



Blood donors with 'medium' or 'minor' risk factors for human immunodeficiency virus infection: are they eligible for donation?

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ABSTRACT

Background and Objectives. We conducted a longitudinal prospective study to assess the eligibility to blood donation of donors with 'minor' risk factors (i.e. minor surgery, professional exposure, cohabitation with 'high risk' people, occasional use of light drugs) or 'medium' risk factors for human immunodeficiency virus (HIV) infection (i.e. casual sexual relationships, multiple heterosexual exposures, sexual partnership with subjects at risk, regular use of light drugs).

Design and Methods. During a 4-year period we administered a psychosocial questionnaire to all donors attending our Center. In addition we determined anti-HIV, anti-hepatitis C virus (HCV), hepatitis B surface antigen (HBsAg) and syphilis serology (TPHA) at entry to the study and at 6-month intervals.

Results. Of 25,367 donors, 1,535 (6%) reported medium and 8,761 (34%) minor risk. At enrollment into the study, 4 medium risk donors were anti-HIV positive and there was a significantly higher rate of positivity for TPHA (0.33% vs 0.07%) and anti-HCV (1.17% vs 0.63%) in this group than in donors reporting no risk. No anti-HIV positivity was observed in minor or no risk donors. During a median follow-up of 18 months, none of 24,404 donors undergoing 106,503 visits seroconverted to HIV. The incidences of new HCV and syphilis infections were almost one log greater in donors at medium risk (3 and $1 \times 10^{-4}/\text{yr}$, respectively) than in no risk donors (0.4 and $0.1 \times 10^{-4}/\text{yr}$, respectively). Medium risk donors were more frequently males (Odds Ratio=3.2, 95% confidence interval= 2.8-3.7), aged 26-35 yrs (1.52; 1.3-1.78), single (1.4; 1.2-1.6), divorced (2; 1.4-2.8), freelance workers (1.43; 1.1-1.9) and first-time donors (1.8; 1.6-2.1) than no risk donors.

Interpretation and Conclusions. The only 4 HIV positive subjects of the cohort were medium risk donors picked up at enrollment. No HIV seroconversion was observed during the study. On the basis of this study we will continue to defer 'medium' risk donors.

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Key words: donor eligibility, risk factors, HIV infection, blood transmitted diseases

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Although the introduction of routine screening for human immunodeficiency virus (HIV) antibodies caused a dramatic reduction of the incidence of transfusion-transmitted HIV infection, this event is still possible when the donor gives blood during the so-called "window" period.^{1,2} Therefore, additional safety measures have been taken to exclude donors at risk. They include: donor education about risk factors to allow a conscious self-exclusion,³ and the collection of information on personal issues related to the risk of becoming infected with HIV^{4,5} and other viruses for which donors are not currently screened.^{6,7} As far as the latter are concerned, there is general agreement about excluding from donation subjects who are at high risk because of parenteral or sexual exposure to transmissible agents.⁸ Despite the unquestioned benefits of these measures, the recent spread of infections by heterosexual contacts among the general population with no identifiable risk factors suggests more selective criteria should be adopted to define eligibility to donate blood. In this regard, it has been questioned whether donors with 'medium' risks (i.e. multiple heterosexual experiences, use of non-intravenous illicit drugs), and 'minor' risks (i.e. healthcare workers, minor surgery exposure, household contact with 'at risk' people, dental care and invasive diagnostic procedures) should be excluded.⁹⁻¹²

To define whether subjects at minor or medium risk are eligible for donation, over a period of 4 years we examined a large cohort of blood donors in whom risk factors were assessed using a psychosocial questionnaire.¹³

Design and Methods

We evaluated risk factors and knowledge about AIDS in the cohort of all allogeneic donors attending our Center during a 4-year period (1995-1998). A total of 25,367 donors, 15% first-time, 85% repeat, were enrolled in the study. We used a psychosocial questionnaire consisting of direct and indirect questions on social items, risk factors and HIV awareness.¹³

