

Occupational Exposure of Health Care Workers to HIV - Are We Doing Enough?

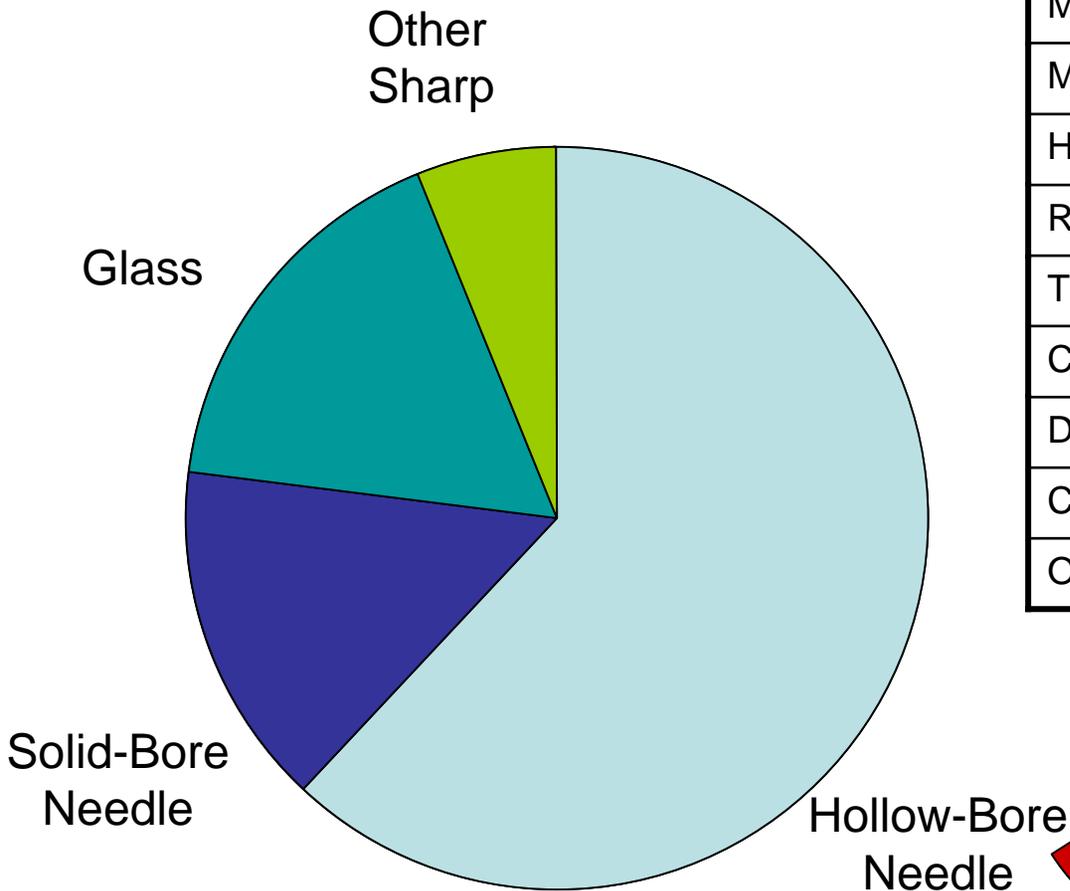
Talk Outline

- Preventing occupational exposures to HIV
- Improving management of occupational at risk exposures

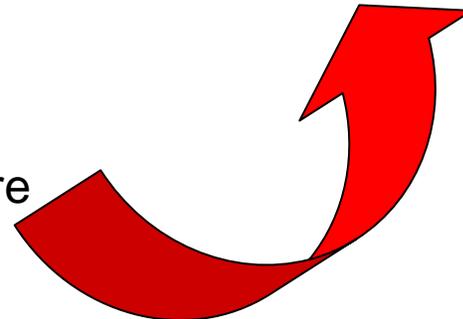
At Risk Exposures



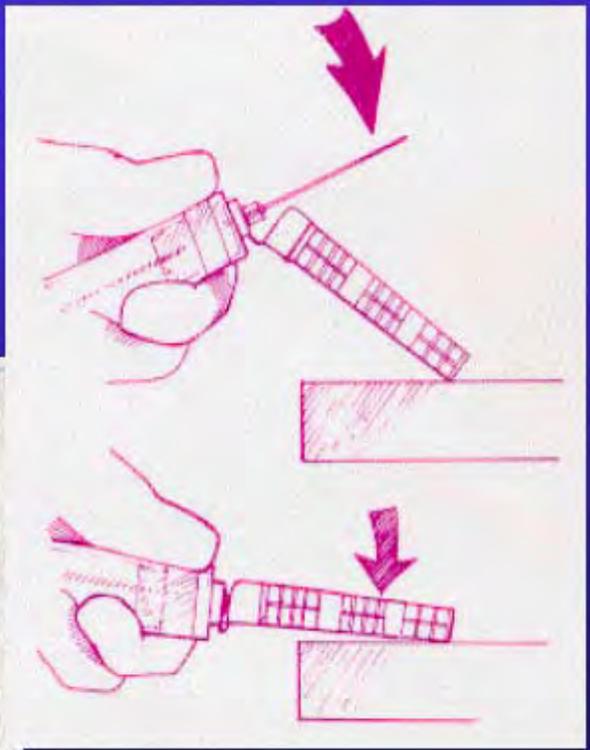
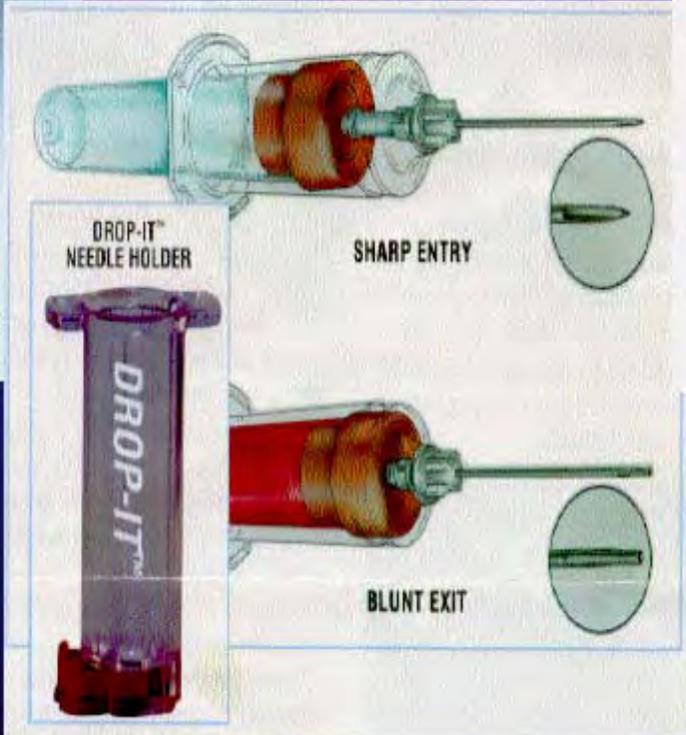
Percutaneous Injuries



Cause	%
Manipulating the needle in the patient	27
Manipulating IV lines	8
Handling/passing device during/after use	10
Recapping needles	5
Transferring specimens	5
Collision with HCW or Sharp	8
Disposal-related causes	22
Cleanup	11
Other	4

