Impact of changes to policy for Mexican risk travel on Canadian blood donor deferrals

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Background. Travel to malaria risk areas such as Mexico is a common source of donor deferral in Canada. On February 21st, 2011 the deferrable regions in Mexico were revised to permit donation if donors travelled to the state of Quintana Roo, Mexico, a popular ocean-side resort area.

Materials and methods. Canadian travel data and malaria deferral rates since 2007 were plotted to examine trends. Deferral records in one centre were accessed from January to April, 2011 to tabulate travel destinations of deferred donors immediately before and after the change.

Results. Travel to Mexico and the Caribbean accounts for 63% of general population travel, and travel to Mexico has been increasing ($P < 0.05$). Deferral for short-term malaria risk travel has a strong seasonal trend with peaks in the winter and troughs in the summer. Approximately 36,000 fewer donations were lost following the change, a reduction of 37% from the previous year. Deferrals in one centre increased for Caribbean/Central America after the change ($P < 0.05$) consistent with the seasonal trend, but decreased for Mexico ($P < 0.05$).

Discussion. Deferrals for malaria risk travel are substantial. Careful revision and refinement of risk areas of travel can significantly reduce the burden of deferral.

Keywords: malaria, Quintana Roo, donor deferral, blood safety.

Introduction

Numerous criteria must be met to be eligible to donate blood; compliance with these criteria is intended to improve safety for both the recipient and the donor[1]. For diseases that may be transmissible by transfusion but would only be acquired in another part of the world, travel deferrals are often applied. In Canada, as in the USA, permanent deferrals have been applied for time spent in the United Kingdom, France and Western Europe to reduce the risk of variant Creutzfeldt-Jakob Disease[2]. Malaria risk travel is a common reason for temporary deferral in the USA[3] and Canada[4]. However, travel deferral strategies lack specificity such that large numbers of safe donors are excluded to reduce very small risks, and revision of policies tends to be sporadic.

Malaria is a serious mosquito-borne parasitic infection in many tropical and sub-tropical countries, with an estimated 216 million people infected[5]. The highest risk is in sub-Saharan Africa, but many countries report endemic cases including Mexico, some countries in the Caribbean, Central and South America and Asia. However, the risk is often not present in all regions of the country, varies by altitude and season, and may be mitigated by living conditions that reduce contact with mosquitoes and by chemoprophylactic treatment. Thus, although travel to countries in which malaria is endemic has become increasingly common, malaria in Canada is rare and when identified is most frequently in immigrants from endemic countries. With increasing travel, deferral places an increasing strain on the donor base to reduce a very small risk[6].

In Canada donors who have visited an area with malaria risk are deferred for 12 months from the date of return for donation of cellular components, such as whole blood and platelets. Donors who have lived in a risk country are deferred for 3 years and donors are permanently deferred if they have a history of malaria. The deferrable areas are regularly updated to reflect current risk, but due to the lack of detail of specific risk areas and for ease of implementation are broader than necessary.

Like residents in the USA, many Canadians travel to resorts in Mexico and the Caribbean, particularly during the long, cold winter. Although there may be some cases of malaria reported in residents of these countries, the risk of malaria from holiday resort travel is extremely low, and for some areas essentially non-existent such that a broad classification of risk travel can result in a high rate of deferrals of safe donors[3,6,7]. In June 2012 the Food and Drug Administration[8] released a draft Guidance for Industry for comments proposing that travellers to the very low-risk states of Quintana Roo and Jalisco in

Mexico be eligible to donate. The draft document also proposes permanent deferral of donors with a history of malaria without proof of successful treatment. Prior to this, on February 21, 2011, Canadian Blood Services revised the deferral policy to permit travel to the state of Quintana Roo, Mexico which increased the range of tourist resort areas that was acceptable. We evaluated the impact of this change and report the results.

Materials and methods

Travel of the Canadian general population

The estimated number of visits by Canadian residents in the general population to Mexico and the Dominican Republic was obtained from the Statistics Canada website for the years from 2007 to 2010 and plotted to examine trends in travel behaviour[9]. Statistics Canada uses survey data from travellers and administrative data on entry into Canada from the Canadian Border Services Agency to estimate the number of visits by a Canadian resident to different countries. The slope of the line was compared with a slope of zero to determine whether there had been a significant increase in travel.

A dataset of all general population travel data for the year 2009 was obtained from Statistics Canada and malaria risk countries were identified based on the USA Center for Disease Control Yellow Book classification. The frequencies of visits to each country and the percentages of all visits to malaria risk areas were calculated. The data are limited to the country of travel and cannot be broken down to specific parts of the countries visited, but can assist in an evaluation of the possible impact of changes in areas considered at risk.

