NORTHWEST AIDS EDUCATION AND TRAINING CENTER

Opportunistic Infections I

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Outline

- **Opportunistic Infections I** – April 5, 2012
  - General Principles and Epidemiology
  - OI prevention and prophylaxis
  - Diagnosis and management of *Pneumocystis jiroveci* Pneumonia
- **Opportunistic Infections II** – April 12, 2012
  - Immune Reconstitution Inflammatory Syndrome
  - HAART in setting of acute OI's – ACTG 5142
  - Diagnosis and Management of MAC, Histoplasma, Candida

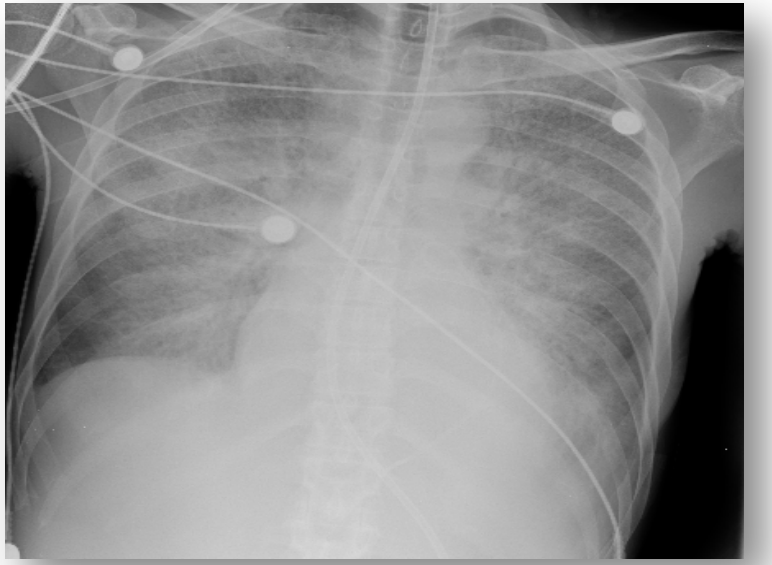
Historical Context – MMWR 1981

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.

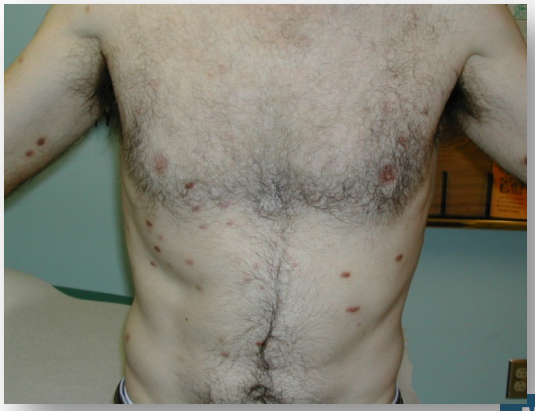
Patient 1: A previously healthy 33-year-old man developed *P. carinii* pneumonia and oral mucosal candidiasis in March 1981 after a 2-month history of fever associated with elevated liver enzymes, leukopenia, and CMV viruria. The serum complement-fixation CMV titer in October 1980 was 256; in May 1981 it was 32.* The patient's condition deteriorated despite courses of treatment with trimethoprim-sulfamethoxazole (TMP/SMX), pentamidine, and acyclovir. He died May 3, and postmortem examination showed residual *P. carinii* and CMV pneumonia, but no evidence of neoplasia.

