HIV-Postexpositionsprophylaxe
beim Krankenhauspersonal

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Übertragungsmöglichkeiten im Gesundheitsbereich

- Relevant: Blut, blutige Flüssigkeiten oder Viruskonzentrat
- Stich/Schnittverletzung (perkutane Verletzung), Schleimhautexposition, Kontakt von nicht intakter Haut/offenen Wunden mit infektiösem Material

Übertragungswahrscheinlichkeiten HIV

- 0,1 bis 1 Infektion pro 100 Kontakte/Expositionen
- Durchschnittliches Risiko einer HIV-Infektion nach perkutaner Exposition mit Blut (messbare Viruslast): 0,3%

Table 1. Summary transmission probabilities for contaminated accidental needlestick or sharp injuries and blood product transfusion, under various inclusion criteria and for pooled data and weighted average methods.

		p_{sz}* (95% CI)		p_p** (95% CI)
Needlestick and other sharps injury				
Included studies (Table 1) [20–45]	0.24%	(14/5810; 0.14–0.40)	0.23%	(0.00–0.46)
Excluded studies[a] [69–78]	0.59%	(7/1179; 0.29–1.22)	0.42%	(0.00–1.23)
Studies explicitly stating no other risk factors present [20,21,25,31,34–37,43,79,80]	0.22%	(4/1833; 0.08–0.56)	0.13%	(0.00–0.54)
AIDS patients only[b] [20,22,29,34,35,38]	0.41%	(5/1231; 0.17–0.95)	0.37%	(0.00–1.00)
All symptomatic patients (AIDS and ARC)[c] [20–23,29,34,35,38,42,45]	0.40%	(7/1745; 0.19–0.83)	0.35%	(0.00–0.86)
Blood product transfusion				
Included studies [46–55]	80.2%	(438/546; 76.7–83.3)	82.2%	(79.0–85.4)
Excluded studies [81–83]	68.8%	(11/16; 44.4–85.8)	68.1%	(45.7–90.5)
Included studies, donations proved to be contaminated[d] [49,50,52–55]	91.9%	(374/407; 88.8–94.2)	92.5%	(89.0–96.1)

ARC, AIDS-related complex; CI, confidence interval; *p_{sz}: estimate weighted by sample size; **p_p: estimate weighted by precision (adapted inverse variance method) – see details in method.

[a]Does not include reports of prospective studies superseded by a more recent publication.

[b]Estimate includes Tokars *et al.* [38], which did not control for zidovudine post-exposure prophylaxis. Excluding this study gave a pooled estimate of 0.30% (1/332; 95% CI, 0.05–1.69) and a weighted average of 0.05% (95% CI, 0.00–1.51).

[c]Estimate includes Tokars *et al.* [38], which did not control for zidovudine post-exposure prophylaxis, and Nelsing *et al.* [42], in which a 'large majority' were AIDS patients. Excluding these studies gave a pooled estimate of 0.49% (3/614; 95% CI, 0.17–1.43) and a weighted average of 0.28% (95% CI, 0.00–1.50).

[d]Donors proven to have been infected with HIV at the time of donation, or donation tested and shown to be contaminated.

Baggaley et al., risk of HIV-1 transmission for parenteral exposure and blood transfusion: a systematic review and meta-analysis. AIDS 2006

HIV seroconversion rate: review of the literature and results of the current study

