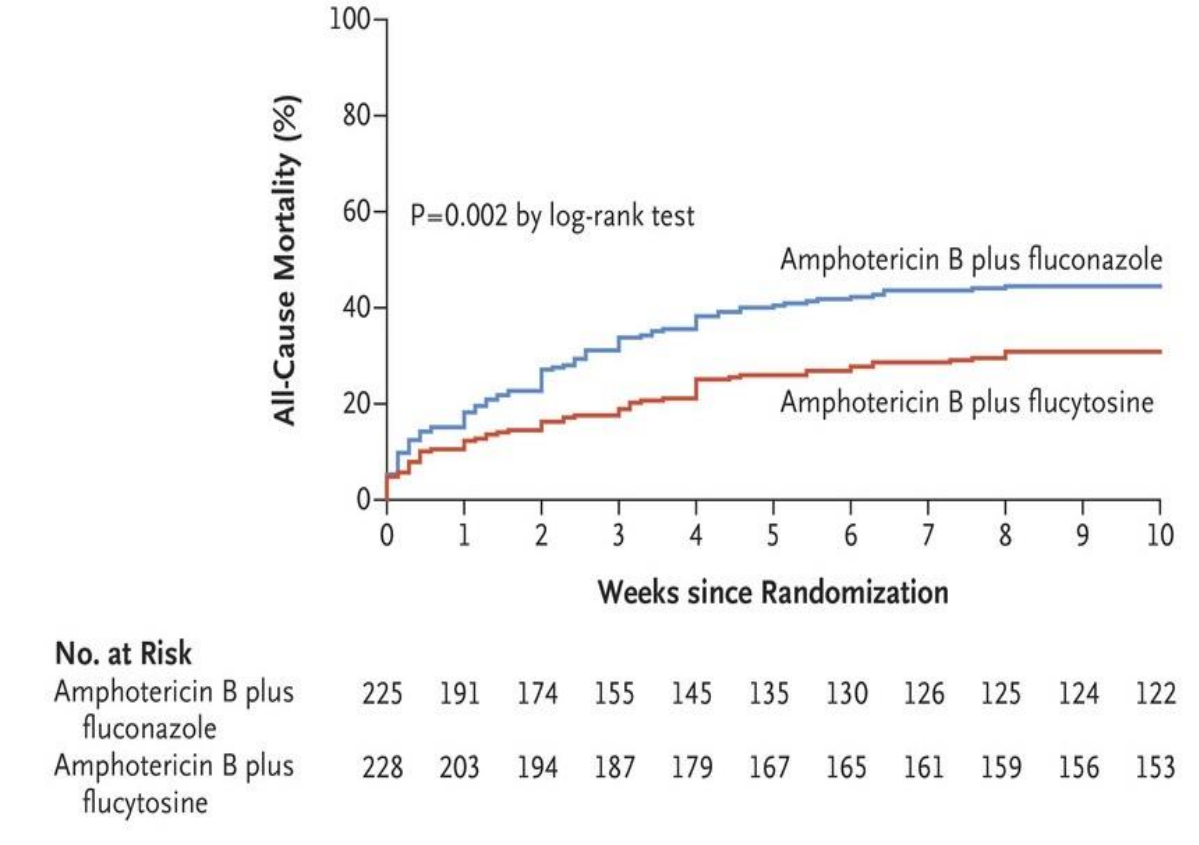


No. at Risk											
Fluconazole plus flucytosine	225	200	192	181	171	167	161	159	155	147	144
Amphotericin B, 1 wk	224	196	180	169	164	152	148	143	142	141	139
Amphotericin B, 2 wk	229	198	188	173	160	150	147	144	142	139	136

0-week mortality
5% to 39%

Molloy SF et al. NEJM 2018; 378:1004-1017

ACTA Trial: flucytosine is superior to fluconazole



45%
31%

Molloy SF et al. NEJM 2018; 378:1004-1017

MRI Imaging Features of CNS Disease in PWH: Diagnosis by Pattern Recognition

Meningitis/meningoencephalitis

- Cryptococcal meningitis
- TB meningitis
- CMV/VZV
- IRIS

Mass Lesions

- CNS toxoplasmosis
- Primary CNS lymphoma
- PML

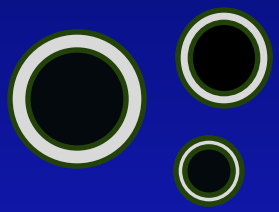
Rules are meant to be broken…

- Cryptococcoma
- Tuberculoma

Adapted from Sakai. Jpn J Radiol. 2021 Nov;39(11):1023-1038

MRI Imaging Features of CNS Disease in PWH: Diagnosis by Pattern Recognition of Focal Lesions

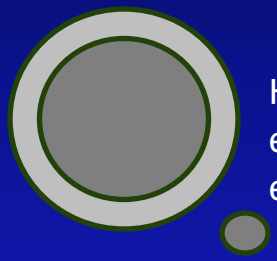
Toxoplasmosis



Ring enhancing

- Basal ganglia, thalamus, subcortical white matter, cerebellum
- PET: Hypometabolic
- SPECT: Cold

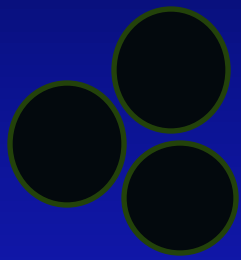
PCNSL



Homogenous enhancing or ring enhancing

- Corpus callosum, periventricular white matter
- PET: **Hypermetabolic**
- SPECT: Hot

