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Transfusion Transmitted Injuries Surveillance System

Project Progress Report 2001-2002

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Transfusion Transmitted Injuries Section
Blood Safety Surveillance and
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Preface

The Transfusion Transmitted Injuries (TTI) Section of the Blood Safety Surveillance and Health Care Acquired Infections Division at Health Canada has been assigned to carry out activities to support the development of a National Transfusion Transmitted Injuries Surveillance System (TTISS). The objectives of the TTISS are:

- To capture data on moderate and severe adverse events of transfusion
- To capture data on serious errors/near misses of blood/blood transfusions
- To capture delayed adverse events of transfusion including transmission of infectious diseases due to transfusion of blood/blood products
- To perform risk assessment:
  - Data analysis and measuring the magnitude of risks
  - Monitor trends over time
  - Measure the risks in relation to epidemiological characteristics (person/time/place)
- To produce reports and disseminate information to support risk management activities and regulatory actions.

Given the advances in testing technology, the risk of acquiring a viral infectious disease through blood transfusion is now extremely low in Canada which has one of the safest blood supplies in the world. The viral risks for HIV, HCV and HBV are now estimated to be 1 in 10 million, 1 in 2,857,000 and 1 in 72,000 units of blood transfused respectively (Chiavetta et al, CMAJ 2003; 169:767-773).

However, bacterial contaminations and non-infectious hazards related to blood transfusion continue to occur at a much higher frequency. They can frequently go unrecognized and are often underreported. The non-infectious hazards can have multiple causes, some related to the transfusion practices at the hospital, others to the clinical condition of the recipients or because of some interactions between the biological product being transfused and the recipient's characteristics.

The TTISS is a voluntary surveillance system that has been implemented to improve transfusion reaction reporting, which can enable us to have a better knowledge of the frequency of transfusion reactions occurring in Canada and assist us in program planning to reduce transfusion risks. This system is in addition to and does not replace the current existing regulatory requirements in place at Health Canada for reporting of serious adverse events related to transfusion of blood products and components.

The present document is the first progress report on the current status of the surveillance system launched in 1999. It addresses adverse events reported to the TTISS for the period April 1, 2001 to June 30, 2002, by the provinces of British Columbia, Quebec, Nova Scotia and Prince Edward Island. The provinces of Ontario, New Brunswick, Alberta and Manitoba joined the surveillance system in April 2002. Data from these locations were either not available or not within the reporting period, due to the start-up time required to produce data. Their data will be included in subsequent reports.

The TTISS project has been a success and a great example of collaboration between health care professionals working together to build a surveillance system aimed at monitoring adverse transfusion reactions. It is important to remember that the results presented in this document are those of a project during its pilot stage. The project has since been expanded and is now a national system. Tremendous progress has been made to improve the system, based on the limitations found in the pilot project. Case definitions have been refined, signs, symptoms and laboratory results are provided in order to validate the cases, and a more in-depth investigation of the cases is now conducted. A Data Review group, with experts across Canada has been instituted to review the data twice a year, make recommendations for enhancing the system, and provide suggestions on any major issues identified. Moreover, denominator data on the number of units of blood transfused will be provided by the provinces/territories for the estimation of risks of the adverse events. This will allow for the comparison of our data to other international hemovigilance systems. An error surveillance system is being developed and methods to capture delayed infections related to transfusion are being addressed.

Implementation of the TTISS would not have been possible without the involvement of the pilot provinces representatives of British Columbia, Dr. David Pi; Québec, Dr. Pierre Robillard; Nova Scotia, Dr. David Anderson; Prince Edward Island, Dr. Linda Van Til as well as the Blood Manufacturers, Canadian Blood Services and HÉMA-QUÉBEC representatives, and the regulatory groups of Health Canada.

Specifically, I would like to express my gratitude to these representatives for the tremendous work accomplished in the development of the surveillance system, mainly in reaching agreement on the data elements to be collected and transferred to Health Canada, the standardized definitions to be used for the data elements and the standardized form for reporting the data elements.

I am indebted as well to the staff of the TTI Section, Blood Safety Surveillance and Health Care Acquired Infections Division, Nancy McCombie, Magalie Cator, Nick Karitsiotis and his team, Mary-Ann Wotherspoon and Marlène Huard, who worked diligently in the development of the surveillance system and in the preparation of this report.

The contribution of all participants and the continuous support of our collaborators are greatly appreciated. I look forward to the future involvement of the remaining provinces and territories for a comprehensive national surveillance system in the next year.

