

HIV and opportunistic infections

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Agenda



Introduction

Case Study 1: < 200 cells/uL

Case Study 2: < 100 cells/uL

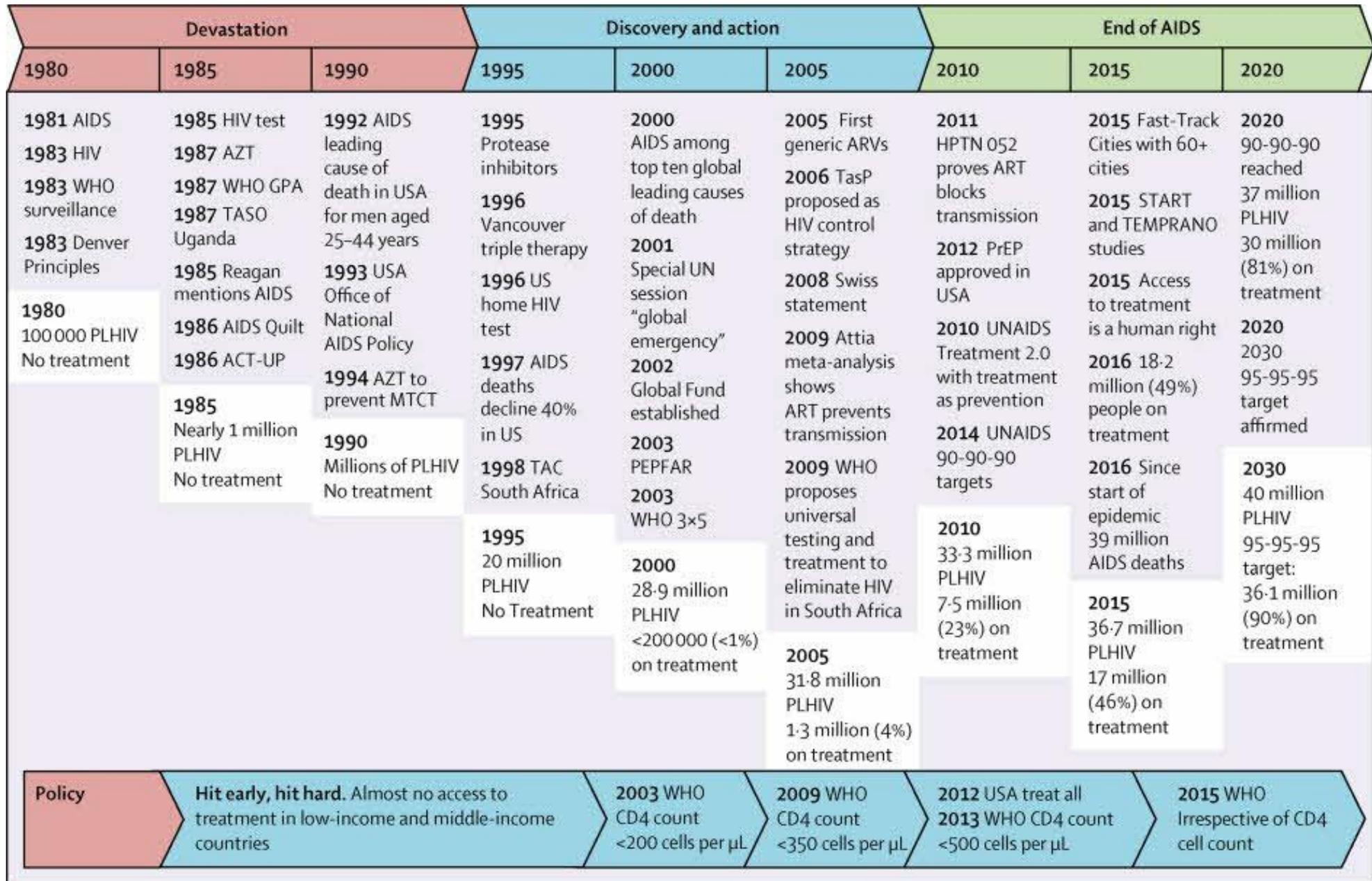
Case Study 3: < 50 cells/uL

Others to consider





Introduction



The State of HIV Now



Global HIV data

	2000	2005	2010	2020	2024
People living with HIV	27.9 million [25.3 million - 31.1 million]	29.9 million [27.1 million - 33.4 million]	32.2 million [29.2 million - 36.0 million]	38.9 million [35.3 million - 43.5 million]	40.8 million [37.0 million - 45.6 million]
New HIV Infections	2.9 million [2.3 million - 3.7 million]	2.5 million [2.0 million - 3.2 million]	2.2 million [1.7 million - 2.8 million]	1.5 million [1.2 million - 1.9 million]	1.3 million [1.0 million - 1.7 million]
AIDS related deaths	1.8 million [1.4 million - 2.4 million]	2.1 million [1.6 million - 2.7 million]	1.4 million [1.1 million - 1.8 million]	740 000 [570 000 – 960 000]	630 000 [490 000 – 820 000]