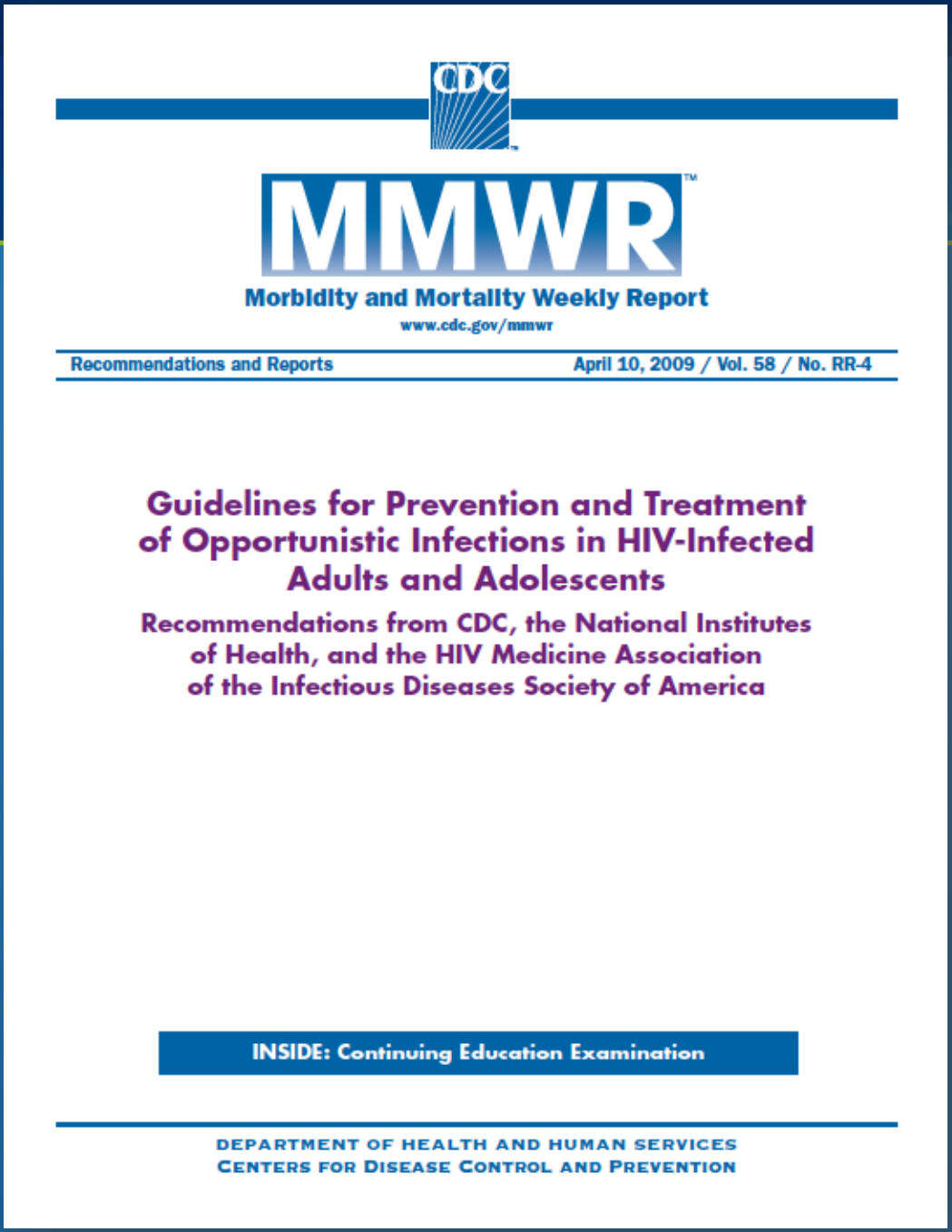
Patient 2: A previously healthy 30-year-old man developed *P. carinii* pneumonia in April 1981 after a 5-month history of fever each day and of elevated liver-function tests, CMV viruria, and documented seroconversion to CMV, i.e., an acute-phase titer of 16 and a convalescent-phase titer of 28* in anticomplement immunofluorescence tests. Other features of his illness included leukopenia and mucosal candidiasis. His pneumonia responded to a course of intravenous TMP/SMX, but, as of the latest reports, he continues to have a fever each day.