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I Introduction

In order to improve adverse transfusion reaction reporting in Canada, Health Canada put together the following expert working group in March 1998: The Surveillance and Epidemiology of Transfusions (SET) Working Group. After many consultations, reviewing the literature and how adverse transfusion reactions were reported in other western countries, the SET Working Group issued its report on February 28, 1999[1]. A comprehensive surveillance scheme was proposed that included estimation of the risks of adverse transfusion reactions in Canada. Surveillance indicators were proposed including rates of transfusion transmitted infections, of transfusion induced injuries and of adverse reactions, both for fresh blood components and fractionation products. Data elements to be collected by the surveillance system were also identified in that report as well as the governance mechanism for such a reporting system. One of the major recommendations of the SET report was that the federal, provincial and territorial governments develop a new surveillance system for adverse transfusion reactions and sponsor the development of definitions of such reactions, of a standardized reporting mechanism and of guidelines for the investigation of suspected adverse transfusion reactions.

In March 1999, a federal/provincial/territorial meeting was convened to address some of the SET report recommendations, particularly those related to the proposed new surveillance system. Health Canada announced its decision to fund pilot projects for surveillance of transfusion transmitted injuries (including infections) in Canada. Provinces and territories were invited to submit proposals and four did: British Columbia, Quebec, Nova Scotia and Prince Edward Island.

The new surveillance system was called the Transfusion Transmitted Injuries Surveillance System (TTISS). In the following two years, a surveillance scheme was developed by a core working group composed of representatives from Health Canada, the four pilot provinces, the Canadian Blood Services, and HÉMA-QUÉBEC. This scheme included the scope of the surveillance system, the data elements to be collected and those to transfer to Health Canada, a set of standardized definitions for the data elements, a standardized form for reporting adverse events (Appendix 1), a database for data entry, and some predefined analyses. The form and definitions were inspired by those used by the Quebec hemovigilance system, which had already developed such tools in 1998 and 1999 and started reporting adverse transfusion reactions provincially in February of 2000. Hence, there was compatibility between the two surveillance schemes, that of Quebec and the national pilot system.

Throughout this process, all the provinces were kept informed and able to provide input through the TTISS Federal/Provincial/Territorial Steering Committee that met regularly. Hence, once the pilot projects were completed, there would be the basis for a national surveillance system of adverse transfusion reactions.

1 Kleinman, et al. The Surveillance and Epidemiology of Transfusions Working Group, Final Report. Health Canada, February 28, 1999.

After numerous discussions, there was agreement by all four pilot provinces and Health Canada on all data elements to collect on a standardized reporting form. A Microsoft (MS) Access database to be used by the participating hospitals and provinces was developed by Health Canada. The database visually reproduced the reporting form and included extensive search capabilities, predefined reports and an export mechanism to send data that had been made anonymous to Health Canada. Quebec already had developed an electronic reporting format so it did not use the Health Canada database for collection, and British Columbia developed its own electronic reporting mechanism.

The type of cases and the data elements to export to Health Canada by the provinces were agreed upon (Appendices 2 and 3) as well as the governance for the analyses which, for the duration of the pilot project, would lie with the members of the Core Working Group. Data started being sent to Health Canada in April 2002 for the period starting April 1, 2001. There were biannual transfers thereafter.

The data presented in this report cover a 15-month period (April 1, 2001 to June 30, 2002). Only descriptive analyses were performed because of the lack of denominator data from all provinces on the number of blood recipients from which the reactions arose or on the number of units transfused. All severe reactions reported during that period were included in this report even if, for reactions related to fractionated products, data were far from being complete. Special attention in the report is given to bacterial contamination and deaths. Finally, recommendations for the future of TTISS are given at the end of the report including a status on where the project stands as of March 31, 2003.

II Methodology

2.1 Transfusion Reaction Reporting

The mechanism of transfusion reaction reporting varies across the provinces.

2.1.1 British Columbia

The Provincial Blood Coordinating Office (PBCO), which coordinates the British Columbia (B.C.) Blood Surveillance project, the B.C. Adverse Event Reporting System (AERS), selected eight hospitals with six blood banks to participate in the TTISS project according to the 'specific monthly transfusion volumes of red blood cells, their commitment to quality improvement in transfusion and their willingness to participate in the development of a standardized reporting system'. These hospitals transfuse approximately 50% of blood products in the province. They worked with the PBCO to assess and redesign adverse reaction reporting, resulting in the establishment of a standard process for data collection and reporting. Forms and guidelines were developed and software made available for the collection and reporting of transfusion reactions to the PBCO. These are different from the TTISS form, User's Manual and database but compatible. Definitions of transfusion reactions were similar to those used by the other provinces. Seven hospitals/sites started reporting data on April 2001, and another one began in November 2001. Since this date, there has been ongoing rollout and reporting from facilities across the province.

Following a transfusion reaction, a team consisting of a nurse, a technologist and a pathologist worked together at each site to investigate and report the reaction to the PBCO. Transfusion reactions data were collected either through the manual reporting form or the electronic transmission of the data to the PBCO.

Manual reporting

Once a transfusion reaction was reported to the blood bank, the designated technologist conducted a preliminary review to ensure the form was complete and determined if the cases met TTISS requirements for reporting. For serious reactions, an investigation was performed, and when completed, the case was faxed to the PBCO for data entry into the PBCO master AERS system that was set up to export the cases to Health Canada.

