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No. 1

# 医薬品 研究報告 調査報告書

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| 一般的名称 | 人血清アルブミン | | | | | |
| 販売名(企業名) | 赤十字アルブミン20(日本赤十字社)<br>赤十字アルブミン25(日本赤十字社)<br>赤十字アルブミン20%静注4g/20mL(日本赤十字社)<br>赤十字アルブミン20%静注10g/50mL(日本赤十字社)<br>赤十字アルブミン25%静注12.5g/50mL(日本赤十字社) | | 研究報告の公表状況 | Tortajada C, de Olalla PG, Pinto RM, Bosch A, Cayla J. Euro Surveill. 2009 Apr 16;14(15). pii: 19175. | 公表国<br>スペイン | |

| 研究報告の概要 | 使用上の注意記載状況・その他参考事項等 |
|---|---|
| ○2008年9月～2009年3月に発生したスペインのバルセロナにおける男性と性的関係を持つ男性(MSM)間のA型肝炎のアウトブレイク<br>2008年9月1日～2009年3月9日の期間に、バルセロナにおいてA型肝炎症例150例が報告され、これは過去2年間の同期間と比較して3倍に増加した。ほとんどの症例は、MSMであることを報告した87名を含む、成人男性に発生した。以上のことは、MSM集団にアウトブレイクが発生中である可能性を示し、このコミュニティを標的とした有効な予防接種プログラムの必要性を強調している。 | 赤十字アルブミン20<br>赤十字アルブミン25<br>赤十字アルブミン20%静注4g/20mL<br>赤十字アルブミン20%静注10g/50mL<br>赤十字アルブミン25%静注12.5g/50mL<br><br>血液を原料とすることに由来する感染症伝播等 |

| 報告企業の意見 | 今後の対応 |
|---|---|
| 2008年9月1日～2009年3月9日の期間に、スペイン、バルセロナにおいてA型肝炎症例150例が報告され、MSM集団におけるアウトブレイクの可能性が示されたとの報告である。<br>これまで、本製剤によるHAV感染の報告はない。さらに最終製品についてHAV-NAT陰性であることを確認している事から本製剤の安全性は確保されていると考える。 | 本製剤の安全性は確保されていると考えるが、本製剤の重要なウイルス除去・不活化工程である液状加熱に抵抗性のある遺伝子型の存在が示唆されたので、今後もウイルスの検出や不活化する方策について情報の収集に努める。なお、日本赤十字社は、輸血感染症対策として、問診で肝炎の既往があった場合、A型肝炎については治癒後6ヶ月間、家族に発症した人がいる場合は1ヶ月間献血不適としている。また、男性と性的接触を持った男性は1年間献血不適としている。 |

別紙2

JRC2009T-025

Rapid communications

# Outbreak of hepatitis A among men who have sex with men in Barcelona, Spain, September 2008 – March 2009

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Between 1 September 2008 and 9 March 2009, 150 cases of hepatitis A were reported in Barcelona, representing a threefold increase compared with the same period in the previous two years. The majority of the cases occurred in adult men, including 87 who reported having sex with men. This indicated the possibility of an outbreak ongoing in the population of men who have sex with men (MSM) and emphasised the need to target this community with more effective vaccination programmes.

## Introduction

In Spain, hepatitis A is a reportable disease defined by acute hepatitis symptoms combined with the presence of immunoglobulin M antibodies to hepatitis A virus (IgM anti-HAV) [1]. Physicians and laboratories report cases to the local public health agencies. The Public Health Agency of Barcelona is the relevant office for the city of Barcelona, covering a population of 1,600,000 inhabitants. The Health Department of the Government of Catalonia collects cases from all the regional agencies of Catalonia and reports them to the National Centre of Epidemiology in Madrid.

Since September 2008, an increase in the number of reported cases of hepatitis A in the municipality of Barcelona has been observed. Between 1 September 2008 and 9 March 2009, a total of 150 confirmed cases of hepatitis A were reported from the area. In the same period in 2006-7 and 2007-8 the numbers of notified cases were 54 and 55 respectively.

The notification data indicated that the increase may affect predominantly men who have sex with men (MSM). An outbreak alert was raised after five cases had been notified in one day, including four men aged 23-25 years of whom three were known to be MSM. For comparison, in the previous two years, the average number of notifications ranged from 0 to 12 cases per month. This prompted us to undertake a survey among the reported adult male cases, to determine whether they belonged to the group of MSM and whether they engaged in activities associated with an increased risk of hepatitis A infection [2-5].

The outbreak is still ongoing and notifications occur at a frequency of one case per day.

## Methods

For the purpose of the outbreak investigation, a case was defined as a man over 18 years old who had sex with men, was resident in Barcelona city and had symptoms of acute hepatitis with onset from 1 September 2008 and positive result of IgM anti-HAV test.

To identify cases according to the above definition, all reported hepatitis A patients who were male and older than 18 years, resident in Barcelona city and had symptoms onset from September 2008 were interviewed with a modified questionnaire based on the standard questionnaire for hepatitis A of the Health Department of the Government of Catalonia but with additional questions on sexual behaviour. The interviews were done by telephone or e-mail. Cases that had been reported before the outbreak alert but could fulfil the case definition criteria were re-interviewed retrospectively, using the modified questionnaire.

Questions included having sex with men, number of sexual partners, visiting bathhouses, bars and discos, use of the internet to look for sexual partners, having group sex, and working as sex worker during the two months before symptoms onset, as well as hepatitis A immunisation status and infection with human immunodeficiency virus (HIV).

Contact-tracing was performed according to standard procedures, as done routinely by the local Public Health Agency for every case of hepatitis A reported. During the interview, the patient is asked to identify close contacts. These people are then contacted directly by the Agency and informed about the risk of infection and offered vaccination or postexposure prophylaxis. Vaccination and immunoglobuline is provided free of charge in the Agency offices or, in some cases, administered by healthcare workers visiting the contacts.

