

# IVIg - Guidelines and Use in Hematologic Disorders

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Canadian Blood Service

Transfusion Update May 2009

Sydney, Australia



# IVIIG - Guidelines and Use in Hematologic Disorders

- Development of Canadian guidelines
  - why
  - how
- Guidelines in selected hematologic conditions
  - compare Canadian guidelines with Australian & UK guidelines
- Adverse effects of IVIG administration
- Outcomes of guideline process in Canada



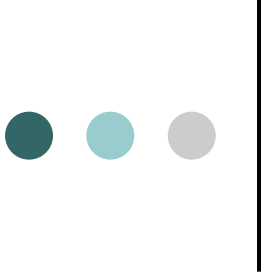
# Canadian Blood Services

- federally regulated
- provincially and territorially funded
- monopoly service provider in all 9/10 provinces & all 3 territories
  - Héma-Québec is the blood supplier for the province of Québec
- blood components & plasma protein products provided "free" of charge to hospitals

# Canada

Political Regions



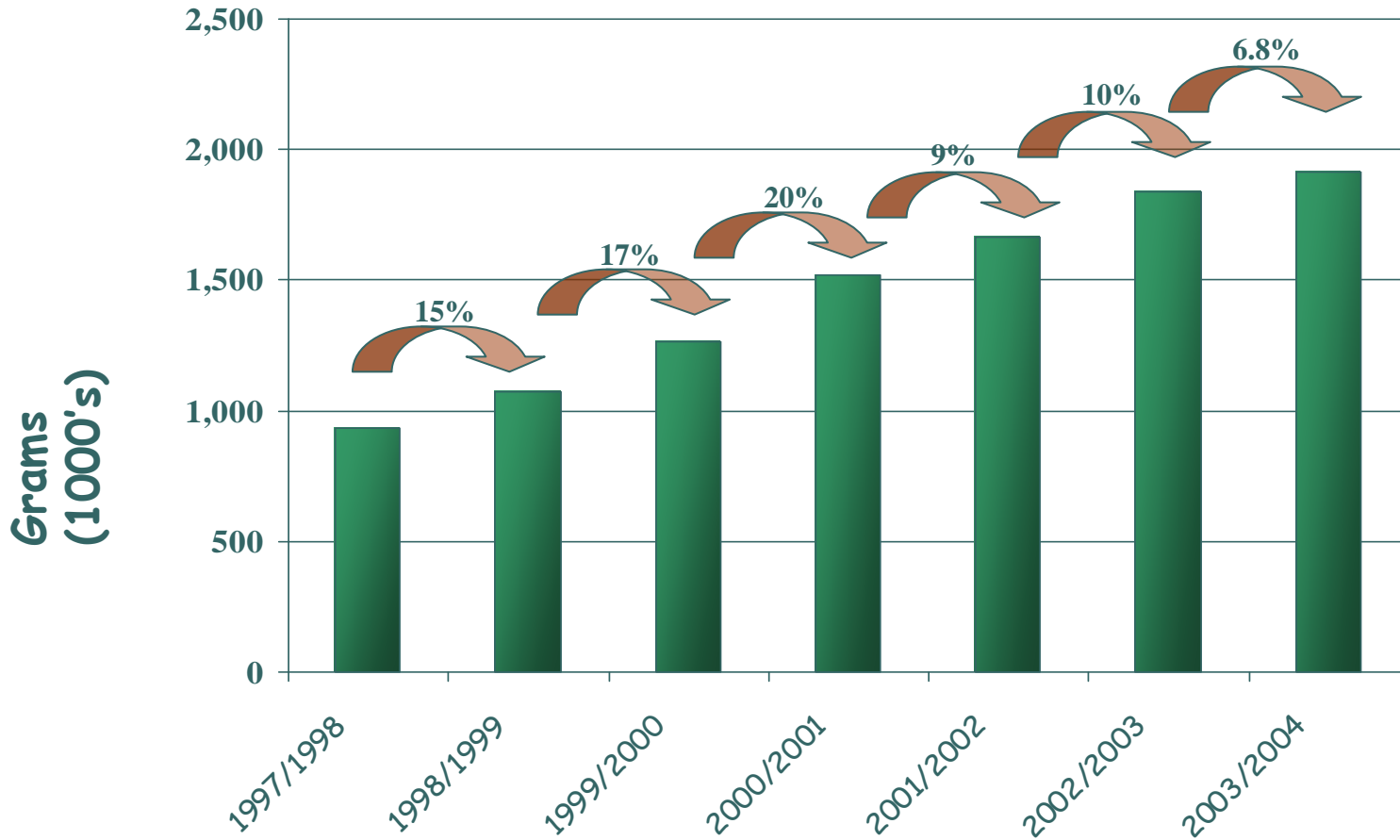


# IVIG Self- sufficiency

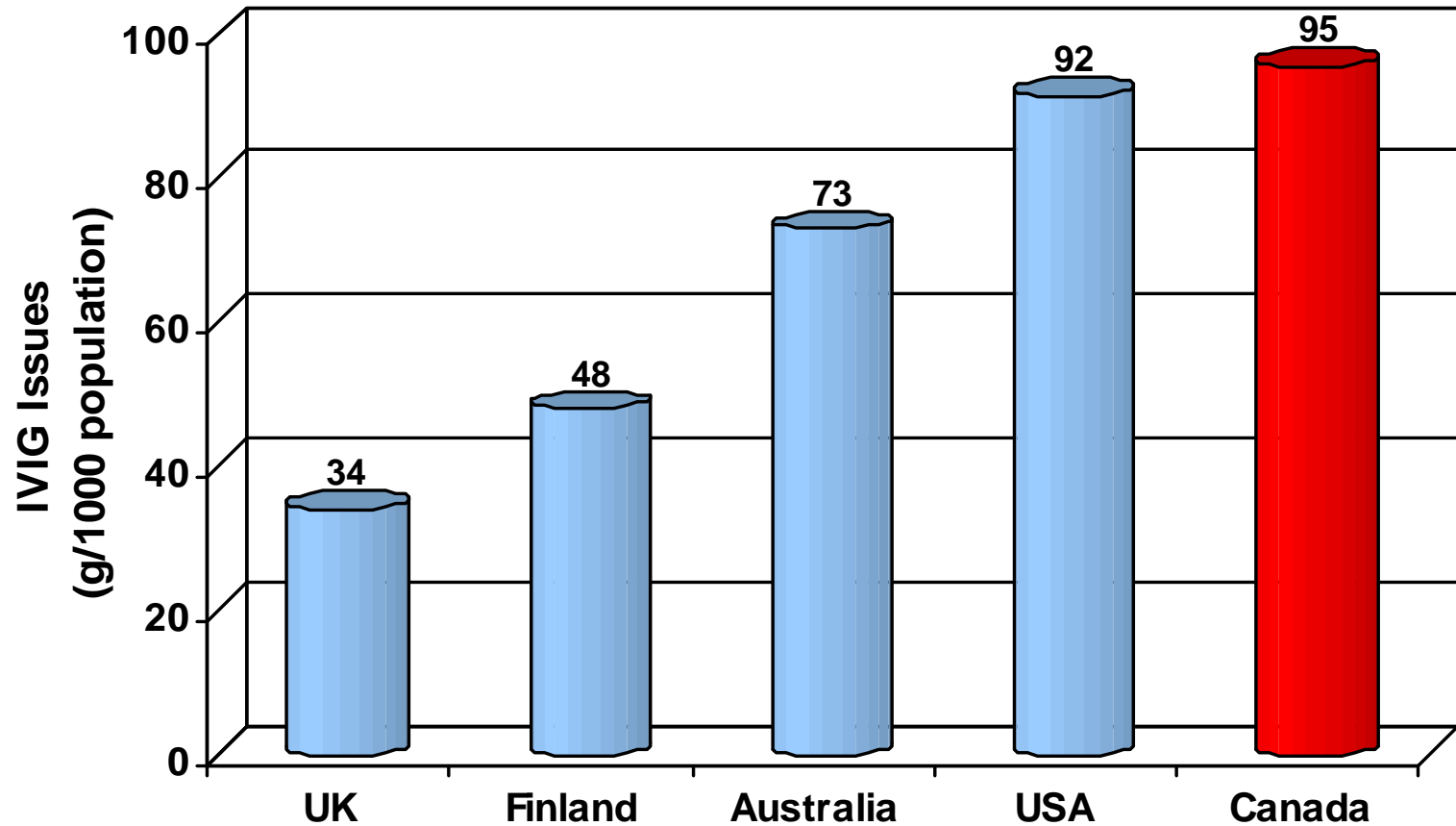
	Plasma from own donors	Purchased product
Australia	73%	27%
Canada	28%	72%