Author	Years of study	Year of publication	Country	Known HIV-positive source	Type of injury	No. of accidents	Documented HIV seroconversion, n (%)	Use of antiretroviral therapy
Moss et al[9]	NR	1986	United States	Yes	Overall	29	0 (0)	NR
Arva et al[10]	1986–1989	1990	Norway	Yes	Overall	924	0 (0)	NR
Puro et al[11]	1986–1988	1990	Italy	Yes	Overall	53	0 (0)	NR
Heptonstall et al[12]	1985–1992	1993	United Kingdom	Yes	Overall	134	2 (1.5)	Zidovudine in 1 HCW, after percutaneous exposure; seroconverted
					Percutaneous	99	2 (2)	
					Mucocutaneous	35	0 (0)	
Ippolito et al[8]	1986–1990	1993	Italy	Yes	Overall	1,488	2 (0.13)	NR
					Percutaneous	1,003	1 (0.1)	
					Mucocutaneous	485	1 (0.21)	
Tokars et al[13]	1983–1992	1993	United States	Yes	Overall	1,245	4 (0.32)	Zidovudine in 848 HCWs; 1 seroconverted
					Percutaneous	1,103	4 (0.36)	
					Mucocutaneous	142	0 (0)	
Gerberding[14]	1984–1992	1994	United States	Yes	Overall	725	1 (0.14)	NR
					Percutaneous	327	1 (0.31)	
					Mucocutaneous	398	0 (0)	
Huertas et al[15]	1987–1993	1995	Mexico	Yes	Overall	54	0 (0)	NR
Romea et al[16]	1986–1992	1995	Spain	Yes	Overall	98	0 (0)	NR
Roberts et al[17]	1990	1999	United States	Yes	Overall	39	0 (0)	Zidovudine in 27 HCWs
Gutierrez et al[18]	1998–2002	2005	Brazil	Yes	Overall	44	0 (0)	Zidovudine-lamivudine, or 2 RTIs + nelfinavir, or indinavir-ritonavir
Davanzo et al[19]	2004–2006	2008	Italy	Yes	Overall	1	0 (0)	PEP used not specified
Gupta et al[20]	2003–2005	2008	India	Yes	Overall	88	0 (0)	Zidovudine-lamivudine, or zidovudine-lamivudine-indinavir
Shriyan et al[21]	2009–2011	2012	India	Yes	Percutaneous	7	0 (0)	Zidovudine-lamivudine-indinavir
Villarroel et al[22]	1998–2008	2012	Chile	Yes	Overall	6	0 (0)	Zidovudine-lamivudine
Pérez-Diaz et al[23]	2009–2014	2015	Colombia	Yes	Overall	2,403	1 (0.04)	21.5% received PEP. Zidovudine-lamivudine, lopinavir-ritonavir, or emtricitabine-tenofovir. Other PEP used includes abacavir-lamivudine, atazanavir, efavirenz, and raltegravir.
					Percutaneous	2,213	1 (0.05)	
					Mucocutaneous	190	0 (0)	
Sheth et al[24]	2003–2015	2016	India	Yes	Overall	48	0 (0)	81.3% received PEP. Zidovudine-lamivudine, tenofovir-emtricitabine, zidovudine-lamivudine-indinavir, stavudine-lamivudine-indinavir, tenofovir-emtricitabine-lopinavir-ritonavir, or zidovudine-lamivudine-lopinavir-ritonavir
Current study	2002–2015	2016	United States	Yes	Overall	266	0 (0)	21.2% received PEP. Lamivudine-zidovudine-lopinavir-ritonavir, or emtricitabine-tenofovir-raltegravir
					Percutaneous	140	0 (0)	
					Mucocutaneous	115	0 (0)	
Average						7,652	10 (0.13)	

HCW, health care worker; *NR*, not reported; *PEP*, postexposure prophylaxis; *RTIs*, reverse-transcriptase inhibitors.

Chibueze A. et al, Seroconversion rate among health care workers exposed to HIV-contaminated body fluids: the university of Pittsburgh 13-year experience, Am Journal of Infection control 45 (2017) 896-900

DOCUMENTED AND POSSIBLE OCCUPATIONALLY ACQUIRED HIV INFECTION (OAI): ALL REPORTS, BY OCCUPATION

OCCUPATION	Documented OAI	Possible OAI	Total
Nurse/midwife**	56	72	128
Doctor/medical students	14	28	42
Surgeon	1	17	18
Dentist/dental worker	-	8	8
Clinical lab worker*	17	22	39
Ambulanceman/paramedic	-	13	13
Non-clinical lab worker	3	4	7
Embalmer/morgue technician	1	3	4
Surgical technician/ODA	2	3	5
Dialysis technician	1	3	4
Respiratory therapist	1	2	3
Health aide/attendant/nurse aide	2	19	21
Housekeeper/porter/maintenance	3	15	18
Other/unspecified HCW**	5	29	34
Total	106	238	344

* In the US phlebotomists are classified as clinical laboratory workers, and in France Italy and Spain nurses are usually responsible for phlebotomy. All other cases involving phlebotomists have been classed under nurses.

** 1 nurse and 1 unspecified HCW that were previously as documented cases for the 1999 Report have now been reclassified as possible cases.

http://webarchive.nationalarchives.gov.uk/20140714095709/http://www.hpa.org.uk/webc/HPAwebFile/HPAweb_C/1194947320156: Data from health protection agency, UK.

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)

Case-control study of health care workers with occupational percutaneous exposure to HIV-infected blood (33 case patients, 665 controls).

