Transfusion Reaction Education for BC Pathologists – Module 2 October 20, 2011 – Dr. Kate Chipperfield

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Speaker

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Disclosure:

Dr. Chipperfield :

- Is the principal investigator of a randomized controlled trial using a novel instrument produced by LightIntegra Technology. She has no financial interest in the company.
- Received an honorarium from CSL Behring for attending an advisory board meeting.

2011-10-20

Contents of Module 2

- · Goals and Objectives of the module
- Serious Reactions
 - Transfusion Associated Circulatory Overload (TACO)
 - Severe Allergic reactions or Anaphylaxis
 - Transfusion Related Acute Lung Injury (TRALI)
 - Bacterial Contamination
 - Acute Hemolytic Transfusion Reaction (AHTR)
 - Post Transfusion Purpura (PTP)
 - Transfusion-associated Graft vs Host Disease (TA-GvHD)
- Note:
 - Immunoglobulin- related serious reactions:
 - to be discussed in Module 4
 Transfusion Associated Dyspnea (TAD)

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Key Points - Serious Reactions

- · require hospitalization or prolongation of hospital stay
- · directly attributable to the transfusion.
- signs and symptoms may overlap with those of low severity, common reactions.
- All transfusion reactions should be reported to the Transfusion Medicine Service (TMS/laboratory).
- It may be necessary to treat the recipient and/or provide additional components/products before an investigation is completed.

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· Clinical management is required for all recipients.





	Signs & Sy serious tra	mptoms of a nsfusion reaction:
	System	Signs and Symptoms
	cardiovascular	 hypertension hypotension tachycardia shock
	inflammatory	 fever
20	11-10-20	7



I	Signs & Symptoms of a serious transfusion reaction:				
	System	Signs and Symptoms			
	respiratory	 dizziness dyspnea (shortness of breath) wheezing hypoxemia Sp02< 90% on room air Pa02 < 60 mm Hg on room air Pa02 < 60 mm Hg 			
	gastrointestinal/ renal	nausea/vomiting ·Other clinical evidence of hypoxemia red or brown urine oliguria			
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ĺ	Signs & S serious tra	ymptoms of a ansfusion reaction:		
	System	Signs and Symptoms		
	pain	 headache joint/muscle pain, back pain, chest pain heat/pain at IV site 		
	cutaneous	 flushing skin rash jaundice diffuse hemorrhage 		
	other	 restlessness/anxiety 		
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Overlap of Signs & Symptoms Serious or Common Low-severity Acute Transfusion Reaction				
Signs and Symptoms	Differential Diagnosis			
Hives / itching	Allergic – low or high severity Anaphylaxis			
Fever	FNHTR, AHTR, TRALI, sepsis (bacterial contamination)			
Hypotension	Anaphylaxis, AHTR, septic shock, less likely TRALI			
Sense of doom, flank pain, hemoglobinuria	AHTR			
Shortness of breath	TACO, TRALI, TAD allergic/anaphylactic - bronchospasm			
11-10-20	10			







Case Study 1- SOB							
 75 year old male 1 unit of RBC transfused over 2 hours Report of shortness of breath, chest pain, and anxiety within 30 minutes of completion. Afebrile. 							
	BP Pulse T (C)						
	Baseline	130/85	85	36.2			
2011-10-2	13						

Transf	usion
Assoc	iated
Circul	atory
Overl	load
(TAC	CO)
2011-10-20	14

			Ye	ar		
Reaction Type	2008 (N=911)		2009 (N=789)		2010 (N=795)	
	Total	%	Total	%	Total	%
TACO	23	2.5%	7	0.9%	24	3.0%
Severe Anaphylactic / Anaphylactoid	6	0.7%	1	0.1%	4	0.5%
Acute Hemolytic	2	0.2%	3	0.4%	5	0.6%
Possible TRALI	2	0.2%	2	0.3%	0	0
TRALI	0	0	0	0	0	0



TACO Symp	TACO Symptoms and Signs				
Symptoms include:	Signs include:				
 non-productive cough dyspnea 	 tachypnea/orthopnea pulmonary edema raised jugular venous pressure hypertension cyanosis and tachycardia 				
2011-10-20	16				



