
Evolution of the Treatment and Prophylaxis of Opportunistic Infections in HIV-Infected Persons

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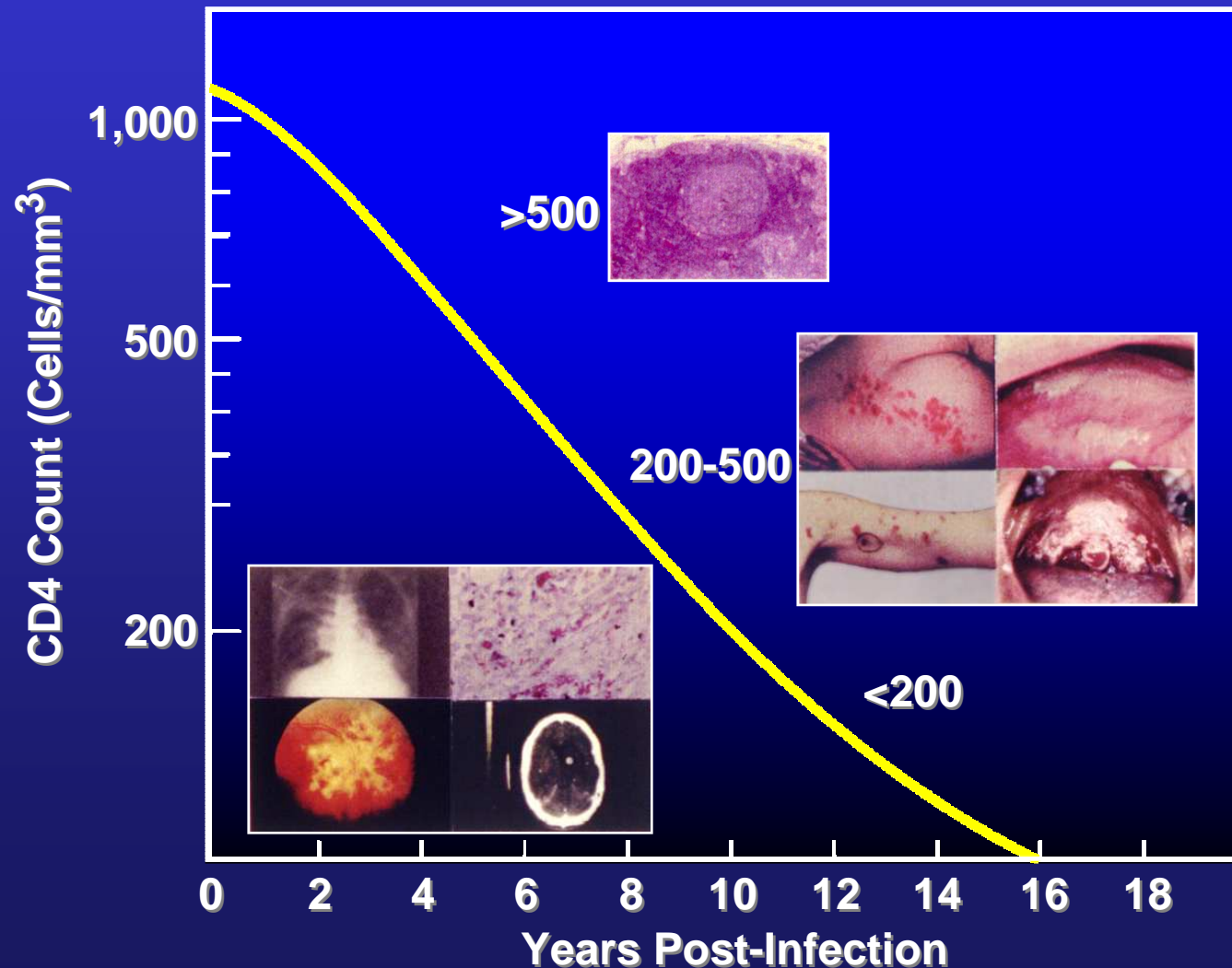
Early Misconceptions about AIDS

UFO aliens are spreading AIDS

THE AIDS virus is being spread by spaceships that are bombarding our planet from outer space with a deadly ray.

They're using the disease to take over the planet!