At each donation the questionnaire was confidentially administered to all donors by a physician, during a pre-donation medical interview lasting on average 7 minutes. We arbitrarily classified donors into three groups: medium risk donors, minor risk donors and no risk donors, on the basis of the reported risk factors. Medium and minor risk factors are listed in Table 1. At enrollment and periodically at six-month intervals (every donation for women, every two donations for men) we tested all donors for anti-HIV^{1,2} and anti-HCV (Ortho-Clinical Diagnostics, Raritan, NJ, USA), HBsAg (Murex Diagnostics, Dartford, Kent, UK), TPHA (Fujirebio, Tokyo, Japan). Anti-HIV and anti-HCV positivites were confirmed by Western-blot (Genelabs Diagnostics, Singapore) and by RIBA III (Ortho-Clinical Diagnostics) respectively. 'Medium' risk donors were also tested for HTLV I/II (Genelabs Diagnostics) every six months and for HIV provirus (gag region) by an in-house polymerase chain reaction assay, at the time of risk detection. Donor data including demographic information, health history, laboratory test results, and codes of risk factors were recorded on a computerized medical record (Oracle, Oracle Italia, Milan, Italy).¹⁴

Statistical analysis

Proportions were compared by means of the chi-square test. The incidence of HIV positivity was calculated by using the number of subjects who became positive during the follow-up divided by the duration of the follow-up. Relative risk was calculated as the ratio of the incidence of positives among each risk group and the incidence in the no risk group. Odds ratio and their 95% confidence intervals (C.I.) were determined in order to study the association between epidemiological characteristics and donor category of risk.

Results

From the original number of 25,367 donors enrolled in this study, 123 initially reporting high risk experiences (use of heavy drugs either intravenously or not, homosexual experiences) were excluded from further evaluations. Of the remaining 25,244 subjects examined, 14,948 (59%), 8,761 (35%) and 1,535 (6%) reported no, minor and medium risks, respectively.

The epidemiological characteristics of blood donors at medium and minor risk as compared with the group reporting no risk are shown in Table 2. The results of serologic tests performed in the 3 groups at enrollment and during follow-up are shown in Tables 3 and 4. The follow-up was performed on 24,401 donors, as 823 donors were deferred for reasons not related to blood

Table 1. Definition of medium and minor risk factors.

Medium risks	
a.	Heterosexual relationships with a casual partner in the last year
b.	Heterosexual relationships with more than 3 partners in the last year
c.	Sexual partnership with subjects described in points a and b in the last year
d.	Current or previous sexual partnership with users of non-intravenous heavy drugs (cocaine, ecstasy)
e.	Current or previous regular use of light drugs (cannabis)
Minor risks	
a.	Minor surgery such as acupuncture in medical settings, invasive diagnostic procedures, minor surgical operations, dental care in the last year
b.	Professional exposure such as health care workers, ambulance crew, etc. in the last year
c.	Household contact with anti-HIV and anti-HCV positive subjects and with intravenous drug-users in the last year
d.	Sexual relationship with 2-3 partners in the last year
e.	Occasional use of light drugs more than one year previously

Table 2. Epidemiological characteristics of 25,244 donors grouped by type of risk. Minor and medium risk donors have been compared with no risk donors. (Odds ratios and 95% confidence intervals).

Variable	Donors		
	Minor risk N=8,761	Medium N=1,535	No risk N=14,948
Gender			
Female	3,144	230	5,391
Male	5,617	1,305 ¹	9,557
Age class (years)			
18-25	2,221	319	3,587
26-35	2,945	648 ²	4,783
36-45	1,593	297	2,840
46-55	1,447	205	2,392
56-65	555	66	1,346
Marital status			
Single	3,883	815 ³	6,857
Divorced/separated	286	77 ⁴	448
Married	4,485	638	7,464
Widowed	107	5	179
Level of education			
Medium	2,628	445	4,484
High	4,818	813	8,221
Graduate	1,315	277	2,243
Profession			
Director	573	132	972
White collar worker	3,838	578	6,597
Tradesperson	398	118	891
Blue collar worker	852	171	1,165
Freelance worker	586	151 ⁵	775
Student	1,501	318	2,690
Pensioner/housewife	939	46	1,753
Unemployed	74	21	105
Migration status			
Native	6,483	1,090	11,062
Non-native	2,278	445	3,886
Donor status			
Repeat	6,045	828	10,314
First-time	2,716	707 ⁶	4,634

¹OR 3.2 (95% CI 2.8-3.7) when references are females; ²OR 1.52 (95% CI 1.3-1.78) when reference is 18-25 year age class; ³OR 1.4 (95% CI 1.2-1.6) when references are married donors; ⁴OR 2.0 (95% CI 1.4-2.8) when references are married donors; ⁵OR 2.2 (95% CI 1.8-2.8) when references are white collars; ⁶OR 1.8 (95% CI 1.6-2.1) when references are repeat donors.