Changes to deferrable travel criteria 2007-2012

The list of deferrable travel destinations is updated as changes in malaria risk occur, at least once per year but more frequently if required. Prior to February 21, 2011 donors could donate if they visited parts of Mexico including the popular resort town of Cancun in the state of Quintana Roo and the state of Jalisco. However, travel to other parts of Quintana Roo, including many popular tourist resorts and areas frequently visited in day trips from Cancun, was a cause for deferral. On February 21, 2011 a new list was implemented that permitted travel anywhere in Quintana Roo, as well as the northeastern state of Tamaulipas which is not a common tourist area. Travel to many tourist resort areas in the Dominican Republic, including many cities in Puerto Plata, is acceptable, while travel to the interior of the country is considered a malaria risk; these criteria did not change substantially. There were also a number of changes to specific areas within other countries, mainly based on the US CDC Yellow Book for malaria risk. For example, travel to anywhere in El Salvador had been a cause for donor deferral but was changed to only parts of the country, and travel to south mainland China had also been a cause for deferral (although major destinations such as Beijing, Shanghai, Hong Kong and Macao were acceptable) but was further reduced to only two provinces. A list of areas causing deferral is maintained on the Canadian Blood Services' website which classifies countries as "no risk", "partial risk" or "all risk". For the changes to destinations causing deferral in Mexico the web-site list was not revised and listed simply as partial risk.

Deferral data

The National Epidemiology Donor Database (NEDD), which is maintained with SAS software (SAS Institute Inc., Cary, NC, USA) contains donation and deferral data on all Canadian blood donors except those donating in the province of Québec. In this study, deferral records for all allogeneic whole blood donors presenting to donate (N =1,625,432 excluding directed donations) between January 1, 2007 and July 30, 2012 were included. The rate of malaria deferrals for each month was calculated as the number of deferrals divided by whole blood collections plus deferrals and plotted to examine trends over time. To determine the change in deferrals before and after the change in policy in February, 2011, autoregressive models were fitted and means of the monthly deferral rates before and after February 2011 were compared. A P value less than 0.05 was considered statistically significant. The total numbers of donations lost due to malaria short-term travel deferral before and after the change were estimated using the sum of deferrals and an estimate of the number of donations that would have been made during the deferral period for the periods of February 21, 2010 to February 20, 2011 and February 21, 2011 to February 20, 2012. To estimate the number of donations that would have been made had the donors not been deferred, the product of the number of donors deferred and the average number of undeferred donors who returned was calculated considering the median donation interval. This was also calculated using the average number of deferred donors who returned because some deferred donors are eligible to return in less than 1 year (deferral for travel is for 1 year from the date of travel, not the date of deferral) which was subtracted from the number of donations expected from undeferred donors to get the number of donations that deferred donors would have made. This was done separately for first-time and repeat deferred donors and then summed The 95% confidence intervals were estimated using Monte Carlo simulation.

In addition, data from all telephone and on-site deferral records at North/East Ontario and Nunavut

Region (NEON, which includes the city of Ottawa) between January 1 and April 30, 2011 were manually extracted from paper records and the numbers of deferrals for different travel destinations were tabulated for the period before February 21, and the period after. This region accounts for approximately 10% of whole blood collections. The rates of donors deferred before and after the change in criteria were compared using the chi-squared test.

Results

Figure 1 shows the number of visits by Canadians in the general population to Mexico and the Dominican Republic from 2007 to 2010. Travel to Mexico increased over the period ($P < 0.05$) but remained steady for the Dominican Republic. Analysis of general population travel in 2009 showed that of approximately 3.9 million visits by Canadians to countries for which any part was endemic for malaria (about 12% of the Canadian population), 1.2 million (about 30% of visits) were to Mexico. An additional 1.3 million (33% of visits) were to endemic parts of the Caribbean, mainly to the Dominican Republic (0.9 million visits). The next most frequently visited area was Asia was about 0.8 million visits, of which mainland China travel accounted for 0.26 million. There were 0.27 million visits to endemic countries in Africa, and 0.18 million to Central America (only 3,300 to El Salvador).

Figure 2 shows the number of donors deferred over the period from 2007 to 2012. There is a strong seasonal trend for short-term travel deferral with a peak during the winter months, and a trough during the summer months. The mean deferral rate decreased from 5.0% to 3.4% after February 2011 ($P < 0.0001$). During the year before the change on February 21, 2011 there were 46,530 donors deferred plus there were an estimated 53,070 additional donations that these donors would have made during the time they were deferred (had they been

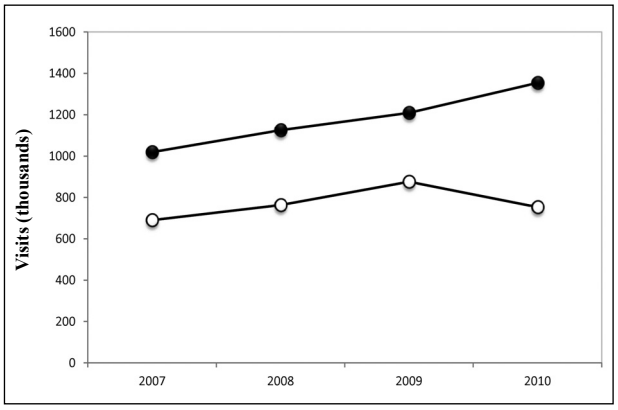

Figure 1 - The number of visits by Canadians to Mexico (●) and Dominican Republic (○).