Correlation Between CD4 Count and Clinical Manifestations of HIV-1 Infection



AIDS 1981 to 1996

- **Medical problems**

- Prevention and treatment of opportunistic infections
- Therapy against the virus itself was poor

- **Social problems**

- Stigmatization of persons with the disease
- Lack of understanding and denial about how HIV was acquired led to high rates of transmission

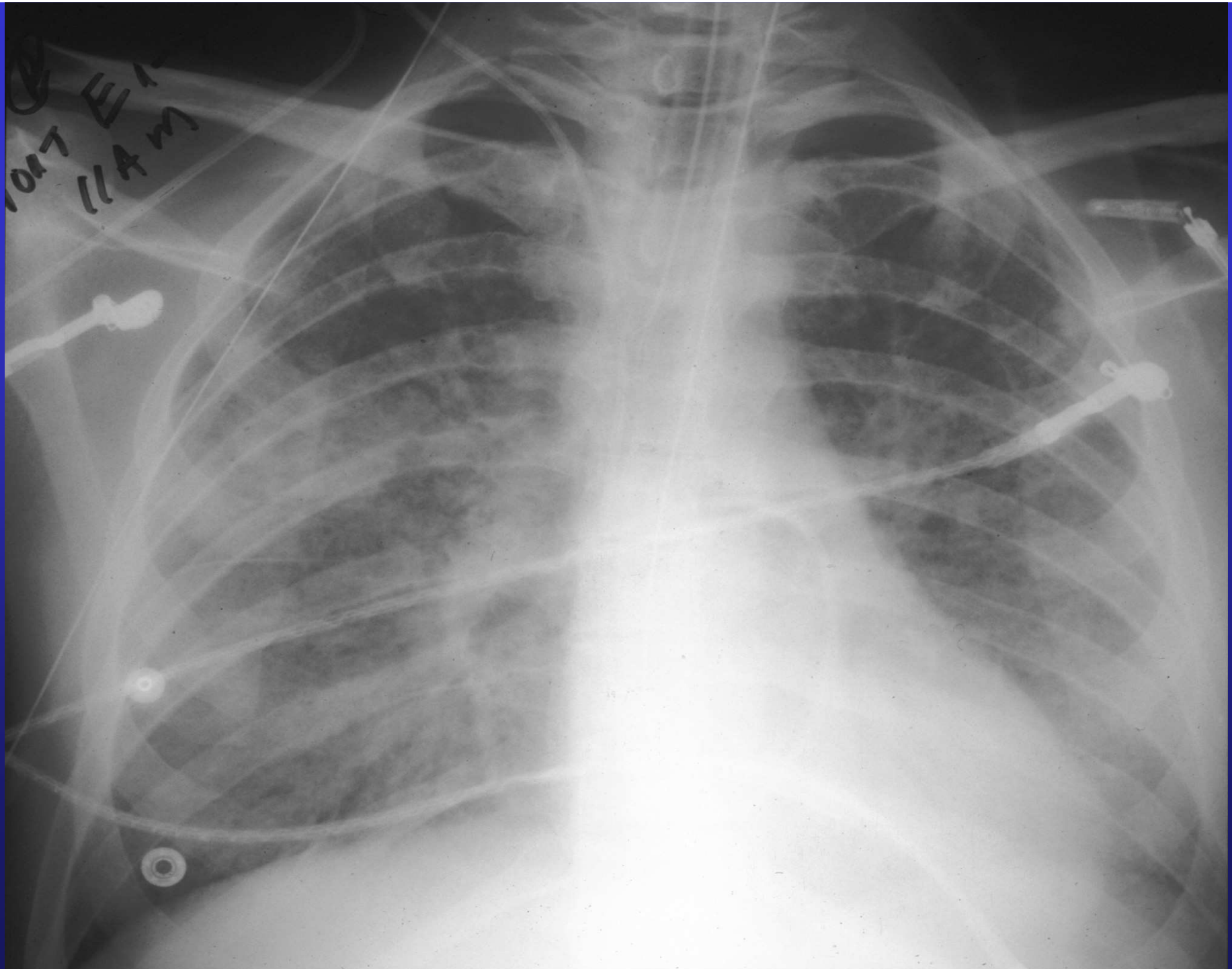
- **Political**

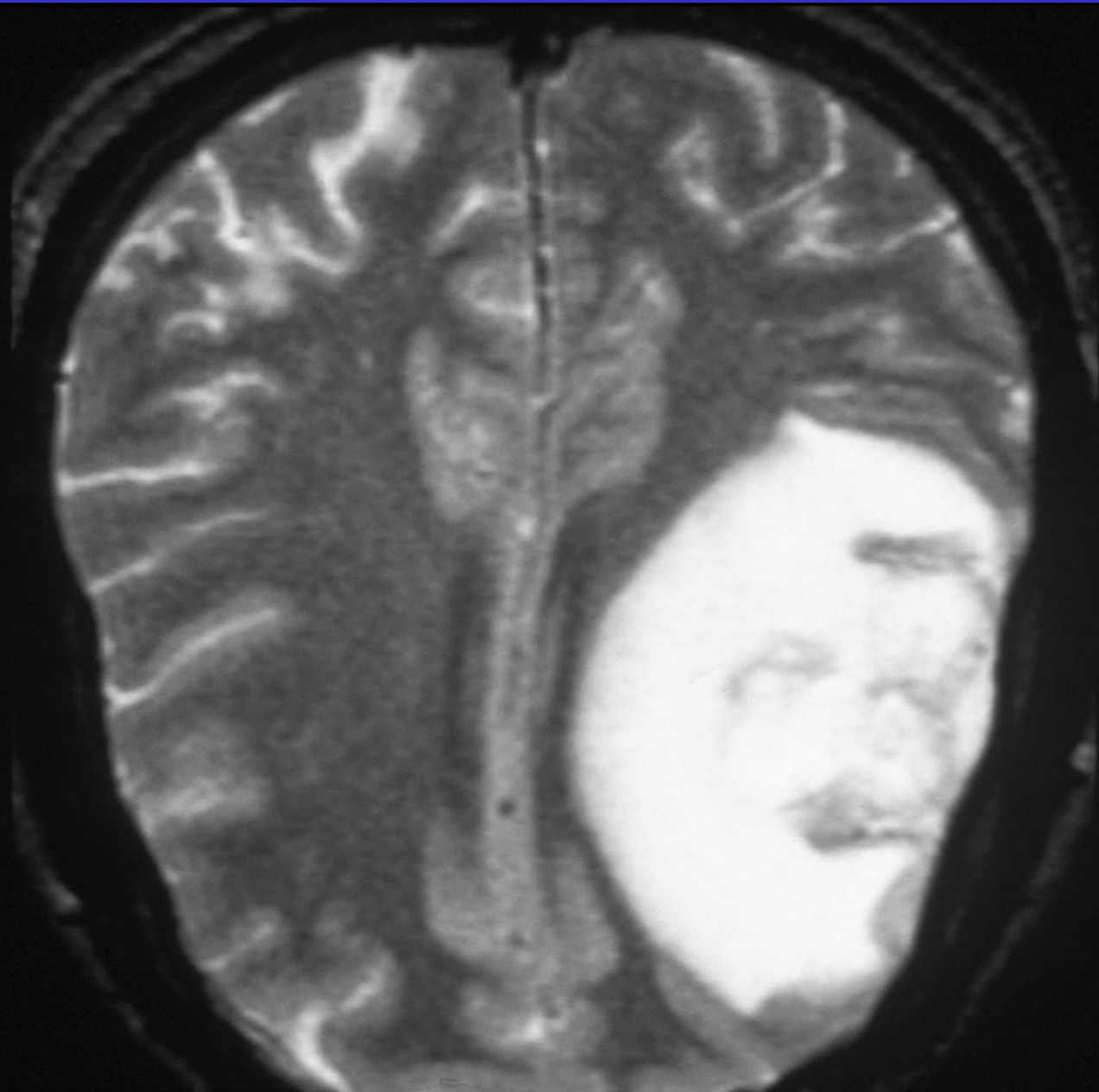
- Failure of nations to recognize and accept the problem
 - Disintegration of the public health infrastructure
 - Lack of education about transmission and prevention
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AIDS 1981 to 1996