יו	ГАСО	
C	Cause	volume overload rapid infusion rate complicating pre-existing patient condition
C	Onset	 within 6 hours of completion of transfusion relates to patient's condition, volume administered and administration rate
F	requency	 1/700 transfusion recipients 1/100 "at-risk" patients (risk of cardiac overload, history of previous transfusion reactions, and/or unstable condition)
R re	Results of eaction	 acute pulmonary edema cardiac arrhythmia death
2011-10-	-20	17

TACO Prevention patients:	is key, particularly for at risk	
Vulnerable patients include:	 risk of cardiac overload (CHF, COPD, ARF, seve anemia), history of previous TACO, and/or unstable condition pediatric 	re
2011-10-20		18

TACO Recommendations:		
"At-risk" patient	 Give each unit of red cells slowly (50 mL/hour) maximum rate is 4 hours from removal from temperature controlled storage units may need to be split The patient may require additional diuretic therapy (for example I.V. furosemide). Oxygen may be required. Closely monitor the patient for signs and symptoms of TACO. 	
Differential diagnosis	TRALI, TAD	
2011-10-20	19	

Case Study – Further Investigation

- · History of cardiac disease
- Patient received platelets 1 hour before the red cells (volume about 250 mL)
- Patient had angina prior to the red cell transfusion and was self-medicating with nitroglycerin.
- Symptoms resolved 1 hour after reaction noted.

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- Lab investigation is normal/negative.
- Clerical check OK.

Case Study –	Conclusion
	Result
Pathologist Conclusion	Transfusion associated circulatory overload
Relationship to transfusion	Definite / Probable Possible / Doubtful
Severity	Non-severe (grade 1)
Outcome	Minor (no sequelae)
2011-10-20	21









Severe Allergic reaction or Anaphylaxis- Symptoms and Signs			
Symptoms include:	Signs include:		
 skin itching dyspnea wheezing chest or abdominal pain nausea 	 urticaria/pruritus bronchospasm hypotension vomiting periorbital and laryngeal edema erythema 		
2011-10-20	24		



Severe Allergic reaction or Anaphylaxis	
Cause	 Anaphylaxis occurs when IgE antibodies (usually patient's) combine with the corresponding (donor) antigen.
	 Some patients with severe IgA deficiency can develop antibodies to IgA and severe anaphylaxis may occur if transfusion exposes them to IgA.
Onset	within the first hour
Frequency	1/1,600 platelet pools1/23,000 red cell units
Results of reaction	 potentially fatal (3% of cases) disseminated urticaria and severe bronchospasm may result from reaction
2011-10-20	25



	Severe Suggeste	Allergic reaction or Anaphylaxis ed treatment and recommendations:	
	For all patients	Stop the transfusion. Do NOT restart. Return the unit to the TMS for further investigation. Send EDTA samples.	
		 Provide medical treatment as indicated by symptoms and severity of the reaction. – Laryngeal /Lower Respiratory Tract symptoms may require epinephrine. – Other symptoms may require IV diphenhydramine 25 - 50 mg. 	
	Differential diagnosis	 reactions to other allergens such as tape, latex, or drug coincidental clinical conditions TRALI or TACO with dyspnea 	
	2011-10-20	26	

I	Severe Suggeste	Allergic reaction or Anaphylaxis d treatment and recommendations:
	Future	Consider IgA deficiency:
•	transfusion	 send pretransfusion sample for quantification of immunoglobulins and Anti-IgA levels assess family history Note: CBS does assays for low level IgA and IgA antibodies.
	lgA	Requires:
	deficient patient	washed RBC
		IgA deficient plasma-containing components
		Note: IgA deficient plasma protein products are not available.
201	1-10-20	27



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Severe All Suggested tre	ergic reaction or Anaphylaxis eatment and recommendations: • Requires any plasma OR cellular product to be from an IgA deficient donor.
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Case Study 2 – Further Investigation

- No bronchospasm reported
- Rapid response to combination therapy
 (antihistamine, epinephrine and steroid IV)
- Multiple concurrent exposures ?alternate allergens