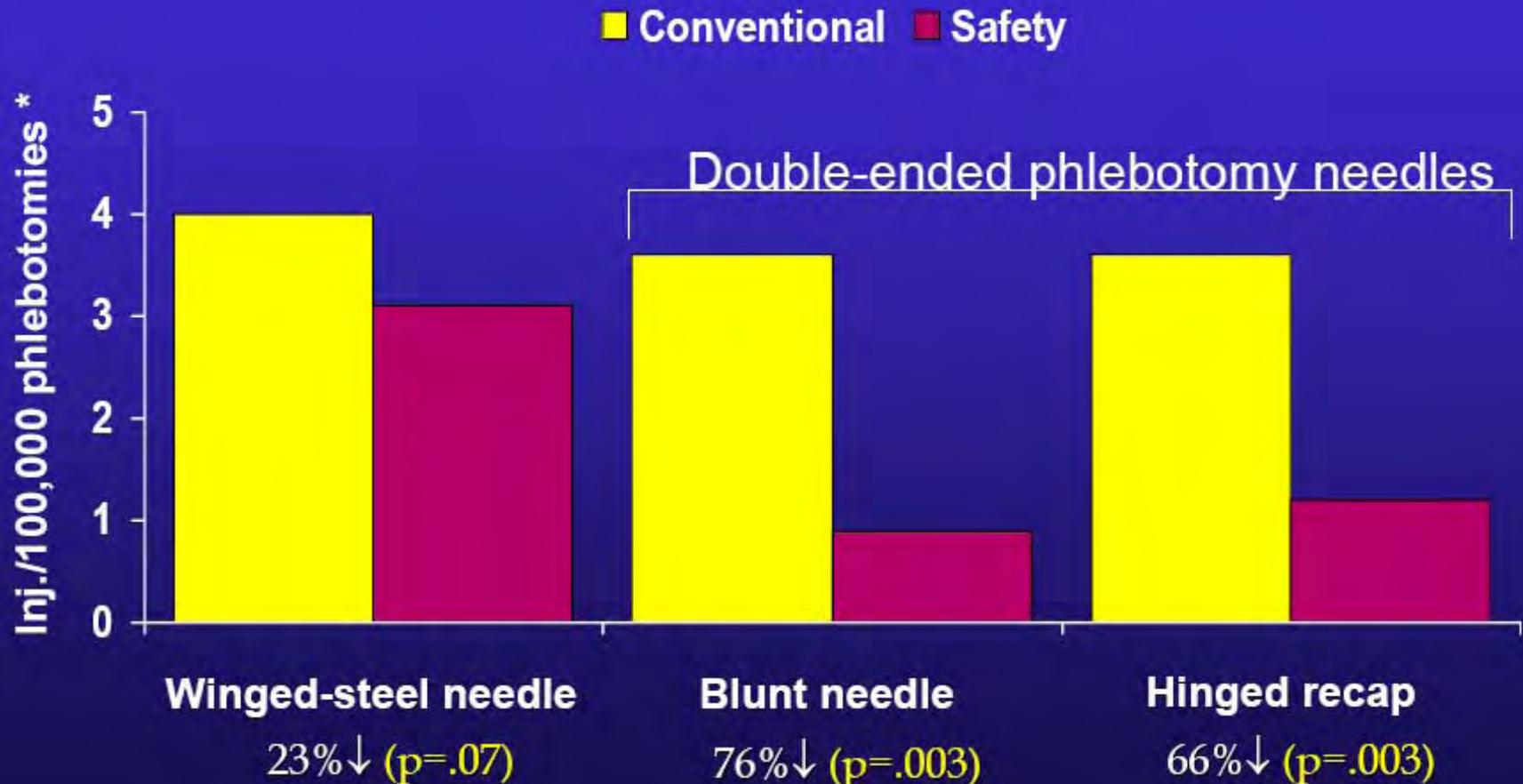


Safety Phlebotomy Devices



Rate of Phlebotomy-Related Injuries

Conventional vs. Safety Devices



* Adjusted for underreporting

Source: CDC MMWR Jan 17, 1997



Minimize post-hoc handling of needles



Improving Sharps Disposal





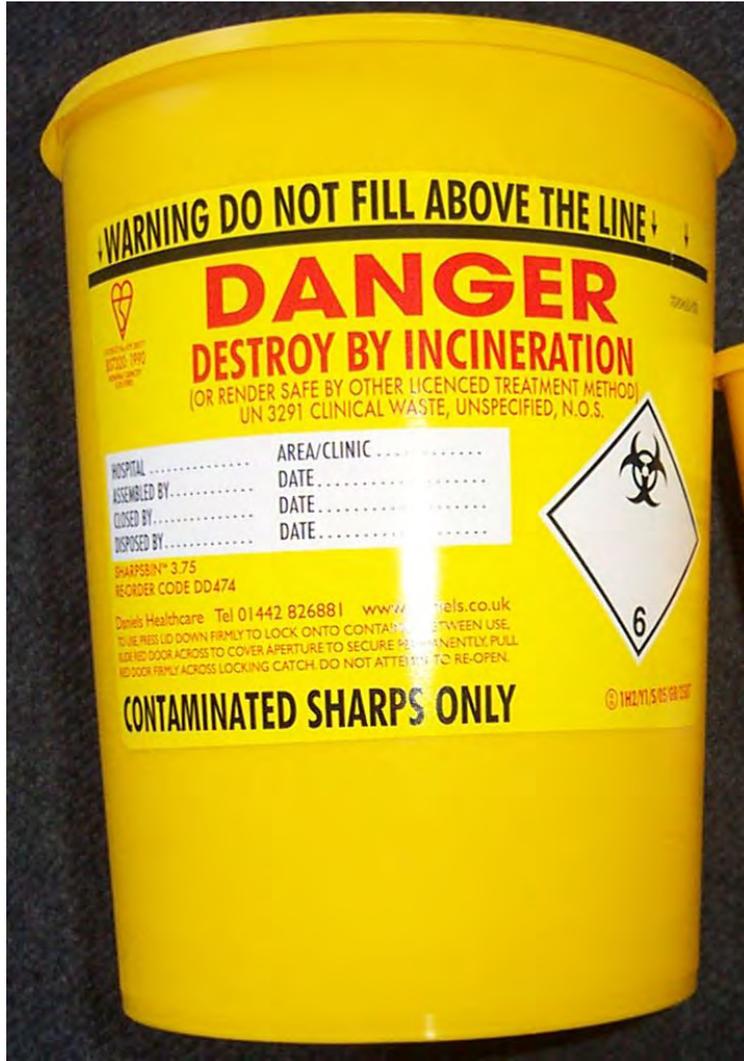