Table 3. Anti-HIV, anti-HCV, HBsAg and TPHA positive serology in 25,244 donors grouped by type of risk at enrollment; odds ratios (OR) and 95% confidence intervals (CI) of medium and minor risk donors as compared with no risk donors are reported. Only statistically significant comparisons are shown.

Risk type	Total donors N.	Anti-HIV+ N. (row%)	Anti-HCV+ N. (row%)	HBsAg+ N. (row%)	TPHA+ N. (row%)
Medium risk	1,535	4 (0.26)	18 (1.17) #	11 (0.72)	5 (0.33)*
Minor risk	8,761	0 (0.0)	32 (0.37)	13 (0.15)	5 (0.06)
No risk	14,948	0 (0.0)	94 (0.63)	55 (0.37)	10 (0.07)

#OR=1.9 (95% CI 1.1-3.2); *OR= 4.9 (95% CI 1.7-14.4).

transmittable infections. The 4 anti-HIV positive subjects observed throughout the study were detected at enrollment among medium risk donors: 2 of 62 whose partners were cocaine users, 1 of 804 who had had casual intercourse in the previous year, 1 of 167 who had had more than 3 sexual partners in the previous year. All other medium risk donors tested negative for HIV DNA and anti-HTLV I-II antibody determinations.

Medium risk donors with heterosexual risks more frequently reported having used non-intravenous illicit drugs more than 1 year previously than minor and no risk donors (23% versus 6%, $p < 0.01$). As far as other sexual risks are concerned, in the subgroup of donors who had had casual or multiple heterosexual risk experiences, 57% did not use protection and 22% had had sex with natives of an area with a high incidence of HIV infection.

Awareness of HIV infection was not different in the 3 groups, being excellent (=4/4 correct answers) in 10% of medium, 9.4% of minor and in 9.6% of no risk donors, moderate (=2-3/4 correct answers) in 54% of medium, 52.7% of minor and in 53% of no risk donors, and scanty (=1 or 0/4 correct answer) in the remaining donors.

Discussion

In this prospective study we investigated some 'at risk' behaviors and conditions reported by a large cohort of donors and we evaluated the incidence of HIV and of more common transfusion-transmitted infections. For this study we used a psychosocial questionnaire because of the well known improvement of the reliability of self-reported behavior when a face to face interview is performed in an empathic relationship.¹⁵⁻¹⁷ The ability of reducing seroprevalence of HIV in collected blood through the use of direct oral questions to prospective donors was evaluated by Johnson *et al.*⁵ Despite some positive findings, that study did not provide information about serologic and demographic profiles of excluded donors. This information may be of particular interest in order to define donor recruitment areas and to address educational programs to prevent HIV infection. Our data show that medium risk donors, as classified by our criteria, are the target 'risk' population, as the only 4 HIV positive results were found among these subjects. Moreover, a higher rate of transfusion-transmitted infection markers was detected in this group, similarly to what Lackritz *et al.*¹ described concerning donors infected by HIV. The analysis of epidemiological characteristics showed some differences between the group of medium risk donors and that of no risk donors: in particular the former group contained a higher proportion of men, of persons aged 25-35 years, of single or divorced people, of freelance workers and of first-time donors than the latter. This information could be useful to define groups of people in our area who need specific educational and health interventions. Other authors, who investigated sexual lifestyle of donors screened for the presence of antibodies to herpes simplex virus type 2, found that 'risk' donors had similar age and marital status as our 'risk' population.¹⁸ This may indicate that these conditions are related to behavioral risk experience. It is worth noting the relation between 'risk' donors and professions, suggesting the influence

Table 4. Incidence of HIV, HCV, HBsAg and TPHA seroconversion among the cohort of 24,401 donors grouped by type of risk and monitored in 106,503 attendances during a 4-year period. Medium and minor risk donors have been compared with no risk donors (ref); Rate ratios and 95% confidence intervals (CI) are also presented.

