

1 **Manuscript Title:** Decreasing trends in HTLV-1/2 but steady HIV-1 infection among
2 replacement donors in Argentina

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20 **Running Head:** human retroviruses, blood, Buenos Aires

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24 ABSTRACT

25 In Argentina, current procedures to ensure safety of the blood supply for
26 transfusion include reviewing the records of blood donors with particular attention to the
27 serologic detection of specific blood borne infections. Data of 28,483 blood donations
28 received from 1st January 2003 to 31st December 2008 in a public hospital in Buenos
29 Aires were analyzed.

30 Of the 28,483 blood donations, 7,442 (26.1%) were female donors, 14,582
31 (51.2%) were younger than 35 years-old, and 23,746 (83.4%) were Argentine. Among
32 all, only 285 (1.0%) were voluntary donations. The prevalence of HTLV-1/2 was 0.1%
33 (95% CI 0.063-0.15), being 0.07% for HTLV-1 and 0.03% for HTLV-2. The prevalence
34 of HIV-1 was 0.2% (95% CI 0.110-0.206). No HIV-1/HTLV-1/2 co-infections were
35 detected among volunteer donors. During this study period, data confirm that HTLV-1/2
36 infection was not endemic in Buenos Aires, and that the prevalence of HTLV-1/2
37 decreased throughout while HIV-1 was stable. Due to the small number of voluntary
38 donations, we could not conduct comparisons to infection rates in replacement donations.
39 Although there have been several ongoing programs aimed at recruiting voluntary blood
40 donations and changing from a mostly repository system to an altruistic system of blood
41 donations, Argentina is still far from reaching this objective. More efforts are needed in
42 order to increase and assure the quality of blood supply in this country.

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44 **Keywords:** HTLV, HIV, blood donors, Argentina

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INTRODUCTION

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Contrary to the recommended recruitment model of altruistic or community volunteer blood donations proposed by the World Health Organization, the Latin-American blood supply, including Argentina, is based mainly on repository or replacement donations (Pan American Health Organization, 1998). Such donations, made by patient-recruited donors, are considered less safe, thus representing a significant challenge to the health-care system (Ministerio de Salud y Ambiente, 2009). In addition to a steady supply of safe donors, current procedures to ensure the safety of blood supply for transfusion include reviewing the records of blood donors with particular emphasis on the serological detection of specific blood borne infections (Schmuñis et al., 2000).

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At present, the detection of markers for HTLV-1/2, HIV, HBV, HCV, *T. cruzi*, *T. pallidum* and Brucella is mandatory in Argentine blood banks. Although the detection of HTLV-1/2 antibodies has been proposed by the Argentine Hematology Association since 1997, it only became mandatory in blood banks in December 2004, after endemic areas for these infections were detected in the Northern provinces of the country (Biglione et al., 2005; Salud Pública, 2005). Since this mandate, no data have been published regarding the prevalence of HTLV-1/2 among blood donors.

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The main objective of this study was to estimate the prevalence and the trends in infection prevalence of HTLV-1/2 and HIV-1 antibodies among voluntary and replacement blood donors attending a public blood bank in Buenos Aires, Argentina, over a five year period from 2003 to 2008.

MATERIALS AND METHODS

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71 A retrospective analysis of serial cross-sectional data collected at the blood bank
72 of the “Juan A. Fernandez” public Hospital in Buenos Aires was conducted. Data from
73 consecutive blood donations was collected from blood bank records from January 2003 to
74 December 2008. Blood donors were classified as either replacement blood donors (if they
75 stated that the reason for donating was that they had a friend or relative in the hospital) or
76 as voluntary donors (those who made altruistic, not-remunerated donations). All potential
77 blood donors underwent a medical interview and could refuse to donate by self-exclusion.
78 Samples were tested first as singletons and reactive samples were repeated in duplicate on
79 the same assay. Samples with at least two positive results were considered repeatedly
80 reactive. HTLV-1/2 screening was performed by ELISA (Vironostika HTLV-I/II,
81 bioMérieux, Boxtel, The Netherlands; Murex HTLV I+II, Abbott, Dartford, Kent, UK or
82 Bioelisa HTLV-I+II(r), Biokit, Barcelona, Spain). Repeatedly reactive samples for
83 HTLV-1/2 infection were confirmed by Western blot (WB) (HTLV blot 2.4, Genelabs
84 Diagnostics, Science Park, Singapore). HIV-1 screening was performed by ELISA
85 (Vironostika HIV-1 Antigen, bioMérieux, Boxtel, The Netherlands; Vironostika HIV
86 Uni-Form II plus O, bioMérieux, Boxtel, The Netherlands; Vironostika HIV Uni-Form II
87 Ag/Ab, Organon Teknika, Boxtel, Netherlands; Murex HIV-1.2.O, Murex, Biotech Ltd,
88 Kent, UK or Anti-HIV TETRA ELISA, Biotest, Dreieich, Germany). Repeatedly reactive
89 samples for HIV-1 infection were confirmed by WB (Novapath HIV-1, Immunoblot,
90 BioRad, California, USA).

