NOVA SCOTIA PROVINCIAL BLOOD COORDINATING PROGRAM

Blood and Blood Product Adverse Reactions in Nova Scotia

January 1, 2007 to December 31, 2007

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Preface

In the 1997 Report of the Commission of Inquiry on the Blood System in Canada, Justice Horace Krever emphasized the importance of surveillance and tracking of blood products/components, referring to the concept of vein to vein management of blood.

In March 1998, Health Canada convened a multidisciplinary Surveillance and Epidemiology of Transfusions (SET) Working Group, with a mandate to explore issues related to the development of a comprehensive blood surveillance system model for Canada.

In February 1999, the SET Working Group released its final report. It included a recommendation for provincial-level surveillance initiatives to work toward developing an effective national surveillance system. Health Canada began the development of a national transfusion surveillance system through the *Transfusion Transmitted Injuries Surveillance System (TTISS) Pilot Project*. The intent of this pilot project was to capture adverse reactions related to the transfusion of blood and blood components, and to serve as an early warning system as well as an education vehicle. Nova Scotia was one of four provinces selected to participate in the pilot.

During the initial participation in TTISS from 2001 to 2004, reporting within Nova Scotia represented 52 percent of transfusions occurring within the province. Continued participation with TTISS has led to the development and expansion of adverse transfusion reaction reporting to 100 percent of all transfusions occurring within the province.

In 2004, through collaborative efforts of the Nova Scotia Provincial Blood Coordinating Program, Canadian Blood Services (Halifax) and the Atlantic Regional Adverse Reporting Centre (ARARC) it was agreed that the Canadian Transfusion Adverse Event Reporting form (CTAER) would be used for reporting all reactions. Discussions with and agreement from CBS Halifax and ARARC led to the development of a provincial standard for reporting of *all* adverse transfusion reactions within Nova Scotia. This provincial standard incorporated recommendations from the Nova Scotia Joint CJD Review[1] regarding standardization of language and access to a centralized phone number with coverage twenty-four hours a day/seven days a week for response on emergent issues. The provincial standard was implemented January 1, 2005.

The TTISS is a voluntary surveillance system that has been implemented to support 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 reactions related to transfusion of blood components and products.

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I Introduction

Nova Scotia has nine District Health Authorities (DHAs), and the IWK Health Centre, consisting of 41 sites encompassing adult, pediatric and tertiary care facilities as well as community-based hospitals and day clinics. TTISS was implemented in Nova Scotia in 2001 with initial pilot sites capturing 52 percent of transfusions occurring within the province. An established process was in place with the initial sites for reporting of adverse reactions. The Transfusion Practice Coordinator with the NSPBCP functioned as the provincial Transfusion Safety Officer receiving, reviewing, obtaining missing information and entering all cases reported.

Development of a provincial strategy/approach was identified as vital to ensure complete and comprehensive reporting. The established process required amending and expansion to include the remaining 48 percent of transfusions which were not being captured. Canadian Blood Services (CBS) and the Atlantic Regional Adverse Reporting Centre (ARARC) were also identified as crucial to the success of the province wide implementation of the Canadian Transfusion Adverse Event Reporting (CTAER) form (Appendix 1). Discussions with and agreement from both parties led to the development of a provincial standard for reporting of *all* adverse transfusion reactions within Nova Scotia (Figure 1).

A process for the addition of the remaining sites was developed in conjunction with the laboratory manager, medical director, and clinical nursing educators of each site. The remaining sites identified a key contact person from within the laboratory to maintain document control of the CTAER forms and completion follow up.

The provincial implementation of the TTISS at the remaining sites involved a one day workshop for key contact laboratory technologists and nurses as well as a telehealth session for physicians/ pathologists responsible for classification of adverse transfusion reactions. The culmination of all the preparation allowed for the provincial algorithm for reporting to be implemented January 1, 2005.