- **Medical problems**

- Prevention and treatment of opportunistic infections (OIs) provided most of the improvements in survival and decreases in morbidity associated with care of the HIV-infected person
 - Pneumocystis jiroveci pneumonia (PCP)
 - Mycobacterium avium complex (MAC)
 - Toxoplasma gondii encephalitis
 - Candida esophagitis
 - Cytomegalovirus (CMV) retinitis
 - **HOWEVER**, OIs would frequently recur when treatment was discontinued; several OIs required continuous, lifelong treatment (toxoplasmosis, CMVR)
 - Therapy against the virus itself was poor
 - Antiretroviral therapy could only slow the relentless decrease in the CD4+ T cell counts of HIV-infected persons
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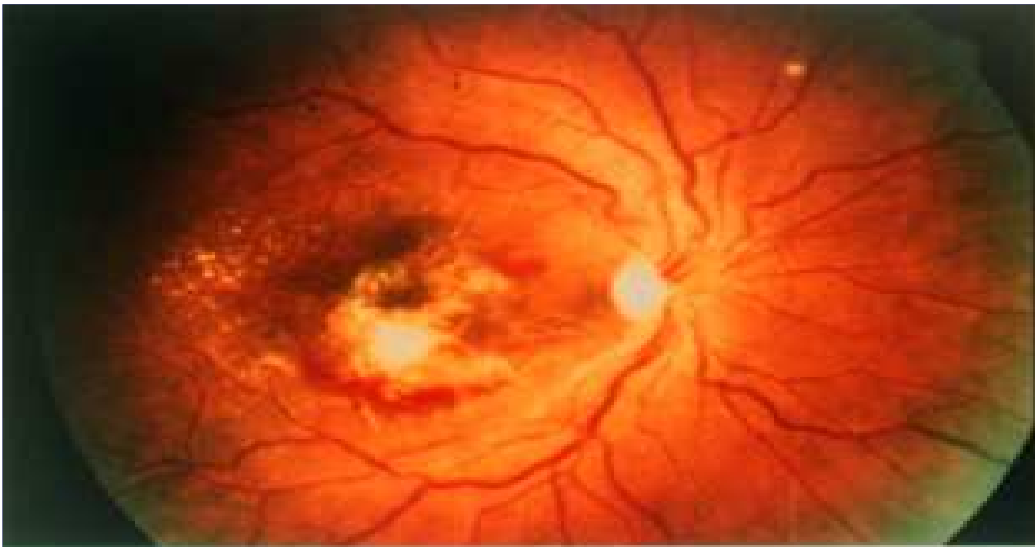




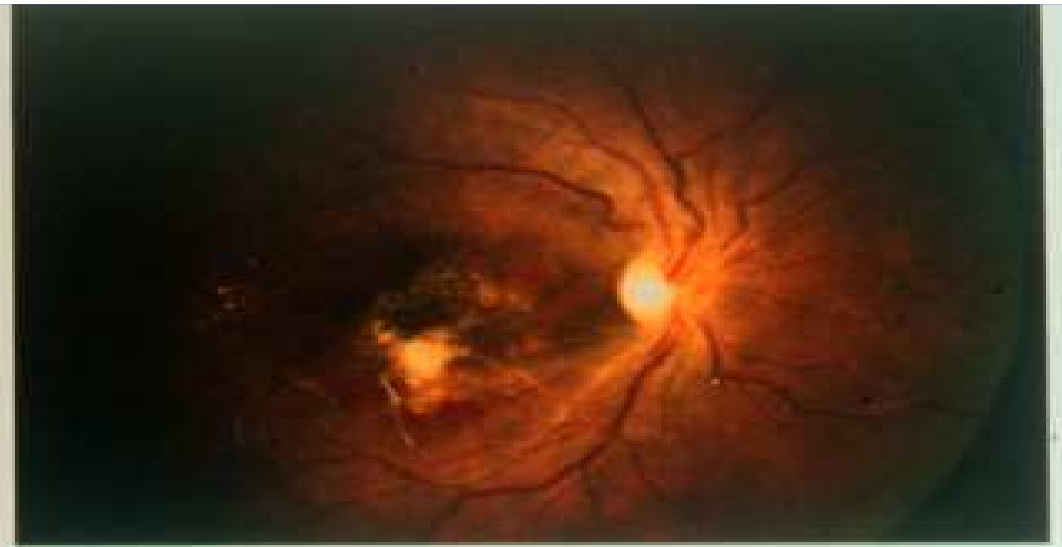
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Survival in Persons with CMV Retinitis and HIV Infection

