

Opportunistic infections in Men who have sex with MEN (MSM)

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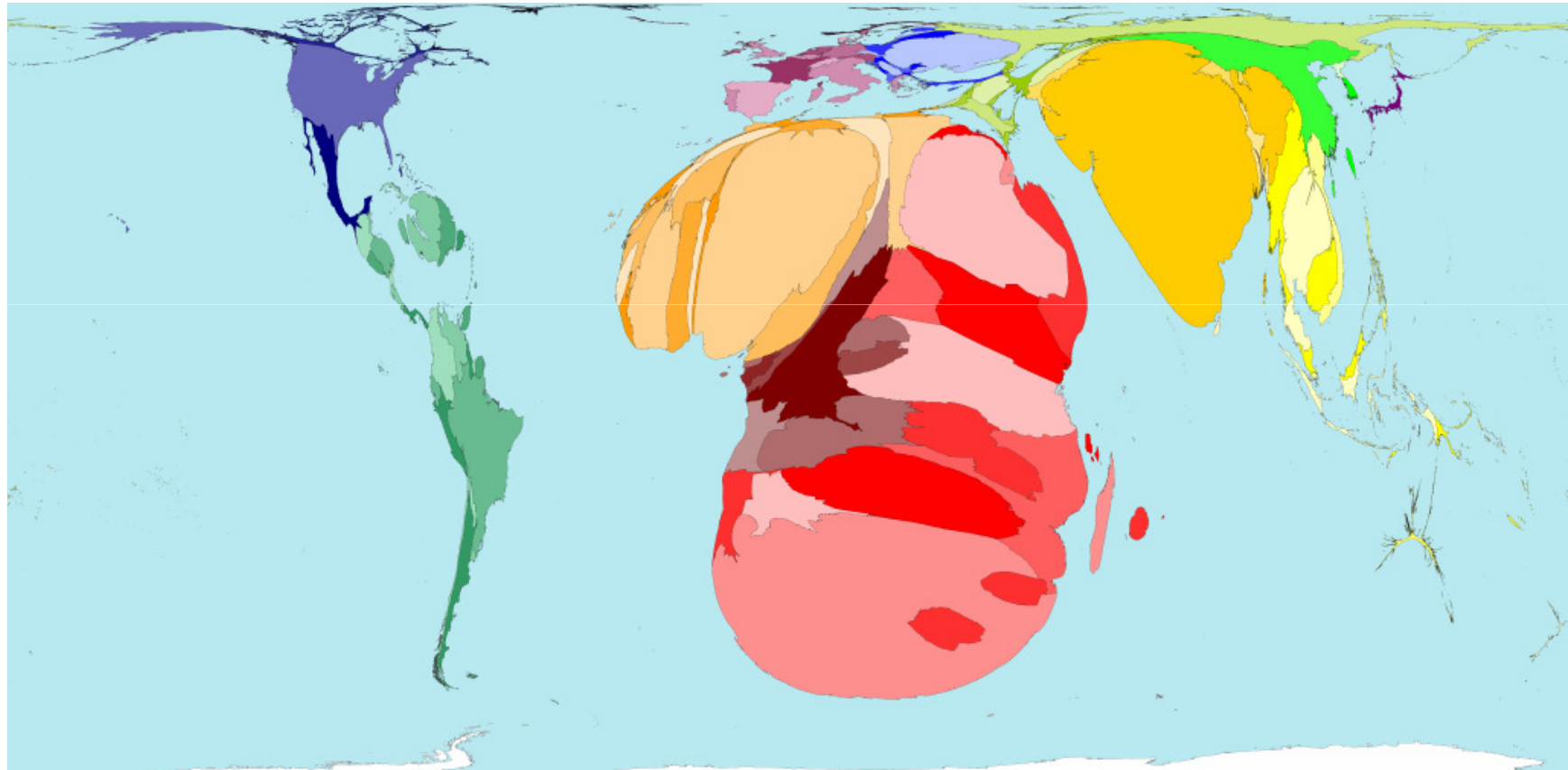


