Prevention and Assessment of Opportunistic Infections: Case Presentations

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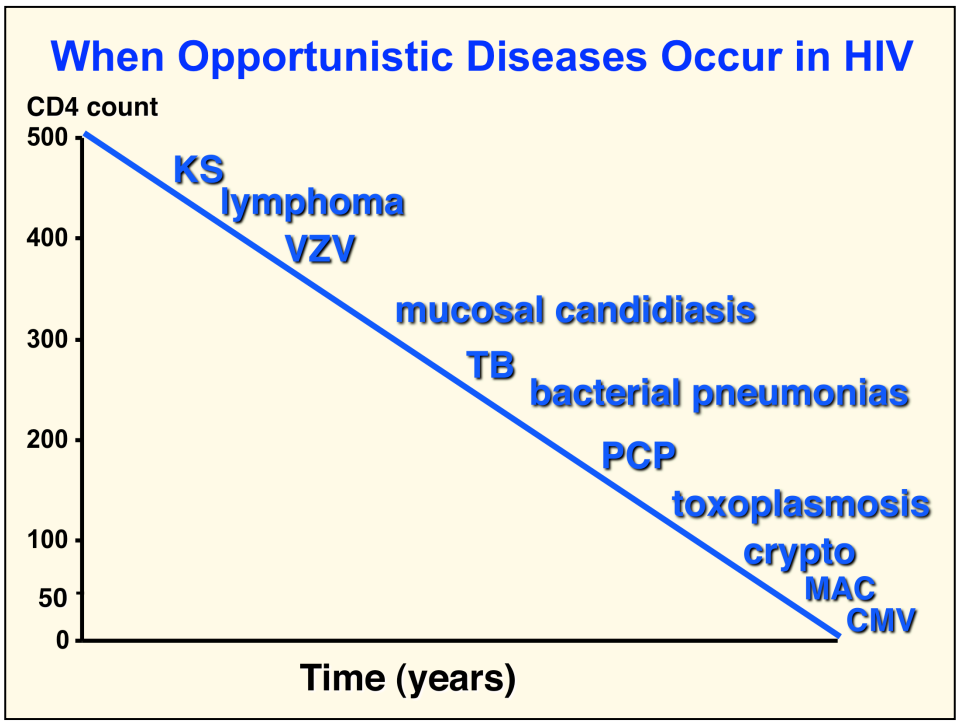
Disclosures

I have received honoraria or participated in advisory boards for the following companies:

- Pfizer
- Janssen Pharmaceutica
- Schering-Plough
- Fujisawa
- Merck
- Astellas



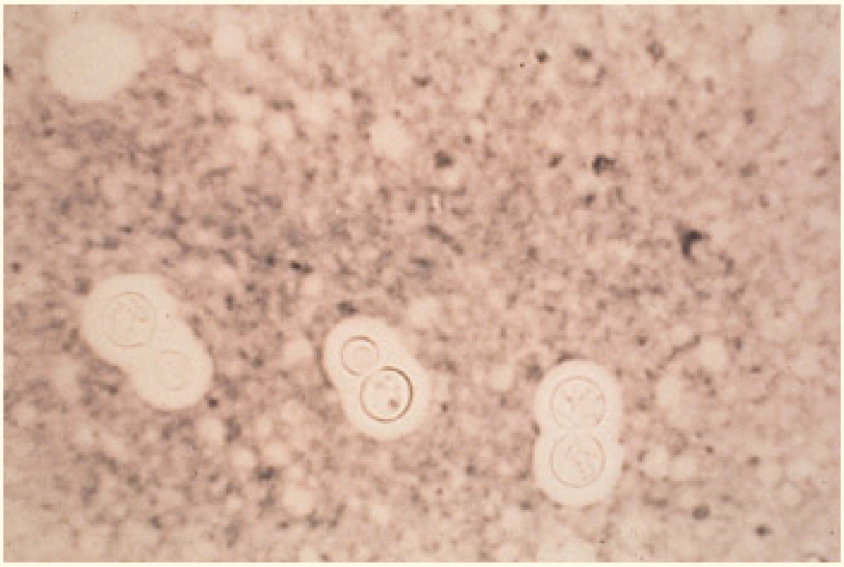
- Knowing the CD4 count when patients present with symptoms is essential in being able to make a differential diagnosis.
- Kaposi's sarcoma (KS) and Lymphoma can occur at any CD4 count.
- Most commonly Pneumocystis jiroveci (carinii) pneumonia (PCP) is seen in patients with CD4 counts in the range of 200
- At a low CD4 count any of the opportunistic infections (OI's) can occur

