Clinical Challenges in the Use of IVIG: Managing Adverse Reactions with Appropriate Product Selection

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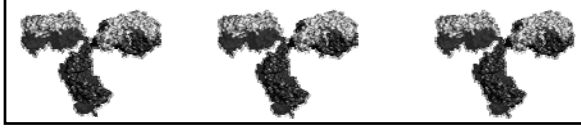


Disclosure

- Jerry Siegel Pharm.D. FASHP
  - Consultant for Cangene Corporation
  - Consultant for Amgen

This presentation was peer reviewed and found to have no conflicts.

Learning Objectives

- Describe the rationale and mechanisms for prioritization of IGIV use.
- Summarize the clinical and pharmaceutical considerations in tailoring IGIV therapy to a patients individual risk profile.
- Explain the evidence for the use of IGIV in various conditions.
- Describe keys to formulary product selection and utilization management

Frequently Asked Questions

- What is IGIV (IVIG)?
- How does it work?
- What is it used for?
- Can it only be infused intravenously?
- What is a “normal” dose?
- Why is the infusion rate important?

FDA approved indications:

- **Primary immunodeficiencies**
- **Idiopathic thombocytopenic purpura (ITP)**
- **Chronic lymphocytic leukemia (CLL)**
- **Kawasaki syndrome**
- **Chronic Inflammatory Demylenating Polyneuropathy (CIDP) (2008)**
- **Bone marrow transplantation (BMT)**
- **Pediatric HIV**

FAQ's: Appropriate Indications

- Why are there so few FDA approved indications?
- How strong is the evidence for commonly used indications?
- Are placebo controlled trials ethical for these indications
- Are there trials comparing one IGIV product to another?
- Is one product better than another for certain indications?
- What are the newest indications for IGIV.

IGIV: Off-Label Uses

- **Allergy/asthma**
- **Dermatologic disorders**
  - **AMBD**
- **Hematologic diseases**
  - **Fetal alloimmune thrombocytopenia**
- **Infectious diseases**
  - **Chronic infection with parvovirus B19**
  - **Adult HIV infection/AIDS**
  - **Adult/neonatal sepsis**
  - **Prophylaxis in preterm neonates**
  - **Toxic shock syndrome**
- **Neurologic diseases**
  - **Drug of choice in:**
    - **GBS**
    - **MMN**
- **Neurologic diseases (cont'd)**
  - **Proven efficacy in:**
    - **CIDP**
    - **Dermatomyositis**
    - **Lambert-Eaton myasthenic syndrome**
    - **Stiff person syndrome**
  - **Probably effective in:**
    - **Myasthenia gravis**
    - **Polymyositis**
- **Organ transplantation/vasculitic diseases**
  - **Cardiac transplantation**
  - **Renal transplantation**

AIDS = acquired immunodeficiency syndrome; AMBD = autoimmune mucocutaneous blistering disease.

Novel Use: Alzheimer's Disease

- Alzheimer's Disease
  - Aggregation of beta-amyloid
  - Causes synaptic blockade in the brain
- IGIV
  - Helps endogenous antibodies bind to beta-amyloid and reverse plaque formation
- Belkin et al Phase I trial showed 2.5 pt. improvement in mini-mental status scores
- Tsakanikas et al Phase II trial showed increase in cognition scores by 5.4 pts. in 9 months

Ohio State University Medical Center IGIV Utilization

Areas of utilization	1993 % Patients N= 76	1999 % Patients N= 100	2002 % Patients N = 117	2007 % Patients N= 173
FDA Approved Indications	76.3%	36%	21%	49%
Neurology	17.1%	52%	68%	36%
Other	6.6%	12%	11%	15%

Chronology of IGIV Developments

1944–1979	Only ImIgG* (aggregates caused severe reactions when given IV)
1979	1st IGIV was Fc cleaved and only for PID
1981	1st intact IGIV also indicated for ITP
mid-1980s	Low-IgA products developed
1990	NIH consensus conference • all IGIV products clinically comparable

