AMERICAN COLLEGE OF EMERGENCY PHYSICIANS
SCIENTIFIC ASSEMBLY
1999

To Treat or Not to Treat: An Approach to High-Risk Exposures

The emergency department often is the first referral and counseling resource for the lay public as well as hospital employees who have been exposed to potentially transmissible disease. Today, one must be cautious of contracting tuberculosis, HIV, and hepatitis. The presenter will discuss the risks associated with the various types of exposures, along with the current published recommendations for prevention and chemoprophylaxis.

- Discuss the risk associated with bodily fluid and needlestick exposures and how to effectively counsel with regard to the risk of disease transmission, hepatitis and HIV prophylaxis, and follow-up.
- Analyze published recommendations regarding chemoprophylaxis after an exposure, including chemoprophylaxis after rape.
- Discuss the appropriateness of the BCG vaccine in the prevention of tuberculosis.
- Understand the risk of developing bacterial meningitis following occupational exposure

TU-75
Tuesday, October 12, 1999
9:00 AM - 10:55 AM
Room # N242
Las Vegas Convention Center

FACULTY

Peter E Sokolove, MD

Assistant Professor, Medicine, UC Davis School of Medicine, Davis, California; Associate Residency Director, Emergency Medicine, UC Davis Medical Center, Sacramento, California

VARICELLA-ZOSTER VIRUS (VZV)

Overview

- 4 million Chicken Pox cases each year in the U.S
- 15% eventually develop Shingles
- Childhood chicken pox -- fever, malaise, rash (250-500 lesions, 5-7 days)
- Complications in children - bacterial superinfection, acute cerebellar ataxia, cerebritis, Reye's syndrome (rare), others (nephritis, myocarditis, arthritis, coagulation defects)
- Congenital VZV - abnormalities of skin, lungs, eyes, CNS- 2% of births with VZV in first or second trimesters

B. *Epidemiology*

- Mainly in kids less than 8 years old
- After age 12, 10% are susceptible
- Adults becoming more susceptible (immigration from tropical countries)

C *Primary Varicella in Adults*

- Adults have 9-25 times risk of complications compared to children
- About 1% of adults require hospitalization
- Most common complication is VZV pneumonia
- Diffuse, bilateral, miliary pattern characteristic on CXR
- Less than 100 deaths per year in the U.S.
- Adults are 2% of cases but 50% of deaths
- Only 25% of deaths are in immunocompromised patients

D *Transmission*

- Airborne droplets or direct contact with infected lesions
- Incubation period 14-16 days (but can be 10-21 days)
- Infectious prior to onset of rash
- Moderate to high infectivity -- household secondary attack rate of 85%
- Unclear exactly what constitutes an exposure

E. *Treatment of Adults -- Acyclovir*

1. *PO Acyclovir*

- Wallace (1992): Acyclovir 800 mg 5 times a day for 7 days vs. Placebo
- Beneficial if given within 24 hours of rash
- Not for pregnant patients with varicella
- Valacyclovir reasonable alternative (1 g TID for 7 days)

IV Acyclovir

- For immunocompromised patients with varicella or zoster
- Patients with significant complications of varicella

F. *Prevention -- Varicella-Zoster Immune Globulin (VZIG)*

- Can prevent or modify course of varicella
- Does not work once disease is established
- Given within 48 hours of exposure, not after 96 hours
- For susceptible individuals at high risk of complications
- Not for normal adults
- Exposure after 5 days following rash onset is lower risk

- Main indications:
  - -- immunocompromised
  - -- pregnancy (helps mother, maybe fetus)
  - -- newborns (maternal rash 5 days before to 2 days after delivery)
- One vial (125 units/l.25 cc) per 10 kg IM up to 5 vials
- Costs about $75 per 125 units
- Modified infection may not give life-long immunity

G *Prevention -- VZV Vaccine*

1. *Overview*

- Varivax (Merck) - live attenuated vaccine licensedby the FDA in 1995
- Vaccination of susceptible healthcare workers is cost-effective

2 *Vaccine Safety*

- Common adverse reactions: local (25%), sparse rash within 1 month (5%)
- Children with leukemia have 50% incidence of rash
- Leukemic children given the vaccine may transmit VZV to others, but secondary cases were subclinical or mild
- Case reports of transmission from healthy patients who are vaccinated to others

Zoster Incidence

- Eight cases of zoster occurred in 9,000 vaccinated healthy kids after 10 years
- This is the same rate of zoster for natural infection
- No severe or disseminated cases occurred
- Vaccinated leukemic children had a lower incidence of zoster