Cryptococcal Meningitis in AIDS

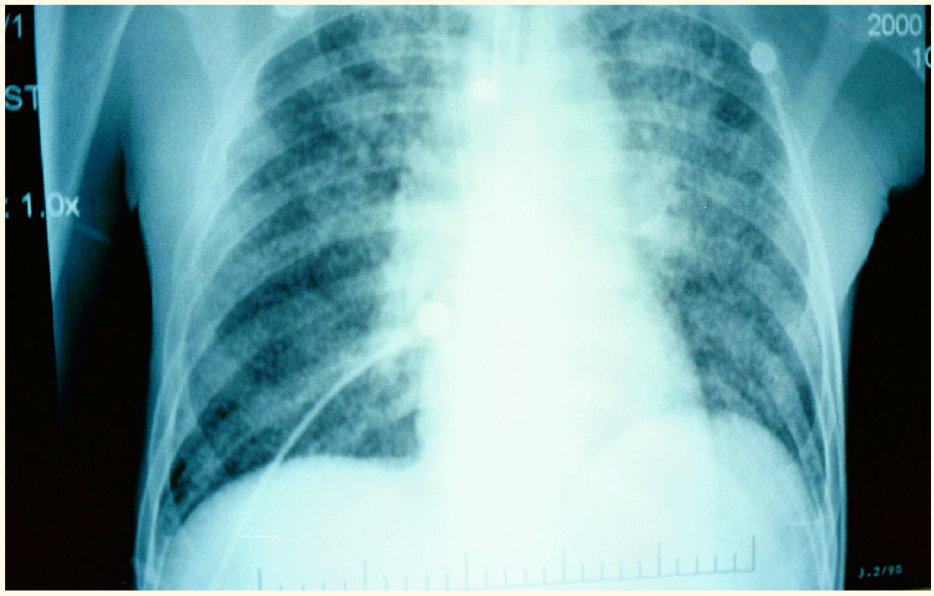
Presentation: (n=45)	Percentage
Headache	67
Fever	62
Altered mentation	18
Cough or SOB	18
Dizzyness	9
Seizures	9
Syncope	7
Skin lesions	7
Psychosis	4

Rev Infect Dis 1990;12:768

- Headache, as a symptom of Cryptococcal Meningitis, is only seen in 2/3 patients.
- Other symptoms occurring simultaneously also make it difficult to diagnose this OI.



- Cryptococcus identified in the CNS



• This chest x-ray shows miliary pulmonary cryptococcosis, which is much less common than AIDS-related cryptococcal meningitis.

AIDS-Related Cryptococcal Meningitis

	% positive
Serology	
• cryptococcal antigen	
- serum	99%
- CSF	>90%
India ink smear	75-88%

NEJM 1989
Rev Infect Dis 1990;12:768

Common Treatable CNS Diseases in AIDS

Syndrome	Etiology	Test
Meningitis	Cryptococcus, syphilis (TB, Listeria rare)	• serum antigen • RPR & TPPA
Mass lesion	Toxoplasmosis 1^0 CNS lymphoma	• trial of therapy • stereotactic Bx CSF EBV PCR
Focal white matter lesions	JC virus (PML)	• CSF JCV PCR stereotactic Bx

Toxoplasmosis Prophylaxis

Indication:	CD4 <100/mm^3 plus Toxoplasma IgG+
Recommended:	a) TMP-SMX 1DS tab daily
	or b) dapsone 50mg/day + pyrimethamine 50mg/wk + leucovorin 25mg/wk
	or c) atovaquone 1500mg (+/- pyrimethamine 25 mg + leucovorin 10 mg) daily

