

**2005 Annual Conference
Japanese Society for AIDS Research
Kumamoto, Japan**

Mandate for Early HIV Detection



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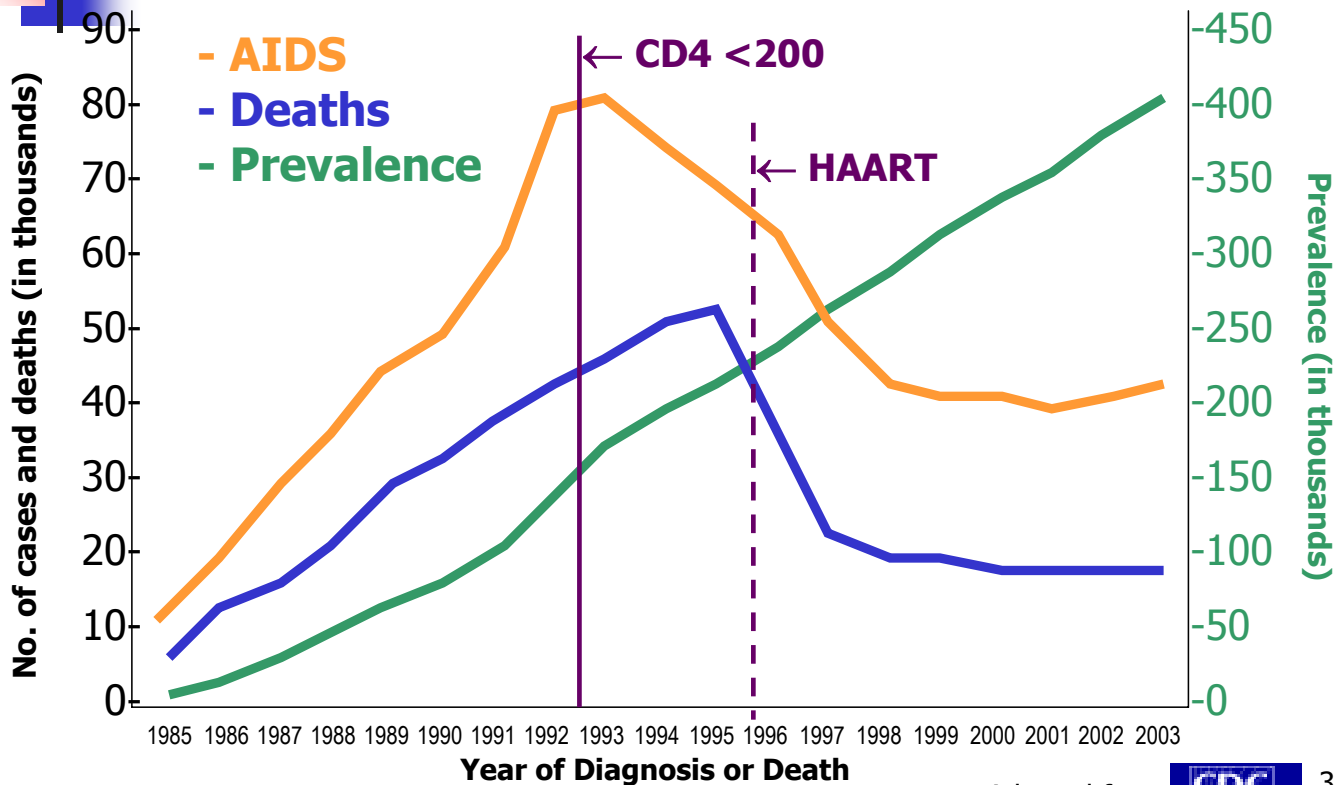


Reasons for Early HIV Detection

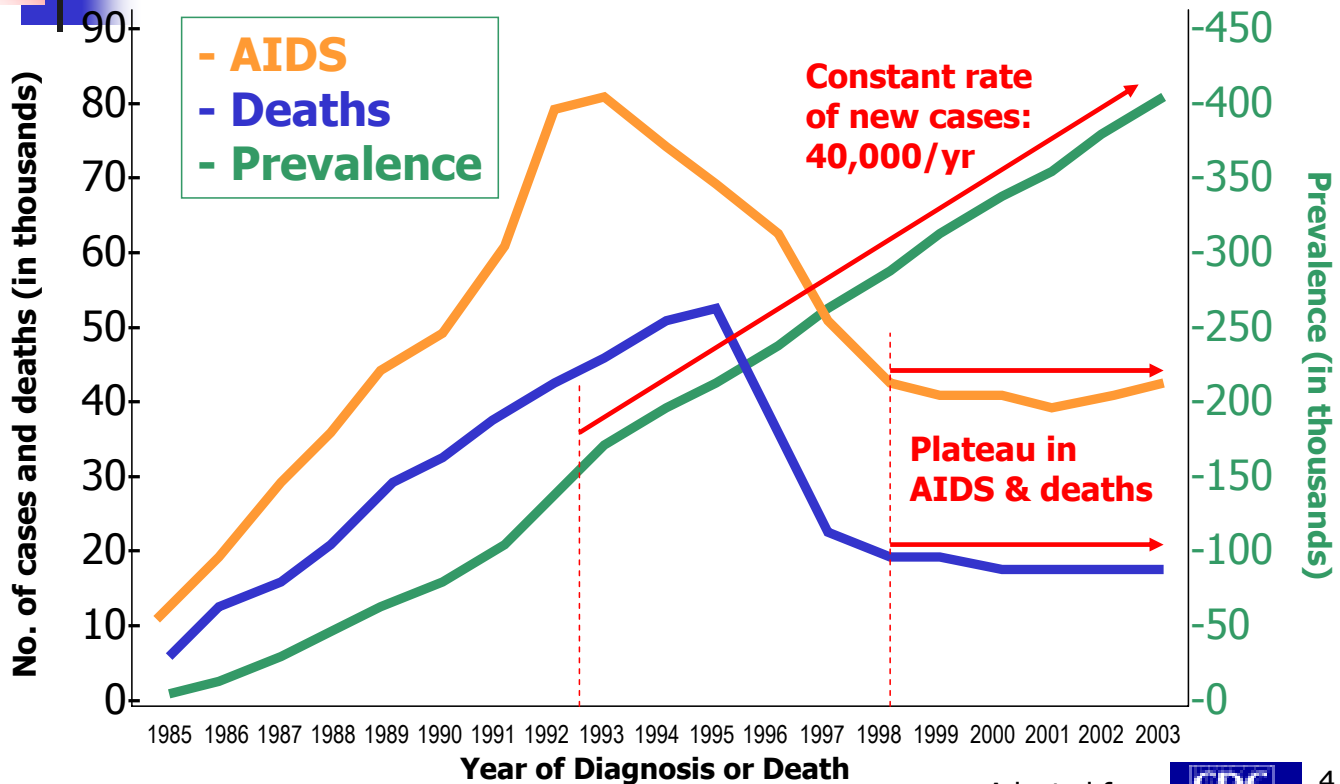
OUTLINE

- Continued expansion of HIV pandemic
 - US: steady rate new cases, plateau AIDS & deaths
 - International: increasing cases & rates
- Transmission prevention
 - Inadequate knowledge of HIV sero-positivity
 - STD resurgence, continued high risk behavior, transmitted drug resistance
 - Reduced STDs, risk & transmission when know HIV+
- Availability of effective interventions
 - Rapid testing in routine medical care
 - Effective risk reduction strategies

Estimated Number of AIDS Cases, Deaths, and Persons Living with AIDS, 1985-2003, U.S.