Kaposi's Sarcoma and *Pneumocystis* Pneumonia Among Homosexual Men – New York City and California

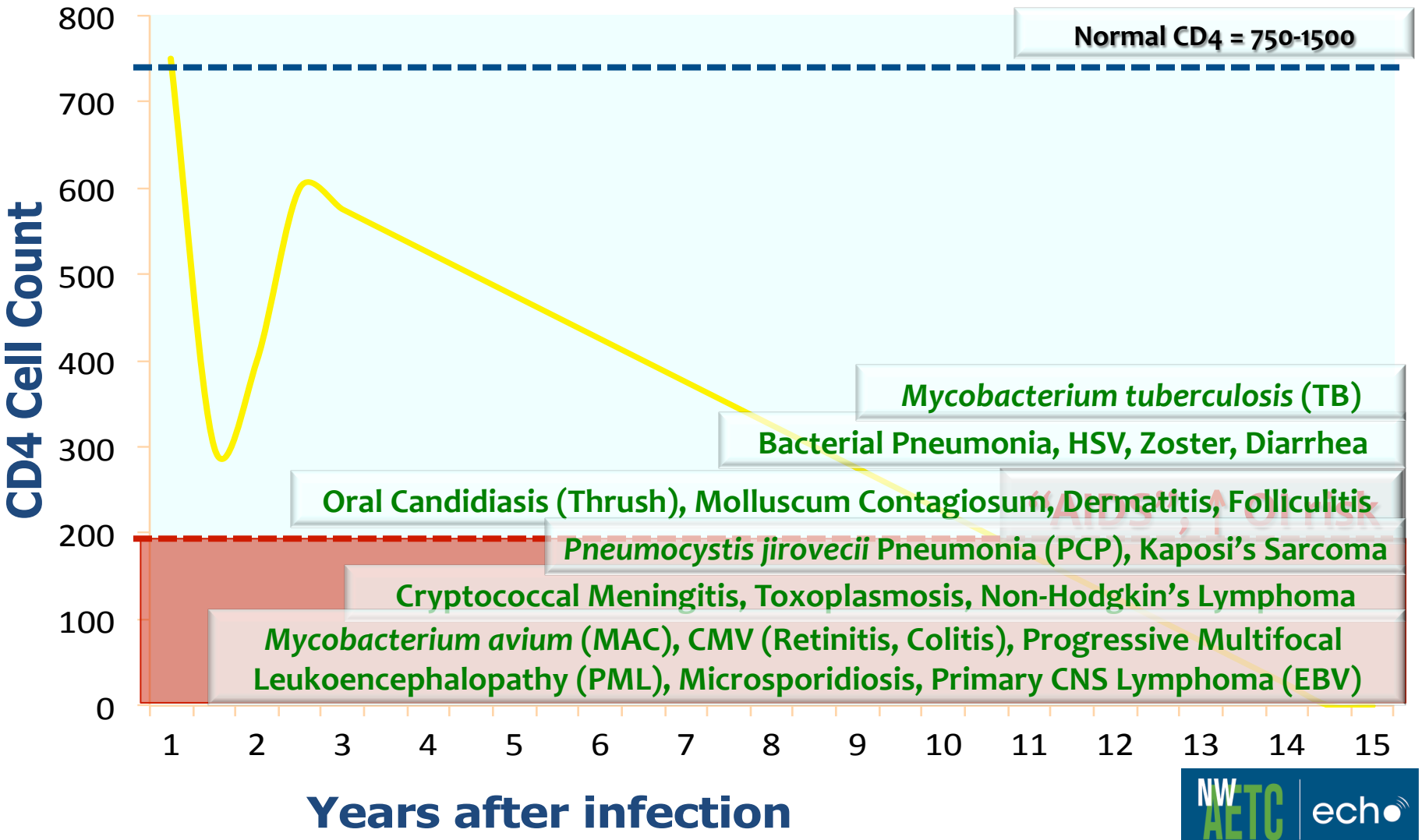
During the past 30 months, Kaposi's sarcoma (KS), an uncommonly reported malignancy in the United States, has been diagnosed in 26 homosexual men (20 in New York City [NYC]; 6 in California). The 26 patients range in age from 26-51 years (mean 39 years). Eight of these patients died (7 in NYC, 1 in California)—all 8 within 24 months after KS was diagnosed. The diagnoses in all 26 cases were based on histopathological examination of skin lesions, lymph nodes, or tumor in other organs. Twenty-five of the 26 patients were white, 1 was black. Presenting complaints from 20 of these patients are shown in Table 1.