*ImIgG, intramuscular immunoglobulin G

Chronology of IGIV Developments

mid-1990s	HCV transmitted in IGIV ▪ New antiviral steps added (S/D; pasteurize) • Manufacturing facilities upgraded
Late 1990s	Sucrose nephropathy warnings
2000	Product commodity vs. differentiation
2002	ADE/thrombosis warnings • Off-label use predominant/novel uses • Reimbursement issues
2003	New advances in IGIV safety
2006	SCIG marketed (Vivaglobin)
2008	New Indications (CIDP)

Patient Case: PID Infusion Problems

- A 12 year old boy has been receiving IGIV at a medical center infusion clinic monthly for the indication of a primary immune deficiency
- It has become increasingly more difficult to infuse because of fever, chills and headaches following the infusions as well as overall malaise. The infusion time is now over 8 hours and at least two days of school is missed per month post infusion
- Venous access has also been a major issue as a catheter was placed but had to be removed due to infection.

What is the next best course of Action?

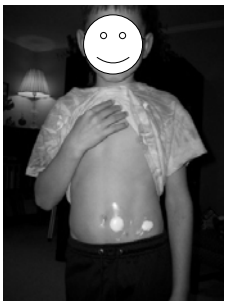
1. Discontinue the use of IGIV
2. Give high dose prednisone as pre-medications
3. Increase rate of infusion
4. Consider SCIG
5. Give smaller doses more often
6. Both 4 and 5

Immune Globulin Administration Routes

- Intravenously
- Intramuscularly
- Subcutaneously
- Orally

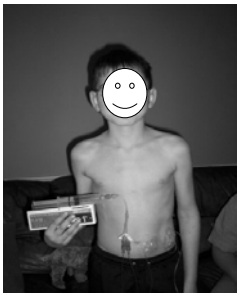
SCIG Infusion sites

- The best sites for SCIG infusion are abdominal or anterior thigh
- Two to Four sites are usually used for infusion
- 15 ml is the limit per infusion site



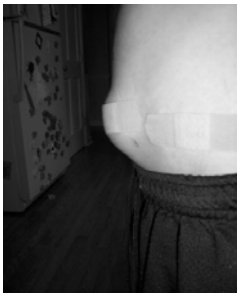
SCIG Infusion

- A simple infuser pump can be used to complete the infusion
- Rate of infusion is <20 ml/hr
- Infusion set can be multiple . Usually two to four sites
- Depending on dose the total infusion time is usually 30 to 45 minutes



Post Infusion SCIG

- The post-infusion “goose bump” will usually go down in a few hours
- Injection site swelling and mild inflammation is normal
- Rare but more serious site reactions have been reported



What is a “normal” IGIV dose?

- Original Doses were for replacement therapy
  - 100-150mg/kg
  - Goal was to achieve an IgG level >600mg/dL
- ITP doses
  - Usually 1gm/kg X 3 days
  - Or 500mg/kg X 4 days
- Some doses as high as 2gm/kg
- Round doses to nearest vial size
- Dose adjusted for morbid obesity

‘Expected’ IGIV Adverse Events

- Infusion rate related
  - Hypo/Hypertension
  - Headache
- ‘Nature of the Beast’
  - Anaphylactoid reactions
    - IgA deficiency
  - Amphotericin-like reaction, fever and shakes
  - Severe back and leg pain
  - Rash
  - Flu-like symptoms
- Post-infusion
  - Severe headache - Aseptic Meningitis

