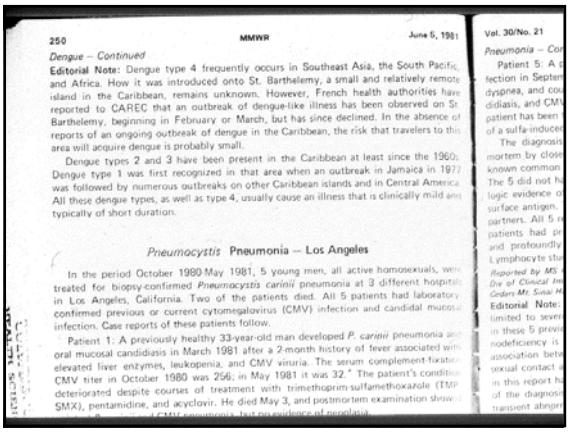


250 MMWR June 5, 1981 Vol. 30/No. 21

Dengue – Continued

Editorial Note: Dengue type 4 frequently occurs in Southeast Asia, the South Pacific, and Africa. How it was introduced onto St. Barthelemy, a small and relatively remote island in the Caribbean, remains unknown. However, French health authorities have reported to CAREC that an outbreak of dengue-like illness has been observed on St. Barthelemy, beginning in February or March, but has since declined. In the absence of reports of an ongoing outbreak of dengue in the Caribbean, the risk that travelers to this area will acquire dengue is probably small.

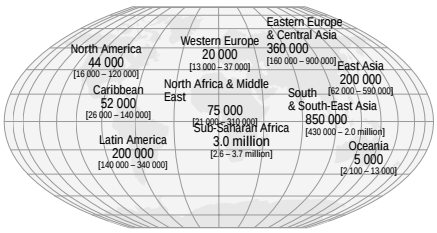
Dengue types 2 and 3 have been present in the Caribbean at least since the 1960s. Dengue type 1 was first recognized in that area when an outbreak in Jamaica in 1977 was followed by numerous outbreaks on other Caribbean islands and in Central America. All these dengue types, as well as type 4, usually cause an illness that is clinically mild and typically of short duration.

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

Estimated number of adults and children newly infected with HIV during 2003



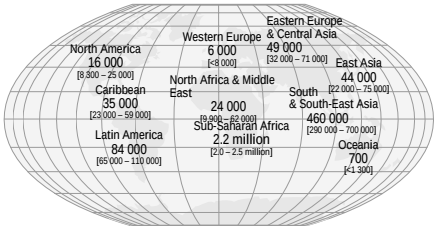
Total: 4.8 (4.2 – 6.3) million

00003-E-4 – July 2004

HIV Transmission

- Blood
  - transfusion
  - injection drug use
- Sexual Intercourse
  - heterosexual
  - male to male
- Perinatal
  - intrapartum
  - breast feeding

Estimated adult and child deaths from AIDS during 2003



Total: 2.9 (2.6 – 3.3) million

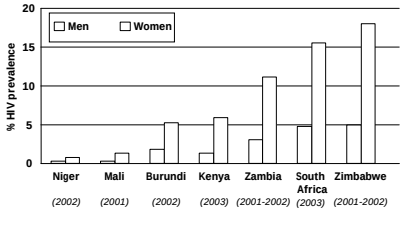
00003-E-5 – July 2004

Global estimates for adults and children end 2003

• People living with HIV	37.8 million [34.6 – 42.3 million]
• New HIV infections in 2003	4.8 million [4.2 – 6.3 million]
• Deaths due to AIDS in 2003	2.9 million [2.6 – 3.3 million]

00003-E-3 – July 2004

HIV prevalence among 15–24-year-olds in selected sub-Saharan African countries, 2001–2003

