

The Early-Treatment Era: 1987-1995

1987: 1st AIDS Drug Zidovudine (AZT/ZDV)



The Early-Treatment Era: 1987-1995

**1987: Treatment Investigational New Drugs
Accelerated Drug Approval Process Begins**



U.S. Food and Drug Administration

The Early-Treatment Era: 1987-1995



1987: Activists protest high cost of AZT



The Early-Treatment Era: 1987-1995

1987: US congress emergency funding for AZT



**AIDS
EMERGENCY
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The Early-Treatment Era: 1987-1995

1987: WHO Global Program on AIDS founded



The Early-Treatment Era: 1987-1995

1987: Condoms indicated for HIV prevention



The Early-Treatment Era: 1987-1995

1987: First human HIV vaccine trial



The Early-Treatment Era: 1987-1995

1987: Japanese Foundation for AIDS Prevention created



The Early-Treatment Era: 1987-1995

1987



FDA

ACT UP

AIDS Coalition to Unleash Power



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EMERGENCY
FUND



AIDS
J F A P

The Early-Treatment Era: 1987-1995

1988: Women with AIDS outnumber men



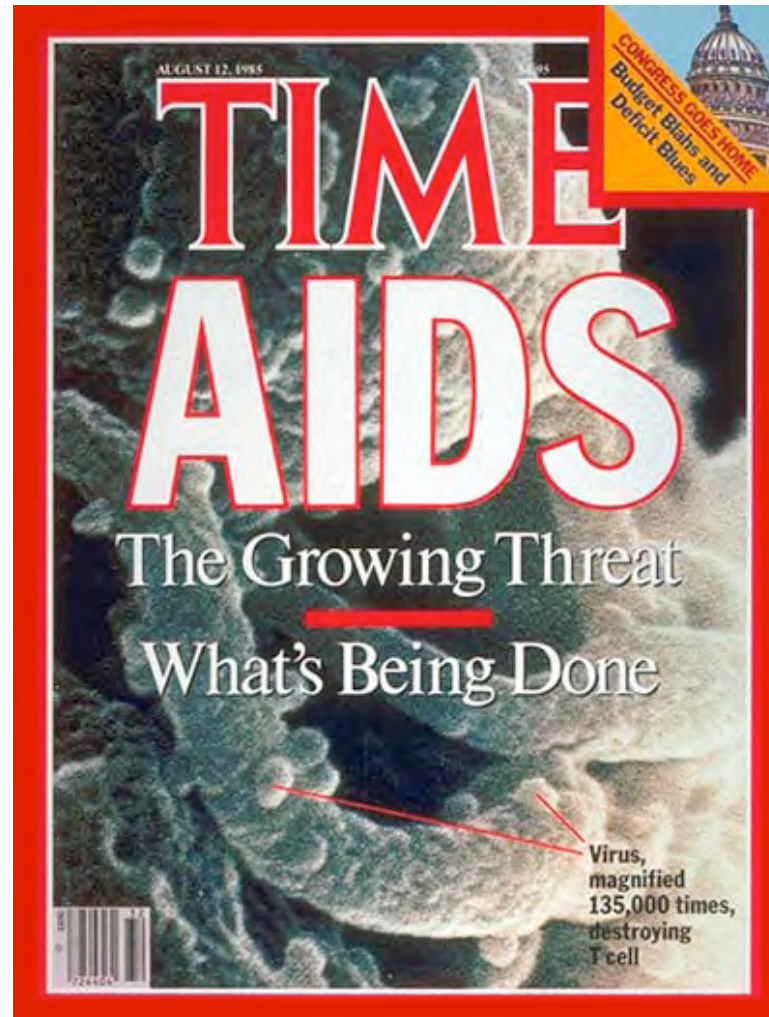
The Early-Treatment Era: 1987-1995

1988: Protests lead to FDA Expanded Access Program for drugs still in trials



The Early-Treatment Era: 1987-1995

1988: Growing media attention



The Early-Treatment Era: 1987-1995

1988: US Office of AIDS Research founded



The Early-Treatment Era: 1987-1995

1988: US AIDS Education and Training Centers founded