Epidemiology of HIV in Singapore

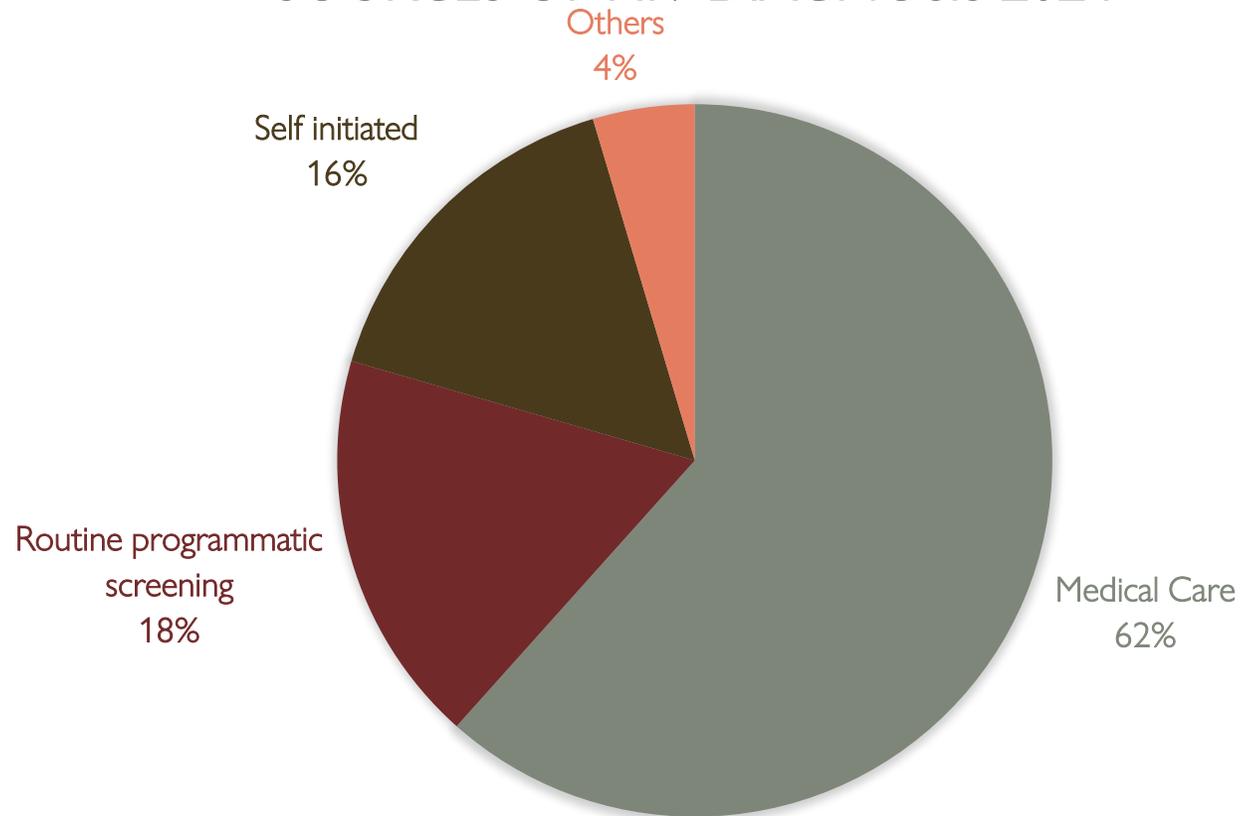


- ❖ The number of new cases have remained stable from between 400 to 500 per year from 2007 to 2017
- ❖ This dropped to 151 cases in 2024.
- ❖ 93.4% of cases are transmitted through sexual intercourse.
- ❖ Heterosexual transmission accounted for 38.4% of the cases, while 50.3% of the cases were from MSM transmission and 7.3% were among bisexual men.

Modes of Transmission

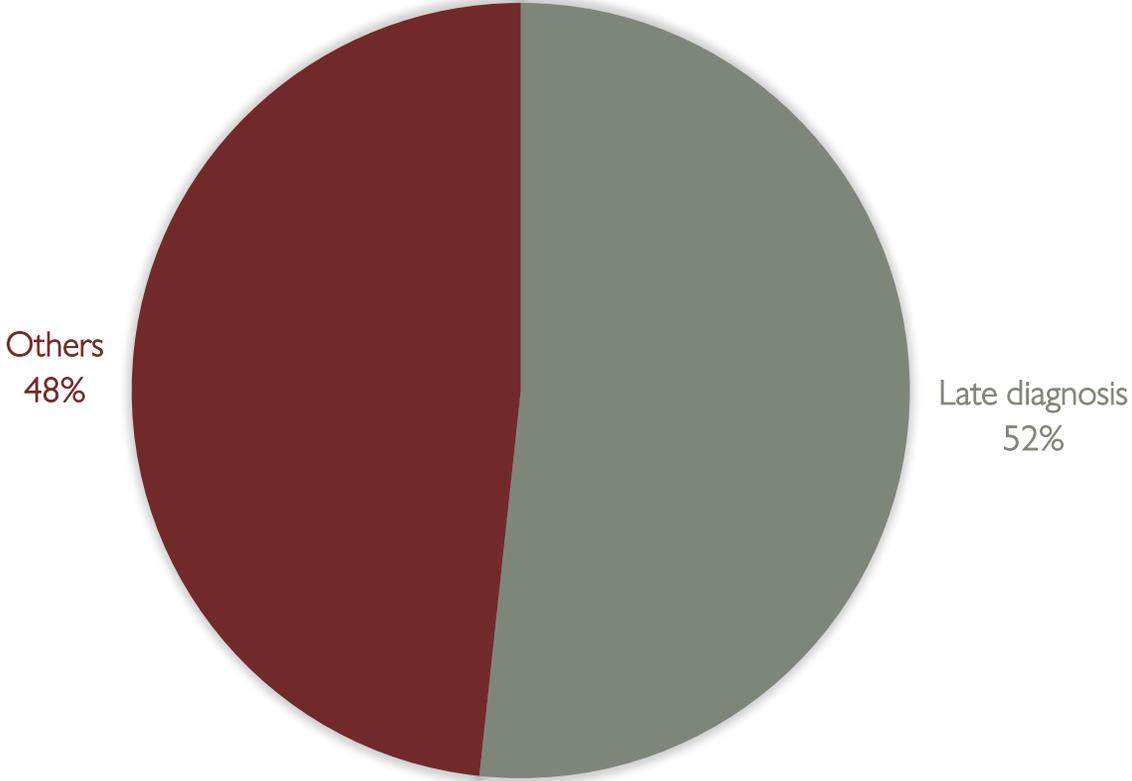
Mode of Transmission	1985 - 2019	2020	2021	2022	2023	2024	Total
Sexual Transmission							
Heterosexual	4704	96	82	75	66	58	5081
Men having sex with men	2850	125	147	102	119	76	3419
Bisexual	652	28	8	10 [^]	12	11	721
Intravenous drug use	126	3	3	3	1	1	137
Blood Transfusion	3	0	0	0	0	1 [*]	4
Renal Transplant overseas	5	0	0	0	0	0	5
Perinatal (mother to child)	34	0	0	0	0	0	34
Uncertain/Others	244	9	10	12	11	4	290
Total	8618	261	250	202	209	151	9691

SOURCES OF HIV DIAGNOSIS 2024



Adapted from Update on the HIV/AIDS Situation in Singapore 2024 (May 2025), CDA

PROPORTION OF LATE-STAGE HIV INFECTION AT DIAGNOSIS 2024



Adapted from Update on the HIV/AIDS Situation in Singapore 2024 (May 2025), CDA

HIV/AIDS Situation in Hong Kong [2024]



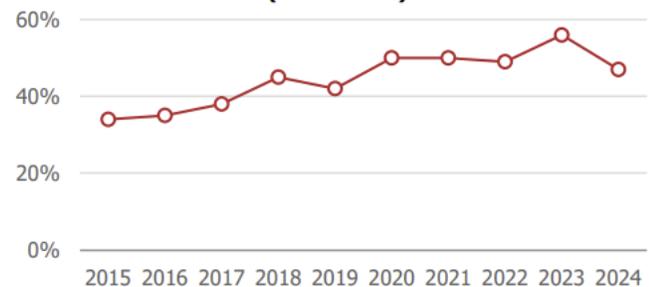
The number of newly reported HIV infection has decreased for the ninth consecutive year

The first case of HIV infection in Hong Kong was reported in 1984. As of 2024, the Department of Health has received a cumulative total of 12,403 reports of HIV infection and 2,557 AIDS cases under the HIV/AIDS voluntary reporting system (Figure 1). The number of newly reported HIV infection in 2024 was 365, representing an 8.1% decrease

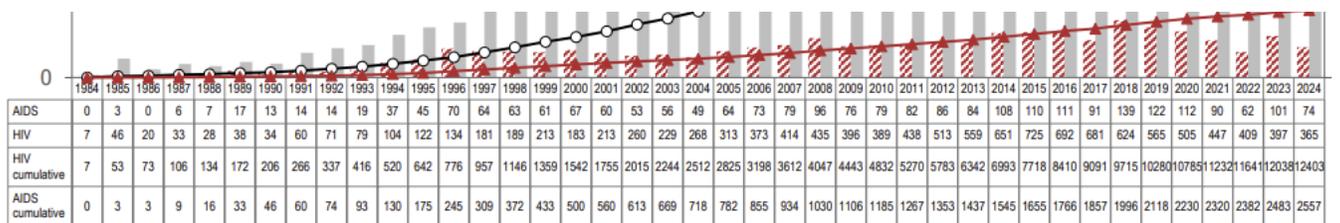
Almost half of the newly reported HIV cases were late presenters

Late presenters refer to individuals whose CD4 cell count is less than 200 cells/mm³ or who have progressed to AIDS at the time of HIV diagnosis. Late presentation leads to increased risk of opportunistic infections, higher mortality, and increased risk of HIV transmission in the community. The proportion of late presenters among newly reported HIV cases has risen to over 40% in recent years (Figure 8), indicating that many were not diagnosed and put on treatment in a timely manner at the early stage of infection.