4. *Immunogenicity and Effectiveness*

- Cell-mediated immunity (CMI) most important, but titers correlate with CMI
- Seroconversion 97% ages 1-12 years (1 dose), 94% for adults given 2 doses
- Not known low long immunity lasts:
  - -- 25 Japanese children all had antibodies at 20 years after vaccination
  - -- Of 214 U.S. children 95% had antibody up to 6 years after vaccination
  - -- Of 40 adults, 82% had antibodies at 7 to 13 years
- Breakthrough cases are usually mild (< 50 lesions)

Cost

- Cost to physician approximately $39 per dose
- Cost to test antibodies approximately $68 to $77 per dose

6. *Recommendations for vaccine*

- One subcutaneous dose (0.5 cc) for kids 1-12 years old without prior VZV
- 2 doses 4 to 8 weeks apart for adolescents and adults
- Unknown if boosters will be needed for adult
- Not for immunocompromised patients or those with recent steroid use
- Probably safe for patients using inhaled steroids only
- Not for pregnant patients (or pregnancy planned within 3 months)
- Avoid salicylates for 6 weeks

7. *Vaccine for ED Personnel -- Special Concerns*
   - Check antibody levels at 6 weeks after second vaccination to assess response
   - Can return to work, but watch for rash, malaise, or fever
   - Avoid immunocompromised, newborn. or seronegative pregnant patients

H. *Emergency Department Exposure*
   - Determine if significant exposure: ventilation, time, activity
   - Attack rates of 5-10% after exposure
   - Check VZV titer (not reliable if immunocompromised)
   - VZIG only if immunocompromised and not known to be immune
   - Off for days 10 to 21 if significant exposure
   - Acyclovir within 24 hours of rash
   - Room ventilation - depends on air changes per hour, 1 hour probably safe

IL BACTERIAL MENINGITIS -- *Neisseria Meningitidis*

A *Overview and Epidemiology*
   - Gram negative diplococcus
   - Multiple serogroups (A, B, C, X, Y, Z, 29-E, and W-135)
   - Second leading cause of bacterial meningitis in adults (IO-35% of U.S. cases)
   - Serotypes B and C most common in U.S. (each causes 45% of invasive cases)
   - Serotype A often associated with epidemics around the world

B. *Transmission*
   - Asymptomatic colonization of upper respiratory tract (1-35% per year)
   - Transrmssion by droplets of respiratorv secretions
   - Usually attacks age <5 years, peaks ages 3-5 months
   - Transmission facilitated by close contact, low socioeconomic conditions, temperature and humidity, concomitant viral infections, smoking, non-secretor of Lewis blood group.
   - Outbreaks in semi-closed communities
   - Increased risk for disease: terminal complement deficiency (C5-9), asplenia
   - Incubation period l-10 days, usually <4 days
   - Infectious for about 24 hours after starting antibiotics
   - Disease risk after contact: 57% week 1, 18% week 2. 9% week 3. 16% weeks 4-6

C *Disease Prevention*
   - Risk group includes all ages
   - Household contacts attack rate 4/1000
   - Relative risk: household contacts 1245, day care 76, nursery school 23
   - Chemoprophylaxis indications (preferably within 24 hours):
     -- Household, day care, and nursery school contacts
     -- People contacting oral secretions of index case (kissing, sharing food or drink)
     -- HCWs with exposure to secretions (mouth-to-mouth, intubation. suctioning)

D. *Chemoprophylaxis Regimens*

- Rifampin 10 mg/kg/dose BID x 4 doses (up to 600 mg/day)
  - -- About 95% effective
  - -- Resistance reported when used extensively
- Ceftriaxone 125 mg IM if age <1 year, or 250 mg for adults (choice for pregnancy)
  - -- 97% effective in Saudi Arabia Group A outbreak
- Sulfisoxazole (if known susceptible) for 2 days
  - -- 500 mg q.d. age <1 year
  - -- 500 mg b.i.d. age 1-12 years
  - -- 1 g b.i.d. age > 12 years
- Ciprofloxacin 500 mg po x 1 also effective (not used in children or pregnancy)
  - -- Several studies show 93-97% effective

E. *Meningococcal Vaccine*

- Quadrivalent: A, C, Y, W-135 (50 mcg of each purified capsular polysaccharide)
- Single 0.5 cc SQ dose
- Kids <18 months need 2 doses (3 months apart)
- Group A immunogenic in age >3 months, Group C in >2 years
- Lasts probably <3 years, especially if given at very young age
- Indications:
  - -- high risk children >2 years old (terminal complement deficiency, asplenia)
  - — chemoprophylaxis adjunct if caused by a vaccine serogroup
  - -- travelers to areas with hyperendemic or epidemic disease
- Adverse reactions: localized erythema 1-2 days, unknown if safe in pregnancy