	Canada CBS	Québec Héma-Québec	ARCBS
Population	25.7 x 10 <sup>6</sup>	7.8 x 10 <sup>6</sup>	21.5 x 10 <sup>6</sup>
WB donations	915,858	245,594	1,021,517
Plateletpheresis donations	39,637	26,656	243,868
Plasmapheresis donations	55,244	9,454	36,000
Hospitals served	732	99	~825

# Canadian Blood Services IVIG UTILIZATION



## International Comparison of IVIG Issues for 2004



Data Sources: BPL, Sanquin Oy, ARCBS, Market Research Bureau and CBS.



# Labelled vs Off Label Use of IVIG

- Notion in Canada that off-label use represented at least 50% of use
  - Not identical for all IVIG brands/countries
  - On-label does not necessarily = indicated
  - Off-label does not necessarily = inappropriate use
- Great concern to funders!!
- Led to
  - Establishment of the National Advisory Committee on Blood & Blood Products
  - IVIG guideline development

# Health Canada approved indications for IVIG products available from CBS

Brand (Manufacturer)	Immunodeficiency		Pediatric HIV	Allogeneic BMT	Kawasaki Syndrome	ITP	CIDP
	1°	2°					
<b>Gamunex IGVInex (Talecris)</b>	X	X	X	X		X	X
<b>Gammagard S/D (Baxter)</b>	X	X			in USA	X	
<b>Gammagard Liquid (Baxter)</b>	X	X (CLL)				X	
<b>Sandoglobulin NF (CSL Bering)</b>	X	X					
<b>Privigen (CSL Bering)</b>	X	X				X	
<b>Vivaglobin (CSL Bering)</b>	X						

# Therapeutic Goods Administration approved indications for IVIG products available in Australia

Labelled Indicatons	Sandoglobulin NF Liquid (CSL Limited)	Intragam P (CSL Limited)	Octagam (Octapharma)
<b>replacement therapy in:</b> • Primary immunodeficiency (PID) syndromes	X	X	X
• Multiple myeloma, CLL	X	X	X
• Congenital AIDS	X (in children)	X	X (in children)
<b>immunomodulatory therapy in:</b> • ITP (children and adults)	X	X	X
• Guillain-Barré Syndrome	X	X	X
• Kawasaki Disease	X	X	X
• Allogeneic bone marrow transplantation	X	X	X

# Cost Comparison

**GOLD**



**\$41  
Aus**

**IVIG**



**\$69 Cdn  
(\$79 Aus)**

**PLATINUM**



**\$53  
Aus**

# Example of Cost of ITP Treatment

- 70 kg patient at 1 g/kg/day x 2 days

- \$9660 Cdn!



Prednisone 150 mg/day X 1 month < \$32 Cdn



# Advantages of Evidence-Based Guidelines

Lin W et al. ASH Educational Book Dec 2008

- Improve patient care
- Increase consistency of care
- Influence funding
- Influence public policy
  - research & research funding



# Canadian IVIG Guideline Development

- Began (in 2004) with hematologic and neurologic disorders - published in 2007
- Now completing guidelines for use of IVIG in primary immunodeficiency & solid organ transplantation
- Funding - unrestricted educational "value added fund" from Bayer to CBS



# Canadian IVIG Guideline Development

- For each set of IVIG guidelines
  - defined the clinical questions
  - performed extensive literature reviews
  - established panels that included
    - a methodological expert in clinical practice guideline development
    - recognized Canadian experts in given fields
    - representation from CBS & the NAC
  - panel developed recommendations
  - external review

**EVIDENCE**

*An **Evidence-informed** Approach  
Incorporating Consensus from Experts*

**CONSENSUS**

**EXPERTS**

# Guidelines Published

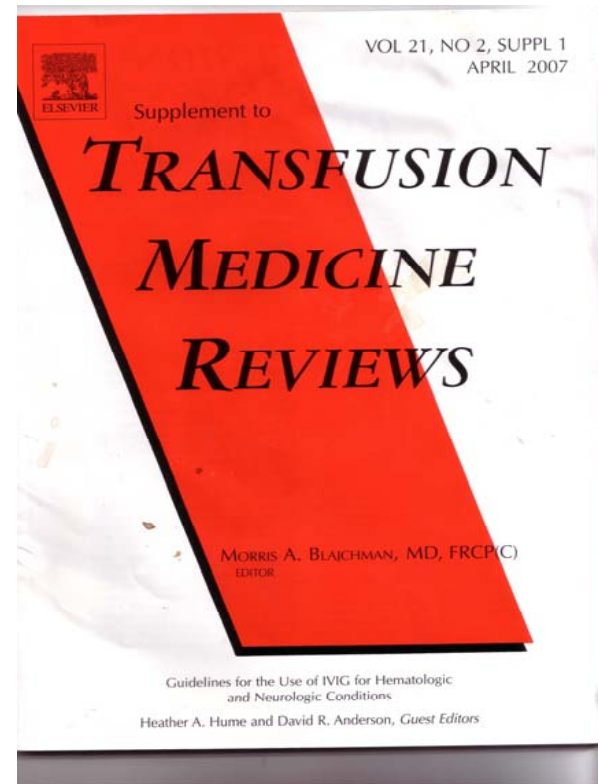
- *Transfusion Medicine Reviews*  
(April 2007 Supplement)

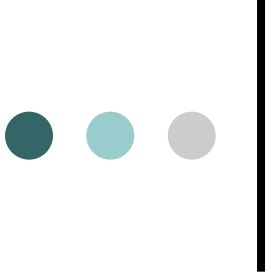
- **Hematology**

- 20 indications

- **Neurology**

- 23 indications





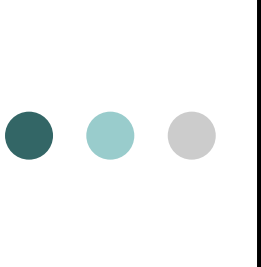
# IVIIG guidelines - Comparisons

- Guidelines for the Use of IVIG for Hematologic and Neurologic Conditions. Transfusion Medicine Reviews 2007; 21(2) Suppl 1
- Criteria for the Clinical Use of IVIG in Australia
  - Dec 2007, revisions Feb 2009
  - [www.nba.gov.au/ivig/pdf/criteria.pdf](http://www.nba.gov.au/ivig/pdf/criteria.pdf)
  - [www.nba.gov.au/ivig/pdf/criteria-revisions.pdf](http://www.nba.gov.au/ivig/pdf/criteria-revisions.pdf)
- UK National Health Service Clinical Guidelines for Immunoglobulin Use, 2<sup>nd</sup> Ed, May 2008
  - [www.ivig.nhs.uk](http://www.ivig.nhs.uk)



# IVIIG Guidelines - Hematology

- ITP
  - children
  - adults
- HSCT
- Acquired hypogammaglobulinemia
- HDN
- Sickle cell disease



# Adult ITP IVIG Studies Reviewed for the Canadian Guidelines

<i>Studies</i>	<i>Designs</i>	<i>Total # patients</i>	<i>Outcomes</i>
Acute ITP	1- RCT, not blinded (2002) 1 – non RCT (1998)	161	IVIG superior in 1 study, not in the other
Chronic ITP	3 RCTs, not blinded (1993, 1998, 2003)	84	1 study some advantage for IVIG (but ? clinical significance)
Acute & chronic ITP	2 RCTs, not blinded (1989, 1996)	44	No significant differences