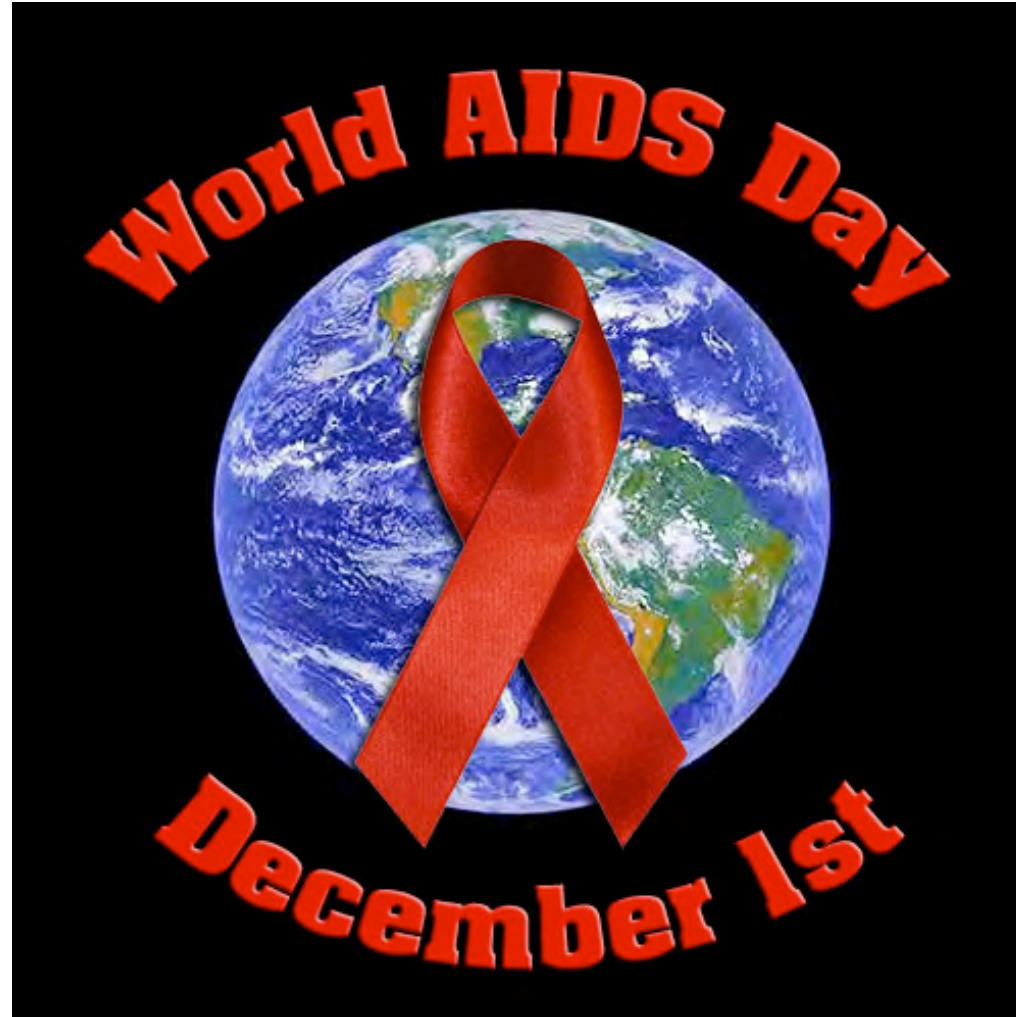
The Early-Treatment Era: 1987-1995

1988: 1st comprehensive needle exchange program



The Early-Treatment Era: 1987-1995

1988: WHO declares World AIDS Day



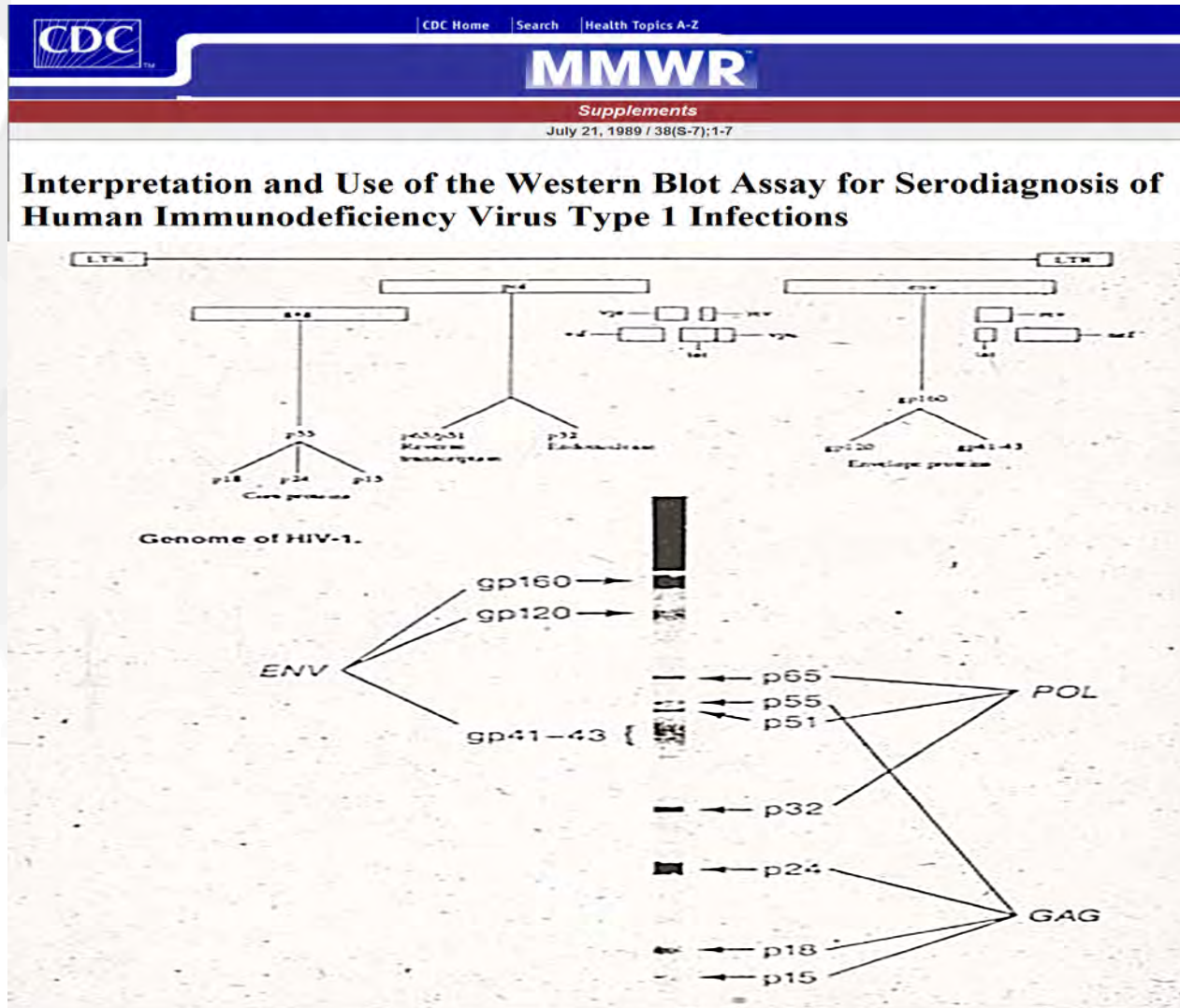
The Early-Treatment Era: 1987-1995

1987 1988



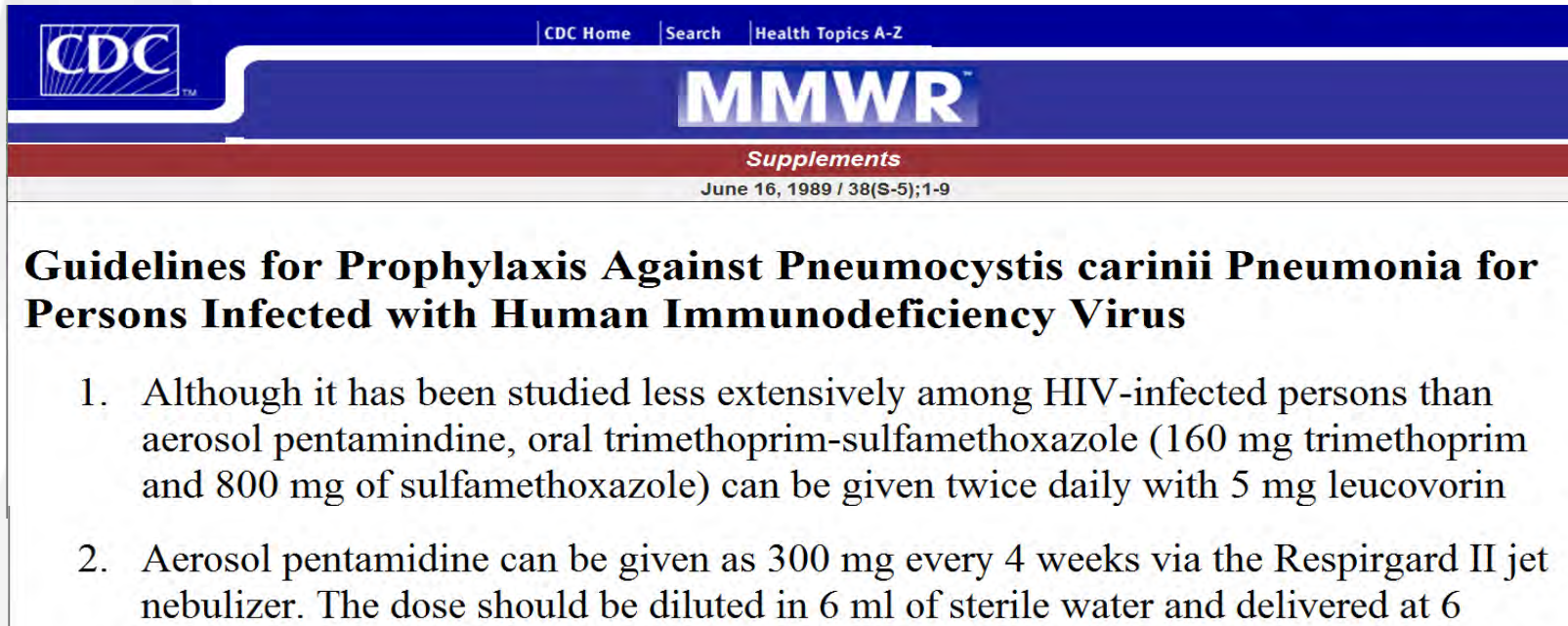
The Early-Treatment Era: 1987-1995

1989: CDC HIV-1 western blot interpretation guidelines



The Early-Treatment Era: 1987-1995

1989: CDC PCP prevention guidelines



The image is a screenshot of a CDC MMWR Supplements page. At the top left is the CDC logo. To its right are links for 'CDC Home', 'Search', and 'Health Topics A-Z'. The main title 'MMWR' is in large white letters on a dark blue background, with 'Supplements' in smaller white letters below it. The date 'June 16, 1989 / 38(S-5);1-9' is printed in small black text. The main heading is 'Guidelines for Prophylaxis Against Pneumocystis carinii Pneumonia for Persons Infected with Human Immunodeficiency Virus'. Below this are two numbered list items.

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MMWR
Supplements

June 16, 1989 / 38(S-5);1-9

Guidelines for Prophylaxis Against *Pneumocystis carinii* Pneumonia for Persons Infected with Human Immunodeficiency Virus

1. Although it has been studied less extensively among HIV-infected persons than aerosol pentamidine, oral trimethoprim-sulfamethoxazole (160 mg trimethoprim and 800 mg of sulfamethoxazole) can be given twice daily with 5 mg leucovorin