Electronic reporting

For sites reporting electronically, all cases for which an investigation was completed were exported monthly to the PBCO on a diskette. These cases were then imported into the PBCO master system. The master AERS system at the PBCO contains only completed cases that have been investigated and validated.

Sites that reported adverse events of transfusion received, on a monthly basis, a summary of all reactions received at the PBCO and were asked to review them in order to ensure that no cases were missed. On a quarterly basis, a summary of all data submitted by the sites was once again sent back to them for review and reconciliation prior to exporting the cases in an encrypted text file to Health Canada.

2.1.2 Quebec

In Quebec, all 33 hospitals that were already participating in the Hemovigilance System participated in the 'Quebec Blood Surveillance Project' funded by Health Canada. These hospitals are served by 43 blood banks and transfuse about 80% of components in the province. All adverse transfusion reactions are reported to the Quebec Blood Secretariat since February 2000. Data reporting to Health Canada started in April 2002, with data collected since April 2001.

Manual reporting

At the beginning of Quebec's project, hospitals were reporting transfusion reactions manually. A standardized reporting form similar to the TTISS form was completed and signed by a transfusion safety officer. The diagnosis and association with transfusion were validated and signed by the hematologist in charge of the blood bank and the form was then sent to the Quebec Blood Secretariat where further validation was done by a provincial transfusion safety officer. The data were entered into a MS Access database and all serious adverse reactions were reviewed and validated by the project director.

Electronic reporting

An online reporting system, using the Lotus Notes messaging system, was implemented in health care facilities in April 2001 and most hospitals have been reporting online. A provincial transfusion safety officer reviewed submissions from hospitals on a daily basis and took steps to validate the data. As with the manual reporting, electronic forms for serious adverse events were reviewed and validated by the project director. Data on serious adverse events meeting TTISS requirements for reporting were extracted and an Excel file sent to Health Canada.

2.1.3 Nova Scotia

The Nova Scotia Blood Surveillance Project created and implemented a surveillance process for adverse reactions in eight hospitals/sites that transfuse approximately 52% of blood products in the province. Two sites started reporting transfusion data in June and October 2001, respectively, and another one in January 2002. The five remaining sites have reported transfusion reactions since mid June 2002.

The process of transfusion reaction reporting for each site was developed and implemented with a key laboratory partner, medical director and laboratory staff member. The implementation process involved education sessions on transfusion reactions to laboratory and nursing staff at each site.

Transfusion reaction information was sent by the blood bank laboratory staff to the project office by fax. The project coordinator who also functioned as a transfusion safety officer gathered the required information. Data were entered into a database at the project office after validation by the Blood Transfusion Service Medical Director and exported in an encrypted text file to Health Canada.

2.1.4 Prince Edward Island

The Prince Edward Island (P.E.I.) project on Transfusion Transmitted Injuries Surveillance was implemented province-wide through creation of a provincial Central Transfusion Registry that captures all transfusions and associated reactions. All seven P.E.I. hospitals participated in the surveillance project. Two blood banks, associated with these hospitals, provide 100% of blood products in the province.

When a transfusion reaction occurred, the hospitals filled out the TTISS form and initiated the investigation of the reaction. Forms were collected by a transfusion safety officer during quarterly on-site visits. The transfusion safety officer reviewed the forms and results of the investigation. The forms were submitted to the medical director for approval and validation of the diagnostic category and association with transfusion. The cases were then entered into the database installed by Health Canada and relevant data were exported to Health Canada, in a Microsoft Access Database (MDB) file.

2.2 Analyses

Data received from the provinces were compiled in a MS Access database, maintained in the TTI Section and exported to SPSS 10.0 for analysis. Descriptive analyses of the data reported were conducted, including number and proportion of each category of adverse events, their distribution by age and by sex, and their severity and relationship to transfusion. Suspected blood products implicated in these reactions were also analyzed. For the purpose of this analysis, only adverse events occurring during the period April 1, 2001 to June 30, 2002 were included.

III Results

3.1 Overall Results

From April 1, 2001 to June 30, 2002, a total of 99 adverse reactions were reported by participating provinces to the TTI Section, Health Canada. The highest proportion of reported reactions were “major allergic/anaphylactic (39%), followed by ”bacterial contamination" (24%) (Table 1).