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- No prior transfusion history
- Testing for IgA deficiency negative

Case Study 2 – Conclusion		
	Result	
Pathologist Conclusion	Allergic reaction	
Relationship to	Definite / Probable	
transfusion	Possible / Doubtful	
Severity	Severe (grade 2)	
Outcome	Minor (no sequelae)	
2011-10-20	30	







TRALI – Symptoms and Signs Rapid Onset (within 6 hours of transfusion) of:			
Symptoms include:	Signs include:		
breathlessnesscoughing	 bilateral pulmonary infiltrates and acute dyspnea with hypoxemia tachypnea tachycardia hypotension 		
2011-10-20	– Tever 33		







TRALI – Causes (common theories)		
Antibody hypothesis	 Anti HLA (I or II) or anti-human neutrophil antigen (HNA) in donor plasma, reacts with corresponding antigen present on recipient leukocytes. (In 10% of cases, the antibody is of recipient origin.) 	
Neutrophil priming hypothesis	 Lipid inflammatory mediators in the product prime and activate recipient neutrophils to cause capillary leak/injury. Patient's clinical condition may predispose. 	
Speculative	 direct pulmonary endothelial damage immune complex formation cytokine and or complement activation 	
2011-10-20	36	



I	TRALI		
	Onset	within 6 hours of transfusion start (often within 2 hours)	
	Frequency	 1/1,200 to 1/5,000 (plasma-containing transfusion TRALI is associated with components with a higher plasma content, such as frozen plasma. Rates may decrease as CBS changed to predominantly male donor plasma for frozen plasma 	s)
	Results of reaction	72% of reported cases require mechanical ventilation 5 to 10% of cases are fatal	
201	1-10-20		37



TRALI Suggeste	d treatment and recommendations:
For all	Stop the transfusion. Do NOT restart.
patients	Return the unit to the TMS for further investigation.
	Send EDTA samples.
Contact	The pathologist should contact CBS as soon as the lab is notified of a possible TRALI case.
CBS TRALI	As soon as possible:
investigation	Complete the CBS TRALI form.
	 Collect the TRALI investigation samples.
	 Send form and samples to CBS.
Respiratory	 High concentration of oxygen may be required.
distress	 Mechanical ventilation may be required.
treatment	 IV fluids and vasopressors may be indicated. Diuretics and steroids are not believed to be useful.
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Case Study 3 - Further Investigation

- No prior hypoxia, no cardiac history
- Bilateral crackles on exam, no fever
- Preexisting ascites, no jugular venous distension, no edema
- CXR bilateral pulmonary infiltrates
- Admitted to ICU; maintained on high flow O2, did not require intubation, improvement within 24 hours
- TMS : clerical checks okay, negative investigation
 Reported immediately to CBS: female donor (AB), companion unit quarantined, CBS investigation pending

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Case Study 3 – Conclusion		
	Result	
Pathologist Conclusion	TRALI	
Relationship to	Definite / Probable /	
transfusion	Possible / Doubtful	
Severity	Life-threatening (Grade 3)	
Outcome	Minor / No sequelae	
2011-10-20	40	

Case Study 4 - Fever

- 55 year old male receiving platelets
- After ~30 mL complains of severe chills
- RN observes rigors; vitals include:

	BP	Pulse	T (C)
Baseline	110/82	85	36.7
Reaction	85/50	105	39.5
11-10-20			41





Bacterial Contamination Symptoms and Signs			
Symptoms include:	Signs include:		
 chills shortness of breath nausea 	 rigors fever hypotension tachycardia vomiting collapse 		
2011-10-20	43		

I	Bacteria	al Contamination		
J	Cause	Infusion of a unit contaminated with bacteria		
	Onset	Often within 15 minutes after transfusion start Always within 24 hours		
	Frequency	1/1,000 to 1/3,000 (platelet concentrate) 1/50,000 (RBC unit)		
	Results of reaction	Shock Acute Renal Failure DIC		
		Death frequency: Platelet pools: 1/40,000 RBC unit: 1/500,000		
201	1-10-20		44	