2. Aerosol pentamidine can be given as 300 mg every 4 weeks via the Respirgard II jet nebulizer. The dose should be diluted in 6 ml of sterile water and delivered at 6

The Early-Treatment Era: 1987-1995

1989: Japanese HIV-tainted blood scandal

薬害エイズ事件



Ministry of Health, Labour and
Welfare
厚生労働省

The Early-Treatment Era: 1987-1995

1989: Aerosolized pentamidine approved for PCP prophylaxis

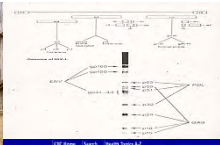
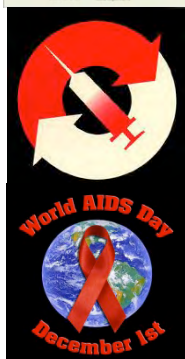


The Early-Treatment Era: 1987-1995

1987 1988 1989



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MMWR

Supplement

Volume 14, Number 12, December 1, 1989

Prophylaxis Against *Pneumocystis carinii* in Patients Infected with Human Immunodeficiency Virus

Japanese HIV-tainted blood scandal
薬害エイズ事件



The Early-Treatment Era: 1987-1995



1990: Governmental liability for HIV-infected blood products

The New York Times
ON THE WEB

British Hemophiliacs Win Compensation for AIDS

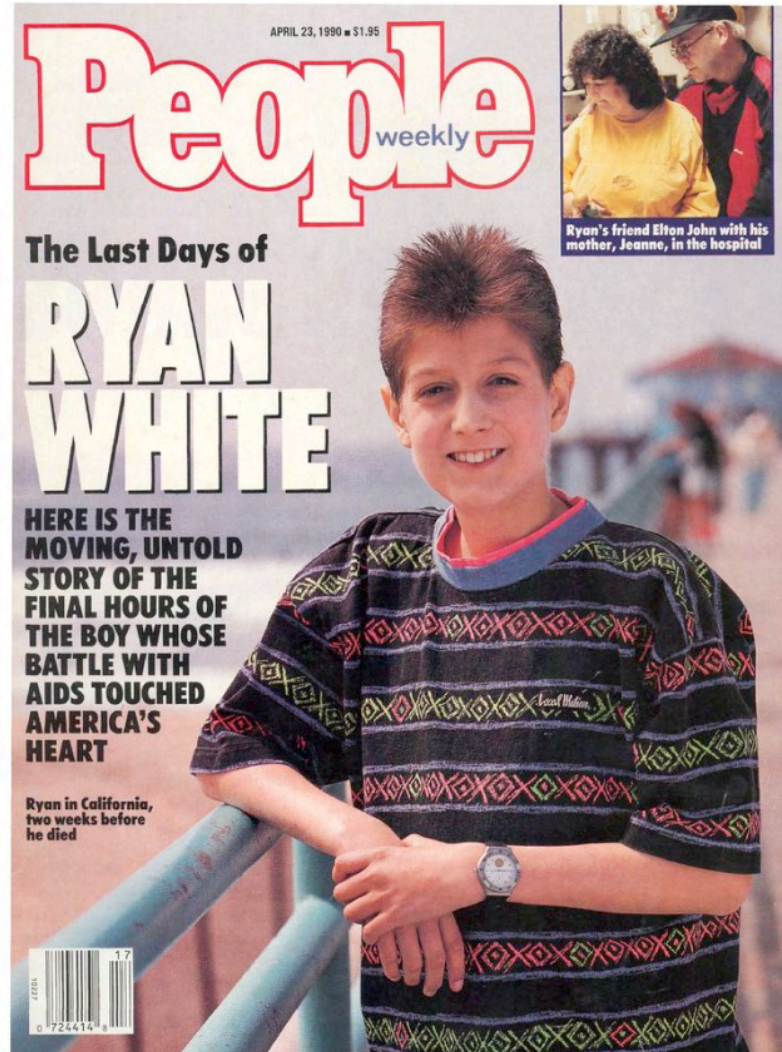
Special to The New York Times
Published: December 13, 1990

Prime Minister John Major has announced that the British Government will increase compensation to hemophiliacs who contracted the AIDS virus after being treated with contaminated blood products thought to have been imported from the United States.

