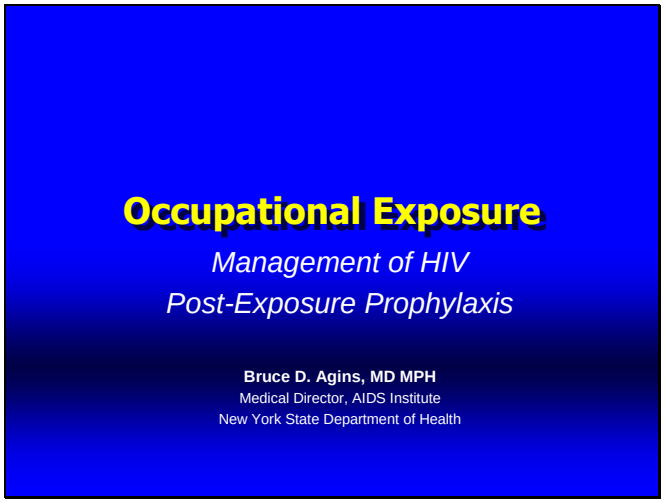
Update on Prophylaxis after Occupational Exposure to HIV

Bruce D. Agins, MD MPH, Instituto del SIDA, Departamento de Salud del Estado de Nueva York, EE.UU.

This session will provide the audience with an overview of current guidelines for the management of HIV prophylaxis following occupational exposure. The rationale for post-exposure prophylaxis (PEP) will be discussed, including a review of the CDC case-control study demonstrating the efficacy of PEP. Following this discussion of the scientific basis for PEP, an the current guidelines and recommendations will be presented. A comparison between the New York State and CDC guidelines will be introduced describing the pros and cons of each approach. Use of newer antiretroviral medications will be included in this discussion. Finally, practical strategies for implementing a PEP program at a hospital will be described, based on the experiences of health care providers in New York State.



RATIONALE

- Magnitude of the problem
- An opportunity for prevention
- Known successes of HIV prophylaxis

Spring 2002 New York State Department of Health AIDS Institute

Occupational HIV Infection

- Occupationally acquired HIV infection among HCW reported through 6/99
  - 137 possible cases of HIV transmission
  - 57 documented cases of HIV infection
  - 26/57 AIDS
- **Most exposures do not result in infection**

Spring 2002 New York State Department of Health AIDS Institute

Occupational HIV Infection

- **Factors influencing transmission**
  - Amount of blood involved in exposure
  - Amount of virus in patient's blood at time of exposure
  - Post-exposure prophylaxis

Spring 2002 New York State Department of Health AIDS Institute

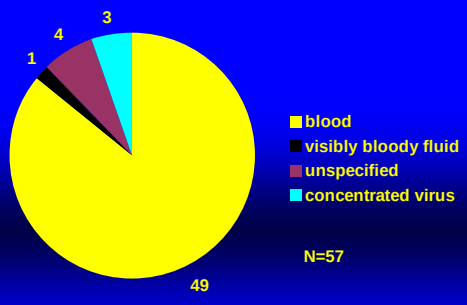
U.S. Health-Care Workers with Documented Occupationally Acquired HIV Infection, by Occupation through June 1999

OCCUPATION	
Nurse	**24**
Clinical laboratory technician	**16**
Physician (non-surgeon)	6
Non-clinical laboratory technician	3
Surgical technician	2
Housekeeper / maintenance worker	2
Morgue technician	1
Emergency med technician/paramedic	1
Respiratory therapist	1
Dialysis technician	1
Total	**57**

Spring 2002 New York State Department of Health AIDS Institute

Source Fluids for Exposures Resulting in Occupational HIV Transmission

US HCW reported through 12/98



Spring 2002 New York State Department of Health AIDS Institute

Risk Factors for HIV Transmission CDC Case Control Study

Risk Factor	Adjusted Odds Ratio (95% CI)	
Deep Injury	**16.2**	**(6.1-44.6)**
Visible blood	6	(1.8-17.7)
Terminal illness	6	(2.2-18.9)
In vessel	4	(1.9-14.8)
ZDV use	0.2	(0.1-0.6)

Cardo et al., NEJM;1997;337:1485-90 (updated)