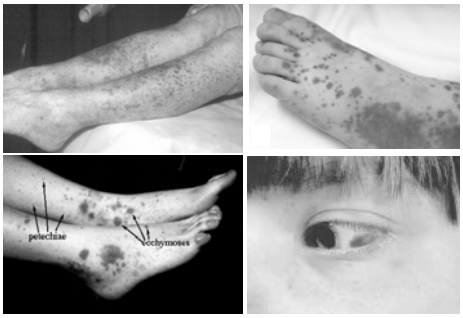
‘Unexpected’ IVIG Adverse Events

- Viral transmission
  - Hepatitis C documented
- Prion transmission
  - Creutzfeldt-Jakob Disease (Prion)
- Renal complications
  - Inc BUN/Cr and renal failure
- Thromboembolic events
  - Pulmonary embolism
  - Deep vein thrombosis
  - MI
  - Hemolytic anemia
- Other
  - Pulmonary embolism

Clinical Case Study

- 39-year-old man
  - Acute ITP (platelet count, 2000)
  - Creatinine clearance,19 mL/mn
- Can IGIV be used?
  - What considerations need to be made?
- What alternatives can be offered?

Clinical Presentation of ITP



Available at: http://www.revolutionhealth.com. Accessed June 7, 2008.

Can IGIV be used?

1. Yes… It should be considered because the ITP is severe.
2. No because the patient has renal insufficiency
3. IGIV should not be used because the ITP is severe
4. Platelet transfusion is the best option

What are the best alternatives to IGIV in this case?

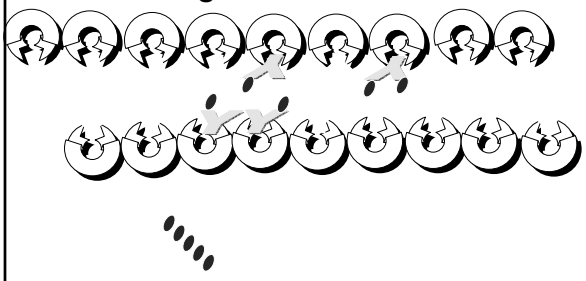
- 1. High Dose Steroids
- 2. High Dose Rho(D) antibody
- 3. mycophenolate
- 4. rituximab
- 5 thrombopoetin mimetic
- 1 & 2 only

First-line Treatment: Intravenous Immunoglobulin (IVIg)

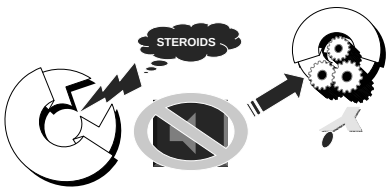
- Dose: 400 mg/kg/day x 5 days or 1 g/kg/day x 2 days
  - Total dose of 140 g
- Initial infusion could take up to 4 hours
- Efficacy:
  - Increased platelet count: 75-92% of patients
  - Complete remission: 50-65% of patients
  - Rapid increase in platelet count
  - Effective in patients with life-threatening blood loss
  - Can be used with corticosteroid use and platelet infusions

Nakhoul IN, et al. *Clin Adv Hematol Oncol.* 2006;4:136-144,153; Stevens E, et al. *Neth J Med*. 2006;64:356-63.

"Running the IVIG Gauntlet!"



Proposed MOA of Steroids



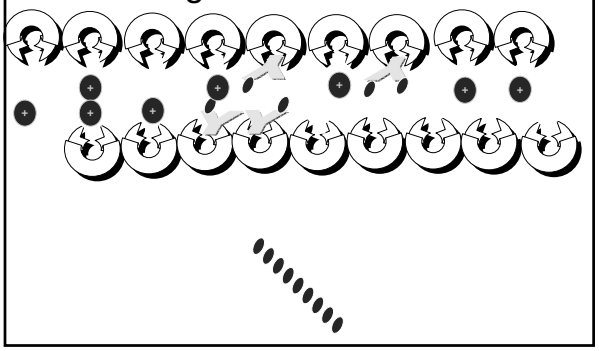
First-line Treatment: IV Anti-D: Rho (D) Immune Globulin

- Single injection of 50 mcg/kg
  - Can be infused over 15-30 minutes
  - Can also be administered as a divided dose on separate days
- No premedication required prior to infusion

IV Anti-D: Rho (D) Immune Globulin

- Efficacy:
  - 66% response rate (65 of 98 patients with chronic ITP and platelet counts <30,000)
    - Response rate is better in patients with platelet counts over 20,000 to less than 10,000
  - Median time to platelet response – 3 days
  - Duration of response – 22 days
- Adverse events:
  - ~50% of patients experienced bleeding at baseline
  - 30% of patients experienced bleeding at day 8

"Running the anti-D Gauntlet!"