Cardo DM, Culver DH, Ciesielski CA, et al; Centers for Disease Control and Prevention Needlestick Surveillance Group. A casecontrol study of HIV seroconversion in health care workers after percutaneous exposure. *N Engl J Med* 1997;337(21):1485-1490

Wirksamkeit der PEP

- postexpositionelle Prophylaxe allein mit Zidovudin (ZDV) hat vermutlich einen Schutzeffekt in der Größenordnung von 80% (Cardo et al. 1997)
- Irvine et al. 2015: Review/Metaanalyse PEP bei Primaten: Risiko der HIV/SIV-Serokonversion 89% niedriger mit PEP. Signifikante Assoziation zwischen Zeit bis zum Beginn der PEP und Serokonversionsrate
- Makaken-Versuch (SIV):
  - PEP für 28 Tage -> keine Infektion
  - PEP für 10 Tage -> 50% nicht infiziert
  - PEP für 3 Tage -> alle infiziert

  - Start PEP innerhalb 24 Stunden -> nicht infiziert
  - Innerhalb 48 Stunden -> 50% nicht infiziert
  - Innerhalb 72 Stunden -> 75% infiziert

Irvine C et al., Efficacy of HIV postexposure prophylaxis: systematic review and meta-analysis of nonhuman primate studies, Clinical Infectious diseases, 2015:

Empfehlungen

Beginn:

so schnell wie möglich (optimal innerhalb 2 Stunden)

Nach > 72 Stunden in der Regel nicht mehr indiziert (einzelne Ausnahmen)

Dauer: 28-30 Tage

Wann PEP?

Expositionsereignis	VL bei Indexperson >50 Kopien/ml oder unbekannt	VL bei Indexperson <50 Kopien/ml
Massive Inokulation (>1 ml) von Blut oder anderer (Körper-) Flüssigkeit mit (potentiell) hoher Viruskonzentration	Empfehlen	Empfehlen
(Blutende) Perkutane Stichverletzung mit Injektionsnadel oder anderer Hohlraumnadel; Schnittverletzung mit kontaminiertem Skalpell, Messer o.ä.	Empfehlen	Anbieten
Oberflächliche Verletzung (z. B. mit chirurgischer Nadel) ohne Blutfluss Kontakt von Schleimhaut oder verletzter/geschädigter Haut mit Flüssigkeit mit potentiell hoher Viruskonzentration	Anbieten	Nicht indiziert
Perkutaner Kontakt mit anderen Körperflüssigkeiten als Blut (wie Urin oder Speichel) Kontakt von intakter Haut mit Blut (auch bei hoher Viruskonzentration) Haut- oder Schleimhautkontakt mit Körperflüssigkeiten wie Urin und Speichel	Nicht indiziert	Nicht indiziert

PEP-Regime

Deutsch-österreichische Leitlinien(2013):

Tenofovir/Emtricitabin plus Raltegravir

Raltegravir + Tenofovir-DF/Emtricitabin ≡ **Isentress®** + **Truvada®**[1]

Dosierung: **Isentress** 400 mg 1 - 0 - 1
+**Truvada** 245/200 mg 1 - 0 - 0

US-Leitlinien (2013):

Tenofovir/Emtricitabin plus Raltegravir

EACS-Guidelines (2017):

Tenofovir/Emtricitabin plus Raltegravir oder Darunavir/Ritonavir oder Lopinavir/Ritonavir

Wichtig zu bedenken

Schwangerschaft?

Indexpatient antiretroviral (vor-)behandelt? mögliche Resistenzen?

Vorerkrankungen der zu behandelnden Person? (z.B. schwere Niereninsuffizienz?...)

Dauermedikation?

Alternative PEP-Regime

Deutsch-österreichische Leitlinien(2013):

Statt Tenofovir/Emtricitabin: Zidovudin/Lamivudin

Statt Raltegravir: Lopinavir/Ritonavir

US-Leitlinien (2013):

Statt Tenofovir/Emtricitabin: Zidovudin/Lamivudin

statt Raltegravir: Darunavir/Ritonavir, Atazanavir/Ritonavir, Lopinavir/Ritonavir, Rilpivirin

EACS-Guidelines (2017):

Statt Tenofovir/Emtricitabin: Zidovudin/Lamivudin

statt Raltegravir oder Darunavir/Ritonavir oder Lopinavir/Ritonavir: Dolutegravir