Source: 2009 DHHS Opportunistic Infection Guidelines. (aidsinfo.nih.gov)

Risk of Opportunistic Infection by CD4



AIDS-defining Conditions

Pneumocystis jirovecii pneumonia	Invasive Cervical Carcinoma (HPV)
Cryptococcosis, cryptococcal meningitis (C. neoformans)	Non-Hodgkin's Lymphoma , Burkitt's Lymphoma, Primary CNS Lymphoma (EBV)
Esophageal (or respiratory) Candidiasis (C. albicans)	Progressive Multifocal Leukoencephalopathy (PML, JC virus)
Kaposi's Sarcoma (HHV-8)	HIV Encephalopathy
Cerebral Toxoplasmosis (T. gondii)	HIV Wasting Syndrome
CMV Infection (retinitis, colitis)	Cryptosporidia
	Isospora
Histoplasma capsulatum (disseminated or extrapulmonary)	Recurrent Pneumonia (≥ 2 episodes/yr)
Coccidioidomycosis (C. immitis)	Mycobacterium avium (MAC)
Herpes simplex: chronic ulcer, esophageal or pulmonary disease	Non-typhoidal Salmonella septicemia
Tuberculosis (extra-pulmonary)	

Approaches to OI's

- **Primary Prophylaxis**
  - Offered to everyone to prevent infection
- **Secondary Prophylaxis**
  - Offered after OI treatment to prevent recurrence
- **Vaccination**
- **OI Treatment**
- **ART**

Prophylaxis to prevent OI's

Primary

- PCP
- TB
- Toxo
- MAC
- VZV
- *S. pneumoniae*
- HBV
- HAV
- Influenza

Secondary

- PCP
- Toxo
- MAC
- CMV
- Cryptococcosis
- Histoplasmosis
- Coccidioidomycosis
- Recurrent *Salmonella* bacteremia
- Recurrent HSV
- Recurrent Candidiasis