25th May 2011

Outline of talk

- Risk factors for HIV Infection in MSM
- Acute HIV Infection (AHI)
- Main focus on the following HIV related opportunistic Infections:
 - Tuberculosis
 - Pneumocystis Jirovecci Pneumonia
 - Syphilis
 - Cryptococcal Meningitis
- Other important Infections
- Concluding remarks

HIV burden of disease



www.worldmapper.org/

Death related to HIV infection



www.worldmapper.org/

Risk factors for HIV infection In MSM

- Receptive anal intercourse^{1, 2}
- Unsafe sex ^{1, 2}
- High number of life time partners
- Sexually transmitted infections¹ (especially syphilis)
- IDU (intravenous drug use)²

1) Risk factors for HIV-1 infection among MSM in costal Kenya CROI March 2011

2) Parry et al. Drug and Alcohol Dependence 95 (2008) 45-53

Opportunistic Infections

- Principal cause of serious morbidity and mortality in HIV infected persons.
- Are infections or neoplasms (the latter induced by viral infections)
- Are infections with less virulent organisms or are unusually severe
- Most major opportunistic infections are AIDS-defining illnesses (WHO stage 4)

TABLE 1. REVISED WHO CLINICAL STAGING OF HIV/AIDS FOR ADULTS AND ADOLESCENTS

<p>Primary HIV Infection</p> <ul style="list-style-type: none"> Asymptomatic Acute retroviral syndrome
<p>Clinical stage 1</p> <ul style="list-style-type: none"> Asymptomatic Persistent generalized lymphadenopathy (PGL)
<p>Clinical stage 2</p> <ul style="list-style-type: none"> Moderate unexplained weight loss (<10% of presumed or measured body weight) Recurrent respiratory tract infections (RTIs, sinusitis, bronchitis, otitis media, pharyngitis) Herpes zoster Angular cheilitis Recurrent oral ulcerations Papular pruritic eruptions Seborrhoelic dermatitis Fungal nail infections of fingers
<p>Clinical stage 3</p> <p><i>Conditions where a presumptive diagnosis can be made on the basis of clinical signs or simple investigations</i></p> <ul style="list-style-type: none"> Severe weight loss (>10% of presumed or measured body weight) Unexplained chronic diarrhoea for longer than one month Unexplained persistent fever (intermittent or constant for longer than one month) Oral candidiasis Oral hairy leukoplakia Pulmonary tuberculosis (TB) diagnosed in last two years Severe presumed bacterial infections (e.g. pneumonia, empyema, pyomyositis, bone or joint infection, meningitis, bacteraemia) Acute necrotizing ulcerative stomatitis, gingivitis or periodontitis <p><i>Conditions where confirmatory diagnostic testing is necessary</i></p> <ul style="list-style-type: none"> Unexplained anaemia (<8 g/dl), and or neutropenia (<500/mm³) and or thrombocytopenia (<50 000/mm³) for more than one month

Clinical stage 4

Conditions where a presumptive diagnosis can be made on the basis of clinical signs or simple investigations

HIV wasting syndrome

Pneumocystis pneumonia

Recurrent severe or radiological bacterial pneumonia

Chronic herpes simplex infection (orolabial, genital or anorectal of more than one month's duration)

Oesophageal candidiasis

Extrapulmonary TB

Kaposi's sarcoma

Central nervous system (CNS) toxoplasmosis

HIV encephalopathy

Conditions where confirmatory diagnostic testing is necessary:

Extrapulmonary cryptococcosis including meningitis

Disseminated non-tuberculous mycobacteria infection

Progressive multifocal leukoencephalopathy (PML)

Candida of trachea, bronchi or lungs

Cryptosporidiosis

Isosporiasis

Visceral herpes simplex infection

Cytomegalovirus (CMV) infection (retinitis or of an organ other than liver, spleen or lymph nodes)

Any disseminated mycosis (e.g. histoplasmosis, coccidiomycosis, penicilliosis)

Recurrent non-typhoidal salmonella septicaemia

Lymphoma (cerebral or B cell non-Hodgkin)

