Antiviral Therapy

Effect on Sexual Transmission of HIV

?

Deductive Logic

Biological Plausibility

Clinical and Population Studies

Transmission of HIV: Biological Requirements

Infectiousness → Susceptibility

Inoculum (concentration)

Phenotypic factors

Hereditary resistance

Innate resistance

Acquired (immune) resistance

…from Cohen and Galvin

Nature Microbiology Reviews 2:33-42, 2004

Inoculum and Sexual Transmission of HIV

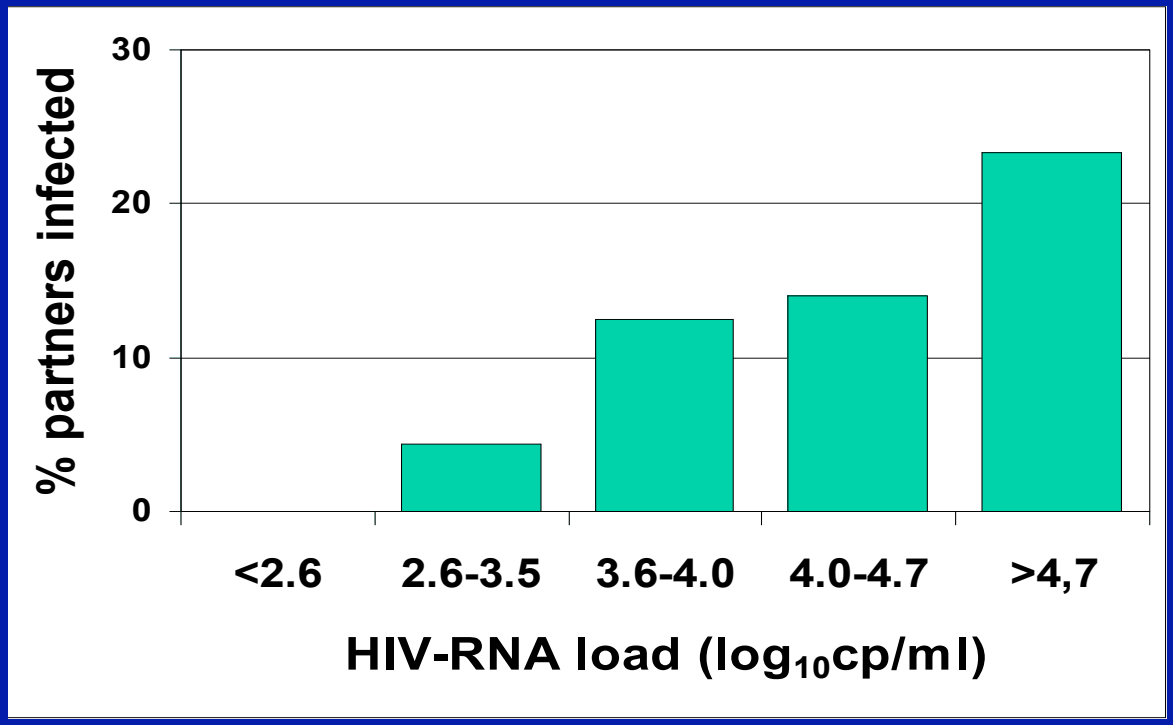
- **Quinn TC, Wawer MJ, Sewankambo N, Serwadda D, Li CJ, Wabwire-Mangen F, Meehan MO, Lutalo T, Gray H. Viral load and heterosexual transmission of human immunodeficiency virus type 1. N Engl J Med 2000;342:921-9**

- **Fideli US, Allen SA, Musonda R, et al. Virologic and immunologic determinants of heterosexual transmission of human immunodeficiency virus type 1 in Africa. AIDS Res Hum Retroviruses 2001;17(10):901-10**

- **Tovanabutra S, Robison V, Wongtrakul J, Sennum S, Suriyanon V, Kingkeow D, Kawichai S, Tanan P, Duerr A, Nelson KE. Male viral load and heterosexual transmission of HIV-1 subtype E in northern Thailand. J AIDS, 2002; 29:275-83.**