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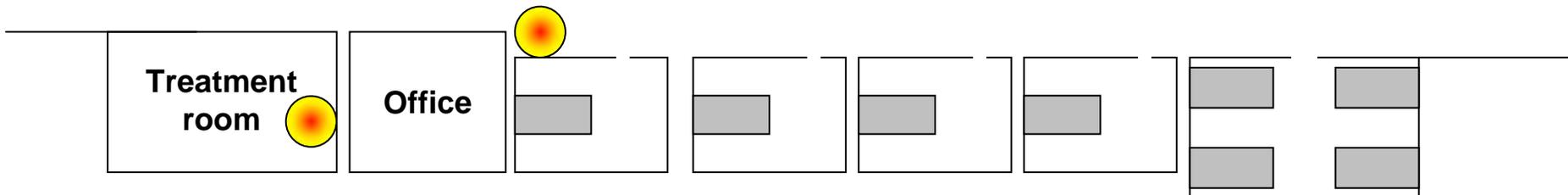
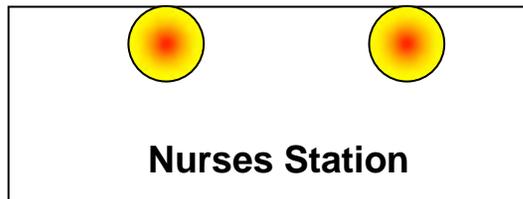
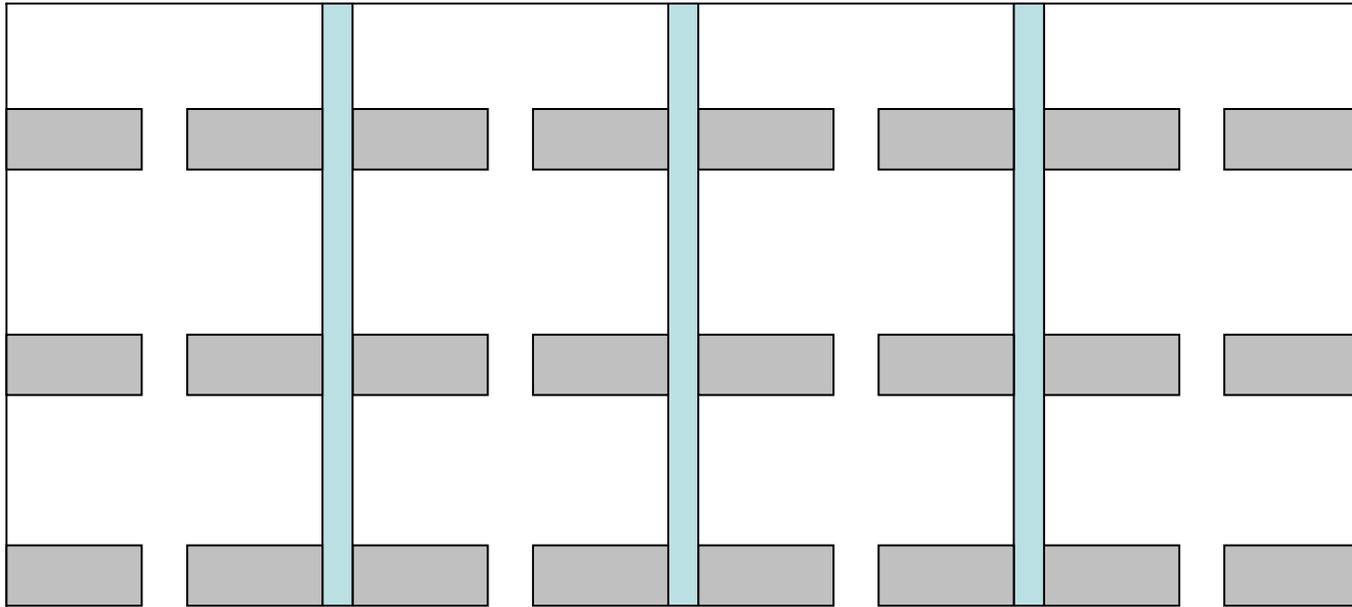
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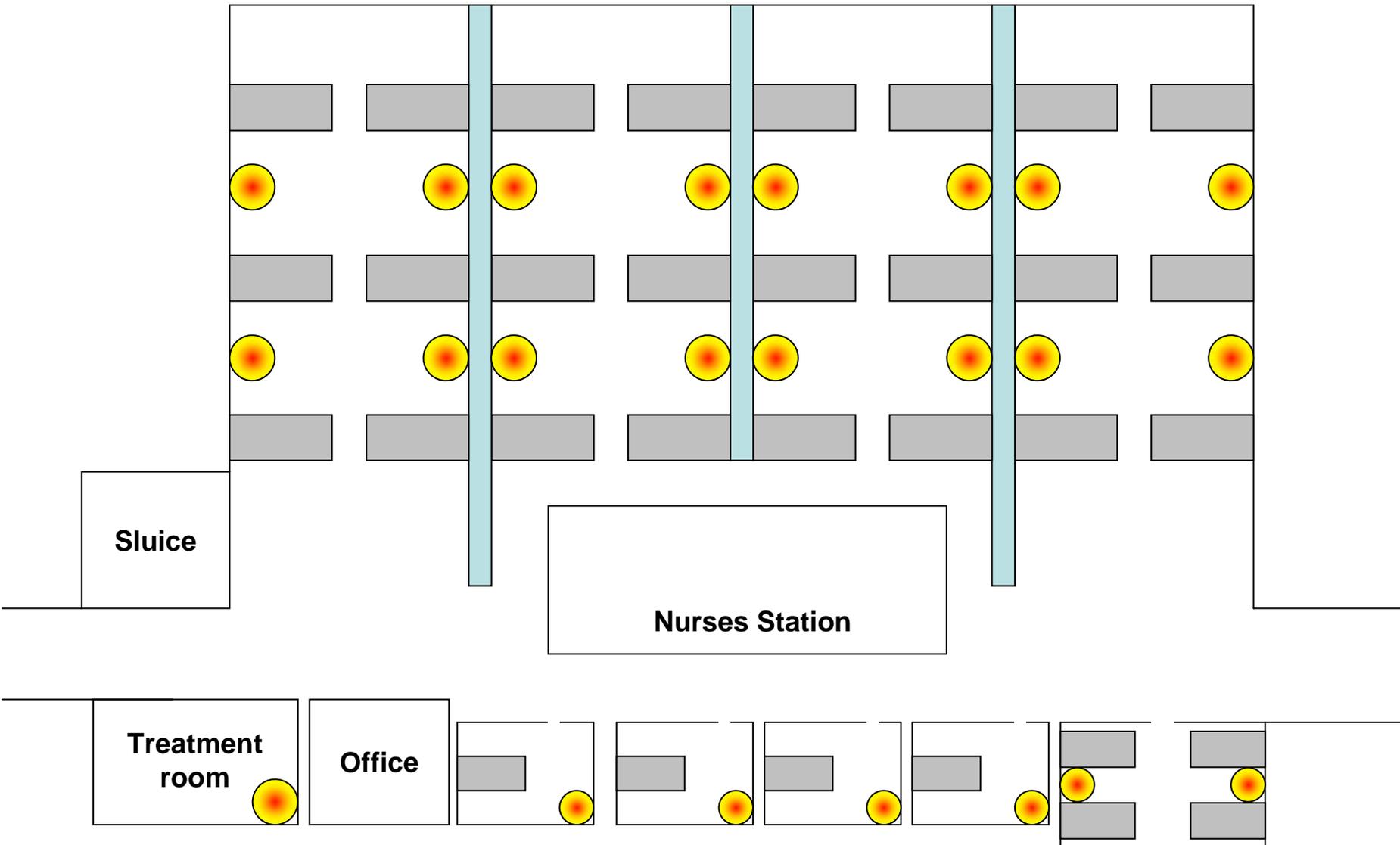
Proper Disposal of Sharps and Blunts



