FDA Workshop on Behavior-Based Donor Deferrals in the NAT Era

Lister Hill Auditorium, NIH
Bethesda, Maryland
March 8, 2006

Summary of the Workshop

Andrew I. Dayton, M.D., Ph.D., CBER

Cees van der Poel, Sanquin

- European Blood Alliance decided not to change the present policy of permanent deferral of potential donors who have a history of MSM.
- Questionnaire 2005 (G. Follea, France) 15/15 countries have permanent deferral of donors with sexual behaviour which puts them at high risk of acquiring severe infectious diseases.

Committee on Equal Rights

- The case of 4 MSM against 4 blood banks:

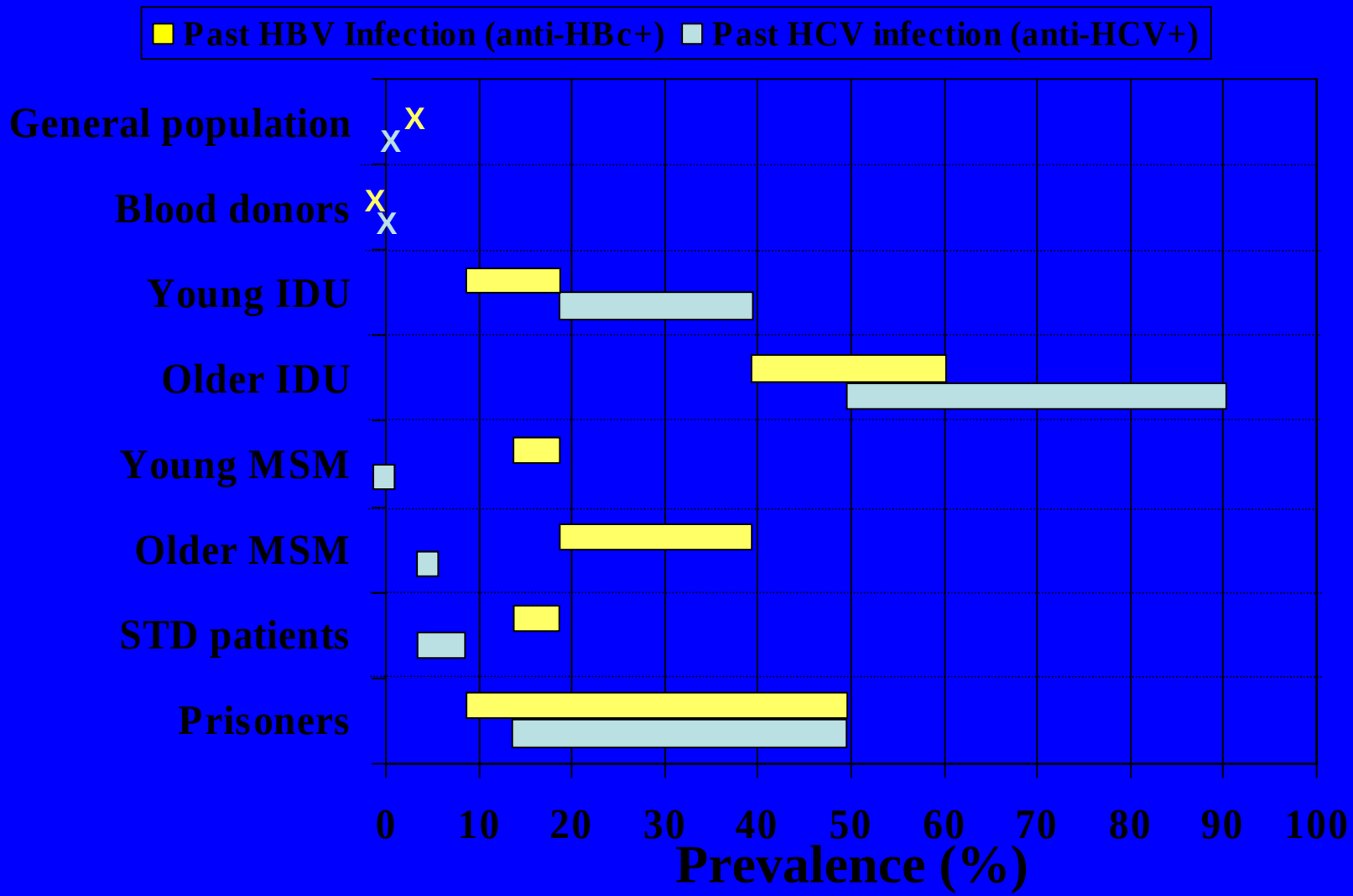
1. Equal Treatment Act forbids discrimination in offering goods or services.
2. MSM is a manifestation of sexual orientation.