Invasive cervical carcinoma

Visceral leishmaniasis

HIV seroconversion illness

- Often missed
- Clinical presentation:
 - Often asymptomatic
 - Symptoms
 - Flu-like symptoms (fever, headache, fatigue, malaise)
 - Rash
 - Lymphadenopathy
 - Night sweats

Pulmonary Tuberculosis

- More commonly smear negative
- Chest X-Ray atypical, subtle or normal
- Extra-pulmonary TB more common
- More rapid clinical deterioration
- Especially when CD₄ <200
- Critical delays in treatment initiation

MDR-TB

- High mortality in HIV-infected patients
 - Delayed diagnosis, disseminated TB, opportunistic infections, bacterial infections
 - Appropriate diagnosis & rapid treatment initiation crucial, in cases of MDR-TB to limit transmission, morbidity and prevent XDR-TB.
- Diagnosis:
 - Sputum (may be smear and culture negative)
 - Aspirate or biopsy may be the only way of making a diagnosis

Extra-pulmonary Tuberculosis

common sites

- Lymphadenitis
- Abdominal
- Miliary /disseminated
- CNS
 - Meningitis (TBM)
 - Tuberculoma

Treatment

Regimen	Intensive Phase	Continuation Phase	Notes
Regimen 1	R/H/Z/E 2 months	R/H 4 months	
Regimen 2	R/H/Z/E/S 3 months	R/H/E 5 months	Streptomycin = 40 doses
MDR-TB	E/Z/O/Eth/A 6 months minimum	E/Eth/O 18 months or 12 months after last negative culture	Initial culture should be sent at 3 months
XDR-TB	An MDR strain plus resistance to any fluoroquinolone and any one of kanamycin, amikacin or capreomycin		
R=Rifampicin, H=Isoniazid, Z=Pyrazinamide, E=Ethambutol, S=Streptomycin Eth=Ethionamide, A=Amikacin, O=Ofloxacin			

Pneumocystis Jirovecci Pneumonia (PJP)