ED Exposure to Meningococcal Meningitis

- Organism identification by gram stain, CIE, latex agglutination, or culture
- Determine exposure -- intubation, suctioning, secretion contact, ≥ 8 hours
- Begin prophylaxis within 24 hours
- Vaccinate if appropriate serotype
- Do not wear contact lenses if taking rifampin

III. NEEDLESTICK INJURIES

Overview

- ED workers are at high risk of blood-borne pathogen exposure
- Universal precautions are imperfect
- Many HCWs come to the ED for evaluation and management
- Under-reporting is common (housestaff do not report 60 - 95%)
- Timely evaluation and treatment is important

Hepatitis B Virus (HBV)

1. *Overview*

- About 300,000 cases in the U.S. each year
- Risk groups: area of high prevalence - Asia/Africa, IVDA, dialysis, homosexual males, sexual partners of those with HBV
- 12,000 HCW infections and 200-300 deaths each year

2. *Clinical Course*

- Most are asymptomatic
- 25% acute hepatitis
- 6-10% chronic hepatitis
- 2-3% cirrhosis
- Increased risk of hepatocellular carcinoma

3. *Serologic Markers*

- Surface antigen (HBsAg) = active infection, transmissible
- Surface antibody (HBsAb) is protective
- E antigen (HBeAg) = peak virus replication levels

Transmission

- Up to 30% of high-risk workers are already infected
- Much more transmissible than HIV
- Not all patients can transmit disease
- Once symptomatic, HBsAg usually present for one month
- Risk of transmission 2 % (HBeAg absent) to 40% (HBeAg present)

Hepatitis B Immune Globulin (HBIG)

- Passive immunization for non-immune individuals
- Derived from pooled human plasma
- No evidence of transmitting disease
- Should be given < 72 hours after exposure
- Of questionable value beyond 7 days

6. *Hepatitis B Vaccine*

- Recombinant vaccine from yeast cells containing HBsAg gene
- Initial IM injection, then at 1 and 6 months
- Adverse reactions: redness, low-grade fever, rash, nausea, joint pain or mild fatigue
- Safe to give during pregnancy

Hepatitis B Vaccine -- Immune Response

- Antibody drawn 4-6 weeks after series completed (desired titer ≥ 10 SRU)
- Three doses immunogenic in 90% of adults and 95% of children
- Non-responder risk factors: obesity, age > 50, smoking, immunosuppressed
- May need extra doses or intradermal vaccine
- About 100% effective if 3 doses and respond
- Duration of protection undetermined (at least S years)
- 25-50% of responders lose “protective” Ab levels within 5-7 years, but still protected against clinical disease

8. *Post-Exposure Prophylaxis*

- May require vaccine, HBIG, both or neither
- Depends upon vaccination and antibody response of HCW
- See *MMWR* Table 5

Hepatitis C Virus (HCV)

1. *Overview*

- 1.8% of Americans are infected (3.9 million)
- 40% of HCV infected persons do not know they are infected
- Acquired from IVDA, blood transfusions, sexually (minor)
- Transfusion risk is now low

Clinical Course

- Often asymptomatic or mild
- Symptoms usually appear SO days after exposure
- 85% chronic hepatitis
- 60-70% elevated LFTs
- 10-20% cirrhosis
- 1-5% hepatocellular carcinoma

Seroconversion

- Antibodies at 10 weeks- 10 months after exposure (l-8 months after symptoms)
- Usual delay in HCV antibody development is 4-6 months
- Incidence of seroconversion following HCV positive needlestick is about 1.8% (estimates range 0-7%)
- Vaccine is not available (high heterogeneity, rapid mutation rate)
- Immune globulin not helpful after exposure

Human Immunodeficiency Virus (HIV)

1. *Overview*

- 12-14 million HIV+ worldwide, 1.5 million in U.S.
- Marcus et al -- 9% of ED patients HIV+
- John Hopkins University ED seroprevalence study (1987) -- 5.2% HIV+, 13.6% penetrating trauma, only 23% known symptomatic

Seroconversion in HCWs

- As of 6/97 -- 52 US HCWs with occupational seroconversion
- 114 additional HCWs with possible occupational HIV
- 81% acute retroviral syndrome (median 25 days)
- Antibodies begin at 3 weeks, almost always HIV+ by 6 months
- Rare reports of seroconversion at 6-12 months (HCV co-infection)

Risk of Transmission

- High risk fluids: blood, semen, amniotic fluid, blood-tinged fluids
- Lower risk fluids: urine, tears, saliva (little to no measurable virus)
- HIV negative patients can transmit disease (very unlikely)
- Mucocutaneous -- large volume, prolonged contact, portal of entry
- No reports of seroconversion via exposure to intact skin
- Probably not transmitted by aerosol
- Gloves may decrease blood transmitted by 46-86% (Mast et al.)