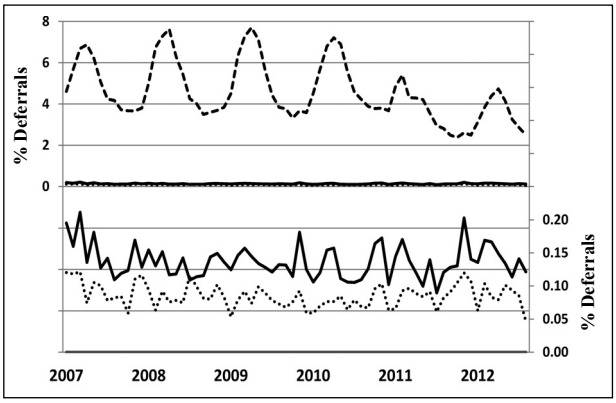

Figure 2 - Split graph of the percentage of whole blood donors deferred from 2007 to 2012 for short term travel to and endemic area (12 month deferral) (– – –), former resident of an endemic area (3 year deferral) (—) and history of malaria (permanent deferral) (·····).

eligible), the sum of which is 99,600 (85,356-113,804) donations lost. In the year after the change there were only 29,782 donors deferred, and an estimated 33,475 additional donations that these donors would have made during the deferral period for a total of 63,257 (54,459-72,055) donations lost. The difference in donations lost between the 2 years was 36,343 donations, a reduction of 37%. Short-term travel accounts for the vast majority of deferrals for malaria risk (94.1% in 2011) with deferrals for residency in a malaria risk country and for a history of malaria accounting for very small proportions of deferrals for malaria risk (3.5% and 2.4%, respectively, in 2011); the deferral rates for these reasons do not have any seasonal trend and were not different after the change in criteria ($P > 0.05$). Over the period considered 82.1% of the short-term travel deferrals were in repeat donors, but most of those deferred for residency in an area endemic for malaria or with a history of malaria were first-time donors (74.8% and 84.7%, respectively).

Table I shows the rate of deferred donors by travel destination at the NEON Region from January 1 to April 30, 2011. Before February 21, the number of donors deferred for travel to Mexico was 157 per 10,000; this dropped to 25 per 10,000 after that date ($P < 0.05$); likewise, most Mexico deferrals before February 21 were for travel to Qunitana Roo, while the number was only 2 per 10,000 after. Over the same period deferral for Caribbean, Central /South American travel increased, as it did for most other destinations ($P < 0.05$). Deferrals for Asia decreased ($P < 0.05$) but involved a small number of donors.

Discussion

Analysis of deferral rates over time showed that the majority of travel deferrals were for short-term

Table I - The rate per 10,000 donors in North and East Ontario and Nunavut Region deferred for short-term travel between January 1 and April 30, 2011 by travel destination before and after February 21st when the regions resulting in deferral were changed.

	Before Feb 21, 2011 (12,628 donors)	After Feb 21, 2011 (16,012 donors)	P-value
Mexico	157	25	<0.05
Quintana Roo	138	2	
Other States	19	23	
Caribbean	185	304	<0.05
Central/South America	63	132	<0.05
Middle East	48	18	<0.05
Africa	29	51	NS
Asia	67	45	<0.05
Total 2011	**550**	**575**	
Total 2010	**493**	**778**	

travel with a strong seasonal trend that had a trough during the summer months and a peak during the cold winter months when travel to sunny destinations is very popular. Approximately 80% of Canadian Blood Services' donors are repeat donors who would be deferred on their next appointment or donation attempt. As this would be within a few months of returning from travel, the deferral rates largely reflect travel from a few months before. Deferral for residency in an endemic country (3 years from the date of immigration) or for history of malaria has no seasonal trend because these deferrals are mainly for first-time donors and because immigration is less seasonal.