Sera from 14 cases who fulfilled the case definition were sent to the Enteric Virus Laboratory of the Department of Microbiology of the University of Barcelona for genetic analysis.

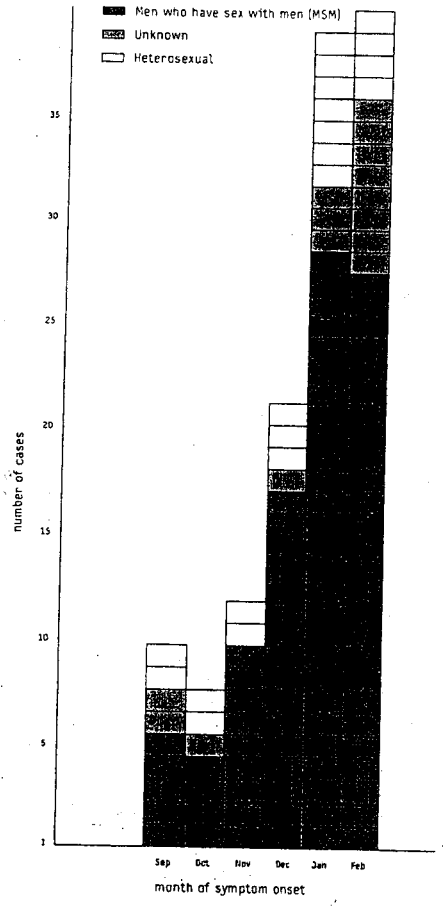
## Results

From 1 September 2008 to 9 March 2009, a total of 150 laboratory-confirmed hepatitis A cases were reported. Of the 150 cases, 137 (91%) were older than 18 years, and of these, 126

(84% of the total) were men and 11 (7% of the total) were women. In the equivalent period in 2006-7, of the 54 hepatitis A cases reported, 29 (54%) were older than 18 years, including 21 (39%) men. Similarly, in 2007-8, there were 55 cases in total, 24 (43%) of whom were over 18 years old, including 13 (23%) men.

FIGURE

**Number of cases of hepatitis A among men older than 18 years, by month of onset of symptoms and sexual behaviour, Barcelona, 1 September 2008 - 9 March 2009 (n=122, preliminary data)**




Source of data: Public Health Agency of Barcelona, Spain

Of the 126 adult male patients, 107 were interviewed using the modified questionnaire. In response, 87 (69%) declared to have had sex with men and 20 (16%) defined themselves as heterosexual. For the remaining 19 notified cases (15%) this information was not available (Figure).

As a result, 87 persons fulfilled the case definition criteria. The median age of these cases was 33 (IC 95%: 31-34) years. Ten (11%) were HIV-positive. Only one had been vaccinated against hepatitis A and another one had received only one ddse of the vaccine.

A considerable proportion of MSM cases reported engaging in activities that may be associated with increased risk of infection. The mean number of sexual partners was four (IC 95%: 3-6), 14 cases (16%) used the internet to look for sexual partners, 26 (30%) frequented discos or bars and 19 (22%) visited bathhouses.

The virological analysis showed HAV genotype IA in sera obtained from 14 patients. The results of phylogenetic analysis are not available yet.

**Control measures**

Vaccination against hepatitis A of all cases' contacts and postexposure prophylaxis of close contacts and sexual contacts within 15 days of the last exposure has been recommended. Vaccination and immunoglobuline is offered free of charge in the Public Health Agency of Barcelona.

We performed contact-tracing and offered vaccination and immunoglobuline to those identified. In cases when patients did not have or did not want to give this information (address or telephone), we advised them to inform their partners and close contacts to get the vaccination or immunoglobuline.

In addition, we have also strengthened the existing recommendations for vaccination of MSM by distributing fliers and posters in collaboration with the Spanish "Coordinadora Gai-Lesbiana" a federation which coordinates the activity of gay non-governmental organisations (NGO) and other associations.

The vaccination program for hepatitis A and B in gay bathhouses, which has been in place in Barcelona since 2004, has been reinforced, as well, by increasing the number of visits of healthcare workers and by covering more establishments.

To raise awareness about the possible outbreak, e-mail alerts were sent to microbiology laboratories, local practitioners and hospitals to enhance notification.

Gay organisations were informed about the hepatitis A outbreak affecting MSM, and information about the outbreak was published on some gay websites.

**Discussion**

An increase in the number of reported hepatitis A cases in Barcelona has been observed since September 2008. Of the 150 cases reported between 1 September 2008 and 9 March 2009, 87 were identified as MSM.

An increase in the number of notifications has recently been observed in other regions of Spain, as well. The data available are from the period between week 36 of 2008 and week 4 of 2009. Andalucia has reported an increase from 175 and 125 cases for that period in 2006-7 and 2007-8, respectively, to 350 in 2008-9; Madrid has reported an increase from 95 and 75 to 230 and Castilla – La Mancha has registered an increase from 15 and 20 cases to 60 [6]. It is not clear whether these increases are due to outbreaks and whether they affect a particular risk group but investigations are ongoing.

In Spain vaccination for hepatitis A is not included in the routine immunisation schedule, but is recommended for certain risk groups, including MSM [7].

In recent years, 2002-3 and 2004, two outbreaks of hepatitis A among MSM, affecting 48 and 60 people respectively, were detected in Barcelona. Most of them (80%) were bathhouse users [data from the Public Health Agency of Barcelona, not published]. Similar venues have also been associated with hepatitis A outbreaks elsewhere in Europe [2-5]. The strain identified in the current outbreak is different from the one detected in the MSM outbreaks in 2002-3 and 2004.

Since 2004 a special vaccination programme for hepatitis A and B has been targeted at those who frequent gay bathhouses. Healthcare workers from the Public Health Agency of Barcelona visit these venues and offer information about hepatitis A, B, C and sexually transmitted infections (STI), perform rapid tests for HIV and administer vaccinations for hepatitis A and B. To date, 3,000 bathhouse guests have used this opportunity [data from the Public Health Agency of Barcelona, unpublished].