Continued Expansion of HIV Epidemic



Adapted from




UNAIDS HIV/AIDS Estimates: Annual Increases (Decreases)

Region	Adults & Children Living with HIV: End 2004	Adults & Children Living with HIV: 03→04 End 2003		Adults & Children Living with HIV: 01→03/yr End 2001	
	Sub-Saharan Africa	25.4 mill.	400 K	25.0 mill.	600 K
No. Africa & Mid. East	540,000	60 K	480,000	70 K	340,000
So. & SE Asia	7.1 mill.	600 K	6.5 mill.	300 K	5.9 mill.
East Asia	1.1 mill.	200 K	900,000	110 K	680,000
Latin America	1.7 mill.	100 K	1.6 mill.	100 K	1.4 mill.
Caribbean	440,000	10 K	430,000	15 K	400,000
E. Europe & Central Asia	1.4 mill.	100 K	1.3 mill.	205 K	890,000
W. & Central Europe	610,000	30 K	580,000	20 K	540,000
North America	1.0 mill.	0	1.0 mill.	25 K	950,000
Oceania	35,000	3 K	32,000	4 K	24,000
TOTAL	39.4 mill.	1.6 mill.	37.8 mill.	1.45 mill.	34.9 mill.

Reasons for Early HIV Detection

OUTLINE

- Continued expansion of HIV pandemic
 - US & international case increases
- **Transmission prevention** 
 - Inadequate knowledge of HIV sero-positivity
 - STD resurgence, continued high risk behavior, transmitted drug resistance
 - Reduced STDs, risk behaviors & transmission when know HIV+
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Inadequate Knowledge of HIV Sero-Status



* Based on tested patients not returning for results

Fleming et al, CROI 2002;
CDC, CROI 2003: #2

Inadequate Knowledge of HIV Sero-Status

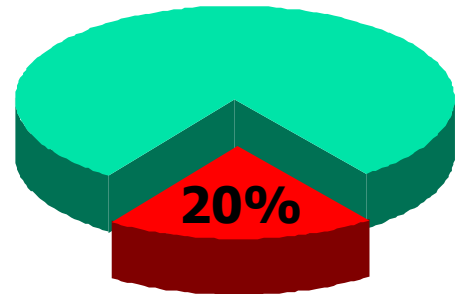
- **34% of 329 HIV+** children born 1995-96 to mothers NOT tested before birth

Lindegren. JAMA 1999;282:531--8.

- Reasons for no test:
 - No prenatal care, e.g. substance abuse
 - Refused: test not emphasized by doc.

CDC MMWR 2001;50(RR19):59-86.

4 million women give birth each year in the US



800,000 DO NOT KNOW their HIV status at delivery

(CDC 1998)

Knowledge of HIV Status: Erroneous & Inadequate

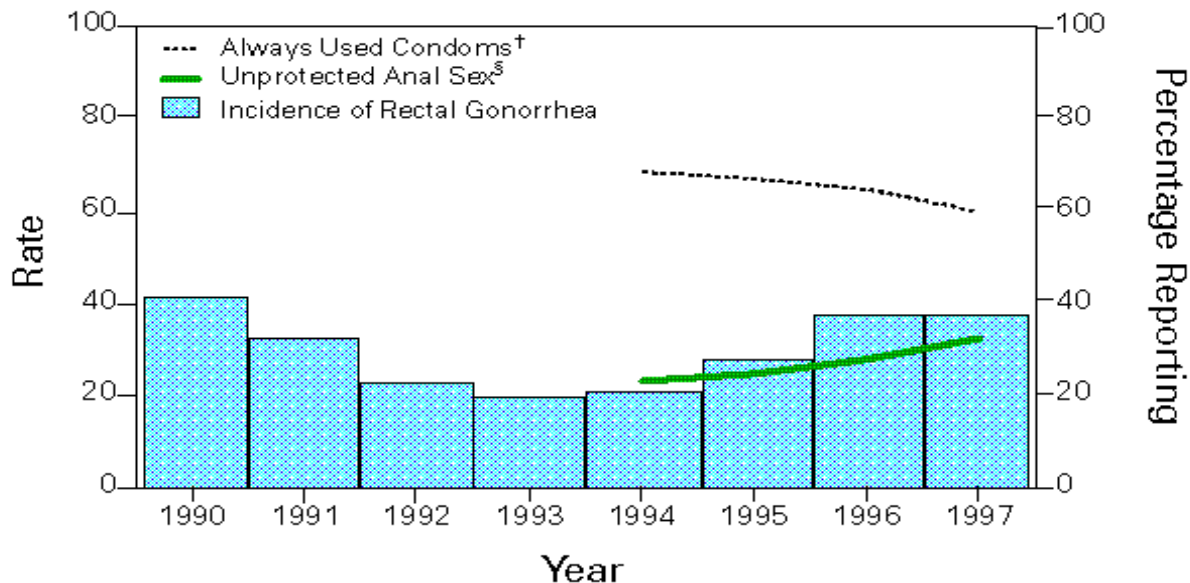
- San Francisco cohort, gay/ bisexual men, ages 18-29 yr

Perceived HIV Status	Actual HIV Test Result		
	HIV-Neg.	HIV-Pos.	Total
HIV-neg.	244	11 (4%)	255
HIV-pos.	0	51	51
Don't Know	52	6 (10%)	58
Total	296	68 (18.7%)	364

25% of HIV+'s didn't know status.

Resurgent Risk Behaviors & STDs

FIGURE 1. Percentage of men who have sex with men reporting selected sexual behaviors, and rate* of male rectal gonorrhea — San Francisco, 1990–1997



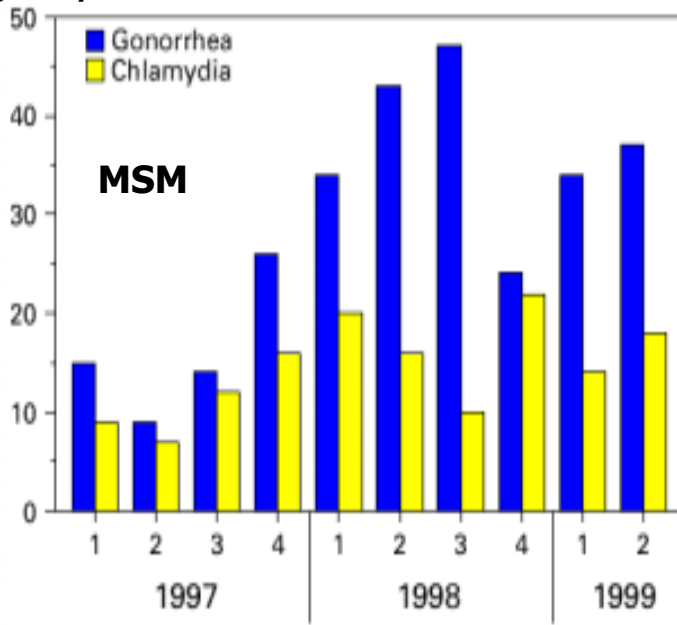
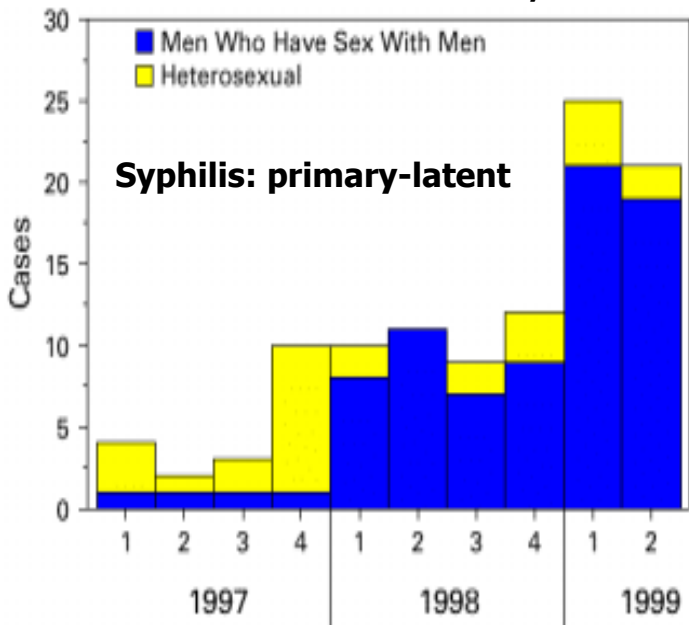
*Per 100,000 men aged ≥ 15 years.