# ITP in Adults

	<b><i>Australia 2009</i></b>	<b><i>Canada 2007</i></b>	<b><i>UK 2008</i></b>
Acute ITP		<ol style="list-style-type: none"><li>1. Severe or life-threatening bleeding (with other treatment)</li><li>2. No/slow response or contraindication to corticosteroids</li></ol>	
Chronic ITP		<ol style="list-style-type: none"><li>1. Possible steroid-sparing treatment post-splenectomy</li></ol>	



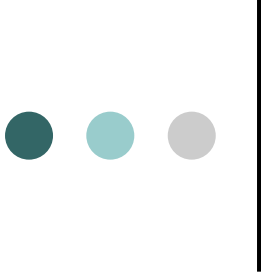
# ITP in Adults

	<b><i>Australia 2009</i></b>	<b><i>Canada 2007</i></b>	<b><i>UK 2008</i></b>
Acute ITP	<ol style="list-style-type: none"><li>1. Life-threatening bleeding</li><li>2. Unresponsive to or contraindication to corticosteroids</li><li>3. PC &lt; 30 X 10<sup>9</sup>/L and moderate to severe bleeding</li></ol>	<ol style="list-style-type: none"><li>1. Severe or life-threatening bleeding (with other treatment)</li><li>2. No/slow response or contraindication to corticosteroids</li></ol>	
Chronic ITP	<ol style="list-style-type: none"><li>1. Life-threatening bleeding</li><li>2. Failure or contraindication to other therapy including splenectomy</li><li>3. Prior to surgery</li></ol>	<ol style="list-style-type: none"><li>1. Possible steroid-sparing treatment post-splenectomy</li></ol>	



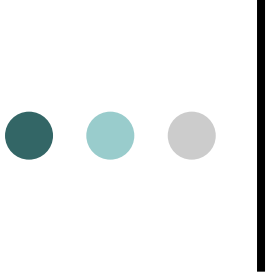
# ITP in Adults

	<b><i>Australia 2009</i></b>	<b><i>Canada 2007</i></b>	<b><i>UK 2008</i></b>
Acute ITP	<ol style="list-style-type: none"> <li>1. Life-threatening bleeding</li> <li>2. Unresponsive to or contraindication to corticosteroids</li> <li>3. PC &lt; 30 X 10<sup>9</sup>/L and moderate to severe bleeding</li> </ol>	<ol style="list-style-type: none"> <li>1. Severe or life-threatening bleeding (with other treatment)</li> <li>2. No/slow response or contraindication to corticosteroids</li> </ol>	<ol style="list-style-type: none"> <li>1. Persistent or life-threatening bleeding and a PC &lt; 30 X 10<sup>9</sup>/L</li> <li>2. Bleeding, unresponsive to other treatment</li> </ol>
Chronic ITP	<ol style="list-style-type: none"> <li>1. Life-threatening bleeding</li> <li>2. Failure or contraindication to other therapy including splenectomy</li> <li>3. Prior to surgery</li> </ol>	<ol style="list-style-type: none"> <li>1. Possible steroid-sparing treatment post-splenectomy</li> </ol>	<ol style="list-style-type: none"> <li>1. Not recommended</li> </ol>



# Childhood ITP IVIG Studies Reviewed for the Canadian Guidelines

<i>Studies</i>	<i>Designs</i>	<i>Total # patients</i>
Acute ITP	10 RCTs not blinded 1985-2002	656
Chronic ITP	1 RCT not blinded 1984	9
Acute & chronic ITP	1 RCTs not blinded 1997	12



# Corticosteroids vs IVIG for the Treatment of Children with ITP: Systematic Review and Meta-analysis of RCTs

Beck CE et al. J Pediatr 2005;147:521-7

- 1<sup>o</sup> outcome = # of patients with a platelet count  $\geq 20 \times 10^9/L$  48 hr after ***treatment initiation***
- Results
  - 10 studies included
  - RR: CS vs IVIG for 1<sup>o</sup> outcome was 0.74 (95% CI: 0.65, 0.85)
  - NNT: 4.55 (95% CI: 3.23, 7.69)



# Severe hemorrhage in children with newly diagnosed ITP

Neurnert CE et al. Blood 2008;112:4003-8

- Intercontinental Childhood ITP Study Group prospective registry
  - UK, USA, Canada, Switzerland
- Severe hemorrhage at diagnosis & up to 28 days
- 863 eligible, evaluable children
  - 665 (77%) no/mild bleeding at diagnosis
  - 173 (20%) moderate bleeding at diagnosis
  - 25 (2.9%) severe bleeding at diagnosis



# Severe hemorrhage in children with newly diagnosed ITP

<i>Presentation</i>	<i>Total #</i>	<i># developing severe bleeding within 28 days</i>
No/mild bleeding PC < 20 X 10 <sup>9</sup> /L	505	3 (0.6%)
Moderate bleeding	173	3 (1.7%)

Development of bleeding unrelated to management



# ITP in Children

	<b><i>Australia 2009</i></b>	<b><i>Canada 2007</i></b>	<b><i>UK 2008</i></b>
Acute ITP		<ol style="list-style-type: none"><li>1. Life-threatening bleeding (with other treatment)</li><li>2. One option for 1st line treatment if <math>PC &lt; 20 \times 10^9/L</math></li></ol>	
Chronic ITP		<ol style="list-style-type: none"><li>1. One option for treatment (other being anti-D if appropriate)</li></ol>	



# ITP in Children

	<b><i>Australia 2009</i></b>	<b><i>Canada 2007</i></b>	<b><i>UK 2008</i></b>
Acute ITP	<p><i>Emerging role</i></p> <ol style="list-style-type: none"> <li>1. Life-threatening bleeding</li> <li>2. PC &lt; 30 X 10<sup>9</sup>/L and moderate to severe bleeding</li> </ol>	<ol style="list-style-type: none"> <li>1. Life-threatening bleeding (with other treatment)</li> <li>2. One option for 1st line treatment if PC &lt; 20 X 10<sup>9</sup>/L</li> </ol>	
Chronic ITP	<p><i>Emerging role</i></p> <ol style="list-style-type: none"> <li>1. Life-threatening bleeding</li> <li>2. PC &lt; 30 X 10<sup>9</sup>/L and moderate to severe bleeding without other options</li> <li>3. Prior to surgery</li> </ol>	<ol style="list-style-type: none"> <li>1. One option for treatment (other being anti-D if appropriate)</li> </ol>	



# ITP in Children

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Chronic ITP	<p><i>Emerging role</i></p> <ol style="list-style-type: none"> <li>1. Life-threatening bleeding</li> <li>2. PC &lt; 30 X 10<sup>9</sup>/L and moderate to severe bleeding without other options</li> <li>3. Prior to surgery</li> </ol>	<ol style="list-style-type: none"> <li>1. One option for treatment (other being anti-D if appropriate)</li> </ol>	<ol style="list-style-type: none"> <li>1. Not recommended.</li> </ol>



# IVIG & Preventions of Acute GVHD in BMT

- IVIG licensed for this use based on studies (1980-90s) showing a decreased rate of acute GVHD
  - but no decrease in overall survival
- Cordonnier study 2003



## IVIg in Allogeneic HSCT

Cordonnier C et al. Ann Intern Med 2003;139:8-18

- 200 patients undergoing HSCT from HLA matched siblings
- RCT, double-blinded, 4 arms
  - IVIg 50, 250, 500 mg/kg or placebo
- Results
  - no significant differences in GVHD, infection, mortality
  - severe veno-occlusive disease occurred more frequently as the IVIg dose increased ( $p < .01$ )



# Ig prophylaxis in Hematological Malignancies & HSCT

## Cochrane Review Oct 8 2008

- Objective - to determine if IVIG prophylaxis reduces mortality or affects other outcomes
- 40 RCTs
  - 30 HSCT
  - 10 lymphoproliferative disorders
- HSCT - routine prophylaxis with IVIG is not supported
  - no difference in all-cause mortality
  - increased risk for VOD
- LPD - may be considered for those with hypogammaglobulinemia & recurrent infection