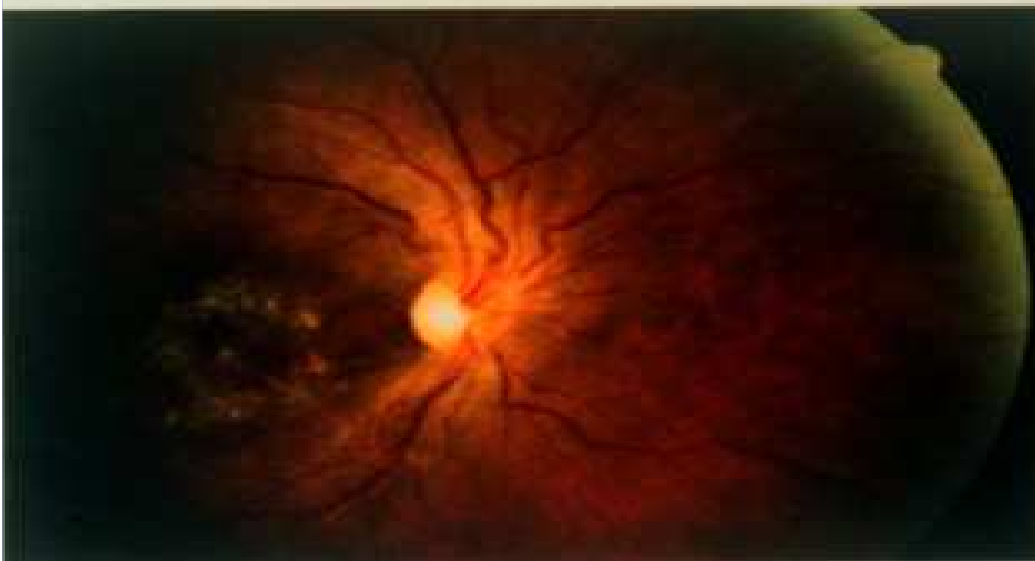
- **1981 - 1987**
 - (pre-ganciclovir, ARVs) 2 to 6 months
 - **1988 - 1990**
 - (ganciclovir, AZT) 8 to 9 months
 - **1991 - 1996**
 - (foscarnet, NRTIs) 12 to 14 months
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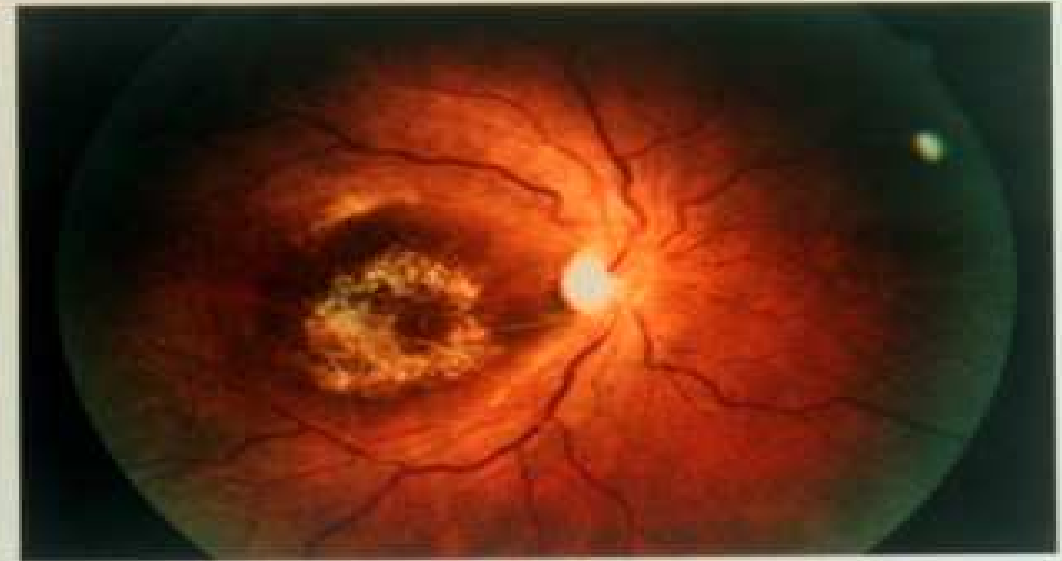
Week 0
Active CMV retinitis