Exposure	Seroconversion Risk
Needlestick	1/300 (0.3%)
Mucous membrane	< 1/1000
Transfusion 1 unit screened PRBC	< 1/300,000
Receptive anal intercourse	1/100
Female to male sexual transmission	1/1500

Risk factors for HIV transmission after percutaneous blood exposure (Cardo DM, et al., *NEJM*, 1 1/97)

Risk Factor	Odds Ratio	95% CI
Deep injury	1s	6-41
Blood visible on device	6.2	2.2-21
Procedure with needle placed directly into artery or vein	4.3	1.7-12
Terminal AIDS in source patient	5.6	2-16
Post-exposure zidovudine	0.19	0.06-0.52

4. *Viral Load and HIV Transmission*

- Viral load measures HIV RNA
- Animal studies show increased risk of transmission with higher viral load
- Plasma viral load reflects only cell-free virus in blood
- Does not measure cell-associated virus or other areas (e.g. lymphatics)
- Transmission may still occur at low viral loads

Host Immune Response

- Unclear if this is an important factor in transmission
- Small study of HIV-exposed but uninfected HCWs (Pinto LA, et al.)
- HIV-specific cytotoxic T-lymphocyte response by stimulated monocytes
- Similar response in uninfected HCWs with repeated exposures
- May represent a protective response or just a marker for exposure

6. *Theoretical Basis for Post-Exposure Prophylaxis*

- "Window of opportunity" before infection is established
- Animal studies -- initial targets are skin dendritic cells
- These help initiate infection of CD4 cells in regional lymph nodes
- PEP may prevent or limit HIV replication in dendritic cells or nodes

Evidence Supporting Post-Exposure Prophylaxis

- Animal studies are mixed in methodology and outcomes
- Demonstrated beneficial outcomes include:
  - -- Delayed viremia or antigenemia
  - -- Development of cellular immune response
  - -- Prevention of infection
- AZT during pregnancy decreased perinatal transmission by 67% (AIDS Clinical Trial Croup protocol 076)
- CDC case-control study (*MMWR* 1995, *NEJM* 1997)

8. *Post-Exposure Prophylaxis with Zidovudine (AZT)*

- CDC case-control study in US, France, UK, and Italy
- 33 HCW seroconversions (23 US) vs. 665 controls
- 91% needlesticks (96% hollow), 9% other sharp objects
- Less seroconversion if used AZT (OR 0.2; 95%CI, 0.06-0.52)
- Risk for HIV infection was reduced by 81% (95% CI, 48 - 94%)

Post-Exposure Prophylaxis -- Prospective Studies

- 1987-1989, Burroughs-Wellcome sponsored trial
- AZT vs. placebo for 6 weeks
- Terminated prematurely due to low enrollment
- Placebo-controlled trial now very unlikely

10. *AZT Dosage and Toxicity*

- Nucleoside reverse transcriptase inhibitor
- Divided doses totaling 600 mg daily (e.g. 200 mg TID)
- Treatment is continued for 4 weeks
- Short term toxicity = GI discomfort and fatigue
- 3 1% of HCWs discontinue due to symptoms
- Hematologic toxicity (reversible) is rare in healthy individuals

11. *Multidrug Prophylaxis*

- AZT is the only drug shown to beneficial for PEP in humans
- Combination prophylaxis reasonable due to resistance and synergistic effects in AIDS patients
- Resistance suspected if source not responding to AZT
- One study showed AZT resistance in 11% of new HIV infections
- No direct evidence that combination regimens are beneficial
- AZT worked in ACTG protocol 076 study even if resistant strain

12. *Lamivudine (3TC)*

- Nucleoside reverse transcriptase inhibitor
- Synergistic antiviral activity with AZT
- Decreases emergence of resistant strains
- No increased side effects when added to AZT
- Toxicity = GI symptoms, pancreatitis is rare
- 3TC dose is 150 mg BID (4 weeks)
- Preliminary data -- 24-36% HCWs discontinue AZT + 3TC