Current sharps bin coverage for a typical ward at GSH



Optimal Sharps Bin Coverage for a typical ward at GSH





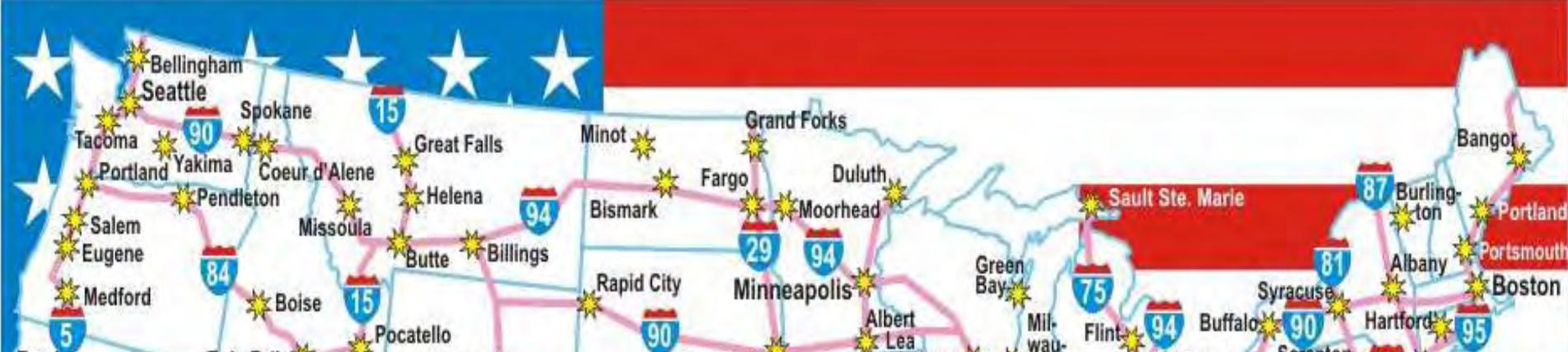


TABLE 1
 PERCUTANEOUS INJURY REPORTING RATE BY OCCUPATION, FROM UNDERREPORTING SURVEYS BY THE NATIONAL SURVEILLANCE SYSTEM FOR HEALTH CARE WORKERS, 1997–1998

Occupation	No. of Respondents	HCWs With ≥ 1 PI	No. of PIs Reported	No. of PIs That Occurred	Reporting Rate* (CI ₉₅)
Surgical medical	2,266	404	236	881	26.8% (20.7%–32.8%)
Nonsurgical medical	1,997	249	171	316	54.1% (47.6%–60.6%)
Nursing	8,896	770	564	1,070	52.7% (48.7%–56.7%)
Technician	1,788	95	81	121	66.9% (55.9%–78.0%)
All others	8,791	176	122	316	38.6% (28.9%–48.3%)
Total	23,738	1,694	1,174	2,704	43.4% (39.5%–47.3%)

HCWs = healthcare workers; PI = percutaneous injury; CI₉₅ = 95% confidence interval.
 *Number of injuries reported divided by the number of injuries that occurred.



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GF Jooste Hospital, Mannenberg, Cape Town

42 doctors polled

- 66% of doctors reported ≥ 1 PCI
- 46% reported the injury
- 59% applied first aid to the wound
- 35% received post-exposure counselling

Mendelson & Meintjes, Submitted



Chris Hani Baragwanath and Johannesburg Hospitals

96 interns polled

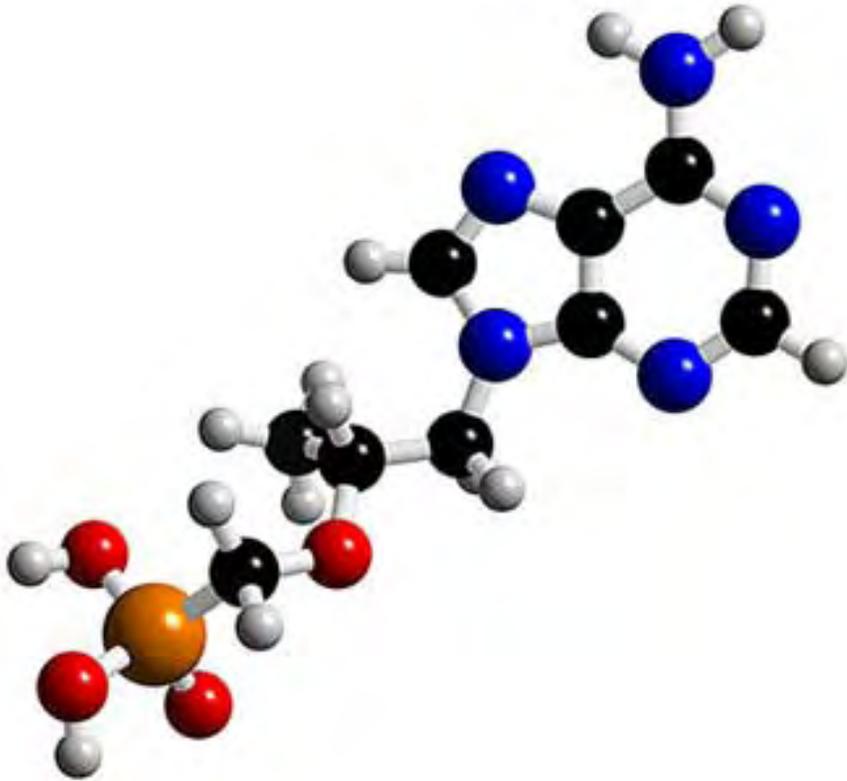
- 69% Interns ≥ 1 PCI
- 33% from an HIV-seropositive source
- 64% PCI involving an HIV-positive source were reported
- 45% mucocutaneous exposures
- 56% recalled PCI during their student training

SAMJ 2001; 91(1): 57-61



**What is the evidence that
HIV PEP works for
occupational exposures?**

Macaque SIV Model of PEP



(R)-9-(2-phosphonylmethoxypropyl)adenine
(PMPA)