Speaking in the House of Commons on Tuesday to the cheers of Conservative Party back Mr. Major said his Government had been able to "agree in principle" to the proposals for compensation put forth by lawyers representing 1,217 people, who are either hemophilia infected with the human immunodeficiency virus, which causes AIDS, or relatives of those who have died.

The Early-Treatment Era: 1987-1995

1990: Ryan White dies at age 18



The Early-Treatment Era: 1987-1995



1990: US Ryan White CARE Act becomes federal law

104 STAT. 576

PUBLIC LAW 101-381—AUG. 18, 1990

Public Law 101-381
101st Congress

An Act

Aug. 18, 1990
[S. 2240]


To amend the Public Health Service Act to provide grants to improve the quality and availability of care for individuals and families with HIV disease, and for other purposes.

Be it enacted by the Senate and House of Representatives of the United States of America in Congress assembled,

SECTION 1. SHORT TITLE.

This Act may be cited as the “Ryan White Comprehensive AIDS Resources Emergency Act of 1990”.

Ryan White
Comprehensive
AIDS Resources
Emergency Act
of 1990.
42 USC 201 note.



The Early-Treatment Era: 1987-1995

1990: Woman infected by HIV+ dentist



The screenshot shows the header of the CDC's Morbidity and Mortality Weekly Report (MMWR). It features the CDC logo on the left, navigation links for 'CDC Home', 'Search', and 'Health Topics A-Z' in the top right. The 'MMWR' logo is prominently displayed in the center, with the word 'Weekly' underneath it. Below this, the issue information 'July 27, 1990 / 39(29):489-493' is shown.

Possible Transmission of Human Immunodeficiency Virus to a Patient during an Invasive Dental Procedure

CDC received a case report of acquired immunodeficiency syndrome (AIDS) in a young woman for whom an epidemiologic investigation had not established a source for her human immunodeficiency virus (HIV) infection (i.e., documented behavioral or other risk factors, including intravenous (IV)-drug use, sex with an HIV-infected person, or receipt of a blood transfusion or blood components). However, investigation revealed that 24 months before her AIDS diagnosis she had two teeth extracted by a dentist who had AIDS. Information on the dental procedure was obtained from interviews with the patient and reviews of her dental records

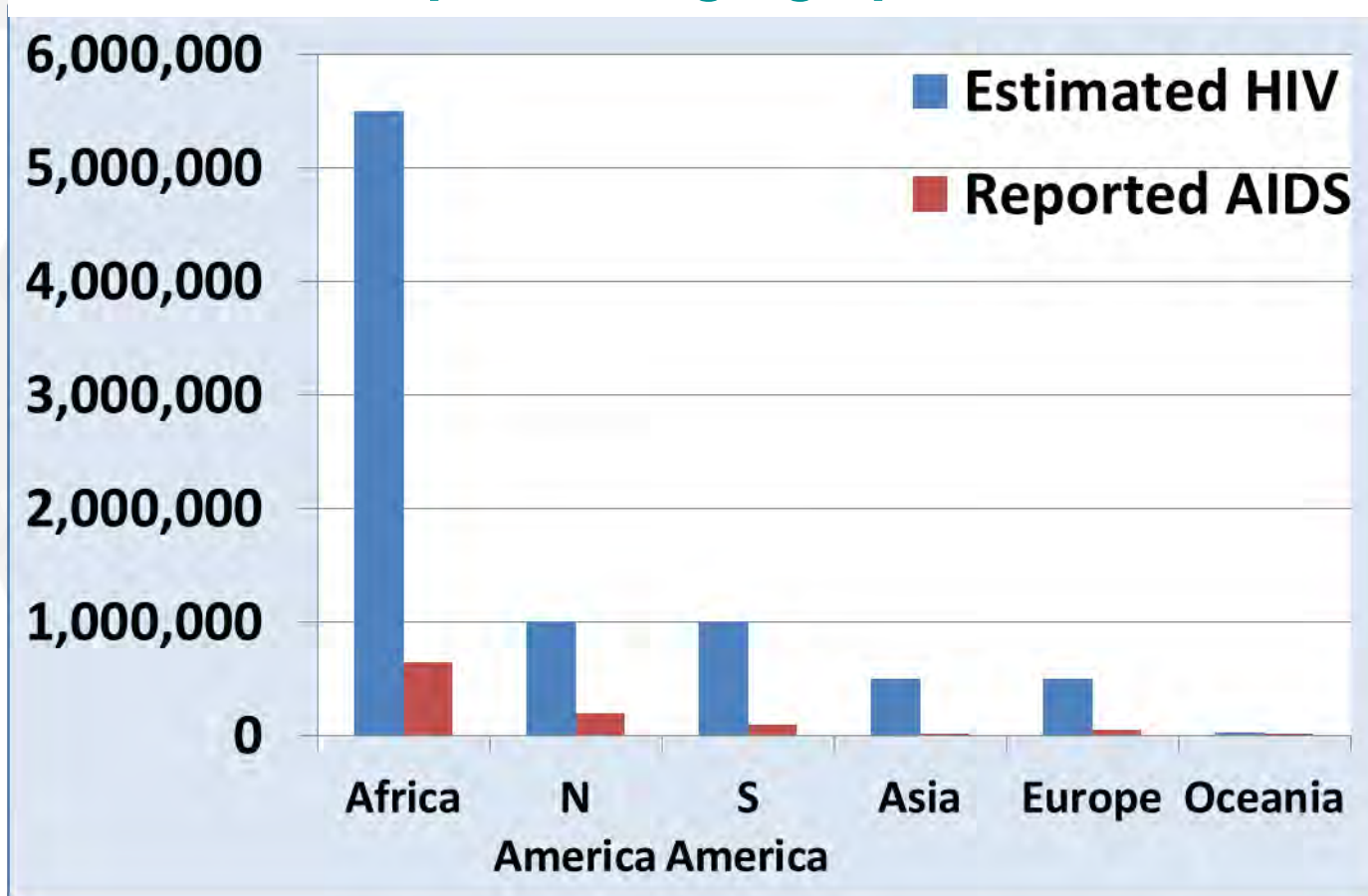
The Early-Treatment Era: 1987-1995

1990: Last International AIDS Conference in the US due to prohibition against entry of HIV+ foreigners



The Early-Treatment Era: 1987-1995

1990: WHO reports surging epidemic in Africa



The Early-Treatment Era: 1987-1995

1987 1988 1989 1990



The Early-Treatment Era: 1987-1995

1991: Red ribbon AIDS awareness symbol



The Early-Treatment Era: 1987-1995

1991: Thailand launches massive
AIDS prevention and control program.