BloodViral load and HIV-1 transmission

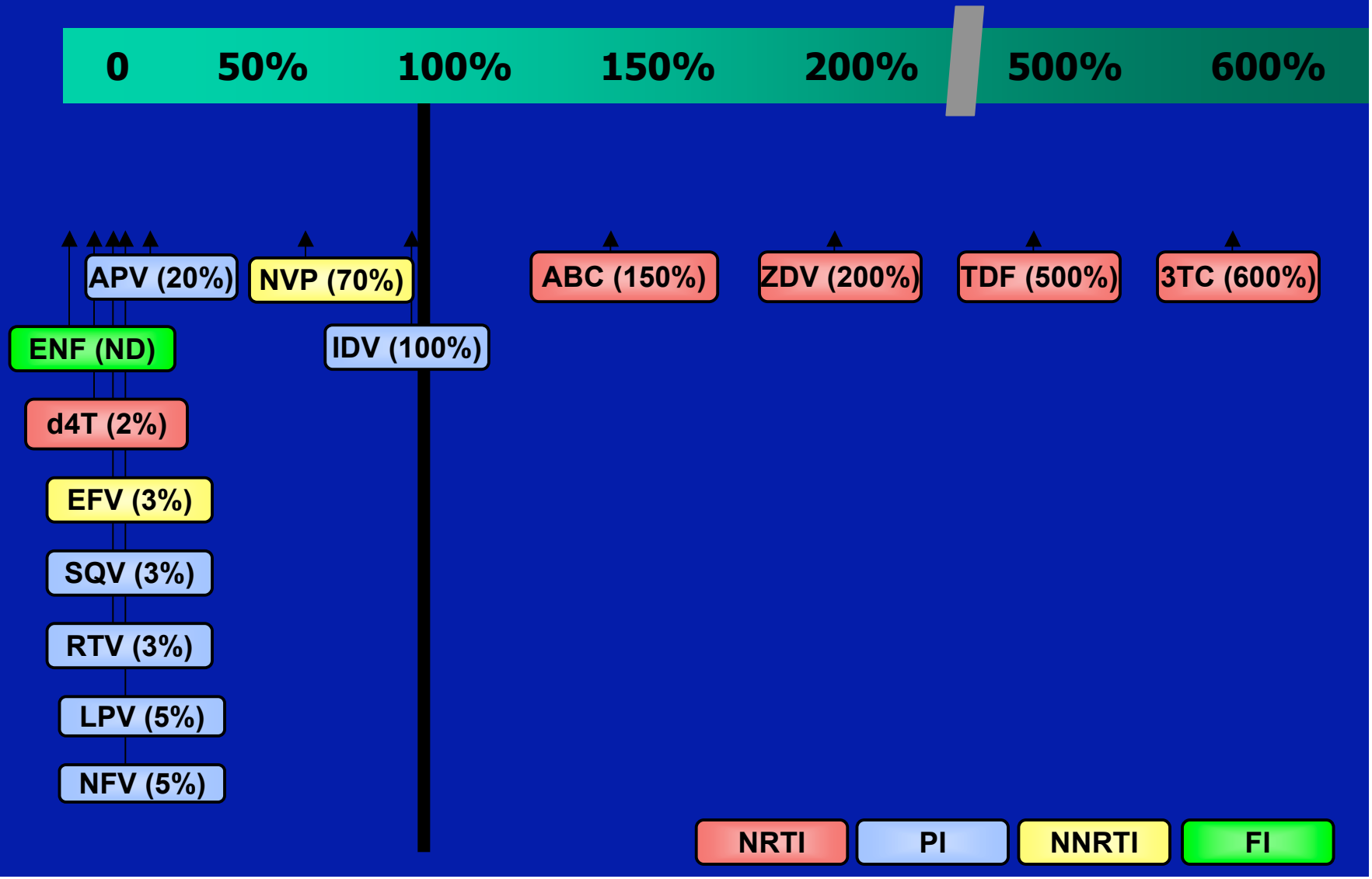
Quinn TC et al, NEJM, 2000,342:921



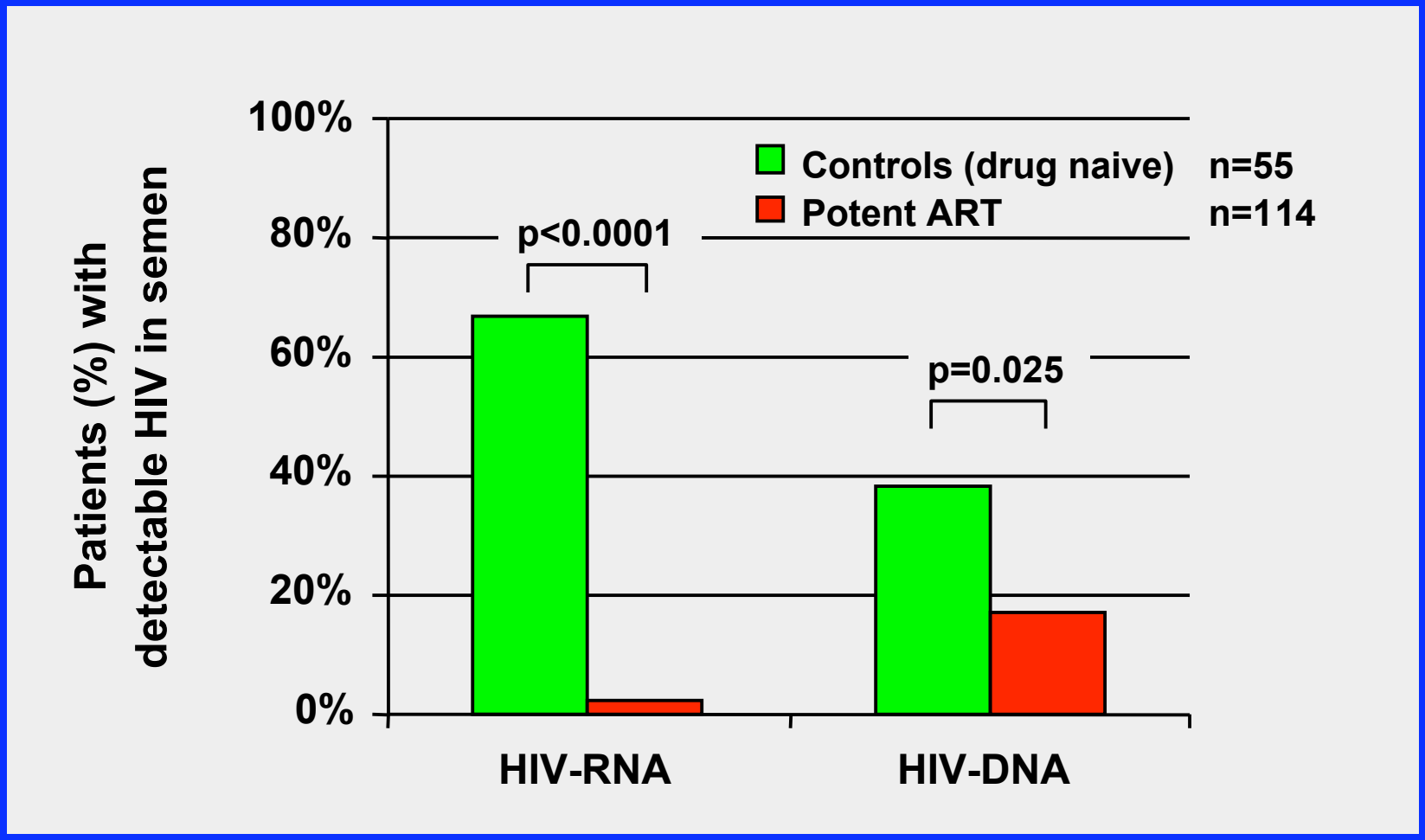
Male Genital Tract Exposure

percent of blood plasma

Kashuba et al. and CROI 13 Abstract 569 (Vourvahis), 13th CROI Abstracts 396 (Stekler), Abstract 618 (Katzenstein)



Semen HIV in patients with suppressed viral load



Vernazza et al., AIDS, 2000

ART Effects Sexual Transmission of HIV

Retrospective Analysis

Musicco *et al*. Archives Internal Medicine 154: 1971; 1994

Castilla *et al.* JAIDS 40, 96, 2005

Kayitenkore *et al*. IAS Abstracts, 2006

Epidemiological/Ecological Analysis

Katz *et al.* Am J. Public Health 92: 388, 2002

Porco *et al.* AIDS 18:81, 2004

Fang *et al.* JID, September 2004

Turner et al. JAIDS 15:1627, 2004

Modeling

Blower (Science, 2000), Law (AIDS, 2003), Blower (Lancet ID, 2003), Garnett (Nature Medicine, 2003), Blower (AIDS Rev, 2003), Auvert 2004 (S. Africa), Garnett (PLOS, 2006), 13th CROI 5 Abstracts …and on and on forever and ever!!

HPTN 052/CHAVI007: ART for Prevention
(Pilot Phase Completed)

Arm 1: Immediate ART (CD4 count 350–550 cells/mm^3)