Prevention of Opportunistic Infections

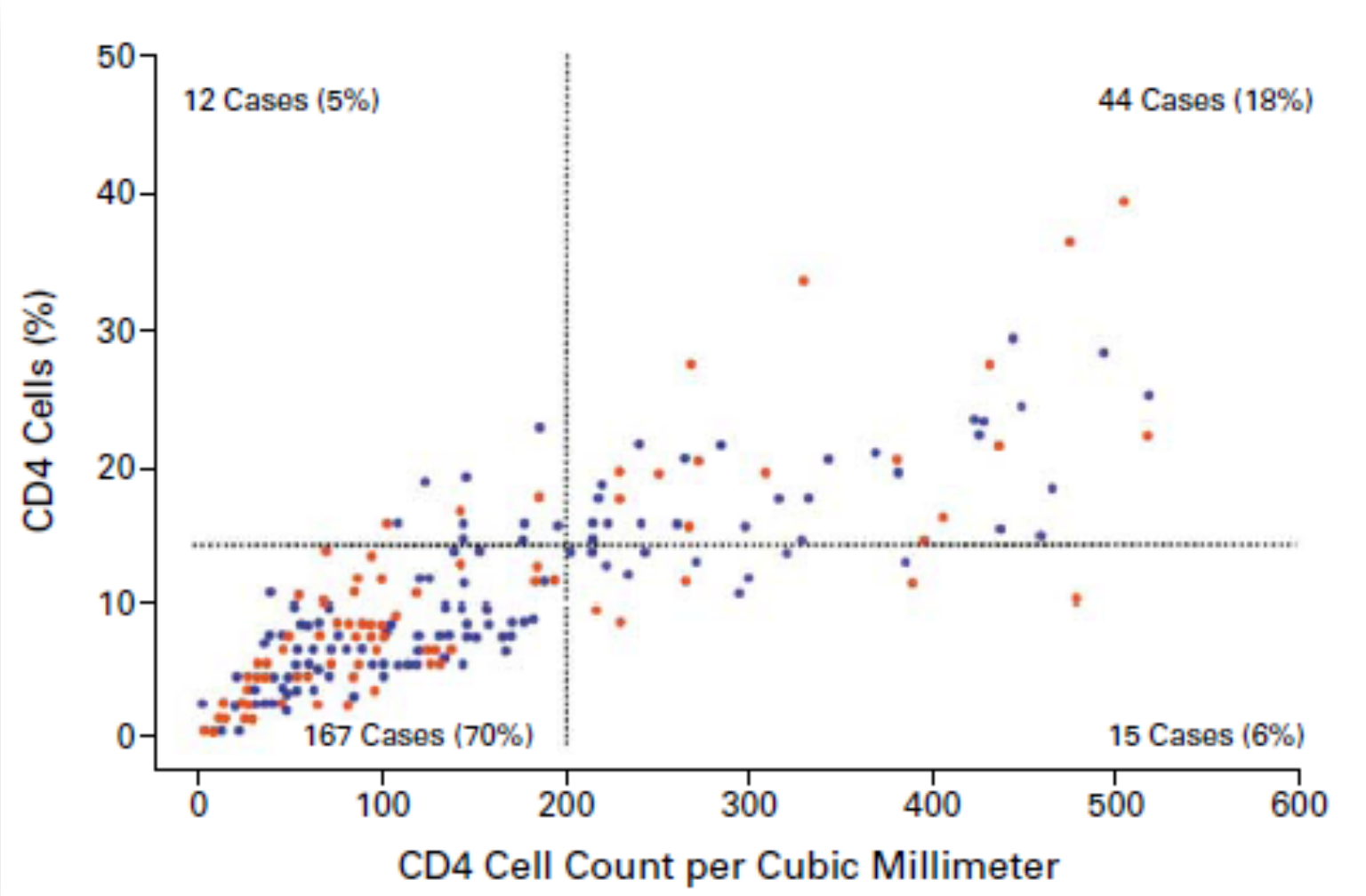
Disease	Major Indication	Prophylaxis
Pneumocystis pneumonia	CD4 < **200** cells/mm^3 *or* Oropharyngeal candidiasis	Trimethoprim-sulfamethoxazole (Bactrim, Septra)
Toxoplasma encephalitis	CD4 <**100** cells/mm^3 *and* Toxoplasma IgG positive	Trimethoprim-sulfamethoxazole (Bactrim, Septra)
Disseminated *Mycobacterium avium* complex	CD4 < **50** cells/mm^3	Azithromycin

Alternatives to Trimethoprim/Sulfamethoxazole

- **TMP/SMX i DS tab PO QD***
  - TMP/SMX i SS tab PO QD or i DS tab PO TIW
  - Dapsone 100 mg PO QD
  - Dapsone 50 mg PO QD + Pyrimethamine 50 mg PO QWeek + Leukovorin 25 mg PO QWeek
  - Aerosolized Pentamidine 300 mg/2.5 mL saline Q3 weeks.
  - Atovaquone 1,500 mg PO QD