[†]Condoms always used during anal sex during the previous 6 months.

[§]Unprotected anal sex with two or more partners during the previous 6 months.

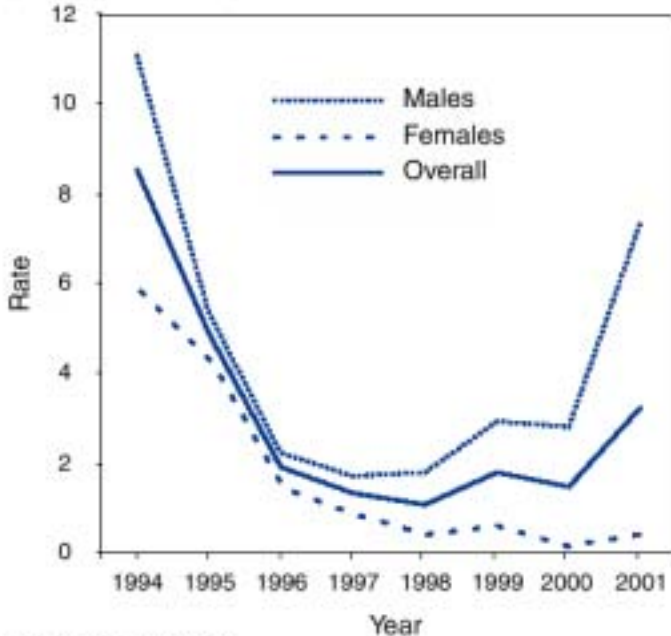
Resurgent STDs in Era of HIV / AIDS

Resurgent STD's among MSM: Seattle, Washington, 1997-1999

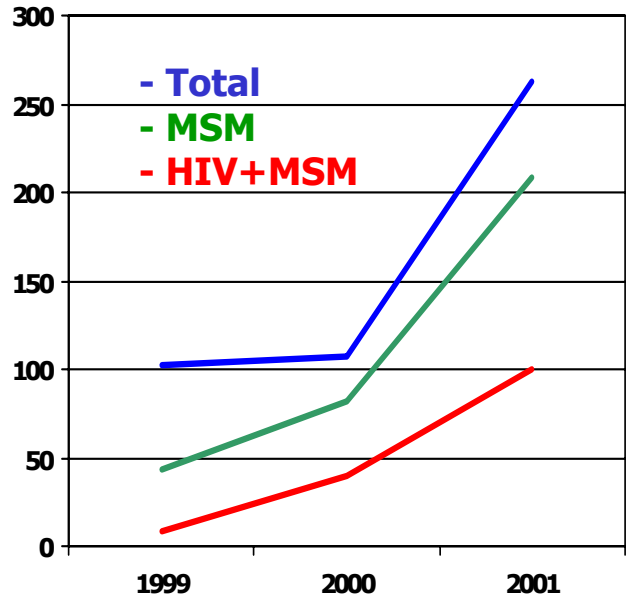


Resurgent STDs in Era of HIV / AIDS

Primary & Secondary Syphilis in New York City



* Per 100,000 population.



CDC MMWR 2002;51(38):853-6

Continued Sexual Risk Behavior Following HIV Diagnosis

Range of **sexual risk behavior prevalence** among US HIV+ persons **aware of their HIV sero-status**

RISK (Author & year)	Sample	Behaviors post diagnosis
Blood Donors (Cleary 1991)	153 men 43 women	40% men & 38% women / past week: unprotected vag. or anal sex
Hetero-1° partners (Kline 1994)	214 women	52% not always used condoms w/ 1° partners / past 4 weeks
Substance Users (Kalichman 1997)	115 men (74% het.)	61% / mo: unprotected vag. sex 20% / mo: unprotected anal sex
MSM (Wolitski 1998)	242 men	22% / 12 mo unprotected insertive anal sex w/ HIV- or unkn.

Heterosexual Transmission: Increased at Higher VL

Heterosexual Transmission in US Hemophiliacs

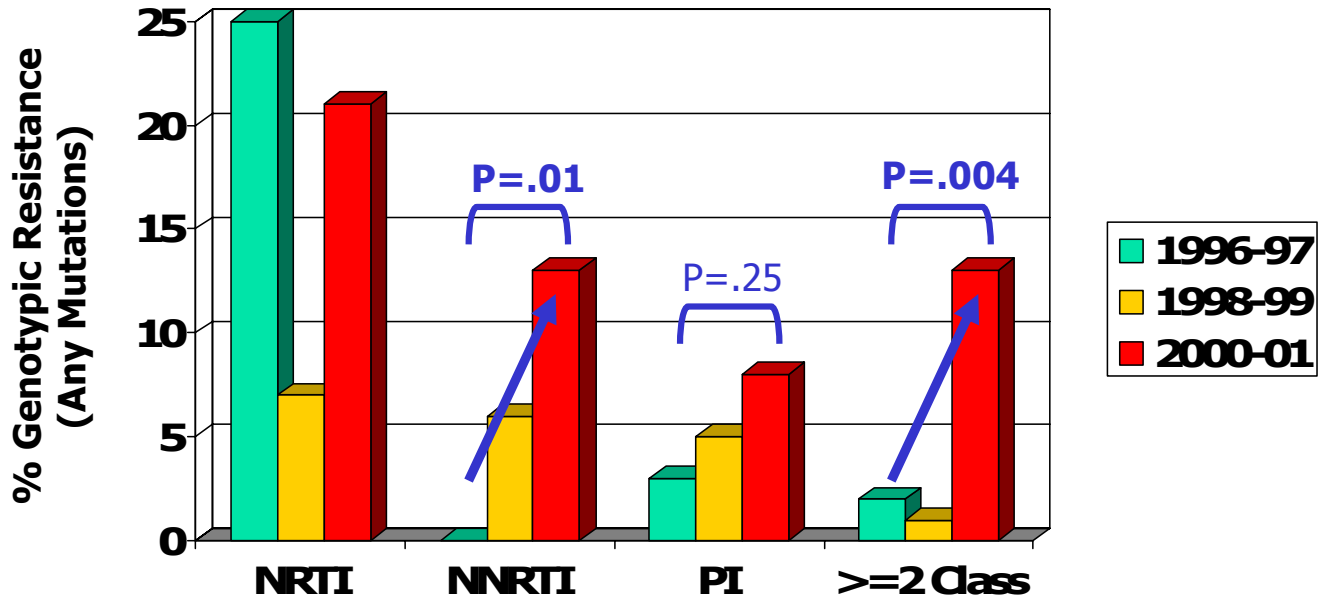
	Transmitters	Non-Transmitters
Number (%)	5 (13%)	34 (87%)
Median CD4	245 ± 91	260 ± 28
Median VL	121,800	12,800
<1,000	0 (0%)	1 (3%)
1,000-9,999	1 (20%)	14 (41%)
10,000-99,999	1 (20%)	16 (47%)
≥ 100,000	3 (60%)	3 (9%) p=0.027