# Indications for the Use of IVIG in Hematologic Malignancies

	<i>Australia 2009</i>	<i>Canada 2007</i>	<i>UK 2008</i>
Acquired hypogammaglobulinemia in hematologic malignancies		Recommended for infection prophylaxis in selected patients Not recommended for routine use in children	
Acquired hypogammaglobulinemia in HSCT		Not recommended	
Prevention of treatment of GVHD		Not recommended	



# Indications for the Use of IVIG in Hematologic Malignancies

	<i>Australia 2009</i>	<i>Canada 2007</i>	<i>UK 2008</i>
Acquired hypogammaglobulinemia in hematologic malignancies	NHL, CLL, MM: hypoGG and recurrent severe infection or unresponsive to vaccines	Recommended for infection prophylaxis in selected patients Not recommended for routine use in children	
Acquired hypogammaglobulinemia in HSCT	Not recommended	Not recommended	
Prevention of treatment of GVHD		Not recommended	



# Indications for the Use of IVIG in Hematologic Malignancies

	<i>Australia 2009</i>	<i>Canada 2007</i>	<i>UK 2008</i>
Acquired hypogammaglobulinemia in hematologic malignancies	NHL, CLL, MM: hypoGG and recurrent severe infection or unresponsive to vaccines	Recommended for infection prophylaxis in selected patients Not recommended for routine use in children	Acute – no Maintenance – selected
Acquired hypogammaglobulinemia in HSCT	Not recommended	Not recommended	Acute – yes Maintenance – selected
Prevention of treatment of GVHD		Not recommended	Grey indication



# Indications for the Use of IVIG in HDN and SCD

	<i>Australia 2009</i>	<i>Canada 2007</i>	<i>UK 2008</i>
Hemolytic disease of the newborn		Recommended as treatment for severe hyperbilirubinemia as per AAP (2004)	
Sickle cell disease - hemolytic transfusion reaction		May be considered if life threatening	



# Indications for the Use of IVIG in HDN and SCD

	<i>Australia 2009</i>	<i>Canada 2007</i>	<i>UK 2008</i>
Hemolytic disease of the newborn	May be used in selected cases in consultation with FM and TM experts	Recommended as treatment for severe hyperbilirubinemia as per AAP (2004)	
Sickle cell disease - hemolytic transfusion reaction		May be considered if life threatening	



# Indications for the Use of IVIG in HDN and SCD

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Hemolytic disease of the newborn	May be used in selected cases in consultation with FM and TM experts	Recommended as treatment for severe hyperbilirubinemia as per AAP (2004)	Acute – selected Maintenance – no
Sickle cell disease - hemolytic transfusion reaction		May be considered if life threatening	Used successfully with corticosteroids



# Adverse reactions to IVIG

Common	Rare	Theoretical
Headache	Renal dysfunction	vCJD infection
Cough	Thrombotic events	HIV infection
Nausea/vomiting	Aseptic meningitis	
Fever/chills	Anaphylaxis	
Flushing	TRALI	
Urticaria	<i>Hemolysis</i>	
Malaise	Neutropenia	
Myalgia	HCV infection (1993)	
Hypertension		
Volume overload		



# Case of IVIG Associated Hemolysis

Dr. R. Scuccimarri McGill University, Montreal

- 7 month old boy with Kawasaki Disease
- Hb = 93 g/L at admission
- Treated with IVIG 2g/kg
- Persistent fever - given 2nd treatment of IVIG 2g/kg
- Hb falls to 56 g/L
- Clear of evidence of hemolysis
  - spherocytes, reticulocytosis, increased LDH, decreased haptoglobin
- Group AB, positive DAT, anti-A,B in eluate
- Given RBC transfusion



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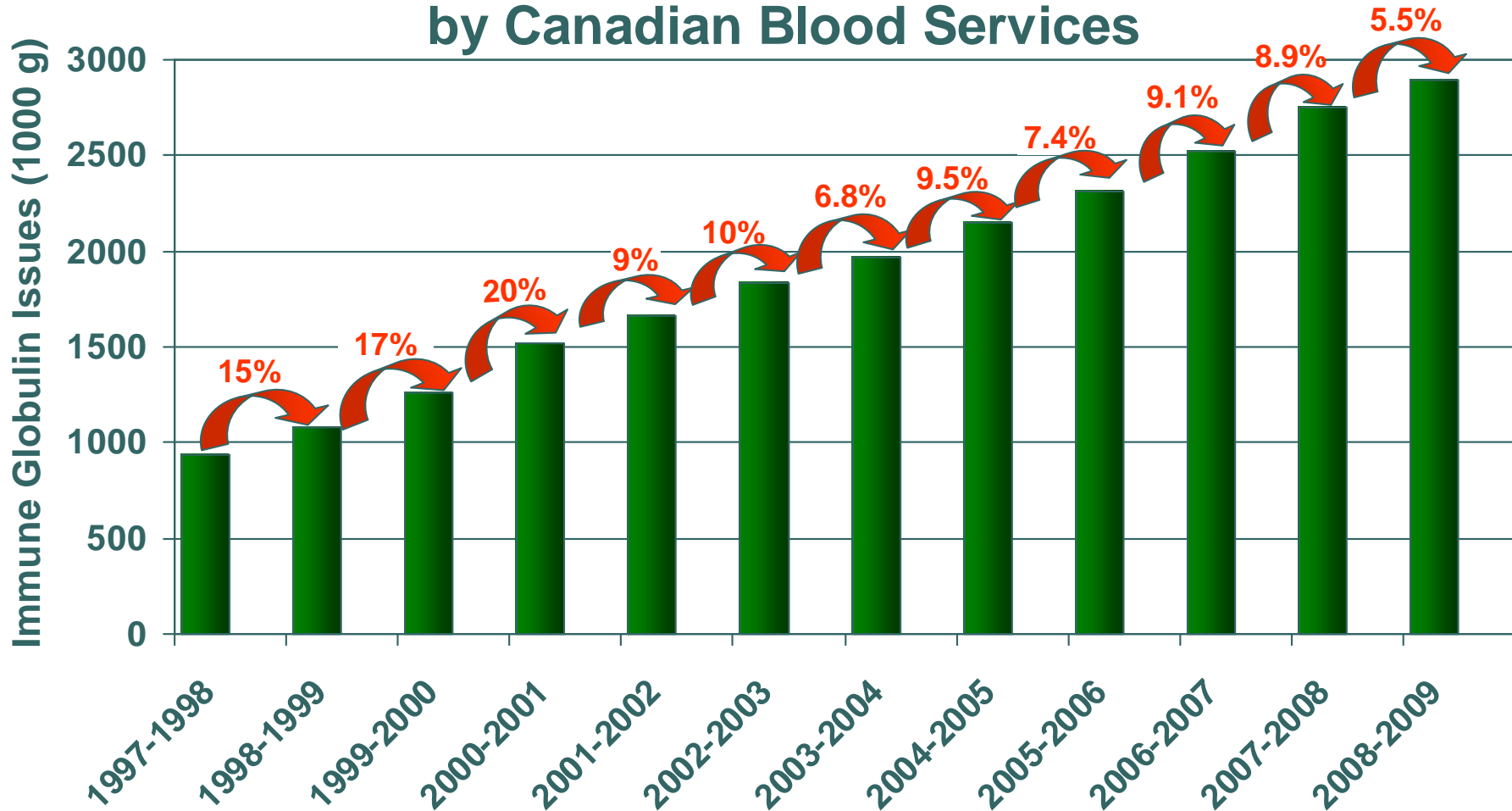
Hemolytic transfusion reactions after IVIG. Daw Z. Transfusion 2008;48:1598-1601



# Have we accomplished anything with our guidelines?

- Funders realize that we are trying to be vigilant about IVIG use
- Are clinicians using the guidelines??
  - about to do an survey of neurologists
- What has happened to IVIG use...
- Some provinces are putting guidelines into practice...