3. Verdict:
4. No direct discrimination. The purpose of selection is to prevent virus infections including HIV.
5. Homosexual men are disproportionately affected by the selection.
6. There is indirect discriminatory distinction, however objectively justified and not disproportional given the interest of the recipients of blood.

Matthew McKenna, CDC

- 450K-500K MSM (lifetime) infected with HIV in the United States
- 250K-300K IDU (lifetime) infected with HIV in the United States
- ~3/4 are diagnosed in both groups
- Incidence in MSM ~2-3% per year in high risk, 1% per year in low risk (stable)
- Incidence in IDU ~0.5-1% per year (declining)
- Overall prevention outcomes impact risk to blood supply

Estimates of Past HBV (anti-HBc) & HCV (anti-HCV) Infection in Selected US Populations, Ian Williams, CDC



EIA Sensitivity to HTLV-II
Ed Murphy, UCSF

- Liu Transfusion 1999 (USA IDU)
  - Camb Biotech EIA 530/557 (95.1%)
  - Abbott 7A92 EIA 554/557 (99.5%)
  - Roche PCR 474/557 (85.1%)

  (but 47 (7.5%) PCR+ among 627 NEG on all EIA's)
- Poiesz Transfusion 2000 (IDU & S. Amer Indian)
  - Vironostika HTLV-I and –II 144/204 (71%)
  - Camb Biotech HTLV-I + rgp21 155/204 (76%)
  - Abbott HTLV-I and –Iib 159/204 (78%)
  - HTLV-II research PCR 200/204 (98%)

HTLV Risk Groups – USA
Ed Murphy, UCSF

HTLV-I (0.01% in Current US Blood Donors)

- Japanese American, Caribbean, Central African ethnicity: 0.1% to 1%
- CSW (7%), STD clinics (0.4%)

HTLV-II (0.02% in Current US Blood Donors)

- IDU: 0.5% to 17.6%, by city
- Sex partner of IDU: ~0.5%
- Native American: 2% - 3%

HTLV-I and –II Residual Risk
Ed Murphy, UCSF

- Has not been estimated since Schreiber NEJM 1996
- Probably still 1-2 per million units
- Cold storage and leukoreduction probably reduce risk but inferential data only

Conclusions from the Uganda Transfusion Study, Sheila Dollard, CDC

- **2.3% of HHV-8 seropositive blood units led to infection of the transfused patient**

- **Criteria for HHV-8 seropositive and seroconverter were very stringent, therefore this estimate is low**

Seroprevalence of HHV-8 in US Populations (Sheila Dollard)

Group	HHV-8 +
US Blood donors (screened)	2-4 %
General Population; hospital control patients, general clinic patients, pregnant women	2-10 %
Injection drug users; heterosexual, HIV-	6-11 %
Injection Drug users; heterosexual, HIV+	13-18 %
Men who have sex with men (MSM), HIV-	12-16 %
MSM; HIV+	40-50 %
Patients with Kaposi's sarcoma	> 95 %

Implications of HHV-8 Prevalence

- Relaxing the MSM deferral to 1 or 5 years would result in an ~ 2% to 5% increase in HHV-8 introduction into the blood supply.

Summary of Error Detection Rates from Investigation of Ab / MP-NAT Discordant Cases, Mike Busch

	Serology Errors	**MP-NAT Errors**
# discordant cases studied	91 (NAT+/Ab-)	566 (Ab+/NAT-)
# FN test errors detected	4 (HCV)	1 (HCV)
# RNA+/Ab+ units screened	14,242	2,716
FN error rate	**0.028 %** (1 in 3,560)	**0.037 %** (1 in 2,716)

If exclude 1st year in system 1, serol error rate = 0.0084%

Odds of Having a Reactive Screening Test Result (Mike Busch)

MSM History	Reactive Test (%)	OR (95% CI)	Adj. OR (95% CI)
< 12 m	12.6	5.3 (2.6-10.4)	2.9 (1.5-5.8)
>12m-5 yrs	34.1	7.1 (1.2-41.7)	4.3 (0.9-21.7)
>5yrs–after 1977	12.5	1.4 (0.7-2.6)	1.0 (0.5-2.2)
1977 or earlier	7.9	1.6 (0.7-3.7)	1.7 (0.8-3.7)
did not report MSM	2.7	1.0	1.0

† Odds ratio adjusted for donor status, test-seeking behavior.

p<0.001

Implications and caveats of 5 yr MSM abstention data.