Heterosexual Transmission: Increased at Higher VL

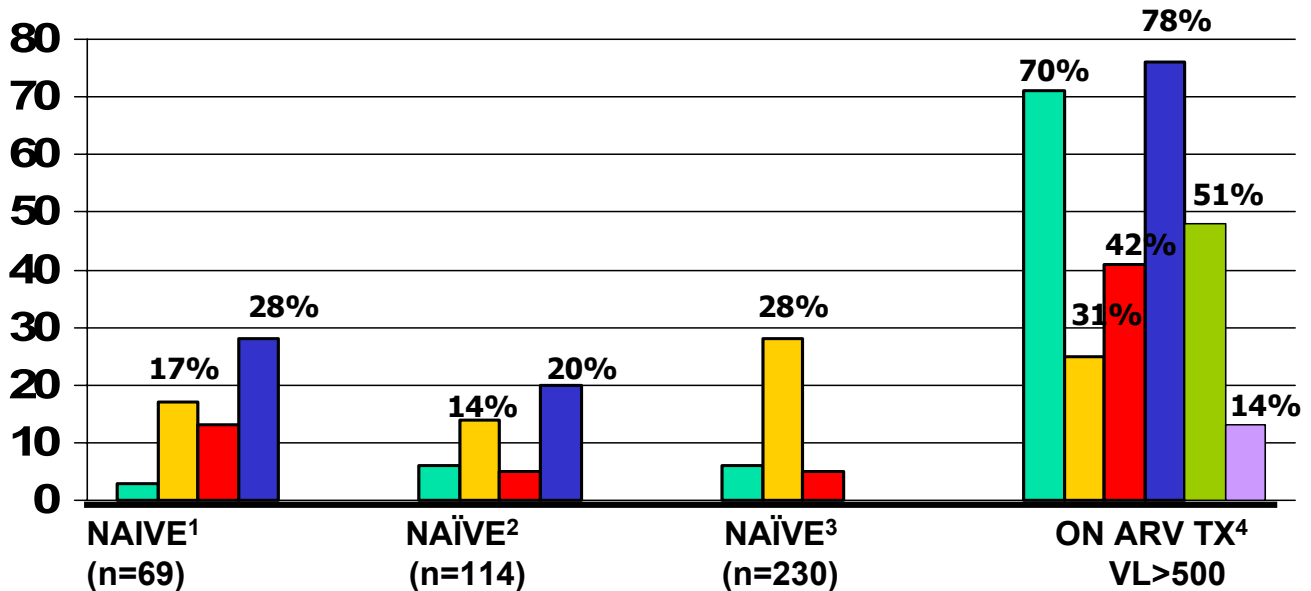
- 415 couples in Uganda x 30mo, 55%men+
- 90 couples (22%) seroconverted:
 - 12%/yr: **M**→**F** = **F**→**M**
 - 23%/yr: VL >50,000 vs 0% VL <1500
 - 2.45 x ↑ risk of transmission
with each 1 log VL ↑ (p<0.0001)

Primary HIV-1 Drug Resistance Among Recently Infected Persons



Resistance Prevalence in the US

■ nRTIs ■ NNRTIs ■ PI's ■ Any drug ■ 2-3 class ■ 3 class



(63% of study pop'n had resistance in 1998, only 3 yr into HAART era)



2 Modes of Drug Resistance Acquisition: The **NEED** for Different Prevention Strategies

■ Primary **Transmitted** Resistance

- From source partner w/ **acquired** resist who:

- Knew he/she was infected
- Had seen a health care provider
- Had been prescribed ARV therapy

} **“Prevention
for
Positives”**

- To a recipient engaging in high risk behavior

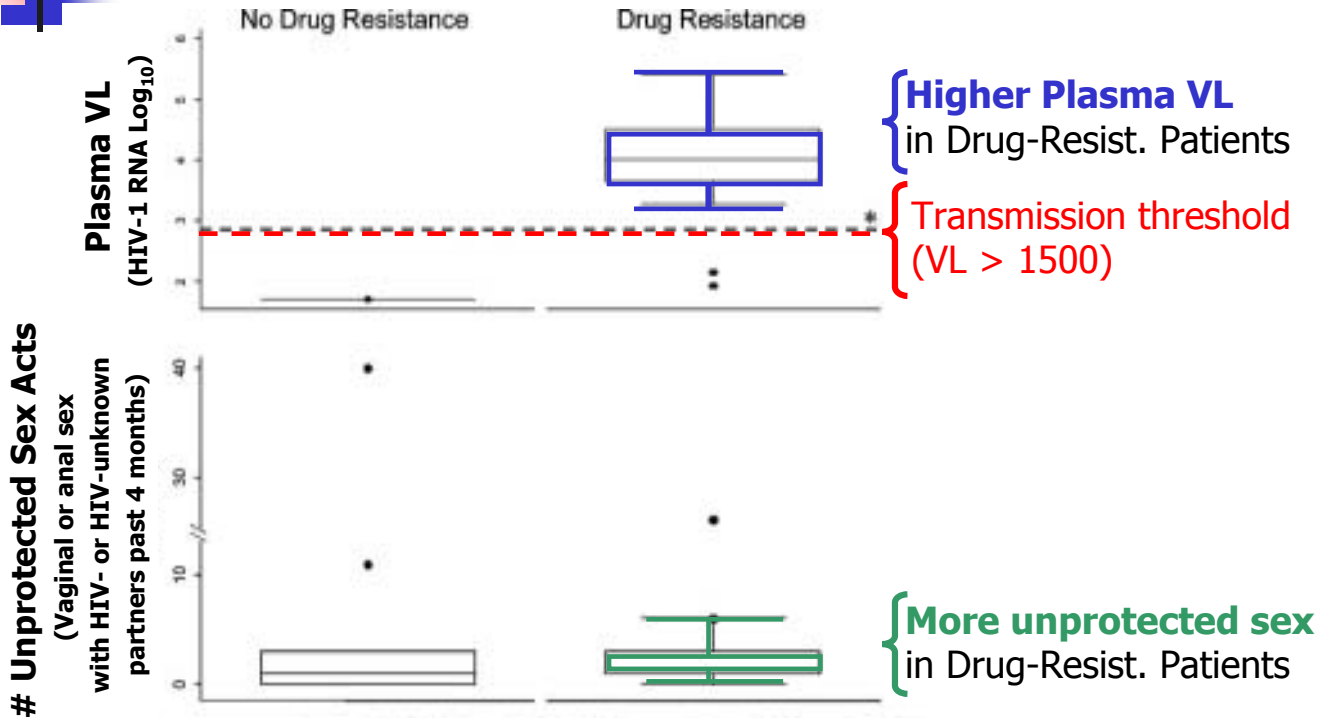
} **“Risk
Reduction”**

■ Secondary **Acquired** Resistance

- Following non-suppressive treatment

} **“Adherence
Counseling”**

High-Risk Sexual Behavior in ARV-Resistant HIV+ Adults



*Broken line represents plasma HIV RNA threshold for HIV transmission (1500 copies/mL) in sexually active adults from a previous study.²²