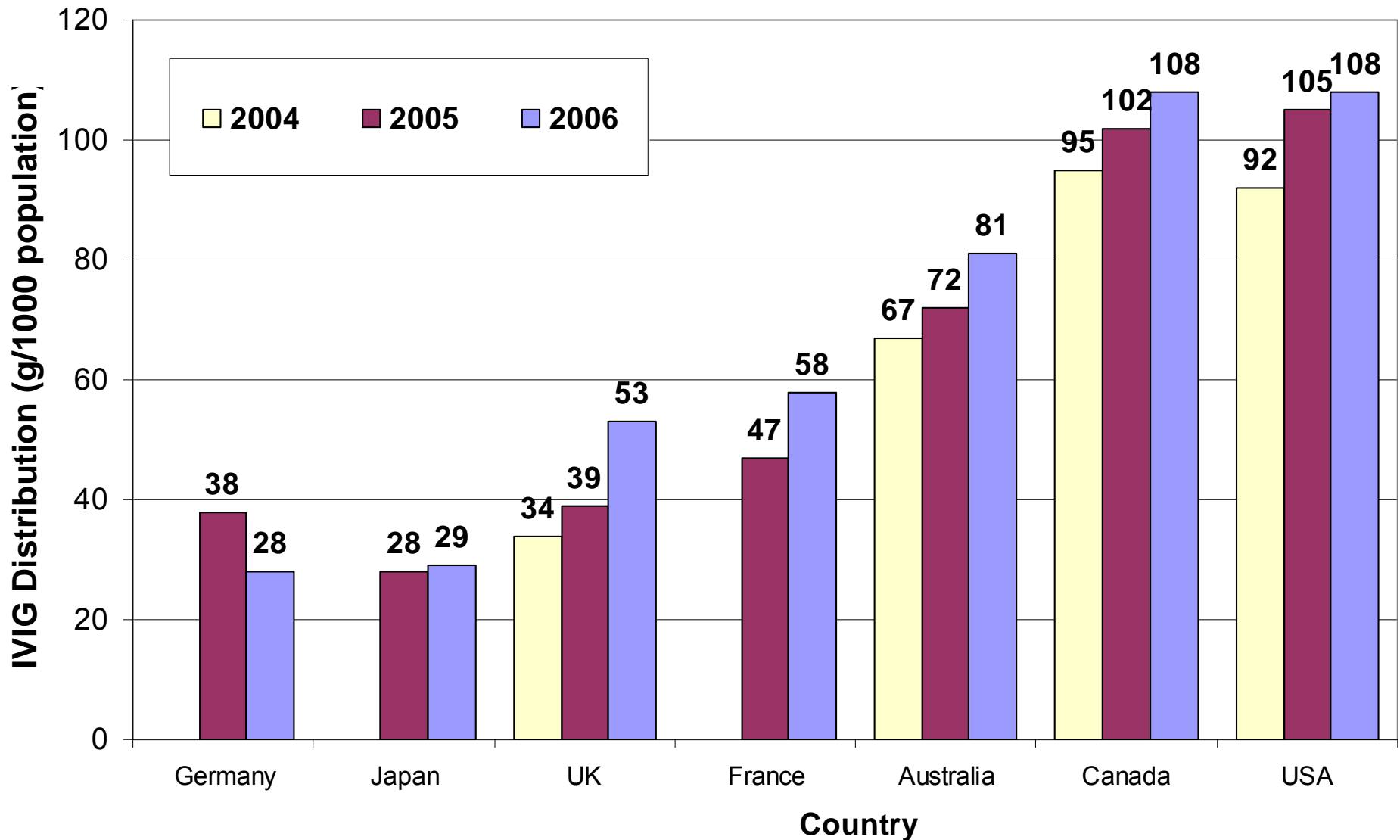
## Overall Immune Globulin Issues by Canadian Blood Services



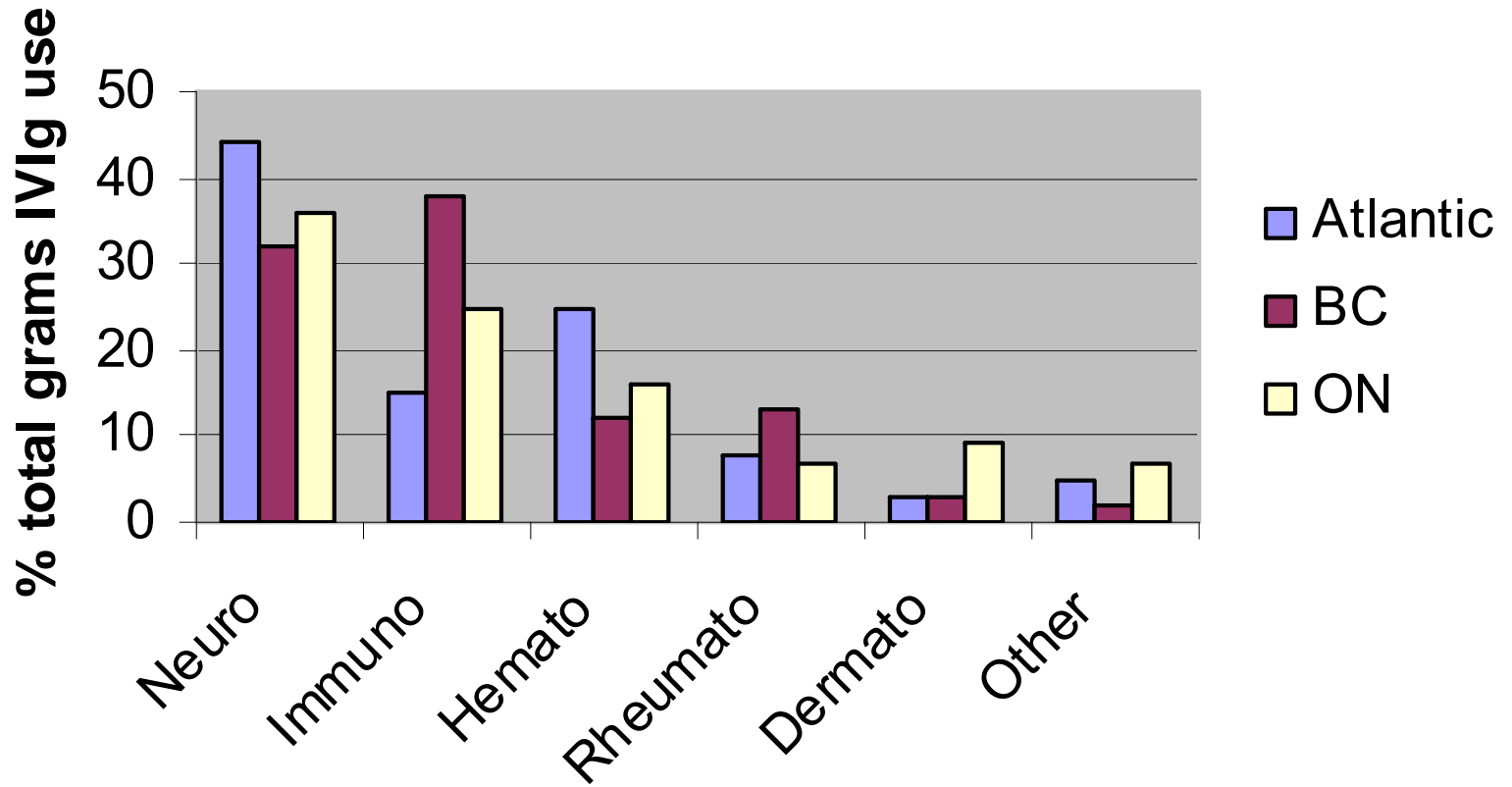
Note: Total issues for 2008/09 include both IVIG and SCIG

