Workgroup: Stratification of Risk Groups for Blood Borne Pathogens

Consensus Conference:
Optimal Testing of Live Donors to Prevent Transmission of Infectious Diseases
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Workgroup

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** Employed by the U.S. Government; non-voting members of WG*
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Motivation

- "Higher Risk Groups" (HRGs)
- If we screen all donors in the same manner, identifying HRGs is irrelevant
- Premise: a living donor belonging to an HRG would undergo more stringent screening than the universal screening recommendations
- "Higher Risk" might be an off-putting term, particularly to lay public

Risk of Stringent Screening

- Feasibility
- Cost
- False positives
- (Unnecessary) Delay-of-game:
  - Standard transplant: more time on dialysis
  - Desensitization: usually starts 1-2 weeks pre-tx
  - KPD: might scuttle an n-way chain/exchange
- Might even exclude donor permanently

Current HRGs

- Men who have had sex with another man in the preceding 5 years.
- Persons who report nonmedical intravenous, intramuscular, or subcutaneous injection of drugs in the preceding 5 years.
- Persons with hemophilia or related clotting disorders who have received human-derived clotting factor concentrates
- Men and women who have engaged in sex in exchange for money or drugs in the preceding 5 years.

Current HRGs

- Persons who have had sex in the preceding 12 months with any person described in items 1–4 above (previous slide) or with a person known or suspected to have HIV infection.
- Persons who have been exposed in the preceding 12 months to known or suspected HIV-infected blood through percutaneous inoculation or through contact with an open wound, nonintact skin, or mucous membrane.
- Inmates of correctional systems

Higher Risk Groups

- Questions to address about a HRG:
  - Is it feasible to identify donors who actually fall into the risk group?
  - Are the estimates of risk for this group reliable?
  - Is the estimated risk high enough to warrant screening beyond universal recommendations?
  - What proportion of donors would meet these criteria and thereby require additional screening?

HRG Framework

- Goal: Identify *a priori* a set of criteria for evaluating HRGs
  - Feasibility of identifying patients
  - Reliability of risk estimates
  - Minimum risk to consider "higher risk"
  - Proportion of donors falling into HRG
- Then: apply this framework to current and potentially new HRGs

Feasibility of Identifying Patients

- We have to be able to classify patients as belonging (or not belonging) to the HRG
- Hierarchy of evidence:
  - Strongest = effects of behavior are detectable by lab tests, physical exam, tox screen, etc
  - Behavior can be documented in a medical record
  - Behavior can only be identified by self-report
  - Weakest = requires report by third party

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Note: Ability to identify patients through more than one criteria would constitute stronger evidence than one alone

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Note: Identification of patients in some HRGs might benefit from screening on more than one occasion

Reliability of Risk Estimates

- We cannot just define a HRG because it "seems to be high risk" – needs to be based on published risk estimates (US/Canada)
- Significant heterogeneity in risk estimates: study design, sample size, study population…
  - Strongest = cohort studies of actual donors
  - Studies of *incidence* in members of the HRG
  - Studies of *prevalence* in members of the HRG

Recent Systematic Reviews

- Kucirka LM, Sarathy H, Govindan P, Wolfe J, Ellison T, Hart L, Montgomery RA, Ros RL, Segev DL. The risk of window period HIV infection in high infectious risk donors: systematic review and meta-analysis. AJT. 2011 Jun;11(6):1176-87.
- Kucirka LM, Sarathy H, Govindan P, Wolfe J, Ellison T, Hart L, Montgomery RA, Ros RL, Segev DL. The risk of window period hepatitis C infection in high infectious risk donors: systematic review and meta-analysis. AJT. 2011 Jun;11(6):1188-200.

HCV Window Period Risk

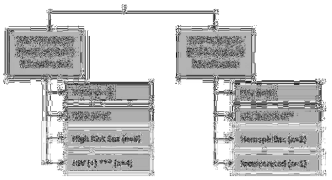

Figure 1: Search/selection. *Some studies reported both HCV prevalence and incidence; unique studies included totaled 103. **A systematic review was recently performed on this topic and the estimates reported in this review were used to calculate the risk of WP HCV infection in donors exposed to HIV infected blood. ***Used to calculate the probability that HIV infected blood was contracted with HCV.

HCV Window Period Risk

Table 2: Risk per 10 000 of an HCV infection occurring during the window period, by ELISA and NAT

HRD category	No. of patients	No. of HCV seroconverted or prevalent	Person-years	Pooled incidence (95% CI) (per 100 person-years)	ELISA WP = 66 days	NAT WP = 7 days
MSM	1341	88*	**	1.8 (1.7–2.0)	32.5 (30.7–36.1)	3.5 (3.3–3.8)
IDU	1955	520	3081.4	15.8 (15.5–16.4)	300.6 (276.1–332.8)	32.4 (29.7–35.3)
Hemophiliac	23 952 636	103	5 851 063	0.0018 (0.0015–0.0022)	0.26 (0.22–0.32)	0.027 (0.023–0.034)
Commercial sex worker	678	182*	**	6.4 (5.5–7.5)	114.9 (105.8–126.6)	12.3 (11.3–13.4)
Sex with a partner in categories 1–4	1361	391*	**	6.4 (5.5–6.9)	114.9 (104.2–123.8)	12.3 (11.1–13.2)
HIV exposed through blood	6736	1674*	***	0.0085**** (0.0019–0.0247)	4 (0.9–11.1)	0.4 (0.09–1.2)
Incarcerated*****	357	2	550.9	0.4 (0.04–1.3)	7.2 (0.7–23.5)	0.8 (0.08–2.5)

*Number of prevalent, not incident infections.
**Prevalence used to estimate incidence using methods previously described.
***Prevalence of HCV among HIV positive persons was estimated and combined with an estimate of per blood exposure risk of HCV to estimate WP infection in this category.
****Probability of infection per exposure.
*****Only one study of intraprison incidence available.