Spring 2002 New York State Department of Health AIDS Institute

Exposure Risk

- **Percutaneous** **0.3%**
- Mucous membrane 0.1%
- Non-intact skin <0.1%

Spring 2002 New York State Department of Health AIDS Institute

Exposure Risk

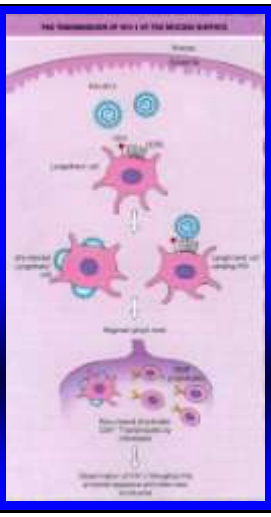
- ***Riskiest***
  - deep parenteral inoculation via hollow needle
  - parenteral inoculation with high viral titers
- ***Less Risky***
  - small volume via non-hollow needle
  - mucosal exposure/non-intact skin exposure
- ***Risk not identified***
  - intact skin exposure
  - exposure to urine, saliva, tears, sweat

Spring 2002 New York State Department of Health AIDS Institute

Rationale for PEP: *The Science*

- What we know about HIV transmission
- Animal Studies
- Immunology data
- *CDC Case-Control Study*
- Other Data
  - Perinatal Transmission Prevention: **ACTG 076**

Spring 2002 New York State Department of Health AIDS Institute



Spring 2002

Outcomes of HIV Exposures

- No infection ⌫ no immune memory
- Aborted infection ⌫ cellular immune response
- Acute infection ⌫ seroconversion

Spring 2002 New York State Department of Health AIDS Institute

Animal Studies of PEP:

Prevention of SIV in macaques with Tenofovir (PMPA)

- **24 macaques**
  - 4 / study arm
- **IV inoculation** of SIV
  - 10 X 50% animal infectious dose
- **Initiation** at 24, 48, 72h post exposure
- **Duration** 3,10, 28 days

Tsai et al, J Virol, 1998;72:4265

Spring 2002 New York State Department of Health AIDS Institute

Animal Studies of PEP: Prevention of SIV in macaques with Tenofovir (PMPA)

Initiation / duration	% Protected
24h / 28d	100%
48h / 28d	50%
72h / 28d	50%
24h / 10d	75%
24h / 3d	0

Tsai et al, J Virol, 1998;72:4265

Spring 2002 New York State Department of Health AIDS Institute

Animal Studies: Observed Outcomes

- Suppression or delay of antigenemia
- Early administration more effective than later
- Larger inocula decrease prophylactic efficacy
- Decreased doses result in decreased efficacy of antiviral prophylaxis

Spring 2002 New York State Department of Health AIDS Institute

Animal Studies: Problems in Interpretation

- No animal model is comparable to humans
- Higher inoculum used in most studies
- Other variables
  - viral strain
  - route of inoculation
  - time of initiation of prophylaxis
  - drug regimen (most ZDV)

Spring 2002 New York State Department of Health AIDS Institute

Human Data

- Controlled clinical trial not feasible
- CDC retrospective study
- Perinatal Transmission Prophylaxis

Spring 2002 New York State Department of Health AIDS Institute

PEP in Humans / HCW

- CDC Case Control Study
  - 33 cases / 679 controls
  - Identify risk factors
  - Logistic regression model
  - ***81% reduction in risk of HIV seroconversion in AZT group***

Spring 2002 New York State Department of Health AIDS Institute

CDC Case Control Study

	cases(%)	controls(%)
First dose < 4 hrs	67	89
Completed 4 wks	44	66
1000 mg ZDV	75	78
Receiving ZDV	71	70

Spring 2002 New York State Department of Health AIDS Institute

Risk Factors For HIV Transmission CDC Case Control Study

Risk Factor	Adjusted Odds Ratio (95% CI)	
Deep Injury	16.2	(6.1-44.6)
Visible blood	6	(1.8-17.7)
Terminal illness	6	(2.2-18.9)
In vessel	4	(1.9-14.8)
ZDV use	0.2	(0.1-0.6)

Cardo et al., NEJM;1997;337:1485-90 (updated)

Spring 2002 New York State Department of Health AIDS Institute

Limitations of CDC Study

- Study design
  - not RCT
  - cases and controls from different cohorts
- Bias
- Small numbers of cases
- Non-standard ZDV use

Spring 2002 New York State Department of Health AIDS Institute

PEP in Humans

- 076 study
  - randomized
  - ZDV last trimester, intrapartum and post-partum vs no rx
  - controls ⌫ 25% rate of transmission
    ZDV ⌫ 7% rate of transmission