Table 1: Diagnosis of Adverse Transfusion Reactions Reported to Health Canada (April 1, 2001 - June 30, 2002) (n = 99)

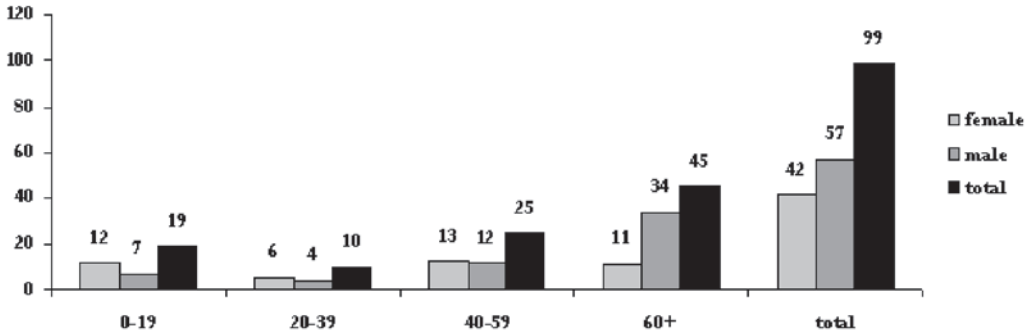
Adverse Reactions	Number	Proportion
Major Allergic /Anaphylactic Reaction	39	39.4%
ABO Incompatibility*	11	11.1%
Acute Hemolytic Reaction	13	13.1%
Viral Infection (Parvovirus B19)	1	1.0%
Bacterial Contamination	24	24.2%
TRALI (Transfusion-related acute lung injury)	6	6.1%
Hypotensive Transfusion Reaction	1	1.0%
Unknown	4	4.0%
Total	**99**	**100.0%**

* Four cases of ABO incompatibility resulted in acute hemolytic reaction.

3.2 Age and Sex

The largest proportion of adverse reactions (46%) occurred in patients aged 60 years and over, followed by those between 40-59 years (25%), and then those 0-19 years (19%). Males represented 58% of the reported reactions (Figure 1).

Figure 1: Adverse Transfusion Reactions by Age and Sex



3.3 Relationship to Transfusion

A high degree of association to transfusion was observed among the reported reactions, 80% being definite or probable (Table 2). Causality was assigned using the definitions listed in Appendix 3.

Table 2: Adverse Transfusion Reactions by Relationship to Transfusion

Adverse Reactions	Relationship to Transfusion			
	Definite	Probable	Possible	Total
Major Allergic/Anaphylactic Reaction	9	27	3	39
ABO Incompatibility	10	1	–	11
Acute Hemolytic Reaction	11	2	–	13
Viral Infection (Parvovirus B19)	–	1	–	1
Bacterial Contamination	1	11	12	24
TRALI (Transfusion related acute lung injury)	3	2	1	6
Hypotensive Transfusion Reaction	–	–	1	1
Unknown	–	1	3	4
Total # (%)	34 (34.3%)	45 (45.5%)	20 (20.2%)	99 (100%)

3.4 Severity of Outcome

There were minor or no sequelae following the occurrence of 57 (58%) adverse reactions, whereas 32 reactions (32%) were life-threatening and eight (8%) resulted in death (Table 3).

Table 3: Adverse Transfusion Reactions by Severity of Outcome

Adverse Reactions	Severity of Outcome					
	Death	Life-threatening	Long-term Sequelae	Minor/No Sequelae	Not Determined	Total
Major Allergic/ Anaphylactic Reaction	1	18	–	20	–	39
ABO Incompatibility	–	1	1	9	–	11
Acute Hemolytic Reaction	1	7	–	5	–	13
Viral Infection (Parvovirus B19)	–	–	–	1	–	1
Bacterial Contamination	1	4	–	18	1	24
TRALI (Transfusion related acute lung injury)	1	2	–	3	–	6
Hypotensive Transfusion Reaction	–	–	–	1	–	1
Unknown	4	–	–	–	–	4
Total # (%)	**8 (8.1%)**	**32 (32.3%)**	**1 (1%)**	**57 (57.6%)**	**1 (1%)**	**99 (100%)**

3.4.1 Deaths

The deaths were definitely associated with transfusion in two cases, probably in three cases, and possibly in three cases. The two deaths definitely associated with transfusion were due to a bacterial contamination of a platelet pool and an acute hemolytic reaction secondary to the transfusion of a wrong ABO red cell unit.

The three with a probable association were a case of TRALI, a case with an anaphylactic reaction and a cancer patient who developed severe hypertension during the transfusion of platelets.

For the three cases possibly associated with transfusion, the patients had been transfused with red blood cells:

Case 1 Very old patient; possible septic shock; no cultures done.

Case 2 Patient in a terminal stage of cancer, was tachypneic on arrival and presented a volume overload.

Case 3 No information available.

No autopsy was performed on all these cases.

3.4.2 Bacterial Contamination

As shown, in Table 4a, there were 12 cases of definite or probable bacterial contamination. Most of these reactions were minor. Platelets were implicated in two thirds of these reactions. A variety of bacteria were isolated in the blood product culture, with predominance of skin contaminants.