The Early-Treatment Era: 1987-1995

1991: European AIDS Clinical Society Established



The Early-Treatment Era: 1987-1995

1991: 2nd AIDS drug: Didanosine (ddl, Videx)

Sequential monotherapy



The Early-Treatment Era: 1987-1995



1991: ACTG 021 proves 1st PCP prophylaxis

THE LANCET

Lancet. 1991 Aug 3;338(8762):265-9.

Effect of zidovudine and *Pneumocystis carinii* pneumonia prophylaxis on progression of HIV-1 infection to AIDS. The Multicenter AIDS Cohort Study.

Graham NM, Zeger SL, Park LP, Phair JP, Detels R, Vermund SH, Ho M, Saah AJ.

Department of Epidemiology, Johns Hopkins School of Hygiene and Public Health, Baltimore, Maryland.

Abstract

Although used widely, the effectiveness of zidovudine therapy and primary prophylaxis for *Pneumocystis carinii* pneumonia (PCP) in HIV-1-infected individuals, has not been assessed in a large cohort. We have done an observational study between October, 1986, and October, 1990, of

The Early-Treatment Era: 1987-1995

1991: HIV transmission through breast milk



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ORIGINAL ARTICLE

Postnatal Transmission of Human Immunodeficiency Virus Type 1 from Mother to Infant — A Prospective Cohort Study in Kigali, Rwanda

Philippe Van de Perre, M.D., Arlette Simonon, Ph.D., Philippe Msellati, M.D., Deo-Gratias Hitimana, M.D., Dolores Vaira, M.S., Anatholie Bazubagira, M.D., Christiaan Van Goethem, M.D., Anna-Maria Stevens, M.D., Etienne Karita, M.D., Danièle Sondag-Thull, M.D., François Dabis, M.D., M.P.H., and Philippe Lepage, M.D.

N Engl J Med 1991; 325:593-598 | [August 29, 1991](#)

The Early-Treatment Era: 1987-1995

1991: Magic Johnson announces HIV



The Early-Treatment Era: 1987-1995

1991: US housing assistance enacted for PLWA



The Early-Treatment Era: 1987-1995

1987 1988 1989 1990 1991

FDA
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AIDS Coalition to Unleash Power

AIDS EMERGENCY FUND

ACTG
AIDS CLINICAL TRIALS GROUP

ACS
J F A P

World AIDS Day
December 1st

MMWR
Morbidity and Mortality Weekly Report
June 16, 1989, 138(10):1-4

Prophylaxis Against Pneumocystis carinii in Persons with Human Immunodeficiency Virus

Japanese HIV-tainted blood scandal
薬害エイズ事件

THE LANCET
Lancet, 1991 Aug 3;338(8762):205-6
Effect of zidovudine and Pneumocystis prophylaxis on progression of HIV-1 infection: Multicenter AIDS Cohort Study.

THE NEW ENGLAND JOURNAL OF MEDICINE
Potential Transmission of Human Immunodeficiency Virus Type 1 from Mother to Infant — A Prospective Cohort Study in Kipili, Rwanda

People
The Last Days of RYAN WHITE
HERE IS THE MOVING, WERLD-STAR OF THE FALL, WHOSE BATTLE WITH AIDS TOUCHED AMERICA'S HEART

THE NEW YORK TIMES
British Hemophiliacs Win Compensation for AIDS

EACS
European AIDS Clinical Society

VIDEX
BMS 200754

AIDS Surges in Africa

HIV/AIDS Housing
U.S. Dept. of Housing and Urban Development

HIV VACCINE

The Early-Treatment Era: 1987-1995

1992: First rapid HIV test



The Early-Treatment Era: 1987-1995

1992: 3rd NRTI: Zalcitabine (ddC, Hivid)

Dual nucleoside therapy approved



The Early-Treatment Era: 1987-1995

1992: Uganda emphasizes prevention



The Early-Treatment Era: 1987-1995

1992: AIDS marches in cities across the US



The Early-Treatment Era: 1987-1995

1992: AIDS #1 cause death US men 25-44yo



The Early-Treatment Era: 1987-1995

1992: ACT-UP message spread worldwide



The Early-Treatment Era: 1987-1995

1987 1988 1989 1990 1991 1992



The Early-Treatment Era: 1987-1995



1993: Viral activity during asymptomatic disease



nature International weekly journal of science

Nature **362**, 355-358 (25 March 1993) | doi:10.1038/362355a0; Received 18 February 1993

HIV infection is active and progressive in lymphoid tissue during the clinically latent stage of disease

Giuseppe Pantaleo^{*}, Cecilia Graziosi^{*}, James F. Demarest^{*}, Luca Butini[†], Maria Montroni[†], Cecil H. Fox[‡], Jan M. Orenstein[§], Donald P. Kotler^{||} & Anthony S. Fauci^{*}

The Early-Treatment Era: 1987-1995

1993: First report of drug resistance.

Era of sequential monotherapy

Science

The New York Times
ON THE WEB

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January 1, 1993

New H.I.V. Strains Resist AIDS Drug

Forum

- [Join a Discussion on AIDS Epidemic](#)

By THE ASSOCIATED PRESS

WASHINGTON -- In increasing numbers of patients infected with H.I.V., the virus that causes AIDS, it is showing early resistance to AZT, the drug most commonly used against it, and researchers say there is an urgent need to develop new drugs to combat the epidemic.

The Early-Treatment Era: 1987-1995

1993: No benefit in taking AZT in early disease



**Early AZT takes a pounding in
French-British 'Concorde' trial J Cohen**

Science 9 April 1993: 157

The Early-Treatment Era: 1987-1995

1993: Fourth NRTI: Stavudine (d4T, Zerit)

