Managing Occupational Exposures to Bloodborne Pathogens

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Disclosure: Spouse works for Merck, Inc.

Presentation Includes: Discussion of unapproved off-label and/or investigational uses (prophylaxis) of one or more products (antiretrovirals and interferon-alfa).
Managing Occupational Exposures to Bloodborne Pathogens

- Historical Perspective - Epistemology
- The Magnitude of Occupational Risks
- Primary and Secondary Prevention
- PEP for HIV Exposures – Rationale and Guidelines
- Managing HCV Exposures
- Managing Infected Providers

How Many Occupational HIV Infections Have Occurred Among Health Care Workers?
### HIV Seroconversions

<table>
<thead>
<tr>
<th></th>
<th>U.S.</th>
<th>Other</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parenteral Exposures</td>
<td>52*</td>
<td>45</td>
<td>97</td>
</tr>
<tr>
<td>Mucocutaneous Exposures</td>
<td>7*</td>
<td>4</td>
<td>11</td>
</tr>
<tr>
<td>Total†</td>
<td>58</td>
<td>49</td>
<td>107</td>
</tr>
</tbody>
</table>

* Includes two individuals who had both parenteral and mucosal exposures
† Data complete through January 2014


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**What is the magnitude of risk for occupational HIV infection associated with a single parenteral exposure to blood from an HIV-infected patient?**
### Risk for Occupational HIV Infection Following Percutaneous Exposures

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of Studies</td>
<td>21</td>
</tr>
<tr>
<td>Number of Participants</td>
<td>6,267</td>
</tr>
<tr>
<td>Number of Percutaneous Exposures</td>
<td>6,498</td>
</tr>
<tr>
<td>Number of Seroconversions</td>
<td>21</td>
</tr>
<tr>
<td>Infection Rate per Participant</td>
<td>0.34%</td>
</tr>
<tr>
<td>Infection Rate per Exposure</td>
<td>0.32%</td>
</tr>
</tbody>
</table>

### Comparative Risks for Hepatitis B Transmission

- Risk for Transmission of Hepatitis B following a parenteral occupational exposure to ‘e’ antigen positive blood: 27 - 43%
- Risk for clinical hepatitis severe enough to require hospitalization: 6 - 24%
Occupational Risk for Infection with Hepatitis C

Number of Studies 25
Number of Percutaneous Exposures 2357
Number of Infections 44
Infection Rate per Exposure 1.9%
Range of Infection Rates 0 – 22.2%


Primary Prevention

Blood = Risk
Primary Prevention
Reducing Risk for Exposure

- Thoughtful Use of Universal/Standard Precautions
- Education – Retraining Staff about Occupational Risks
- Modification of Procedures and Work Practices
- Modification of Medical/Nursing School Curricula
- Engineered Controls – Use of Technological Advances
- Immunization

Parenteral Injuries/1000 Discharges, 1985 – 2013, NIH Clinical Center
What should you do if you sustain an occupational exposure to HIV?

Postexposure Antiretroviral Chemoprophylaxis for Exposure to HIV

Rationale for Electing to Offer Post-Exposure Chemoprophylaxis for Occupational HIV Exposures

1. Healthcare worker advocacy / PEP can be viewed as “empowering” by the exposed HCW.
Postexposure Antiretroviral Chemoprophylaxis for Exposure to HIV

Rationale for Electing to Offer Post-Exposure Chemoprophylaxis for Occupational HIV Exposures: in vitro data

2. Evidence suggests that antiretrovirals may block the dissemination of HIV from dendritic cells to susceptible T-cells.


3. T-cells from six of eight HIV-exposed (uninfected) healthcare workers produced IL-2 when exposed to HIV peptide antigens.

Clerici et al, JAMA 1994;271[1]:42-6

Postexposure Antiretroviral Chemoprophylaxis for Exposure to HIV

Rationale for Electing to Offer Post-Exposure Chemoprophylaxis for Occupational HIV Exposures: in vitro data

4. Cytotoxic T lymphocyte (CTL) responses to HIV env peptides were detected in 7/20 (35%) HCW exposed to HIV-positive blood.

(Pinto et al., JCI 1995;96[2]:867-76)
What *in vivo* evidence suggests that PEP is effective?

- Rate of transmission precludes a clinical trial
- Efficacy in preventing animal retroviral infection
- Efficacy in preventing maternal-fetal transmission
- Retrospective case-control study of occupational HIV infection
- Clinical experience since 1990

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*In vivo* evidence of PEP efficacy – Efficacy in Animal Models

A. Bottiger administered BEA-005 (2,3’-dideoxy-3’-hydroxymethyl cytidine) for 3 days to macaques and prevented both SIV and HIV-2 infection following either intravenous or intrarectal inoculation – (AIDS, 1997).