Spring 2002 New York State Department of Health AIDS Institute

Other Perinatal Transmission Prophylaxis Data

New York State Observational Study

Timing of Prophylaxis Initiation	Number Born	Percent HIV-Infected
PRENATAL	423	6.1
INTRAPARTUM	50	10.0
BEFORE 48 hours POST-PARTUM	86	9.3
AFTER 48 hours POST-PARTUM	38	18.4
NO THERAPY	342	26.1

Spring 2002 New York State Department of Health AIDS Institute

Other Perinatal Transmission Prophylaxis Data

- UNAIDS PETRA Study:
  - ZDV/3TC initiated intrapartum and administered 1 week post-partum to mother and baby results in 10.8% transmission rate compared with 17.2% in the placebo group
- WITS and other observational NY Studies:
  - HAART substantially lowers transmission rates even further

Spring 2002 New York State Department of Health AIDS Institute

GUIDELINES

- Goal
- Caveat
- Sources
- HAART
- When to Treat
- Recommendations
- Controversies

Spring 2002 New York State Department of Health AIDS Institute

Guidelines: The Goal

- The ultimate goal of PEP is to maximally suppress any limited viral replication that may occur, and to shift the biological advantage to the host cellular immune system to prevent or abort early infection

Spring 2002 New York State Department of Health AIDS Institute

Indications for PEP

NYSDOH CDC

Recommendations are the same

- A mucous membrane, non-intact skin or percutaneous exposure to blood or visibly bloody fluid
- Source is potentially HIV infected

Spring 2002 New York State Department of Health AIDS Institute

Immediate Measures

- **Percutaneous:**
  - wash needlesticks and cuts with soap and water
  - remove foreign materials
- **Non-intact skin exposure:**
  - wash with soap and water or antiseptic
- **Mucous membrane**
  - flush splashes to the nose, mouth or skin with water
  - irrigate eyes with clean water, sterile saline or sterile irrigants

Spring 2002 New York State Department of Health AIDS Institute

Antiretroviral Regimens

NYSDOH	CDC
Universal Regimen ZDV 3TC + Nelfinavir → (Combivir)	Basic Regimen ZDV 3TC → (Combivir) Expanded Regimen Basic + indinavir or nelfinavir or efavirenz or abacavir

Spring 2002 New York State Department of Health AIDS Institute

Alternative Regimens

- Efavirenz – only in men
- Nevirapine – concerns about hepatotoxicity; dose escalation
- Stavudine – if ZDV-intolerance
- Indinavir – tolerability

- Tailoring to the source patient's known drug resistance profile/drug history

Spring 2002 New York State Department of Health AIDS Institute

Initiation of PEP

NYSDOH	vs. CDC
• Up to 36 hours post-exposure (*preferably within 1 hour*) • **Referral to "HIV specialist" within 72 hours**	• As soon as possible; may be appropriate up to one week for exposures of high

Spring 2002 New York State Department of Health AIDS Institute

Duration of Therapy

- Four week course of therapy
- Adherence

Spring 2002 New York State Department of Health AIDS Institute

NYSDOH vs. CDC

	PRO	CON
CDC	•Less expensive •Less toxic •Greater adherence?	•Complex •Imprecise definitions •Basic regimen inadequate for seroconversion •Adherence
NYSDOH	•Scientifically rational •Simplified decision points	•Expensive •Toxic •Adherence

AIDS Institute

ZDV PEP Treatment Failures in HCWs

World-wide Cases
- 21 failures in health care providers
- 5 failures in other settings
- no delay in time to seroconversion
- no adverse effects on natural history

Potential Explanations
- delay in treatment
- dose too low / low drug levels
- resistant virus
- high inoculum exposure
- treatment duration too short
- monotherapy is not efficacious
- host factors

Spring 2002 New York State Department of Health AIDS Institute

Implementation of PEP Programs

Designing a PEP Program

- Indications
- Timing and availability
- Access to therapy
- Testing and counseling

Institutional Procedures

- HAVE A PLAN for immediate evaluation of employees
- HAVE A PLAN for financial provision of PEP
- HAVE A PLAN to protect employee confidentiality about exposure, treatment and test results
- Review and Update annually

Institutional Procedures: Counseling

- Acknowledge and be prepared to address fright
- See the employee again in 2-3 days to answer questions, clarify issues
- Review medication then and again frequently
  - Possible toxicities/interactions; adherence
  - arrange for referral to HIV Specialist as appropriate
  - weekly monitoring while on treatment
- Provide contacts for questions