Table 4a: Characteristics of Definite and Probable Cases of Bacterial Contamination

Bacterial Contamination Status	Blood* Products	Signs and Symptoms	Organism Identified		Severity of Outcome
			Blood Product Culture	Recipient Culture	
Definite	PLT	Fever, chills	*Staphylococcus aureus*	*Staphylococcus aureus*	Death
Probable	RBC	Fever, chills, hypotension, diaphoresis	*Streptococcus*	–	Life-threatening
Probable	PLT	Fever, chills, dyspnea, nausea, vomiting	*Moraxella*	–	Life-threatening
Probable	RBC	Hypotension	*Streptococcus*	–	Life-threatening
Probable	RBC	Fever, chills, vomiting	*Staphylococcus epidermidis*	–	Minor/No sequelae
Probable	PLT	Fever, chills, rigors	Coagulase-negative *Staphylococcus*	–	Minor/No sequelae
Probable	PLT	Fever, chills, urticaria	*Propionobacterium acnes*	–	Minor/No sequelae
Probable	RBC	Fever, flushes	Coagulase-negative *Staphylococcus*	–	Minor/No sequelae
Probable	PLT	Urticaria	*Streptococcus*	–	Minor/No sequelae
Probable	PLT	Fever, urticaria, vomiting	*Staphylococcus*	–	Minor/No sequelae
Probable	PLT	Hypotension, shock, diarrhea	*Oerskovia xanthineolitica*	–	Minor/No sequelae
Probable	PLT	Urticaria	*Streptococcus viridans*	–	Minor/No sequelae

* PLT = Platelets; RBC = Red Blood Cells

Twelve other cases of bacterial contamination were reported as possibly related to transfusion (Table 4b). In one of them the product culture was positive and the result of the recipient culture was unknown. According to the reporting province, the case was classified as possibly related to transfusion because it occurred within a time frame consistent with the administration of the blood product, but the event could also be explained by the recipient's primary or secondary diagnosis, treatment or by the administration of a drug or other agent. (This shows that there is some difference in the classification of bacterial contamination cases across the provinces). Two thirds of these cases were minor as well. Red blood cells (RBC) were implicated in most of these cases.

Table 4b: Characteristics of Possible Cases of Bacterial Contamination

Bacterial Contamination Status	Blood* Products	Signs and Symptoms	Organism Identified		Severity of Outcome
			Blood Product Culture	Recipient Culture	
Possible	RBC	Fever, chills, hypotension, shock, dyspnea, tachycardia	–	Gram-negative bacillus	Life-threatening
Possible	RBC	Fever, chills, hypotension, oligoanuria	–	*Klebsiella pneumoniae*	Minor/No sequelae
Possible	RBC	Fever	–	*Staphylococcus epidermidis* & *Streptococcus mitis*	Minor/No sequelae
Possible	RBC	Fever, dyspnea	–	Group B *Streptococcus*	Minor/No sequelae
Possible	PLT	Fever	–	*Staphylococcus bonivir*	Minor/No sequelae
Possible	FFP	Fever, chills, urticaria wheezing	–	Gram-negative bacilli	Minor/No sequelae
Possible	RBC	Fever, chills	–	Gram-negative bacillus	Minor/No sequelae
Possible	RBC	Fever	–	*Enterococcus faecalis*	Minor/No sequelae
Possible	RBC	Fever, chills	–	*Escherichia coli*	Minor/No sequelae
Possible	RBC	Fever, chills	–	*Citrobacter koseri*	Minor/No sequelae
Possible	FFP	Fever	Coagulase-negative *Staphylococcus*	–	Minor/No sequelae
Possible	RBC	Fever, chills tachycardia	–	*Staphylococcus epidermidis*	Not determined

* RBC = Red Blood Cells; PLT = Platelets; FFP = Fresh Frozen Plasma

3.5 Implicated Blood Products

The majority of the reported reactions (95%) were associated with the administration of fresh blood components. Of these, 54% were related to RBC; 23% to platelets and 18% to fresh frozen plasma (FFP) (Table 5a).

Table 5a: Adverse Transfusion Reactions by Suspect Fresh Blood Components

Adverse Reactions	Fresh Blood Components †													
	RBC		PLT		FFP		Cryo		RBC +FFP		RBC +PLT		Total**	
	No	%	No	%	No	%	No	%	No	%	No	%	No	%
Major Allergic/ Anaphylactic Reaction	15	41.7	10	27.8	9	25	1	2.8	1	2.8	–	–	36	100
ABO Incompatibility	6	54.5	1	9.1	4	36.4	–	–	–	–	–	–	11	100
Acute Hemolytic Reaction	10	90.9	–	–	1	9.1	–	–	–	–	–	–	11	100
Viral Infection (Parvovirus B19)	1	100	–	–	–	–	–	–	–	–	–	–	1	100
Bacterial Contamination	13	54.2	9	37.5	2	8.3	–	–	–	–	–	–	24	100
TRALI (Transfusion-related acute lung injury)	2	33.3	1	16.7	1	16.7	1	16.7	–	–	1	16.7	6	100
Hypotensive Transfusion Reaction	1	100	–	–	–	–	–	–	–	–	–	–	1	100
Unknown	3	75	1	25	–	–	–	–	–	–	–	–	4	100
Total*	**51**	**54.3**	**22**	**23.4**	**17**	**18.1**	**2**	**2.1**	**1**	**1.1**	**1**	**1.1**	**94**	**100**

* % of all adverse reactions
** % of each category of adverse reactions
† RBC = Red Blood Cells; PLT = Platelets; FFP = Fresh Frozen Plasma; Cryo = Cryoprecipitate

The reactions reported with the plasma derivatives (Table 5b) are known adverse effects of these products.