B. Tsai et al. – (PMPA)(Tenofovir®), demonstrated efficacy in a macaque/SIV model – (Science 1995).
**Postexposure Antiretroviral Chemoprophylaxis for Exposure to HIV**

*In vivo* evidence of PEP efficacy – Efficacy in Animal Models – PMPA / SIV

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>Dose</th>
<th>Type of Administration</th>
<th>Number of Infected * (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>5</td>
<td>20mg/kg</td>
<td>48h pre</td>
<td>0/5 (0)</td>
</tr>
<tr>
<td>2</td>
<td>10</td>
<td>30mg/kg</td>
<td>48h pre</td>
<td>0/10 (0)</td>
</tr>
<tr>
<td>3</td>
<td>5</td>
<td>30mg/kg</td>
<td>4h post</td>
<td>0/5 (0)</td>
</tr>
<tr>
<td>4</td>
<td>5</td>
<td>30mg/kg</td>
<td>24h post</td>
<td>0/5 (0)</td>
</tr>
<tr>
<td>5</td>
<td>10</td>
<td>– 0</td>
<td>none</td>
<td>10/10 (100)</td>
</tr>
</tbody>
</table>

* Infection = one or more of the following positive: PMBC culture; PCR; SIV antigen; SIV antibody


C. Further studies in the SIV/PMPA model have shown that:

- Duration is important – All animals treated for 28 days were protected; half those treated for 10 days, and none treated for 3 days, were protected.
- Delay is detrimental – None of the animals treated within 24 hours developed infection; only 50% treated 48 hours and 25% treated 72 hours after infection were protected.

In vivo evidence of PEP efficacy – Efficacy in Preventing Maternal-Fetal HIV Transmission

A. ACTG-076 demonstrated a 67% reduction in vertical HIV transmission. Only 30% of the reduction in transmission was explicable by reduction of maternal RNA.

### Efficacy of Antiretrovirals in Preventing Maternal-Fetal Transmission

<table>
<thead>
<tr>
<th>Study</th>
<th>Regimen</th>
<th>Timing*</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wade (1998)</td>
<td>ZDV</td>
<td>A+L+P</td>
<td>6.1% vs. 26.6%</td>
</tr>
<tr>
<td></td>
<td>ZDV</td>
<td>L+P</td>
<td>10.0% vs. 26.6%</td>
</tr>
<tr>
<td></td>
<td>ZDV</td>
<td>P (&lt;48 hr)</td>
<td>9.3% vs. 26.6%</td>
</tr>
<tr>
<td></td>
<td>ZDV</td>
<td>P (&gt;72 hr)</td>
<td>18.4% vs. 26.6%</td>
</tr>
<tr>
<td>Bulterys (1999)</td>
<td>ZDV</td>
<td>A+L+P</td>
<td>8.2% vs. 15.5%</td>
</tr>
<tr>
<td></td>
<td>ZDV</td>
<td>L+P</td>
<td>8.6% vs. 15.5%</td>
</tr>
<tr>
<td></td>
<td>ZDV</td>
<td>P</td>
<td>8.1% vs. 15.5%</td>
</tr>
<tr>
<td>Blanche (1999)</td>
<td>ZDV+3TC</td>
<td>A+L+P</td>
<td>2.6% vs. 6.5%</td>
</tr>
<tr>
<td></td>
<td>ZDV</td>
<td>A+L+P</td>
<td></td>
</tr>
<tr>
<td>Guay (1999)</td>
<td>ZDV</td>
<td>L+P</td>
<td>25.1% vs. 13.1%</td>
</tr>
<tr>
<td></td>
<td>NVP</td>
<td>L+P</td>
<td></td>
</tr>
</tbody>
</table>

*A - Prenatal therapy (usually beginning at 36 weeks)
L - Therapy during labor and delivery
P - Postpartum treatment of infant
**Postexposure Antiretroviral Chemoprophylaxis for Exposure to HIV**

**What is the Evidence that PEP is Effective – CDC Case-Control Study**

Risk for Occupational Infection Was Increased:

A. For “deep” injuries (p < 0.0001);
B. When blood was visible on the device causing the injury (p = 0.0014);
C. The injuring device had been placed in the source patient’s vein or artery (p = 0.0028);
D. The source patient died within 60 days of the exposure (p = 0.0011);
E. If the HCW did not take zidovudine (p = 0.0026).

**Postexposure Antiretroviral Chemoprophylaxis for Exposure to HIV**

**What is the Evidence that PEP is Effective – Clinical Experience**

A. CDC Case-control study.
B. Case-finding for occupational infections nationwide.
C. Anecdotal case suggesting efficacy in preventing transfusion-associated and occupationally-associated transmission of HIV.