# International Comparison

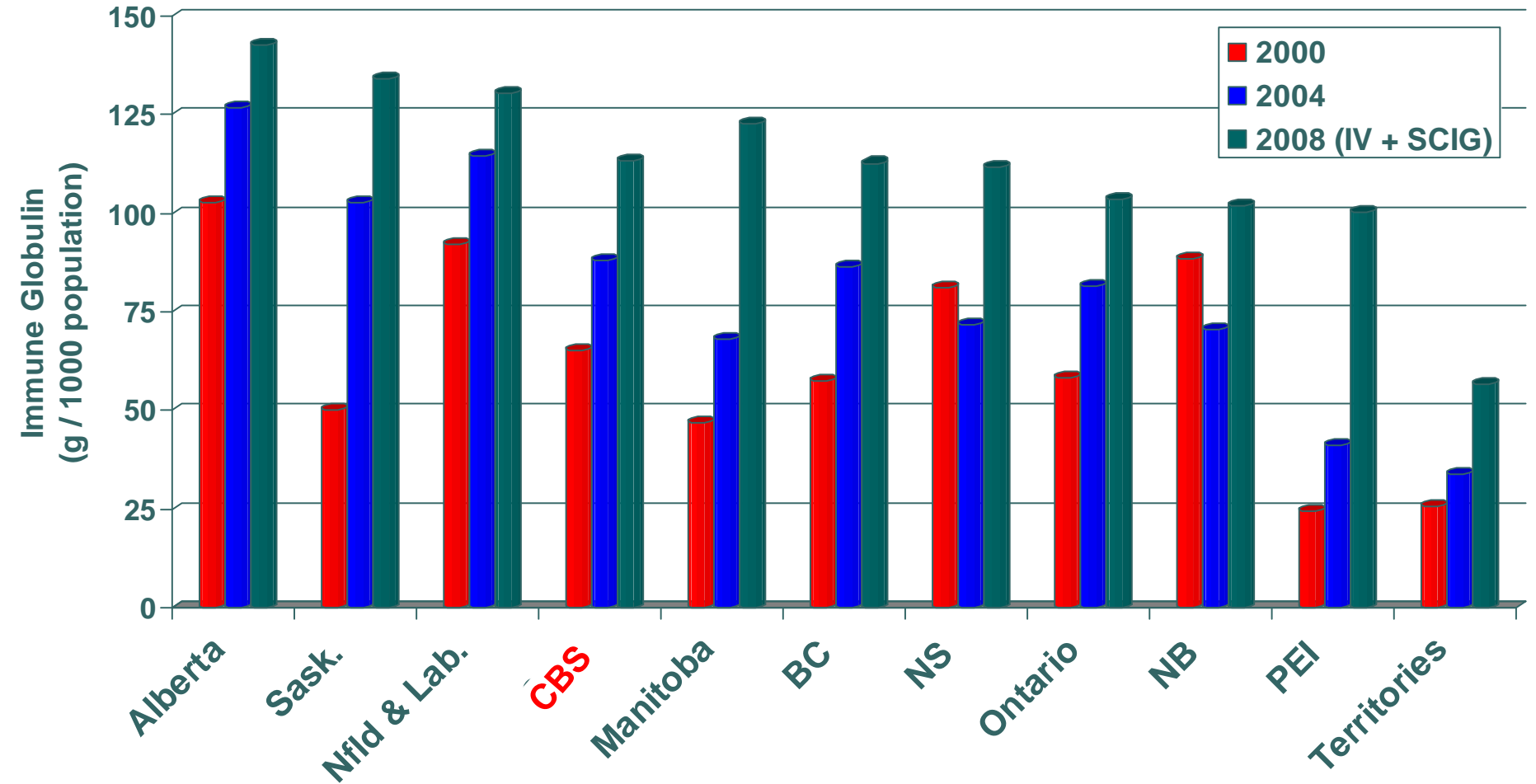
Figure 1: International Comparison of IVIG Distribution (2004-2006)



## IVIg Use in Canadian Provinces



## Immune Globulin Issues per 1000 population





# Ontario IVIG Utilization Audit

- 20 hospitals (70% of ON IVIG use)
- Sept-Nov 2007
- 7 recommendations
  - Including "a provincial guideline for use of IVIG in ON must be created & adopted"



# Atlantic Provinces 2008 IVIg Ordering Process

- Physician completes IVIg standardized order
- Order reviewed by local transfusion laboratory
  - Meets criteria – IVIg issued
  - Criteria not met – discuss with ordering physician
- Expert clinician consultant available provincially to resolve disputes

**PRE-PRINTED ORDER**

Blood Transfusion Service

**Request for IVIG (Adult)**

Patient: \_\_\_\_\_ Weight: \_\_\_\_\_ kg Allergies: \_\_\_\_\_

- The following orders may be used in any patient care area and will be carried out by a qualified health professional only on the authority of a physician.
- All blanks must be completed as appropriate. Use the table below to check off the indication and criteria for the use of IVIG. **Missing information will result in delays.**
- The blood transfusion service **may require a consultation** with a specialist prior to issuing product.

**ORDERS (see reverse for dosing guidelines):**  
 Daily infusion of \_\_\_\_\_ g of IVIG.  
 Expected start date: \_\_\_\_\_ (yyyy/mm/dd)  
 with \_\_\_\_\_ day(s) per treatment  
 Number of weeks between treatments: \_\_\_\_\_  
 Total Number of Treatments: \_\_\_\_\_  
 IgA deficient product required?  Yes  No

	Indication	Criteria – Please Complete Checkboxes	Indication	Criteria – Please Complete Checkboxes
<b>NEUROLOGY</b>	<input type="checkbox"/> <b>CIDP: New Onset/Relapse</b>	No criteria need to be met other than a confirmed diagnosis.	<input type="checkbox"/> <b>CIDP: Long Term Maintenance</b>	Must meet both of the following 2 criteria: <input type="checkbox"/> patient is under the care of a neurologist neurologist name: _____ <input type="checkbox"/> patient is on adjuvant immunosuppressive therapies
	<input type="checkbox"/> <b>Myasthenia Gravis: Acute</b>	Must meet the following criterion: <input type="checkbox"/> severe exacerbation or myasthenic crisis	<input type="checkbox"/> <b>Myasthenia Gravis: Chronic</b>	Must meet the following criterion: <input type="checkbox"/> other agents are being used to treat MG
	<input type="checkbox"/> <b>Guillain-Barré Syndrome: Acute</b>	Must meet both of the following 2 criteria: <input type="checkbox"/> IVIG being given within 4 wks of symptom onset <input type="checkbox"/> Hughes Disability Score is 3 or more (see over) OR score is 2 or less & symptoms are progressing	<input type="checkbox"/> <b>Guillain-Barré Syndrome: Relapses</b>	Must meet both of the following 2 criteria: <input type="checkbox"/> relapse is within 8 wks of the initial symptom onset <input type="checkbox"/> the patient has previously responded to IVIG
	<input type="checkbox"/> <b>Multifocal Motor Neuropathy</b>	Must meet the following criterion: <input type="checkbox"/> the patient is under the care of a neurologist neurologist name: _____	<input type="checkbox"/> <b>Multiple Sclerosis</b>	Must meet the following criterion: <input type="checkbox"/> the patient is under the care of a neurologist neurologist name: _____
	<input type="checkbox"/> <b>Stiff Person Syndrome: Acute</b>	Must meet 1 of the following 2 criteria: <input type="checkbox"/> GABAergic medications were tried & failed <input type="checkbox"/> patient has contraindication to GABAergic meds	<input type="checkbox"/> <b>Stiff Person Syndrome: Chronic</b>	Must meet the following criterion: <input type="checkbox"/> the patient is under the care of a neurologist neurologist name: _____
<b>HEMATOLOGY</b>	<input type="checkbox"/> <b>ITP: Acute</b>	Must meet 1 of the following 3 criteria: <input type="checkbox"/> major bleeding & platelets less than 50x10 <sup>9</sup> /L <input type="checkbox"/> failed to respond to steroids after 3 or more days <input type="checkbox"/> rapid elevation of platelets required for surgery	<input type="checkbox"/> <b>ITP: Chronic</b>	Must meet both of the following 2 criteria: <input type="checkbox"/> IVIG use has already raised platelets by more than 20x10 <sup>9</sup> /L <input type="checkbox"/> other agents are being used to treat ITP
	<input type="checkbox"/> <b>Pregnancy-Associated ITP</b>	Must meet 1 of the following 3 criteria: <input type="checkbox"/> platelets less than 10x10 <sup>9</sup> /L (any trimester) <input type="checkbox"/> platelets between 10 & 30x10 <sup>9</sup> /L (2 <sup>nd</sup> or 3 <sup>rd</sup> trimester) <input type="checkbox"/> need to increase platelets for delivery or epidural	<input type="checkbox"/> <b>Secondary Immuno-deficiency</b>	Must meet 1 of the following 2 criteria: <input type="checkbox"/> a recent life-threatening infection related to low levels of polyclonal immunoglobulin <input type="checkbox"/> recurrent clinically significant infections related to low levels of polyclonal immunoglobulin
<b>OTHER</b>	<input type="checkbox"/> <b>Primary Immune Deficiency Conditions</b>	<b>Specify condition:</b>  IgG levels must be drawn before every 5th dose or more frequently by physician request as follows: <b>IgG levels to be drawn before every _____ dose.</b>	<input type="checkbox"/> <b>Other Indication</b>	<b>Please provide name of indication:</b>