SAFE: CDC Serostatus Approach to Fighting the HIV Epidemic

1. Increase # HIV+ persons aware of serostatus
2. Increase use of HIV preventive services
3. Increase high quality HIV care & treatment
4. Increase HIV treatment adherence
5. Increase # HIV+ persons who sustain HIV-STD risk-reduction behavior



CDC's **SAFE** Initiative: Medical Benefits of HIV Diagnosis

- OI prophylaxis →
 ↓ HIV-related morbidity
- Tx STD's, substance abuse, mental health →
 ↓ HIV transmission / risk behaviors
- Antiretroviral treatment →
 ↓ morbidity, mortality, & transmission



CDC's **SAFE** Initiative:

Public Health Benefits of HIV Diagnosis:

- ↑ Partner protection after aware of diagnosis →
↓ HIV transmission
- ↓ **Viral load in blood & sexual secretions**
via antiretroviral treatment
→ → **Reduced HIV transmission**

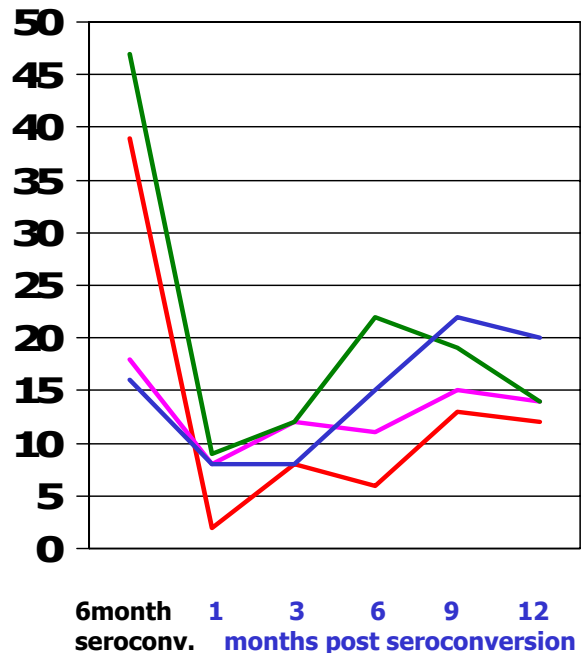
Reduced Sexual Risk Behaviors Following Knowledge of HIV Status

- CDC study, N=142 pts diagnosed previous 6-24mos, predominantly heterosexual black males

Behavior	Men	Women	Total
Before knew HIV+: Always used condoms	12%	15%	13%
Since knowing HIV+: Always used condoms	74%	84%	77%
Since knowing HIV+: Didn't tell status before sex	61%	52%	58%

Reduced High-Risk Sex After Diagnosis – With Recidivism

- 1995+ prospective HIV- MSM vaccine cohort (n=3200)
- 2% newly HIV+ (n=72)
- 59% = high-risk transmitters (unprotected anal sex during 6month seroconversion period):
 - insertive w/ HIV-neg/unknown
 - receptive w/ HIV-neg/unknown
 - insertive w/ HIV-positive
 - receptive w/ HIV-positive



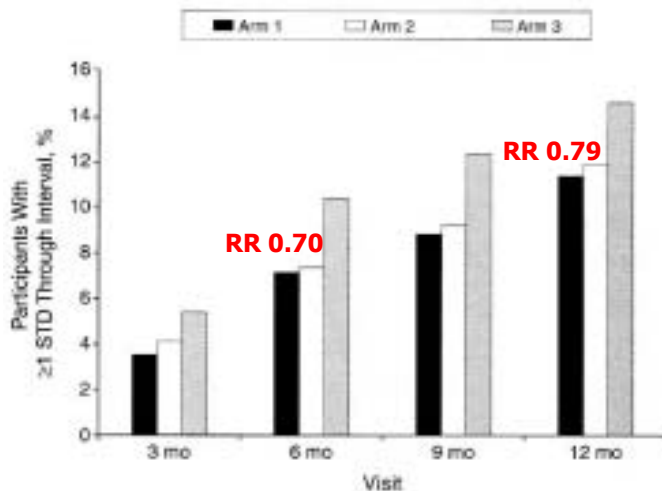
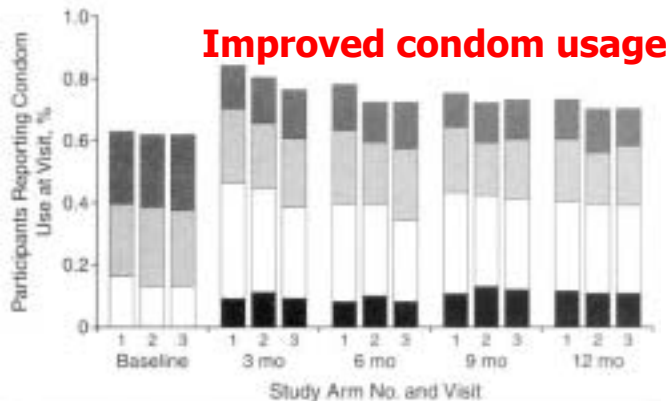
Reduced STDs with Risk-Reduction Counseling

Arm 1: counseling x4/4wks

Arm 2: counseling x2/10d

Arm 3: didactic x2/10d

Fewer STI's in risk- reduction counseling intervention vs standard didactic counseling

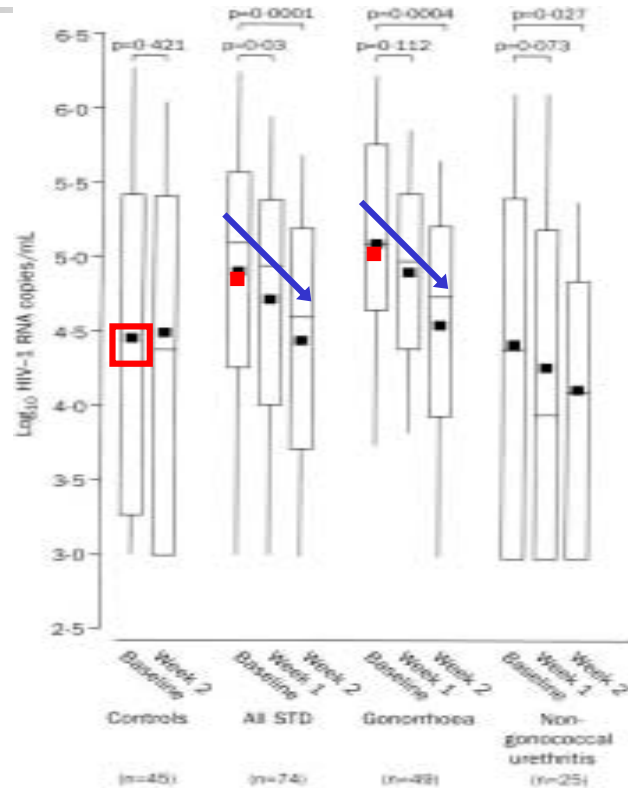


Treatment of STDs → Reduced HIV in Semen

Median seminal plasma HIV-1 RNA:
8x higher in STD group than controls
(12.4 vs 1.5 x 10⁴ copies/mL, p=0.035)