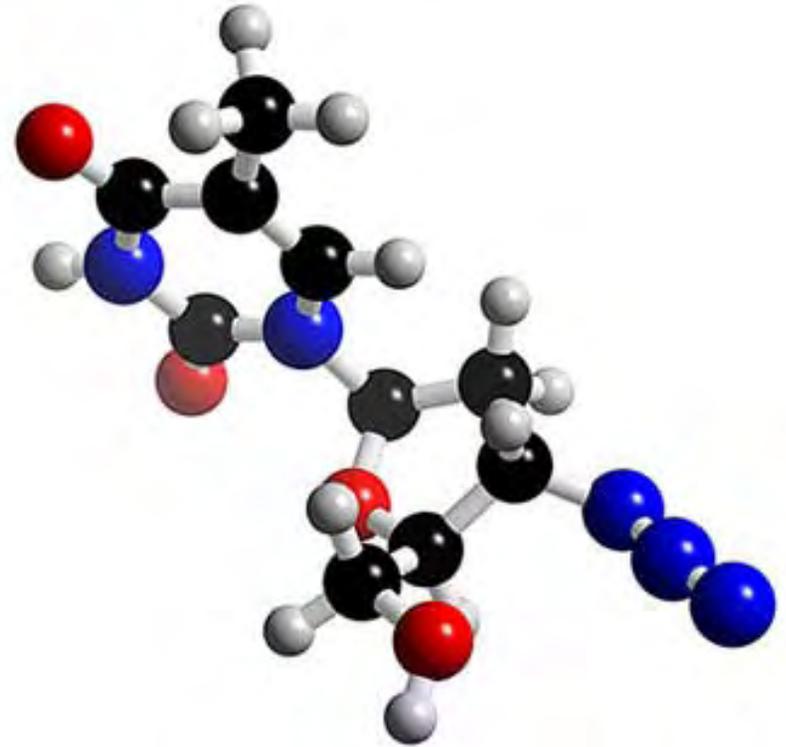
Tenofovir PEP prevents SIV infections in Macaques

- Infection with 10x 50% Monkey infectious dose SIV i.v
- Daily s.c Tenofovir started 48h pre-, 4 or 24 hours p.i
 - continued for 28 days
- Monitoring to 56 weeks
 - p27 antigenaemia & SIV ELISA
 - Cell-free and Cell-associated viral load
 - Inguinal lymph node biopsies
 - Euthanasia and autopsy of 2 animals
- 28/28 macaques protected

Timing & duration of PEP is critical to preventing infection of Macaques

Group	Number infected at week 48
Mock-treated Controls	4/4
24-hour post-exposure, 28 day treatment	0/4
48-hour post-exposure, 28 days treatment	4/4
72-hour post-exposure, 28 days treatment	4/4
24-hour post-exposure, 10 days treatment	2/4
24-hour post-exposure, 3 days treatment	2/4

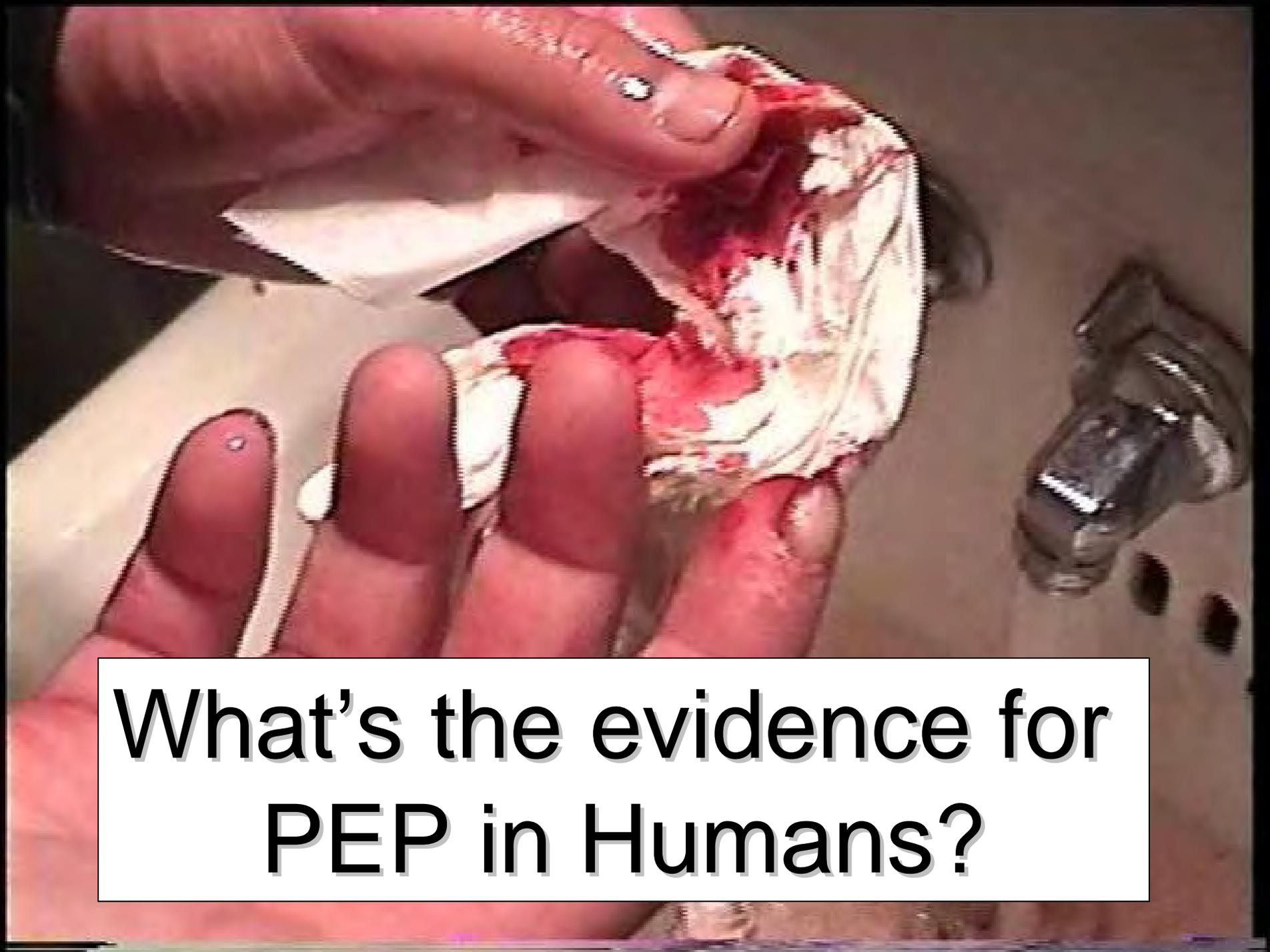
Zidovudine fails to prevent SIV infection in Macaque models but limits viral load



Lindgren B. J Acquir Immune Defic Syndr 1991

Fazely F. J Acquir Immune Defic Syndr 1991

Martin LN. Journal of Infectious Diseases 1993



**What's the evidence for
PEP in Humans?**

Surveillance of HIV Infection and Zidovudine Use among Health Care Workers after Occupational Exposure to HIV-Infected Blood

Jerome I. Tokars; Ruthanne Marcus; David H Culver; Charles A. Schable; Penny S. McKibben; Claudiu I. Bandea; and David M Bell

15 June 1993 / Volume 118 Issue 12 / Pages 913-919

- CDC surveillance project in US Hospitals
- 1245 HCW enrolled following exposure
 - 89% Percutaneous injury
 - 80% source patients had AIDS
 - Follow up to 56 weeks
- 4/1103 serconverted
- Risk = 0.32% (upper limit CI 0.83%)

Volume of blood and VL of source are determinants of risk

TABLE 2. LOGISTIC-REGRESSION ANALYSIS OF RISK FACTORS FOR HIV TRANSMISSION AFTER PERCUTANEOUS EXPOSURE TO HIV-INFECTED BLOOD.