Arm 2: Delayed ART (>200 cells/mm^3 or AIDS-defining illness)*

Study Population: 8 sites

Malawi (2 sites), India (2 sites), Brazil (2 sites), Thailand, Zimbabwe, Boston

Sample size: n=1750 serodiscordant couples

Power: 90% power to detect 35% reduction in sexual transmission of HIV

ART for Prevention

- **Cohen, MS, Hossenipour, M, Butera, S, Kashuba, AA. Antiretroviral therapy to prevent sexual transmission of HIV In *Current Clinical Topics in Infectious Disease*, Remington J and Swarz, M (eds) 2002**

- **Hosseinipour M, Cohen MS, Vernazza PL, Kashuba AD. Can antiretroviral therapy be used to prevent sexual transmission of human immunodeficiency virus type 1? Clin Infect Dis. Vol. 34; 2002:1391-5**

- **Cohen MS, Cellum, C, Kashuba, AK. ART for Prevention. http://www.medscape.com/viewprogram/2671**

- **Cohen, MS, Hosseinipour, M. HIV treatment meets prevention: antiretroviral therapy as prophylaxis. *In The AIDS Pandemic: Impact on Science and Society*, Mayer and Pizer (eds), Elsevier Press 2004**

Cohen, MS, Gay, C, Blower, S and Paxton L. Antiretroviral therapy for the prevention of transmission of HIV Annals of Internal Medicine (invited).