The scenario in the present outbreak seems to be different from the previous two outbreaks since only 22% of the cases identified as MSM were bathhouse users.

Interventions aimed at the sexual contacts of the cases were difficult to carry out since in a considerable proportion of the cases the partners could not be identified in the course of contact-tracing process.

All but two cases among MSM were unvaccinated. Vaccination of MSM could help to control this outbreak and is crucial in preventing future ones. Thus information campaigns and immunisation programmes which effectively reach the MSM community are needed.

References


1. Commission Decision of 28 April 2008 amending Decision 2002/253/EC laying down case definitions for reporting communicable diseases to the Community network under Decision No 2119/98/EC of the European Parliament and of the Council (notified under document number C(2008) 1589) (Text with EEA relevance). 2008/426/EC. Official Journal L 159, 18/06/2008 P. 0046 - 0090. Available from: http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2008:159:0046:01:EN:HTML
2. Leentvaar-Kuijpers A, Kool JL, Veugelers PJ, Coutinho RA, van Griensven GJ. An outbreak of hepatitis A among homosexual men in Amsterdam, 1991-1993. Int J Epidemiol. 1995;24(1):218-22.
3. Reintjes R, Bosman A, de Zwart O, Stevens M, van der Knaap L, van den Hoek K. Outbreak of hepatitis A in Rotterdam associated with visits to 'darkrooms' in gay bars. Commun Dis Public Health. 1999;2(1):43-6.
4. Bell A, Ncube F, Hansell A, Davison KL, Young Y, Gilson R, et al. An outbreak of hepatitis A among young men associated with having sex in public venues. Commun Dis Public Health. 2001;4(3):163-70.
5. Mazick A, Howitz M, Rex S, Jensen IP, Weis N, Katzenstein TL, Haff J, Melb K. Hepatitis A outbreak among MSM linked to casual sex and gay saunas Copenhagen, Denmark. Euro Surveill. 2005;10(5):pii=536. Available from: http www.eurosurveillance.org/ViewArticle.aspx?ArticleId=536
6. Informe semanal de vigilancia 2 de marzo de 2009 [Weekly epidemiologic report, 2 March 2009]. Red Nacional de Vigilancia Epidemiologica. Servic Vigilancia Epidemiologica. Centro Nacional de Epidemiologia. Available fro http://www.isciii.es/htdocs/centros/epidemiologia/boletin_red/IS-090302-WE pdf
7. Protocol d'actuació per al control i prevenció de l'hepatitis A [Protocol action for the control and prevention of hepatitis A]. Generalitat de Catalun Departament de Salut: Barcelona; 2004. Available from: http://www.genca cat/salut/depsalut/html/ca/dir2829/prothepatitis2009.pdf



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別紙様式第2-1

No. 5

# 医薬品 研究報告 調査報告書

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| | | | | 2009. 5. 18 | 該当なし | |
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| 販売名(企業名) | 新鮮凍結血漿「日赤」(日本赤十字社)<br>新鮮凍結血漿-LR「日赤」(日本赤十字社)<br>新鮮凍結血漿-LR「日赤」成分採血(日本赤十字社) | | | | | |

**研究報告の概要**

○入れ墨、ピアスに対する供血延期の再評価
背景:2005年8月に、カナダ血液サービスは、入れ墨や耳・体のピアスに関連する供血延期期間を12ヶ月から6ヵ月に短縮した。本試験では、この変更が血液の安全性および安定供給に及ぼす影響を評価した。
試験デザインおよび方法:最近の供血者40,000名を対象とした匿名郵送調査により、これら行為の実施率を調べた。National Epidemiology Donor Databaseを用いて、感染症(TD)マーカー率を算出した。TD陽性供血者とマッチする対象者間のリスク因子を比較する症例対照試験を実施した。供血延期率は、延期期間の変更前後に評価した。
結果:入れ墨、耳のピアス、ボディピアスの実施率は、それぞれ調査回答者の13.7%、53.6%、10.4%であり、最大0.7%の行為が過去6ヵ月間に行われていた。TDマーカー率は低く安定し、供血延期期間変更前は100,000供血当たり21.6、変更後は100,000供血あたり19.2であった。昔行った入れ墨はHCVリスクと関連付けられたが(オッズ比、5.43; 95%信頼区間1.82～16.2)、最近の入れ墨やピアスは、HCVまたはHBVのリスク因子でなかった。延期期間の短縮により、供血延期の件数は入れ墨で20%、ピアスで32%減少した。
結論:入れ墨およびピアスに対する供血延期期間の短縮後、検知できるほどの安全性に対する影響はなく、血液供給においては、期待値以下ではあるが、好ましい効果があった。現在の血液の安全性に及ぼす影響はごくわずかであることから、他の一時的供血延期の期間について再評価すべきである。

**使用上の注意記載状況・その他参考事項等**

新鮮凍結血漿「日赤」
新鮮凍結血漿-LR「日赤」
新鮮凍結血漿-LR「日赤」成分採血

血液を介するウイルス、細菌、原虫等の感染
vCJD等の伝播のリスク

| 報告企業の意見 | 今後の対応 |
|---|---|
| カナダ血液サービスにおいて、入れ墨や耳・体のピアスに関連する供血延期期間を12ヶ月から6ヵ月に短縮した後、検知できるほどの安全性に対する影響はなく、血液供給においては、期待値以下ではあるが、好ましい効果があったとの報告である。 | 日本赤十字社では、輸血感染症対策として問診時に過去1年以内に入れ墨を入れた人は献血不適としている。ピアス穴を開けた人については、状況によって1ヵ月～1年間、粘膜を貫通している場合は無期限に献血延期としている。今後も情報の収集に努める。 |

(2)

JRC2009T-023

BLOOD DONORS AND BLOOD COLLECTION

# Reassessment of deferrals for tattooing and piercing

*Mindy Goldman, Guoliang Xi, Qi-Long Yi, Wenli Fan, and Sheila F O'Brien*

**BACKGROUND:** In August 2005, the Canadian Blood Services decreased the deferral period for tattooing and ear or body piercing from 12 to 6 months. This study assessed the impact of this change on blood safety and availability.