PML



Non-enhancing T2 hyperintense

- Corpus callosum, periventricular white matter
- PET: Hypometabolic
- SPECT: Cold

Adapted Sakai. Jpn J Radiol. 2021 Nov;39(11):1023-1038

Key Points

- Multiple diagnoses can co-occur in people with low CD4
- CSF analyses can facilitate diagnosis of PML, cryptococcal or tuberculous meningitis and cytomegalovirus encephalitis
- A definitive diagnosis of cerebral toxoplasmosis requires a combination of serological testing, MRI findings, and in certain cases, brain biopsy
- On MRI, toxoplasmosis often manifests with several brain abscesses with predilection for the basal ganglia, whereas PML typically manifests as diffuse white matter lesions with predilection for the subcortical U fibers
- ART initiation in the setting of OIs can lead to a paradoxical worsening of symptoms, caused by IRIS

Immune Reconstitution Inflammatory Syndrome (IRIS)

- Definition: temporarily worsening of symptoms of inflammation or infection related to starting ART
- Occurs after initiation of ART as immunity is restored
- Results from an exaggerated immune response (eg, activation of latent or occult TB)
- Treatment consists of nonsteroidal antiinflammatory drugs for moderate cases and corticosteroids for severe cases

- In adults, IRIS has been most frequently observed following initiation of treatment of individuals with mycobacterial infections, PCP, cryptococcal infection, CMV, Herpes zoster or other herpes virus infections, and hepatitis B and C, toxoplasmosis and progressive multifocal leukoencephalopathy.
- It is also been described in children following BCG administration.

- The ideal time to initiate HAART in the setting of IRIS is not known.
- Delaying HAART to avoid IRIS may increase the risk of rapid and fatal progression of HIV disease.

Guidelines for the Prevention and Treatment of Opportunistic Infections in Adults and Adolescents With HIV

Prevention: Vaccines

Vaccine	All People with HIV	Where Varies by Age	Where Varies by CD4 Cell Count (cells/mm^3)	
			< 200	≥ 200
Pneumococcal conjugate (PCV15 or PCV20)	One dose			
Varicella (VAR)			Contraindicated	Two doses
Zoster recombinant (RZV)		Two doses for ages 18 and older		

https://clinicalinfo.hiv.gov/

Guidelines for the Prevention and Treatment of Opportunistic Infections in Adults and Adolescents With HIV

Prevention: Prophylaxis

Opportunistic Infections	Indication	Preferred
***Mycobacterium avium* complex (MAC) disease**	CD4 count <50 cells/mm^3 **AND** not receiving ART or remains viremic on ART or has no options for a fully suppressive ART regimen **(AI)** Not recommended for those who immediately initiate ART after HIV diagnosis **(AII)** Disseminated MAC disease should be ruled out before starting primary prophylaxis. See the MAC section for more information.	Azithromycin 1,200 mg PO once weekly **(AI)**, *or* Clarithromycin 500 mg PO twice daily **(AI)**, *or* Azithromycin 600 mg PO twice weekly **(BIII)**
***Pneumocystis* pneumonia (PCP)**	CD4 count <200 cells/mm^3 **(AI)**, *or* CD4 <14% **(BII)**, *or* If ART initiation must be delayed, CD4 count ≥200 cells/mm^3 but <250 cells/mm^3 and if monitoring of CD4 cell count every 3 months is not possible **(BII)**	TMP-SMX[c] 1 DS tablet PO daily **(AI)**, *or* TMP-SMX[c] 1 SS tablet daily **(AI)**

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Guidelines for the Prevention and Treatment of Opportunistic Infections in Adults and Adolescents With HIV

Discontinuation of Prophylaxis

Opportunistic Infection	Indication for Discontinuing Primary Prophylaxis	Indication for Restarting Primary Prophylaxis	Indication for Discontinuing Secondary Prophylaxis/Chronic Maintenance Therapy	Indication for Restarting Secondary Prophylaxis/Chronic Maintenance
***Mycobacterium avium* Complex Disease**	Continuing a fully suppressive ART regimen **(AI)**	CD4 count <50 cells/mm^3 and not on fully suppressive ART **(AIII)**	If the following criteria are fulfilled **(AI):** • Completed ≥12 months of therapy, *and* • No signs and symptoms of MAC disease, *and* • Have sustained (>6 months) CD4 count >100 cells/mm^3 in response to ART.	If a fully suppressive ART regimen is not possible and CD4 count is consistently <100 cells/mm^3 **(BIII)**
***Pneumocystis* Pneumonia**	CD4 count increased from <200 to >200 cells/mm^3 for >3 months in response to ART **(AI)** Can consider when CD4 count is 100–200 cells/mm^3 if HIV RNA remains below limits of detection for ≥3 months to 6 months **(BII).**	CD4 count <100 cells/mm^3 **(AIII)** CD4 count 100–200 cells/mm^3 and HIV RNA above detection limit of the assay **(AIII)**	CD4 count increased from <200 cells/mm^3 to >200 cells/mm^3 for >3 months in response to ART **(BII).** Can consider when CD4 count is 100–200 cells/mm^3 if HIV RNA remains below limits of detection for ≥3 months to 6 months **(BII).**	CD4 count <100 cells/mm^3 **(AIII)** CD4 count 100–200 cells/mm^3 and with HIV RNA above detection limit of the assay **(AIII)**

https://clinicalinfo.hiv.gov/

What does the future hold?

- We have made significant advancements in disease prevention and we have the tools to prevent and treat OIs
- Ongoing disparities lead to delays in testing and treatment and we must address social determinants of health to eliminate AIDS


Thank you
for your attention