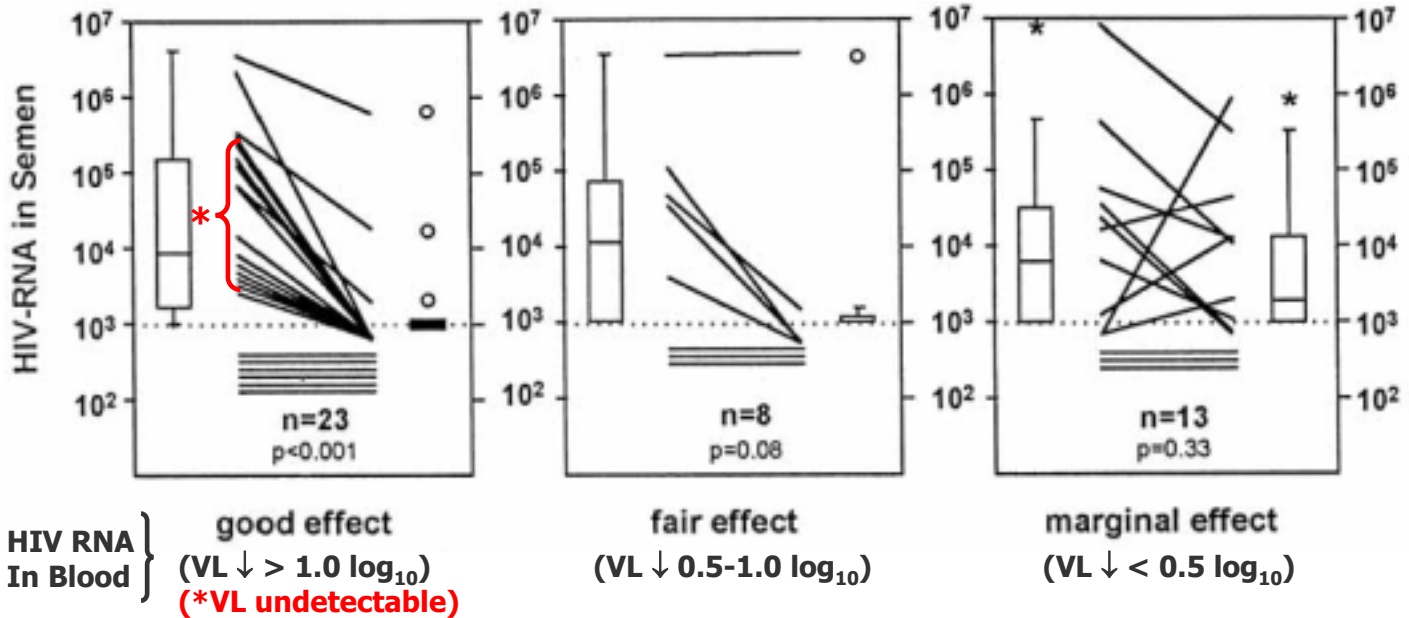
Significant reduction of seminal HIV-1
after treatment of urethritis

**Potential reduction in sexual
transmission of HIV-1
by treatment of STDs**




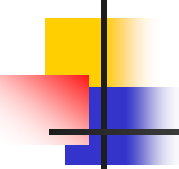
ARV Reduction in Plasma VL → Reduced HIV in Semen

N=44 ARV-naïve or experienced patients



ARV in Pregnancy →

Reduced Perinatal Transmission



1994	■ AZT monotherapy:			
	■ ACTG 076	Wk 14+	22.6%	→ 7.6%
1998	■ Thailand	Wk 36+	19%	→ 9%
	■ USA	L & D+	27%	→ 10%
	■ NVP single dose:			
1999	■ HIVNET 012 (+BrFd)	1 dose	21%	→ 12%
	■ AZT + 3TC (IP/PP):			
1999	■ PETRA (Afr,+BrFd)	L & D+	15%	→ 6%
	■ Triple therapy:			
2003	■ DITRAME-1.1 (AZT/3TC+sdNVP)			→ 5 %
	■ USA: w/ AZT & PI	std. tx		→ 1.2%
2000's+	■ Current US observed transmission on HAART			0-2%!

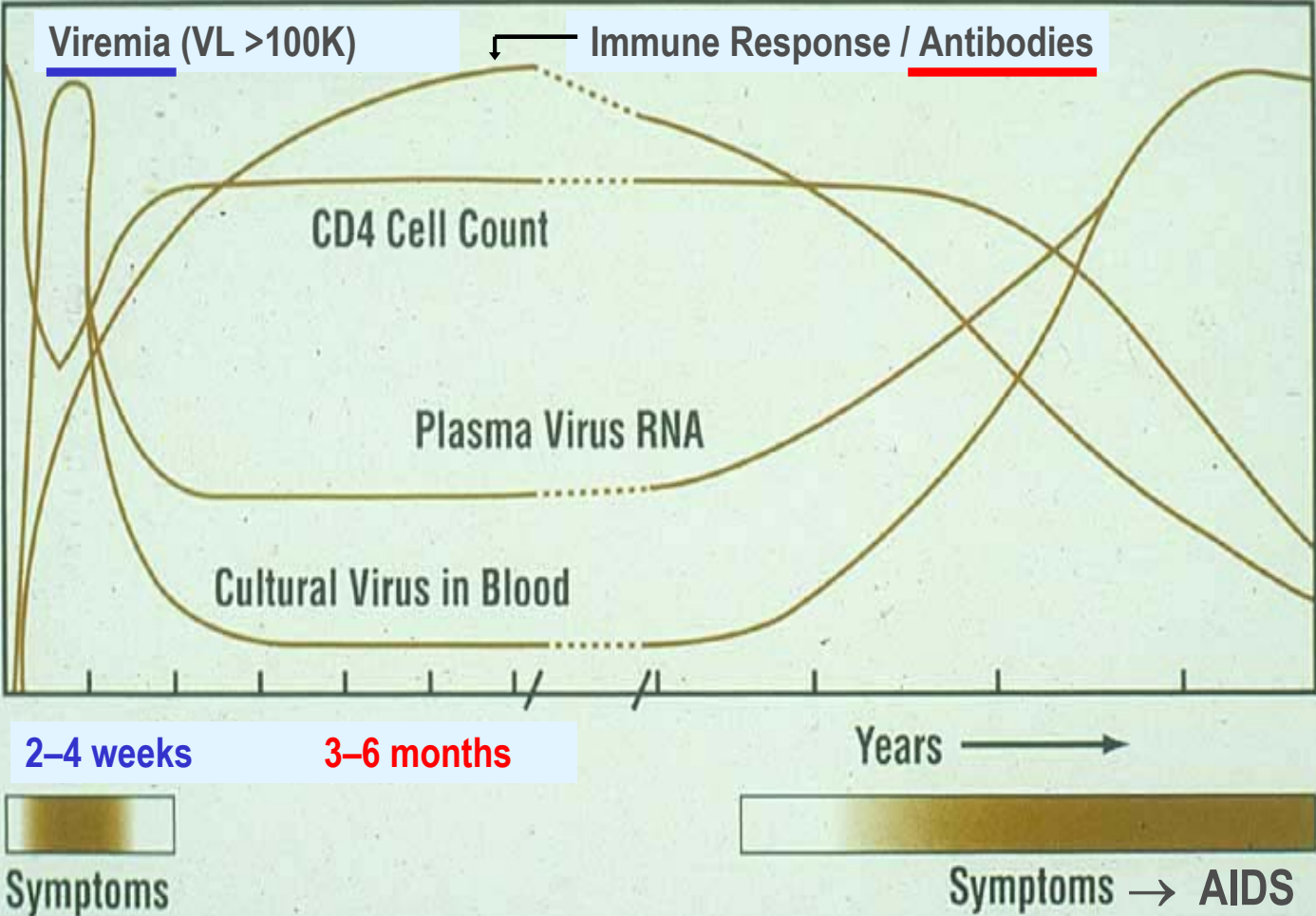


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HIV Infection: Acute Viremia & Development of Antibodies