- True of first time and repeat donors.
- Possibly atypical population (had already donated despite deferral policy)
- Suggests “5 yr abstention” identifies a “safe subset”.
- Underscores value of prospective, national study of MSM abstention history and STD, TTVI positivity.

Quarantine Release Errors Calculated from Biological Product Deviation Reports

Sharon O'Callaghan & Andrew Dayton

Rate of Quarantine Release Errors in Hospitals is ~18 Times That of Blood Centers

	Blood Centers	Hospitals
Confirmed Positive	0.5 / 10,000	
Repeat Reactive	0.4 / 10,000	7 / 10,000

Conclusions:
Change in Infectious Risk as % of Current Risk

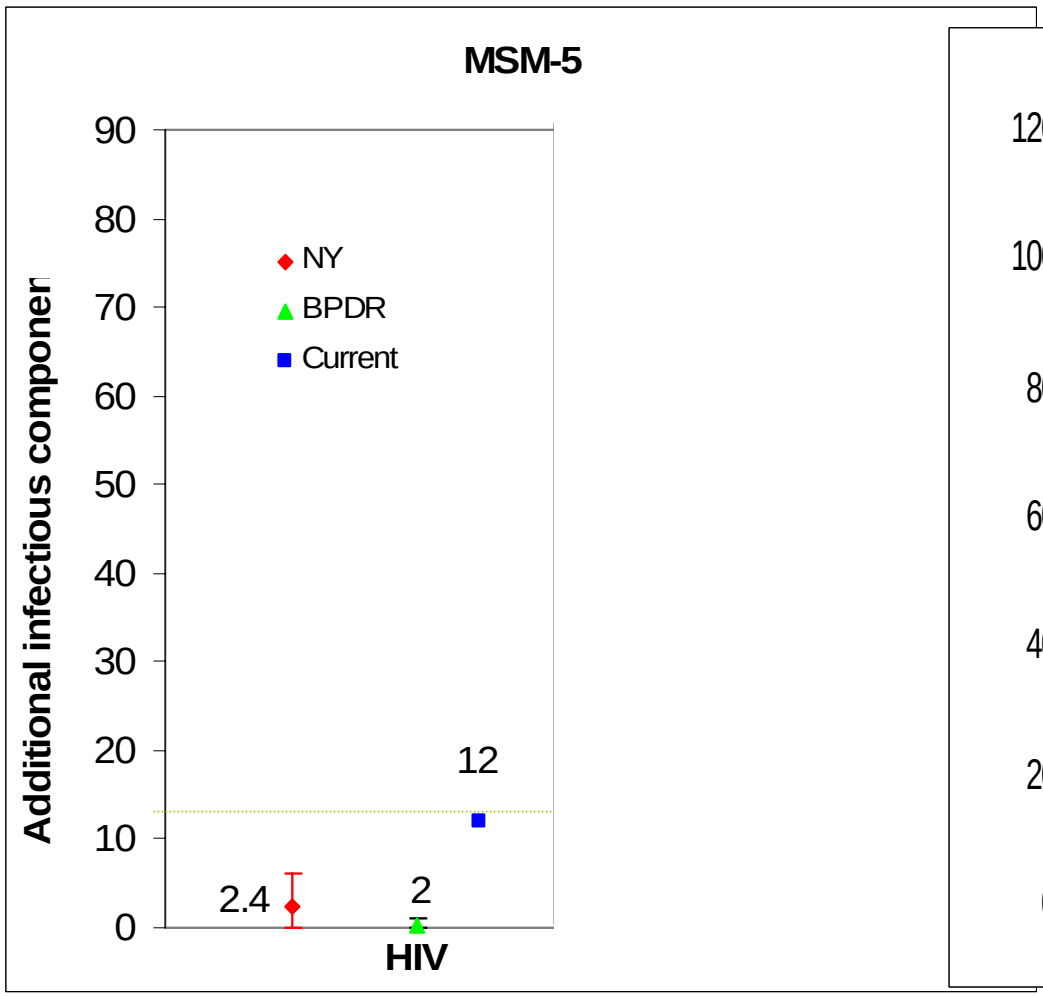
Behavior	Agent	ΔE* BPDR%	ΔE* NY Data%
MSM 5yr	HIV	1.7 %	25 %
	HBV	<0.2 %	<3 %
MSM 1 yr	HIV	2.5 %	40 %
	HBV	<0.4 %	<6 %
IDU 1 yr	HIV	5 %	75 %
	HBV	<2.4 %	2.8-7 %
	HCV	40 %	60 %
	HTLV	2100 %	2200 %