RISK FACTOR	U.S. CASES*	ALL CASES†
	adjusted odds ratio (95% CI)‡	
Deep injury	13 (4.4–42)	15 (6.0–41)
Visible blood on device	4.5 (1.4–16)	6.2 (2.2–21)
Procedure involving needle in artery or vein	3.6 (1.3–11)	4.3 (1.7–12)
Terminal illness in source patient§	8.5 (2.8–28)	5.6 (2.0–16)
Postexposure use of zidovudine	0.14 (0.03–0.47)	0.19 (0.06–0.52)

*All risk factors were significant ($P < 0.02$).

†All risk factors were significant ($P < 0.01$).



Reported Instances of Failure of Postexposure Zidovudine To Prevent HIV Infection in Health Care Workers after Percutaneous Exposure to HIV-infected Blood

Report	Country	Year	Sharp Object	Hours to First Dose	Regimen†		Onset of Retroviral Illness	Time Seroconversion Documented‡	Source Patient on Zidovudine	Reference
					mg	Days				
1	South Africa	1992	IV cannula	0.5	1200	42	None	6 wk	No	(29)
2	United States	1991	22-gauge phlebotomy needle	0.75	800	10	2 wk	3 mo	Yes	§
3	A Western European country	1992	18- to 20-gauge IV cannula	1	1000	42	2 wk	56 d	Yes	
4	France	1990	Phlebotomy needle	1.5	1000	21	16 d	52 d	Yes	(30)
5	United States	1992	21-gauge syringe needle	2	1000	17	38 d	121 d	No	This report
6	United States	1990	16-gauge IV cannula	3 to 7	1000	8	36 d	94 d	Yes	§
7	Australia	1990	Hollow needle	6	1000	54	5 wk	6 wk	Yes	(31)
8	South Africa	1990	Lancet	12	1200	21	17 d	24 d¶	No	(29)

* HIV = human immunodeficiency virus; IV = intravenous.

† Regimens are expressed as milligrams of zidovudine per day and number of days taken. Report 5: 500 mg/d for 1 day, then 1000 mg/d for 16 additional days.

‡ By enzyme immunoassay and Western blot.

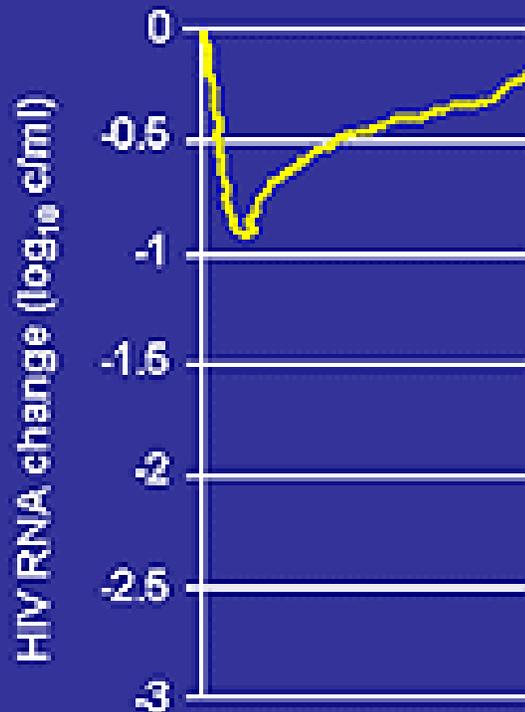
§ C. Ciesielski, unpublished CDC data.

|| Confidential communication from the country's national public health authority to D. Bell, CDC; cited with permission; and also **Anonymous**: HIV seroconversion after occupational exposure despite early prophylactic zidovudine therapy. *Lancet*. 1993;341:1077-8.

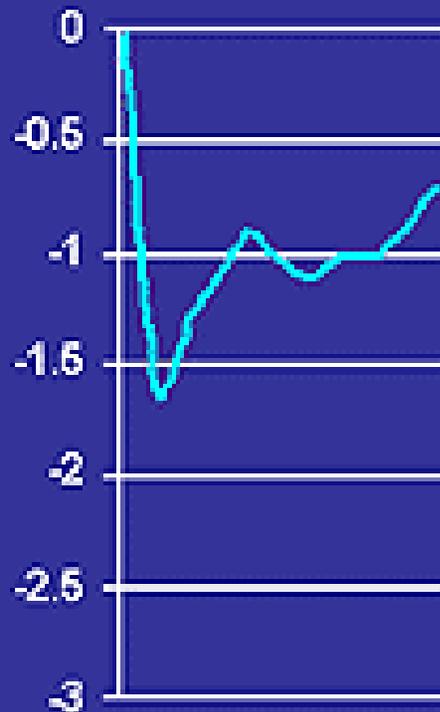
¶ At 24 days, reactive by enzyme immunoassay and weakly positive by Western blot. At 3 months, enzyme immunoassay had a higher optical density reading, and Western blot had strongly positive bands.

Antiretroviral Activity: 1987-1997

1987: AZT
monotherapy



1994:
Two-drug therapy



1997: Three drugs
including PI



Fischl. NEJM. 1987.

Eron. NEJM. 1995.

Gulick. NEJM. 1997.

Hammer. NEJM. 1996.

Cameron. Lancet. 1998.

TABLE 1. Recommended HIV postexposure prophylaxis (PEP) for percutaneous injuries

Exposure type	Infection status of source				
	HIV-positive, class 1*	HIV-positive, class 2*	Source of unknown HIV status†	Unknown source‡	HIV-negative
Less severe¶	Recommend basic 2-drug PEP	Recommend expanded ≥3-drug PEP	Generally, no PEP warranted; however, consider basic 2-drug PEP** for source with HIV risk factors††	Generally, no PEP warranted; however, consider basic 2-drug PEP** in settings in which exposure to HIV-infected persons is likely	No PEP warranted
More severe§§	Recommend expanded 3-drug PEP	Recommend expanded ≥3-drug PEP	Generally, no PEP warranted; however, consider basic 2-drug PEP** for source with HIV risk factors††	Generally, no PEP warranted; however, consider basic 2-drug PEP** in settings in which exposure to HIV-infected persons is likely	No PEP warranted

* HIV-positive, class 1 — asymptomatic HIV infection or known low viral load (e.g., <1,500 ribonucleic acid copies/mL). HIV-positive, class 2 — symptomatic HIV infection, acquired immunodeficiency syndrome, acute seroconversion, or known high viral load. If drug resistance is a concern, obtain expert consultation. Initiation of PEP should not be delayed pending expert consultation, and, because expert consultation alone cannot substitute for face-to-face counseling, resources should be available to provide immediate evaluation and follow-up care for all exposures.

† For example, deceased source person with no samples available for HIV testing.

‡ For example, a needle from a sharps disposal container.

¶ For example, solid needle or superficial injury.

** The recommendation “consider PEP” indicates that PEP is optional; a decision to initiate PEP should be based on a discussion between the exposed person and the treating clinician regarding the risks versus benefits of PEP.

†† If PEP is offered and administered and the source is later determined to be HIV-negative, PEP should be discontinued.

§§ For example, large-bore hollow needle, deep puncture, visible blood on device, or needle used in patient’s artery or vein.

