Public Health Agency of Canada
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Transfusion Transmitted Injuries Surveillance System

Program Report 2002-2003

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This report can also be accessed through the Public Health Agency
of Canada website at: http://www.phac-aspc.gc.ca/hcai-iamss/tti-it

Cat. No. HP37-1/2003
ISBN 662-69188-1

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Program Report
2002-2003

Transfusion Transmitted Injuries Section
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June 2005

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Acknowledgement

A national surveillance system is only as strong as the participating federal/provincial/territorial partners and the Transfusion Transmitted Injuries Surveillance System is no exception. The Public Health Agency of Canada recognizes the invaluable contributions of all the stakeholders in the system including but not limited to transfusion safety officers, laboratory technologists, nurses, and blood bank physicians. Without their timely provision of data on adverse transfusion events, there could be no analysis of the national importance of these occurrences. The advice and collaboration of all participating sites and of the two blood manufacturers (Canadian Blood Services and Héma-Québec) as well as the members of the regulatory branch of Health Canada is essential to the system and to have a meaningful positive effect on the health of Canadians.

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List of Acronyms

ATE	Adverse Transfusion Event
CMVIg	Cytomegalovirus immune globulin
IBCT	Incorrect Blood Components Transfused
IVIg	Intravenous immune globulin
MS ACCESS	Microsoft Access
NTTISS WG	National Transfusion Transmitted Injuries Surveillance System Working Group
NWPDR	National Working Party for Data Review
PHAC	Public Health Agency of Canada
PTP	Post-Transfusion Purpura
RSVIg	Respiratory syncitial virus immune globulin
SHOT	Serious Hazards of Transfusion
SPSS	Statistical Package for Social Science
TRALI	Transfusion Related Acute Lung Injury
TTISS	Transfusion Transmitted Injuries Surveillance System
UK	United Kingdom

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1 Introduction

The Transfusion Transmitted Injuries Surveillance System (TTISS) is maintained by the Public Health Agency of Canada (PHAC) to collect data on adverse transfusion events (ATEs) resulting from the therapeutic use of blood, blood components, plasma derivatives and recombinant products* across the country.

The TTISS began as a pilot project to carry out voluntary surveillance of both infectious and non-infectious transfusion related injuries in four provinces, for the period of 1999-2002. Implementation of the TTISS has continued to expand since the pilot project and it is now a national program in various stages of implementation in all provinces and territories.

The pilot provinces collaborated with PHAC to develop standardized materials for the reporting of ATEs. The primary tools developed are a Canadian Transfusion Adverse Event Reporting Form and a Canadian Transfusion Adverse Event Reporting User's Manual. These tools, along with standardized definitions for reporting ATEs, ensure consistent reporting across Canada. The Canadian Transfusion Adverse Event Reporting Form is endorsed by both blood manufacturers (Canadian Blood Services and Héma-Québec) and the two relevant regulatory directorates of Health Canada: the Marketed Health Products Directorate and the Biologics and Genetic Therapies Directorate, both of the Health Products and Food Branch.

TTISS is advised by two working groups: the National Transfusion Transmitted Injuries Surveillance System Working Group (NTTISS WG) and the National Working Party for Data Review (NWPDR).

The NTTISS Working Group advises the program on the direction, quality and effectiveness of TTISS as a national surveillance system. Its core membership is composed of representatives of each province and territory, two representatives from Health Canada's regulatory branch, as well as the two blood manufacturers.

The NWPDR reviews and evaluates the data produced by the system on the safety of blood, blood components and products intended for use in the treatment of human diseases. Members include professionals knowledgeable in the fields of public health, infectious diseases, epidemiology and transfusion medicine. The Working Party focuses on identifying, from the data submitted, from the literature and from their expertise, phenomena or unusual adverse events that require further investigation by PHAC. It also assists in developing research questions and hypotheses for investigation by PHAC.

* Refers to recombinant hemostatic agents distributed by blood banks

The data presented in this report cover a two-year period (2002-2003) and are presented under three headings:

- overall results,
- events related to blood components, and
- events related to plasma derivatives and recombinant products.

Special attention is given to specific ATEs related to blood components, such as ABO incompatibility, acute hemolytic reactions, and bacterial contamination. Fatalities are also reported separately. Rate calculations were performed for blood components only, as methods for transferring denominator data for plasma derivatives and recombinant products are still under discussion. The report concludes with a discussion of the data and its limitations and recommendations for improving the surveillance system.

2 Methodology

Data on adverse transfusion events were collected and investigated at participating hospital sites. Data were usually reported to a provincial or territorial blood co-ordinating office on a standardized paper form or transferred electronically according to standardized definitions. Non-nominal data on moderate and severe adverse events were then transferred electronically as per provincial/territorial/federal agreement to the PHAC. These cases were exported to PHAC through a Microsoft Access (MS-ACCESS) datafile after encryption of the file to ensure security of the transfer process. In some instances these non-nominal data were transferred electronically directly from the participating hospitals to the PHAC as per agreement with the provincial/territorial authority.

Training on the use of the form, the definitions, and the database, supplied by PHAC, was provided to each participating province/territory. In some instances, a data validation process was performed at the provincial level to ensure that the reported ATEs met the required standards. Relationship of ATEs to transfusion and severity of ATEs were assigned by reporting hospitals.

Relationship of ATEs to transfusion was defined as follows:

- **Definite**
  If a clinical and/or laboratory event occurred within a time period consistent with the administration of the blood product and was proven by investigation to have been caused by transfusion.
- **Probable**
  If a clinical and/or laboratory event occurred within a time period consistent with the administration of the blood product and did not seem to be explainable by any other cause.
- **Possible**
  If the clinical and/or laboratory event occurred within a time period consistent with the administration of the blood product but a concurrent disease or the administration of a drug or other agent could not be excluded as a possible cause of the event.

Severity of ATEs was graded as follows:

- **Death**
  If the recipient's death was felt to be the consequence of a transfusion.
- **Life threatening**
  If the recipient required major intervention following the transfusion (vasopressors, intubation, transfer to intensive care).

- **Long-term sequelae**
  If the recipient developed either an infection with a persistent infectious agent (HIV, hepatitis C, hepatitis B), or a transfusion reaction with severe sequelae or the anticipation of difficulty with future transfusions (e.g. development of one or many antibodies to very high frequency antigens (≥95%)).
- **Minor or no sequelae**
  If the recipient developed antibodies to low or medium frequency antigens (<95%) or other minor reactions.
- **Not determined**
  If the consequences of the transfusion reaction were not certain.

Data received at the PHAC were reviewed by the TTISS epidemiologists and medical advisors for completeness and validity. When required, additional information such as signs, symptoms, and/or laboratory results were requested from the reporting hospitals. In some instances, cases were excluded because they were reported with insufficient information to enable analysis or because cases did not meet TTISS standard definitions or cases were minor and not reportable. Data were then exported to the Statistical Package for Social Sciences (SPSS) for epidemiological analysis. Only ATEs definitely, probably or possibly related to transfusion were considered for analysis.

Participating provinces were also asked to provide the number of hospitals that had been participating in TTISS for each year and the proportion of total blood components transfused in the province attributed to the participating hospitals. They were also asked to provide the number of transfused units in the participating hospitals for each category of blood component.

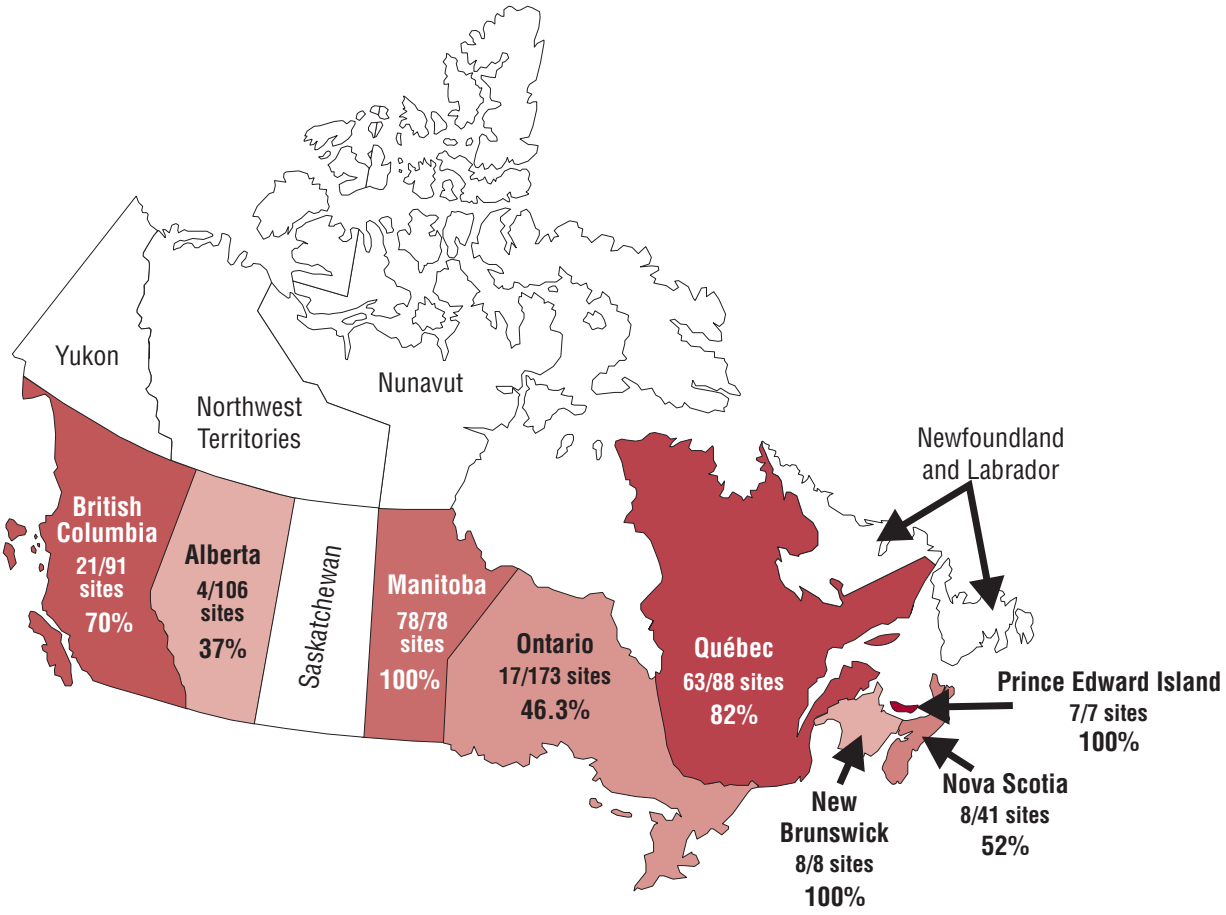
The incidence of ATEs was calculated using the total number of units of blood components transfused in the three provinces where reporting was considered to be optimal. ATEs from these three provinces represented 97% of the reported cases.