Figure 8. Proportion of late presenters (2015–2024)



Note: Cases with incomplete information were excluded.

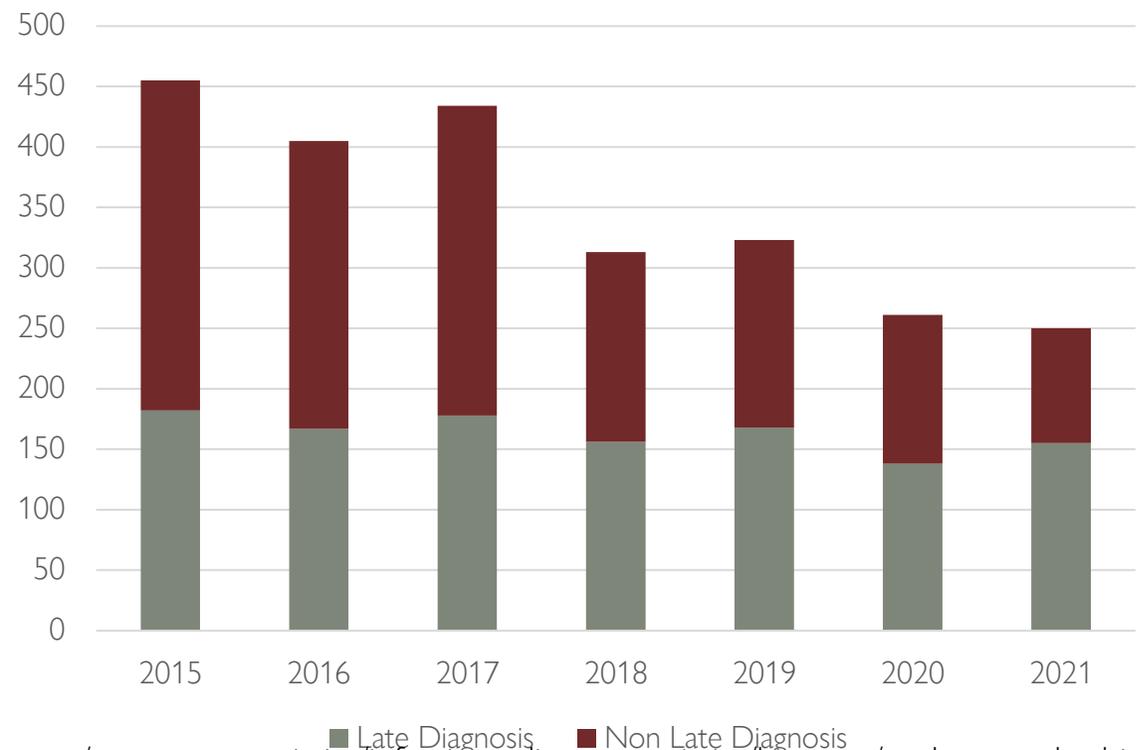


Most newly reported HIV cases were men, Chinese and young adults

Late presentation in Singapore

- Late presentation in Singapore is defined as a CD4 count of 200 cells/uL or less at the time of diagnosis, or development of an AIDS-defining illness within 1 year of diagnosis, or both
- As the number of newly diagnosed HIV infections has declined in recent years, the proportion of late diagnoses has increased

Late vs Non-Late Diagnosis among Newly Notified HIV Infections in Singapore, 2015-2021



1. [https://www.moh.gov.sg/resources-statistics/infectious-disease-statistics/hiv-stats/update-on-the-hiv-aids-situation-in-singapore-2021-\(june-2022\)](https://www.moh.gov.sg/resources-statistics/infectious-disease-statistics/hiv-stats/update-on-the-hiv-aids-situation-in-singapore-2021-(june-2022))

HIV Testing and Screening- Why is it important?

Reducing onward transmission from undiagnosed HIV-infected

- Evidence shows that persons living with HIV who are unaware of their HIV diagnosis have a markedly higher HIV transmission rate when compared with those who are aware of their HIV diagnosis^{2,3}