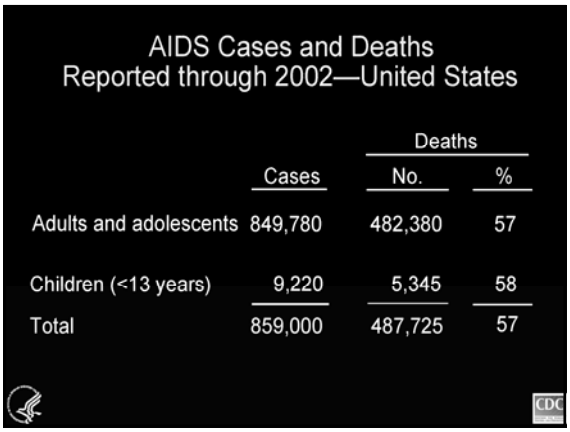


Sources: Burundi (Enquete Nationale de Seroprevalence de l'Infection par le VIH au Burundi. Bujumbura, Décembre 2002). Kenya (Kenya Demographic and Health Survey 2003. Mali (Enquête Démographique et de Santé. Mali 2001). Niger (Enquête Nationale de Séroprévalence de l'infection par le VIH dans la population générale âgée de 15 à 49 ans au Niger (2002). South Africa 1)Pettifor AE, Rees HV, Steffenson A, Hlongwa-Madikizela L, MacPhail C, Vermaak H, Kleinschmidt I. HIV and sexual behaviour among young South Africans: a national survey of 15-24 year olds. Johannesburg: Reproductive Health Research Unit, University of Witwatersrand, 2004). Zambia (Zambia Demographic and Health Survey 2001-2002). Zimbabwe (The Zimbabwe Young Adult Survey 2001-2002).

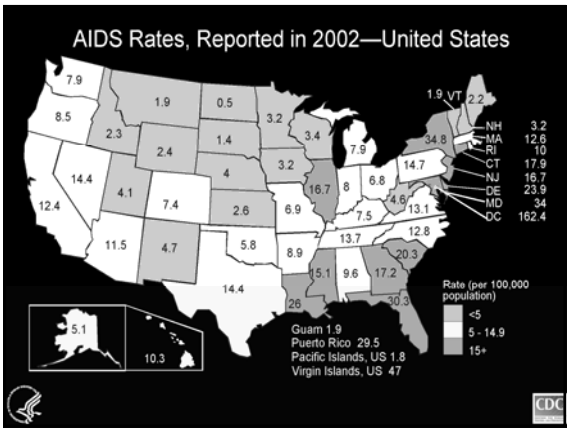
2004 Report on the Global AIDS Epidemic (Fig 7)

AIDS Cases and Deaths Reported through 2002—United States

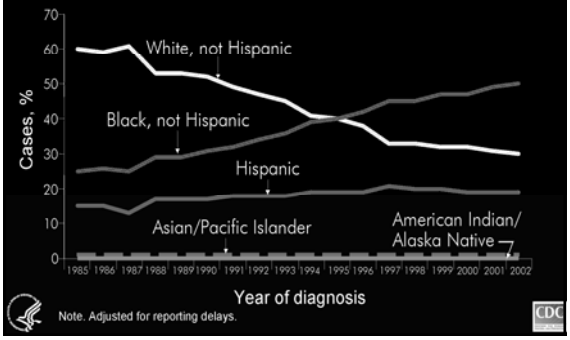
	Cases	Deaths	
		No.	%
Adults and adolescents	849,780	482,380	57
Children (<13 years)	9,220	5,345	58
Total	859,000	487,725	57



AIDS Rates, Reported in 2002—United States

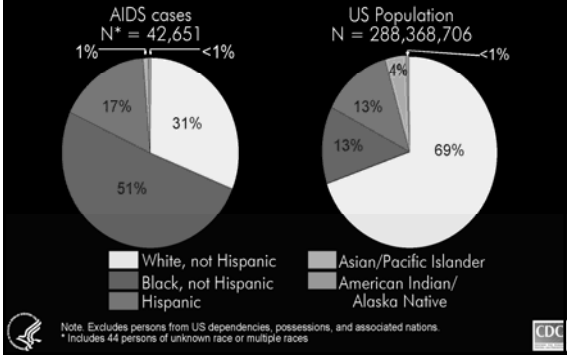


Proportion of AIDS Cases, by Race/Ethnicity and Year of Diagnosis, 1985–2002—United States



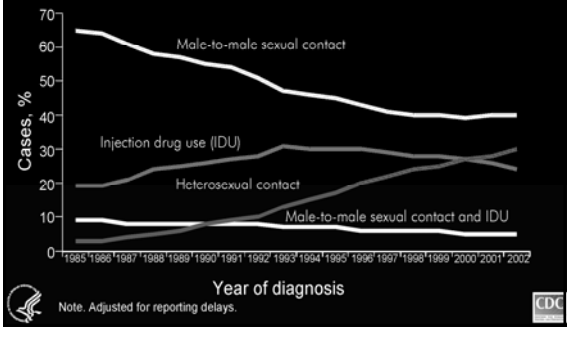
Note. Adjusted for reporting delays.