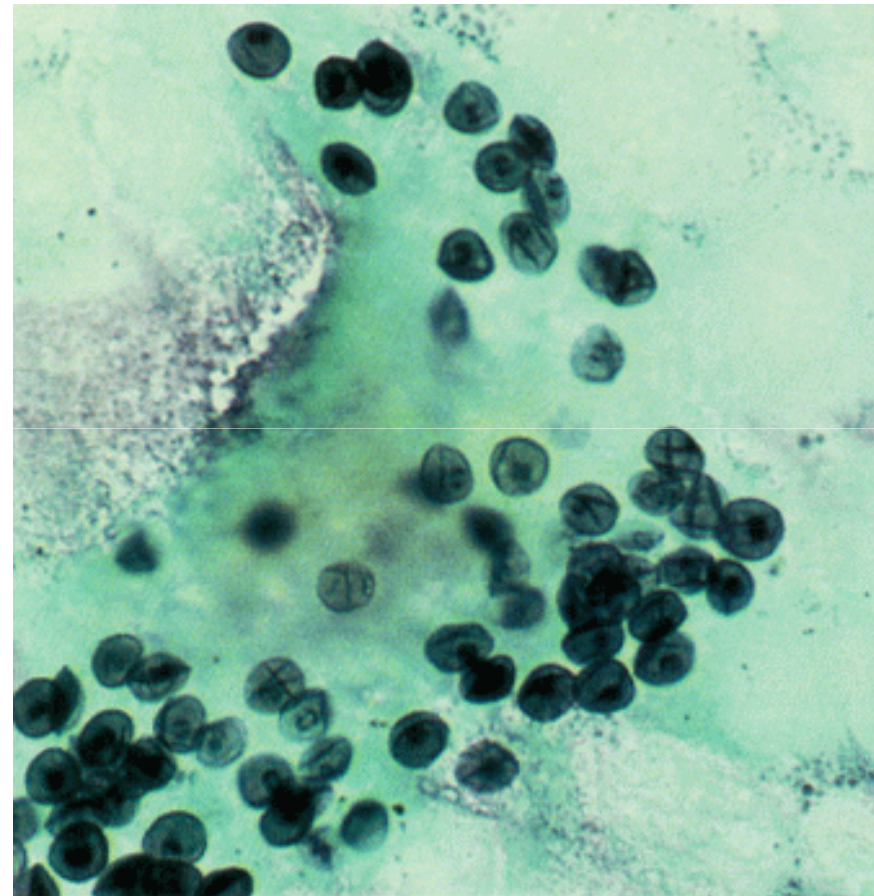


Bilateral Interstitial infiltrate lower zones

- CD₄ usually <200 cells/ μ L
- Subacute onset
 - 1-3 weeks
 - Progressive dyspnoea
 - Dry cough
- Examination
 - Marked tachypnoea
 - Chest clear (or late inspiratory crackles)
 - CXR abnormalities subtle or absent
 - Hypoxia (late manifestation)

Diagnosis of PJP

- Clinical picture combined with CXR usually sufficient to make diagnosis.
- Induced sputum
- Bronchoscopy and lavage
 - Direct fluorescent antigen test (DFAT)
 - Silver stain
 - PCR



Silver stain of bronchoalveolar lavage showing cysts of PJP

Treatment of PJP

- Co-trimoxazole (480mg tablets)- 3 weeks
 - 1 tablet for each 4kg body weight / day in a tds or qds dose. Maximum 4 tabs qds.
- Steroids
 - Hypoxic patients ($pO_2 < 8\text{kpa}$)
 - 40mg bd for 5 days followed by 40mg od 5 days then 20mg od for 11 days.
- Alternative regimen
 - Clindamycin 600mg tds plus Primaquine 15mg od

Syphilis

- Common in HIV-infected MSM
- **Presentation characterized by wide range symptoms**
- Latent syphilis associated with prolonged time to serologic response
- **Re-infection common observed rate ~10% per year**

**Table 2:
Clinical Presentations and Diagnosis
Delays (N=118)**

Symptom (most to least common)	N (%)	N (%) with delay in dx from onset of symptom	Median delay in days
Generalized rash	70 (59%)	16 (23%)	25
Rash on palms and soles	44 (37%)	4 (9%)	7
Sore throat	25 (21%)	14 (56%)	44
Cervical LAD	23 (19%)	12 (52%)	56
Subjective fever	18 (15%)	7 (39%)	42
Inguinal LAD	13 (11%)	6 (46%)	36
Chancre	13 (11%)	6 (46%)	73
Mouth ulcers	13 (11%)	9 (69%)	78
Asymptomatic + RPR	9 (8%)	-	-

54(46%) had a delay in diagnosis from onset of any symptom to treatment

L Siegel, L Drusin, R Gulick, T Wilkin
Weill-Cornell Medical College, New York-Presbyterian
Hospital; New York, NY Poster CROI 2009

- Primary, secondary, early latent
 - Treatment: Benzyl penicillin G IM stat
- Late latent or tertiary-cardiovascular or gummatous disease
 - Treatment: Benzyl penicillin G IM weekly for 3 weeks
- Neurosyphilis (ocular & auricular)
 - Treatment: penicillin G 3-4 MU 4 hrly (18-24 MU/day) ivi 10 to 14 days
- Neurocognitive Impairment in HIV-infected individuals with previous Syphilis ¹
 - Among participants cognitive decline was not related to whether they had or had not been treated for syphilis

1) Neurocognitive Impairment in HIV-infected individuals with previous syphilis poster-CROI March 2011

Cryptococcal Meningitis

- Yeast infection (varieties-*neoformans* & *gattii*)
- Most infections in HIV
 - *C.neoformans* var *neoformans*
- Ecology
 - Avian excreta (pigeons), trees
 - Ubiquitous -spores
- **Estimated 957 900 cases & 624 700 deaths world wide (vast majority in sub-Saharan Africa)¹**
- CD₄ usually <200 cells/μL
- Inhalation →pulmonary infection →systemic →CNS
- Presentation:
 - Headaches
 - Vomiting
 - Visual disturbances/diplopia
 - Confusion
 - Focal neurology