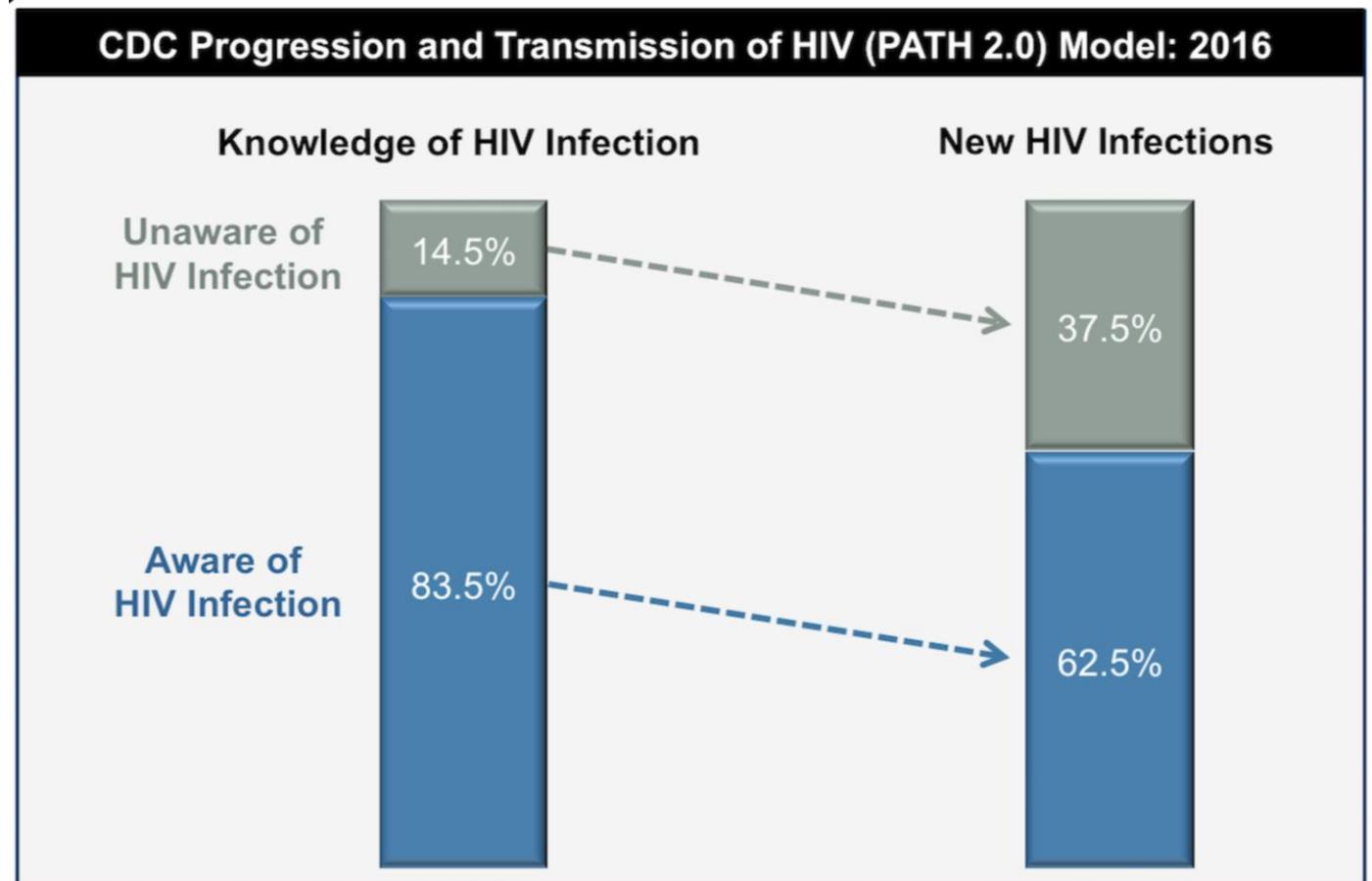
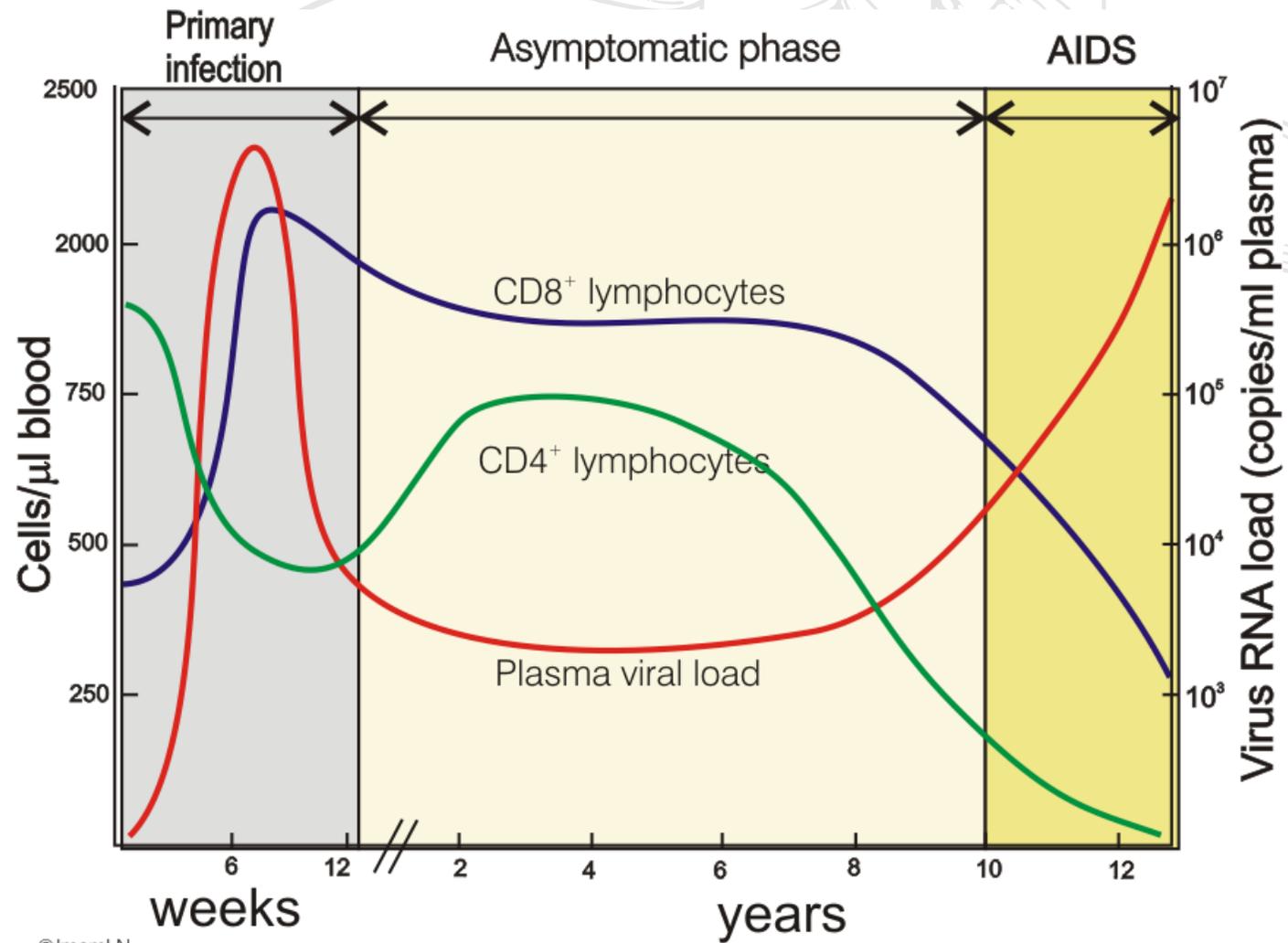


Figure 4 - HIV Transmissions in the United States in 2016 Based on Awareness of HIV Infection

In this Progression and Transmission of HIV (PATH 2.0) model, investigators from the CDC estimated HIV transmissions and transmission rates in the United States in 2016, including stratification based on awareness of HIV infection. As shown, persons unaware of their HIV infection account for a disproportionate percentage of HIV transmissions.

Natural Progression of HIV



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AIDS defining illnesses



Bacterial infections, multiple or recurrent*

Candidiasis of oesophagus, bronchi, trachea, lungs

Cervical cancer, invasive[§]

Coccidioidomycosis, disseminated or extrapulmonary

Cryptococcosis, extrapulmonary

Cryptosporidiosis (>1 month's duration)

Cytomegalovirus disease (other than liver, spleen, or nodes), onset at age >1 month

Cytomegalovirus retinitis (with loss of vision)[†]

Encephalopathy, HIV related

Herpes simplex: chronic ulcers (>1 month's duration) or bronchitis, pneumonitis, or oesophagitis (onset at age >1 month)

Histoplasmosis, disseminated or extrapulmonary

Isosporiasis, chronic intestinal (>1 month's duration)

Kaposi sarcoma[†]

Lymphoid interstitial pneumonia

Lymphoma, Burkitt (or equivalent term)

Lymphoma, immunoblastic (or equivalent term)

Lymphoma, primary, of brain

Mycobacterium avium complex or *Mycobacterium kansasii*, disseminated or extrapulmonary[†]

Mycobacterium tuberculosis of any site,

Mycobacterium, other species or unidentified species, disseminated[†] or extrapulmonary[†]

***Pneumocystis jirovecii* pneumonia**[†]

Pneumonia, recurrent^{†§}

Progressive multifocal leukoencephalopathy

Salmonella septicemia, recurrent

Toxoplasmosis of brain, onset at age >1 month[†]

Wasting syndrome attributed to HIV

Common Opportunistic Infections

CD4 count	Opportunistic Infections
< 200 cells/uL	Pneumocystic pneumonia
< 100 cells/uL	The Five Cs: <ul style="list-style-type: none">- CMV- Cryptococcus meningitis- Cerebral toxoplasmosis- Candidiasis- Cryptosporidium
< 50 cells/uL	Mycobacterium avium complex , PML
Anytime	Tuberculosis, regardless of CD4 count