Spring 2002 New York State Department of Health AIDS Institute

Institutional Procedures: Counseling

- Provide counseling about sexual and reproductive issues
- Avoid breastfeeding
- Avoid donation of blood, plasma, organs, tissue or semen

Spring 2002 New York State Department of Health AIDS Institute

Procedures: Access to Therapy

- Access to the full course of PEP drugs should be covered by the employer/facility
- Should be made available at no cost to the employee: no OOP or insurance
- A 3-day supply should be immediately available
- **24 hr/7-day availability of services**

Spring 2002 New York State Department of Health AIDS Institute

Occupational Exposure & PEP: The Central Issues

- Assess the nature of the exposure, invoking significant risk standard
- Rapid initiation of PEP

Spring 2002 New York State Department of Health AIDS Institute

Reality of PEP

- Uncertain science but tremendous opportunity
- Rapid evaluation / implementation
- Adverse effects → adherence
- Comprehensive agency planning

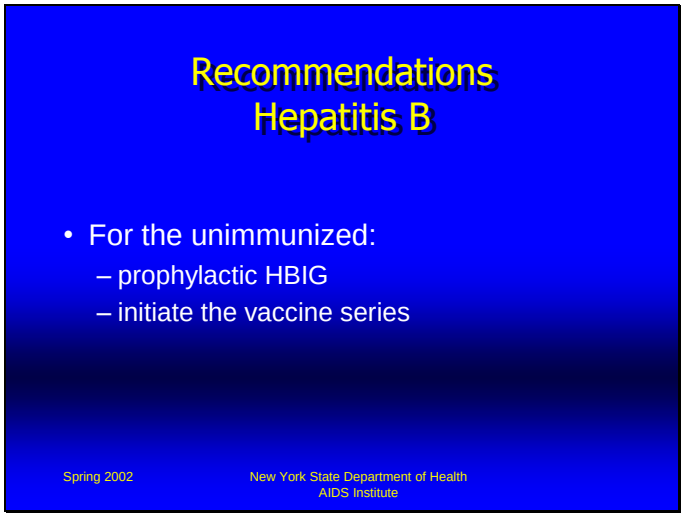
Spring 2002 New York State Department of Health AIDS Institute

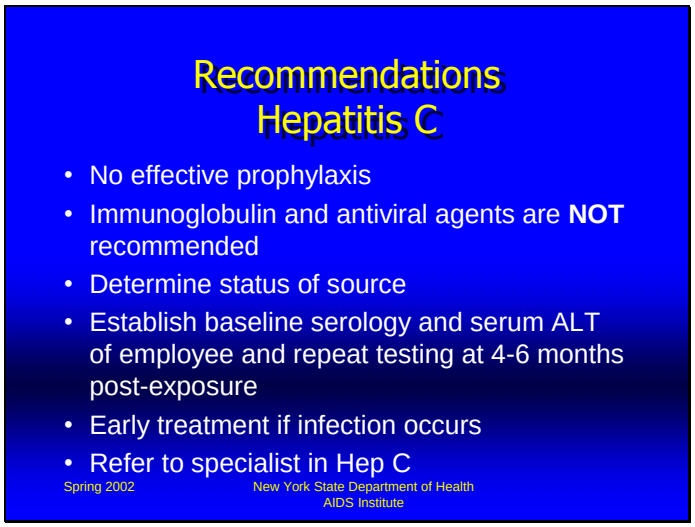
Acknowledgments

- Michael Foltzer, MD — Bassett Healthcare
- Lou Smith, MD — Albany Medical Center
- Barkat Fazal, MD — Bronx Lebanon Medical Center

- AIDS Institute
  - Mark Waters, RN MPH
  - Alvaro Carrascal, MD MPH

Spring 2002 New York State Department of Health AIDS Institute


Recommendations
Hepatitis B
• For the unimmunized:
– prophylactic HBIG
– initiate the vaccine series
Spring 2002
New York State Department of Health
AIDS Institute


Recommendations
Hepatitis C
• No effective prophylaxis
• Immunoglobulin and antiviral agents are NOT recommended
• Determine status of source
• Establish baseline serology and serum ALT of employee and repeat testing at 4-6 months post-exposure
• Early treatment if infection occurs
• Refer to specialist in Hep C
Spring 2002
New York State Department of Health
AIDS Institute