Occupational HIV Infections by Year of Exposure Reported to CDC 1985 – 2013

Data Courtesy of Elise Beltrami, M.D., Denise Cardo, M.D., Lisa Panlilio, M.D. and David Kuhar, M.D., all from DHQP, CDC

Potential Factors Contributing to the Observed Decrease in Occupational HIV Transmissions

- Efficacy of HAART in lowering patients’ viral burdens.
- Efficacy of Primary Prevention (i.e., fewer exposures due to use of Universal/Standard Precautions).
- Decreased reporting to CDC / less aggressive case-finding.
- Efficacy of HAART in decreasing hospitalizations, as well as the numbers and types of procedures required.
- Presumed efficacy of Secondary Prevention (i.e., efficacy of antiretroviral PEP).
HIV PEP – Management of Occupational Exposure in Pregnancy

1. Pregnancy should not preclude the use of optimal PEP.
2. The counseling responsibility is redoubled for pregnant HCWs.
   • Risks for infection
   • What is known (and not known) about adverse drug effects for the HCW and her fetus.
3. Concern expressed about:
   • Potential for lactic acidosis and death with the ddI/d4t regimen,
   • The potential for mitochondrial toxicity in the newborn (nucleoside analogues),
   • Potentially carcinogenic and teratogenic Nelfinavir contaminant.

Resistance to Antiretroviral Agents: Implications for PEP

• Resistance to antiretroviral drugs occurs frequently in 2013;
• Transmission of resistant virus reported infrequently;
• Relevance of exposure to resistant virus is not well understood;
• Patients take many drugs; difficult to know to which drug(s) virus may be resistant (without genetic testing);
• Cross-resistance within drug classes.
Recommendations for Postexposure Management of Occupational HIV Exposure

HIV exposures with a recognized transmission risk

RAL + TDF + FTC

? DOL + TDF + FTG

ALTERNATIVE REGIMENS

**USPHS Recommendations for Postexposure Management of Occupational HIV Exposure**

**ALTERNATIVE ANTIRETROVIRAL AGENTS FOR USE AS PEP ONLY WITH EXPERT CONSULTATION**

<table>
<thead>
<tr>
<th>Agent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abacavir (Ziagen®; ABC)</td>
</tr>
<tr>
<td>Efavirenz (Sustiva®; EFV)</td>
</tr>
<tr>
<td>Enfuvirtide (Fuzeon®; T20)</td>
</tr>
<tr>
<td>Fosamprenavir (Lexiva®; FOSAPV)</td>
</tr>
<tr>
<td>Maraviroc (Selzentry®; MVC)</td>
</tr>
<tr>
<td>Saquinavir (Invirase®; SQV)</td>
</tr>
<tr>
<td>Stavudine (Zerit®; d4T)</td>
</tr>
</tbody>
</table>


**USPHS Recommendations for Postexposure Management of Occupational HIV Exposure**

**ANTIRETROVIRAL AGENTS GENERALLY NOT RECOMMENDED FOR USE AS PEP**

<table>
<thead>
<tr>
<th>Agent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Didanosine (Videx EC®; ddI)</td>
</tr>
<tr>
<td>Nelfinavir (Viracept®; NFV)</td>
</tr>
<tr>
<td>Tipranavir (Aptivus®; TPV)</td>
</tr>
</tbody>
</table>

**ANTIRETROVIRAL AGENTS CONTRAINDICATED AS PEP**

<table>
<thead>
<tr>
<th>Agent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nevirapine (Viramune®; NVP)</td>
</tr>
</tbody>
</table>

Current Antiretroviral Medications

NRTI
- Abacavir ABC
- Didanosine DDI
- Emtricitabine FTC
- Lamivudine 3TC
- Stavudine D4T
- Zidovudine ZDV
- Tenofovir TDF

NNRTI
- Delavirdine DLV
- Efavirenz EFV
- Etravirine ETV
- Nevirapine NVP
- Rilpivirine RPV

COMBINATION PRODUCTS
- Combivir (ZDV/3TC)
- Epzicom (ABC/3TC)
- Truvada (TDF/FTC)
- Trizivir (ZDV,3TC,ABC)
- Atripla (EFV,TDF,FTC)

PI
- Amprenavir APV
- Atazanavir ATV
- Darunavir DRV
- Fosamprenavir FPV
- Indinavir IDV
- Lopinavir/RTV LPV/RTV
- Nelfinavir NFV
- Ritonavir RTV
- Saquinavir SQV
- Tipranavir TPV
- Darunavir DRV

NNRTI
- Delavirdine DLV
- Efavirenz EFV
- Etravirine ETV
- Nevirapine NVP
- Rilpivirine RPV

COMBINATION PRODUCTS
- Combivir (ZDV/3TC)
- Epzicom (ABC/3TC)
- Truvada (TDF/FTC)
- Trizivir (ZDV,3TC,ABC)
- Atripla (EFV,TDF,FTC)

FUSION INHIBITOR
- Enfuvirtide T-20

CCR 5 RECEPTOR ANTAGONIST
- Maraviroc MVC

INTEGRASE INHIBITORS
- Raltegravir RAL
- Dolutegravir DOL

Significant Guideline Changes

- Changes
  - Complexity of recommendations (i.e., simplification)
  - No risk stratification (2 vs. 3 drugs)
  - Recommended regimens
  - Acceptable and non-acceptable agents
  - Follow-up –If 4th generation combination HIV p24 - HIV antibody test is used, testing may be concluded at 4 months after exposure