II Methodology

2.1 Transfusion Reaction Reporting

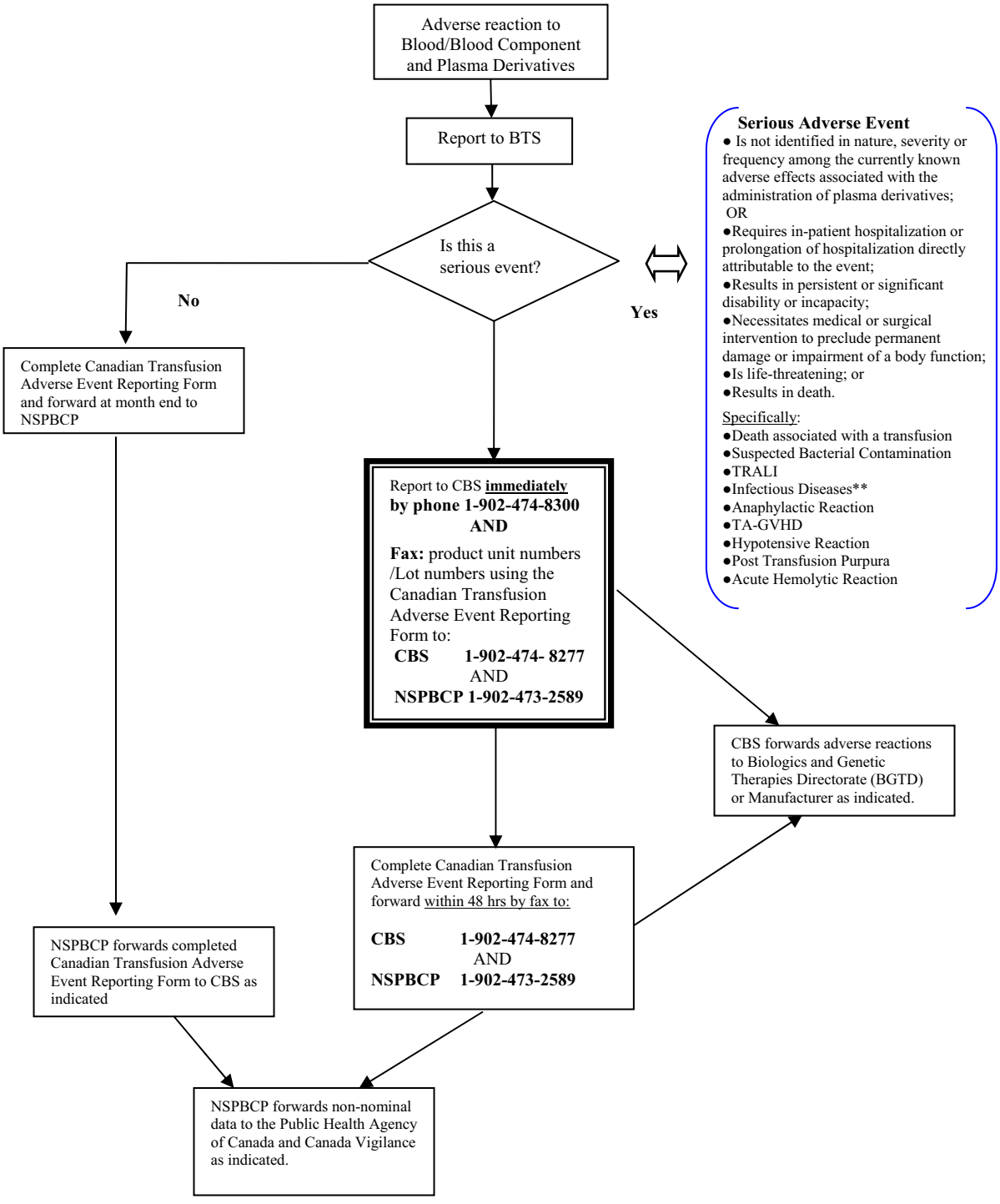
Upon receipt of an adverse transfusion reaction report, the designated blood transfusion technologist conducts a preliminary review and ensures the CTAER form is completed as per the algorithm in Figure 1 and determines if the case has all the requirements for reporting. *For serious reactions*, an investigation is initiated and pertinent information is faxed immediately to CBS Halifax and the NSPBCP. At 48 hours the CTAER form is faxed again including updated information regarding the adverse reaction. When the investigation is completed and the case closed, it is sent to the NSPBCP for inclusion into the TTISS database.

All non-serious cases are sent to the NSPBCP at month end and reviewed by the NSPBCP for validation and completeness of reporting prior to entry into the database. It is important to note that any cases involving plasma derivatives are faxed to Canada Hemovigilance, formerly the ARARC, as outlined in the algorithm in Figure 1.