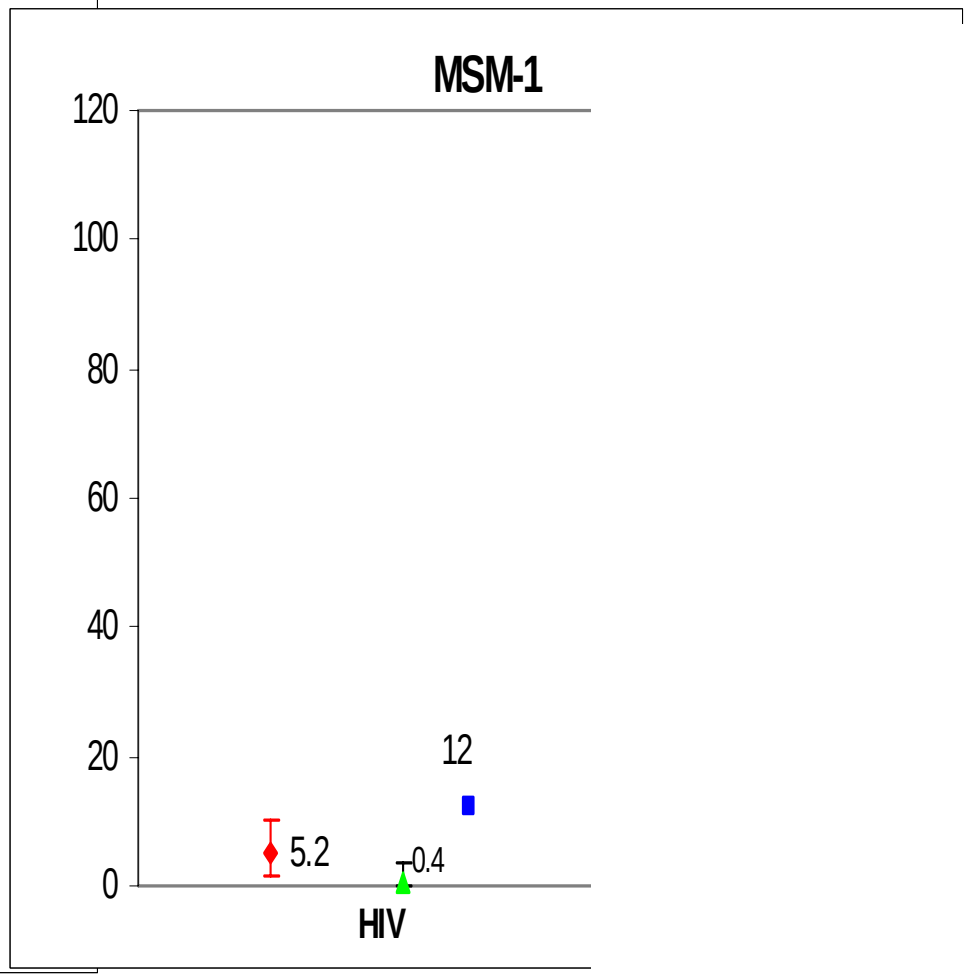
*Infectious Components

- Prevalence invariant w.r.t. abstinence
- Effective prevalence
- NY data suggests caution (HIV/MSM)
- IDU dangerous (HCV & HTLV)

IV. Number additional potentially infectious units enter supply – MSM >5yr and MSM >1yr

Comparison Results <u>EQR NY State – Linden data</u> and <u>EQR BPDR data</u> - to current risk (Steve Anderson)





Commentary, Roger Dodd

- EIDs do not appear to have any overall common characteristics with respect to class of organism, transmission route or pathogenesis. Consequently, they cannot be considered as a homogeneous group
- All transfusion transmitted infections must necessarily have a blood-borne phase.
- This does not however, assure transmissibility by sexual or low-volume non-parenteral routes.
- Consequently, risk behaviors associated with such transmission routes are not common to all TTIs

However,

- Although there is no guarantee that “The Next Virus” will be disproportionately prevalent in MSM, the real question is whether there is a high probability that such will be the case.
- MSM does represent a major risk factor for 2 of the 5 major screened TTVI.

Conclusions, Celso Bianco

- Rapid HIV tests [used for pretesting] are not compatible with the cGMP requirements for collection facilities licensed by FDA
- Pre-testing of first time donors would have a severe impact on blood availability
- Substantial operational improvements in the past few years have reduced risk of inappropriate release of marker positive components.

Questionnaire Issues (Kristen Miller)

- Factors Impacting Response Accuracy
- Sensitive/stigmatizing behaviors
- Motivation
- Literacy
- Respondent burden
- Time frame / memory problems
- Donor knowledge & understanding of risk

Conclusion

- FDA is having extensive discussion with NIH and CDC to try to arrive at a consensus recommendation.