HIV Diagnostic Tests

■ ANTIBODY TESTS

- ELISA Serum run twice
- WB Confirmatory

■ Specimens

- Venous Lab standard
- Rapid "Ora-Quick" & others
- Oral "Ora-Sure" (mail)
- Home "Home Access"

■ VIRAL RNA TESTS

- PCR or bDNA Earliest diagnosis

**TEST
RESULT
TIMES:**

1-7 days

3-20 minutes

1-2 weeks

1-2 weeks

1-2 weeks

FDA-Approved Rapid HIV Tests

Tests	OraQUICK	UNI-GOLD	REVEAL
Samples	-Oral fluid -Whole blood -Plasma	-Whole blood -Plasma -Serum	-Plasma -Serum
Sensitivity	99.3*-99.6%	100%	99.8%
Specificity	99.8*-100%	99.7-99.8%	98.6-99.1%
Time	20-40 minutes	Exactly 10 min.	In 3 minutes

CLIA-waived (except *italic tests* - require centrifuge)

Negative results = **conclusive** (if outside of window period)

Positive results - must be **confirmed** with Western Blot

(even if lab EIA negative), note: blood "slightly" more sens.

OraQuick ADVANCE[®] Rapid HIV-1/2 Test

SPECIMEN COLLECTION

Venipuncture



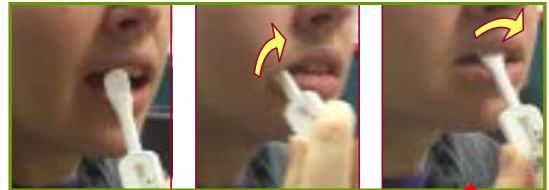
or

Fingerstick



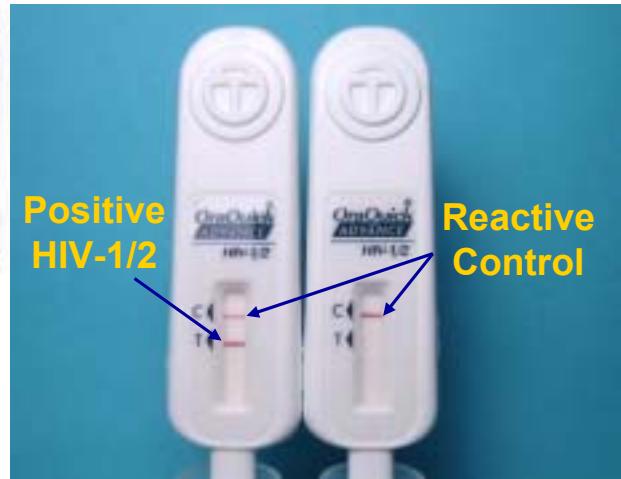
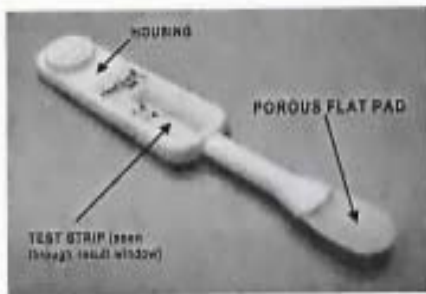
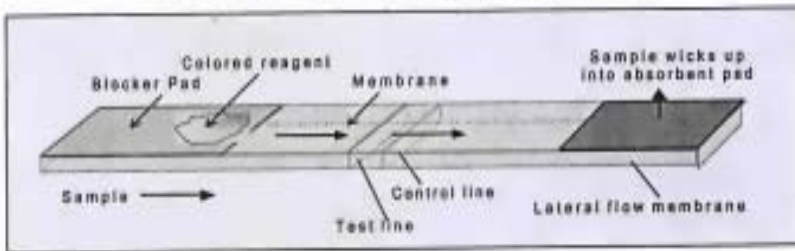
or

Buccal Swab



OraQuick ADVANCE® Rapid HIV-1/2 Test – cont'd

OraQuick® Assay Design



Read results in 20 – 40 minutes

Put this between
your cheek and gum
for 2 minutes.

Believe it or not,
you've just taken
an accurate new
test for HIV.

Elisa + Western Blot

Introducing OraSure, the first
noninvasive HIV testing system.

- The OraSure HIV-1 oral specimen collection device is designed to draw antibodies – not virus – from the tissue of the cheek and gum (not saliva)
- 99.97% of 3570 people in clinical trials received the correct result
- Safer than blood
- Easy to use: in mouth for few minutes, mail device to company, receive results by mail in 2 weeks

Results in Known HIV Negative People				
Number Tested	EIA Negative	EIA Repeat Reactive (17)		
		WB Negative	WB Indeterminate	WB Positive
2897	2890	13	4	0

OraSure EIA testing correctly identified 2890 of 2897 confirmed HIV negative people as HIV negative.

Results in Known HIV Positive People				
Number Tested	EIA Negative	EIA Repeat Reactive (672)		
		WB Negative	WB Indeterminate	WB Positive
673	1	0	7	665

OraSure EIA testing correctly identified 672 of 673 confirmed HIV positive people as EIA repeatedly reactive. Of 673 people total, 665 were positive, 7 were indeterminate.

OraSure
Oral HIV-1 Antibody Testing System

No needles. No blood.
Just accurate results.

To start testing with OraSure
Call 1-800-ORASURE



HIV Testing Indications: 3 Categories

1) Risk Factors for HIV Infection

- Sex, IV drugs, blood, contact with at-risk person (*see next section*)

2) Manifestations of HIV Infection

- Acute retroviral syndrome
- Chronic non-specific symptoms of HIV ←
- AIDS conditions

3) Medical Conditions Affected by HIV ←



HIV Testing Indications:

2. Manifestations of HIV

A. Acute retroviral syndrome:

- Fever, adenopathy, pharyngitis, rash, etc.
- 50-80%, within first 6wks

B. Non-specific, early HIV S/Sx:

- Lymphadenopathy, onychomycosis, shingles, recurrent vaginitis, hypergamma-globulinemia, neutropenia, thrombocytopenia, etc.

C. AIDS opportunistic infections / cancers:

- PCP, esophagitis, diarrhea, lymphoma, etc.



Low Prevalence Group Members: **Risk May be High**

REAL CASES:

- 57 yr grandmother univ. secretary – w/ acute “flu”
 - *Divorced with new 39 y/o boyfriend*
- 65 yr married grandmother – recurrent vag.candida
 - *Husband raped at campground*
- 72 yr surgeon’s widow – recurrent thrush, dry cough
 - *Died of late-diagnosed PCP (boyfriend)*
- 43 yr father with pregnant wife – single lymph node
 - *Prior MSM contacts in bars*

HIV Testing Indications:

3. Medical Need to Know

- Pregnancy
 - Perinatal transmission
- Pelvic Inflamm.Disease
 - Abscesses
- Syphilis
 - Neuro-syphilis
- Cervical Dysplasia
 - No-cryotherapy
- HPV Disease
 - Eval for Dysplasia
- Tuberculosis
 - Hi rates concurrence & latent activation!
- HBV & HCV
 - ↑ Morbidity / mortality
- Occupational Expos.
 - Work-Comp



HIV Prevention Measures: “What Works?”