TABLE 2. Recommended HIV postexposure prophylaxis (PEP) for mucous membrane exposures and nonintact skin* exposures

Exposure type	Infection status of source				
	HIV-positive, class 1 [†]	HIV-positive, class 2 [†]	Source of unknown HIV status [§]	Unknown source [¶]	HIV-negative
Small volume ^{**}	Consider basic 2-drug PEP ^{††}	Recommend basic 2-drug PEP	Generally, no PEP warranted ^{§§}	Generally, no PEP warranted	No PEP warranted
Large volume ^{¶¶}	Recommend basic 2-drug PEP	Recommend expanded \geq 3-drug PEP	Generally, no PEP warranted; however, consider basic 2-drug PEP ^{††} for source with HIV risk factors ^{§§}	Generally, no PEP warranted; however, consider basic 2-drug PEP ^{††} in settings in which exposure to HIV-infected persons is likely	No PEP warranted

* For skin exposures, follow-up is indicated only if evidence exists of compromised skin integrity (e.g., dermatitis, abrasion, or open wound).

[†] HIV-positive, class 1 — asymptomatic HIV infection or known low viral load (e.g., <1,500 ribonucleic acid copies/mL). HIV-positive, class 2 — symptomatic HIV infection, AIDS, acute seroconversion, or known high viral load. If drug resistance is a concern, obtain expert consultation. Initiation of PEP should not be delayed pending expert consultation, and, because expert consultation alone cannot substitute for face-to-face counseling, resources should be available to provide immediate evaluation and follow-up care for all exposures.

[§] For example, deceased source person with no samples available for HIV testing.

[¶] For example, splash from inappropriately disposed blood.

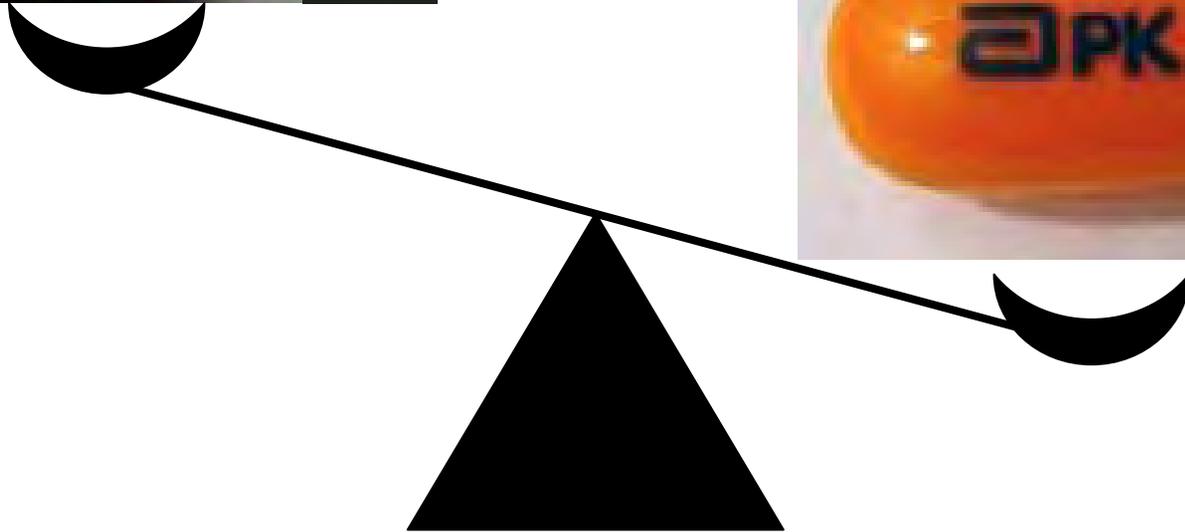
^{**} For example, a few drops.

^{††} The recommendation “consider PEP” indicates that PEP is optional; a decision to initiate PEP should be based on a discussion between the exposed person and the treating clinician regarding the risks versus benefits of PEP.

^{§§} If PEP is offered and administered and the source is later determined to be HIV-negative, PEP should be discontinued.

^{¶¶} For example, a major blood splash.

Dual vs Triple Therapy for PEP



Factors that could influence completion of a 28 day course of PEP

- Adverse drug effects
- Drug resistance
- Psychosocial factors

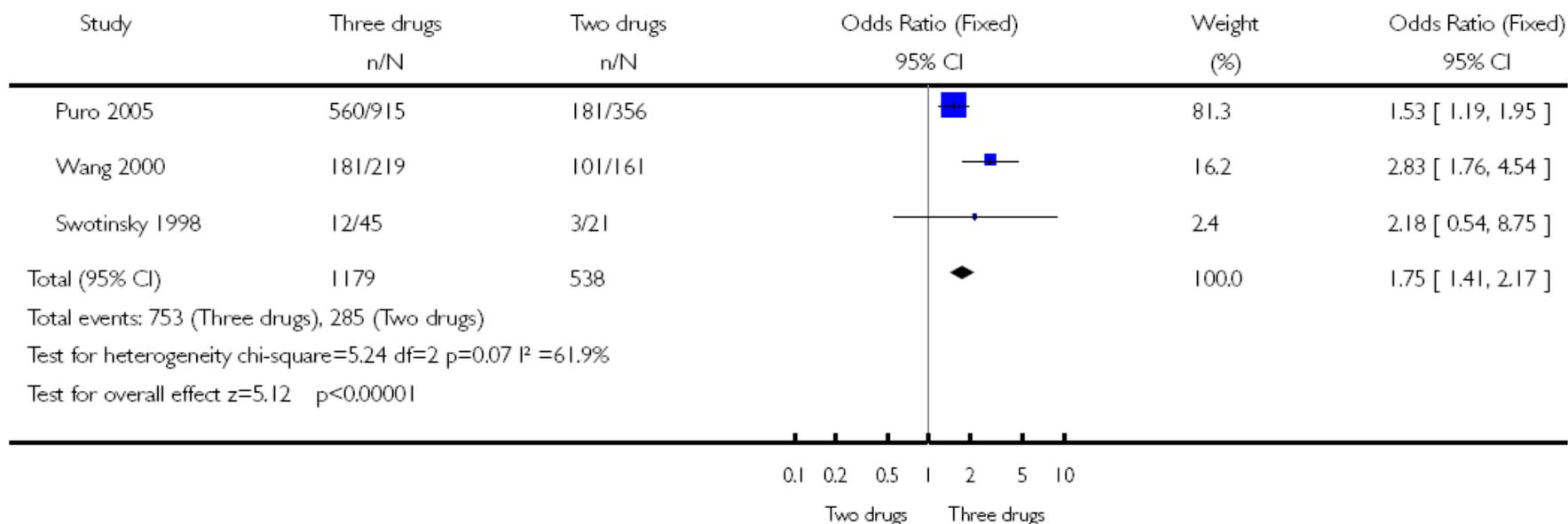
2 vs 3 – Adverse events in PEP

Analysis 01.01. Comparison 01 Two drugs vs three drugs, Outcome 01 Adverse events

Review: Antiretroviral post-exposure prophylaxis (PEP) for occupational HIV exposure