3 Results

As of 31 December 2003, a total of eight provinces were participating in TTISS: British Columbia, Alberta, Manitoba, Ontario, Québec, New Brunswick, Nova Scotia and Prince Edward Island. Figure 1 shows the number of participating hospitals in each province and the proportion of total transfusions captured in each of the provinces by the participating hospitals.

Figure 1

Hospital sites participating in TTISS and proportion of transfusions captured



During the reporting period, participating hospitals across these provinces transfused a total of 1,629,684 units of blood components, more than half being red blood cells (Table 1).

Table 1

Blood components transfused by hospital sites participating in TTISS

Blood components	Number of units transfused by year					
	Year 2002		Year 2003		Total	
	N	%[a]	N	%[a]	N	%[a]
Whole blood	607	0.1	823	0.1	1,430	0.1
Red blood cells	354,696	49.6	487,885	53.3	842,581	51.7
Whole blood derived platelets	192,252	26.9	223,959	24.5	416,211	25.5
Apheresis platelets	11,933	1.7	14,717	1.6	26,650	1.6
Plasma	107,425	15.0	136,232	14.9	243,657	15.0
Cryoprecipitate	47,573	6.7	51,582	5.6	99,155	6.1
Total	**714,486**	**100.0**	**915,198**	**100.0**	**1,629,684**	**100.0**

[a] Proportion of units transfused by year

3.1 Adverse Transfusion Events Included for Analysis

A total of 512 ATEs were reported to the PHAC during the period 1 January 2002 to 31 December 2003. Of these, 216 (42.2%) were excluded from the data analysis. The reasons for exclusion are summarized in Table 2. The main reasons for exclusion were that the event was minor and not to be reported to TTISS (58%), or that the cases did not meet standard TTISS definitions (29%), including cases where the relationship to transfusion was doubtful.

Two hundred ninety-six ATEs (57.8% of reported cases) were included in the analysis, 152 for 2002 and 144 for 2003.

Table 2

Reported, included and excluded adverse transfusion events

Calendar year	Reported adverse transfusion events	Included adverse transfusion events		Excluded adverse transfusion events and reasons for exclusion							
				Non reportable minor events		Incomplete/ missing information		Not meeting standard definitions		Total	
		N	%[a]	N	%[b]	N	%[b]	N	%[b]	N	%[a]
2002	244	152	62.3	52	56.5	6	6.5	34	37.0	92	37.7
2003	268	144	53.7	74	59.7	21	16.9	29	23.4	124	46.3
Total	**512**	**296**	**57.8**	**126**	**58.3**	**27**	**12.5**	**63**	**29.2**	**216**	**42.2**

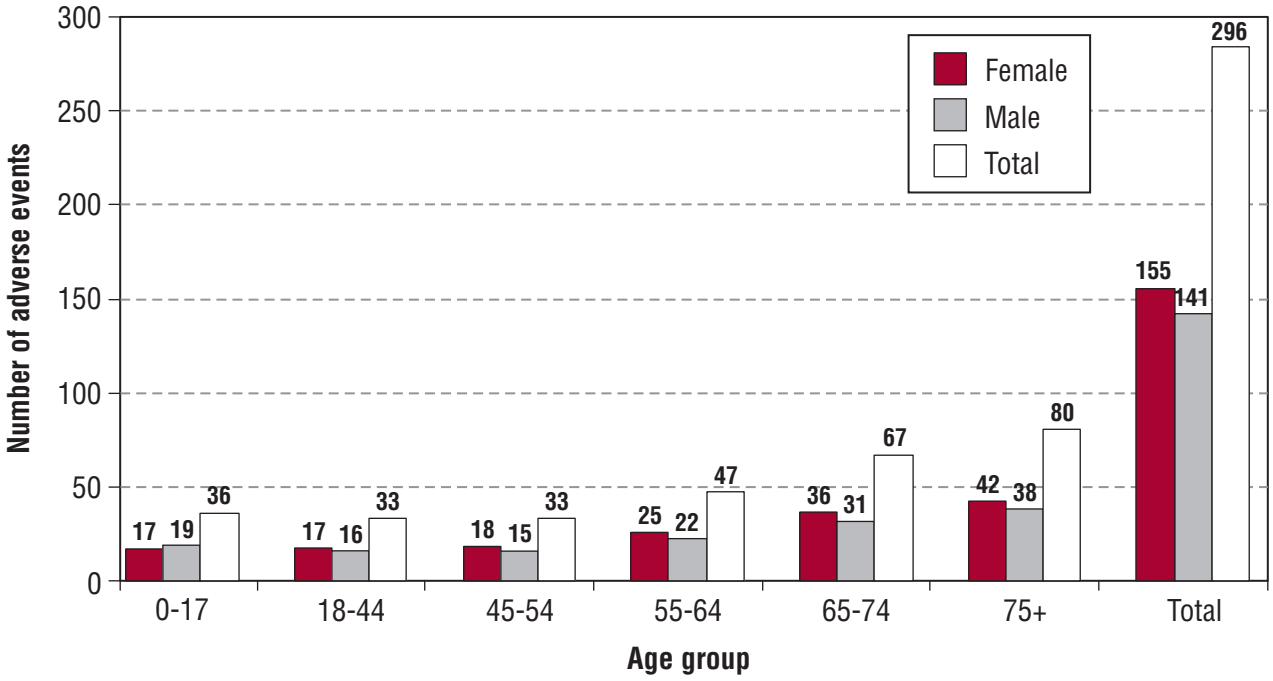
[a] Proportion of reported events per year

[b] Proportion within excluded events by year

Distribution of ATEs by age and gender is shown in Figure 2. Adverse events were distributed evenly among males and females, and no difference was noted in the distribution between 2002 and 2003. However, as denominator data on the number of transfusions by age and gender was not available, we could not report on the risk of ATEs related to age or gender.

Figure 2

Distribution of adverse transfusion events by age and gender



Among the 296 ATEs included in the analysis 90.2% (267) were related to the administration of blood components and 9.8% (29) to plasma derivatives and recombinant products.

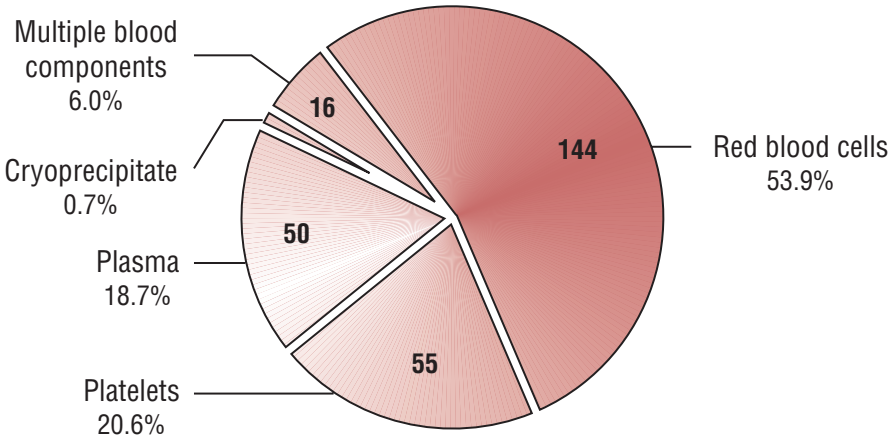
3.2 Adverse Transfusion Events Related to Blood Components

3.2.1 Type of Blood Components Implicated in Adverse Transfusion Events

Of the 267 ATEs related to the administration of blood components, the highest proportion (53.9%) was related to the administration of red blood cells, followed by platelets (20.6%) and plasma (18.7%). Six percent (6%) of ATEs occurred in patients who received multiple blood components (more than one type of component), but no specific component could be related to the ATE. Two cases (0.7%) were related to the administration of cryoprecipitate (Figure 3). There was no significant difference between the proportions of ATEs by category of blood components transfused between 2002 and 2003.

Figure 3

Blood components implicated in adverse transfusion events

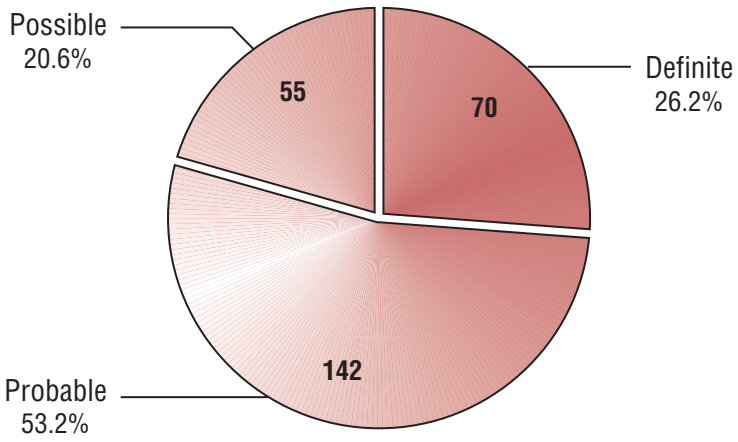


3.2.2 Relationship of Adverse Transfusion Events to Transfusion

Seventy-nine (79%) percent of ATEs were assessed to be definitely or probably related to transfusion, while 21% of cases were possibly related to transfusion (Figure 4). There was no difference in the distribution of relationship to transfusion between 2002 and 2003.

Figure 4

Adverse transfusion events related to blood components by relationship to transfusion



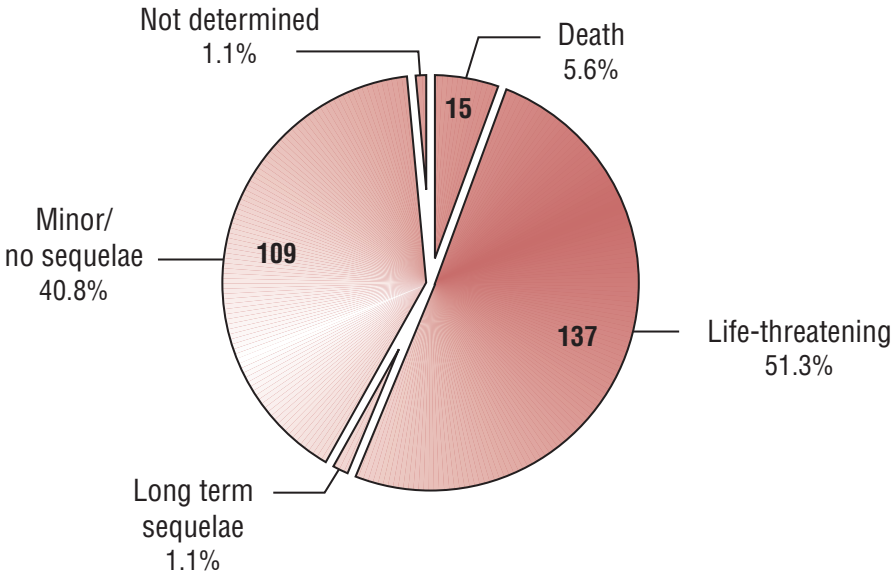
3.2.3 Severity of Adverse Transfusion Events

Approximately half of the reported ATEs related to blood components were graded as life-threatening and in six percent (6%) of the cases, the recipient died, but the death was not necessarily related to the ATE. Forty-one percent (41%) of ATEs were graded as minor or no sequelae (Figure 5). These events (graded as minor/no sequelae) were serious but not life-threatening or did not result in a serious reaction in the recipient. An example is the asymptomatic ABO mistranfusion.