2.2 Analyses

Data received from the facilities were compiled into the TTISS MS Access database. Descriptive analyses of the data reported were conducted, including number and proportion of each category of adverse reactions, their distribution by severity of outcome and the relationship to transfusion. Suspected blood products implicated in these reactions were also summarized. For the purpose of this analysis, only adverse transfusion reactions occurring during the period January 1, 2007 to December 31, 2007 and received by the NSPBCP prior to September 1, 2008, have been included.

Provincial Standard for Hospitals to Report Adverse Reactions to Blood/ Blood Components and Plasma Derivatives in Nova Scotia



** At this time, reporting of post-transfusion Infectious Diseases: Variant Creutzfeldt Jakob disease, Gonorrhea, Hepatitis B, Hepatitis C, Hepatitis D, Human Granulocytic Ehrlichiosis, Human Immunodeficiency virus (HIV), Lyme disease, Malaria, Syphilis, and West Nile Virus (WNV) shall be done through existing notifiable diseases/ lookback/traceback procedures. All others such as: Babesiosis, Chagas', Cytomegalovirus (CMV), Epstein-Barr, Human T-cell Lymphotropic Virus (HTLV), Leishmaniasis are reportable to NSPBCP. In the event that notifiable diseases are reported to the NSPBCP, we will determine if there is/ has been an appropriate connection with Public Health.

III Results

3.1 Overall Results

All sites administering transfusions within Nova Scotia report all adverse reactions to the NSPBCP and all serious adverse reactions to CBS and the NSPBCP. During 2007, 49,019 units of blood components were transfused with red cells comprising approximately 61% of transfusions. Table 1 outlines the blood components transfused in Nova Scotia within six categories. The NSPBCP obtains the number of units transfused from the monthly unit disposition reports submitted by hospital sites.

Table 1: Blood components transfused within Nova Scotia in 2007

Blood Components	Number of units transfused	
	N	Percent per year
Red Blood Cells	29,797	60.79
Fresh Frozen Plasma	2,939*	6.00
Apheresed Fresh Frozen Plasma	3,243	6.62
Platelets	9,602	19.59
Apheresed Platelets	1,152	2.35
Cryoprecipitate	2,274	4.64
Other (granulocytes, whole blood, etc…)	12	0.02
Total	**49,019**	**100**

*Includes cryosupernatant plasma.

In 2007, 562 suspected adverse transfusion reactions were reported to the NSPBCP. Upon investigation the relationship to transfusion for 50 of these were concluded to be either 'ruled out' (7) or 'doubtful' (43). The remaining 512 were deemed to be definitely/possibly/probably) related to transfusion (507) or the relationship was classified as "not determined" (5). 500 were associated with blood components and 12 with plasma derivatives.

3.2 Classification of Adverse Reaction

Classifications of the adverse reactions are based on the definitions in the Version 3.0 TTISS User's Manual and denote the final classification for entry into the TTISS database. Table 2 shows the classification of the 500 adverse reactions related to blood components and the 12 adverse reactions related to plasma derivatives. The largest proportions of adverse reactions to blood components were febrile non-hemolytic (36 %), delayed serological transfusion reaction (34.8%) and minor allergic (22.4%): a combined total of 93.2%. Minor allergic (58.3%) and Hypotensive/Other (41.7%) are the classifications of adverse reactions associated with plasma derivatives.

Table 2: Classification of Adverse Reactions

Classification	Blood Components	%	Plasma Derivatives	%
Febrile Non Hemolytic Transfusion Reaction	180	36.0	0	0.0
Delayed Serological Transfusion Reaction	174	34.8	0	0.0
Minor Allergic Reaction	112	22.4	7	58.3
Circulatory Overload	13	2.6	0	0.0
Hypotensive Transfusion Reaction and Others	10	2.0	5	41.7
Severe/Anaphylactic/Anaphylactoid	6	1.2	0	0.0
Acute and Delayed Hemolytic/Unknown	5	1.0	0	0.0
Total	**500**	**100.0**	**12**	**100.0**

Further examination of the table shows there were 13 cases of circulatory overload reported. The majority involved elderly patients who received red blood cells or plasma. Half of the cases were grade 1 (minor), while the other half were graded 2, 3, or 4 severity (see section 3.4 of this report for severity descriptions).

Seven hypotensive cases involved a systolic drop in blood pressure greater than 30mm/Hg. This is a less common type of reaction and is not well documented in the literature.