HIV Window Period Risk

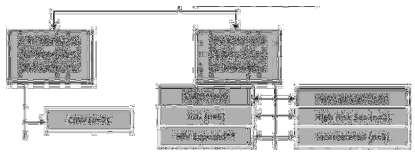

Figure 1: Search/Selection. *Some studies reported both HIV prevalence and incidence; unique studies included totaled 122. **A systematic review was recently performed on this topic and the estimates reported in this review were used to calculate the risk of WP infection in donors exposed to HIV.

HIV Window Period Risk

Table 1: Risk per 10 000 of an HIV infection occurring during the window period, by ELISA and NAT

HRD category	# Patients	# HIV Seroconverted	Person-Years	Pooled incidence (95% CI) (per 100 pya)	ELISA	NAT
MSM	19567	920	53037.2	1.7 (1.6–1.8)	10.2 (9.6–10.9)	4.2 (3.9–4.5)
IDU	9698	207	10248.54	2.0 (1.6–2.3)	12.1 (10.5–13.8)	4.9 (4.3–5.5)
Hemophiliac	23952671	71	5851070	0.0013 (0.0010–0.0016)	0.096[1] (0.086–0.106)	0.035 (0.027–0.043)
Commercial sex worker	1722[2]	129[2]	NA	1.1[2] (0.9–1.2)	6.8 (5.4–7.2)	2.7 (2.2–3.0)
Sex with a partner in categories 1–4	1454	40	3228.1	0.12 (0.09–0.16)	0.7 (0.5–0.9)	0.3 (0.2–0.4)
HIV exposed through blood	5810	3	3	0.0024[3] (0.0014–0.0040)	1.5 (0.8–2.4)	0.6 (0.4–1.0)
Incarcerated	5168	11	2831.5	0.4 (0.2–0.7)	2.3 (1.3–4.1)	0.9 (0.5–1.7)

[1]Pooled incidence among blood donors was used to calculate residual risk of infection in blood supply using the upper estimate of the WP of the NAT used in blood screening (n = 11 days). Residual risk in the blood supply was used to calculate the risk of WP infection in hemophiliacs, making the very conservative assumption that they received 1 unit of blood per day for the duration of the ELISA or NAT WPs.
[2]Incidence calculated by pooling studies of prevalence then converting to incidence using previously described methods.
[3]Per exposure estimate taken from a systematic review of postneedlestick HIV seroconversion. Risk of WP infection was calculated using per needlestick risk × risk of exposure occurring during the WP.

Minimum Risk

- HRG classification → more stringent testing
- So HRG individuals should carry a higher risk of window period HIV or HCV seroconversion than the general public (otherwise why test?)
- Absolute or relative
- Workgroup: Absolute risk of window period HIV or HCV infection in 1:10,000 individuals in a given category merits more testing

Proportion of Donors

- If a given HRG definition captures 100% of donors, no longer useful to discriminate those requiring universal vs. more stringent testing
- Workgroup: Any definition expected to capture >5-10% of donor pool would capture too many donors

Categorization

- Current "high infectious risk donor" classification is dichotomous
- But risk is very heterogeneous (active injection drug user versus hemophiliac with no recent transfusions)
- Could be more than one risk level (with each "higher" level of risk would come more stringent testing)

Current Risk Groups

Category	Feasibility of Identifying Patients	Reliability of Risk Estimates	Beyond Minimal Risk?	Proportion of Donors
MSM	self-reported	somewhat strong	Yes	Less than 5-10%
IDU	somewhat detectable by physical exam/tox screen	somewhat strong	Yes	Less than 5-10%
Hemophiliac	strongly detectable	very weak	No	Less than 5-10%
CSW	self-reported at best (unlikely to report)	somewhat strong	Yes	Less than 5-10%
Sex with Categories 1-4	self-reported at best (somewhat unlikely to report or to even know)	very weak	Unable to ascertain (very weak literature)	Probably less than 5-10% but unknown
Exposed to HIV	self-reported (probably somewhat reliable)	somewhat strong	Probably	Less than 5-10%
Incarcerated	strongly detectable if current; self-report +/- record search if previous	somewhat strong	Yes	Less than 5-10%

Potential Risk Groups

Category	Feasibility of Identifying Patients	Reliability of Risk Estimates	Beyond Minimal Risk?	Proportion of Donors
IN Cocaine, Heroin	self-reported +/- tox screen	somewhat weak	Probably	Less than 5-10%
Recent Genital Ulcers	self-reported (unlikely that physical exam will cover this)	very weak	Probably not (but weak lit)	Probably less than 5-10% but unknown
Recent STI*	self-reported (maybe medical records)	very weak	Depends on timing	Less than 5-10%
Recent Travel to Endemic Areas	self-report	maybe somewhat strong for natives, very weak for visitors	Unable to ascertain	Less than 5-10%

* and/or seeking testing or treatment of STI