Dual NRTI, "d-NRTI" pancreatitis and neuropathy



The Early-Treatment Era: 1987-1995

1993: Women's cohort studies begin



WHHS
Women's Interagency HIV Study



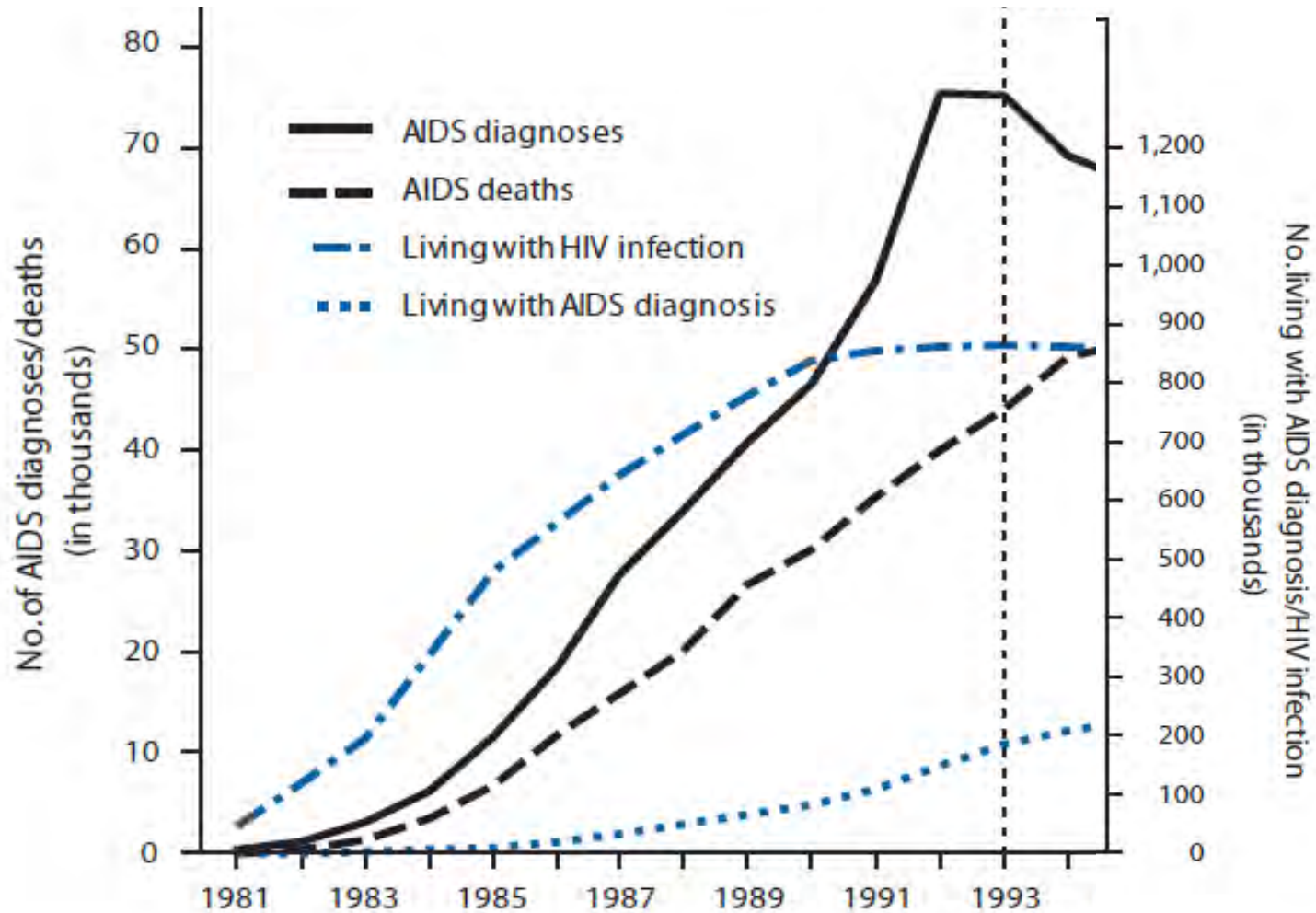
The Early-Treatment Era: 1987-1995

1993: Female condom licensed



The Early-Treatment Era: 1987-1995

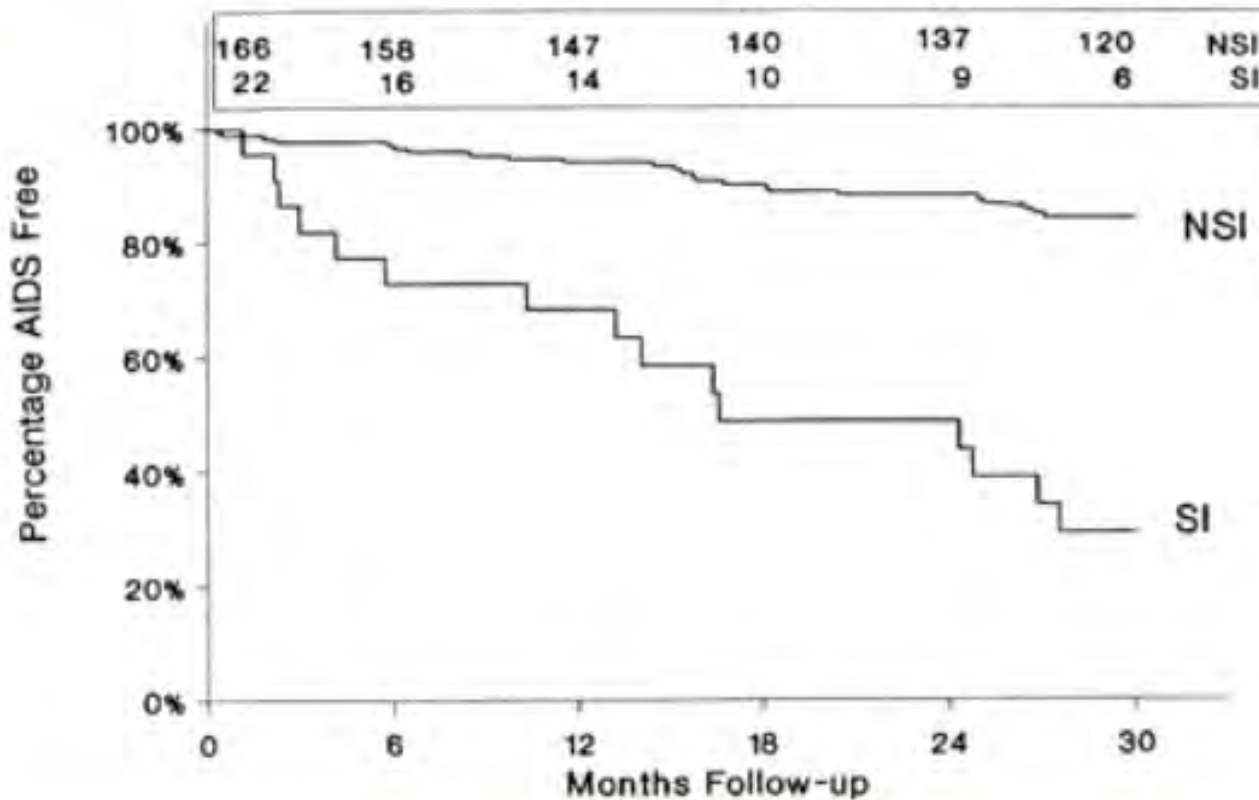
1993: CDC AIDS case definition includes CD4 <200