13. *Other Nucleoside Reverse Transcriptase Inhibitors*

- Combivir = AZT 300 mg plus 3TC 150 mg (taken BID)
- Danosine (ddI), zalcitabine (ddC), and stavudine (d4T) are alternatives
- 3TC is generally first line

14 *Protease inhibitors -- Overview*

- Inhibit HIV aspartyl protease (very specific)
- Potent antiviral activity in vitro and in vivo

- Do not require phosphorylation
- Recommended for high risk exposures
- Indinavir or nelfinivir is preferred
- Alternatives include saquinivir (poor bioavailability) and ritonavir (more side effects, start gradually)

15. *Protease inhibitors -- Dosing and Toxicity*

- IDV dose is 800 mg TID
- IDV toxicity = GI, hyperbilirubinemia (10%), renal stones (4%)
- Nelfinavir dose is 750 mg TID
- Nelfinavir toxicity = diarrhea
- All PIs can cause hyperglycemia (even DKA)

16. *Non-nucleoside Reverse Transcriptase Inhibitors*

- Nevirapine and delaviridine
- Rapid onset and highly potent
- More pronounced side effects
- Alternative agents available
- Not recommended for routine PEP

17. *Who Needs Post-Exposure Prophylaxis?* -- Figure 1 (*MMWR* S/l 5/98)

18. *Timing of Post-Exposure Prophylaxis*

- Animal models may not be relevant and human data is limited
- Shih et al. gave SCID-hu mice IV dose of HIV that infects 100%
- AZT single dose intraperitoneal then 2 weeks in drinking water

Time to drug after exposure	Infection rate
2 hours	0%
4 hours	10%
8 hours	20%
24 hours	60%
36 hours	80%
48 hours	100%

- Case-control study 89% of cases started AZT within 4 hours
- Best to start promptly, preferably within 1 hour of exposure

19 *Cost of Post-Exposure Prophylaxis*

Drug	Daily	4 weeks
Zidovudine	$7.62	$213
Lamivudine	$6.14	$172
Indinavir	$12	$336
Triple Therapy	$25.76	$721

20. *Cost -Effectiveness (Pinkerton et al)*

- Hypothetical cohort of 100,000 exposed HCWs
- Total program costs = $4.8 million
- Cost per averted infection = $400,000
- Cost per quality-adjusted life year saved:

Exposure Risk	cost / QALY
Low (0.1%)	$136,000
Base Case (0.3%)	$37,000
High (0.5%)	$17,000
Very high (1%)	$2,400

- PEP does not save money
- PEP is cost-effective when using PHS guidelines
- Triple therapy saves money if only minimally superior (79.02% vs 79% efficacy)

Summary of ED Needlestick Exposures

1 *Evaluation*

- Complete incident report
- Assess risk of disease transmission:

Injury	Source	HCW
Infectious material	HIV and hepatitis risk factors	Medical history
Instrument	Clinical symptoms	Immunizations
Procedure	CD4 count	Pregnancy
Depth	Vial load	
Volume	HIV therapy	

- Test source blood: HBsAg, HCV, HIV (consent)
- Test HCW: HBsAb, HIV, pregnancy test
- Testing of sharp instruments not recommended or reliable

Acute Management

- Wash with soap and water / flush mucous membranes
- Address tetanus status
- Administer HBIG and/or HB vaccine as indicated (see Table 5)
- Chose PEP regimen based upon exposure and HIV status
- Discuss HIV PEP with HCW
- Clinician's Hotline -- (888) 448-4911