IV Anti-D - Rho (D) Immune Globulin Cont.

- Serious adverse effects:
  - Hemolysis, especially with doses over 75 mcg/kg[1]
- Common adverse effects:
  - Chills, headache, pyrexia
- Reduce dose to 25-40 mcg/kg if patient's Hb<10 g/dL[2]
- Important drug interaction:
  - Live virus vaccines (eg, measles, mumps, polio, rubella) should not be administered within 3 months after Rho(D) immune globulin
- AWP for 350 mcg ~$1,500

1. Aledort LM, et al. *Hematology.* 2007;12:289-295; 2. Psaila B, Bussel JB. *Hematol Oncol Clin North Am* 2007;21:743-59.

Case Study: 65-Year-Old Woman With Suspected GBS

- A 65-year-old woman is admitted to the hospital with suspected GBS
- Patient has a history of MI
- Serum creatinine level is 2.0 mg/dL
- Body weight, 120 kg

GBS = Guillain–Barré syndrome; MI = myocardial infarction.

What are the treatment options for this patient?

1. IGIV with high osmolarity and low volume
2. Sucrose stabilized IGIV
3. Plasmaphoresis
4. IVIG with low osmolarity and non-carbohydrate stabilizers
5. 3 & 4 are the best choices

What IGIV dose and infusion guidelines would you recommend?

- 1. Actual body weight of 120 kg with dose 120gm/day for 4 days with rapid infusion protocol
- 2. Ideal Body weight dose of 60 kg and dose of 60grams/day for 4 days
- 3. Adjusted Dosing weight of 90 kg with dose of 45grams for 4 days
- 4. Actual body weight of 120kg with dose of 60 grams for 4 days

FAQ's: What Weight to Use

- Licensing studies all done with actual body weight. Doses were 100-400mg/kg
- Does IVIG distribute to FAT?
- What matters more: Peak or total dose?
- Is there a a maximum dose per/day or infusion?
- Should I use ideal body weight?
- How should I adjust the weight?
- Do I need to consider the weight to calculate infusion rate.
- Do I need to consider the total protein or carbohydrate infusion per hour?

IGIV Product Features Potentially Affecting Tolerability

Finding the "right match" for the patient is a critical clinical concern

- Volume load (rate of infusion)
- Osmolality
- Sodium content
- Sugar content
- IgA content
- pH

Management of Adverse Events

- Different brands have different side-effect profiles that can be patient specific
- Every patient has a maximum infusion rate that they can tolerate, which may differ between brands
- 'Rate' is everything !

Management of Adverse Events

- Hypo/Hypertension and/or Headache
  - Occurs during the infusion
  - Treatment
    - Reduce rate of infusion
    - Monitor BP pre and post infusion & at home
  - Most patients develop tolerance
  - If intolerable, consider switching brands
  - Generally, pre-medication unnecessary

Management of Adverse Events

- Anaphylactoid Reactions
  - Incidence ~1 in 3333
  - May be related to IgA deficiency with anti IgE or anti IgG antibodies against IgA
  - Prevention
    - If true IgA deficiency, use Gammagard S/D™ (low IgA) with caution or do not use IGIV at all
  - Treatment
    - Stop infusion
    - Methylprednisolone, Diphenhydramine, Epinephrine
    - Consider SQ or long-term infusion

Patient Case (Rigors)