91 Prevalence was estimated as the proportion of confirmed positive tests among the
92 total screened population by year of testing; 95% confidence intervals (CI) were

93 calculated assuming a binomial distribution. Prevalence and changes in prevalence over
94 time were analyzed by chi-square test, stratified by nationality, age and sex. Statistical
95 analyses were performed using the SPSS software, release 11.5.0, 2002, Chicago, IL,
96 USA.

RESULTS

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98 Of the 28,483 blood donations, 7,442 (26.1%) were female donors, 14,582
99 (51.2%) were younger than 35 years-old, and 23,746 (83.4%) were Argentine. Of the
100 total donations, 285 (1.0%) were voluntary, mostly of Argentine nationality (n=243;
101 85.3%), and principally males (n=180; 85.3%). Less than one in five voluntary donations
102 (n=55; 19.3%) were from 18 repeat volunteer donors. The number of donations varied
103 from a low of 3,912 in 2006 to a high of 5,223 in 2004. Table 1 shows the prevalence of
104 HTLV-1/2 and HIV-1 by year and gender. The prevalence of repeatedly reactive samples
105 for HTLV-1/2 was 0.8% (221/28,483) (95% CI 0.67-0.88) and further WB confirmatory
106 testing yielded a final prevalence of 0.1% (28/28,483) (95% CI 0.063-0.15). There was a
107 decreasing trend in HTLV-1/2 infection, especially among men (p=0.004), and no
108 HTLV-1/2 infection was observed among voluntary donations. When comparing the
109 prevalence of HTLV-1/2 before and after the resolution for mandatory detection in blood
110 banks was passed, no significant difference was observed although the number of positive
111 individuals decreased considerably in 2007 and 2008.

112 Out of the 28 confirmed HTLV-1/2 seropositive individuals, 21 were HTLV-1
113 (0.07%) and seven were HTLV-2 (0.03%). Among the HTLV-1 positive individuals, nine
114 were Argentine (five from Buenos Aires city and surroundings, three from Jujuy and one
115 from Misiones), four Paraguayan, four Peruvian, two Chilean, and one Bolivian. As for
116 the HTLV-2 positive cases, three were Argentine (from Buenos Aires), two Peruvian and
117 one Uruguayan. Information on two individuals was not available (Table 2).

118 Out of the 21 HTLV-1 positive blood donors, four were positive for hepatitis B virus
119 (HBV) core antibody (anti-HBc). Of these four cases, two were co-infected with

120 *Trypanosoma cruzi* (*T. cruzi*) and one of them also with *Treponema pallidum* (*T.*
121 *pallidum*). There were no HIV-1/HTLV-1/2 coinfections. No associations were found
122 between HTLV-1/2 and co-infections with HBV, *T. cruzi* and *T. Pallidum* ($p>0.05$).

123 The screening prevalence for HIV-1 was 0.3% (82/28,483) (95% CI 0.22-0.35)
124 and 0.2% (45/28,483) (95% CI 0.110-0.206) after WB confirmation. Out of the 45 HIV-1
125 positive individuals, 33 were Argentine (23 from Buenos Aires city and surroundings,
126 two from Misiones, two from Corrientes, one from Jujuy, one from La Rioja and one
127 from Santiago del Estero), seven Paraguayan, three Peruvian and two Uruguayan.
128 Information on three individuals was not available.

129 Among the 45 confirmed HIV-1 positive blood donors, 7 were positive for anti-
130 HBc. Of these seven cases, one was positive for antibodies to hepatitis C virus (HCV),
131 two were co-infected with *T. cruzi* and one of them also with *T. pallidum*. A total of two
132 HIV/HCV co-infections and two HIV-1/*T. pallidum* were detected. HIV-1 prevalence
133 was stable, over the study period but HIV-1 infection was significantly higher among
134 male compared to female donors ($p< 0.05$). No HIV-1 infection was detected among
135 voluntary donations.