3. *HCW Follow-Up Management*

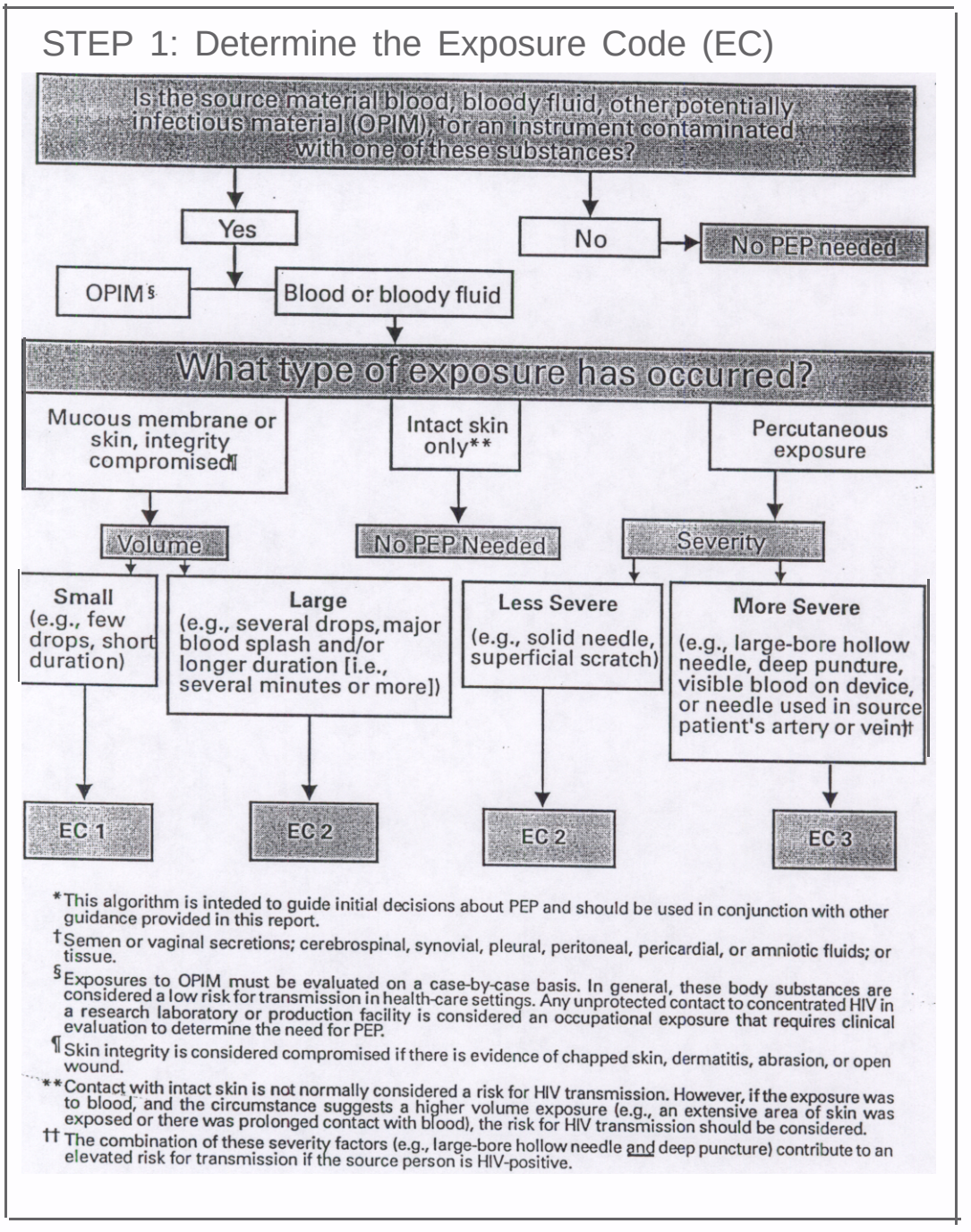
- HIV test baseline, 6 and 12 weeks, 6 months (12 months optional)
- HIV test if acute retroviral syndrome at any time
- If source has hepatitis C or IVDA -- test for hepatitis C antibody and ALT at baseline, 3 and 6 months, and one year
- If PEP used -- CBC, Chem-7, LFTs at baseline and 2 weeks
- Antiemetics or antidiarrheal agents may be used

TABLE 5. Recommendations for hepatitis B prophylaxis following percutaneous or permucosal exposure

Exposed person	Treatment when source is found to be: HBsAg-positive	HBsAg-negative	Source not tested or unknown
Unvaccinated	HBIG x 1[a] and initiate HB vaccine[b]	Initiate HB vaccine[b]	Initiate HB vaccine[b]
Previously vaccinated Known responder	Test exposed for anti-HBs 1. If adequate,[c] no treatment 2. If inadequate. HB vaccine booster dose	No treatment	No treatment
Known nonresponder	HBIG x 2 or HBIG x 1 plus 1 dose HB vaccine	No treatment	If known high-risk source, *may treat as if source were HBsAg-positive*
Response unknown	Test exposed far anti-HBs 1. if inadequate.' HBIG x 1 plus HB vaccine booster dose 2. If adequate, no treatment	No treatment	Test exposed for anti-HBs 1. If inadequate'. HB vaccine boaster dose 2. If adequate, no treatment

[a]HBIG dose 0.06 ml/kg IM.
[b]HB vaccine dose - see Table 3.
[c]Adequate anti-HBs is ≥10 SRU by RIA or positive by EIA.