Again, no difference in the distribution of severity between 2002 and 2003 was noted.

Figure 5

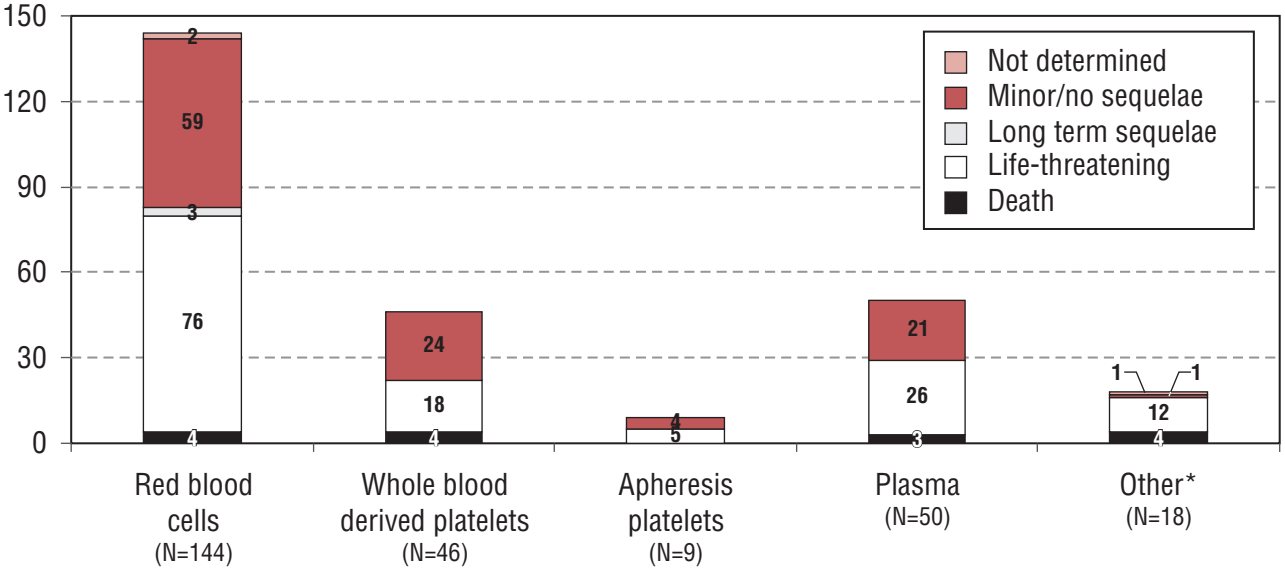
Adverse transfusion events related to blood components by severity



The severity of adverse events by type of blood components transfused is shown in Figure 6. The proportion of events graded as minor was highest with whole blood derived platelets.

Figure 6

Severity of adverse transfusion events by type of blood components



* Includes multiple blood components and cryoprecipitate.

3.2.4 Diagnosis of Adverse Transfusion Events Related to Blood Components

The type of ATEs related to each type of blood component transfused is shown in Table 3. The largest proportion of ATEs reported was major allergic/anaphylactic reaction (36%). This was the case for all blood components. For plasma and platelets, it represented more than 50% of the ATEs.

Transfusion related acute lung injury (TRALI), circulatory overload, acute hemolytic reactions and bacterial contamination with respective proportions of 13.1%, 12.7%, 11.6% and 10.1% were also reported in significant numbers.

It should be noted that, although they represented only 2.6% of the reported ATEs, seven cases of post-transfusion purpura occurred in the two-year period (one in 2002 and six in 2003). Only one case of West Nile virus infection was reported to TTISS in 2002, but PHAC is aware of two other transfusion related cases reported to Health Canada's regulatory branch in 2002.[†]

[†] Of the 2 other cases of WNV reported to Health Canada's regulatory branch in 2002, one was life-threatening and probably related to transfusion, and one was minor and definitely related to transfusion.

Table 3

Diagnosis of adverse transfusion events related to blood components

Adverse transfusion event	Red blood cells			Whole blood derived platelets			Apheresis platelets			Plasma			Total[a]		
	2002[b]	2003[b]	Total[b]	2002[b]	2003[b]	Total[b]	2002[b]	2003[b]	Total[b]	2002[b]	2003[b]	Total[b]	2002	2003	Total
Major allergic / anaphylactic reaction	21 (28.0)	14 (20.3)	35 (24.3)	16 (51.6)	8 (53.3)	24 (52.2)	1 (50.0)	5 (71.4)	6 (66.7)	11 (50.0)	16 (57.1)	27 (54.0)	**50 (36.2)**	**46 (35.7)**	**96 (36.0)**
TRALI	10 (13.3)	8 (11.6)	18 (12.5)	1 (3.2)	2 (13.3)	3 (6.5)	-	-	-	2 (9.1)	5 (17.9)	7 (14.0)	**18 (13.0)**	**17 (13.2)**	**35 (13.1)**
Circulatory overload	14 (18.7)	10 (14.5)	24 (16.7)	1 (3.2)	-	1 (2.2)	-	-	-	4 (18.2)	3 (10.7)	7 (14.0)	**19 (13.8)**	**15 (11.6)**	**34 (12.7)**
Acute hemolytic transfusion reaction	12 (16.0)	18 (26.1)	30 (20.8)	-	1 (6.7)	1 (2.2)	-	-	-	-	-	-	**12 (8.7)**	**19 (14.7)**	**31 (11.6)**
Bacterial contamination	5 (6.7)	5 (7.2)	10 (6.9)	9 (29.0)	1 (6.7)	10 21.7	-	2 (28.6)	2 (22.2)	3 (13.6)	2 (7.1)	5 (10.0)	**17 (12.3)**	**10 (7.8)**	**27 (10.1)**
ABO incompatibility	6 (8.0)	3 (4.3)	9 (6.3)	-	2 (13.3)	2 (4.3)	1 (50.0)	-	1 (11.1)	1 (4.5)	1 (3.6)	2 (4.0)	**8 (5.8)**	**6 (4.7)**	**14 (5.2)**
Hypotensive transfusion reaction	4 (5.3)	3 (4.3)	7 (4.9)	2 (6.5)	-	2 (4.3)	-	-	-	-	1 (3.6)	1 (2.0)	**6 (4.3)**	**5 (3.9)**	**11 (4.1)**
Post-transfusion purpura	-	3 (4.3)	3 (2.1)	-	1 (6.7)	1 (2.2)	-	-	-		-	-	**1 (0.7)**	**6 (4.7)**	**7 (2.6)**
Delayed hemolytic transfusion reaction	1 (1.3)	2 (2.9)	3 (2.1)	-	-	-	-	-	-	-	-	-	**1 (0.7)**	**2 (1.6)**	**3 (1.1)**
Viral infection[c]	-	-	-	-	-	-	-	-	-	-	-	-	**1 (0.7)**	**-**	**1 (0.4)**
Other[d]	2 (2.7)	3 (4.3)	5 (3.5)	2 (6.5)	-	2 4.3	-	-	-	1 (4.5)	-	1 (2.0)	**5 (3.6)**	**3 (2.3)**	**8 (3.0)**
Total N	**75**	**69**	**144**	**31**	**15**	**46**	**2**	**7**	**9**	**22**	**28**	**50**	**138**	**129**	**267**
%[e]	**(54.3)**	**(53.5)**	**(53.9)**	**(22.5)**	**(11.6)**	**(17.2)**	**(1.4)**	**(5.4)**	**(3.4)**	**(15.9)**	**(21.7)**	**(18.7)**	**(51.7)**	**(48.3)**	**(100.0)**

[a] This total includes 16 events related to multiple components (4 anaphylactic/anaphylactoid reactions, 2 circulatory overload, 1 hypotensive reaction, 3 post-transfusion purpura, 5 TRALI and 1 viral infection) and 2 TRALI related to cryoprecipitate, not shown in the table, that were added to the respective categories.

[b] Proportion of reported ATEs for each type of blood component.

[c] West Nile virus (the recipient received multiple blood components).

[d] Other ATEs reported included hypocalcemia, hyperkalemia, transfusion-associated dyspnea, atypical pain syndrome, Rh incompatibility and one case of unknown diagnosis.

[e] Proportion of specific blood components involved in ATEs.

3.2.5 Type of Adverse Transfusion Events by Relationship to Transfusion

A high proportion of ATEs had a probable relationship to transfusion. This was the case for circulatory overload (73.5%), bacterial contamination (70.4%), major allergic/anaphylactic reaction (65.6%), and TRALI (45.7%), as shown in Table 4.

All the ABO incompatibility cases were definitely related to transfusion. The relationship to transfusion was also unsurprisingly definite for the majority of acute hemolytic transfusion reactions (51.6%).

Hypotensive reaction had a high proportion of possible relationship to transfusion (63.6%).

Table 4

Type of adverse transfusion events by relationship to transfusion

	Relationship to transfusion							
	Definite		Probable		Possible		Total	
Adverse transfusion event	N	%[a]	N	%[a]	N	%[a]	N	%[b]
Major allergic /anaphylactic reaction	14	14.6	63	65.6	19	19.8	**96**	**36.0**
TRALI	9	25.7	16	45.7	10	28.6	**35**	**13.1**
Circulatory overload	5	14.7	25	73.5	4	11.8	**34**	**12.7**
Acute hemolytic transfusion reaction	16	51.6	10	32.3	5	16.1	**31**	**11.6**
Bacterial contamination	4	14.8	19	70.4	4	14.8	**27**	**10.1**
ABO incompatibility	14	100.0	-	-	-	-	**14**	**5.2**
Hypotensive transfusion reaction	-	-	4	36.4	7	63.6	**11**	**4.1**
Post-transfusion purpura	3	42.9	-	-	4	57.1	**7**	**2.6**
Delayed hemolytic transfusion reaction	3	100.0	-	-	-	-	**3**	**1.1**
Viral infection[c]	-	-	1	100.0	-	-	**1**	**0.4**
Other[d]	2	25.0	4	50.0	2	25.0	**8**	**3.0**
Total	**70**	**26.2[e]**	**142**	**53.2[e]**	**55**	**20.6[e]**	**267**	**100.0**

[a] Proportion of relationship for each ATE.
[b] Overall proportion of specific ATEs.
[c] West Nile virus.
[d] Includes: hypocalcemia, hyperkalemia, transfusion associated dyspnea, atypical pain syndrome, Rh incompatibility and unknown.
[e] Overall proportion of relationship to transfusion for ATEs.