Table 5b: Adverse Transfusion Reactions by Suspect Plasma Derivatives

Adverse Reactions	Plasma Derivatives †					
	IVIG		RhIG		Total**	
	No	%	No	%	No	%
Major Allergic/ Anaphylactic Reaction	2	66.7	1	33.3	3	100
Acute Hemolytic Reaction	–	–	2	100	2	100
Total*	**2**	**40**	**3**	**60**	**5**	**100**

* % of all adverse reactions
** % of each category of adverse reactions
† IVIG = Intravenous Immune Globulin
RhIG = Rh Immune Globulin

IV Discussion

Reporting transfusion reactions in a standardized manner throughout four provinces and more than 50 hospitals proved to be quite a challenge. Developing a set of standardized definitions for transfusion reactions and a set of data to transfer to Health Canada that was agreeable to all parties involved was a process that lasted 18 months. As well, the reporting tools (forms and database) went through several drafts. Since reporting started, in a period of 15 months, 99 serious adverse transfusion reactions were reported to Health Canada by the 56 hospitals participating in the TTISS in the four pilot provinces.

These data should not be considered as national figures and caution must be used in interpreting them. This is a new surveillance system and very few Canadian hospitals participated. In addition, there was no certainty regarding the true level of standardization achieved. There was very little information transferred to Health Canada to interpret the diagnoses and accept cases as valid. In many instances there were no signs or symptoms provided and no laboratory results as well as no text description of the event. This situation has been improved and, for future transfers, data on symptoms, signs and laboratory results will be provided and an agreement is anticipated for the transfer of a narrative description of a reaction. This will ensure a better classification at the national level.

Within the TTISS project, the only reactions being reported to Health Canada are severe reactions. This, in conjunction with the fact that only a small fraction of Canadian hospitals participated during the pilot project, explains the small number collected by the TTISS.

Other surveillance programs such as the Canadian Adverse Drug Reaction Program which collects information on all adverse events to fractionated blood products may have a higher number of reports, but the quality of the TTISS reports is expected to be better as each case has been investigated and validated at the provincial level. It is not possible to evaluate the extent of underreporting since a clinical condition must be recognized first at the primary level as a transfusion reaction within a hospital and some of the reactions were possibly missed.

The absence of denominators from all provinces on the number of blood recipients and on products transfused in the participating hospitals prevented the calculation of rates of adverse transfusion reactions. These data are essential for a surveillance system and should certainly be included for future transfers in order to enable the estimation of risks of adverse reactions.

There were two deaths definitely associated with transfusions that were reported, including one case of acute hemolytic reaction, secondary to a human error, the transfusion of a wrong ABO red cell unit, and one of bacterial contamination. It is difficult to definitely relate the other deaths to transfusion. However, the death associated to the TRALI case is most probably related to transfusion.

Of the adverse events reported, only five were related to fractionated products. Caution is needed with respect to the data on fractionated products. There was no agreement on what reactions should be reported with respect to this type of product and reporting varied significantly from one province to the other. It can be assumed that there was significant underreporting of adverse events related to fractionated products during the reporting period.

TTISS has shown that it can work in pilot settings despite the difficulties inherent in a national surveillance system. It should now expand beyond the pilot provinces and hospitals and, in fact, as of March 2003, almost all provinces and territories have agreed to participate in the TTISS, and the surveillance system will gradually be deployed in Canadian hospitals over the next two years.

TTISS has its limitations in the capacity to capture transmission of viral infections because of the current inability to link with public health data. Such a link is necessary as these infections are often not recognized until weeks or months later when the patient is no longer in hospital. Treating physicians in the community will then notify public health authorities of these cases but only for those infections that are reportable. A pilot project is being planned to look at how this could be done.

Finally, TTISS should expand in the future to include surveillance of major errors in transfusion medicine. There is, currently, an initiative to develop and pilot a system for error surveillance that would eventually be incorporated into TTISS so that the national surveillance system would be more comprehensive.