Generally, individuals with **CD4 counts > 200 cells/uL** and are **virologically suppressed** are not considered immunocompromised

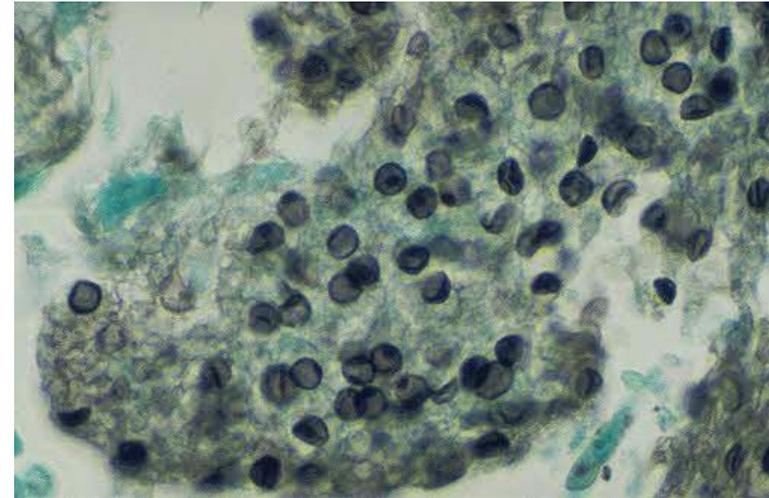
PCP in HIV Infection

- Techniques

- Induced sputum
- Bronchoscopic Alveolar Lavage (BAL)
- Transbrochial biopsy
- Open lung biopsy

- Diagnosis

- Can not be cultured
- Classified as fungus but shares characteristics with protozoa
- Staining of cyst wall, or cyst and trophozoite staining



Silver staining of PCP cyst wall with Gomori-Methenamine Silver (GMS) stain
<http://library.med.utah.edu/WebPath/INFEHTML/INFEC005.html>

PCP in HIV Infection Treatment

Preferred treatment for moderate to severe PCP

- Trimethoprim-sulfamethoxazole (TMP-SMX): [15–20 mg TMP and 75–100 mg SMX]/kg/day IV administered q6h or q8h (AI), may switch to PO after clinical improvement (AI)
- Duration of therapy: 21 days (AII)

Preferred treatment for mild to moderate PCP

- Same daily dose of TMP-SMX as above, administered PO in 3 divided doses (AI); or
- TMP-SMX (160 mg/800 mg or DS) 2 tablets tid (AI)
- Duration of therapy: 21 days (AII)

MAINTENANCE THERAPY

TMP-SMX (1-2 tablets) od until CD4 >200cells/ul >3mo

PRIMARY PROPHYLAXIS when CD4 <200

TMP-SMX (1-2 tablets) od

Dapsone 100mg od (if unable to tolerate TMP-SMX)

Nebulised pentamidine 300mg once monthly (if unable to tolerate TMP-SMX or dapso

Alternative therapy for moderate to severe PCP

- Pentamidine 4 mg/kg IV daily infused over ≥60 minutes (AI), certain specialists reduce dose to 3 mg/kg IV daily because of toxicities (BI); or
- Primaquine 15–30 mg (base) PO daily plus clindamycin 600–900 mg IV q6h to q8h or clindamycin 300–450 mg PO q6h to q8h (AI)

Alternative therapy for mild-to-moderate PCP

- Dapsone 100 mg PO daily and TMP 15 mg/kg/day PO (3 divided dose) (BI); or
- Primaquine 15–30 mg (base) PO daily plus clindamycin 300–450 mg PO q6h to q8h (BI); or
- Atovaquone 750 mg PO bid with food (BI)

Indications for corticosteroids (AI)

PaO₂ <70 mmHg at room air or alveolar-arterial O₂ gradient >35 mmHg

Prednisone doses (beginning as early as possible and within 72 hours of PCP therapy) (AI):

Days 1–5 40 mg PO bid

Days 6–10 40 mg PO daily

Days 11–21 20 mg PO daily

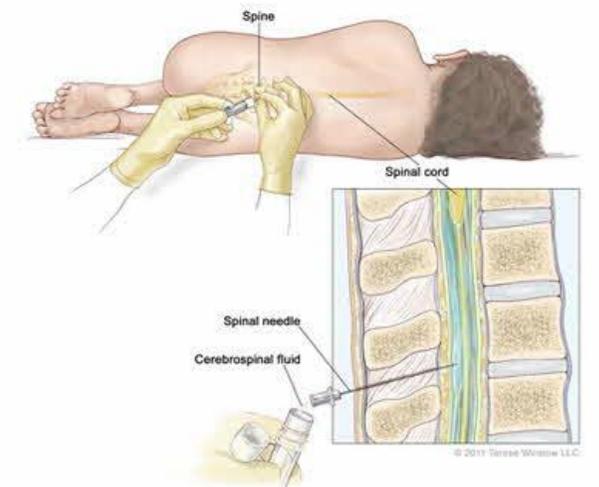
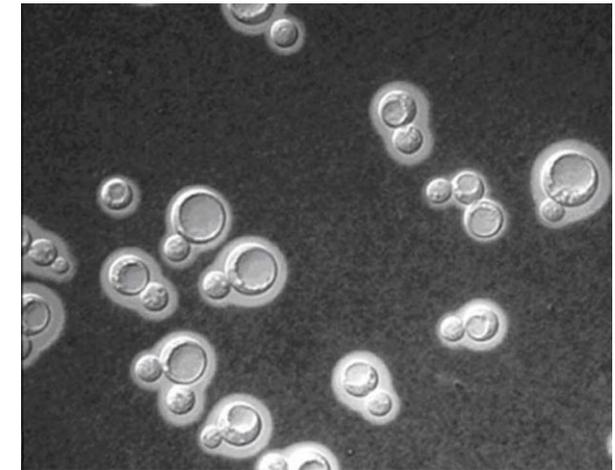
IV methylprednisolone can be administered as 75% of prednisone dose

Benefits of corticosteroid if started after 72 hours of treatment is unknown, but a majority of clinicians will use it in patients with moderate t

Whenever tested for primaquine Steroids should be initiated concurrently with PCP treatment

Common Opportunistic Infections: CRYPTOCOCCAL MENINGITIS

CAUSE	<i>Cryptococcus neoformans</i> or <i>Cryptococcus gatti</i> ; yeast
RISK FACTORS	CD4 < 100
SYMPTOMS	Headache; fever; malaise
SIGNS	Fever, neck stiffness, photophobia, signs of raised intracranial pressure
INVESTIGATIONS	Serum Cryptococcal Antigen Positive Lumbar Puncture: raised opening pressure CSF: high protein, low-normal glucose, lymphocytes; India Ink stain positive, culture positive for <i>Cryptococcus</i>
MANAGEMENT	Induction: IV Amphotericin B + PO Flucytosine x 2 weeks THEN Consolidation: PO Fluconazole 400mg x at least 8 weeks THEN Maintenance: PO Fluconazole 200mg x at least 12 months



What are the other “c”