The Early-Treatment Era: 1987-1995

1993: Poor prognosis with Syncytium-Inducing (SI) virus

Prognostic Value of HIV-1 Syncytium-Inducing Phenotype for Rate of CD4+ Cell Depletion and Progression to AIDS



The Early-Treatment Era: 1987-1995

1993: AIDS deaths continue unabated



The Early-Treatment Era: 1987-1995

1993: Estimated 98,000 HIV+ orphans in Romania



The Early-Treatment Era: 1987-1995

1994: First oral HIV test



The Early-Treatment Era: 1987-1995

1994: Fifth NRTI: Lamivudine (3TC, Epivir)



The Early-Treatment Era: 1987-1995

1994: 10th International AIDS Conference



Yokohama Japan

The Early-Treatment Era: 1987-1995

1994: Public condom promotion campaigns



The Early-Treatment Era: 1987-1995

1994: C-Section halves mother-to-child transmission



The NEW ENGLAND
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Mother-to-Child Transmission of the Human Immunodeficiency Virus

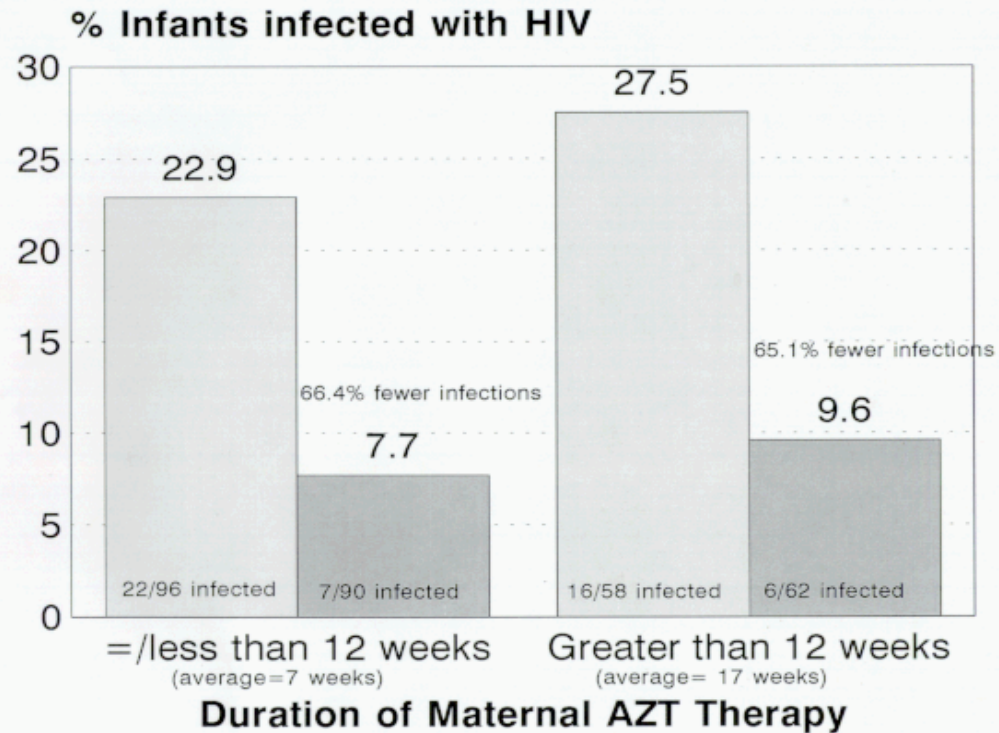
Catherine Peckham, M.D., and Diana Gibb, M.D.

N Engl J Med 1995; 333:298-303 | August 3, 1995

The Early-Treatment Era: 1987-1995

1994: Reduction in perinatal transmission

Effect of Duration of AZT Therapy on Infant Infections *
Data from ACTG 076



* Data Presented by ACTG 076 researchers to
Data Safety Monitoring Board, February, 1994

The Early-Treatment Era: 1987-1995



1994: Herpes virus linked to Kaposi's Sarcoma

Science. 1994 Dec 16;266(5192):1865-9.

Identification of herpesvirus-like DNA sequences in AIDS-associated Kaposi's sarcoma.

Chang Y, Cesarman E, Pessin MS, Lee F, Culpepper J, Knowles DM, Moore PS.

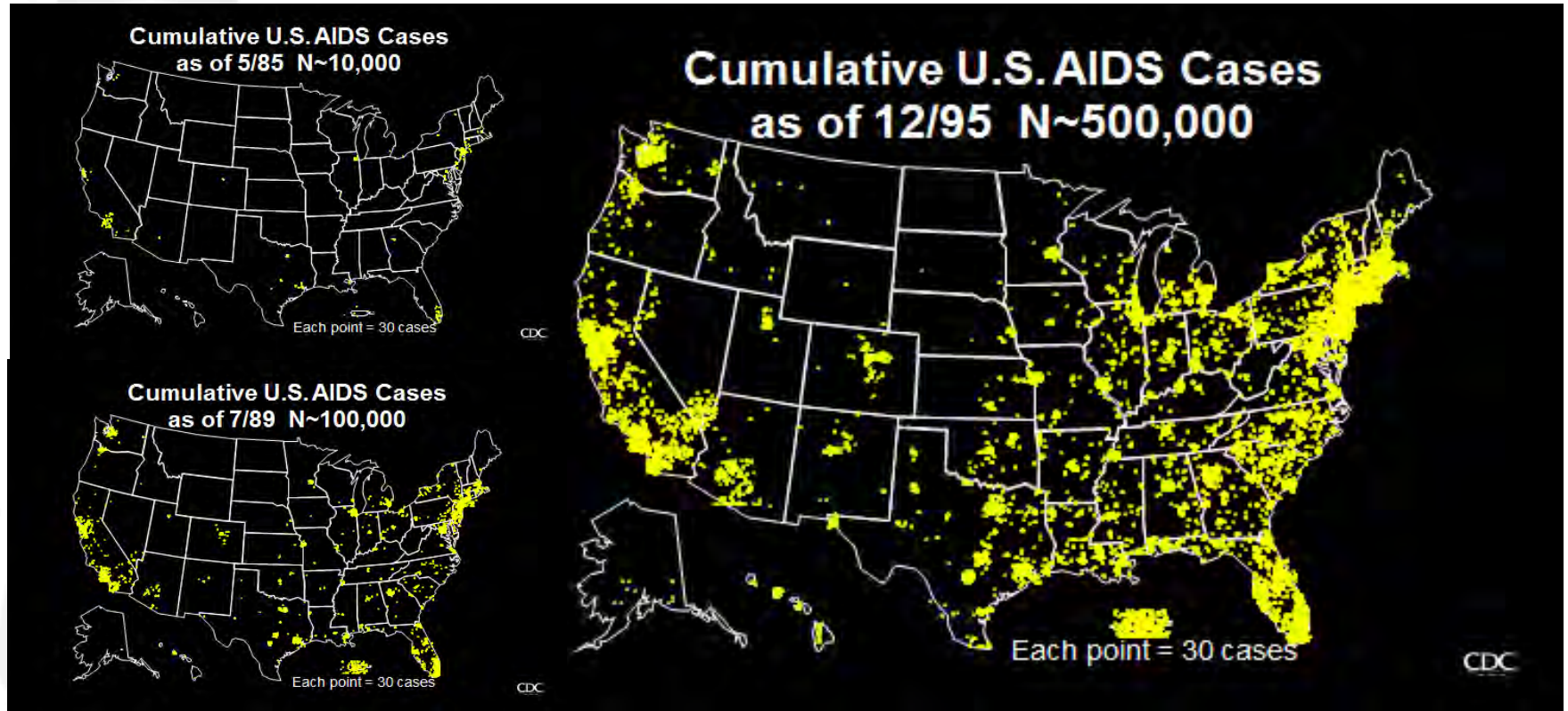
Department of Pathology, College of Physicians and Surgeons, Columbia University, New York, NY 10032.