Basis- und Kontrolluntersuchungen

	Index-person°	Ausgangs-untersuchung	2 Wochen	6 Wochen	3 Monate	6 Monate
HIV-Antikörper	X	X		X	X	(X)
HBsAg^	X	X				
Anti HBc- und Anti HBs-Antikörper		X		X*	X*	X*
HCV-Antikörper	X	X		X*	X*	X*
Weitere STDs	X*	X*	X*	X*		
ärztliche Untersuchung		X	X	X		
Medikamentenanamnese	X[1]	X[2]	X[2]			
Blutbild		X	X	X		
Transaminasen/ aP/ γ-Gt		X	X	X	X**	X**
Kreatinin/ Harnstoff		X	X	X		
Blutzucker		X	X	X		

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REPORTED OCCUPATIONALLY ACQUIRED HIV INFECTIONS IN HEALTHCARE WORKERS AND ESTIMATED HIV/AIDS PREVALENCE BY COUNTRY

REGION	Estimated current HIV/AIDS Prevalence*	Documented OAI	Possible OAI	Total
EUROPE				
France	100 000	13	31	44
Spain	130 000	5	-	5
Italy	100 000	5	-	5
Germany	41 000	5	33	38
United Kingdom	49 500†	5	14	19
Belgium	8100	-	3	3
Switzerland	19 000	2	1	3
Netherlands	17 000	-	2	2
Denmark	3800	-	1	1
Sub Total		35	85	120
REST OF WORLD				
Australia	12 000	6	-	6
Canada	55 000	1	2	3
South Africa	4 700 000	4	1	5
Argentina	130 000	1	-	1
Zambia	1 000 000	1	-	1
Mexico	150 000	-	9	9
Israel	2700	-	1	1
Brazil	600 000	1	-	1
Trinidad & Tobago	17 000	-	1	1
Sub Total		14	14	28
USA	890 000	57	139	196
TOTAL		106	238	344

* UNAIDS/WHO Report on HIV/AIDS Global Epidemic 2002 Update; up until end of 2001.

† Health Protection Agency, SCIEH, ISD, National Public Service for Wales, CDSC Northern Ireland and the UASSG. Renewing the focus. HIV and other Sexually Transmitted Infections in the United Kingdom in 2002. London: Health Protection Agency, November 2003.

http://webarchive.nationalarchives.gov.uk/20140714095709/http://www.hpa.org.uk/webc/HPAwebFile/HPAweb_C/1194947320156: Data from health protection agency, UK.

Report	See also Table/case( )	Year	Exposure	Time to 1st dose	HIV antibody test results Days before(-)/after(+) exposure		Onset of retroviral illness	ART drugs prescribed for HCW	Source patient on PEP
					Negative(s)	First pos.			
18†	T3(43)	1993	mucocutaneous splash	NR	3+	42+	5th week	AZT	NR
19	T3(44)	1996	deep needlestick while recapping after obtaining arterial sample for blood gases	90 minutes	0	97+	day 45	AZT + ddI for 48 hours then AZT only	no
20	T3(45)	1997	deep needlestick with a blood-filled needle (large gauge) incorrectly discarded in waste plastic bag	90 minutes	4+	55+	day 40	AZT + 3TC + IDV for 48 hours then D4T+3TC+IDV	yes
21	T3(App A31)	1998	21G Butterfly	40 minutes	0	83+	~10 weeks post-exposure	AZT + 3TC + IDV + ddI	yes
22†	T3(46)	1999	needlestick in finger web while clearing up. Needle hidden beneath some swabs	95 minutes	0	~90+	day 26	AZT + 3TC + IDV initially then d4T,ddI + nevirapine; ddI discont. after 8 days, rest of drugs cont. for the 4 wks.	yes
23†	T3(App A33)	NR	'probable hollowbore needle' (sharp not identified)	2 hours	0,14+	42+	6th week	AZT + 3TC initially, then ddI, d4T, nevirapine + hydroxyurea after 6 hrs. ddI discont. after 3 days, rest of drugs cont. for the 4wks.	yes
24	T3(108)	2002	21G phlebotomy needle	2 hours	0	80+	~11th week	AZT + 3TC (Combivir) + IDV	yes

* = Table number NR = not reported † = partial AZT post-exposure prophylaxis

Sofortmaßnahmen

Stich- oder Schnittverletzung, Kontamination geschädigter Haut

Spülung mit Wasser und Seife bzw. einem Antiseptikum, welches begrenzt viruzide Wirksamkeit aufweist

Kontamination von Auge oder Mundhöhle

Spülung mit Wasser (Auge, Mundhöhle)

Entscheid über systemische, medikamentöse Postexpositionsprophylaxe

Unfalldokumentation (D-Arzt/ Betriebsarzt)

Erster HIV-Antikörper-Test, Hepatitis-Serologie