Nearly two-thirds of Canadian visits to endemic areas are to Mexico and the Caribbean, thus changes to the deferrable region list in this part of the world would have the greatest potential impact on deferral rates. The remaining one third of travellers' destinations are distributed around the globe and any changes for other countries could only have a minor impact on the deferral rate. Examination of Canadian general population travel trends suggests that travel to Mexico has been increasing since 2007, a trend which is reflected in donor deferrals. As there were no changes to the deferrable regions of the Dominican Republic, the change to accept travellers to anywhere in the state of Quintana Roo (formerly just Cancun), Mexico was almost certainly responsible for the sudden drop in donor deferrals resulting in about 36,000 fewer donations lost. In addition, our comparison in one centre of the 2 months before and after the change showed a significant drop in deferrals for Mexico, specifically for Quintana Roo travel although this observation cannot be directly extrapolated to other parts of Canada. Over the same time, deferral for other areas was either unchanged or increased, coinciding with the seasonal trend.

In Canada transfusion-transmitted malaria (TTM) is extremely rare, the last documented case being in 1995[10], and no cases have been reported since accepting travellers to Quintana Roo. In the USA a case of TTM is reported every year or two, but in both the USA and Canada, TTM is almost exclusively related to former residents of endemic areas and not travellers born in Canada or the USA[11-13]. Risk modelling in the USA using two different approaches has reported extremely low risk from short-term travellers to endemic areas, and this is especially true for travel to Mexico compared with Africa[6,7]. Even with very conservative assumptions, eliminating deferral for travel to all areas in Mexico except the state of Oaxaca, the risk in the USA would only be increased to one potentially infectious unit every 20 years, even without considering the present decline in malaria incidence in Mexico[7]. Seventy per cent of US travel deferrals for Mexico are attributable to travel to Quintana Roo[7]. Our analysis shows that re-definition of the specific regions for malaria risk travel can have a dramatic effect on deferral rates. In this case, a decrease resulted. Conversely, there is also potential for an increase resulting from changes in travel patterns or in popular destinations considered to be at-risk, resulting in substantial donation loss. In order to address the impact on sufficiency, both real and potential, over the last decade some countries such as the UK (England/Northern Wales), Australia and New Zealand have implemented selective testing policies which reduce the deferral period to 4 months (6 months in England/Northern Wales)[14-16]. This is not an option in Canada or the USA at this time because there is no assay licensed for blood donor screening. Nevertheless, continual change in both donor behaviours and risk abroad necessitate regular revision of travel deferral policies to balance safety with sufficiency.

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References

1) 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.
2) O'Brien SF, Chiavetta JA, Goldman M, et al. Predictive ability of sequential surveys in determining donor loss from increasingly stringent variant Creutzfeldt-Jakob disease deferral policies. Transfusion 2006; **46**: 461-8.
3) Leiby DA, Nguyen ML, Notari EP. Impact of donor deferrals for malaria on blood availability in the United States. Transfusion 2008; **48**: 2222-8.
4) O'Brien SF, Fan W, Xi G, et al. Donor loss due to malaria-risk travel deferral. Transfusion 2008: **48** (2S); 62A.
5) World Health Organization. World malaria report 2011 Available at: http://www.who.int/malaria/world_malaria_report_2011/en/. Accessed on 09/01/2013.
6) Spencer B, Steele W, Custer B, et al. Risk of malaria in United States donors deferred for travel to malaria-endemic areas. Transfusion 2009; **49**: 2335-45.
7) Spencer B, Kleinman S, Custer B, et al. Deconstructing the risk for malaria in United States donors deferred for travel to Mexico. Transfusion 2011; **51**; 2398-410.
8) Guidance for industry. Recommendations for donor questioning, deferral, re-entry and product management to reduce the risk of transfusion-transmitted malaria. Food and Drug Administration. Available at: http://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/Blood/ucm077061.htm. Accessed on 28/08/2012.
9) Travel by Canadians to foreign countries. Statistics Canada. Available at: http://www.statcan.gc.ca/tables-tableaux/sum-som/l01/cst01/arts37a-eng.htm. Accessed on 28/09/2012.
10) Slinger R, Giulivi A, Bodie-Collins M, et al. Transfusion-transmitted malaria in Canada. Can Med Assoc J 2001; **164**: 377-9.
11) Mungai M, Tegtmeir G, Chamberland M, Parise M. Transfusion-transmitted malaria in the United States from 1963 through 1999. N Engl J Med 2001; **344**: 1973-8.
12) Mali S, Kachur SP Arguin PM. Malaria Surveillance - 2010. MMWR 2012; **61**: 1-18.
13) Mali S, Kachur SP Arguin PM. Malaria Surveillance - 2009. MMWR 2011; **60**: 1-15.
14) Kitchen AD, Chiodini PL. Malaria and blood transfusion. Vox Sang 2006; **90**: 77-84.
15) Seed CR, Cheng A, Davis TM, et al. The efficacy of a malarial antibody enzyme immunoassay for establishing the reinstatement status of blood donors potentially exposed to malaria. Vox Sang 2005; **88**: 98-106.
16) Reesink HW, Panzer S, Wendel S, et al. The use of malaria antibody tests in the prevention of transfusion-transmitted malaria. Vox Sang 2010; **98**: 468-78.

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