FIGURE 1. Determining the need for HIV postexposure prophylaxis (PEP) after an occupational exposure*



*This algorithm is inteded to guide initial decisions about PEP and should be used in conjunction with other guidance provided in this report.

†Semen or vaginal secretions; cerebrospinal, synovial, pleural, peritoneal, pericardial, or amniotic fluids; or tissue.

§Exposures to OPIM must be evaluated on a case-by-case basis. In general, these body substances are considered a low risk for transmission in health-care settings. Any unprotected contact to concentrated HIV in a research laboratory or production facility is considered an occupational exposure that requires clinical evaluation to determine the need for PEP.

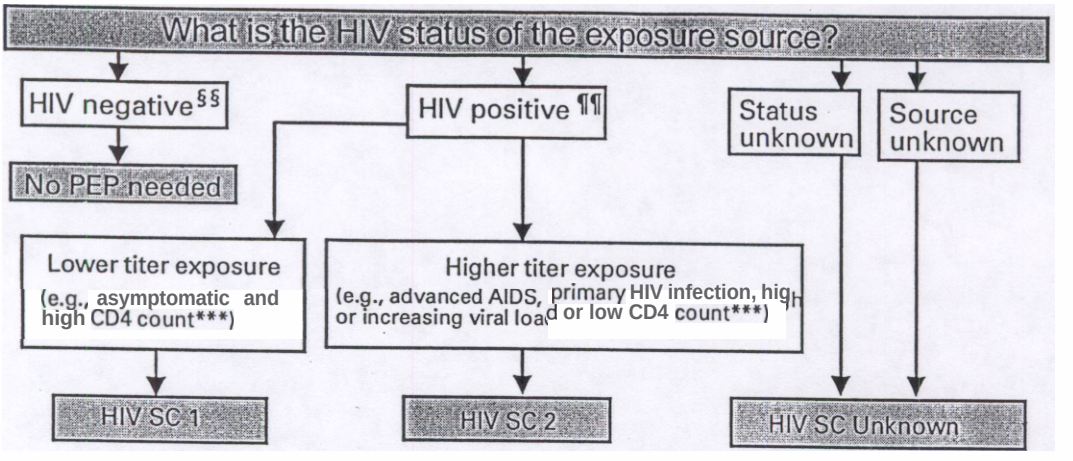
¶Skin integrity is considered compromised if there is evidence of chapped skin, dermatitis, abrasion, or open wound.

**Contact with intact skin is not normally considered a risk for HIV transmission. However, if the exposure was to blood, and the circumstance suggests a higher volume exposure (e.g., an extensive area of skin was exposed or there was prolonged contact with blood), the risk for HIV transmission should be considered.

††The combination of these severity factors (e.g., large-bore hollow needle and deep puncture) contribute to an elevated risk for transmission if the source person is HIV-positive.

FIGURE 1. Determining the need for HIV postexposure prophylaxis (PEP) after an occupational exposure* — Continued

STEP 2: Determine the HIV Status Code (HIV SC)



§§ A source is considered negative for HIV infection if there is laboratory documentation of a negative HIV antibody, HIV polymerase chain reaction (PCR), or HIV p24 antigen test result from a specimen collected at or near the time of exposure and there is no clinical evidence of recent retroviral-like illness.

¶ A source is considered infected with HIV (HIV positive) if there has been a positive laboratory result for HIV antibody, HIV PCR, or HIV p24 antigen or physician-diagnosed AIDS.

* Examples are used as surrogates to estimate the HIV titer in an exposure source for purposes of considering PEP regimens and do not reflect all clinical situations that may be observed. Although a high HIV titer (HIV SC 2) in an exposure source has been associated with an increased risk for transmission, the possibility of transmission from a source with a low HIV titer also must be considered.

STEP 3: Determine the PEP Recommendation

EC	HIV SC	PEP recommendation
1	1	**PEP may not be warranted.** Exposure type does not pose a known risk for HIV transmission. Whether the risk for drug toxicity outweighs the benefit of PEP should be decided by the exposed HCW and treating clinician.
1	2	**Consider basic regimen.†††** Exposure type poses a negligible risk for HIV transmission. A high HIV titer in the source may justify consideration of PEP. Whether the risk for drug toxicity outweighs the benefit of PEP should be decided by the exposed HCW and treating clinician.
2	1	**Recommend basic regimen.** Most HIV exposures are in this category; no increased risk for HIV transmission has been observed but use of PEP is appropriate.
2	2	**Recommend expanded regimen.§§§** Exposure type represents an increased HIV transmission risk.
3	1 or 2	**Recommend expanded regimen.** Exposure type represents an increased HIV transmission risk.
Unknown		If the source or, in the case of an unknown source, the setting where the exposure occurred suggests a possible risk for HIV exposure and the EC is 2 or 3, consider PEP basic regimen.