3.2.6 Type of Adverse Transfusion Events by Severity

As previously mentioned, about half of the reported ATE cases were graded as life-threatening. Circulatory overload accounted for the highest proportion of cases that were graded as life-threatening (94%). However, for this ATE only the severe cases were reportable to TTISS. TRALI followed with 74.3% and major allergic/anaphylactic reaction with 49% (Table 5).

ABO incompatibility and acute hemolytic reactions represented the largest proportion of cases that were graded as minor (71.4% and 61.3% respectively). All these cases irrespective of severity were reportable to TTISS.

Transfusion was not the likely cause of death in all of the cases graded as death shown in Table 5 (see section 3.4 on fatalities); death may have occurred in some cases (5) as a result of recipient's underlying conditions.

Table 5

Type of adverse transfusion events by severity

	Severity of adverse event											
	Death		Life-threatening		Long term sequelae		Minor/ no sequelae		Not determined		Total	
Adverse transfusion event	N	%[a]	N	%[a]	N	%[a]	N	%[a]	N	%[a]	N	%[b]
Major allergic/anaphylactic reaction	1	1.0	47	49.0	-	-	47	49.0	1	1.0	**96**	**36.0**
TRALI	3	8.6	26	74.3	-	-	6	17.1	-	-	**35**	**13.1**
Circulatory overload	2	5.9	32	94.1	-	-	-	-	-	-	**34**	**12.7**
Acute hemolytic transfusion reaction	-	-	8	25.8	3	9.7	19	61.3	1	3.2	**31**	**11.6**
Bacterial contamination	4	14.8	4	14.8	-	-	19	70.4	-	-	**27**	**10.1**
ABO incompatibility	-	-	3	21.4	-	-	10	71.4	1	7.1	**14**	**5.2**
Hypotensive transfusion reaction	2	18.2	7	63.6	-	-	2	18.2	-	-	**11**	**4.1**
Post-transfusion purpura	2	28.6	4	57.1	-	-	1	14.3	-	-	**7**	**2.6**
Delayed hemolytic transfusion reaction	-	-	3	100.0	-	-	-	-	-	-	**3**	**1.1**
Viral infection[c]	1	100.0	-	-	-	-	-	-	-	-	**1**	**0.4**
Other[d]	-	-	3	37.5	-	-	5	62.5	-	-	**8**	**3.0**
Total	**15**	**5.6[e]**	**137**	**51.3[e]**	**3**	**1.1[e]**	**109**	**40.8[e]**	**3**	**1.1[e]**	**267**	**100.0**

[a] Proportion of grade of severity related to each ATE.
[b] Overall proportion of specific ATEs.
[c] West Nile virus.
[d] Includes: hypocalcemia, hyperkalemia, transfusion associated dyspnea, atypical pain syndrome, Rh incompatibility and unknown.
[e] Overall proportion of grade of severity in ATEs.

3.2.7 Analysis of Specific Type of Adverse Transfusion Events

3.2.7.1 ABO Incompatibility

All of the 14 reported ABO incompatibility cases reported were unintended. Nine cases (64.3%) were related to red blood cells; three (21.4%) to platelets (the cases related to platelets were included as they were error-related) and two (14.3%) to plasma. Most of the events in recipients (71.4%) were graded as minor or no sequelae, but three (21.4%) were graded as life-threatening. Six ABO incompatibility cases resulted in acute hemolytic reactions. No deaths occurred.

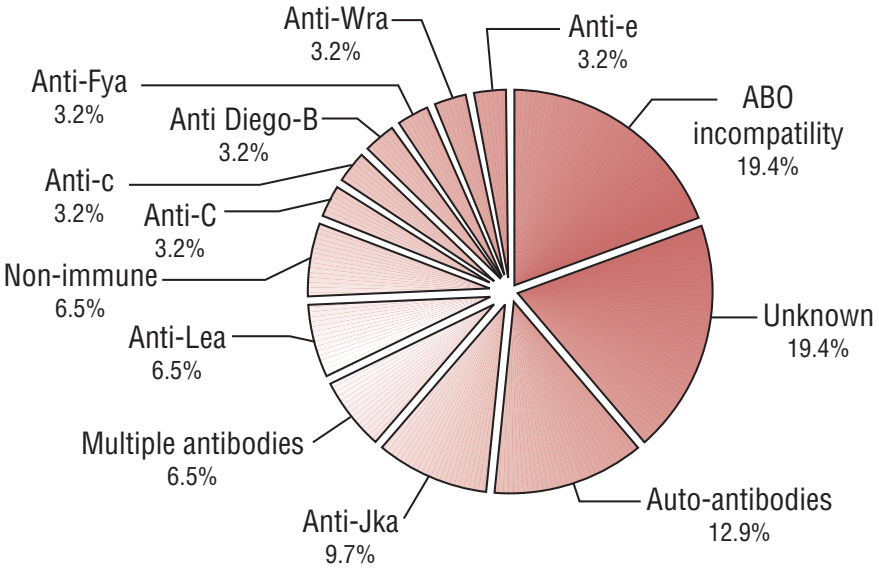
Of the three cases graded as life-threatening, one patient ID was not verified at the bedside and the wrong patient was sampled in two cases.

3.2.7.2 Acute Hemolytic Transfusion Reactions

Acute hemolytic transfusion reactions were reported in 31 cases. This category of adverse event accounted for about 12% of all reported ATEs. Most of the acute hemolytic reactions (96.8%) were related to the administration of red blood cells while one (3.2%) was related to the administration of whole blood derived platelets. The causes of these reactions are presented in Figure 7.

Figure 7

Causes of acute hemolytic transfusion reactions



Sixty-one percent (61%) of these cases (19) were graded as minor and 25.8% (8) as life-threatening. Three cases resulted in long-term sequelae while the severity of the event was not determined in one case.

All eight life-threatening cases of acute hemolytic reaction received red blood cells. The cause of the reaction was ABO incompatibility in three cases; irregular antibodies were identified in four cases and the cause of the reaction was not determined in the other case.

3.2.7.3 Delayed Hemolytic Transfusion Reactions

Three cases of delayed hemolytic transfusion reaction were reported; only severe cases were reportable to TTISS. The three reported cases were definitely related to transfusion and all were graded as life-threatening. Multiple irregular antibodies were identified in two cases and an anti-Jka was identified in the other case.

3.2.7.4 Bacterial Contamination

A) Bacterial Contamination by Relationship to Transfusion

A total of 27 cases of bacterial contamination definitely, probably or possibly related to transfusion were reported, 63% having been reported in 2002.

In the *Canadian Adverse Event Reporting Form User's Manual*, bacterial contamination is defined as follows:

Bacterial contamination is considered **Definite** if it meets ALL of the following criteria:

- The same bacteria are found in the recipient and the blood product.
- Contamination of the blood sample or the laboratory is not suspected.

Bacterial contamination is considered **Probable** if it meets the following criteria:

- Positive blood product culture.
- Contamination of the blood sample or the laboratory is not suspected.
- The recipient is symptomatic (nothing else explains it).
- The recipient blood culture was not done.
  - No specimen was available.
  - A blood culture was not ordered.
- The recipient's blood culture is negative.
  - The recipient is already taking antibiotics.
  - There were problems with the recipient's blood culture.

Bacterial Contamination is considered **Possible** if it meets the following criteria:

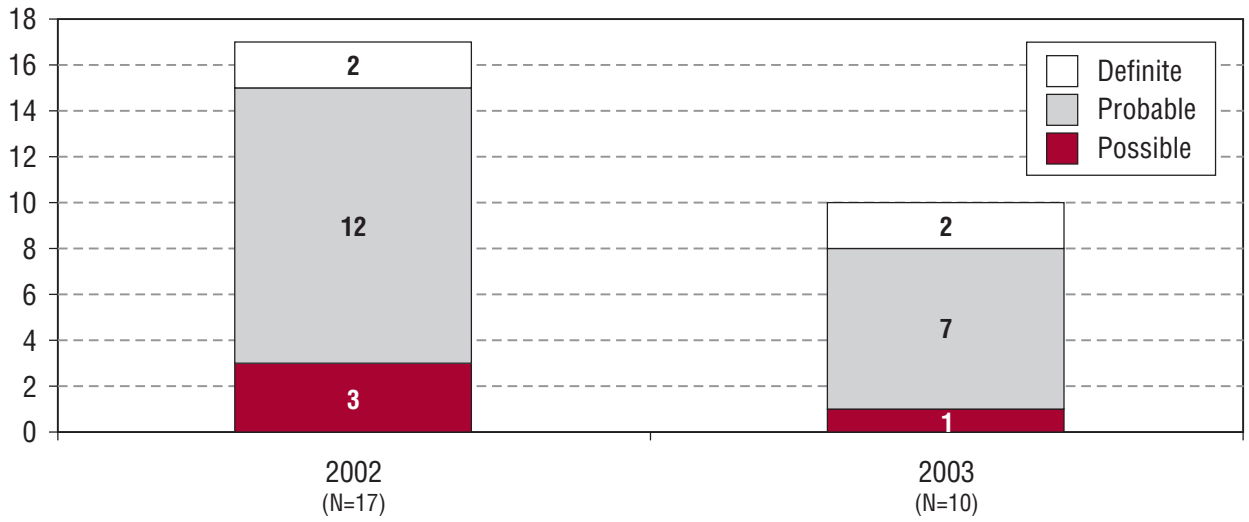
- The recipient's blood culture is positive.
- Contamination of the blood sample and the laboratory is not suspected.
- The recipient is symptomatic (nothing else explains it).

- A blood product culture was not done.
  - No specimen was available.
- The blood product culture is negative.
  - There were problems with the culture of the blood product.

For the two years, two-thirds of bacterial contamination cases (19) were probably related to transfusion, 14.8% (four cases) were definitely related to transfusion and 14.8% (four cases) were possibly related to transfusion. Distribution of relationship to transfusion by year is presented in Figure 8.