Week 2
Active retinitis resolving



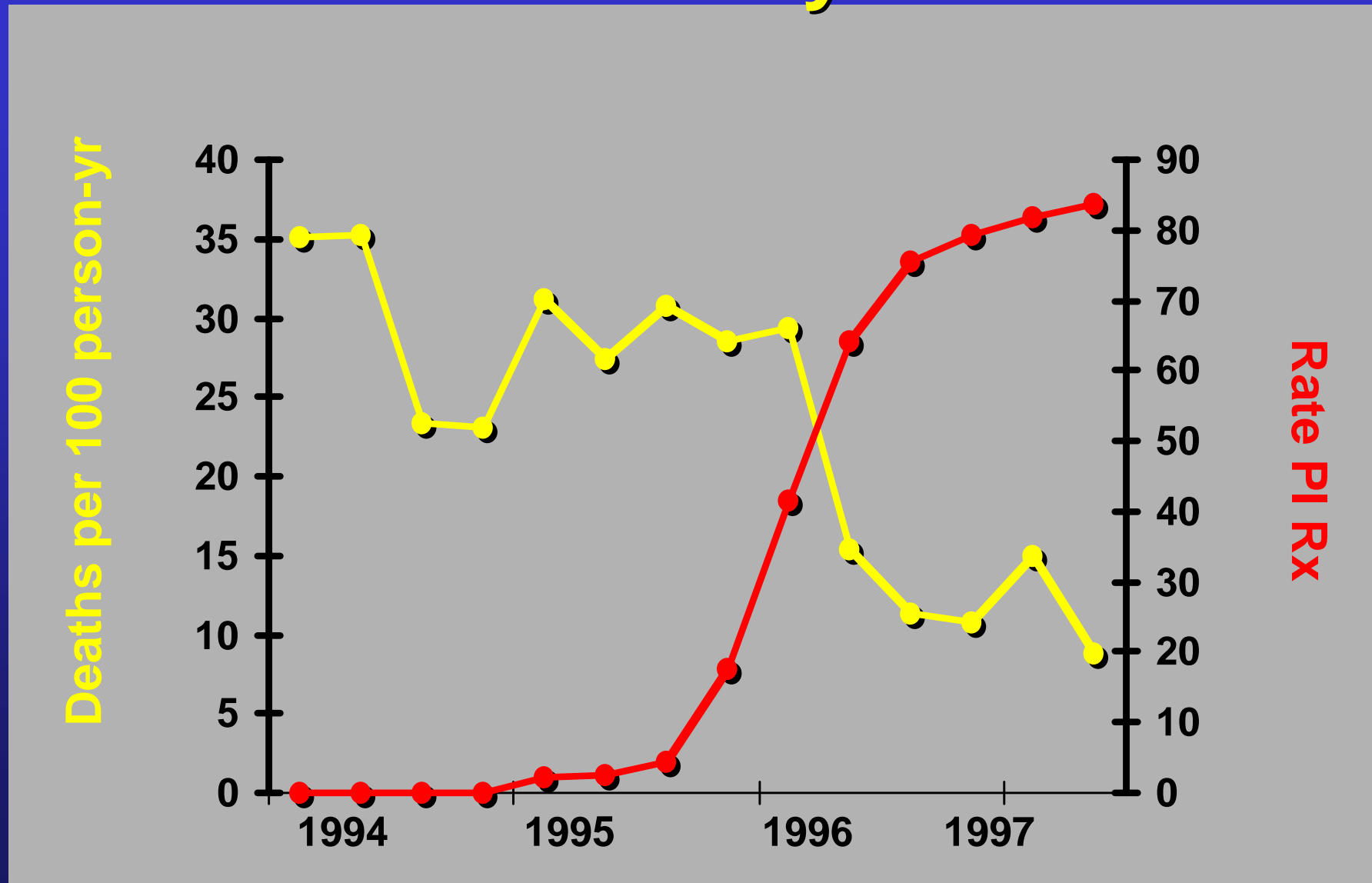
Week 7
Inactive retinitis



Week 18
Appearance of new CMV lesions



Decline in HIV Mortality with HAART



Palella FJ, Jr., et al. *NEJM* 1998,338:853-60

Objective

- To determine if persons with stable CMV retinitis on potent antiretroviral therapy could safely discontinue their specific anti-CMV therapy without reactivation of their retinitis or increase in HIV in plasma
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Whitcup, et al, JAMA, 1999.