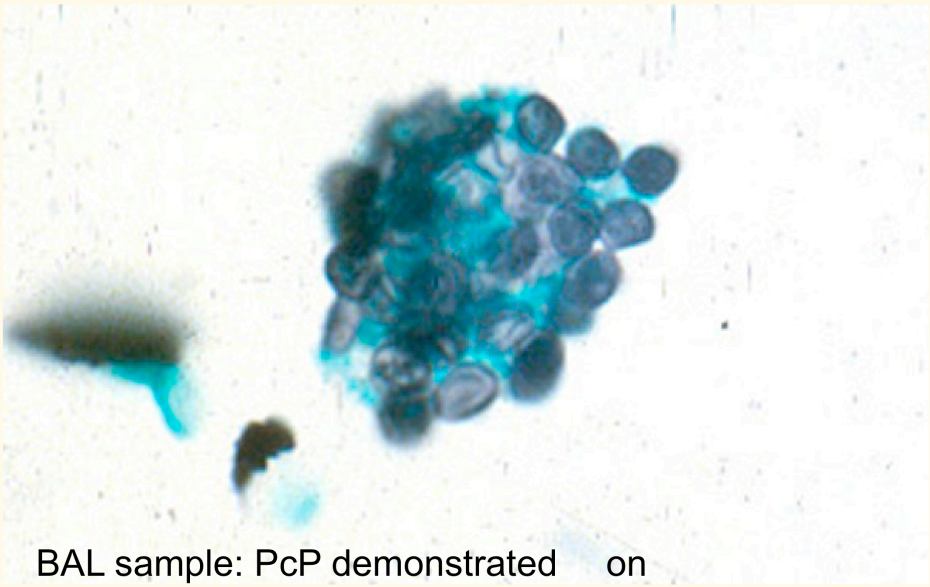
MMWR 2009;vol 58(RR-4):1-206 [CDC/NIH/HIVMA/IDSA]

PCP - Primary Prophylaxis

Indication:	CD4 count < 200, or CD4 <14%, or oral candidiasis
1st choice:	TMP - SMX 1DS or SS tab/day
Alternatives:	• dapsone 100 mg/day
	• aerosol pentamidine 300mg/mo
	• atovaquone 1500 mg/day

MMWR 2009;vol 58(RR-4):1-206 [CDC/NIH/HIVMA/IDSA]

- Approximately 10% of patients with PCP will have a normal CXR. It relates to time of presentation; if patient presents at early onset of PCP, then CXR can be normal.
- Important to consider CD4 fraction. If fraction is below 14%, it is an indication of prophylaxis.



BAL sample: PcP demonstrated on Toluidine blue stain (cytology more sensitive)

- Result from bronchoscopy showing PCP on Toluidin blue stain

Identifying HIV patients for TB isolation

- **Other risk factors: e.g. IDU, homeless, prior + PPD/ TB, recent exposure⊙**
- **History: – prolonged symptoms? (cough & fever > 1 wk, wt loss)**
  – failing Rx for "pneumonia" (CAP)
- **CXR: – mediastinal, hilar adenopathy**
  – cavity or miliary pattern

⊙ *MMWR 2005;54(RR12);1-81*

• Patients don't always present with prolonged symptoms of 3-4 weeks. Sometimes patients diagnosed with pulmonary TB have only had symptoms for a week.

Screening for TB in HIV

Background: WHO screening: if cough ≥ 2wks

Study: SE Asia N= 267/1748 (15% TB)

gold standard: + culture (sputum x3, blood, urine, stool, +/- lymph node)

Symptoms	Sensitivity	Specificity	NPV
• cough ≥ 2 wk	33%	82%	87%
• combination: cough, or fever (any duration), or NS ≥ 3 wk	93%	36%	97%

NEJM 2010;362;707

TB Diagnosis: Nucleic Acid Amplification (NAA)Tests

Sputum/BAL	Sensitivity	PPV*
• AFB smear	45-80%	50-80%
• NAA tests	50-80% for AFB-neg	>95% for AFB-pos

*PPV, positive predictive value if nontuberculous mycobacteria common

Guideline: NAA test for ≥1 respiratory sample on *all* pts with possible pulm. TB

CDC (Atlanta) MMWR 2009;58(01);7-10

TB - Primary Prophylaxis

Indication:	• TST (ppd) > 5 mm
or	• recent TB exposure
or	• prior pos. TST, untreated
or	• history of inadequately treated healed TB
1st choice §:	INH 300 mg/d x 9 months
	(+ pyridioxine 50 mg/day)

§ after excluding active TB

MMWR 2009;vol 58(RR-4):1-206 [CDC/NIH/HIVMA/IDSA]

- A positive skin test is considered > 5mm in HIV positive individuals. In HIV negative individuals a skin test is positive >10 mm
- Recent TB exposure is an indication of prophylaxis, without the need for a skin test. This is because the risk for development of active TB is much greater in HIV positive individuals.