- Issues not changed
  - Recommended duration of therapy
  - ‘Kinetics’ of administration

Postexposure Prophylaxis for Occupational HIV Exposures

Basic Principles

- Treatment must be immediately accessible
- Make certain an exposure has occurred
- Choose a regimen that can be taken
- Be cognizant of source-patient’s therapy and viral burden (where available)
- Be familiar with the agents, their side effects, and the management of toxicity
- Anticipate and prophylactically treat side effects
- Monitor for toxicity and for adherence
- Access to and use of expert consultants

PEPline

National Clinicians’ Post-Exposure Prophylaxis Hotline (PEPline)
Free consultation for clinicians treating occupational exposures to HIV and other bloodborne pathogens...
24 hours a day
7 days a week
1-888-HIV-4911
http://pepline.ucsf.edu/pepline

a joint program of UCSF/SFGH CPAT / EPI Center supported by HRSA and CDC
Occupational HCV Exposure and Infection

Management – NIH Clinical Center Approach

- Test source patient for HCV antibody and, when appropriate, by PCR;
- Serologies, PCR and ALT for exposed healthcare worker at baseline and then periodically;
- Staff who develop repeatedly positive PCRs are either treated or referred to Hepatology service;
- “Preemptive Therapy” versus “Watchful Waiting”;
- ? Postexposure prophylaxis on the immediate horizon.

Occupational HCV Exposure and Infection

Why Treat Early?
Evidence from the Therapy of ‘Acute Hepatitis C’

- All patients received 5 million units of interferon - a2b subcutaneously daily for one month, then three times a week for 20 weeks.
- 42/43 evaluable patients were free of HCV RNA 24 weeks after therapy was completed (one patient lost to follow-up).

Why Treat Early?

Evidence from the Therapy of ‘Acute Hepatitis C’

• 14/44 had occupational exposures (e.g., needlestick injuries as the source of infection.
• Time from infection to first symptoms of hepatitis was 54 days (range 15 to 105 days)
• Time from infection to the initiation of therapy was 89 days (range 30 to 112 days)
• All had HCV RNA; in all 44 RNA became undetectable. Mean time to disappearance was 3.2 weeks (range 2 to 12).


Relevance of Treatment of ‘Acute Hepatitis C’

• Patients who develop “Acute Infection” with HCV are an unusual subset of HCV patients.
• Treating “Acute Infection” (as defined) may not be equivalent to “Preemptive Therapy”.
• Toxicity will likely be substantial; adherence will be a significant issue.
**Occupational HCV Exposure and Infection**

Arguments for ‘Preemptive Therapy’

- Viral genomic diversity is lowest early in infection; thus, infection may be more easily immunologically ‘defeated’.
- Acute infection is clearly more easily eradicated than is chronic infection (98% versus 65%).
- Hit hard; hit early.

*Ho D. NEJM 1995;333:450-1*

Arguments for ‘Watchful Waiting’

- Immunomodulators may be more effective after an initial cellular response; perhaps not relevant agents that have direct antiviral properties.
- ‘Natural clearance’ likely occurs with higher frequency than has been suspected (e.g., for “acute HCV hepatitis” 50% or more may recover spontaneously.
- Waiting will preclude substantial side effects and cost for those who clear spontaneously.

Occupational HCV Exposure and Infection

‘Preemptive Therapy’ or ‘Watchful Waiting’ – Codicils

- Data base as yet inadequate to make definitive recommendations.
- We do not know yet what fraction of HCWs mount a brisk cellular immune responses to HCV infection, resulting in complete resolution of infection.
- Generalizing from results of treatment of acute infection to preemptive therapy may be problematic.

‘Wildcards’

- Role of new HCV antivirals – administered as postexposure prophylaxis has not been assessed.
- Both protease inhibitors (e.g., Telaprevir, Boceprevir and Simeprevir) and Nucleoside analogs (e.g., Sofosbuvir) are marketed.
- More than 100 drugs in development; some are on the immediate horizon (e.g., Ledipasvir)
- True PEP for HCV may become a reality soon.
Nosocomial Epidemiology of Bloodborne Pathogen Infections

- Patient to provider transmission
- Patient to patient transmission
- Provider to patient transmission

\{ \textit{ALOccur} \}

Nosocomial Epidemiology of Bloodborne Pathogen Infections

- Patient to provider transmission – \textit{Common}
- Patient to patient transmission – \textit{Infrequent}
- Provider to patient transmission – \textit{Rare}
Primum non Nocere

Hepatitis B Transmission – Provider-to-Patient

1. Through 1994, investigators at the CDC identified 42 instances of provider-to-patient HBV transmission (375 patients).
   