1) SAMJ April 2011, Vol. 101, No.4



Diagnosis

Lumbar puncture

- Diagnosis
 - India ink stain
 - Cryptococcal Latex Antigen test (CRAG)
 - Cryptococcal culture
 - Opening pressure
 - Cell count, Gram stain, protein & glucose
 - Bacterial culture
 - TB culture, syphilis
- When to CT scan?
 - If neurological signs
 - But do not delay LP & treatment

Treatment of initial & subsequent episodes of CM

Relapse thought to be attributable to inadequate primary therapy (dose/or duration) or failure of compliance with consolidation or maintenance therapy

Initial

- Induction phase
 - Amphotericin B 1mg/Kg/day ivi for 2 weeks
- Consolidation phase
 - Fluconazole 800mg po daily for 8 weeks
- Secondary prophylaxis
 - Fluconazole 200-400mg po daily for life or until CD₄ >200 cells/μL for more than 6 months on ART (at least 12 months fluconazole in total)

- **Induction phase**
 - Amphotericin B 1mg/Kg/day ivi for 4-10 weeks.
- **Consolidation phase**
 - Fluconazole 800-1200mg po daily for 10-12 weeks
- **Secondary prophylaxis**
 - Fluconazole 400mg po daily for life or until CD₄ >200 cells/μL for more than 6 months on ART (at least 12 months fluconazole in total)

Managing raised intracranial pressure



The South African Journal of HIV Medicine-
2007

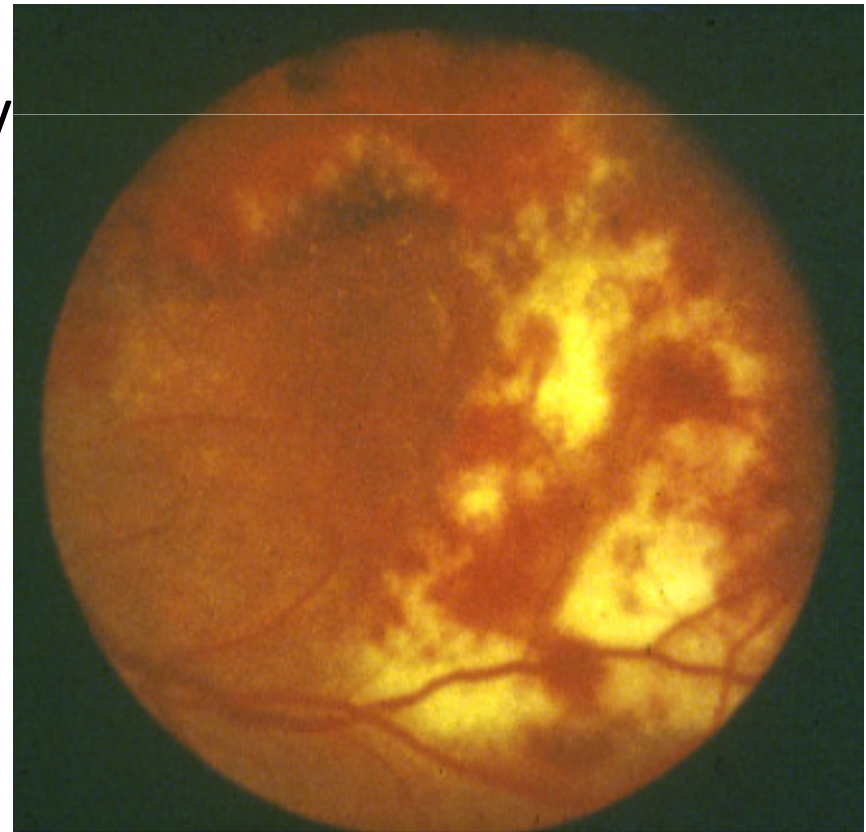
- Opening pressure >25cmH₂O
- Remove up to 20-30 ml of CSF (to decrease opening pressure by 20-50%)
- **Repeat LP for pressure relief dictated by:**
 - Worsening headache
 - Ophthalmoplegia
 - Papilloedema
 - Hearing loss
 - Visual loss
 - Depressed level of consciousness
- **Many patients need daily LP initially**