**STUDY DESIGN AND METHODS:** The prevalence of these activities was assessed on an anonymous mail-out survey of 40,000 recent donors. Transmissible disease (TD) marker rates were calculated using the National Epidemiology Donor Database. A case-control study was performed comparing risk factors in TD-positive donors with matched controls. Donor deferral rates were assessed before and after the change in deferral period.

**RESULTS:** The prevalence rates of tattoo, ear piercing, and body piercing were 13.7, 53.6, and 10.4 percent in survey respondents, respectively, with up to 0.7 percent of activity likely to represent deferrable risk. TD marker rate was low and stable at 21.6 per 100,000 donations before and 19.2 per 100,000 donations after the change in deferral length. Remote tattoo was associated with hepatitis C virus (HCV) risk (odds ratio, 5.43; 95% confidence interval, 1.82-16.2), but neither recent tattoo nor piercing was a risk factor for HCV or hepatitis B virus. Shortening of the deferral period reduced deferrals by 20 percent for tattoo and 32 percent for piercing.

**CONCLUSION:** There was no measurable adverse effect on safety and a positive but less than expected effect on blood availability after shortening the deferral period for tattoo and piercing. The length of other temporary deferrals should be reassessed, since their current contribution to blood safety may be negligible.

Blood donor selection criteria are an important part of blood safety. Criteria must balance recipient and donor risk, against the ever-increasing need for blood and the challenges of ensuring adequacy of supply. It is important to reassess both the need for and the duration of specific deferral criteria, particularly as other aspects of blood safety, such as transmissible disease (TD) testing and good manufacturing procedures, are strengthened.[1] Tattooing and ear and body piercing are reasons for temporary deferral of varying lengths in different regulatory jurisdictions. A US Food and Drug Administration (FDA) memorandum issued in April 1992 stipulated a 12-month deferral for donors who have had ear piercing or tattoo in which sterile procedures were not used.[2] A decade later, an FDA Blood Products Advisory Committee voted to continue these deferrals, but recommended a reexamination of the duration of deferral.[3] Presentations made to the committee at that time underlined the limited evidence of any safety benefit of these criteria.[3]

Blood donation does not exist in a vacuum, but is affected by societal trends in behaviors and infectious disease rates, which will influence donor deferral and TD rates. The frequency of both tattooing and body piercing is increasing in the general population, particularly in younger individuals, as assessed by population surveys and individual observations on a stroll down any city

**ABBREVIATIONS:** CBS = Canadian Blood Services; DHAQ = donor health assessment questionnaire; IVDU = intravenous drug use; TD = transmissible disease.

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street on a summer day.[4-7] Temporary deferrals result in donation loss on that day and may also decrease donor return rates, particularly when they happen early in an individual's donation career.[8] In Canada, the deferral period for these activities decreased from 12 months to 6 months in August 2005. We aimed to examine the impact of this change on safety by assessing both TD rates and the association between these behaviors and TD before and after the change in deferral period. We also estimated the prevalence of piercing and tattoos in our donor population and assessed the positive impact of a shorter deferral period on adequacy of supply.

## MATERIALS AND METHODS

### Anonymous donor survey

An anonymous questionnaire was mailed to a total of 40,000 whole blood donors on a monthly basis throughout 2006. The sample was stratified by region proportional to the number of donors in each region, and first-time donors were oversampled such that there were 20,000 first-time and 20,000 repeat donors in the sample. A sample was drawn from donors who had donated during a given month, and the questionnaire mailed within 2 weeks of the end of the month. To increase the response rate, a second questionnaire with an accompanying letter and reminder card were sent 2 and 4 weeks after the initial questionnaire, respectively. The questionnaire included a code that denoted the region of index donation, donation status, and whether it was the first or second mailing, but did not include donor identifiers. In total, 20,037 donors (50%) completed a survey questionnaire, including 7382 first-time donors (37%). Of total responders, 4357 (21.7%) were from the second mailing. To identify possible duplicate questionnaires an algorithm comparing the first and second mailings for age, sex, donation status, donation times, country of birth, first three digits of residence postal code, marital status, ethnic origin, and highest level of education was applied. The handwriting on potential duplicate questionnaires was compared, and if duplication was likely, the second mailing item was removed. Frequencies of demographic characteristics of respondents were compared with those in the 2006 general donor base to confirm representativeness. To account for the differential sampling probability (first-time and repeat donors), sampling weights were created for each of the respondents based on their representation in the 2006 donor population by age, sex, donation status, and region.

Donors were asked if they had ever had a tattoo, ears pierced, or any other body piercing and whether or not they had participated in the activity in the past 6 months. The survey was approved by the Canadian Blood Services (CBS) Research and Ethics Board.

### Assessment of donor deferral rates

All donors are queried about tattoo, ear piercing, and body piercing, in the self-administered section of the CBS donor health assessment questionnaire (DHAQ). For donors who answer affirmatively, the date and type of activity are noted on the DHAQ, and the donor is coded in the CBS donor database. However, deferral codes are not entirely specific for a given risk factor and include donors with other risk factors, such as needle-stick injury. Manual revision of the DHAQ was done for the central and north eastern regions of Ontario, which include Toronto, Ottawa, and surrounding areas. These two regions represent about 23 percent of CBS collections. The exact reason and start date of deferral was obtained from the DHAQ. For the purpose of analysis these were divided into two groups: Group 1, the 16 months before the change in donor deferral period (April 1, 2004, to July 31, 2005) and Group 2, the 16 months after the change in deferral duration (September 1, 2005, to December 31, 2006). The month of August 2005 was excluded to avoid the inclusion of potential errors relating to operational issues in the early phase of implementation.