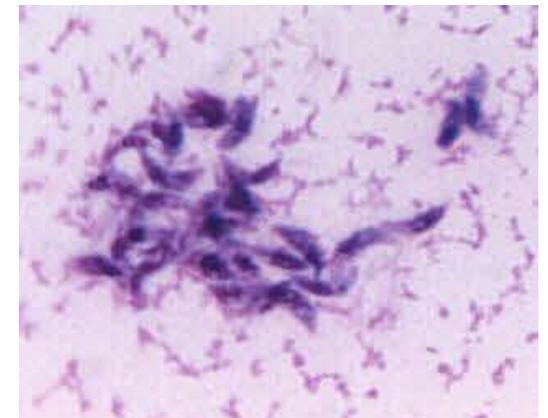
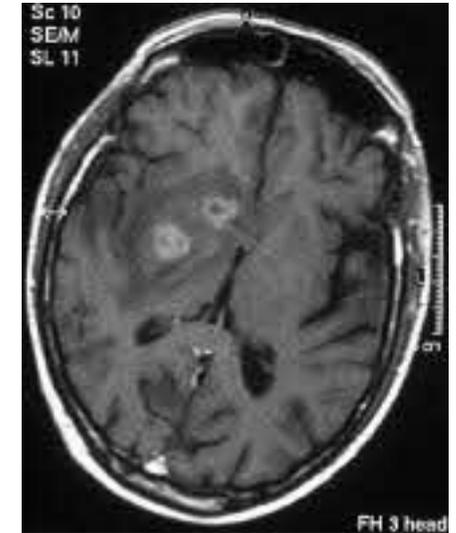
Common Opportunistic Infections: CANDIDIASIS

CAUSE	<i>Candida</i> species; yeast
RISK FACTORS	CD4 < 200
SYMPTOMS	Whitish coating on tongue, oral mucosa, back of throat Pain on swallowing if affecting oesophagus
SIGNS	Whitish coating on hyperaemic base on oral and oesophageal mucosa
INVESTIGATIONS	Clinical diagnosis
MANAGEMENT	Oral candidiasis: Oral Fluconazole 200mg once then 100mg OM x 1 week Nystatin Oesophageal candidiasis: Fluconazole 400mg once then 200mg OM x 2 weeks



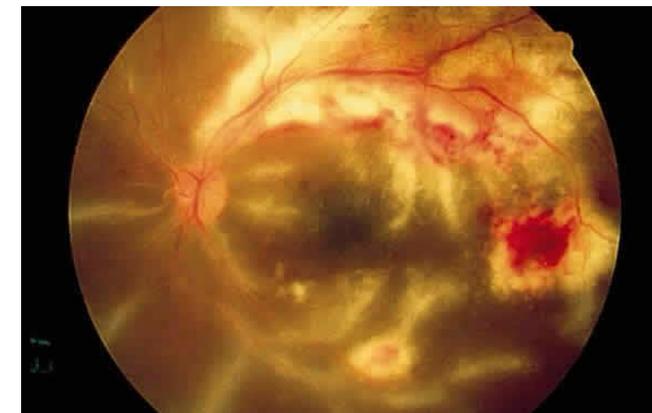
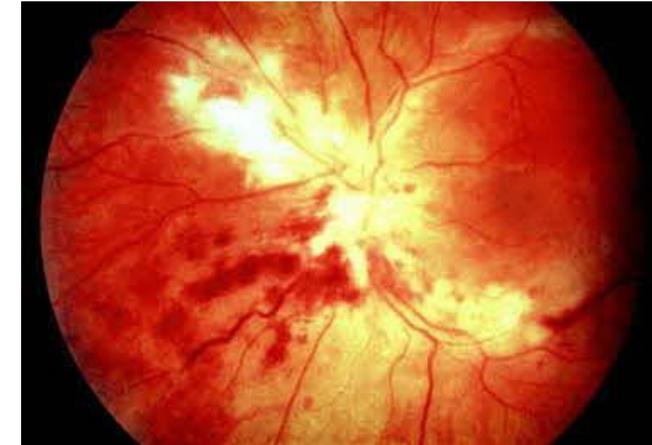
Common Opportunistic Infections: CEREBRAL TOXOPLASMOSIS

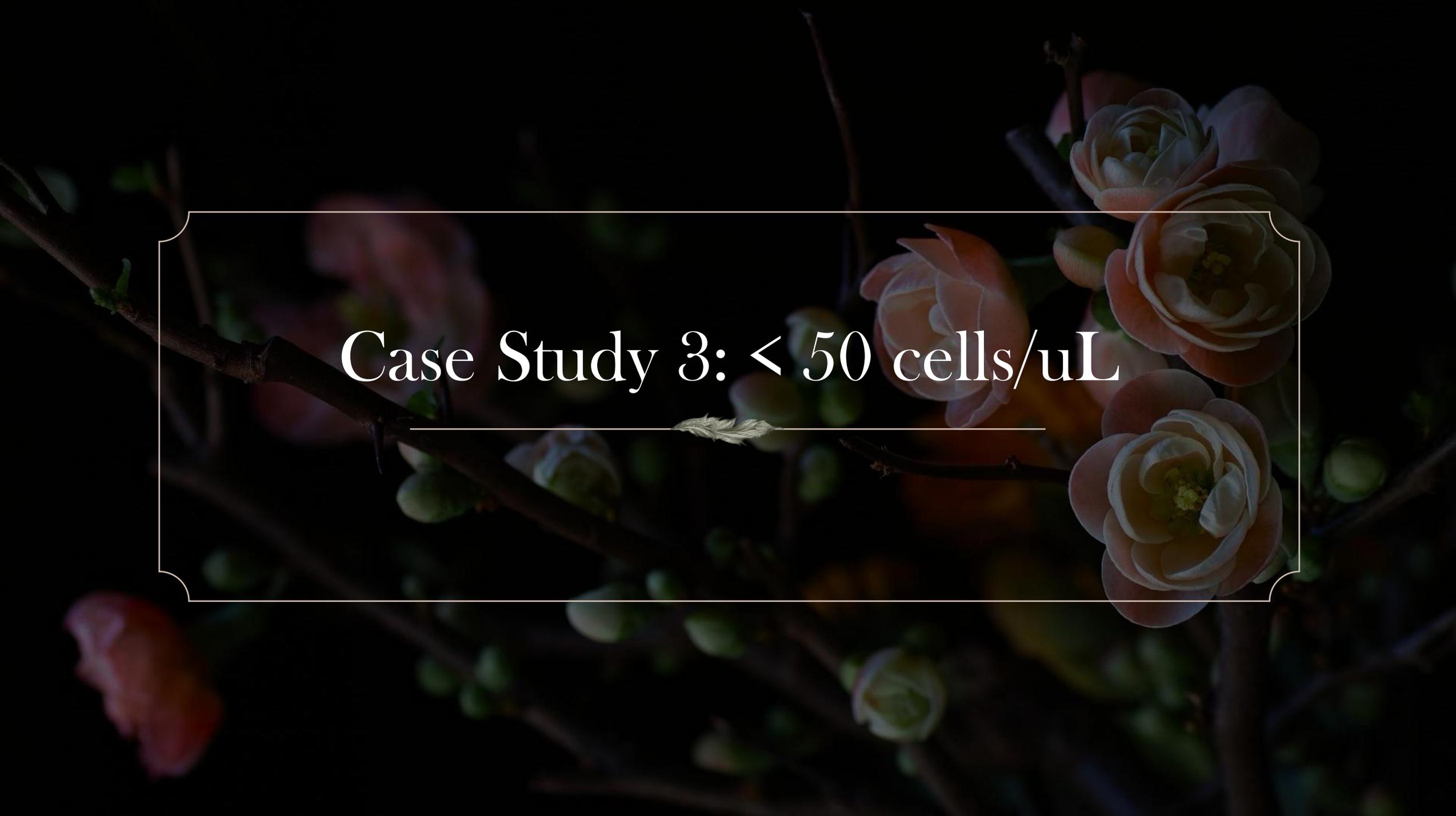
CAUSE	<i>Toxoplasma gondii</i>
RISK FACTORS	Rare if CD4 > 200; Highest risk when CD4 < 50; Toxoplasma IgG Positive
SYMPTOMS	Headache, fever, altered mental state, weakness
SIGNS	Focal neurological deficits; seizures, depressed conscious level, coma
INVESTIGATION S	Serum Toxoplasma IgG positive Neuroimaging (CT or MRI Brain): Multiple ring-enhancing lesions in the brain parenchyma with a predilection for the basal ganglia
MANAGEMENT	Prophylaxis: 2 tabs (single-strength) Bactrim daily Treatment: Pyrimethamine + Sulfadiazine + Leucovorin x at least 6 weeks - Maintenance therapy thereafter Start HAART after clinical improvement; 2-3 weeks after Toxo Rx