New developments preventive strategies

- Data from Cape Town
 - In 707 patients initiating ART
 - 13% CD₄ <100 cells/μL serum sample tested positive CRAG
 - Prospective screening for CRAG would be 100% predictive for CM
 - 73% of ART-naive presenting with CM have been diagnosed with HIV for median of 4 months before CM.
- Suggested strategy:
 - Doing serum CRAG patients with CD₄ <100 cells/μL
 - Asymptomatic CRAG +ve patients.
 - Fluconazole 400mg daily for 8 weeks
 - Followed by fluconazole 200mg daily for at least 10 months (or CD₄ >200 cells/μL).
 - Starting ART after initial 2 weeks of fluconazole

Painless visual loss

- Commonest cause of painless visual loss in HIV (CD₄ count <50 cells/ μ L) is CMV retinitis.
- Presentation is gradual deterioration of visual fields over months
 - It may be unilateral initially
- Diagnosis
 - Fundoscopy
 - Vitreous PCR
- Differential diagnosis
 - Toxoplasmosis
 - Varicella-zoster virus
 - HIV



Space Occupying Lesions

Toxoplasmosis



- *Toxoplasma gondii* reactivation in the brain
- CD₄ usually <100 cells/μL
- Presentation:
 - Focal neurology
 - Seizures
 - Confusion
 - Headaches
 - Fevers
- Single or multiple ring-enhancing lesions on CT scan
- Positive serum Toxoplasma IgG supports the diagnosis
- Treatment: Co-trimoxazole

Gastrointestinal presentation

Oesophageal candidiasis

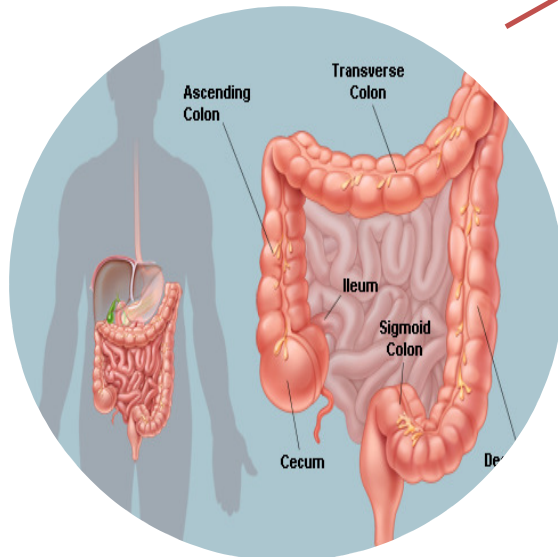
- Common in advanced disease
- Usually presents with dysphagia and or odynophagia
- Usually associated with oral candidiasis
- Differential diagnosis:
 - Major ophthous ulcers
 - CMV
- Treatment:
 - Does not respond to topical therapy
 - Oral fluconazole 200mg daily 14 days

Chronic Diarrhoea

- Common in advanced HIV

Small bowel




- Large volume
- Frequency ++
- Blood, mucus & WBC absent
- Differential:
 - Cryptosporidium
 - Isosporiasis
 - Microsporidium
 - HIV enteropathy



Large bowel

- Small volume
- Frequency +
- Blood, mucus & WBC present
- Differential:
 - Cytomegalovirus

Diagnosis

- 2 stools for microscopy (special stains)
 - Pathogen found  Treat pathogen
 - Mild no pathogen  Antimotility treatment
 - Severe no pathogen  Endoscopy & biopsy
(upper & lower GI scopes)