Proportion of AIDS Cases and Population, by Race/Ethnicity 2002—United States



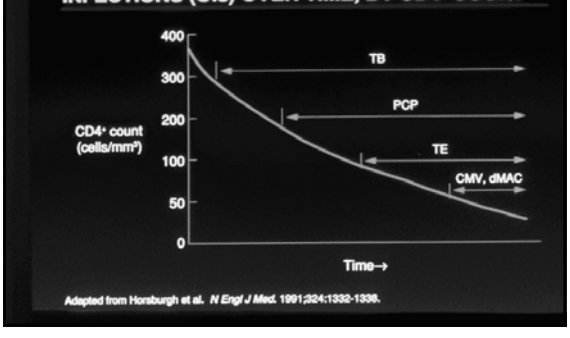
Note. Excludes persons from US dependencies, possessions, and associated nations.
* Includes 44 persons of unknown race or multiple races

Proportion of AIDS Cases among Adults and Adolescents, by Exposure Category and Year of Diagnosis 1985–2002—United States

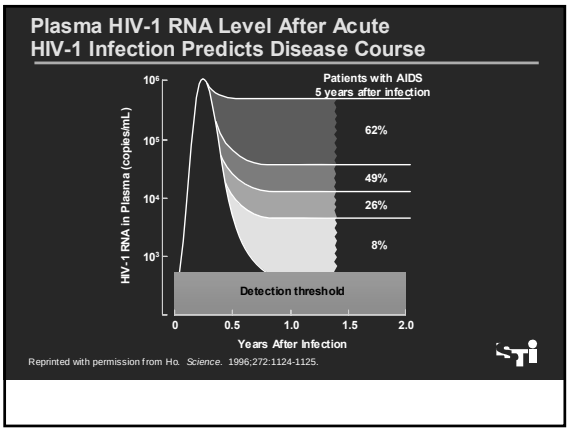


Note. Adjusted for reporting delays.

INCIDENCE OF SELECTED OPPORTUNISTIC INFECTIONS (OIs) OVER TIME, BY CD4+ COUNT



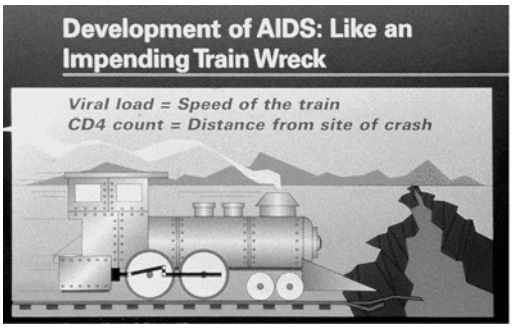
Adapted from Horsburgh et al. *N Engl J Med.* 1991;324:1332-1336.



Frequency of HIV 'Non-Progressors'

- San Francisco City Clinic Cohort
  - 539 HIV+ Gay men with known seroconversion date.
  - After 10 years of follow up:
    92% had either: died, developed AIDS or had CD4<200.

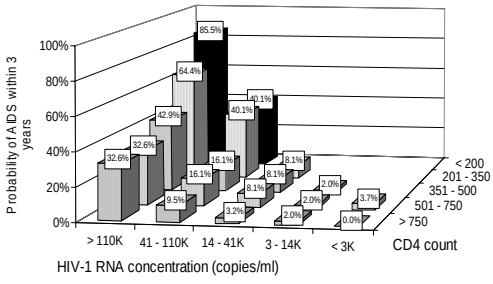
[Buchbinder et al. AIDS 1994;8:1123.]



Explaining the variability of HIV disease

- Viral Factors
  - Nef deletion
  - Non-clade B subtypes
- Host Factors
  - Chemokine co-receptors
  - Immune response
  - Gender?
- Environmental Factors
  - Infection, diet?, stress?

Probability of AIDS over 3 years



HIV Co-receptors

CD4 necessary but not sufficient for infection.

Beta chemokine receptors act as HIV co-receptors.

CXCR4 (lymphocyte) CCR5 (macrophage)

Homozygous CCR5 deletion found in <1%.

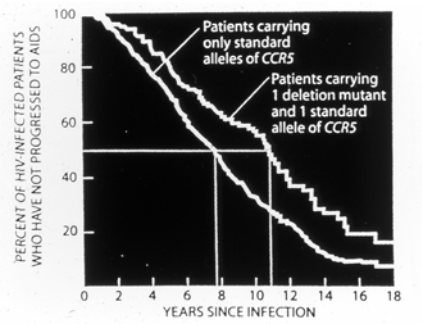
MACS High risk cohort:

No HIV+ among those homozygous for deletion.

3.6% of HIV Negative were homozygous.

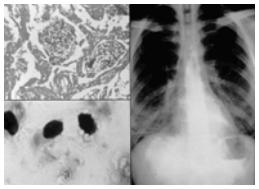
Among persistently HIV Neg: up to 33% were homozygous.

Effect of Co-receptor Heterozygosity



Pneumocystis pneumonia in AIDS

- Commonest life threatening complication of AIDS in U.S.
- Subacute illness (fever, cough, dyspnea).
- Diffuse interstitial infiltrate on x-ray.
- Addition of corticosteroids to antimicrobials cuts mortality in severe disease 50%.
- Fully preventable with trimethoprim-sulfa.