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DISCUSSION

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140 This study reports the prevalence of HIV-1 and HTLV-1/2 before and after its
141 detection became mandatory in blood banks from Argentina as well as the trends in these
142 transfusion-related infections at a public blood bank setting in Buenos Aires.

143 Studies conducted in the 1990s in Argentina, before the screening for HTLV-1/2
144 antibodies became compulsory, showed prevalence of 0.03%, 0.07% and 0.21%,
145 respectively, which are in agreement with our results (Schmuñis et al., 2000; Del Pino et
146 al., 1994; Perez Bianco et al., 1993). However we did observe a higher screening
147 prevalence in this sample compared to data from the Ministry of Health (MoH) (Informe
148 del Control de Sangre a Transfundir, 2007). This may be due to the use of commercial
149 kits which are not the best in terms of sensitivity for HTLV-1/2 detection (Berini et al.,
150 2008). Nevertheless, the final prevalence (0.1%) after WB confirmation is low, despite
151 the high prevalence of these retroviruses among high-risk populations and the high
152 immigration rates from HTLV-1/2 endemic areas to the capital city (Biglione et al., 2005;
153 Lombardi et al., 1991; Pampuro et al., 1993). Regarding this point, it is interesting to note
154 that almost half of the persons with HTLV-1/2 antibodies were from neighboring
155 countries such as Peru, where HTLV-1 is known to be endemic. When examining the
156 decreasing trend of HTLV-1/2 infection over the years studied, it is noted that the
157 detection of HTLV-1/2 antibodies in blood banks became mandatory in December 2004
158 and could have contributed to the reduction in the number of infected individuals coming
159 for further donations.

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161 Ccomparison of HTLV-1/2 infections with other markers for co-infections did not
162 show any significant association, suggesting that the transmission of HTLV-1/2
163 infections is not associated with risk exposures for infection with other infections
164 assessed in this study.

165 With respect to HIV-1, the epidemic in Argentina was principally focused in men
166 who have sex with men (MSM) and injecting drug user communities in mid 1980's. The
167 infection has disseminated to the heterosexual population and it is especially affecting
168 sexually active women (Ministerio de Salud y Ambiente, 2008).

169 Previous studies conducted among blood donors in 1993 and 2000 reported a final
170 prevalence of 0.21% and 2.42-3.36 per 1,000 donations respectively, similar to the
171 findings presented in this study (Schmuñis et al., 2000; Perez Bianco et al., 1993).
172 Although constant efforts are being made to promote HIV testing, there were no
173 significant changes in HIV-1 seropositivity over the last few years.

174 In summary, HTLV-1/2 infection prevalence decreased in blood donors between
175 2003 to 2008, indicating that Buenos Aires city is a non-endemic area. Although there
176 was only a small number of voluntary donors in this study, neither HTLV-1/2 nor HIV
177 infections were observed in this population, suggesting, as is widely known, that the use
178 of these donations for blood and blood components is safe (Saguier et al., 2003). This
179 situation is similar in other Latin American countries, including Chile, El Salvador,
180 Guatemala, Mexico, Nicaragua, Paraguay, Peru and Venezuela, where the majority of
181 blood supplies come from repository donors (Schmuñis et al., 2005). The national
182 programs launched in the last decade in Brazil for recruiting voluntary blood donors have
183 significantly boosted this type of donation (Schmuñis et al., 2005).

184 Several strategies are being implemented nationwide aimed at increasing
185 voluntary blood donations; however, the number of voluntary donors is still far from
186 covering the needs of the national blood supply system. Therefore, big efforts are being
187 made to implement national programs aimed to boost voluntary, altruistic and habitual
188 blood donations in Argentina as well as to assure the quality of screening for infection
189 markers and to conduct appropriate surveillance and prevention measures at local levels.

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REFERENCES

204 Berini C, Pascuccio S, Bautista C, Gendler S, Eirin ME, Rodriguez C, Pando MA,
205 Salomon H, Biglione MM. 2008. Comparison of four commercial screening assays for
206 the diagnosis of Human T-cell Lymphotropic virus types 1 and 2. *Journal of Virological*
207 *Methods* 147(2), 322--327.

208 Biglione MM, Astarloa L, Salomon HE. 2005. High prevalence of HTLV-I and
209 HTLV-II among blood donors in Argentina: a South American health concern. *AIDS*
210 *Research and Human Retroviruses* 21(1), 1--4.