2. Subsequently, two additional clusters of HBV infection occurred (both from HBeAg-positive surgeons).
   * Four patients acquired clinical hepatitis B infection from an orthopedic surgeon.
   * 19 patients of a thoracic surgery resident became infected.

3. No specific events or breaks in technique were identified in either cluster that could explain the transmissions, although the surgical resident did not wear double gloves.
Hepatitis B Transmission – Provider-to-Patient

4. Since 1996 there have been an additional ten reports of hepatitis B transmission from providers to patients.
   - These cases are generally associated with HBV infected surgeons; one case associated with an infected dentist;
   - Only one relatively recent report has been described from North America – 75 patients were infected from procedures involving placement of subdermal EEG electrodes by an HBeAg positive technician.


5. In four unconnected cases of acute hepatitis B infections, surgery was identified as a possible source. UK investigators tested the surgical teams. In each case a surgeon was found to be infected with so-called ‘precore mutants’ that were incapable of making ‘e’ antigen.


6. Because of several published instances of HBeAg-negative surgeons transmitting hepatitis B infection, some experts propose HBV DNA quantitation of HBeAg-negative workers to determine infectivity, as well as to provide a basis for deciding whether they should be allowed to perform exposure-prone procedures.

1. Provider-to-patient transmission of hepatitis C has been rarely reported in the US. Four documented reports in the literature since testing for this virus became widely available in 1990.

2. Conversely, in Europe, and particularly in the UK, transmission has been detected with a higher frequency.
   - Ten separate instances; 269 cases of HCV infection in patients

3. Healthcare provider intravenous substance use has been a common feature of several clusters.

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### Hepatitis C Transmission, Provider-to-Patient, U.S.*

<table>
<thead>
<tr>
<th>Type of HCW</th>
<th>Year</th>
<th>Cases Reported</th>
<th>Mode</th>
</tr>
</thead>
<tbody>
<tr>
<td>OP surgical tech</td>
<td>1991-92</td>
<td>~ 40</td>
<td>IVDU**</td>
</tr>
<tr>
<td>Anesthesiologist</td>
<td>1994</td>
<td>1/347 (0.3%)</td>
<td>Possible IVDU**</td>
</tr>
<tr>
<td>Cardiac surgeon</td>
<td>2001</td>
<td>14/937 (1.5%)</td>
<td>Exposure prone procedures</td>
</tr>
<tr>
<td>Nurse anesthetist</td>
<td>2004</td>
<td>16/142 (11.3%)</td>
<td>IVDU**</td>
</tr>
<tr>
<td>Surgical technician</td>
<td>2009</td>
<td>~ 23</td>
<td>IVDU**</td>
</tr>
</tbody>
</table>

** Contaminated needles or narcotics used for self-injection

* Courtesy of Joseph Perz, DrPH, MA. Division of Healthcare Quality Promotion, CDC
Historical risk associated with an exposure to blood from a hepatitis C infected source ranges between 0.5 and 2%.

Attack rates in UK lookbacks including index cases is 0.18%; excluding the index case 0.12% (also excludes studies with no transmissions).

Newer recommendations suggest determining risk based on circulating viral burden.

Nine cases, four providers, 25 years.
- Six cases associated with one US dentist
- Two cases in France, associated with two providers, one an orthopedic surgeon, the other a nurse providing postoperative care
- One case in Spain, in which a gynecologist apparently transmitted to a single patient during a C-section
HIV Transmission, U.S. – Dental Care

- Patient A - six visits; two third molar extractions, numerous procedures
- Patient B - 21 visits; extractions, prophylaxis, prosthodontics
- Patient C - 14 visits; extractions, periodontal scaling, restorative fillings
- Patient E - 14 visits; prophylaxis, fillings, crowns, endodontics
- Patient G - two visits; endodontics, restorative filling
- Patient I - one to three visits; prophylaxis, restorative fillings

HIV Transmission, U.S. – Dental Care

- Unique, and becomes more so with each passing day.
- Still a source of controversy; some investigators remain skeptical.
- No explanation for transmission.
HIV Transmission, U.S. – Dental Care

The Florida Case Cluster

Number of Patients in the Practice ~2000
Number of Patients Tested for HIV ~1100
Patients Infected with the Dentist’s Strain 6
Attack Rate 0.54%

Guidelines

Zero Risk vs.
“Significant Risk”
What is ‘Significant Risk’ for Transmission?

“Significant Risk – Standard essentially set by “the reasonable medical judgment of public health officials” (Arline vs. School Board of Nassau County)

Factors characterizing a risk as “significant”*

- Nature of the risk (route[s] of transmission)
- Duration of the risk (period of infectivity)
- Severity of the risk (potential for harm)
- Probability of transmission and harm

* From an Amicus curiae brief filed in Arline vs School Board of Nassau County filed on behalf of the American Medical Association

Existing Guidelines – U.S.