### TD testing

Antibody to human immunodeficiency virus (HIV)-1/2, hepatitis C virus (HCV), and human T-lymphotropic virus (HTLV)-I/II, and hepatitis B surface antigen (HBsAg) were detected with a chemiluminescent assay (Abbott PRISM HIV O Plus, Abbott Diagnostics Division, Wiesbaden, Germany). Confirmatory testing for HIV was performed using the HIV-1 Western blot (Calypte Biomedical Corp., Rockville, MD), for HCV using a third-generation recombinant immunoblot assay (Chiron Corp., Emeryville, CA), for HBsAg using the Abbott PRISM confirmatory assay, and for HTLV-I/II using the HTLV Western blot assay (Version 2.4, Genelabs Diagnostics Ltd., Singapore Science Park, Singapore). Nucleic acid testing (NAT) was performed for HIV and HCV (Roche Molecular Systems, Branchburg, NJ) using 24-unit minipools.

### National Epidemiology Donor Database

The National Epidemiology Donor Database is maintained with computer software (SAS, SAS Institute, Inc., Cary, NC) and contains donation and demographic data such as age, sex and geographic location on all Canadian blood donors except those in the province of Québec. All allogeneic blood donations (whole blood, plasma, and platelet donations) were included in the TD rates.

### Case-control study

A case-control study to examine predictors of TD in blood donors was carried out in 2005 and 2006. Because very few





donors test positive for the presence of HIV or HTLV in Canada, we have focused on risk factors for HCV- and HBsAg-positive donors. The method has been described previously.[9] In brief, all donors who tested positive for the presence of HBsAg or HCV in 2005 or 2006 were invited to participate in a telephone interview about risk factors. For each positive donor who participated, 4 control donors who had tested negative for all markers matched according to age (±5 years), sex, donation type, donation status (first time or repeat), and geographic region were randomly selected. All TD-positive donors received a standard notification letter informing them of their test results and permanent deferral from donation and advising them to seek medical attention. Donors were subsequently sent a letter inviting them to participate in the telephone interview and then were telephoned to conduct the interview. Once an HBsAg- or HCV-positive donor had completed an interview, control donors were selected and invited to participate in the same way. If a control donor refused to participate or could not be contacted, another was randomly selected among the eligible donors until 4 control donors had been interviewed for each positive donor. The telephone interview used a scripted questionnaire that asked about known and potential risk factors and demographic factors.[9] The interview was completed by 181 of 318 TD-positive donors (57%) and 737 of 1252 matched controls (59%). The study was approved by the CBS Research and Ethics Board.

### Statistical analysis

*Donor survey data*

The percentage of donors with a risk factor was calculated and the 95 percent confidence interval (CI) was estimated using the normal approximation method or the Poisson exact method for small percentages.

*TD rate*

The rate for each TD marker was expressed as the number of positive donations per 100,000 donations, and CIs were estimated using the Poisson exact method.

*Case-control study*

Odds ratios (ORs) and 95 percent CIs were estimated for the studied potential risk factors separately for HBsAg- and HCV-positive donors. To determine the independent association of the risk factors with positivity, multiple logistic regression models were constructed separately for each marker. Only those risk factors that had significant ($p < 0.05$) ORs in univariate analysis were included in the model. To determine whether there was any difference in the ORs before and after the change in deferral duration, models for before and after were constructed separately for each marker and the ORs compared.

*Deferral data*

Deferral data were tabulated (frequency and percentage) for each specific deferral reason in the two time periods as well as the duration between the risk behavior and the deferral date (<6 or ≥6 months). The differences in proportions between two time periods (Groups 1 and 2) were compared using the chi-square test. A relative decreasing rate was calculated as: (number of deferred donors in Period 1 – number of deferred donors in Period 2)/number of deferred donors in Period 1 multiplied by 100(%). The deferral frequencies of each group were compared using the chi-square test for a one-way frequency table. In all analyses, a p value of less than 0.05 was considered to be significant.

## RESULTS

### Prevalence of tattoo, ear piercing, and other body piercing

As shown in Table 1, the prevalence of tattoo, ear piercing, or body piercing is high in donors. Furthermore, it is relatively common for donors to have engaged in these behaviors in the past 6 months (the duration of deferral when the 2006 donor survey was performed). After adjustment for donation status, there were approximately 5265 CBS donors in 2006 (95% CI, 4616-5911) who had one of these risk factors in the past 6 months but who had donated within the past few weeks.

### TD rates

TD rates for all CBS donors did not change over the duration of the study. In the 16 months before the change in the duration of deferral there were 270 confirmed positive donations for all TD markers and 1,247,706 total donations for a rate of 21.6 per 100,000 (95% CI, 19.1 to 24.4). In the 16 months after shortening of the duration of deferral there were 249 confirmed positive donations and 1,295,561 total donations, for a rate of 19.2 per 100,000 (95% CI, 16.9 to 21.8; $p > 0.05$).

**TABLE 1. Prevalence of tattoo and piercing, 2006 donor survey (n = 20,037)***

| Risk factor | Ever | In the past 6 months |
|---|---|---|
| Tattoo | 13.7 (13.2-14.1) | 0.4 (0.3-0.5) |
| Ear piercing | 53.6 (52.8-54.2) | 0.7 (0.6-0.8) |
| Body piercing, other than ear piercing | 10.4 (10.0-10.8) | 0.3 (0.2-0.4) |

* Data are reported as percentage (95% CI).