211 Del Pino N, Martínez Peralta L, Pampuro S, Pimentel E, Libonatti O, 1994. HTLV-I/II
212 seroprevalence and coinfection with other pathogens in Blood Donors in Buenos Aires.
213 *Journal of Acquired Immune Deficiency Syndrome* 7, 206--207.

214 Informe del Control de Sangre a transfundir. 2007. Available at www.anlis.gov.ar
215 Accessed December 30, 2008.

216 Lombardi V, Carrillo MG, Alimandi M, Boxaca M, Rossi P, Libonatti O, 1991. Overt
217 and latent HIV 1 and HTLV-I infection in cohorts of at high risk individuals in
218 Argentina. *Molecular and Cellular Probes* 5(6), 409--417.

219 Ministerio de Salud y Ambiente de la Nación: Boletín sobre VIH/SIDA en la
220 Argentina. Año XI, Número 25, Agosto 2008. Pg. 7.

221 Ministerio de Salud y Ambiente. Seguridad Transfusional. Available
222 at [www.msal.gov.ar/html/plan-nacional-donacion-sangre/documentos/seguridad-](http://www.msal.gov.ar/html/plan-nacional-donacion-sangre/documentos/seguridad-transfusional.doc)
223 [transfusional.doc](http://www.msal.gov.ar/html/plan-nacional-donacion-sangre/documentos/seguridad-transfusional.doc). Accessed January 7, 2009.

224 Pampuro SE, Rabinovich RD, Martínez Peralta L, Gallo D, Hanson C, Libonatti O,
225 1993. Presence of human T-cell lymphotropic virus types I and II and coinfection with
226 human immunodeficiency virus in different groups at risk in Argentina. *Journal of*
227 *Acquired Immune Deficiency Syndrome* 6(7), 851--852.

228 Pan American Health Organization, 1998. Blood bank situation in Latin America,
229 1996: serological markers for communicable diseases in blood donors. *Epidemiology*
230 *Bulletin* 19, 12--14.

231 Perez Bianco R, Santarelli MT. 1993. Analysis of a national survey for diseases
232 transmitted by blood transfusion. *Medicina (B Aires)* 53(6), 491--496.

233 Saguier MC, Góngora GN, Houriet S, Reybaud JF, Blejer JL, Galli AC, Salamone HJ,
234 2003. Seroprevalencia en donantes voluntarios de sangre. Rev Arg Transf. 29: 38.

235 Salud Pública Resolución 58/2005. B.O. 31/01/05 -MSA-Normas Técnicas y
236 Administrativas de la Especialidad Hemoterapia. Available at www.femeba.org.ar
237 Accessed March 22, 2009.

238 Schmunis GA, Zicker F, Segura EL, del Pozo AE. 2000. Transfusion-transmitted
239 infectious diseases in Argentina, 1995 through 1997. Transfusion 40(9),1048--1053.

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APPENDIX

266 For HBV antigen Hepanostika HBsAg Uni-Form II, bioMérieux, Boxtel, The
267 Netherlands and for HBc, Hepanostika anti-HBc Uni-Form, bioMérieux, Boxtel, The
268 Netherlands; Bioelisa anti-HBc, Biokit, Barcelona, Spain and Enzygnost Anti-HBc
269 monoclonal, Dade-Behring, Marburg, Germany were used.

270 For HCV antibodies Antibody to HCV Core Antigen ELISA Test System, Ortho
271 Clinical Diagnostics, Raritan, New Jersey, USA; anti-HCV ELISA, Wiener Laboratories
272 S.A.I.C., Rosario, Argentina; Bioelisa HCV, Biokit, Barcelona, Spain, or Murex HCV
273 4.0, Abbott Laboratories, Abbott, Illinois, USA, were used.

274 For Chagas HAI Chagas, Polychaco S.A.I.C., Buenos Aires, Argentina; Chagatest
275 HAI, Wiener Laboratories S.A.I.C., Rosario, Argentina; SERODIA Chagas, Fujirebio
276 Inc, Tokyo, Japan; Chagatek ELISA, bioMérieux, Buenos Aires, Argentina or Chagatest
277 ELISA recombinante v.3.0, Wiener Laboratories S.A.I.C., Rosario, Argentina were used.

278 For *T. pallidum* VDRL test, Wiener Laboratories S.A.I.C., Rosario, Argentina or
279 VDRL-SEPSSI, Britania, Buenos Aires, Argentina were used.