- HCWs who are infected with HIV or HBV and are ‘e’ antigen positive should not perform exposure-prone procedures unless they have sought the counsel of an expert review panel and been advised under what circumstances, if any, they may continue to perform these procedures. Such circumstances would include notifying prospective patients of the HCW’s seropositivity before they undergo exposure-prone invasive procedures.

Subsequently, in 1991 Congress passed P.L. 102-141 mandating states to adopt “CDC guidelines or their equivalent”.

CDC attempted to develop a list of exposure-prone invasive procedures with the help of professional medical associations but no consensus was reached.

In 1992 Dr. William Roper, then CDC Director, in a letter to state health departments, noted that the states, not CDC, would certify equivalency and further stated that “... exposure-prone procedures are best determined on a case-by-case basis, taking into consideration the specific procedure, as well as the skill, technique, and possible impairment of the infected health-care worker.”

Thus, as a result, substantial variability exists in state guidelines, and the role of the expert review panel is underscored.
How Much Variability? How Outdated?

In 2009, we reviewed existing laws and policies and interviewed State Health Department officials in all 50 States to review current practices:

- To evaluate existing variability among State approaches to this issue;
- To determine how many State laws require prospective notification and/or the convening of Expert Review Panels;
- To determine if policies have been modified since the early 1990’s to incorporate new scientific knowledge.


How Much Variability?

- Only 3/50 States adopted the CDC Guidelines directly;
- 42/50 States require an Expert Review Panel;
- One State requires prospective notification of all patients;
- One State requires prospective notification if transmission is shown to have occurred;
- 19 States require infected providers to notify patients of providers’ bloodborne pathogen infections; however, under highly variable circumstances
- Twenty-two States do not require prospective notification;
- Nine States’ guidelines do not address notification
How Outdated?

• Only 3 of 50 States have modified policies or laws since their initial passage in the early 1990’s;
• Only one State includes HCV in its statute;
• No State guideline, policy, or statute advocates the use of molecular methods or circulating viral burdens to assess provider risk.
• Since only 18% of states report that they have had to deal with this issue in the last 5 years, we conclude that problems with providers:
  ➢ not being detected,
  ➢ are not occurring commonly, or
  ➢ are being managed at levels below State Health Departments

Existing HBV Guidelines – U.K.

• HBV-infected providers who are ‘e’-antigen positive may not conduct exposure-prone invasive procedures.
• HBV-infected providers who are ‘e’- antigen negative, but have HBV DNA levels >1000 genome equivalents/ml may not conduct exposure-prone invasive procedures;
**Existing HBV Guidelines – U.K.**

- HBV-infected providers who are ‘e’- antigen negative, but have HBV DNA levels <1000 genome equivalents/ml may conduct exposure-prone invasive procedures, but must be retested at least every 12 months.
- UK currently considering whether those treated with antivirals who one year later have HBV DNA levels <1000, as well as those who are ‘e’ negative and have HBV DNA levels <1000 on treatment should be permitted to perform exposure prone procedures.

**Existing HCV Guidelines – U.K.**

- HCV-infected providers who have circulating HCV RNA may not conduct exposure-prone invasive procedures; trainees found to have circulating HCV RNA should be restricted from starting training in exposure-prone invasive procedures; HCV-infected providers who have circulating HCV RNA who receive antiviral treatment and become HCV RNA negative for a period of six months can be permitted to return to performing exposure-prone invasive procedures (retest in six months).
Existing HIV Guidelines – U.K.

**Either**

Be on effective combination antiretroviral therapy, **and**
Have a plasma viral load <200 copies/ml

**Or**

Be an ‘elite controller,’ be subject to plasma viral load monitoring every three months, be under joint supervision of a consultant occupational physician and their treating physician, and be registered with the UKAP Occupational Health Monitoring Register

HBV Recommendations – European Consensus Group

- HBV-infected providers who are ‘e’ antigen positive, should not perform exposure-prone procedures.
- HBV-infected providers who are ‘e’- antigen negative, but have HBV DNA levels <10,000 genome equivalents/ml **may** conduct exposure-prone invasive procedures, but must be retested at least annually.
- HCWs shown to transmit HBV **should not** perform exposure-prone procedures.
- HBV-infected providers who have been treated and whose post-treatment DNA levels have fallen to <10,000 genome equivalents/ml **may** conduct exposure-prone procedures, but must be retested every three months.
HCV Recommendations – European Consensus Group

- No consensus could be reached for HCV-infected providers, “on balance it is not recommended that exposure-prone procedures be forbidden for HCV-infected HCWs.”