Early indicators of HIV Infection

CD4 count predicts risk of PCP

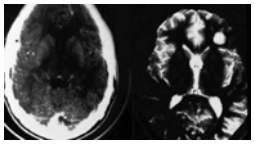
TABLE 1. Cumulative incidence* of *Pneumocystis carinii* pneumonia (PCP) according to CD4+ count at baseline among the MACS seroprevalent cohort†

CD4+ count at baseline	N	PCP	Percentage with PCP		
			6 mo.	12 mo.	36 mo.
< 200	77	19	8.4	18.4	33.3
201-350	217	47	0.5	4.0	22.9
351-500	389	39	0.0	1.4	9.0
501-700	483	43	0.0	0.4	8.3
> 700	499	20	0.0	0.0	3.8

Key features of OIs in AIDS

- HIV causes profound defect mostly restricted to T cell-based immunity (restricted range of pathogens)
- OIs usually reflect reactivation of latent infections.
- Reinfection may occur (eg: tuberculosis)
- Chronic suppression needed after acute treatment.
- Immune reconstitution with anti-retroviral therapy may reverse OI susceptibility

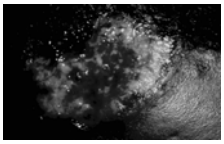
CNS toxoplasmosis

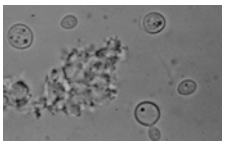


- Protozoon parasite; cats shed oocysts; farm animals incidental hosts; humans infected from cysts, uncooked meat.
- Commonest cause of focal CNS disease in AIDS.
- Serum IgG antibody reliable marker of past infection.
- Reactivation in AIDS associated with CD4<100.

Cryptococcal disease in AIDS

- Ubiquitous soil fungus.
- Initial assymptomatic pneumonia.
- Reactivation in advanced HIV disease (CD4<100).
- Meningitis commonest presentation but wide dissemination frequent.



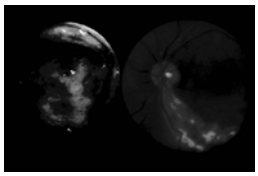


Prophylaxis of Opportunistic Infections

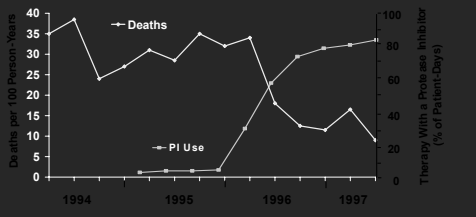
Pathogen	Indication	Regimen
PCP	CD4<200	Trimethoprim-sulfa
Toxo	CD4<100 and IgG+	Trimethoprim-sulfa or Dapsone +Pyrimethamine
MAC	CD4<50	Clarithro/Azithromycin
TB	+PPD (5mm)	INH (9 months)

CMV disease in AIDS

- Common viral infection (50% adult seroprevalence).
- Reactivation at CD4<50
- Retinitis commonest.
- Other sites: Colon, CNS.



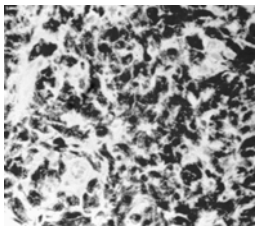
Mortality and Frequency of Use of PI-Containing Regimens Among HIV+ Patients with CD4+ Counts <100 cells/mm³*



*Data from 1255 HIV patients who were followed at 9 HIV-specialty clinics in 8 US cities. Reprinted with permission from Palella. *N Engl J Med*. 1998;338:853-860.

Disseminated Mycobacterium-avium complex (MAC) disease in AIDS|

- Common in environment (water).
- Local lung disease known prior to AIDS.
- Widespread visceral dissemination in AIDS.
- Diagnosis by blood culture.
- Absence of inflammation in tissue sites.



OI Guidelines November, 2001 Comparison of Indications to Discontinue Primary and Secondary Prophylaxis

Agent	Recommendation
PCP	1º CD_4 > 200 X 3 months 2º CD_4 > 200 X 3 months
Toxo.	1º CD_4 > 200 X 3 months 2º CD_4 > 200 X 6 months + initial Rx + asymptomatic
MAC	1º CD_4 > 100 X 3 months 2º CD_4 > 100 X 6 months + 12 mo Rx + asymptomatic

Immune Reconstitution with HIV Therapy

- Focal MAC adenitis
- Inflammatory flare of CMV retinitis
- Worsening of previously stable hepatitis
- Development of cavitary TB