Suspect bacterial contamination of the product if the
patient shows these signs or symptoms:

- Fever defined as an oral temperature \ge 38°C **AND** \ge 1°C rise in temperature above the pre-transfusion baseline **PLUS** any of the following signs and symptoms: 1.
 - rigors (involuntary shaking)
 - _
 - _ _
 - rigors (involuntary shaking) nausea or vomiting dyspnea (shortness of breath) hypotension (systolic BP drop of ≥ 30mmHg below the pre-transfusion baseline) tachycardia (pulse rise > 40bpm above the pre-transfusion baseline) shock
- Fever defined as an oral temperature ≥ 39°C AND ≥ 1°C rise in oral temperature above the pre-transfusion baseline with no other signs and symptoms OR OR 2.
- Fever not responding to antipyretics **OR** 3.
- 4. A high suspicion of sepsis even in the absence of fever

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ĺ	Bacterial Contamination Suggested treatment and recommendations				
	For all patients	Stop the transfusion. Do NOT restart.			
		Return the unit to the TMS for further investigation. Send EDTA samples per facility instructions.			
	For all patients with suspected transfusion transmitted bacterial contamination	Monitor the patient closely Aerobic and anaerobic blood cultures should be set up on the patient and the component/product. Patient may need aggressive supportive therapy, including broad spectrum antibiotics.			
		DO NOT WAIT FOR RESULTS OF BLOOD CULTURES PRIOR TO STARTING ANTIBIOTIC THERAPY.			
201	1-10-20	46			







Case Study 4 – Conclusion		
U	Result	
Pathologist Conclusion	Bacterial contamination	
Relationship to transfusion	Definite	
Severity	Life threatening (3)	
Outcome	Major, Long term sequelae	
2011-10-20 49		

Case Study 5 – Red Urine

- 38 year old female in OR
- 6 hours into procedure, anesthesia team notes red urine in catheter bag
- Monitored vitals remain stable
- 2 units PRBC have been transfused, the most recent 2 hours ago

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What may have happened?

How can this be confirmed?



Acute Hemolytic Transfusion Reactions			
Symptoms include:	Signs include:		
 chills feeling of apprehension agitation pain at IV site flushing pain in chest, back or abdomen shortness of breath 	 fever hypotension hemoglobinuria/-emia, bleeding from puncture sites collapse vomiting 		
2011-10-20	52		



ļ	Acute Hemolytic Transfusion Reactions Onset Always within 24 hours Otten within minutes of initiation of transfusion			
	Frequency (BBC units)	Transfuse wrong blood to patient (error rate)	1/14,000	
	(1120 0(0)	Transfuse wrong blood to patient and blood is ABO INCOMPATIBLE	1/38,000	
		(reaction rate)		
		Fatal (reaction rate)	1/800,000	
	Results of reaction	 >50% of ABO incompatible trans serious morbidity, most common Acute Renal Failure Disseminated Intravascula 	ifusions result in ly: ar Coagulation (DIC)	
201	1-10-20	<10% result in Death	53	





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Ī	Acute Hem Suggested	Acute Hemolytic Transfusion Reactions Suggested treatment and recommendations:			
	For all patients	Stop the transfusion. Do NOT restart.			
		investigation.			
		Send transfusion reaction samples and form.			
If applicable, contact the Health Authority TM team					
		Monitor the patient closely.			
		Seek expert hematologist /nephrologist advice.			
	For patient with	In addition to all measures above,			
	5.0	components .			
201	1-10-20		55		









Case Study 5 – Conclusion			
		Result	
Pathologist Conclusion		Incompatible Transfusion, Unintentional, ABO	
Relationshi transfusion	p to	Definite	
Severity		Life threatening (grade 3)	
Outcome		Major, Long term sequelae	
2011-10-20 58			



TA-GvHD Symptoms and Signs			
Symptoms include:	Signs include:		
 diarrhea skin rash	 profound pancytopenia abnormal liver function bone marrow failure 		
2011-10-20	60		