DONORS	Total N.	Attendances N.	HIV incidence rate/yr (rate ratio: 95%CI)	HCV incidence rate/yr (rate ratio: 95%CI)	HBsAg incidence rate/yr (rate ratio: 95%CI)	TPHA incidence rate/yr (rate ratio: 95%CI)
Medium risk	1,420	8,527	0	3x10 ⁻⁴ (7.5:3.3-17.3)	1x10 ⁻⁴ (2.5: 0.5-11.4)	1x10 ⁻⁴ (10:3.1-32.8)
Minor risk	8,451	35,140	0	1x10 ⁻⁴ (2.5: 1.2-5.3)	0	0.5x10 ⁻⁴ (5:1-16.4)
No risk (ref)	14,530	62,836	0	0.4x10 ⁻⁴	0.4x10 ⁻⁴	0.1x10 ⁻⁴

of psychosocial and environmental factors (such as psychological stress, less stability, less commitment) on individual 'risk' behavior.¹⁹ Despite the donors' efforts to maintain good health,²⁰ the use of condoms by medium risk donors was less widespread than that described in a sample of French individuals who declared the same risk exposure (i.e. casual sexual intercourse).²¹ This can indicate that these blood donors have a low perception of risk with regards to their own experiences, or that socio-cultural influence makes these two groups not comparable. We observed a higher prevalence of risk factors in first-time than in repeat donors, a finding in agreement with those of other authors.^{22,23} The absence of seroconversion for HTLV I/II may be due to the limited size of our sample. In our series, donors who admitted the use of light drugs reported a higher frequency of heterosexual risk experiences. It can be hypothesized that the behavioral impairment produced by these drugs may make people more prone to sexual risk experiences, as already described for alcohol abuse.²⁴ However, the exclusion of donors who use light drugs (cannabis) seems to be rather impractical, as this habit is widespread among young metropolitan groups.^{25,26} Some authors found a higher incidence of HIV infection in cocaine-crack users than in the general population.²⁷ We did not follow-up cocaine users, because we consider them high risk people; however, our data show that also being partner of a cocaine user may represent a risk factor for HIV infection, as 2 HIV positive cases were found among 60 subjects in this condition. Moreover, this finding highlights the importance of also asking questions about the donor's sexual partner, in particular prospective female donors, who may be more vulnerable in sexual relationships.⁹ The vast majority of people infected by HIV do not transmit the virus except by the well-recognized routes. Nevertheless, some cases of HIV infection have been reported during the provision of health care in both institutional and home settings.^{12,28,29} Our data seem to confirm the low probability of becoming infected after exposure to minor risk factors. In fact, no HIV seroconversion has been observed in minor risk donors, even if a slightly higher incidence of HCV seroconversion has been observed in these donors than in no risk ones. This may be due to the relatively small size of our sample or to the good socio-economical level of our donors and suggests that donors with 'minor risk' can be admitted to donate blood.

The deferral of 'medium' risks donors results in the loss of 6% of prospective donors in our Center: this deferral rate is rather high in consideration of the current shortage of blood and the early detection of HIV antibodies by the cur-

rent tests. Nevertheless, these donors are a potential source of HIV infections because they could be in the window period, a rare but possible event.³⁰ Moreover, this blood could transmit other infections acquired by sexual contacts such as those caused by mutants of hepatitis B⁶ and other retroviral infections,³¹ including human herpes virus type 8³² for which donors are not screened. The use of these donor selection criteria would be particularly useful in those countries in which serologic screening is not yet performed or only incompletely so.³³

Contributions and Acknowledgments

CS and GS conceived and designed the study. CS and LV wrote the paper and performed the follow-up of the donors. ET was responsible for statistical analysis. PR, DP, FM contributed to interpretation of data and revision of the manuscript. GS was responsible for the critical evaluation and final approval of this version. The order of authorship is in accordance with these contributions.

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Disclosures

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Potential implications for clinical practice

- ◆ We found an association between some behavioral risk factors and serologic markers of blood-borne infections. This could be useful for updating and improving current criteria for blood donor selection.

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