Common Opportunistic Infections: CYTOMEGALOVIRUS RETINITIS

CAUSE	Cytomegalovirus (CMV)
RISK FACTORS	CD4 < 50 May be unmasked by IRIS
SYMPTOMS	Visual floaters, blind spots, peripheral visual field defects, painless visual loss
SIGNS	Typical appearance of characteristic retinal changes: retinal haemorrhages and hard exudates
INVESTIGATIONS	CD4 < 50 CMV IgG POS; CMV viraemia may be present
MANAGEMENT	Local: intravitreal ganciclovir injections or implants Systemic: ganciclovir/valganciclovir to reduce risk of contralateral eye disease

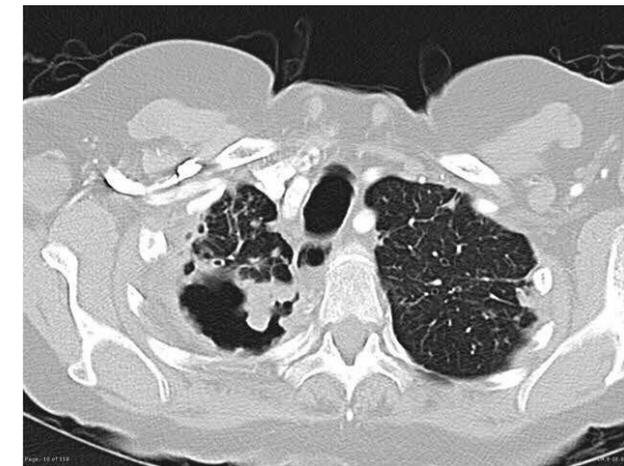
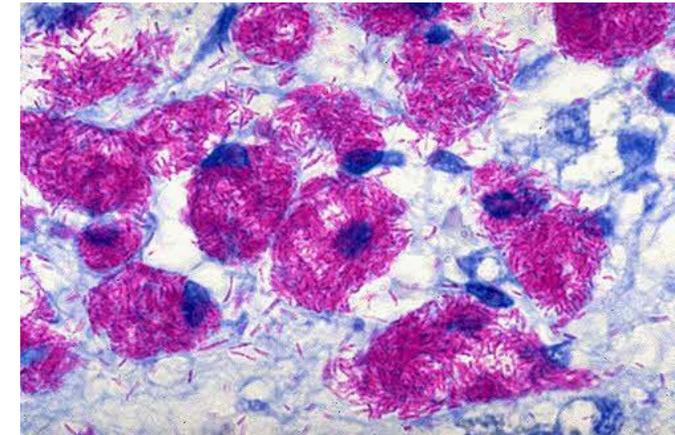




Case Study 3: < 50 cells/uL

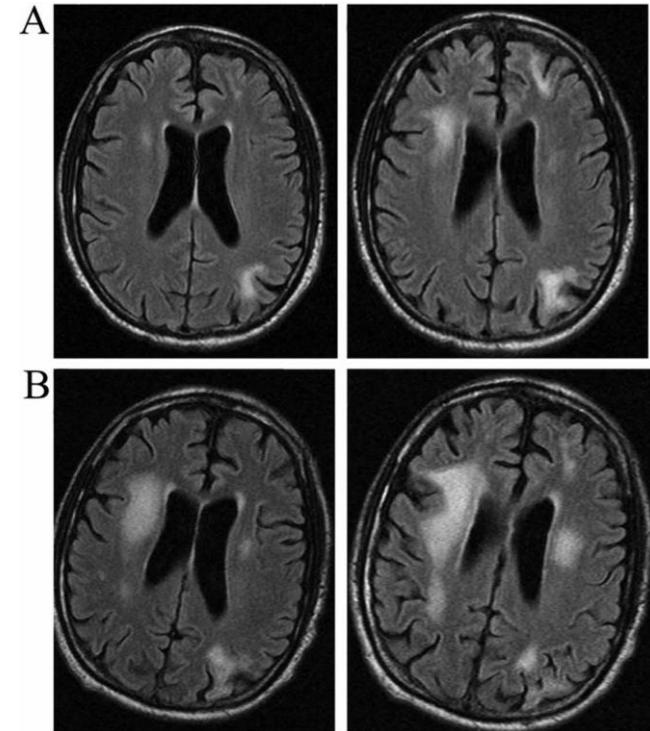
Common Opportunistic Infections: DISSEMINATED MYCOBACTERIUM AVIUM-INTRACELLULAR COMPLEX INFECTION

CAUSE	<i>Mycobacterium intracellulare-avium</i> complex; mycobacterium
RISK FACTORS	CD4 < 50 May be unmasked by IRIS
SYMPTOMS	Fever, night sweats, weight loss, fatigue, diarrhoea, abdominal pain
SIGNS	Fever, hepatomegaly, splenomegaly, lymphadenopathy May present as localised disease: pneumonitis, pericarditis, osteomyelitis, skin or soft tissue abscesses, CNS infection
INVESTIGATIONS	Anaemia, raised ALP Blood AFB culture positive Imaging: organomegaly, lymphadenopathy
MANAGEMENT	Prophylaxis: Clarithromycin or Azithromycin Treatment: Clarithromycin + Ethambutol +/- Rifabutin (if CD4 < 50)



Common Opportunistic Infections: PROGRESSIVE MULTIFOCAL LEUCOENCEPHALOPATHY

CAUSE	JC Virus; human polyoma virus
RISK FACTORS	CD4 < 50; risk increased with lower CD4 and duration of low CD4 May occur as part of immune reconstitution inflammatory syndrome (IRIS)
SYMPTOMS	Focal neurologic deficits – progressively worsening and generalising Cognitive impairment
SIGNS	Focal neurological deficits;
INVESTIGATIONS	MRI Brain: multiple brain white matter T2 hyperintense lesions without surrounding oedema CSF JC Virus positive
MANAGEMENT	Immune reconstitution with highly active antiretroviral therapy Trials of Mefloquine, Maraviroc etc