Effect of ART & OI prophylaxis

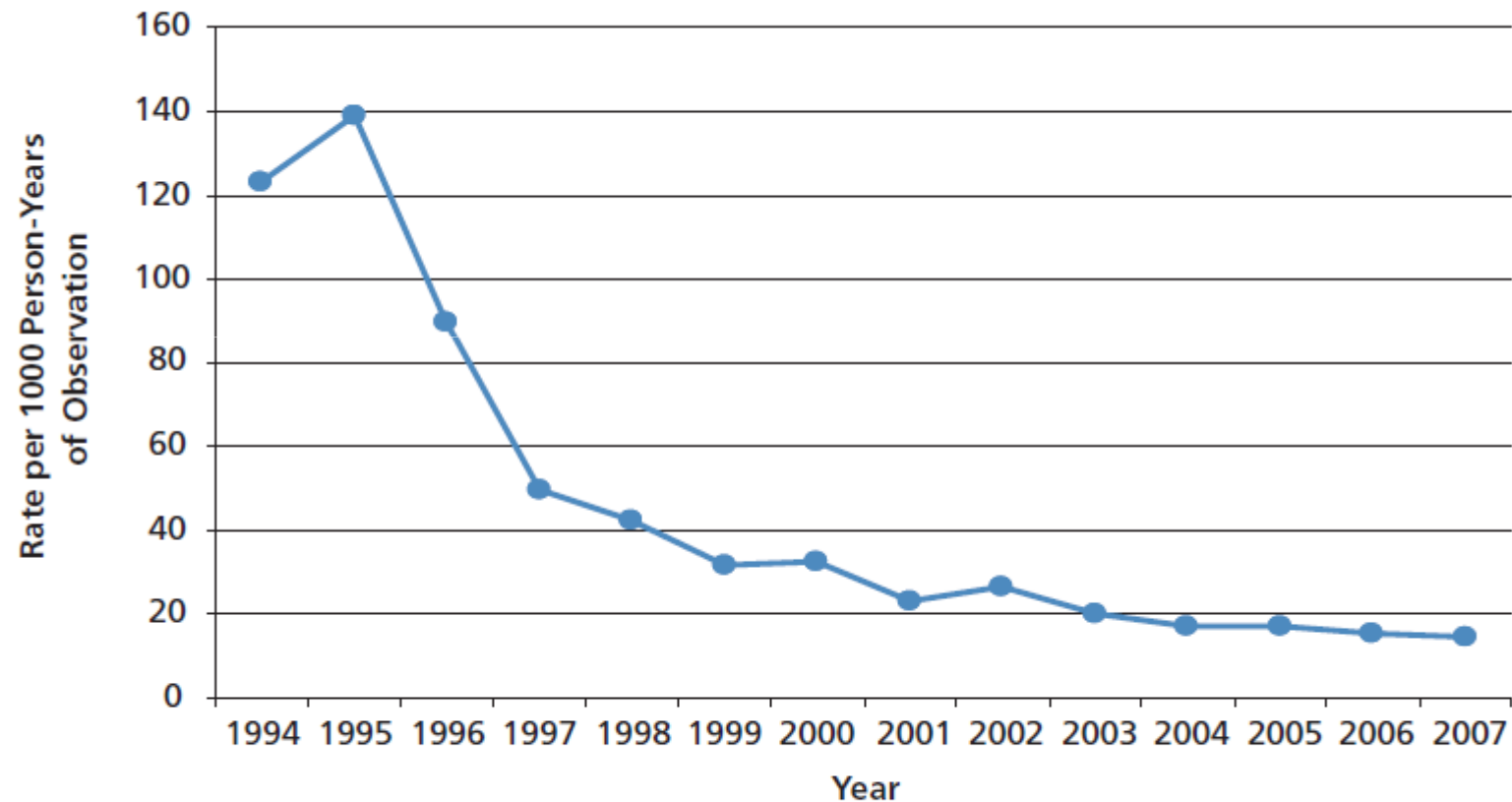


Figure 1. Annual incidence of first AIDS-defining opportunistic infection in the HIV Outpatient Study, 1994–2007. Figure adapted from Brooks et al, *Clin Infect Dis*, 2009.⁴

Conclusion

- Prompt diagnosis of AHI represents a tremendous opportunity for prevention of onward HIV transmission
- Opportunistic infections reduce quality of life & longevity
- Retesting for syphilis in MSM important
- Routine CRAG screening for HIV-infected patients with low CD₄ counts

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