HIV-related fevers: Non-specific presentation

CD4	Non IDU	IDU
>200	as for HIV neg, *plus* TB, lymphoma	as for HIV neg, TB, lymphoma (NHL) *plus* endocarditis (IE)
< 200	PCP, cryptococcus TB, NHL, etc	PCP, crypto, IE, TB, NHL, etc.
< 50	MAC, CMV, PCP, crypto TB, NHL, etc	MAC, CMV, IE, PCP, crypto TB, NHL, etc

Mycobacterium avium complex (MAC) - Primary Prophylaxis

Indication: CD4 < 50

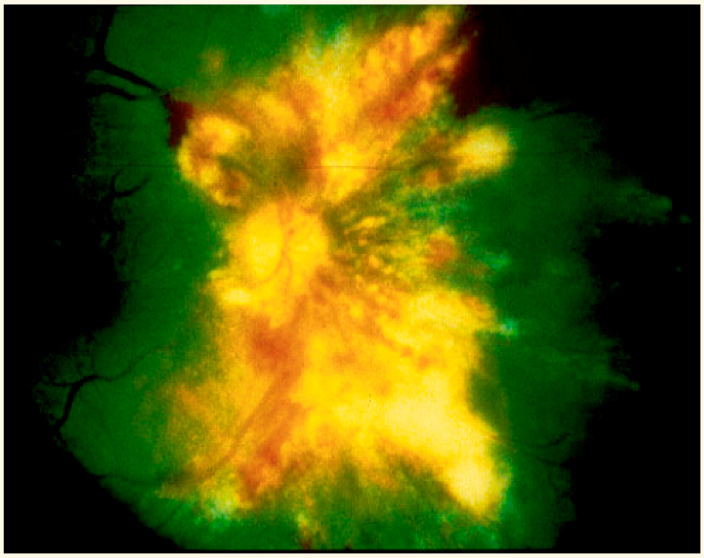
1st choice:
- azithromycin 1200 mg once weekly *or*
- clarithromycin 500 mg bid

Alternatives: rifabutin 300 mg/day

MMWR 2009;vol 58(RR-4):1-206 [CDC/NIH/HIVMA/IDSA]

CMV Disease

Normal Host	Immunocompromised
*mononucleosis (79% EBV, 21% CMV)	retinitis
hepatitis	colitis or esophagitis
congenital	pneumonitis
	hepatitis
	encephalitis



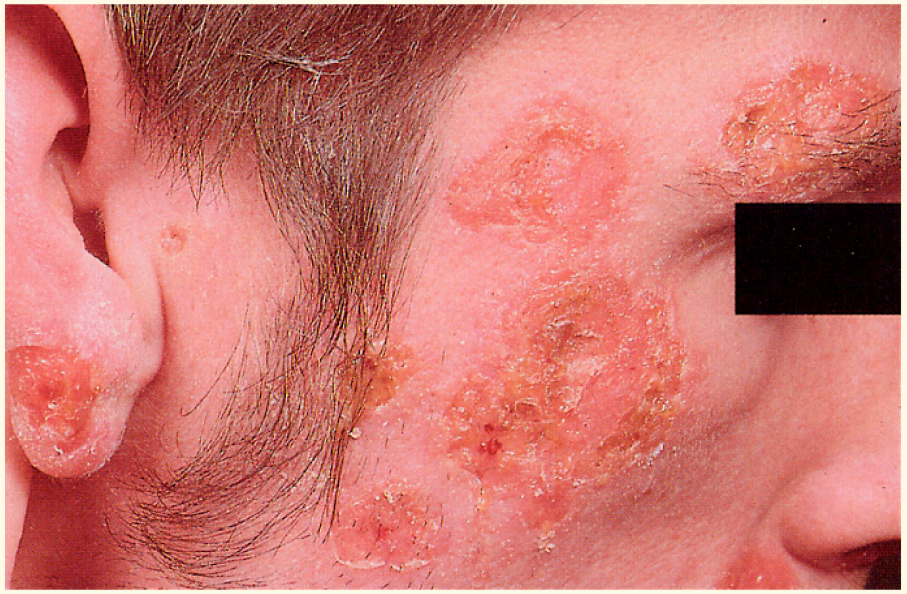
CMV retinitis

- This picture shows extensive hemorrhaging .
- At this stage, vision can not be restored, but progression can be stopped with treatment.
- Early diagnosis is key.