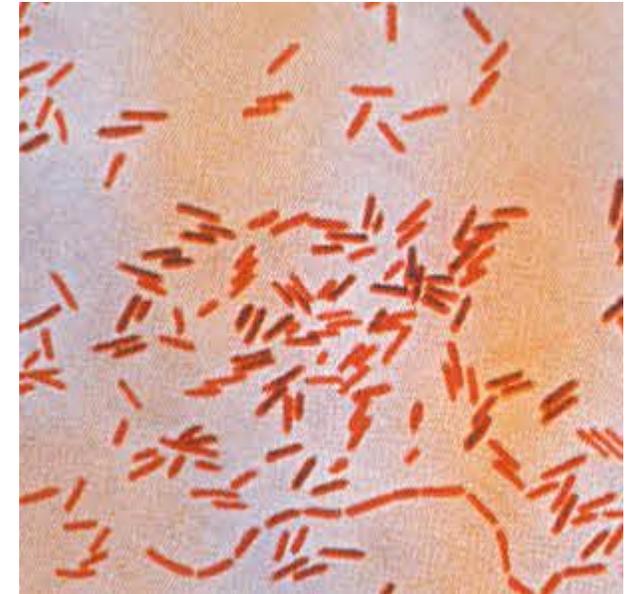




Others to consider

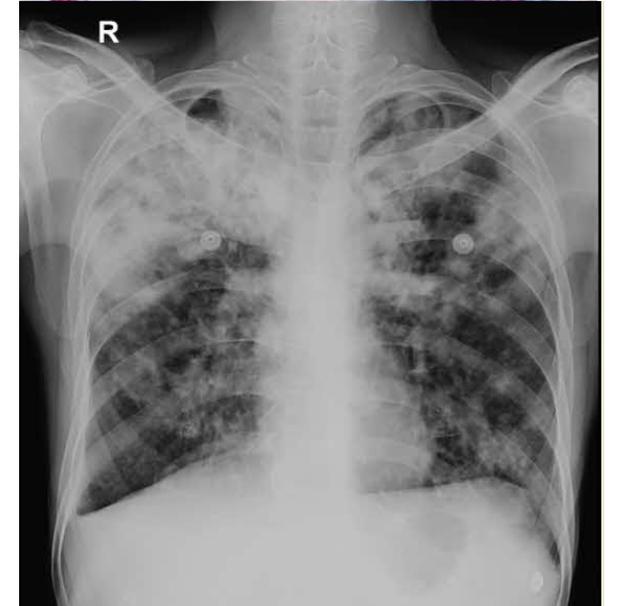
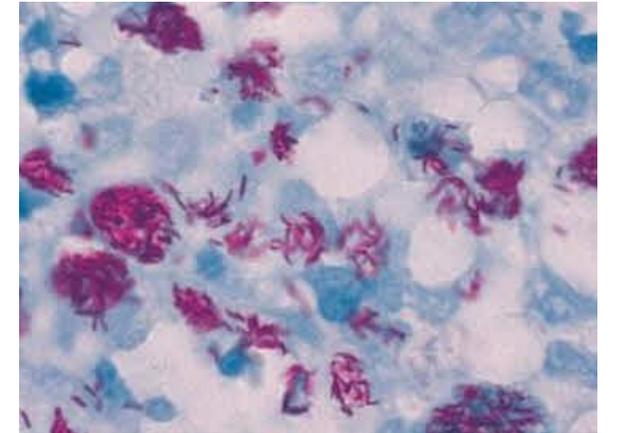
Common Opportunistic Infections: NON-TYPHOIDAL SALMONELLOSIS

CAUSE	<i>Salmonella</i> species
RISK FACTORS	Risk increased with lower CD4
CLINICAL FEATURES	<ul style="list-style-type: none">• Self-limited gastroenteritis• More severe and prolonged diarrhoeal disease, associated with fever, bloody diarrhoea and weight loss• Bacteraemia associated with extra-intestinal involvement, with or without concurrent or preceding gastrointestinal illness
INVESTIGATIONS	Blood culture positive CT: intra-abdominal collections possible
MANAGEMENT	Antibiotic therapy (Ceftriaxone, fluoroquinolones, ampicillin) Drainage of collections if present



Common Opportunistic Infections: PULMONARY TUBERCULOSIS

CAUSE	<i>Mycobacterium tuberculosis</i> , mycobacterium
RISK FACTORS	Any CD4; exposure to positive TB contacts
SYMPTOMS	Fever, night sweats, chills and rigors, productive cough, haemoptysis, loss of weight
SIGNS	Lung crepitations, lymphadenopathy , weight loss, fever
INVESTIGATIONS	CXR: consolidations, cavities, nodules CT Thorax: Consolidations, tree in bud appearance, lymphadenopathy Sputum acid-fast bacilli (AFB) smear and culture, TB PCR
MANAGEMENT	Antituberculous therapy: Rifampicin + Isoniazid + Ethambutol + Pyrazinamide x 2 months THEN Rifampicin + Isoniazid x 4 months Pyridoxine while Isoniazid is being given (peripheral neuropathy)







What is kaposi sarcoma?

- Angioproliferative disease that requires infection from human herpes 8 virus for its development
- 4 types of Kaposi Sarcoma:
 - Classic type
 - Iatrogenic
 - Endemic
 - Epidemic

AIDS related Kaposi sarcoma

- AIDS defining illness
- 300 times more common in people with AIDS compared to other immunosuppressed population
- 10 times more common in MSM or bisexual men compared to other men who acquired HIV through different routes in developed countries
- Other risk factors:
 - Male gender
 - CD4 <200. Rate ratio 18.9 compared with individuals with CD4 > 500 cells/mm³ developing KS
 - HHV- 8 infection required for development
 - Inherited variation in immunomodulating genes
 - Smoking is protective

Clinical manifestations

Cutaneous	Visceral
Common places: lower extremities, face (especially the nose), oral mucosa, genitalia	Possible sites involvement: lymph nodes, liver, pancreas, heart, testes, bone marrow, bone, skeletal muscle
Usually elliptical, arrange in linear fashion along skin tension lines	Most frequent: oral cavity (1/3 of patients), GI (40% of patients), respiratory system (10% of patient with AIDS, 25% with cutaneous lesions)
Symmetrical	
Lymphedema	

J Am Dent Assoc. 1993;124(11):78.

Am J Gastroenterol. 1991;86(6):715.

Prognosis in pre-HAART era

- Average interval from the diagnosis of pleural KS to death was 4 [+ or -] 3 months (range 0.5 to 13 months)
- The median survival from diagnosis of KS to death was 205 days (mean 249 days) for patients with pleuropulmonary KS and 338 days (mean 382 days) for those without pleuropulmonary KS ($p < 0.01$).

Choice of Treatment

Disease	Chemotherapy
Kaposi Sarcoma	First line: pegylated liposomal doxorubicin or liposomal daunorubicin ¹ Others: Etoposide, vincristine, vinblastine, bleomycin
Kaposi Sarcoma Herpes Virus- associated Inflammatory Cytokine Syndrome	Unclear: possible rituximab, liposomal doxorubicin and antiviral therapy ²
Multicentric Castleman Disease (with concurrent Kaposi Sarcoma)	Without life threatening organ failure: Weekly Rituximab, pegylated liposomal doxorubicin and ganciclovir

¹HIV Med. 2008;9(6):336.

²The Oncologist 2017;22:1–3

Thank you