The six anaphylactic/anaphylactoid cases involved patients experiencing urticaria over greater than ¼ of their body along with other symptoms such as shortness of breath, tachycardia, and nausea and vomiting.

The "unknown" cases related to blood components were a grade 1 severity with minor or no sequelae outcome. These cases were classified unknown since they did not fit the current classification definitions. Recipient signs and symptoms either did not match any classification, fit the criteria of two different classifications, or did not have an essential symptom criteria present.

3.3 Serious Adverse reactions

All serious adverse events were reported to CBS and NSPBCP according to the Provincial Standard for Hospitals to Report Adverse Reactions. (Figure1). After further investigation, two cases received a non-severe classification but the appropriate processes were initiated. The remaining cases fit the criteria of a serious adverse event using the algorithm (Figure 1) and the TTISS definitions[2] of:

- The recipient requires in-patient hospitalization or prolongation of hospitalization directly attributable to the event (level 2 severity)
- The adverse event results in persistent or significant disability or incapacity (level 2 severity)
- The adverse event necessitates medical or surgical intervention to preclude permanent damage or impairment of a body function (level 2 severity)
- Life-threatening (level 3 severity)
- Death (level 4 severity)

A possible TRALI case was subsequently concluded as circulatory overload upon completion of donor and patient testing and case review. This is congruent with recent literature stating 80% of initial TRALI reports are subsequently diagnosed as transfusion associated circulatory overload (TACO) [3].

These cases highlight the experience to date using the provincial algorithm for reporting of all transfusion reactions in Nova Scotia. The algorithm has proven to be timely in aiding the quarantine of companion products. As well, the use of a single phone number reporting mechanism available 24/7 has shown to be practical for the user.

3.4 Severity of Outcome

Severity is based on a grading system and is based on the measures taken during the adverse reaction.

- Grade 1 (Non-severe) is described as the patient may require medical intervention but the lack of such intervention would not result in permanent damage or body function impairment.
- Grade 2 (Severe) is defined as patient requiring hospitalization, prolongation of hospitalization, or the adverse event results in persistent or significant disability or permanent damage or body function impairment.
- Grade 3 (Life-threatening) is defined as the patient requiring a major intervention such as vasopressors, intubation or transfer to ICU.
- Grade 4 (Death) refers to a patient's death which was suspected to be the consequence of the transfusion.

Figure 2 shows that 97% majority of the 500 adverse reactions to blood components received were Grade 1, with the remaining 3% considered Grade 2 (Severe), Grade 3 (Life Threatening) or Grade 4 (Death).

Figure 2: Adverse Reactions by Severity: Blood Component

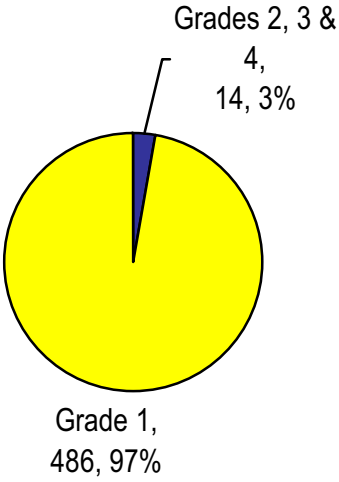
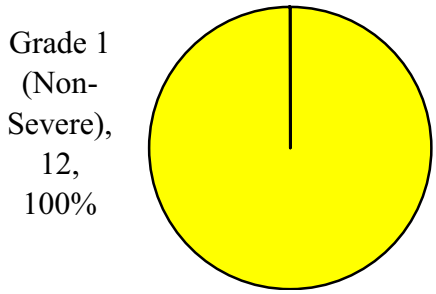


Figure 3 shows that all the adverse reactions related to plasma derivatives in Nova Scotia were grade 1 (non-severe).

Figure 3: Adverse reactions by Severity: Plasma Derivatives



3.5 Incidence of Adverse Transfusion Reactions by Blood Components

The incidence of each type of adverse reaction for 2007 is presented in Table 4. The table highlights the incidence in relation to blood components and shows that, of the adverse transfusion reactions reported, 372 were in relation to red blood cells, 63 involved platelets (apheresis or whole blood derived) and 65 reactions involved plasma.