<b>For Lab Use Only</b>	Dose	Date (yyyy/mm/dd)	Dose	Date (yyyy/mm/dd)	Dose	Date (yyyy/mm/dd)
	<input type="checkbox"/> 1		<input type="checkbox"/> 5		<input type="checkbox"/> 9	
	<input type="checkbox"/> 2		<input type="checkbox"/> 6		<input type="checkbox"/> 10	
	<input type="checkbox"/> 3		<input type="checkbox"/> 7		<input type="checkbox"/> 11	
	<input type="checkbox"/> 4		<input type="checkbox"/> 8		<input type="checkbox"/> 12	

Bar Code

Physician's Signature: \_\_\_\_\_ Date(yyyy/mm/dd): \_\_\_\_\_

Physician's Name \_\_\_\_\_ CPSNS No. \_\_\_\_\_

NEUROLOGY	<input type="checkbox"/> <b>Myasthenia Gravis: Acute</b>	Must meet the following criterion: <input type="checkbox"/> severe exacerbation or myasthenic crisis	<input type="checkbox"/> <b>Myasthenia Gravis: Chronic</b>	Must meet the following criteria: <input type="checkbox"/> other agents are being used
	<input type="checkbox"/> <b>Guillain-Barré Syndrome: Acute</b>	Must meet both of the following 2 criteria: <input type="checkbox"/> IVIG being given within 4 wks of symptom onset <input type="checkbox"/> Hughes Disability Score is 3 or more (see over) OR score is 2 or less & symptoms are progressing	<input type="checkbox"/> <b>Guillain-Barré Syndrome: Relapses</b>	Must meet both of the following criteria: <input type="checkbox"/> relapse is within 8 wks of onset <input type="checkbox"/> the patient has previously
	<input type="checkbox"/> <b>Multifocal Motor Neuropathy</b>	Must meet the following criterion: <input type="checkbox"/> the patient is under the care of a neurologist neurologist name: _____	<input type="checkbox"/> <b>Multiple Sclerosis</b>	Must meet the following criteria: <input type="checkbox"/> the patient is under the care of a neurologist neurologist name: _____
	<input type="checkbox"/> <b>Stiff Person Syndrome: Acute</b>	Must meet 1 of the following 2 criteria: <input type="checkbox"/> GABAergic medications were tried & failed <input type="checkbox"/> <del>patient has contraindication to GABAergic medications</del>	<input type="checkbox"/> <b>Stiff Person Syndrome: Chronic</b>	Must meet the following criteria: <input type="checkbox"/> the patient is under the care of a neurologist neurologist name: _____
HEMATOLOGY	<input type="checkbox"/> <b>ITP: Acute</b>	Must meet 1 of the following 3 criteria: <input type="checkbox"/> major bleeding & platelets less than $50 \times 10^9/L$ <input type="checkbox"/> failed to respond to steroids after 3 or more days <input type="checkbox"/> rapid elevation of platelets required for surgery	<input type="checkbox"/> <b>ITP: Chronic</b>	Must meet both of the following criteria: <input type="checkbox"/> IVIG use has already raised platelets to more than $20 \times 10^9/L$ <input type="checkbox"/> other agents are being used
	<input type="checkbox"/> <b>Pregnancy-Associated ITP</b>	Must meet 1 of the following 3 criteria: <input type="checkbox"/> platelets less than $10 \times 10^9/L$ (any trimester) <input type="checkbox"/> platelets between $10$ & $30 \times 10^9/L$ (2 <sup>nd</sup> or 3 <sup>rd</sup> trimester) <input type="checkbox"/> need to increase platelets for delivery or epidural	<input type="checkbox"/> <b>Secondary Immuno-deficiency</b>	Must meet 1 of the following criteria: <input type="checkbox"/> a recent life-threatening infection <input type="checkbox"/> low levels of polyclonal immunoglobulins <input type="checkbox"/> recurrent clinically significant infections <input type="checkbox"/> response to high doses of immunoglobulin to low levels of polyclonal immunoglobulins
OTHER	<input type="checkbox"/> <b>Primary Immune Deficiency Conditions</b>	<b>Specify condition:</b> _____ IgG levels must be drawn before every 5th dose or more frequently by physician request as follows: <b>IgG levels to be drawn before every ____ dose.</b>	<input type="checkbox"/> <b>Other Indication</b>	<b>Please provide name of indication:</b> _____

<b>For Lab Use Only</b>	<b>Dose</b>	<b>Date (yyyy/mm/dd)</b>	<b>Dose</b>	<b>Date (yyyy/mm/dd)</b>	<b>Dose</b>	<b>Date (yyyy/mm/dd)</b>
	<input type="checkbox"/> 1		<input type="checkbox"/> 5		<input type="checkbox"/> 9	
	<input type="checkbox"/> 2		<input type="checkbox"/> 6		<input type="checkbox"/> 10	
	<input type="checkbox"/> 3		<input type="checkbox"/> 7		<input type="checkbox"/> 11	
	<input type="checkbox"/> 4		<input type="checkbox"/> 8		<input type="checkbox"/> 12	