### Importance of tattoo and piercing as risk factors for HCV and HBV

Tables 2 and 3 show the risk factors identified in all CBS donors confirmed positive for the presence of HCV or HBV in 2005 and 2006. Separate models were constructed for before and after the deferral change and there was no difference in the ORs when the two time periods were compared for either HCV or HBV; hence the data are presented for the 2-year period. For HCV, tattoo was found in 22.7 percent of cases and 10.9 percent of controls with an adjusted OR of 3.47 (95% CI, 1.49 to 8.07). To determine the impact of the date of receiving a tattoo, the model was also constructed with tattoo divided into those donors who had received a tattoo more than 10 years ago and those donors who had only received a tattoo in the past decade. Having received a tattoo more than 10 years ago was a significant predictor of HCV positivity (OR, 5.43; 95% CI, 1.82-16.2), but receiving a tattoo within the past decade was not (OR, 2.35; 95% CI, 0.77-7.22). Ear or body piercing was not a risk factor for HCV on univariate or multiple logistic regression analysis. Major risk factors for HCV, shown in Table 2, were intravenous drug use (IVDU), country of birth in Africa or Asia, sex with an IVDU, blood transfusion, and needle-stick injury. For HBV, neither tattoo nor piercing was an important risk factor for infection on univariate or multiple logistic regression analysis. Major risk factors for HBV, shown in Table 3, were country of birth in Asia or Africa, living in a closed institution, a family history of death from liver disease, or living with someone who had hepatitis or liver disease.

**TABLE 2. HCV risk factors, logistic regression model, 2005-2006***

| Risk factors | Case (n = 88) | Control (n = 349) | Adjusted OR | 95% CI |
|---|---|---|---|---|
| IVDU | 18 (20.5) | 1 (0.3) | 69.02 | 8.05-592.02 |
| Born in Africa or Asia | 14 (16.3) | 14 (4.0) | 14.44 | 5.18-40.25 |
| Sex with IVDU | 14 (17.3) | 7 (2.1) | 8.80 | 2.46-31.50 |
| Blood transfusion | 21 (25.6) | 27 (7.2) | 6.70 | 3.04-14.80 |
| Needle-stick injury | 14 (15.9) | 14 (4.0) | 4.04 | 1.45-11.29 |
| Tattoo | 20 (22.7) | 38 (10.9) | 3.47 | 1.49-8.07 |

* Data are reported as number (%).

**TABLE 3. HBV risk factors, logistic regression model, 2005-2006***

| Risk factors | Case (n = 69) | Control (n = 275) | Adjusted OR | 95% CI |
|---|---|---|---|---|
| Ethnic origin | | | | |
| East or Southeast Asia | 24 (34.8) | 7 (2.5) | 151.41 | 38.6-593.84 |
| Arab or Africa | 14 (20.3) | 5 (1.8) | 74.42 | 17.34-319.29 |
| South or West Asia | 9 (13.0) | 16 (5.8) | 23.08 | 6.48-82.17 |
| European | 18 (26.1) | 236 (85.8) | 1.00 | |
| Other | 4 (5.8) | 11 (4.0) | 9.59 | 1.64-56.03 |
| Lived in a closed institution | 8 (11.6) | 6 (2.2) | 39.67 | 2.00-17.82 |
| Death in the family resulting from liver disease | 9 (13.6) | 7 (2.6) | 22.85 | 4.77-109.39 |
| Living with someone who had hepatitis or liver disease | 15 (23.8) | 13 (4.7) | 5.68 | 1.49-21.72 |

* Data are reported as number (%).

### Impact of change in deferral period on deferral rates

There were 329,203 donor visits in Group 1 and 341,848 donor visits in Group 2, for the two Ontario regions examined. Table 4 summarizes the number of donors deferred for tattoo or ear or body piercing in these two time frames. Deferrals are divided into whether the donor stated that the activity had occurred less than 6 months or 6 to 12 months before the attempted donation. After the decrease in the deferral period (Group 2), no donors should have been deferred for tattoo or piercing that occurred more than 6 months before their donation attempt. The 10 donors in this category may have been deferred in error, shortly after the criteria were changed. For comparison, the number of donors temporarily deferred for other risk factors in the self-administered portion of the DHAQ is noted for the two time frames. These deferrals varied in length from 1 day for activities such as dental cleaning to 12 months for activities such as contact with an individual with hepatitis or jaundice. Overall, the 1017 deferrals for tattoo and piercing in Group 1 and the 723 deferrals in Group 2 represent 35.5 and 28.4 percent of total donor deferrals based on the DHAQ before and after change in the deferral duration, respectively ($p < 0.0001$). This does not include deferrals due to donor hemoglobin (Hb), malaria risk travel, or vital signs assessment. The number of donors deferred for tattoo decreased by 21 percent while the number of donors deferred for piercing decreased by 32 percent after the change in deferral duration; the number of other temporary donor deferrals based on the self-administered portion of the questionnaire decreased by 3 percent, which was not significant ($p = 0.80$). In Group 1, risk activities were not evenly distributed in the 6 to 12 months versus less than 6 months before the donation attempt ($p < 0.0001$). For tattoo and piercing, respectively, 61 and 65 percent of reported risk activities occurred less than 6 months before donation. Since many of the other temporary deferrals in the comparison group were of very short duration, one would expect the majority of these to occur less than 6 months before the donation attempt, as seen in Table 2.

**TABLE 4. Impact of change in deferral duration, Central and North Eastern Ontario**

| Deferral reason and interval before donation attempt | Group 1, n = 329,203 (April 1, 2004, to July 31, 2005) | | | Group 2, n = 341,848 (September 1, 2005, to December 31, 2006) | | |
|---|---|---|---|---|---|---|
| | <6 months | >6 months | Total | <6 months | >6 months | Total |
| Tattoo | 187 | 117 | 304 | 237 | 4 | 241 |
| Piercing | 465 | 248 | 713 | 476 | 6 | 482 |
| Other temporary deferrals self-administered questions | 156 | 35 | 191 | 146 | 40 | 186 |
| Total deferrals DHAQ* | 2074 | 787 | 2861 | 2335 | 208 | 2543 |

* Not including deferrals due to donor Hb, malaria risk travel, or vital signs assessment.





## DISCUSSION

Our results demonstrate that there was no increase in TD rates after a shortening of the deferral period for tattoo or ear and body piercing. Furthermore, engaging in these activities, at least in the past 10 years, was not a risk factor for HCV and HBV positivity, the only two markers with enough positive donors to permit analysis. Piercings and tattoos, occurring in the past 6 months, were not infrequent in people who had recently successfully donated and had negative TD testing results. Shortening of the deferral period had a positive effect on our inventory, although less than one would have expected.