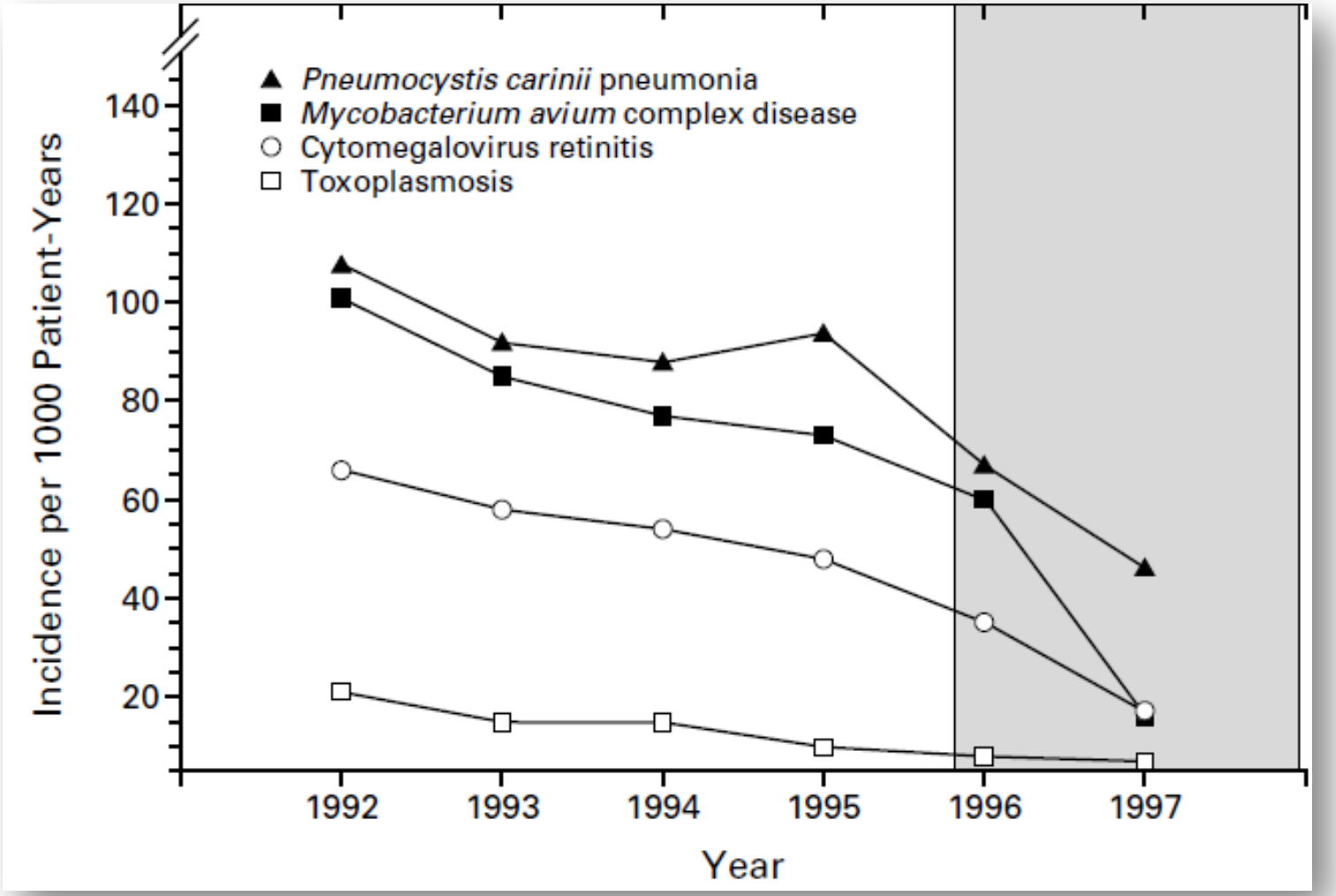
* Preferred

Precision of OI Prophylaxis Criteria



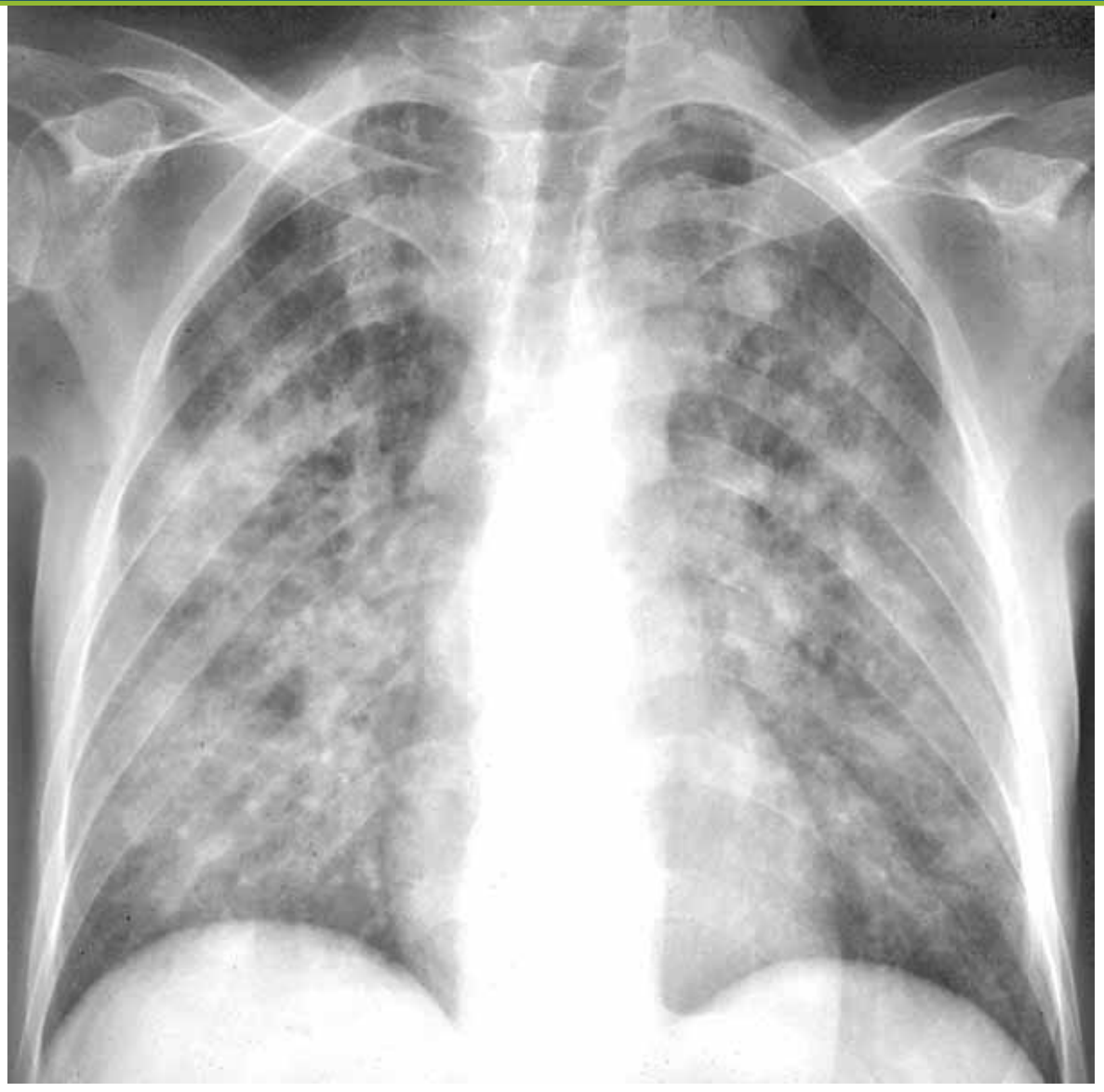
Phair J et al, NEJM 1990;322(3): 161-5
Kovacks JA and Masur H, NEJM, 2000:324 (19): 1416-29