HBV Recommendations – The Netherlands

- HBV-infected providers who have HBV DNA levels <100,000 genome equivalents/ml may conduct exposure-prone invasive procedures, but must be retested at least every annually.
**HIV Recommendations – German Association for the Control of Viral Diseases**

- “With a permanent viral burden of less than or equal to 50 copies/mL, HIV-positive HCWs are allowed to perform any surgery and any invasive procedure, as long as the infected HCW uses double-gloving, undergoes follow-up routinely by occupational medicine professionals, undergoes a quarterly examination of viral burden, and has a regular medical examination by a physician who has expertise in the management of HIV.
- Unrestricted professional activity is only possible with a strict compliance to take antiretroviral therapy and if the HIV-infected HCW strictly adheres to the recommended infection control procedures. Complete compliance with the recommendation almost certainly leads to no HIV transmission risk in patient care.”

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**SHEA Guideline – 2010**

- SHEA assembled a panel of experts to assess the existing SHEA position paper (1997) and to determine whether an update was needed.
- First conclusion – lots of progress in the BBP field since 1997 – not incorporated into the SHEA guidance.
- This group ultimately took the bold position that the data assembled over the last quarter century provided strong footing – when coupled with new molecular methods – for a new, rational set of guidelines.
- These guidelines were published in February 2010
**SHEA Guideline for Management of Healthcare Workers Who Are Infected with Hepatitis B Virus, Hepatitis C Virus, and/or Human Immunodeficiency Virus**

David K. Henderson, MD; Louise Dembkosky, MD, MS, MBA; Neil O. Fishman, MD; Christine Grady, RN, PhD; Tammy Landstreet, MD, IE; Tara N. Pahmore, MD; Kent A. Sepkowitz, MD; David J. Weber, MD, MPH.

for the Society for Healthcare Epidemiology of America

**EXECUTIVE SUMMARY**

This guideline provides the updated recommendations of the Society for Healthcare Epidemiology of America (SHEA) regarding the management of healthcare providers who are infected with hepatitis B virus (HBV), hepatitis C virus (HCV) or human immunodeficiency virus (HIV), and for hepatitis B virus (HBV) carriers. HBV carriers will be defined as having detectable hepatitis B surface antigen (HBsAg) and negative hepatitis B surface antibody (anti-HBs).

Circulating Viral Burden of Clinical Frequency of Testing

<table>
<thead>
<tr>
<th>Circulating Viral Burden</th>
<th>Categories of Clinical Activities</th>
<th>Recommendation</th>
<th>Frequency of Testing</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;10⁴ GE/mL</td>
<td>I, II, and III</td>
<td>No restrictions**</td>
<td>Twice annually</td>
</tr>
<tr>
<td>&gt;10⁴ GE/mL</td>
<td>I and II</td>
<td>No restrictions**</td>
<td>NA</td>
</tr>
<tr>
<td>≥10⁴ GE/mL</td>
<td>III</td>
<td>Restricted**#</td>
<td>NA</td>
</tr>
</tbody>
</table>

* Guideline emphasizes case-by-case management and encourages providers to work with their Occupational Medicine Staff and their physicians.

** Consonant with State laws, with codicils

# Permissible only when viral burden is <10⁴ GE/mL.
Infected Provider “No Restriction” Codicils

No restrictions recommended, so long as the infected healthcare worker:

1. is not detected as having transmitted infection to patients;
2. obtains advice from an Expert Review Panel about continued practice;
3. undergoes follow-up routinely by Occupational Medicine staff (or an appropriate public health official), who test the provider twice per year to demonstrate the maintenance of a viral burden of less than the recommended threshold;
4. also receives follow-up by a personal physician who has expertise in the management of her or his infection and who is allowed by the provider to communicate with the Expert Review Panel about the provider’s clinical status;
5. consults with an expert about optimal infection control procedures (and strictly adheres to the recommended procedures, including the routine use of double-gloving for Category II and Category III procedures and frequent glove changes during procedures, particularly if performing technical tasks known to compromise glove integrity [e.g., placing sternal wires]), and
6. agrees to the information in and signs a contract or letter from the Expert Review Panel that characterizes her or his responsibilities.
### 2010 SHEA Guideline – Hepatitis C*

<table>
<thead>
<tr>
<th>Circulating Viral Burden</th>
<th>Categories of Clinical Activities</th>
<th>Recommendation</th>
<th>Frequency of Testing</th>
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</thead>
<tbody>
<tr>
<td>&lt;10⁴ GE/mL</td>
<td>I, II, and III</td>
<td>No restrictions**</td>
<td>Twice Annually</td>
</tr>
<tr>
<td>≥10⁴ GE/mL</td>
<td>I and II</td>
<td>No restrictions**</td>
<td>NA</td>
</tr>
<tr>
<td>≥10⁴ GE/mL</td>
<td>III</td>
<td>Restricted**#</td>
<td>NA</td>
</tr>
</tbody>
</table>

* Guideline emphasizes case-by-case management and encourage providers to work with their Occupational Medicine Staff and their physicians
** Consonant with State laws, with codicils
# Permissible only when viral burden is <10⁴ GE/mL