Figure 8

Bacterial contamination by relationship to transfusion

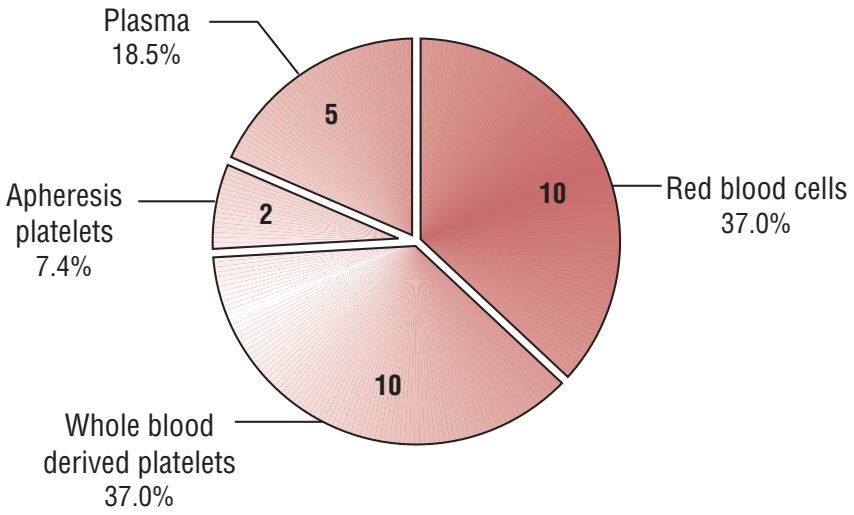


B) Bacterial Contamination by Type of Blood Components Transfused

As shown in Figure 9, of the 27 cases of bacterial contamination, 10 (37%) were related to red blood cells; 10 (37%) to whole blood derived platelets; two (7.4%) to apheresis platelets and five (18.5%) to plasma.

Figure 9

Type of blood components related to bacterial contamination



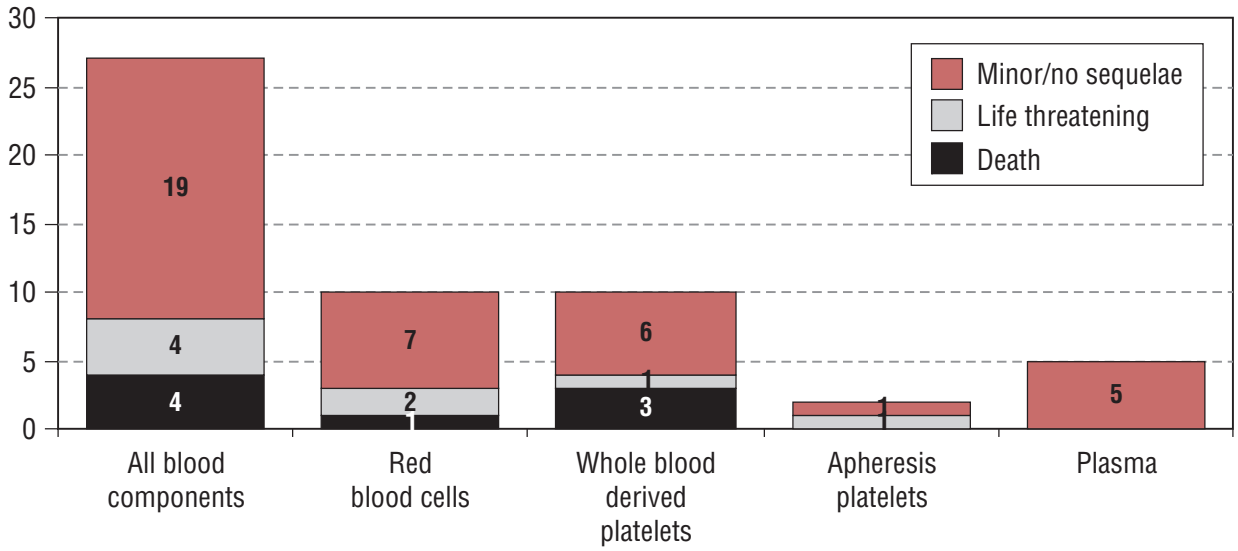
C) Bacterial Contamination by Severity of Adverse Transfusion Events

Most cases of bacterial contamination (70.4%) were graded as minor, four cases (14.8%) as life-threatening and four cases (14.8%) were fatal.

As shown in Figure 10, the proportion of severe cases was slightly higher for whole blood derived platelets than for other components.

Figure 10

Severity of bacterial contamination cases by type of blood components transfused



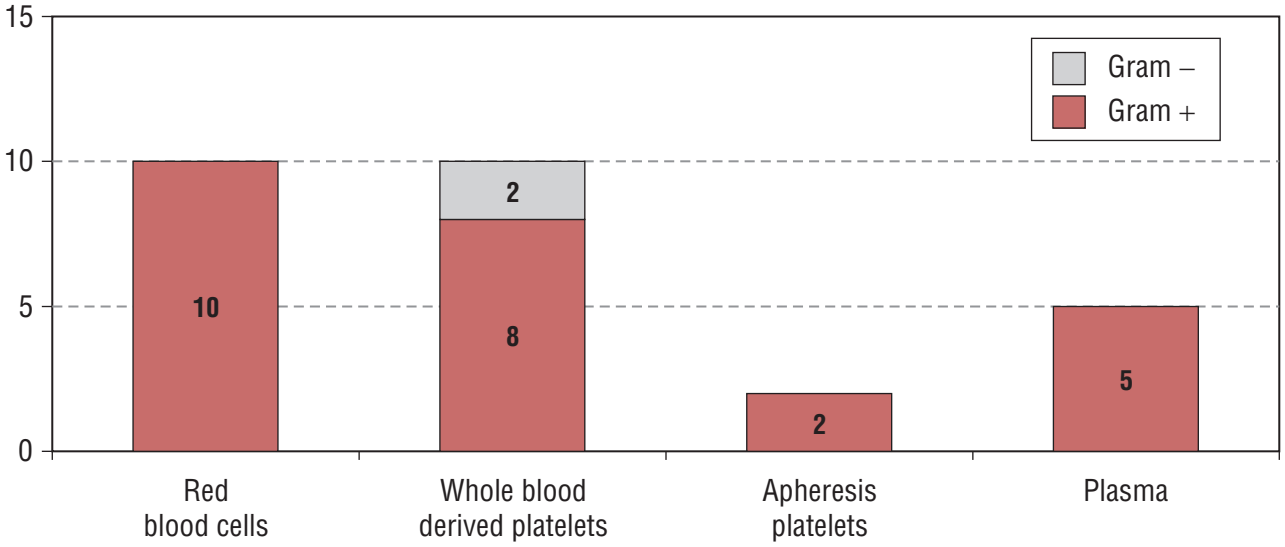
D) Bacterial Contamination by Type of Pathogens Involved

Almost all bacteria implicated in bacterial contamination cases were gram positive (Figures 11 and 12). It is worth noting that all bacterial contaminations related to red cells were gram positive bacteria.

Two gram negative bacteria were identified in bacterial contamination cases possibly related to transfusion. They were related to the administration of whole blood derived platelets.

Figure 11

Bacterial contamination cases by gram stain



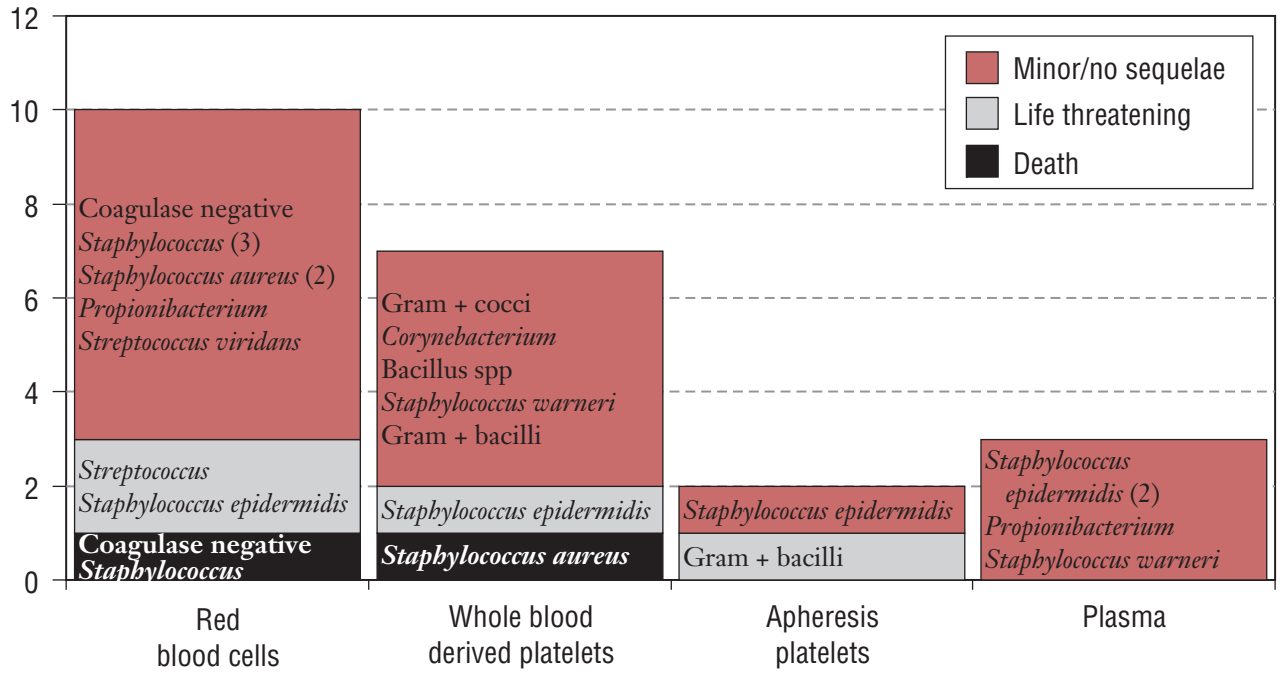
Among the reported cases of bacterial contamination, 23 were definitely or probably related to transfusion, that is, with a positive blood product culture. A variety of organisms were identified in these cases, with a predominance of gram positive cocci such as *Staphylococcus* and *Streptococcus* species (Figure 12).

Two of these cases resulted in death:

- In one case the patient received whole blood derived platelets and the culture of both blood product and recipient grew *Staphylococcus aureus*. The patient's death was definitely related to transfusion.
- The other case was related to red blood cells and the organism implicated was a coagulase negative *Staphylococcus*, which grew only in the blood product culture. Death was assessed to be probably related to transfusion.

Figure 12

Organisms identified in blood product culture



Four cases of bacterial contamination possibly related to transfusion, not shown in Figure 12, were also reported. In these cases, only the recipient's blood culture was positive; the component could not be cultured. Two cases were graded as minor, and the organisms identified were *Pseudomonas* (in one case who received whole blood derived platelets) and *Streptococcus* (in the other case who received fresh frozen plasma).In the other two cases, the recipients died. The blood component received was whole blood derived platelets and the organisms identified were *Staphylococcus aureus* and *Serratia marcescens* respectively.

The death with *Serratia marcescens* was assessed as probably related to transfusion although it was a possible case of bacterial contamination according to the definitions on pages 15 and 16. The other death, with *Staphylococcus aureus*, was possibly related to transfusion.