Table 3 also indicates the three most commonly reported adverse reactions in Nova Scotia (for blood components) are febrile non hemolytic reaction (FNHR) with an incidence of 1:272, delayed serological transfusion reaction (1:282) and minor allergic with an incidence of 1 in 438. Literature indicates that FNHR's are reported most often with RBC's and platelets and rarely with plasma[3]. While Nova Scotia's data supports this literature, incidence rates remain lower than expected for both FNHR and minor allergic reactions. Some studies suggest that FNHR and minor allergic reactions have a higher incidence of 1 in 45-227 and 1 in 250 respectively[3]. As the NSPBCP database becomes

more robust over time it is anticipated that the incidence of both febrile non-hemolytic and minor allergic will be even more reflective of this literature.

It is important to note that some adverse reaction classifications are not reported in table 4 as there were no confirmed adverse reactions of: an ABO incompatible transfusion, TRALI, possible TRALI, bacterial contamination or post transfusion purpura in Nova Scotia in 2007.

Table 3: Incidence of adverse transfusion reactions by Blood Component

ATEs	All products*		Literature Incidence rates*
	49019		
	N	Ratio	
	500	49019	
Febrile Non Hemolytic Transfusion Reaction	180	1: 272	RBC 1:227 to 1:2500 PLT 1:45 to 1:1666
Minor Allergic Reaction	112	1: 438	1:250
Severe / Anaphylactic / Anaphylactoid	6	1: 8170	RBC 1:23,300 PLT Pools 1:3,889
Delayed Serological Transfusion Reaction	174	1: 282	N/A
Transfusion Associated Circulatory Overload	13	1: 3771	1:356 to 1:4075
Hypotensive Transfusion Reaction and Other	10	1: 4902	1:11,000
Acute and Delayed Hemolytic and Unknown	5	1: 9804	N/A
TOTAL	500	1: 98	

* Popovsky, M.A. (2007). Transfusion Reactions (3rd edition). Maryland: AABB Press

3.6 Implicated Plasma Derivatives

The total number of adverse reactions reported in 2007 was 512; with 12 cases being associated with plasma derivatives. Due to the absence of denominator data for plasma derivatives, incidence rates on these reactions are unavailable. The adverse reactions related to these products were Minor Allergic Reaction, Hypotensive Transfusion Reaction, and Other. Plasma derivatives implicated were IVIG (83.33%) and albumin (16.67%)

IV Discussion

Nova Scotia has been participating in the National TTISS since its inception in 2001. Currently, the NSPBCP database houses over 2600 cases and it is anticipated the numbers will rise as more health care professionals recognize and report adverse transfusion reactions. Although we have seen steady increases in cases reported to NSPBCP, 2007 showed a slight decrease in cases reported. There were 551 cases reported in 2007, 40 less cases than was reported in 2006. This may be indicative of a plateau often experienced by other hemovigilance systems[7] or it may indicate a need to further increase awareness of monitoring and reporting adverse transfusion reactions.

Educational initiatives by the NSPBCP during September-December 2007 included site visits to each DHA and IWK and lectures to Licensed Practical Nursing students and Baccalaureate nursing students in Nova Scotia. The presentations main focus was to increase awareness about monitoring, recognizing, managing and reporting adverse transfusion reactions. It is expected that the results of this education will be seen in the 2008-2009 data as these health care workers continue, or begin, transfusing blood components and blood products more diligently.

V Conclusions

We have been successful achieving 100 percent compliance from all facilities in Nova Scotia, in reporting adverse reactions in accordance with the Provincial Algorithm. We have seen the majority of reactions reported related to non-hemolytic febrile, and minor allergic. Serious adverse reactions are being reported immediately to CBS and to the NSPBCP as indicated in the algorithm.

Although reporting of transfusion associated circulatory overload reactions (TACO) is increasing in Nova Scotia, it is likely that this reaction, along with bacterial contamination and TRALI, continues to be underreported. Upon review and comparison of the current literature with the Nova Scotia data, the results are in keeping with what has been documented in hemovigilance systems in other countries.

In closing, the evolution of the surveillance system for Nova Scotia is timely for both compliance with the Canadian Standards Association Z902-04 blood and blood components standard, and enhancing patient safety. The NSPBCP in partnership with key stakeholders has established a solid framework for surveillance within Nova Scotia. The NSPBCP looks forward to sustaining the current success of the surveillance system and collaborating with health care professionals to continue to recognize and report adverse transfusion reactions.

VI References

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