### 2010 SHEA Guideline – HIV*

<table>
<thead>
<tr>
<th>Circulating Viral Burden</th>
<th>Categories of Clinical Activities</th>
<th>Recommendation</th>
<th>Frequency of Testing</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;5 X 10² GE/mL</td>
<td>I, II, and III</td>
<td>No restrictions**</td>
<td>Twice Annually</td>
</tr>
<tr>
<td>≥5 X 10² GE/mL</td>
<td>I and II</td>
<td>No restrictions**</td>
<td>NA</td>
</tr>
<tr>
<td>≥5 X 10² GE/mL</td>
<td>III</td>
<td>Restricted**#</td>
<td>NA</td>
</tr>
</tbody>
</table>

* Guideline emphasizes case-by-case management and encourage providers to work with their Occupational Medicine Staff and their physicians
** Consonant with State laws, with codicils
# Permissible only when viral burden is <5 X 10² GE/mL
Rationale for Viral Burden Cutoffs

• For HBV and HCV cutoffs, one modeling experiment suggested that a suture needlestick exposure to a provider who had a viral burden of $10^4$ GE/mL would be associated with an exposure to less than 1 virion?


• For the HIV cutoff, since allowing HIV-infected practitioners to participate in category III procedures is virtually unprecedented, we chose a more conservative cutoff. Since HIV infected individuals who have “undetectable” viral burdens occasionally spike to 500 GE/mL, we chose $5 \times 10^2$ as the cutoff.

Sources: Tara Parker-Pope. New York Times, “What Should We Be Scared Of?” October 2007. Primary data sources: Unless otherwise noted, all accidental death information from National Safety Council. Lifetime risk is calculated by dividing 2003 population (290,850,005) by the number of deaths, divided by 77.6, the life expectancy of a person born in 2003. *Shark data represents number of attacks worldwide, not deaths. Iatrogenic HIV infection risk assumes all six infected patients have died.

Compared to What????

<table>
<thead>
<tr>
<th>Risk</th>
<th>Annual Deaths</th>
<th>Lifetime risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart disease</td>
<td>652,486</td>
<td>1 in 5</td>
</tr>
<tr>
<td>Cancer</td>
<td>553,888</td>
<td>1 in 7</td>
</tr>
<tr>
<td>Stroke</td>
<td>150,074</td>
<td>1 in 24</td>
</tr>
<tr>
<td>Hospital infections</td>
<td>99,000</td>
<td>1 in 38</td>
</tr>
<tr>
<td>Flu</td>
<td>59,664</td>
<td>1 in 63</td>
</tr>
<tr>
<td>Car accidents</td>
<td>44,757</td>
<td>1 in 84</td>
</tr>
<tr>
<td>Suicide</td>
<td>31,484</td>
<td>1 in 119</td>
</tr>
<tr>
<td>Accidental poisoning</td>
<td>19,456</td>
<td>1 in 193</td>
</tr>
<tr>
<td>MRSA</td>
<td>19,000</td>
<td>1 in 197</td>
</tr>
<tr>
<td>Falls</td>
<td>17,229</td>
<td>1 in 218</td>
</tr>
<tr>
<td>Drowning</td>
<td>3,306</td>
<td>1 in 1,134</td>
</tr>
<tr>
<td>Bike accident</td>
<td>762</td>
<td>1 in 4,919</td>
</tr>
<tr>
<td>Air/space accident</td>
<td>742</td>
<td>1 in 5,051</td>
</tr>
<tr>
<td>Excessive cold</td>
<td>620</td>
<td>1 in 6,045</td>
</tr>
<tr>
<td>Sun/heat exposure</td>
<td>273</td>
<td>1 in 13,729</td>
</tr>
<tr>
<td>Shark attack*</td>
<td>62</td>
<td>1 in 60,453</td>
</tr>
<tr>
<td>Lightning</td>
<td>47</td>
<td>1 in 79,746</td>
</tr>
<tr>
<td>Train crash</td>
<td>24</td>
<td>1 in 156,169</td>
</tr>
<tr>
<td>Fireworks</td>
<td>11</td>
<td>1 in 340,733</td>
</tr>
<tr>
<td>Iatrogenic HIV Infection</td>
<td>0.2</td>
<td>1 in 18,740,335</td>
</tr>
</tbody>
</table>

Sources: Tara Parker-Pope. New York Times, “What Should We Be Scared Of?” October 2007. Primary data sources: Unless otherwise noted, all accidental death information from National Safety Council. Lifetime risk is calculated by dividing 2003 population (290,850,005) by the number of deaths, divided by 77.6, the life expectancy of a person born in 2003. *Shark data represents number of attacks worldwide, not deaths. Iatrogenic HIV infection risk assumes all six infected patients have died.
**Significant Unanswered Questions???

- Should HCW testing be mandatory?
- What is the optimal way to include a consideration of technical skill/competence?
- Is any level of risk tolerable?
- Does therapy make a difference?

**Contact Information**

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- **Telephone** – 301-496-3515