Body adornment by tattoo and body piercing are increasingly common, with prevalence rates of 8 to 25 percent for tattoos and 14 to 51 percent for body piercing reported in recent surveys conducted in various population groups.[4-7] It is therefore not surprising that tattoo and piercing are relatively common reasons for temporary donor deferral, both for CBS and for other blood suppliers.[10,11] Deferral rates are particularly high in younger donors, who are early in their donation career and may potentially have a negative impact on donor return rates.[8,10] Tattoo and piercing result in temporary deferral periods of 6 to 12 months in various jurisdictions; in some cases, shorter deferrals are permitted if additional testing is performed for HBV or HCV or if the donor states that single use needles were used.[12-14] In the United States, after the FDA granted licence amendments to several blood suppliers, AABB Standards were amended to permit donations if tattoos have been applied in a state-regulated entity with sterile needles and ink that has not been reused; however, this is only possible in states that regulate tattoo establishments.[15,16]

Deferrals for tattoos and piercing were implemented in Canada and other jurisdictions in the 1980s, when TD testing, quality standards, and deferral for other higher risk behaviors did not provide the same level of safety that we have achieved today.[17] The current contribution of these criteria to blood safety has not been extensively evaluated. In our study there was no change in the TD marker rate after shortening of the deferral period, in spite of acceptance of donors who would otherwise have been deferred. If these behaviors were important risk factors, one would expect an increase in TD rates immediately after implementation of the change. Zou and coworkers[18] from the ARC found that returning donors who had been temporarily deferred for potential infectious disease risk did not have a higher prevalence of positive TD markers, compared to other donors.

There are conflicting studies on the importance of tattoo and piercing as risk factors for HBV and HCV in the general population.[3,19,20] However, causal associations are generally difficult to establish and interpretation is limited by the different populations studied and by potential confounding effects of other established risk factors such as incarceration and IVDU, particularly since these carry much stigma and may be less readily acknowledged by study participants than piercings and tattoos. In any event, neither ear or body piercing or tattoos (in the past 10 years) were predictors of HCV or HBV positivity in our study, in spite of their high prevalence in donors, and shortening the length of deferral had no effect on this. Although we could not assess the association between piercings or tattoos and HIV or HTLV due to their low prevalence in donors and in the general population, it may be expected that if these were independent predictors of blood-borne pathogen transmission, they would be identified as such for HCV and/or HBV since these are more prevalent infections in the Canadian population and in the donor population. Furthermore, failure to report these risk factors appears to be fairly common, with an estimated 5265 donors having engaged in one of these behaviors in the last 6 months in 2006, and yet TD rates are very low in Canada, underscoring the nonspecificity of these behaviors as identifiers of risk.

Studies on TD marker rates in the blood donor population have consistently demonstrated much higher rates for first-time versus repeat donors, indicating that almost all infections in the donor population are related to remote rather than recent infections and risk factors.[21-24] There have been several studies examining risk factors in TD-positive donors.[8,23-26] In a large, case-control study performed by the REDS group in 1994 to 1995, ear or body piercing was a weak risk factor for HCV positivity, while tattoo was a risk factor on univariate analysis alone.[25]

Similar results were obtained on an earlier US study.[26] Results of earlier studies may not reflect risks associated with more recent piercings or tattoos, since these activities are currently much more common in the general population and less likely to have occurred in nonprofessional settings, such as jails. More recent studies from Holland and Australia are difficult to interpret because of the lack of a control group or analysis to remove confounding effects of IVDU and incarceration, which may be particularly important for HCV transmission.[23,24]

In Canada, a decrease in the deferral period from 12 to 6 months did result in decreased donor deferral rates for tattoo and piercing. However, a 50 percent decrease in the deferral interval only led to a decrease of 21 percent in deferrals related to tattoos and 32 percent in deferrals related to piercing. Analysis of the interval between donation attempt and reporting of risk behavior in Group 1 demonstrates an uneven distribution of reported risk throughout the 12-month deferral period, with increased reporting of more recent risk. Our donor survey data also indicate that many donors who have donated recently have engaged in one of these behaviors within the previous 6 months. Since there were likely a few weeks between the time when the donor made her or his last donation and completed their survey questionnaire, it is possible that a minority of donors engaged in the behavior after donating, however, most likely failed to report deferrable risk. Donors may judge that more temporally remote risk behaviors that did not result in infection do not actually require reporting and may also have decreased recall of more remote behaviors.[17] In spite of the less-than-expected donation gain, a decrease in deferral period was still advantageous, as it will result in approximately 2000 additional donations annually, without any adverse effect on safety. Additionally, the data generated provide reassurance that a further reduction of the length of deferral would not be expected to have any impact on safety. Interestingly, preliminary results from a study in Spain demonstrated that a reduction in donor deferral period from 12 to 4 months for a variety of risk activities, including tattoos and piercing, did not result in any increase in TD marker rates, but led to a less-than-expected decrease in deferral rates of 17 percent.[27]

In summary, tattoos and piercing are frequent in donors, reflecting their increasing popularity in the general population. Our data suggest that deferral of donors for recent tattoo or piercing has a very limited contribution to blood safety in Canada, since decrease in the deferral period did not change the TD marker rate. Additionally, undisclosed risk is common, the TD marker rate is extremely low, and recent tattoo or piercing are not independent risk factors for HBV or HCV infections in donors. Given that window periods for HCV and HBV are estimated at less than 10 and less than 45 days, respectively, for HCV minipool NAT and HBsAg tests currently performed in Canada, a decrease in the duration of deferral to 4 months, which is the current EU standard, would not be expected to have any negative impact on safety.[21] The value of other temporary deferrals should similarly be reassessed.