ſ	TA-GvH	D	
Ĭ	Cause	Donor lymphocytes in the transfused component engraft and recognize the immunocompromised recipient as foreit	gn.
		May occur in the immunocompetent recipient following directed donation or populations with limited HLA diversity.	in
	Onset	2 to 50 days post transfusion (commonly 8 – 10 days in immunosuppressed patient)	
	Frequency	very rare	
2011-	10-20	1	61



	TA-GvHD			
	Prevention	Prevention is key. Irradiate cellular blood components for at- risk groups Refer to TMAG Guidelines for Irradiation of Products (http://www.pbco.ca)		
	Results of reaction	Almost always fatal. Mortality rate >90% within 3 weeks of onset		
20	1-10-20	62		

TA-GvHD Suggested treatment and recommendations:				
General	There is no effective treatment.			
	Prevention by use of irradiated cellular blood components is essential.			
Refer to	TMAG Guidelines for Irradiation of Products (http://www.pbco.ca)	i		
2011-10-20		63		





PTP Symptoms and Signs			
Symptoms include:	Signs include:		
bruisingbleedingchills	 low platelet count petechia hematoma fever rigors bronchospasm 		
2011-10-20	65		

РТР		
Cause	 patient's platelet-specific alloantibodies trigger an immune reaction which also destroys patients own platelets most often seen in female patients 	ı
Onset	5 to 10 days post platelet transfusion (sometimes > 3 weeks)	
Frequency	very rare	
Results of reaction	 recovery usually within 7 to 48 days to recovery can be fatal (8% mortality) 	
2011-10-20		66



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PTP Sugges	ted treatment and recommendations:
Samples to 0	CBS Collect samples for CBS <i>before</i> starting IVIG therapy.
Diagnosis	Presence of platelet allo-antibody, and corresponding lack of platelet antigen in patient.
	almost all platelet antigens have been implicated.
	most commonly: HPA-1a (PIA1)
	rarely: antibody with HLA specificity
Differential diagnosis	ITP, sepsis, DIC, drug, marrow aplasia, HIT etc
2011-10-20	67



PTP Suggeste	ed treatment and recommendation	s:
Treatment:	Consult with hematologist.	
	Usually a self-limited disease, but consider:	
	 IVIG 500 mg/Kg/day - up to 10 days or 1.0 gm/Kg/day for 2 days –may respond quickly (one dose reported) 	
	 plasmapheresis (~12 days to respond) 	
	 steroids (prednisone 2 mg/Kg/day) 	
Lit	tle or no role for platelet transfusion	
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TAD is characterized by respiratory distress within 24 hrs of transfusion which: - does not meet criteria for TRALI does not meet criteria for TACO _ does not meet criteria for an allergic reaction _ is not explained by patient's underlying _ condition 2011-10-20 70

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 Technical Resource Group (TRG)
 Nursing Resource Group (NRG)

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Date / Time	Торіс	Speaker
November 3, 2011 12:00 to 1:00pm	Signs and Symptoms of Transfusion Reactions:Common Low-severity, Delayed Transfusion Reactions, Delayed Complications	Dr. Jason Doyle MD FRCPC Consultant Pathologist, Transfusio Medicine for the Okanagan, IH
November 17, 2011 12:00 to 1:00pm	Immunoglobulin Related Reactions	Dr. Doug Morrison MD FRCPC Medical Director, Transfusion Medicine Lab, FH
December 1, 2011 12:00 to 1:00pm	Transfusion Reaction Reporting and Surveillance	Dr. Louis Wadsworth MB FRCP(C FRCPath, Clinical Professor, Department of Pathology, UBC
December 15, 2011 12:00 to 1:00pm	Transfusion Reaction Annual Data Reports and Case Studies	Dr. Kate Chipperfield MD FRCPC Regional Medical Leader, Blood Transfusion Medicine, VCH



Next Steps

Visit LearningHub - <u>LearningHub Link</u>

https://edreg.cw.bc.ca/phsaedcalendar/Home.aspx

- Note:
 - Need LearningHub Username and PasswordConfirm your email with LearningHub if not done
- Complete:
 - Participant Evaluation
 - Quiz (Closes midnight October 21, 2011)

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