Appendix 1: Canadian Transfusion Adverse Event Reporting Form

Canadian Transfusion Adverse Event Reporting Form

☐ **Incident** (complete at least Sections 1, 3 & 6 before and after all sections during/after)
☐ **Adverse Reaction** (Complete all Sections)
☐ **Incident & Adverse Reaction** (Complete all Sections)

Facility Identification	
Name of Facility	Phone Number
Address of Facility	City
Province	Postal Code
Hospital Code	

1. Recipient Identification

Last Name	First Name	
Health Card Number	Hospital Card Number	
Address Street		Apt.
City	Province	Postal Code
Home Telephone ( )	Work Telephone ( )	

Date of Birth (Year / Month / Day) Sex M☐ F☐

2. Clinical History

Preg. miscarriages ☐ Yes <3 mo. ☐ Yes >3 mo. ☐ No ☐ Unknown
Transfusions ☐ Yes <3 mo. ☐ Yes >3 mo. ☐ No ☐ Unknown
Immune-Compromised ☐ Yes ☐ No ☐ Unknown
Describe: _____
Principal diagnosis _____ Blood Group: ABO ____ Rh ____ Other _____

3. Incident/Adverse Reaction (Type)

Time and place event occured (Year / Month / Day / Time (hr. min.)) Place Date Reported (Year / Month / Day)

3a. Incident Information

☐ Patient idenfiication incident ☐ Product related incident ☐ Other incident ☐ Product transfused
Specify: _____ Specify: _____ Specify: _____

3b. Use of equipment and premedication

Filter ☐ Used ☐ Defective
Pump ☐ Used ☐ Defective
Pressure device ☐ Used ☐ Defective
Blood warmer ☐ Used ☐ Defective
Reinfusion device ☐ Used ☐ Defective
Other, describe:
Premedication ☐ Yes ☐ No
If yes, specify: _____

3c. Report of possible transfusion related infection

☐ Viral: specify _____ ☐ Bacterial: specify _____ ☐ Other: specify _____

4. Clinical Signs and Laboratory Results

☐ Fever T° before: ____ T° after: ____
☐ Hypotension BP before: ____ BP after: ____
☐ Hypertension BP before: ____ BP after: ____
☐ Oliguria ☐ Diffuse Hemorrhage
☐ Urticaria ☐ Nausea/vomiting ☐ Jaundice ☐ Tachycardia
☐ Chills/rigors ☐ Shortness of breath ☐ Shock ☐ Death
☐ Other skin rash ☐ None
☐ Pain, specify: _____
☐ Hemoglobinuria
☐ Other _____
Abnormal laboratory results: _____ Transfused under anesthesia: ☐ General ☐ Local ☐ None
Date specimen taken: _____

Bacterial Infection:
Blood Culture Recipient Date & Time Taken (Year / Month / Day / Time (hr. min.)) ☐ Number ☐ Neg. ☐ Pos. Organisms Identified
Blood Culture of Product Date & Time Taken (Year / Month / Day / Time (hr. min.)) ☐ Number ☐ Neg. ☐ Pos. If positive, Lot Number

5. Suspect Products

Transfused Blood Product		Group of Unit		Blood Centre			Amount Administered				Transfusion			
Product Code/Name	Hospital Modification	ABO	Rh	Code	Unit No. or Lot No.	Expiry Date	Volume ml	Fraction 1/4	1/2	3/4	Started Date	Hour	Finished Date	Hour

Comment _____

6. Measures Taken

☐ None ☐ Antihistamines ☐ Antibiotics
☐ Transfusion stopped ☐ Steroids ☐ Antipyretics
☐ Supplementary 02 ☐ Vasopressors ☐ Analgesics
☐ ICU required ☐ Diuretics ☐ Product culture
☐ Blood culture
☐ Other, specity: _____

Name (print) ☐ Physician ☐ Transfusion Safety Officer ☐ Technologist ☐ Other, specify: _____

Signature (Area code / Telephone number / Extension) (Year / Month / Day)

7. Results of Investigation and Conclusion

Allergic Reaction: ☐ Minor ☐ Anaphylactic/anaphylactoid Signs & Symptoms _____
Febrile Non-Hemolytic ☐

Incompatibility: ☐ Pre-existing incompatibility ☐ ABO Specify:_____ ☐ Other, specify: _____
☐ New Alloantibodies ☐ ABO Specify:_____ ☐ Other, specify:_____

Hemolytic Reaction: ☐ Acute ☐ Delayed

Viral Infection	☐ Specify _____	Donor:	☐ Infected	☐ Uninfected	☐ Unknown
Bacterial Infection	☐ Specify _____	Donor:	☐ Infected	☐ Uninfected	☐ Unknown
Other Infection	☐ Specify _____	Donor:	☐ Infected	☐ Uninfected	☐ Unknown

☐ TA-GVHD ☐ TRALI ☐ Hemochromatosis ☐ Circulatory Overload ☐ Post Transfusion Purpura ☐ Unknown ☐ Other, specify: _____

Severity:	☐ Death	☐ Life-threatening	☐ Long-term Sequelae	☐ Minor or No Sequelae	☐ Not Determined	
Relationship to Transfusion:	☐ Definite	☐ Probable	☐ Possible	☐ Doubtful	☐ Ruled Out	☐ Not Determined
Hospital Procedure Involved:	Describe:			Actions:		
Equipment/Supplies:	Describe: (include lot/model numbers)			Actions:		
Medical Follow-up:	Treatment or Preventative Measures			Actions:		
Supplier Notified:	☐ Yes	☐ No				
Status of Investigation:	☐ Investigation in Progress	☐ Investigation Concluded	☐ Investigation Cannot Be Conducted	☐ Reason:		

8. Comments

Reporting Physician (print) Signature

or Designate

Area code Telephone number Extension Date Year Month Day Time (hr. min.)