††† Basic regimen is four weeks of zidovudine, 600 mg per day in two or three divided doses, and lamivudine, 150 mg twice daily.

§§§ Expanded regimen is the basic regimen plus either indinavir, 800 mg every 8 hours, or nelfinavir, 750 mg three times a day.

Selected References

Varicella

1) Balfour HH, et al. Acyclovir treatment of varicella in otherwise healthy children. *J Peds* 120(4):627-33.
2) Wallace MR, et al. Treatment of adult varicella with oral acyclovir -- a randomized, placebo-controlled trial. *Ann Int Med.* 117(15):358-63.
3) Dunkle LM, et al. A controlled trial of acyclovir for chickenpox in normal children. *NEJM* 325(22):1539-44.
4) Varicella Vaccine. *The Medical Letter.* 37(951):55-57.
5) Gershon AA, et al Live attenuated varicella vaccine: protection in healthy adults compared with leukemic children. *ID.* 161:661-66.
6) Miller HC and Stephan M. Hemorrhagic varicella: a case report and review of the complications of varicella in children. *Am J Emerg Med.* 11(6):633-38.
7) LaRussa P, et al. Transmission of vaccine strain VZV from a healthy adult with vaccine-associated rash to susceptible household contacts. *J Inf Dis*. 1997. 176: 1072-75.
8) Nettleman MD and Schmid M. Controlling varicella in the healthcare setting: the cost-effectiveness of using vairicella vaccine in healthcare workers. *Inf Control and Hosp Epidem.* 18(7):504-8.
9) White CJ. Varicella-zoster virus vaccine. *Clin Inf Dis* 1997. 24:753-61.

Meningitis

1) Benenson AS. *Control of communicable disease in man.* 16th ed. 1995.
2) Cuevas LE and Hart CA. Chemoprophylaxis of bacterial meningitis. *J Antimicrobial Chemo.* 31(suppl B):79-91.

Needlestick Injuries

1) Cardo DM, et al. A case-control study of HIV seroconversion in health care workers after percutaneous exposure. *NEJM.* 337(21): 1485-90.
2) Case-control study of HIV seroconversion in health care workers after percutaneous exposure to HIV-infected blood -- France, United Kingdom, and United States, January 1988 -August 1994. *MMWR.* 44(50):929-33.
3) Connor EM, et al. Reduction of maternal-infant transmission of HIV type 1 with zidovudine treatment. NWM 1994. 331:1173-80.
4) Ferguson TJ. Needlestick injuries among health care professionals. *West J Med.* 156(4):409.
5) Frazer VJ and Powderly WG. Risks of HIV infection in the healthcare setting, *Annu Rev Med* 46:203-1 1.
6) Friedland LR. Universal precautions and safety devices which reduce risk of occupational exposure to blood-borne pathogens: a review of emergency health care workers. *Ped Emerg Care.* 7(6):356-62.
7) Gerberding JL. Prophylaxis for occupational exposure to HIV. *Ann Int Med.* 125(6):497-501.
8) Henderson, DK. Risks for exposures to and infection with HIV among health care providers in the emergency department. *Emerg Clin N Am.* 13(1):199-211.
9) Lanphear BP. Hepatitis C virus infection in healthcare workers: risk of exposure and infection. *If Control Hosp Epidemiol.* 15(12):745-50.
10) Marcus RM, et al. Occupational blood contact among prehospital providers. *Ann Emerg Med.* 25(6):776-79.
11) Mast ST, et al. Efficacy of gloves in reducing blood volumes transferred during simulated needlestick injury. *J Infect Dis.* 168:15X9-92.

12) Pinkerton SD, et al. Cost-effectiveness of chemoprophylaxis after occupational HIV exposure to *HIV Arch Int Med* 1997. 157:1972-80.
13) Pinto LA, et al. Immune response to HIV in healthcare workers occupationally-exposed to HIV-contaminated blood. *Am J Med* 1997. 102(suppl 5B):21-24.
14) Public Health Service guidelines for the management of health-care worker exposures to HIV and recommendations for postexposure prophylaxis. *MMWR*. 5/15/98. 47(RR-7):1-33.
15) **Shih CC,** et al. Postexposure prophylaxis with zidovudine suppresses HIV type 1 infection in SCID-hu mice in a time-dependent manner. *J Infect Dis* 1991. 163(March):625-27.