3.2.8 Incidence of Adverse Transfusion Events

The incidence of each type of ATE for 2002 and 2003 is presented in Tables 6 and 7 respectively. Data for rate calculations come from the three provinces that reported 97% of the ATEs to TTISS. The comparative rates of ATEs per 100,000 units of blood components transfused for 2002 and 2003 are presented in Figure 13.

It was observed for both years that the highest reported rates were for major allergic reactions. Rates did not differ significantly from one year to the next. The high rate of post-transfusion purpura for 2003 is notable.

Table 6

Incidence of adverse transfusion events reported in 2002

Adverse transfusion event	Blood components					
	Red blood cells (290,000)	Whole blood derived platelets		Apheresis platelets (9,709)	Plasma (83,415)	All products[a] (455,126)[b]
		Units (151,291)	Pools (5) (30,528)			
Major allergic/ anaphylactic reaction	1:13,810	1:9,456	1:1,908	1:9,709	1:8,342	**1:9,288[c]**
TRALI	1:36,250	1:151,291	1:30,528	-	1:83,415	**1:30,341[c,d]**
Circulatory overload	1:20,714	1:151,291	1:30,528	-	1:20,854	**1:23,954**
Acute hemolytic transfusion reaction[e]	1:29,000	-	-	-	-	**1:45,512**
Bacterial contamination	1:58,000	1:16,810	1:3,392	-	1:27,805	**1:26,772**
ABO incompatibility	1:58,000	-	-	1:9,709	1:83,415	**1:65,018**
Hypotensive transfusion reaction	1:72,500	1:75,646	1:15,264	-	-	**1:75,854**
Post-transfusion purpura	-	-	-	-	-	**1:455,126[c]**
Delayed hemolytic transfusion reaction	1:290,000	-	-	-	-	**1:455,126**
Other	1:145,000	1:75,646	1:15,264	-	1:83,415	**1:91,025[c,f]**
Total	**1:4,265**	**1:4,880**	**1:985**	**1:4,855**	**1:4,171**	**1:3,556**

[a] Include cryoprecipitate and granulocytes.
[b] Whole blood derived platelets were counted as pools of 5.
[c] Includes ATEs to multiple components, no single being related to the event.
[d] 2 cases related to cryoprecipitate (ratio: 1:20,855).
[e] 2 cases of ABO incompatibility resulted in acute hemolytic reactions.
[f] Excludes the West Nile virus case.

Table 7

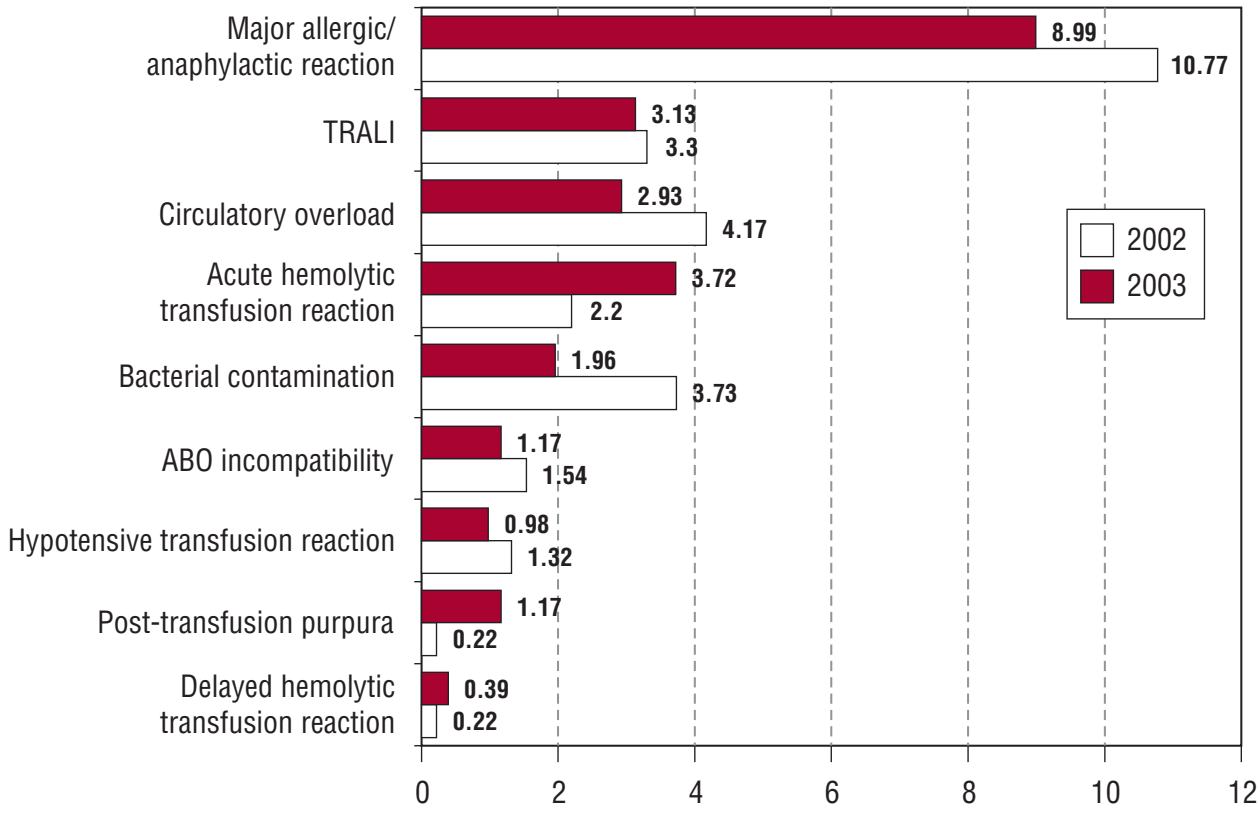
Incidence of adverse transfusion events reported in 2003

Adverse transfusion event	Blood components					
	Red blood cells (326,903)	Whole blood derived platelets		Apheresis platelets (11,694)	Plasma (98,914)	All products[a] (511,364)[b]
		Units (155,944)	Pools (5) (31,189)			
Major allergic/ anaphylactic reaction	1:23,350	1:19,493	1:3,889	1:2,339	1:6,182	**1:11,117[c]**
TRALI	1:46,700	1:77,972	1:15,595	-	1:19,783	**1:31,960[c]**
Circulatory overload	1:32,690	-	-	-	1:32,971	**1:34,091[c]**
Acute hemolytic transfusion reaction[d]	1:18,161	1:155,944	1:31,189	-	-	**1:26,914**
Bacterial contamination	1:65,381	1:155,944	1:31,189	1:5,847	1:49,457	**1:51,136**
ABO incompatibility	1:108,968	1:77,972	1:15,595	-	1:98,914	**1:85,227**
Hypotensive transfusion reaction	1:108,968	-	-	-	1:98,914	**1:102,273[c]**
Post-transfusion purpura	1:108,968	1:155,944	1:31,189	-	-	**1:85,227[c]**
Delayed hemolytic transfusion reaction	1:163,452	-	-	-	-	**1:255,682**
Other	1:108,968	-	-	-	-	**1:170,455**
Total	**1:4,953**	**1:11,139**	**1:2,228**	**1:1,671**	**1:3,533**	**1:4,091**

[a] Include cryoprecipitate and granulocytes.
[b] Whole blood derived platelets were counted as pools of 5.
[c] Includes ATEs to multiple components, no single being related to the event.
[d] Includes 3 cases of ABO incompatibility resulted in acute hemolytic reactions.

Figure 13

Comparative rates of adverse transfusion events per 100,000 units of blood components transfused

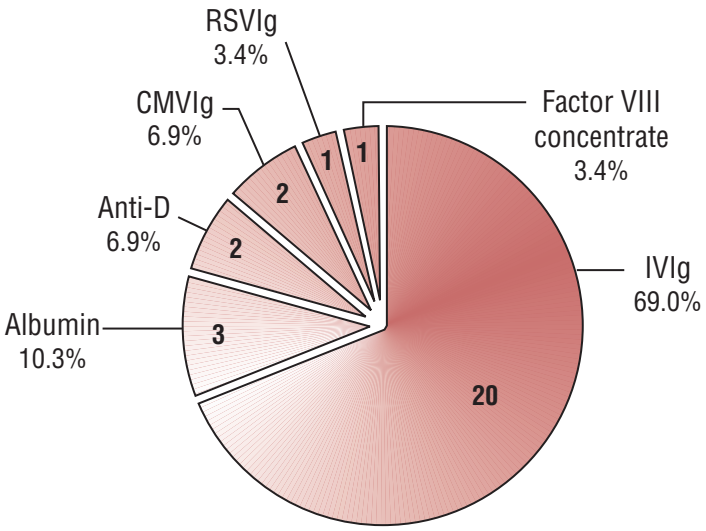


3.3 Adverse Transfusion Events Related to Plasma Derivatives and Recombinant Products

A total of 29 adverse events were related to plasma derivatives and recombinant products (14 in 2002 and 15 in 2003). More than two-thirds of these reactions were related to the administration of intravenous immune globulin (IVIg).

Figure 14

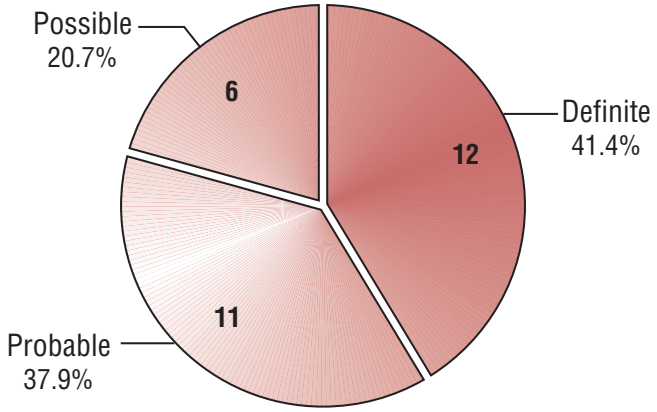
Plasma derivatives and recombinant products related to adverse transfusion events



A higher proportion of adverse events related to plasma derivatives and recombinant products were definitely related to transfusion than was the case for blood components (Figures 15 and 4).