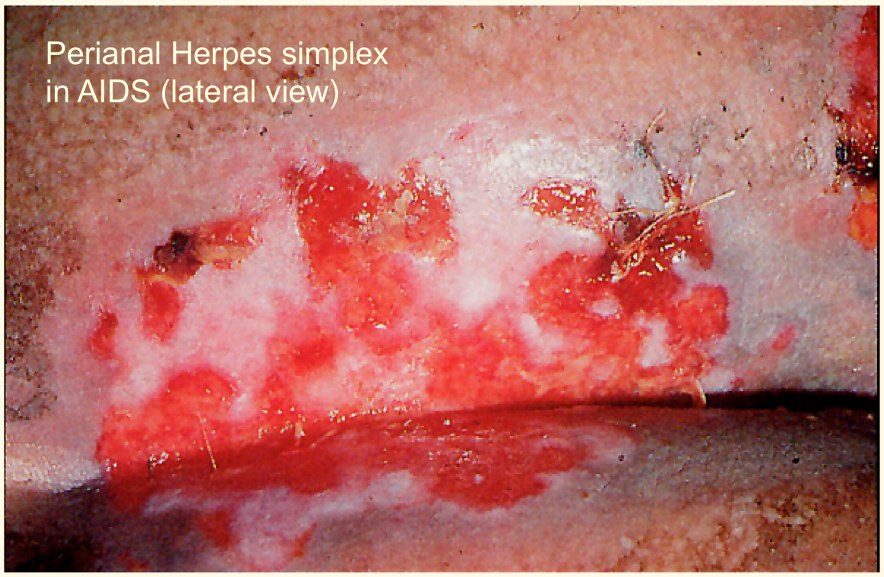
Herpesviruses	Infections in HIV*
Herpes simplex 1,2	mucocutaneous, other sites
Varicella-zoster	varicella, herpes zoster
Cytomegalovirus	retinitis, GI, encephalitis
Epstein-Barr virus	lymphoma; hairy leukoplakia
Human herpesvirus 6	nil (roseola infantum [ex sub])
Human herpesvirus 7	nil (roseola infantum)
Human herpesvirus 8	Kaposi's sarcoma, MCD, PEL
Simian herpes B virus	nil (mucocutan., encephalitis)

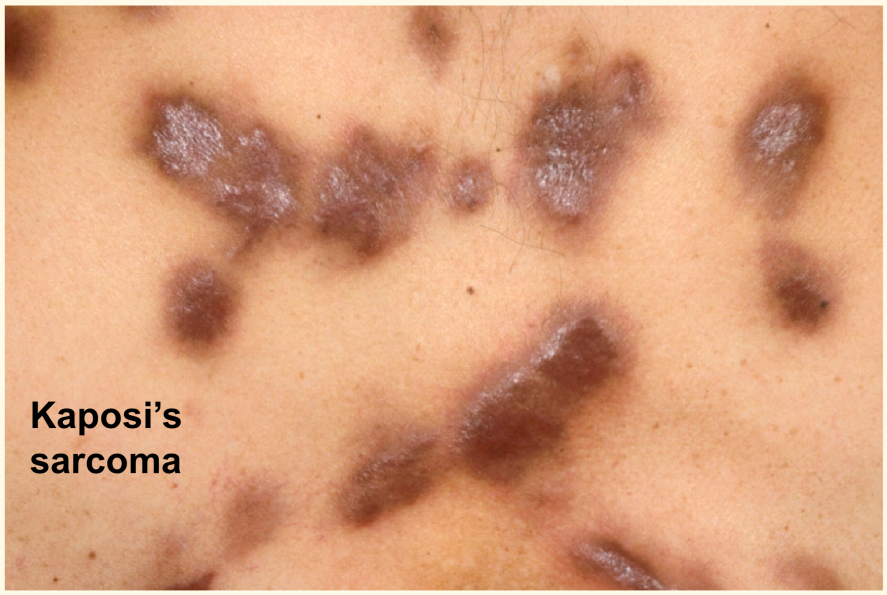
MCD, multicentric Castleman's disease; PEL, primary effusion lymphoma

* Underlined infections are recognized HIV-related opportunistic diseases.



- Herpes Simplex Virus


Perianal Herpes simplex
in AIDS (lateral view)


Kaposi's
sarcoma

Stopping Criteria: Prophylaxis in ART Responders

	1° prophylaxis	2° prophylaxis
•PCP	CD4 > 200¶ x 3mo	CD4 > 200 x 3mo
•TOXO	CD4 > 200 x 3mo	CD4 > 200 x 6mo,& asymptomatic re toxo, & completed initial toxo Rx
•MAC	CD4 > 100 x 3mo	CD4 > 100 x 6mo, asymptomatic re MAC, & completed 12 mo MAC Rx
•CMV retinitis	NA	CD4 > 100 x 3-6mo, plus other criteria*
•Crypto. meningitis	NA	CD4 > 200 x 6mo, asymptomatic re crypto, complete initial Rx, +/- LP*

¶ CD4 >100, if HIV RNA <400 c/ml (*Clin Infect Dis* 2010;51:611)

- Primary prophylaxis guidelines are used when patients have not had the OI before.
- Secondary prophylaxis is for patients who have had previously documented disease.