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## REFERENCES


1. Chiavetta JA, Deeks S, Goldman M, Hannon J, Leach-Bennett J, Megânn H, O'Brien S, Webert K. Proceedings of a consensus conference: blood-borne HIV and hepatitis–optimizing the donor selection process. Transfus Med Rev 2003;17:1-30.
2. Food and Drug Administration. Memorandum: revised recommendations for the prevention of human immunodeficiency virus (HIV) transmission by blood and blood products. (April 23, 1992) Rockville, MD: CBER Office of Communications, Training, and Manufacturers Assistance; 1992.
3. Blood Products Advisory Committee. CBER 2002 Meeting Documents. Discussion on percutaneous exposure of blood and plasma donors: tattoos and body piercing, BPAC March 14, 2002. Available from: http://www.fda.gov/ohrms/dockets/ac/cber02.htm#bloodproducts
4. Deschesnes M, Demers S, Fines P. Prevalence and characteristics of body piercing and tattooing among high school students. Can J Public Health 2006;97:325-9.
5. Mayers LB, Chiffriller SH. Body art (body piercing and tattooing) among undergraduate university students: "then and now". J Adolesc Health 2007;42:201-3.
6. Laumann AE, Derick AJ. Tattoos and body piercing in the United States: a national data set. J Am Acad Dermatol 2006;55:413-21.
7. Stirn A. Body piercing: medical consequences and psychological motivations. Lancet 2003;361:1205-15.
8. Gillespie TW, Hillyer CD. Blood donors and factors impacting the blood donation decision. Transfus Med Rev 2002;16:115-30.
9. O'Brien SF, Fan W, Xi G, Yi QL, Goldman M, Fearon MA, Infante-Rivard C, Chiavetta JA, Willems B, Pi D, Fast M, Delage G. Declining hepatitis C rates in first-time blood donors: insight from surveillance and case-control risk factor studies. Transfusion 2008;48:902-9.
10. Custer B, Johnson ES, Sullivan SD, Hazlet TK, Ramsey SD, Hirschler NV, Murphy EL, Busch MP. Quantifying losses to the donated blood supply due to donor deferral and miscollection. Transfusion 2004;44:1417-26.
11. Zou S, Eder AF, Musavi F, Notari Iv EP, Fang CT, Dodd RY; ARCNET Study Group. Implementation of the Uniform Donor History Questionnaire across the American Red Cross Blood Services: increased deferral among repeat presenters but no measurable impact on blood safety. Transfusion 2007;47:1990-8.
12. European Union Commission Directive 2004/33/EC of March 22/2004, Annex III, Eligibility criteria for donors of whole blood and components. J Eur Union 30.3.2004.
13. UK Blood Transfusion and Tissue Transplantation Services. Professional guidelines, best practice and clinical information. Whole blood and components donor selection guidelines. Available from: http://www.transfusionguidelines.org.uk/
14. Australian Red Cross Blood Services. All about blood. Frequently asked questions. Available from: http://www.donateblood.com.au/
15. Maynard J, Manchester K, Young CT. The effect of the first tattoo variance on your blood supply [abstract]. Transfusion 2003;43 Suppl:73A.
16. Price TH, editor. Standards for blood banks and transfusion services. 25th ed. Bethesda: American Association of Blood Banks; 2008.
17. O'Brien SF, Ram SS, Vamvakas EC, Goldman M. The Canadian Blood Donor Health Assessment Questionnaire: lessons from history, application of cognitive science principles, and recommendations for change. Transfus Med Rev 2007;21:205-22.
18. Zou S, Musavi F, Notari EP, Fujii KE, Dodd RY; ARCNET Study Group. Prevalence of selected viral infections among temporarily deferred donors who returned to donate blood: American Red Cross donor study. Transfusion 2005;45:1593-600.
19. Oot Hayes M, Harkness GA. Body piercing as a risk factor for viral hepatitis: an integrative research review. Am J Infect Control 2001;29:271-4.
20. Hwang LY, Kramer JR, Troisi C, Bull L, Grimes CZ, Lyerla R, Alter MJ. Relationship of cosmetic procedures and drug use to hepatitis C and hepatitis B virus infections in a low-risk population. Hepatology 2006;44:341-51.
21. O'Brien SF, Yi Q, Fan W, Scalia V, Kleinman SH, Vamvakas EC. Current incidence and estimated residual risk of transfusion-transmitted infections in donations made to Canadian Blood Services. Transfusion 2007;47:316-25.
22. Wang B, Schreiber GB, Glynn SA, Kleinman S, Wright DJ, Murphy EL, Busch MP; Retrovirus Epidemiology Donor Study. Does prevalence of transfusion-transmissible viral infection reflect corresponding incidence in United States blood donors? Transfusion 2005;45:1089-96.
23. Polizzotto MN, Wood EM, Ingham H, Keller AJ; Australian Red Cross Blood Service Donor and Product Safety Team. Reducing the risk of transfusion-transmissible viral infection through blood donor selection: the Australian experience 2000 through 2006. Transfusion 2008;48:55-63.
24. Van der Bij AK, Coutinho RA, Van der Poel CL. Surveillance of risk profiles among new and repeat blood donors with transfusion-transmissible infections from 1995 through 2003 in the Netherlands. Transfusion 2006;46:1729-36.
25. Murphy EL, Bryzman SM, Glynn SA, Ameti DI, Thomson RA, Williams AE, Nass CC, Ownby HE, Schreiber GB, Kong F, Neal KR, Nemo GJ. Risk factors for hepatitis C virus infection in United States blood donors. NHLBI Retrovirus Epidemiology Donor Study (REDS). Hepatology 2000;31:756-62.
26. Conry-Cantilena C, VanRaden M, Gibble J, Melpolder J, Shakil AO, Viladomiu L, Cheung L, DiBisceglie A, Hoofnagle J, Shih JW, Kaslow R, Ness P, Alter HJ. Routes of infection, viremia and liver disease in blood donors found to have hepatitis C virus infection. N Engl J Med 1996;334:1691-6.
27. Jimenez-Marco M, Girona E, Sedeno M, Muncunill J. The impact of a reduction in the donor deferral period from 12 months to 4 months [abstract]. Vox Sang 2008;95 Suppl 1:121.