	(MS)	steroid therapy or patients for whom corticosteroid therapy is contraindicated. IVIG may be considered as a treatment option for patients with relapsing-remitting MS who are pregnant or breast feeding or in the immediate postpartum period for women whose exacerbation rate was high before pregnancy and who were on disease modifying agents before pregnancy with plans to recommence therapy after birth or breastfeeding. <b>Dose:</b> 1 g/kg monthly with or without a 5 day induction of 0.4 g/kg daily is a reasonable starting option for treatment of patients with relapsing-remitting MS. A systematic approach should be taken to determine the min. effective dose.
	Stiff Person Syndrome	<b>Acute Setting</b> - GABAergic medications should be first-line treatment for this disorder. IVIG is a reasonable option if GABAergic medications fail or are contraindicated. Acute Dose: 1 g/kg x 2 days or 0.4 g/kg x 5 days in a 4 wk period is a reasonable initial treatment option. <b>Chronic Setting</b> - The patient should be under the care of a qualified expert with specialized knowledge of stiff person syndrome. Efforts should be made to determine the minimum effective dose, and continued use of IVIG should be based on objective measures of its sustained effectiveness. A reasonable treatment dose would be 0.5 to 1.0 g/kg in a 4 wk period. The maximum dose per treatment course should be 2 g/kg. Treatment should be no more frequent than every 4 wks.
H E M A T O L O G Y	Idiopathic Thrombocytopenic Purpura (ITP)	<b>Acute Setting</b> – There must be a diagnosis of ITP and one of the following two: 1) major bleeding and platelet count less than $50 \times 10^9/L$ ; or 2) ITP not responding to steroids after a minimum of three days. IVIG may also be used when preparing a thrombocytopenic patient for surgery when there is insufficient time to depend on steroids. <b>Acute Dose:</b> 1 g/kg per day for 2 consecutive days. <b>Chronic Setting</b> – There must be a diagnosis of ITP and the following 2 criteria: 1) demonstrated responsiveness to IVIG as shown by administration required no more frequently than every 2 wks and a platelet increase greater than $20 \times 10^9/L$ ; and 2) use in conjunction with other agents. There must be a record of the treatments used and platelet counts for review by a specialist with expertise in the management of ITP. Review is to occur every 3 months for the first year then every 6 months thereafter. <b>Chronic Dose:</b> 0.5 to 1.0 g/kg per day, no more frequently than every 2 wks.
	Pregnancy-Associated ITP	Platelet counts greater than $50 \times 10^9/L$ do not routinely need treatment and should not receive steroids or IVIG. Platelet counts between 30 and $50 \times 10^9/L$ in the 1 <sup>st</sup> or 2 <sup>nd</sup> trimester also should not receive treatment. Treatment is required if the platelet count is less than $10 \times 10^9/L$ at any time during the pregnancy or between $10\text{--}30 \times 10^9/L$ in the 2 <sup>nd</sup> or 3 <sup>rd</sup> trimester if there is bleeding. Pregnant women who fail steroids and IVIG should be considered for splenectomy in the second trimester if the platelet count is less than $10 \times 10^9/L$ and there is bleeding. A platelet count of $50 \times 10^9/L$ is sufficient for vaginal or cesarean delivery. IVIG may be useful if very rapid elevation of platelet count is needed before delivery. Platelet count should be greater than $80 \times 10^9/L$ for epidurals. <b>Acute Dose:</b> 1 g/kg per day for 1–2 days.
	Bone Marrow Transplant	Routine use of IVIG for bone marrow transplant is not indicated.
	Secondary Immunodeficiency (Acquired Hypogammaglobulinemia)	IVIG is recommended for infection prophylaxis in adults with malignant hematologic disorders associated with hypogammaglobulinemia or dysfunctional gammaglobulinemia AND either of the following 2 criteria: 1) A recent episode of life-threatening infection that is reasonably thought to be caused by low levels of polyclonal immunoglobulins; OR 2) recurrent episodes of clinically significant infections that are reasonably thought to be caused by low levels of polyclonal immunoglobulins. <b>Dose:</b> Use 0.4 g/kg every 3–4 wks for prophylaxis. For subcutaneous Ig, a dose of 0.1–0.15 g/kg per wk should be used. <b>Reevaluation</b> should be done every 4–6 months by a hematologist. A trough IgG level of greater than 5 g/L should be maintained. Consideration should be given to increasing the target trough level if an appropriate clinical response is not achieved. Using trough IgG levels may not be practical in patients with secondary immunodeficiencies with IgG subclass deficiency and who experience recurrent severe infections. In such cases it would be sufficient to assess the effectiveness of IVIG based on clinical response.
O T H E R	Primary Immune Deficiency Conditions	0.4–0.6 g/kg every 3 to 4 wks

Full  
guide-  
lines  
on the  
back

# Request Navigation Tool for IVIG Request Approval Process

## Blood Transfusion Services

Patient: \_\_\_\_\_ Order Received (yyyy/mm/dd): \_\_\_\_\_

Note: the numbers shown in parentheses are to be used with the Microsoft Excel IVIG utilization data submission tool to track the path that each request follows.

To be completed by lab technologist:	To be completed by pathologist on call, if required:
<p>Is the request for an indication addressed in the request approval process guidelines?</p> <p><input type="checkbox"/> Yes – proceed to next question below</p> <p><input type="checkbox"/> No – product may be issued* (1)</p>	<p>Result of discussion with the ordering MD:</p> <p><input type="checkbox"/> Request revised to meet guidelines (3)</p> <p><input type="checkbox"/> Request withdrawn (4)</p> <p><input type="checkbox"/> Request unchanged – consultation with clinical expert required – see contact info below</p>
<p>Does the request align with the guidelines?</p> <p><input type="checkbox"/> Yes – product can be issued (2)</p> <p><input type="checkbox"/> No – there is a discrepancy with (check all that apply):</p> <p style="margin-left: 20px;"><input type="checkbox"/> Indication    <input type="checkbox"/> Clinical Criteria    <input type="checkbox"/> Dose</p> <p style="margin-left: 20px;"><input type="checkbox"/> Frequency    <input type="checkbox"/> Duration</p> <p>If “No” – the request is to be reviewed by the blood bank pathologist on call</p>	<p>Result of ordering physician’s consult with clinical expert:</p> <p><input type="checkbox"/> Request revised to meet guidelines (5)</p> <p><input type="checkbox"/> Request withdrawn (6)</p> <p><input type="checkbox"/> Request unchanged after consult (7)</p> <p><input type="checkbox"/> Consultation with clinical expert did not occur (8)</p> <hr/> <p>Product can be Issued? <input type="checkbox"/> Yes <input type="checkbox"/> No</p> <p>Comments:</p>
<p>Technologist:</p> <p>Name: _____</p> <p style="text-align: center; margin-left: 100px;">Print</p> <p>Signature: _____</p>	<p>Hematologist/Pathologist:</p> <p>Name: _____</p> <p style="text-align: center; margin-left: 100px;">Print</p> <p>Signature: _____</p>

## Atlantic IVIG Clinical Expert Consult Record Form For Neurology and Hematology IVIG Request Approval Process

Date (YYYY/MM/DD):			
Clinical Expert Name:	[consultant name here]		
Consulting Physician Name:			
<p>Consult pertained to (check indication for IVIG):</p> <table style="width: 100%; border: none;"> <tr> <td style="width: 50%; vertical-align: top;"> <input type="checkbox"/> ITP  <input type="checkbox"/> Pregnancy-associated ITP  <input type="checkbox"/> Bone marrow transplant  <input type="checkbox"/> Acquired hypogammaglobulinemia   <input type="checkbox"/> Other: _____         </td> <td style="width: 50%; vertical-align: top;"> <input type="checkbox"/> CIDP  <input type="checkbox"/> Multifocal motor neuropathy  <input type="checkbox"/> Myasthenia gravis  <input type="checkbox"/> Guillan-Barre syndrome  <input type="checkbox"/> Stiff person syndrome  <input type="checkbox"/> Multiple sclerosis         </td> </tr> </table>		<input type="checkbox"/> ITP <input type="checkbox"/> Pregnancy-associated ITP <input type="checkbox"/> Bone marrow transplant <input type="checkbox"/> Acquired hypogammaglobulinemia  <input type="checkbox"/> Other: _____	<input type="checkbox"/> CIDP <input type="checkbox"/> Multifocal motor neuropathy <input type="checkbox"/> Myasthenia gravis <input type="checkbox"/> Guillan-Barre syndrome <input type="checkbox"/> Stiff person syndrome <input type="checkbox"/> Multiple sclerosis
<input type="checkbox"/> ITP <input type="checkbox"/> Pregnancy-associated ITP <input type="checkbox"/> Bone marrow transplant <input type="checkbox"/> Acquired hypogammaglobulinemia  <input type="checkbox"/> Other: _____	<input type="checkbox"/> CIDP <input type="checkbox"/> Multifocal motor neuropathy <input type="checkbox"/> Myasthenia gravis <input type="checkbox"/> Guillan-Barre syndrome <input type="checkbox"/> Stiff person syndrome <input type="checkbox"/> Multiple sclerosis		
<p>Result of Discussion:</p> <input type="checkbox"/> Agree with physician's order for IVIG <input type="checkbox"/> Revisions to dose or dosing duration/frequency recommended <input type="checkbox"/> IVIG <i>not</i> recommended  <input type="checkbox"/> Other: _____			
<p>Comments:</p>			
Clinical Expert Signature:			



# Potential for international collaboration

- Alliance of Blood Operators (ABO)
  - CBS, ARCBS, UK NBS, US
- All use the same literature
- Literature reviews are expensive
  - evaluation of the quality of the evidence should be similar...
- Exact recommendations could differ