Updated Results

15 patients have been enrolled:

- No patient has had reactivation of CMV retinitis or developed extraocular CMV disease after a mean of more than 60 months
- HIV plasma levels have remained stable (mostly <50 RNA copies/ml)
- Blood and urine culture and CMV PCR on whole blood were intermittently positive in 9 patients, but did not predict reactivation of CMV disease

Guidelines for the Management of Cytomegalovirus Retinitis in Persons with AIDS: 2008

- Current guidelines for the management of CMV retinitis in persons with HIV infection recommend the discontinuation of specific anti-CMV therapy in individuals who have had an increase in their CD4+ cell counts to above 100-150 cells/ μ L
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“Patients with AIDS often have CMV in the lungs but, presumably because of their inability to mount the required T-cell response, do not develop the interstitial pneumonitis seen in transplant recipients. However, if treatment of the human immunodeficiency virus infection successfully leads to correction of this T-cell defect, then according to our hypothesis, CMV pneumonitis will become a major problem in AIDS patients”

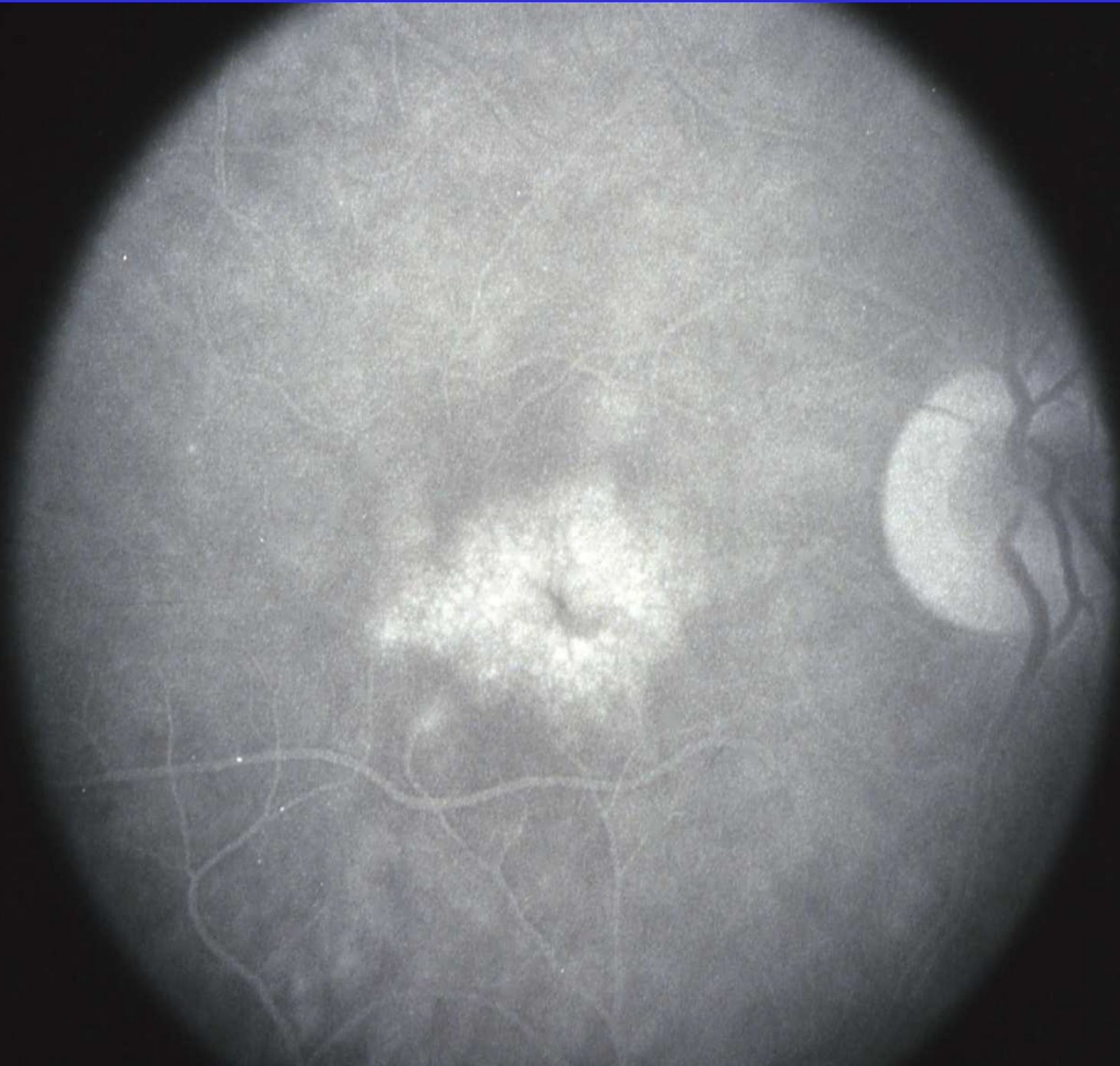
Grundy, Shanley, Griffiths, Lancet, 1987.