Figure 15

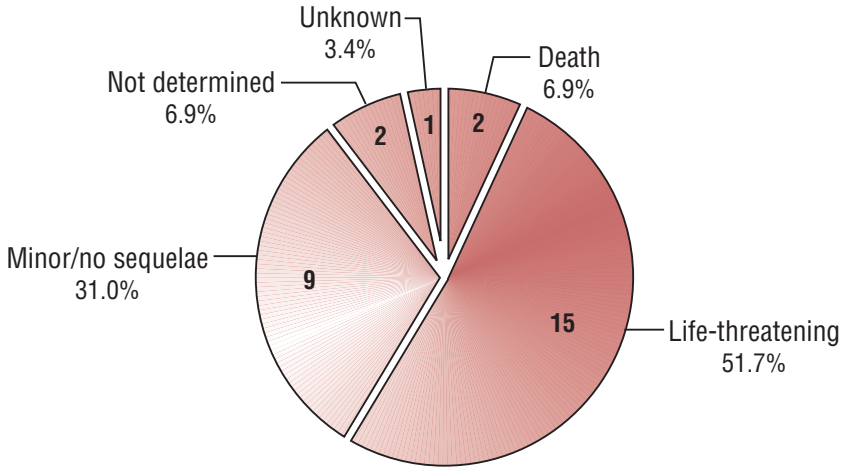
Adverse transfusion events related to plasma derivatives and recombinant products by relationship to transfusion



As in the case of blood components, approximately half of ATEs related to plasma derivatives and recombinant products were graded as life-threatening (51.7%). Thirty-one percent (31%) of cases were graded as minor (Figure 16). Two cases were fatal (see Section 3.4: Fatalities).

Figure 16

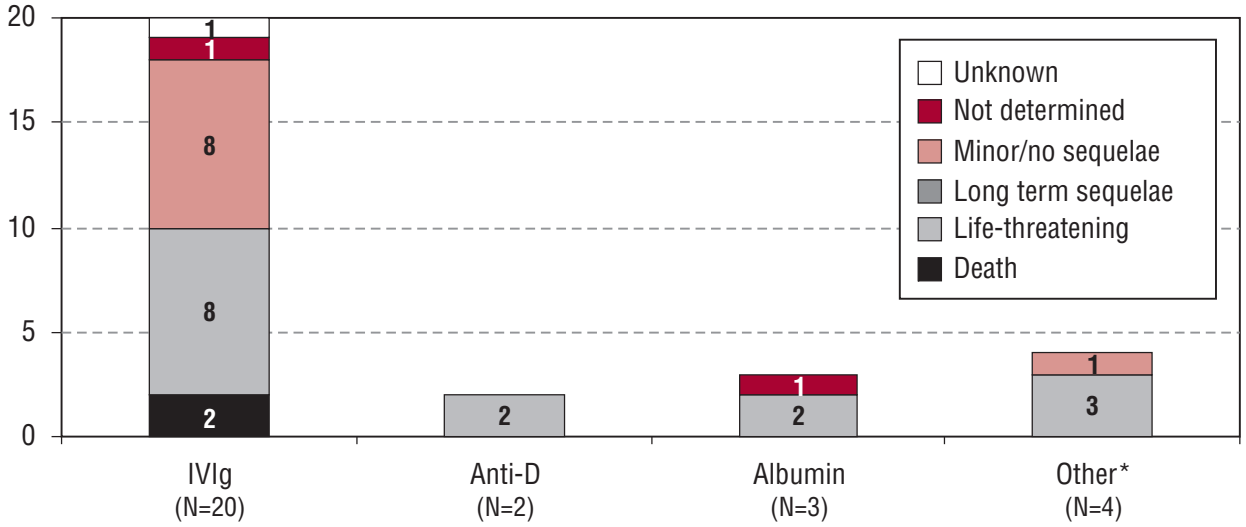
Adverse transfusion events related to plasma derivatives and recombinant products by severity



More than half of the cases graded as life-threatening were related to IVIg (53.3%).

Figure 17

Severity of adverse transfusion event by type of plasma derivatives and recombinant products



* Includes events related to CMVIg (2), RSVIg (1) and factor VIII concentrate (1).

3.3.1 Diagnosis of Adverse Transfusion Events Related to Plasma Derivatives and Recombinant Products

The types of ATEs related to each category of plasma derivatives and recombinant products are shown in Table 8.

Major allergic/anaphylactic reactions were the most frequently reported adverse events (44.8%), followed by aseptic meningitis (20.7%) and hypotensive transfusion reactions (13.8%). These three diagnoses represented 70% of ATEs related to IVIg. Other ATEs less frequently reported included TRALI (1 case), cerebrovascular accident (2 cases) and events classified in the "Other" category: one case of circulatory overload and one case of atypical pain syndrome all associated with IVIg.

Table 8

Diagnosis of adverse transfusion events related to plasma derivatives and recombinant products

Adverse transfusion event	Plasma derivatives and recombinant products											
	IVIg			Anti-D			Albumin			Total[a]		
	2002[b]	2003[b]	Total[b]	2002[b]	2003[b]	Total[b]	2002[b]	2003[b]	Total[b]	2002	2003	Total
Major allergic/ anaphylactic reaction	1 (11.1)	3 (27.3)	4 (20.0)	2 (100.0)	-	2 (100.0)	-	3 (100.0)	3 (100.0)	**6 (42.9)**	**7 (46.7)**	**13 (44.8)**
Aseptic meningitis	3 (33.3)	3 (27.3)	6 (30.0)	-	-	-	-	-	-	**3 (21.4)**	**3 (20.0)**	**6 (20.7)**
Hypotensive transfusion reaction	3 (33.3)	1 (9.1)	4 (20.0)	-	-	-	-	-	-	**3 (21.4)**	**1 (6.7)**	**4 (13.8)**
TRALI	-	1 (9.1)	1 (5.0)	-	-	-	-	-	-	**-**	**1 (6.7)**	**1 (3.5)**
Cerebrovascular accident	-	2 (18.2)	2 (10.0)	-	-	-	-	-	-	**-**	**2 (13.3)**	**2 (6.9)**
Other[c]	2 (22.2)	1 (9.1)	3 (15.0)	-	-	-	-	-	-	**2 (14.3)**	**1 (6.7)**	**3 (10.3)**
Total N (%)[d]	**9 (64.3)**	**11 (73.3)**	**20 (69.0)**	**2 (14.3)**	**-**	**2 (6.9)**	**-**	**3 (20.0)**	**3 (10.3)**	**14 (48.3)**	**15 (51.7)**	**29 (100.0)**

[a] This total includes events related to CMVIg (2 anaphylactic/anaphylactoid reactions), and RSVIg and factor VIII concentrate (1 anaphylactic/anaphylactoid respectively) not shown in the table.

[b] Proportion of reported ATEs for each type of plasma derivative and recombinant product.

[c] Includes: 2 circulatory overload and 1 atypical pain syndrome.

[d] Proportion of plasma derivative and recombinant product involved in ATEs.

3.3.2 Type of Adverse Transfusion Events by Relationship to Transfusion

Major allergic/anaphylactic reactions were more likely to be definitely related to transfusion, and aseptic meningitis probably related to transfusion (Table 9).

Table 9

Type of adverse transfusion events by relationship to transfusion

	Relationship to transfusion							
	Definite		Probable		Possible		Total	
Adverse transfusion event	N	%[a]	N	%[a]	N	%[a]	N	%[b]
Major allergic/anaphylactic reaction	8	61.5	3	23.1	2	15.4	**13**	**44.8**
Aseptic meningitis	2	33.3	4	66.7	-	-	**6**	**20.7**
Hypotensive transfusion reaction	-	-	2	50.0	2	50.0	**4**	**13.8**
TRALI	-	-	-	-	1	100.0	**1**	**3.5**
Cerebrovascular accident	-	-	2	100.0	-	-	**2**	**6.9**
Other[c]	2	66.7	-	-	1	33.3	**3**	**10.3**
Total	**12**	**41.4[d]**	**11**	**37.9[d]**	**6**	**20.7[d]**	**29**	**100.0**

[a] Proportion of relationship to transfusion for each ATE.
[b] Overall proportion of specific ATEs.
[c] Includes: 2 circulatory overload and 1 atypical pain syndrome.
[d] Overall proportion of relationship to transfusion for ATEs.

3.3.3 Type of Adverse Transfusion Events by Severity

Major allergic/anaphylactic reactions were more likely to be graded as life-threatening. The same was true for hypotensive transfusion reactions (Table 10).

Table 10

Type of adverse transfusion events by severity

Adverse transfusion event	Severity of adverse event											
	Death		Life-threatening		Minor or no sequelae		Not determined		Unknown		Total	
	N	%[a]	N	%[a]	N	%[a]	N	%[a]	N	%[a]	N	%[b]
Major allergic/ anaphylactic reaction	-	-	9	62.9	2	15.4	1	7.7	1	7.7	**13**	**44.8**
Aseptic meningitis	-	-	-	-	5	83.3	1	16.7	-	-	**6**	**20.7**
Hypotensive transfusion reaction	-	-	3	75.0	1	25.0	-	-	-	-	**4**	**13.8**
TRALI	-	-	1	100.0	-	-	-	-	-	-	**1**	**3.5**
Cerebrovascular accident	1	50.0	1	50.0	-	-	-	-	-	-	**2**	**6.9**
Other[c]	1	33.3	1	33.3	1	33.3	-	-	-	-	3	**10.3**
Total	**2**	**6.9[d]**	**15**	**51.7[d]**	**9**	**31.0[d]**	**2**	**6.9[d]**	**1**	**3.4[d]**	**29**	**100.0**

[a] Proportion of grade of severity related to each ATE.
[b] Overall proportion of specific ATE.
[c] Includes: 2 circulatory overload and 1 atypical pain syndrome.
[d] Overall proportion of grade of severity in ATEs.

3.4 Fatalities

Among all the reported ATEs related to the administration of both blood components, plasma derivatives and recombinant products, 17 recipients died. However, the relationship of death to transfusion was excluded in four cases: two cases of hypotensive reaction, one case of TRALI and one case of circulatory overload. The relationship to transfusion was doubtful in one case of circulatory overload and not available for the case of West Nile virus infection.

Thus, 11 fatalities were related to transfusion (Table 11).

- The two deaths definitely related to transfusion included:
  - A case of bacterial contamination related to *Staphylococcus aureus* where death resulted from septic shock after a contaminated platelet transfusion
  - A case with post-transfusion purpura where the patient received multiple blood components.

- The seven deaths probably related to transfusion included:
  - A case of bacterial contamination to a coagulase negative S*taphylococcus*
  - A case of bacterial contamination to S*erratia marcescens* related to whole blood derived platelets
  - A case of post-transfusion purpura related to red blood cells
  - A case of circulatory overload
  - A case of anaphylactic reaction related to plasma
  - A case of TRALI related to cryoprecipitate
  - A case of cerebrovascular accident related to IVIg.
- The two deaths possibly related to transfusion included:
  - A case of bacterial contamination to S*taphylococcus aureus* related to whole blood derived platelets
  - A case of TRALI related to red blood cells.

Table 11

Fatal events definitely, probably or possibly related to transfusion

Fatal events	Relationship to transfusion			
	Definite	Probable	Possible	Total
Events related to blood components				
Bacterial contamination	1	2	1	**4**
TRALI	-	1	1	**2**
Post-transfusion purpura	1	1	-	**2**
Circulatory overload	-	1	-	**1**
Anaphylactic reaction	-	1	-	**1**
Events related to plasma derivatives and recombinant products				
Cerebrovascular accident	-	1	-	**1**
Total	**2**	**7**	**2**	**11**

3.4.1 Incidence of Fatal Events Related to Transfusion of Blood Components

Incidence of death associated with blood component is shown in Table 12. Incidence was the highest for bacterial contamination, followed by TRALI and post-transfusion purpura.