Effect of HAART on Incidence of OI's



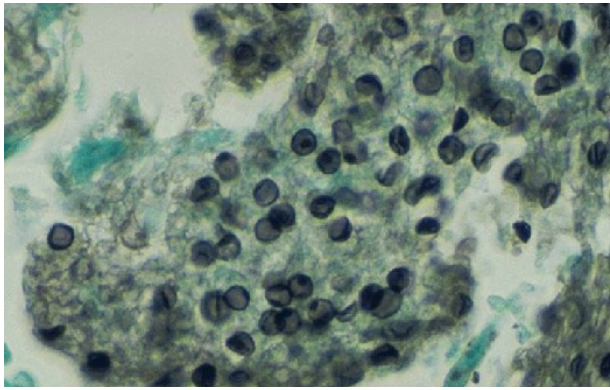
Jones JL et al MMWR 1999;48 (SS-2):1-22, Kovacks JA and Masur H, NEJM, 2000:324 (19): 1416-29

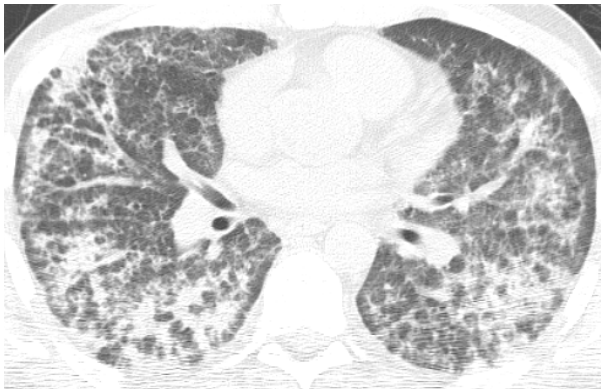
‘PCP’ Pneumonia *(Pneumocystis jiroveci)*