Abstract

Representational difference analysis was used to isolate unique sequences present in more than 90 percent of Kaposi's sarcoma (KS) tissues obtained from patients with acquired immunodeficiency syndrome (AIDS). These sequences were not present in tissue DNA from non-AIDS patients, but were present in 15 percent of non-KS tissue DNA samples from AIDS patients. The sequences are homologous to, but distinct from, capsid and tegument protein genes of the Gammaherpesvirinae, herpesvirus saimiri and Epstein-Barr virus. These KS-associated herpesvirus-like (KSHV) sequences appear to define a new human herpesvirus.

The Early-Treatment Era: 1987-1995

1995: Continued expansion of epidemic across USA



The Early-Treatment Era: 1987-1995



1995: Inherent viral drug resistance mutations

HIV Population Dynamics in Vivo: Implications for Genetic Variation, Pathogenesis, and Therapy

John M. Coffin

Several recent reports indicate that the long, clinically latent phase that characterizes human immunodeficiency virus (HIV) infection of humans is not a period of viral inactivity, but an active process in which cells are being infected and dying at a high rate and in large numbers. These results lead to a simple steady-state model in which infection, cell death, and cell replacement are in balance, and imply that the unique feature of HIV is the extraordinarily large number of replication cycles that occur during infection of a single individual. This turnover drives both the pathogenic process and (even more than mutation rate) the development of genetic variation. This variation includes the inevitable and, in principle, predictable accumulation of mutations such as those conferring resistance to antiviral drugs whose presence before therapy must be considered in the design of therapeutic strategies.

The Early-Treatment Era: 1987-1995

1995: Importance of viral load set point

Advertisement

Annals of Internal Medicine

Established in 1927 by the American College of Physicians

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Article

Quantitation of HIV-1 RNA in Plasma Predicts Outcome after Seroconversion

John W. Mellors, MD; Lawrence A. Kingsley, DrPH; Charles R. Rinaldo, PhD; John A. Todd, PhD; Brad S. Hoo, MS; Robert P. Kokka, DrPH; and Phalguni Gupta, PhD

FIGURE 1. Likelihood of developing AIDS within 3 years*

MACS bDNA	RT-PCR	Plasma Viral Load (copies/mL)	Percent
>30K	>55K	>200	85.5%
10K-30K	20K-55K	201-350	64.4%
3K-10K	7-20K	351-500	42.2%
501-3K	1500-7K	501-750	32.6%
≤500	<1500	>750	16.1%
		201-350	10.1%
		351-500	8.1%
		501-750	2.0%
		>750	0%

*Viral load values represent the actual data obtained on the specimens from the Multicenter AIDS Cohort Study (MACS) as well as the values showing the equivalent expected RT-PCR values. Values shown in this figure differ slightly from those in Table 4 because better discrimination of outcome was achieved by reanalysis of the data using viral load as the initial parameter for categorization followed by CD4+ T cell stratification of the patients. (Adapted from [12])

The Early-Treatment Era: 1987-1995

1995: Generic antiretrovirals production nations



The Early-Treatment Era: 1987-1995

1995: PEPFAR: US President's Emergency Plan for AIDS Relief



The Early-Treatment Era: 1987-1995



1995: First CDC guidelines for OI prevention



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MMWR™

Recommendations and Reports

July 14, 1995 / 44(RR-8);1-34

USPHS/IDSA Guidelines for the Prevention of Opportunistic Infections in Persons Infected with Human Immunodeficiency Virus: A Summary

The Early-Treatment Era: 1987-1995

1995 - December: First protease inhibitor: Saquinavir



The Early-Treatment Era: 1987-1995

1987 1988 1989 1990 1991 1992 1993 1994 1995

1987

FDA

ACT UP

AIDS Coalition to Unleash Power

AIDS EMERGENCY FUND

1988

TIME AIDS

The Growing Threat

What's Being Done

ACTG

AIDS CLINICAL TRIALS GROUP

1989

MMWR

Prophylaxis Against Pneumocystis carinii with Human Immunodeficiency Virus

Japanese HIV-tainted blood scandal

薬害エイズ事件

1990

The New York Times

British Hemophiliacs Win Compensation for AIDS

Ryan White Comprehensive AIDS Resources Emergency Act of 1990.

42 USC 201 note.

AIDS Surges in Africa

1991

EACS

European AIDS Clinical Society

THE LANCET

Effect of zidovudine and Pneumocystis prophylaxis on progression of HIV-1 infection: Multicenter AIDS Cohort Study.

1992

HIV RAPID TESTING

Hivid[®] Didanosine 0.75 mg

100 tablets

AVOIDING AIDS AS EASY AS... AS ABSTAIN BE FAITHFUL C ONDOMISE

1993

nature

Early AZT takes a pounding in French-British 'Concorde' trial | Cohen

Science 9 April 1993: 157

WPHS

Women's Interagency HIV Study

1994

HIV Population Dynamics in Vivo: Implications for Genetic Variation, Pathogenesis, and Therapy

John M. Coffin

CHES 2006

Yokohama Japan

Your Pocket Sex

Europe against AIDS

1995

Cumulative U.S. AIDS Cases as of 12/95 (N=500,000)

HIV/AIDS Housing

IGNORANCE = FEAR

SILENCE = DEATH

FIGHT AIDS ACT UP

World AIDS Day

December 1st

HIV VACCINE

Evolution of HIV treatment paradigms