- Healthcare provider discussions
- Interpersonal skills
- Harm reduction
- Prevention for positives
- International models



Healthcare Provider Discussions

- Bring up at **any and all** clinic visits
- Goals:
 - Risk assessment & rapid testing
 - Risk reduction via skill development
- **Provider Factors**
 - **Comfort with topic = most important!!**
 - “Normalize” subject: e.g. w/ other infections
 - Watch for distractors (e.g. “I’m divorced”)
- Have referrals & resources ready
 - Counseling for psychosocial issues
 - HIV & STD treatment



HIV Risk Factors

- “Unprotected” sexual contact, since 1978
 - Any “STD”, HPV/Pap, OCPs...
- “Recreational” blood exposure
 - IVDU, tattoos, cocaine straws, etc.
- Receipt of tissue or blood products
 - Risk 1:60,000 / 1985 → 1:675,000 / 1996 (USA)
- “PARTNER” with above risks
 - Person from high **prevalence group**
 - Note “6-month” negative window

Sexual Risk Assessment

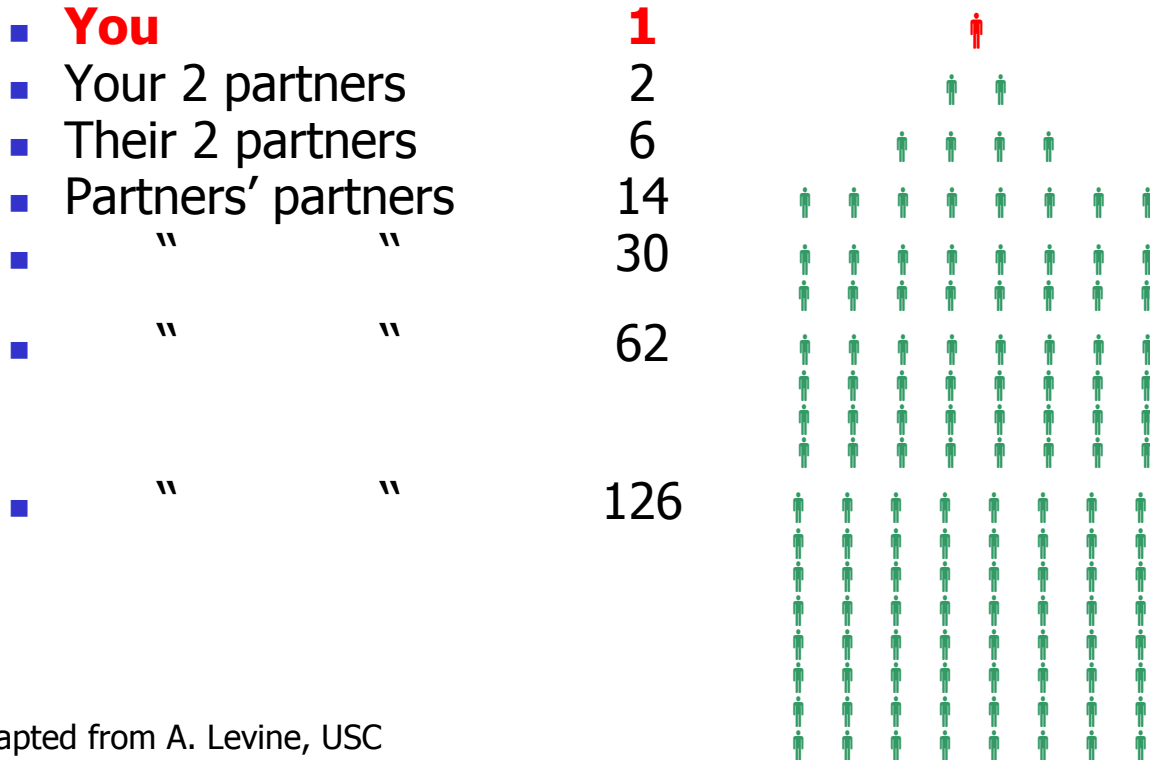
“Have you...?”

- ? Ever had sex since 1978 ?
- ? Used condoms 100% ?
 - ? Used oral contraceptives ?
 - ? Ever been pregnant ?
- ? Ever had:
 - ? A sexually transmitted infection ?
 - ? An abnormal Pap smear ?
- ? Had sex with men, women or both ?
- ? Had sex vaginally, orally or rectally ?

Do you know the above for all of your partners ???

“Know Thy Partner’s History”

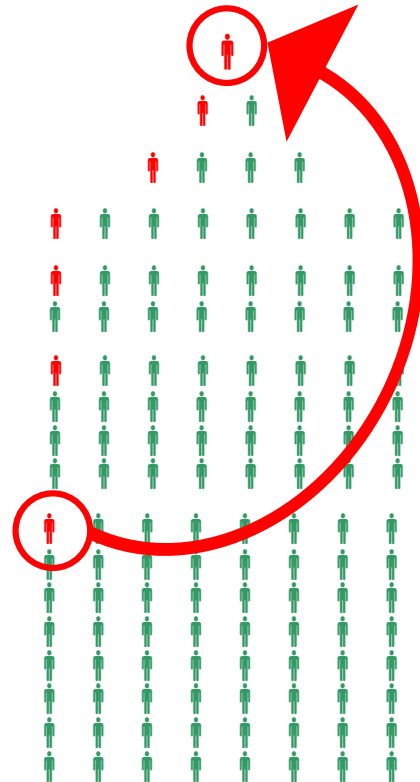
Sex with 2 partners AND their 2 partners



“Know Thy Partner’s History”

Sex with 2 People → *HIV+*

- **You** 1
- Your 2 partners 2
- Their 2 partners 6
- Partners’ partners 14
- “ “ 30
- “ “ 62
- “ “ 126





Interpersonal Prevention Skills

- **LEARN HOW TO ASK PARTNER/S:**
 - History of prior sex / drug partners
 - History of prior sexual infections
 - History of prior HIV testing
- **LEARN HOW TO NEGOTIATE:**
 - Use of condoms / barriers
 - Safer sex / drug practices



Harm Reduction

- Incremental reduction of harm through accomplishable intermediate changes
 - Versus “all or nothing”
- Developed in NY area initially in context of substance abuse
 - Subsequently generalized to HIV context
- **“W.H.O. must give a clear message:
HARM REDUCTION WORKS.”**

Jim Kim, WHO, CROI 2005



Harm Reduction - Application

- Assume continued risk behavior
- Therefore “reduce harm” via “safer” sexual & drug use practices, e.g.:
 - Know HIV sero-status
 - Disclose HIV status
 - Don’t make false assumptions, i.e. “he didn’t tell me – therefore he must be...”
 - Reduce number of partners



Prevention For Positives

- Discuss risk activities at **every** visit
- Inquire about **specific** activities:
 - Having sex? (Using needles?)
 - Disclosing diagnosis?
 - Using protection?
 - Having anonymous sex?
 - Having sex while using drugs?
- Offer **harm reduction**:
 - Condoms, counseling, referrals, etc.
 - Suggest safer practices, counter mis-understandings
 - Partner notification &/or testing



International Prevention Models

“ABC” –and – “CNN”

Abstinence

Condoms

Be Faithful

Negotiation

Condoms

Needle Exchange