Pneumocystis Pneumonia

- **Clinical Manifestations:**
  - Fever, dry cough and dyspnea
- **Pathophysiology:**
  - Probably reactivation and inhalation
  - 90% of patients have CD4 < 200
- **Diagnosis:** Clinical, Chest X-Ray, induced sputum for silver stain and FA, O2 saturation
- **Mortality:**
  - Patients may worsen after starting treatment
  - Steroids indicated if PaO2 < 70%
- **Treatment:**
  - Trimethoprim/Sulfamethoxazole (TMP/SMX) 15-20 mg/kg/day divided Q8 hrs x 14-21 days
  - Steroids beneficial if PaO2 < 70%





Pneumocystis: New Diagnostics

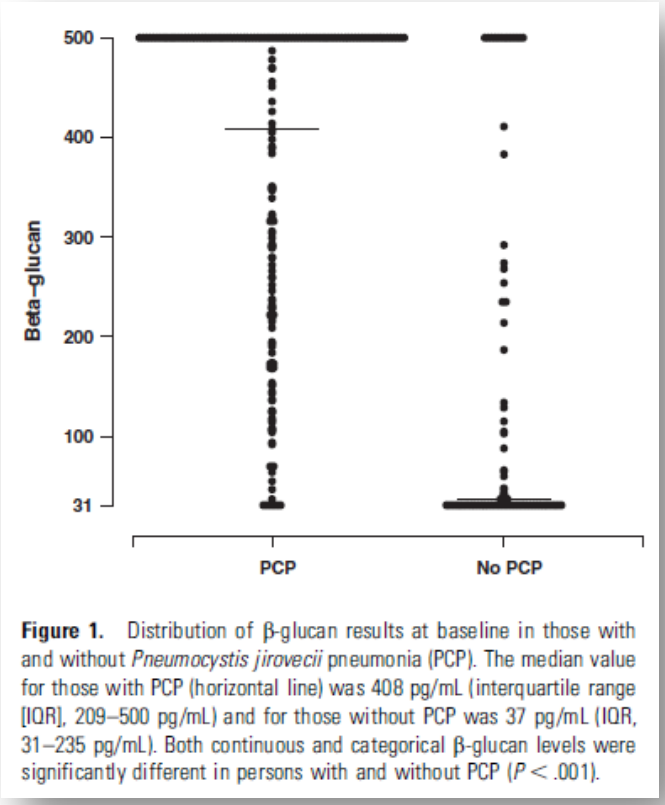


Figure 1. Distribution of β-glucan results at baseline in those with and without *Pneumocystis jirovecii* pneumonia (PCP). The median value for those with PCP (horizontal line) was 408 pg/mL (interquartile range [IQR], 209–500 pg/mL) and for those without PCP was 37 pg/mL (IQR, 31–235 pg/mL). Both continuous and categorical β-glucan levels were significantly different in persons with and without PCP ($P < .001$).

- 1→3 β – D glucan a component of fungal cell wall
- Data extracted from ACTG 5164: 282 pts with acute OI (69% PJP, 14% crypto, 9% bact PNA)
- POSITIVE in 92% of pts with confirmed PCP, but also POSITIVE in 35% of those without PCP
- Sensitivity 92%, Specificity 65%
- PPV 85%, NPV 80%

Sax P, et al *Clinical Infectious Diseases* 2011; Jul 15; 53:197

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Summary: Approach to OI's

- OI's have historical significance in the HIV epidemic, and continue to cause morbidity/mortality
- HAART has reduced the incidence of OI's
- Our main primary preventive strategy is with TMP/SMX and Azithromycin prophylaxis
- *Pneumocystis jiroveci* causes an indolent sub-acute hypoxic pneumonia, treated with TMP/SMX +/- steroids
- Newer diagnostics have arrived! Not perfect, but can be helpful