2005 Annual Conference
Japanese Society for AIDS Research
Kumamoto, Japan

Mandate for Early HIV Detection

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Centro de Salud La Fe HIV/AIDS C.A.R.E. Center
Texas Tech University Health Sciences Center
El Paso, Texas, USA
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.

- AIDS
- Deaths
- Prevalence

Adapted from CDC
Continued Expansion of HIV Epidemic

- AIDS
- Deaths
- Prevalence

Constant rate of new cases: 40,000/yr
Plateau in AIDS & deaths

Adapted from CDC
## UNAIDS HIV/AIDS Estimates: Annual Increases (Decreases)

<table>
<thead>
<tr>
<th>Region</th>
<th>Adults &amp; Children Living with HIV: End 2004</th>
<th>Adults &amp; Children Living with HIV: 03→04 End 2003</th>
<th>Adults &amp; Children Living with HIV: 01→03/yr End 2001</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sub-Saharan Africa</td>
<td>25.4 mill.</td>
<td>400 K</td>
<td>600 K</td>
</tr>
<tr>
<td>No.Africa &amp; Mid.East</td>
<td>540,000</td>
<td>60 K</td>
<td>70 K</td>
</tr>
<tr>
<td>So. &amp; SE Asia</td>
<td>7.1 mill.</td>
<td>600 K</td>
<td>300 K</td>
</tr>
<tr>
<td>East Asia</td>
<td>1.1 mill.</td>
<td>200 K</td>
<td>110 K</td>
</tr>
<tr>
<td>Latin America</td>
<td>1.7 mill.</td>
<td>100 K</td>
<td>100 K</td>
</tr>
<tr>
<td>Caribbean</td>
<td>440,000</td>
<td>10 K</td>
<td>15 K</td>
</tr>
<tr>
<td>E. Europe &amp; Central Asia</td>
<td>1.4 mill.</td>
<td>100 K</td>
<td>205 K</td>
</tr>
<tr>
<td>W. &amp; Central Europe</td>
<td>610,000</td>
<td>30 K</td>
<td>20 K</td>
</tr>
<tr>
<td>North America</td>
<td>1.0 mill.</td>
<td>0</td>
<td>25 K</td>
</tr>
<tr>
<td>Oceania</td>
<td>35,000</td>
<td>3 K</td>
<td>4 K</td>
</tr>
<tr>
<td>TOTAL</td>
<td>39.4 mill.</td>
<td>1.6 mill.</td>
<td>1.45 mill.</td>
</tr>
</tbody>
</table>

Adapted from UNAIDS 2004 & 2005 Reports on Global AIDS Epidemic
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+

- Availability of effective interventions
  - Rapid testing in routine medical care
  - Effective risk reduction strategies
Inadequate Knowledge of HIV Sero-Status

1 Million — (850-950,000)

U.S.A.

HIV/AIDS

CASES

230,000

200,000

130,000

340,000

Learning DIAGNOSIS may counteract misconception that they’re at low / no risk

* 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

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

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

<table>
<thead>
<tr>
<th>Perceived HIV Status</th>
<th>Actual HIV Test Result</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>HIV-Neg.</td>
<td>HIV-Pos.</td>
</tr>
<tr>
<td>HIV-neg.</td>
<td>244</td>
<td>11 (4%)</td>
</tr>
<tr>
<td>HIV-pos.</td>
<td>0</td>
<td>51</td>
</tr>
<tr>
<td>Don’t Know</td>
<td>52</td>
<td>6 (10%)</td>
</tr>
<tr>
<td>Total</td>
<td>296</td>
<td>68 (18.7%)</td>
</tr>
</tbody>
</table>

*25% of HIV+’s didn’t know status.*

Hays: AIDS 1997; Vol.11:1495-1502
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