Table 12

Incidence of fatal events definitely, probably and possibly related to transfusion of blood components

	Red blood cells (616,309)		Whole blood derived platelets				Apheresis platelets (21,403)		Plasma (182,329)		All products[a] (966,490)[b]	
			Units (307,235)		Pools (5) (61,447)							
Fatal events	N	Ratio	N	Ratio	N	Ratio	N	Ratio	N	Ratio	N	Ratio
Bacterial contamination	1	1:616,309	3	1:102,412	3	1:20,482	-	-	-	-	**4**	**1:241,622**
TRALI	1	1:616,309	-	-	-	-	-	-	-	-	**2**	**1:483,245[c]**
Post-transfusion purpura	1	1:616,309	-	-	-	-	-	-	-	-	**2**	**1:483,245[d]**
Major allergic / anaphylactic reaction	-	-	-	-	-	-	-	-	1	1:182,329	**1**	**1:966,490**
Circulatory overload	-	-	-	-	-	-	-	-	1	1:182,329	**1**	**1:966,490**
Total	**3**	**1:205,634**	**3**	**1:102,412**	**3**	**1:20,482**	**-**	**-**	**2**	**1:91,165**	**10**	**1:87,863**

[a] Includes cryoprecipitate and granulocytes.
[b] Whole blood derived platelets were counted as pools of 5.
[c] Includes one ATE related to cryoprecipitate not shown in the table.
[d] Includes ATEs to multiple blood components not shown in the table.

If we consider only the fatalities definitely related to transfusion, the overall incidence was 1:483,245.

In 2002, fatalities definitely related to transfusion included one case of post-transfusion purpura and one case of bacterial contamination with a ratio of 1:455,126 respectively for all products. For bacterial contamination the ratio was 1:151,291 units for whole blood derived platelets or 1:30,528 for platelet pools of five units.

4 Discussion

The Transfusion Transmitted Injuries Surveillance System has continued to evolve from the original four pilot provinces to eight provinces, with a total of 206 hospital sites participating in the surveillance system at the end of 2003, and a steady increase in participation during the reporting period. There has been, however, some variation in the definition of a participating site from province to province. In some provinces, all sites where products were transfused were included, whereas others included only sites with hospital blood banks. Some included only sites that have sent in data, while others included all sites where the TTISS database had been installed and/or training for reporting had been carried out. Since 2004 there has been a standard definition for "site" so that participation data will be comparable between provinces. It should be noted that in the provinces with a small proportion of participating sites, these sites were large as they represented a high proportion of the transfusion activity in these provinces. In the end, almost half of the blood components transfused in Canada were captured in TTISS participating hospital sites.

More than 40% of reported events had to be excluded from analysis. These events were cases not meeting standard definitions or cases with significant missing information that were transferred to PHAC. This may be explained in part by the fact that TTISS was still being implemented in some provinces and a complete validation process was not in place. Also, due to a problem in the transfer module of the TTISS database, some minor reactions were transferred to PHAC that should not have been. This problem has been corrected in a newer version of the database. A meeting was also organized in the last year for TTISS participants to address data quality issues; this will be an annual event in the future.

The relationship to transfusion of the reported events included for analysis was strong with almost 80% being definite or probable, the rest being possible. Even though only serious events had to be reported, some of these events, especially in the categories of major allergic reactions, bacterial contamination and hemolytic reactions were not life-threatening and were therefore graded as 'minor or no sequelae'. Altogether just over half of the events were graded as life-threatening and death occurred in 5.6% of cases. The classification of severity of ATEs in TTISS has led to some confusion because severity of the reaction itself and outcome in the recipient were mixed in some of the categories. In the future, this will be solved by having separate variables for severity of the reaction and outcome in the recipient.

The reported deaths were not all the result of the adverse transfusion event, some being caused by the patient's underlying condition. In fact out of the 17 deaths reported, 11 were possibly, probably or definitely related to transfusion. Only two deaths were definitely related to transfusion, both with blood components (a case of bacterial contamination and a case of post-transfusion purpura). These deaths must be put in perspective with the number of units of blood components transfused in this two-year period (more than 1.5 million) in the participating hospitals and with more than three million units issued in Canada.[1, 2]

The denominator data for plasma derivatives and recombinant products were not available but the number of vials of product issued is also estimated to be around two million for Canada in the two-year period in question.[1,2]

Major allergic or anaphylactoid reactions were the most frequent reactions reported to TTISS during the period, representing respectively 36% and 45% of cases for blood components and plasma derivatives and recombinant products. These data differ significantly from SHOT data[3] in which 'Incorrect Blood Components Transfused (IBCT)' is the most frequent reported event. In Canada, however, only IBCT leading to adverse events are reportable. In France, all reactions, whether minor or serious are reportable to the French Hemovigilance System, and, as in Canada, allergic reactions were the most frequent adverse events reported in 2003.[4]

For blood components, TRALI was the second adverse event most frequently reported with 13% of cases followed by circulatory overload (12.7%), acute hemolytic transfusion reactions (11.6%) and bacterial contamination (10%). The donors implicated in TRALI cases were not all investigated for the presence of HNA or HLA antibodies and the definition used differed from the new consensus definition recently published.[5] Half of the TRALI cases reported were associated with the transfusion of red blood cells.

A number of very different red cell antibodies were involved in the acute hemolytic transfusion reactions reported, only 20% being related to the ABO system. Of the 14 cases of ABO-incompatible transfusions reported, three were life-threatening and were the direct result of an error in patient identification either at the sampling stage for analysis or at the bedside at the time of transfusion. These are preventable cases and strong efforts must be made by hospitals to improve patient identification.

Bacterial contamination is a major risk of transfusion. It is encouraging that the number of cases reported declined by 40% from 2002 to 2003. We will have to await data from the next few years to see if this really represents a downward trend. Only two of the 27 bacterial contaminations reported were with Gram negative bacteria and both were associated with whole blood derived platelets and were not severe cases. In fact, the vast majority of bacterial contaminations were graded as minor and only four cases were graded as life-threatening. Unfortunately four cases resulted in death of the recipient (three with whole blood derived platelets and one with red blood cells). The cases of death were caused by bacteria that may be considered skin contaminants. The fact that many of the reported cases of bacterial contamination were related to plasma transfusions is puzzling and calls into question the quality of the data for this type of reaction. It may be that these cases were the result of laboratory or specimen handling contamination rather than true contamination of the component. More stringent validation of bacterial contamination cases will be required in the future.

Three cases of transfusion-related West Nile virus infections were reported in Canada in 2002. However, of these cases, only one was reported to TTISS. There may be two explanations for this: either the cases occurred in hospitals not participating in TTISS or hospitals

participating in TTISS under-reported. As required by federal regulation, the cases were reported to Health Canada's regulatory branch, but TTISS being a voluntary reporting system, did not receive all the reports. For serious adverse transfusion reactions, especially for infectious diseases, all cases reported in Canada in the future should be compiled in the same report so that a better picture of the transfusion risk in Canada can be made available.

Post-transfusion purpura (PTP) is an uncommon adverse event. The number of cases that were reported in the two-year period (7) is higher than the number reported in the United Kingdom (UK) (6), a country transfusing many more units than Canada, based on the published data for the last three years.[6] The cases were reported by only a few hospitals where there might be enhanced vigilance for this transfusion reaction or just normal fluctuation in the reporting of a rare event. In preliminary 2004 data transferred to PHAC, no cases of PTP have been reported.

In this report we were able to provide rates for adverse transfusion events related to blood components only. The selection of appropriate denominator data was complicated by the fact that quality of reporting varied significantly among the different provinces participating in TTISS. We finally opted to include only cases, both in numerator and denominator, from three provinces where reporting was evaluated to be optimal. This may perhaps have led to a modest overestimate of the rates, but inclusion of denominator data from all provinces, regardless of data quality, would have unduly diluted them, since 97% of ATEs were reported by these three provinces.

As can be seen in figure 13, the rates did not differ significantly between 2002 and 2003. It is however notable that the rate for bacterial contamination in 2003 is almost 50% lower than in 2002. The rates for circulatory overload represent an underestimate of the occurrence of this phenomenon since only the most severe cases are to be reported to TTISS. The situation is the same for delayed hemolytic transfusion reactions. Rates for TRALI are lower than those from prospective studies, but higher than those from other surveillance systems where TRALI is known to be underreported.[5] This reassures us that the decision to use a subset of provinces for rate estimation was prudent.

As expected from the high number of PTP cases reported in 2003, the rate is somewhat higher than some previous published estimates.[7] Since this is considered a rare event, the rate could be reflecting normal annual variation. More data will be needed before we can make meaningful comparisons.

In fact, since TTISS is still an evolving and developing surveillance system in which more provinces and territories and more hospital sites will be participating in the future, it will take some years before we can accurately estimate trends in the incidence of adverse transfusion events for Canada as a whole.

A smaller number or adverse events were reported to TTISS with respect to plasma derivatives and recombinant products. Again it is the category 'major allergic reaction' that was the most frequently reported event followed by aseptic meningitis. Given the frequent use of IVIg in Canada, it is expected that this plasma derivative was the most common one related to the reported events. The reported events related to plasma derivatives and recombinant products are to be expected with the administration of these products; but it is worth mentioning that one case of TRALI was reported in 2003. More adverse events than those reported to TTISS were reported through the Canadian Adverse Drug Reaction Monitoring Program of Health Canada's Marketed Health Product Directorate. It would be interesting in the future to combine data from the two reporting systems in order to have a better picture of the risks associated with these products.

TTISS is not an alert system and is not a substitute to reporting for the manufacturers of blood components, plasma derivatives and recombinant products for action to be taken on the implicated products, nor to Health Canada's regulatory branch. Data that are transferred to TTISS are six months old and therefore useful only for surveillance purposes.

TTISS is a good example of a collaborative effort to develop and implement a nation-wide surveillance system in Canada. Federal public health and regulatory bodies together with provincial and territorial representatives and representatives from the two Canadian blood manufacturers (Canadian Blood Services and Héma-Québec) have been working together since the beginning of the TTISS project. Their dedication has allowed the development of a surveillance system for adverse transfusion events with standards that are as high as those in any other country. This system now being deployed in all provinces and territories will help improve the safety of transfusion in Canada and the well-being of Canadians.

In closing, it is noteworthy that Canada is now actively involved in the international standardization of nosological definitions of adverse transfusion events and of reporting tools. This standardization will allow for better comparisons between different countries and settings and may help identify optimal transfusion practices that will improve blood safety in Canada and elsewhere.

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