Immune Recovery Uveitis in Persons with CMV Retinitis

- In persons with CMV retinitis and HIV infection responding to potent antiretroviral therapy, a new entity has been described.
 - Ophthalmologic findings include:
 - Cystoid macular edema
 - Epiretinal membranes
 - Anterior uveitis
 - Vitreitis
 - Cataracts
-

625.9

6517



Immune Reconstitution Syndromes

Probable

- TB
 - PCP
 - CMV
 - MAC
 - HSV
 - VZV
 - Cryptococcus
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Possible

- Hepatitis C
- PML

Cytomegalovirus in Persons with AIDS: Overview - 2008

- Incidence:
 - Clinical disease was recognized in more than 40% of persons with advanced HIV infection
 - Clinical manifestations:
 - Retinitis, colitis, and esophagitis were most common. Pneumonitis is rare.
 - Standard therapy:
 - Potent antiretroviral therapy
 - Prognosis:
 - Initial response rate of > 90%. **Specific CMV therapy can often be discontinued if antiretroviral therapy can be optimized.**
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Survival in Persons with CMV Retinitis and HIV Infection

- **1981 - 1987**
 - (pre-ganciclovir, ARVs) 2 to 6 months
 - **1988 - 1990**
 - (ganciclovir, AZT) 8 to 9 months
 - **1991 - 1996**
 - (foscarnet, NRTIs) 12 to 14 months
 - **1996 -**
 - (HAART) **Indefinite**
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AIDS 1996 to Present

- **Medical problems**

- Prevention and treatment of opportunistic infections (OIs) **is still required for HIV-infected persons with low CD4+ T cell counts**
 - OIs **no longer** recur when treatment is discontinued **as long as HIV itself is held in check with effective antiretroviral therapy**
 - Therapy against the virus itself **is very good**
 - Antiretroviral therapy **can now reverse the formerly relentless decrease in the CD4+ T cell counts of HIV-infected persons**
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4/15/84

AIDS 1996 to Present

- **Medical problems**

- Prevention and treatment of OIs is greatly improved
 - Problems are still common with coinfection with Tb and of the immune reconstitution inflammatory syndrome
- Therapy against the virus itself is very good
 - Therapy, though, needs to be maintained indefinitely

- **Social problems**

- Stigmatization of persons with the disease
- Lack of understanding and denial about how HIV is acquired leads to high rates of transmission

- **Political**

- Failure of nations to recognize and accept the problem
 - Disintegration of the public health infrastructure
 - Lack of education about transmission and prevention
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Treatment of OIs 1996 to Present

- Replication of the HIV can be reduced to very low levels; the primary prevention and treatment for opportunistic infections is through the appropriate use of antiretroviral therapy
 - HIV transmission and, subsequently, the development of opportunistic infections associated with HIV infection is completely preventable
 - **We have the means to control HIV infection and its associated opportunistic infections**
 - **We now require the support and the will to do so**
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