Syphilis: primary-latent

MSM

CDC MMWR 1999;48:773–7
Resurgent STDs in Era of HIV / AIDS

Primary & Secondary Syphilis in New York City

- Total
- MSM
- HIV+MSM

* 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

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

Marks. AIDS 1999;13(3):297-306
Heterosexual Transmission in US Hemophiliacs

<table>
<thead>
<tr>
<th>Number (%)</th>
<th>Transmitters</th>
<th>Non-Transmitters</th>
</tr>
</thead>
<tbody>
<tr>
<td>5 (13%)</td>
<td>34 (87%)</td>
<td></td>
</tr>
<tr>
<td>Median CD4</td>
<td>245 ± 91</td>
<td>260 ± 28</td>
</tr>
<tr>
<td>Median VL</td>
<td><strong>121,800</strong></td>
<td><strong>12,800</strong></td>
</tr>
<tr>
<td>&lt;1,000</td>
<td>0 (0%)</td>
<td>1 (3%)</td>
</tr>
<tr>
<td>1,000-9,999</td>
<td>1 (20%)</td>
<td>14 (41%)</td>
</tr>
<tr>
<td>10,000-99,999</td>
<td>1 (20%)</td>
<td>16 (47%)</td>
</tr>
<tr>
<td>≥ 100,000</td>
<td>3 (60%)</td>
<td>3 (9%) p=0.027</td>
</tr>
</tbody>
</table>

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)

Quinn. NEJM 2000;342(13):921-929
Primary HIV-1 Drug Resistance Among Recently Infected Persons

% Genotypic Resistance (Any Mutations)

NRTI  NNRTI  PI  >=2 Class


P=.01  P=.25  P=.004

Grant. JAMA 2002; 288(2):181–188
Resistance Prevalence in the US

(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
  - To a recipient engaging in high risk behavior

- **Secondary Acquired Resistance**
  - Following non-suppressive treatment

Adapted from D. Richman. CROI 2005 session #2
High-Risk Sexual Behavior in ARV-Resistant HIV+ Adults

Higher Plasma VL in Drug-Resist. Patients
Transmission threshold (VL > 1500)

More unprotected sex in Drug-Resist. Patients

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

<table>
<thead>
<tr>
<th>Behavior</th>
<th>Men</th>
<th>Women</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before knew HIV+: Always used condoms</td>
<td>12%</td>
<td>15%</td>
<td>13%</td>
</tr>
<tr>
<td>Since knowing HIV+: Always used condoms</td>
<td>74%</td>
<td>84%</td>
<td>77%</td>
</tr>
<tr>
<td>Since knowing HIV+: Didn’t tell status before sex</td>
<td>61%</td>
<td>52%</td>
<td>58%</td>
</tr>
</tbody>
</table>

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 STIs in risk-reduction counseling intervention vs standard didactic counseling

Improved condom usage

Kamb. JAMA 1998; 280(13):1161-1167
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 10^4 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

- **AZT monotherapy:**
    - ACTG 076 Wk 14+ 22.6% → 7.6%
    - 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%!
Reasons for Early HIV Detection

OUTLINE

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- Inadequate transmission prevention
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- Availability of effective interventions
  - Rapid testing in routine medical care
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HIV Infection: Acute Viremia & Development of Antibodies

Viremia (VL >100K) → Immune Response / Antibodies

2–4 weeks 3–6 months
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
## FDA-Approved Rapid HIV Tests

<table>
<thead>
<tr>
<th>Tests</th>
<th>OraQUICK</th>
<th>UNI-GOLD</th>
<th>REVEAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Samples</td>
<td>- Oral fluid</td>
<td>- Whole blood</td>
<td>- Plasma</td>
</tr>
<tr>
<td></td>
<td>- Whole blood</td>
<td>- Plasma</td>
<td>- Serum</td>
</tr>
<tr>
<td></td>
<td>- Plasma</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>- Serum</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sensitivity</td>
<td>99.3*-99.6%</td>
<td>100%</td>
<td>99.8%</td>
</tr>
<tr>
<td>Specificity</td>
<td>99.8*-100%</td>
<td>99.7-99.8%</td>
<td>98.6-99.1%</td>
</tr>
<tr>
<td>Time</td>
<td>20-40 minutes</td>
<td>Exactly 10 min.</td>
<td>In 3 minutes</td>
</tr>
</tbody>
</table>

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
Fingerstick
Buccal Swab

Adapted from OraSure Technologies, Inc., Bethlehem, Pennsylvania
OraQuick ADVANCE® Rapid HIV-1/2 Test – cont’d

Read results in 20 – 40 minutes
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

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

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

Adapted from A. Levine, USC
“Know Thy Partner’s History”

Sex with 2 People $\rightarrow$ HIV+

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

Adapted from A. Levine, USC
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

CDC, CROI 2003: #2
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

CDC, MMWR 7/18/03; 52 (RR-12)
International Prevention Models

“ABC” – and – “CNN”

Abstinence  Condoms
Be Faithful  Negotiation
Condoms  Needle Exchange