Comparison: 01 Two drugs vs three drugs

Outcome: 01 Adverse events



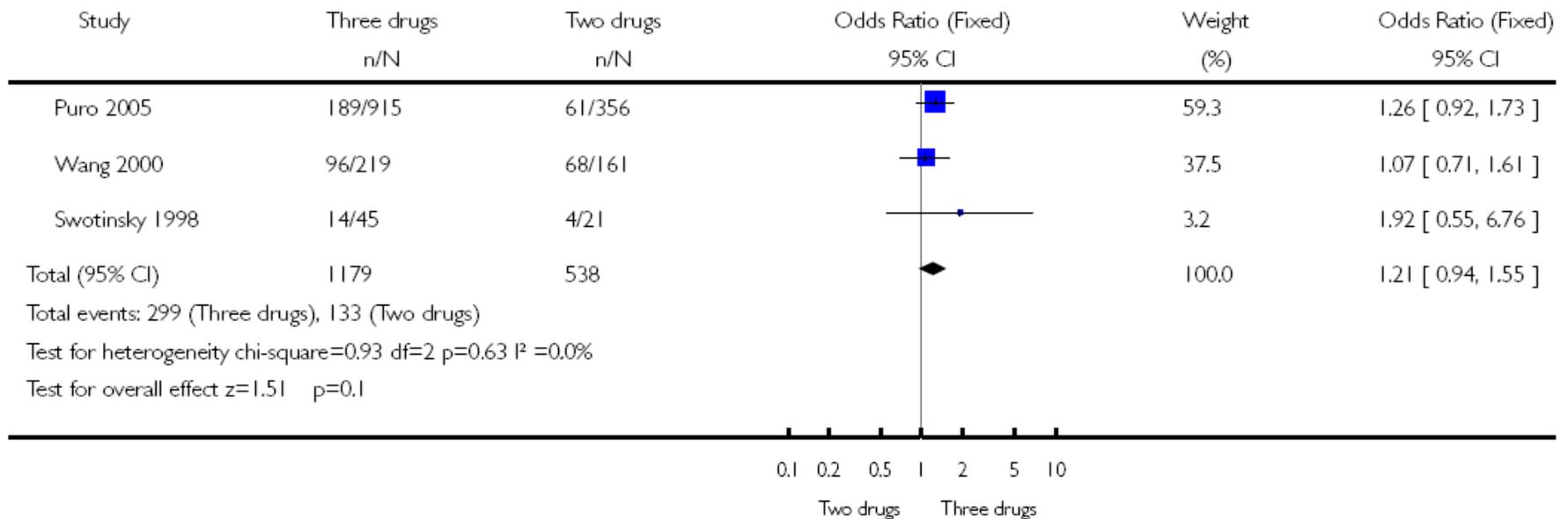
2 vs 3 – Discontinuation rates of PEP

Analysis 01.02. Comparison 01 Two drugs vs three drugs, Outcome 02 Discontinuation

Review: Antiretroviral post-exposure prophylaxis (PEP) for occupational HIV exposure

Comparison: 01 Two drugs vs three drugs

Outcome: 02 Discontinuation



Is AZT the Culprit?

Drug regimen	Total number	Reports of side-effects			Discontinuing prophylaxis			Duration (days)	
		Number	OR (95% CI)	p	Number	OR (95% CI)	p	Median	Mean
ZDV*	647	409 (63.2%)	1		207 (32.0%)	1		8	9
ZDV+3TC†	115	67 (58.3%)	0.82 (0.53–1.25)	0.37	33 (28.7%)	0.86 (0.53–1.34)	0.55	7	10
ZDV+3TC+IDV	191	127 (66.5%)	1.16 (0.82–1.66)	0.44	57 (29.8%)	0.90 (0.62–1.30)	0.63	7	10

ZDV=Zidovudine; 3TC=lamivudine; IDV=indinavir; OR=odds ratio.

*AZT dose = 1000mg daily

†AZT dose = 500 – 600mg daily

Puro et al. Lancet 2000; 355: 1557-8

Use of antiretrovirals with less adverse effects
and
Aggressive but judicious use of antiemetics and antidiarrhoeals

Drug Resistance as a factor in failure of occupational PEP

TABLE 6. Reported instances of failure of combination drug postexposure prophylaxis (PEP) to prevent HIV-infection among health-care personnel exposed to HIV-infected blood through percutaneous injury

Year of incident	Device	PEP regimen ^a	Time to first dose (hrs)	No. of days to onset of retroviral illness	No. of days to document seroconversion [†]	Source-patient		
						HIV-infection status	On anti retrovirals	Virus resistant to antiretrovirals [§]
1992 [¶]	Biopsy needle	ZDV, ddi	0.5	23	23	AIDS, terminally ill	Yes	Unknown
1996 ^{**}	Hollow-bore needle	ZDV, ddi ^{††}	1.5	45	97	Asymptomatic HIV infection	No	Not tested
1997 ^{**}	Large or hollow-bore needle	ZDV, 3TC, IDV ^{§§}	1.5	40	55	AIDS	Yes	No
1998 ^{¶¶}	Hollow-bore needle	ZDV, 3TC, ddi, IDV	0.7	70	83	AIDS	Yes	Yes
1999 ^{***}	Unknown sharp	ddi, d4T, NVP ^{†††}	2.0	42	100	AIDS	Yes	Yes
2001 ^{§§§}	Phlebotomy needle	ZDV, 3TC, IDV ^{†††}	1.6	24	~90	AIDS	Yes	Yes

The role of Psychosocial Support in Occupational PEP

- 20 HCW studied
 - 55% reported acute severe distress
 - 35% persisted moderate distress
 - 30% resigned their posts as a result of the exposure
 - Not knowing source HIV status accentuated stress reaction

GUIDELINES

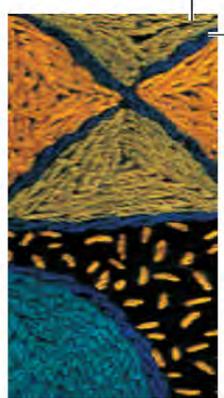
POST-EXPOSURE PROPHYLAXIS



- Significant lack of evidence for the use of specific agents in the PEP setting
- Efficacy of monotherapy, but significant failure rates
- Evidence for use of HAART in treatment settings and now the trend in PMTCT
- Current regimens contain poorly tolerated drugs
- Other equally efficacious ARVs
- The need to improve support through the PEP period

GUIDELINES

POST-EXPOSURE PROPHYLAXIS



7. SELECTING PATIENTS FOR ARV INTERVENTIONS (FIG. 1)

	Status of the Source		
	HIV Positive	Unknown	HIV Negative
Percutaneous exposure to blood or potentially infectious fluids	Triple therapy	Triple therapy	No PEP
Mucocutaneous splash or contact with an open wound, with blood or potentially infectious fluids	Triple therapy	Triple therapy	No PEP
Percutaneous exposure, mucocutaneous splash or contact with an open wound, with non-infectious bodily fluids	No PEP	No PEP	No PEP

Fig. 1. Selecting patients for PEP interventions.

- Drugs
 - Backbone
 - D4T + 3TC or TDF + FTC/3TC or AZT + 3TC
 - Third agent
 - Lopinavir/RTV
 - Saquinavir/RTV
 - Efavirenz
 - Atazanavir/RTV
 - Atazanavir
- Pro-active use of antiemetics & anti-diarrhoeals
- Tightening post-exposure follow-up and support

Are we doing enough?

- No
- Increase in education, access to safety devices and proper waste disposal is key to reducing occupational exposures
- Clear guidelines with rationale use of ARVs with least side effects, proper medical and psychological support of staff on PEP.
- Registry

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