Version 1, May 28, 2001

Appendix 2: Minimum Data Elements for Reporting of Transfusion Related Adverse Events to Health Canada

Minimum Data Elements for Reporting of Transfusion Related Adverse Events to Blood Safety Surveillance and Health Care Acquired Infections Division of Health Canada[2]

Section 1: Recipient Identification

Age (year and month of birth)
Sex (male and female)
Case number (linked to provincial number for follow-up)

Section 3: Time and Place of Incident/Adverse Reaction

Date and time of reaction
Use of equipment (pumps, blood warmer, etc)

Section 4: Clinical Signs and Laboratory Results

Fever (temperature before and after), Hypotension/Hypertension (BP before and after), Oliguria, Diffuse Hemorrhage, Urticaria, Nausea/Vomiting, Jaundice, Tachycardia, Chills/Rigors, Shortness of Breath, Shock, Death, Other skin rash, Pain, Hemoglobinuria, Other

Bacterial Infection:

Blood Culture Recipient: Negative/Positive, Organism Identified
Blood Culture of Product: Negative/Positive, If positive, Lot #, Organism Identified

Section 5: Suspect Products

Transfused product code or name
Hospital modification code
Autologous unit
Expiry date of product
Date and time of transfusion

2 Version 2, April 23, 2003

Section 7: Results of Investigation & Conclusion[3]

Severe Allergic Reactions, e.g., Anaphylactic/Anaphylactoid – Signs and Symptoms
ABO Incompatibility
Acute Haemolytic Reactions
Viral Infections (type)
Bacterial Infections
Other Infections
Transfusion Related Graft-Versus-Host Disease (TR-GVHD)
TRALI
Post Transfusion Purpura
Unknown[4]
Others (specify)[3]
Severity : (Death/Life-threatening/Long-term sequelae/Minor or no sequelae/Not determined)
Relationship to Transfusion: (definite, probable, possible and not determined)

3 All events listed in Section 7, with the exception of Unknown and Others, will be reported to the National level regardless of the severity of the outcome.

4 All Unknown and Other events will only be reported to the National level for Death, Life-threatening and Long-term sequelae (severe).

Appendix 3: Definitions

Adverse Event: An undesirable and unintended occurrence during or after the administration of blood, blood components, or plasma derivatives whether or not considered to be related to the administration of blood, blood components, or plasma derivatives.

Note:The following are considered to be adverse events:

1. **Incident:** An accident or error that could lead to an adverse outcome affecting:

   a) the safety, efficacy or quality of blood, blood components, or plasma derivatives; or

   b) the safety of recipients.

   Accident: An unexpected or unplanned event, not attributable to a deviation from standard operating procedures or applicable laws or regulations that could adversely affect:

   a) the safety, efficacy or quality of blood, blood components, or plasma derivatives; or

   b) the safety of recipients.

   Error: An unexpected, unplanned deviation from standard operating procedures or applicable laws and regulations, usually attributable to a human or system problem, that could adversely affect:

   a) the safety, efficacy or quality of blood, blood components or plasma derivatives; or

   b) the safety of recipients.

2. **Adverse Reaction:** An undesirable and unintended response to the administration of blood, blood components, or plasma derivatives that is considered to be definitely, probably or possibly related to the administration of blood, blood component, or plasma derivatives.

3. **Serious Adverse Event:** An adverse event which:

   - requires in-patient hospitalization or prolongation of hospitalization directly attributable to the event,
   - results in persistent or significant disability or incapacity,
   - necessitates medical or surgical intervention to preclude permanent damage or impairment of a body function,
   - is life-threatening, or
   - results in death.

4. **Unexpected Adverse Event:** An adverse event that is not identified in nature, severity or frequency among the currently known adverse effects associated with the administration of blood, blood components, or plasma derivatives.

Relationship to transfusion

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.

Bacterial contamination is considered "definite" if it meets ALL the following criteria:

1. The recipient must demonstrate any of the following signs and symptoms of sepsis during or within 4 hours of the transfusion (fever, rigors, tachycardia, drop or rise in systolic blood pressure by > 30 mmHg)

2. Positive blood product culture

3. Recipient blood culture growing the same organism as that recovered from the blood product.

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.

Bacterial contamination is considered "probable" if it meets the following criteria:

1. The recipient must demonstrate any of the following signs and symptoms of sepsis during or within 4 hours of the transfusion (fever, rigors, tachycardia, drop or rise in systolic blood pressure by > 30 mmHg)

2. Positive blood product culture.

Possible

If the clinical and/or laboratory event occurred within a time period consistent with the administration of the blood product but could be explained by a concurrent disease or by the administration of a drug or other agent.

Not determined

If it remains to be determined whether the event was related to the administration of the blood product and further information is forthcoming.

Notes

Notes