- 65 year old female with chronic IgG deficiency
- IVIG infused at 40 grams per month (400mg/kg)
- Standard 3–Phase escalation infusion used
- Maximum infusion rate 150ml/hr
- Patient was receiving Panglobulin NF but it was discontinued and product changed to Gammagard Liquid
- After 2nd dosing escalation patient developed severe rigors

The best choice to treat the rigors

- 1. Slow the infusion of IVIG
- 2. Administer meperidine 50mg IVP
- 3. Administer morphine 4mg IVP
- 4. Administer diphenhydramine 100mg IVP

For future treatments

- 1. IGIV can no longer be given
- 2. Change brand to Carimune NF
- 3. Use same product with very slow infusion rate
- 4. Change to SCIG administration
- 5. Use high dose methyl-prednisolone as a pre-medication
- 6. 2, 3 and 4 are reasonable choices

Management of Adverse Events

- Amphotericin-like reaction, fever and shakes (Rigors)
  - Presents like an amphotericin reaction
  - Treatment
  - Triad – Methylprednisolone, Diphenhydramine, (Meperidine)
    - ? Resume infusion (rate?)
  - Prevention
    - Pre-medication (consider tramadol)
    - ? Change brands
    - Consider SQ or long-term infusion

Management of Adverse Events

- Severe back and leg pain
  - Unique reaction
  - Pain is severe
  - Treatment
    - Triad – Methylprednisolone, Diphenhydramine, Narcotics
  - Prevention
    - Will diminish on subsequent infusions
    - Pre-medications
    - ? Switch brands

Management of Adverse Events

- Rash
  - Treatment
    - Methylprednisolone, Diphenhydramine
  - Prevention
    - Pre-treatment with above
    - Switch brands if intolerable
    - Consider SQ or long-term infusion

Management of Adverse Events

- Flu-like symptoms
  - Generally occurs hours to days after infusion
  - Treatment
    - NSAID's or acetaminophen
    - ? Methylprednisolone, Diphenhydramine
  - Prevention
    - Pre-treatment with above
    - Switch brands if intolerable
    - Consider SC or long-term infusion

Management of Adverse Events

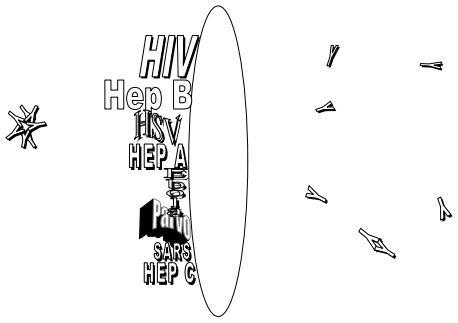
- Post-infusion headache
  - Felt to be an aseptic meningitis
  - Generally occurs hours to days after infusion
  - Often associated with nausea and vomiting
  - Most treatments ineffective
  - Prevention
    - Switch brands if intolerable
    - * Consider SC or long-term infusion

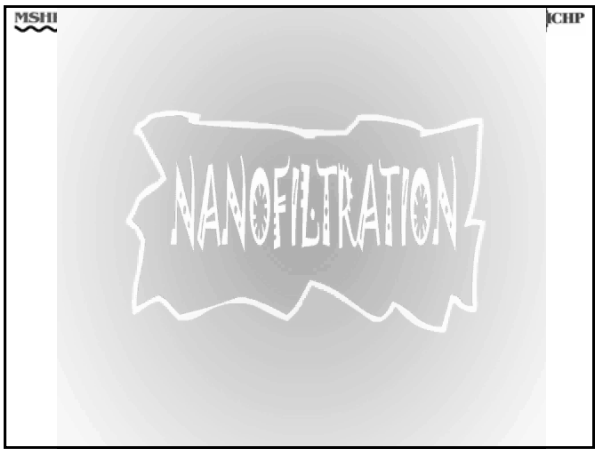
Management of Adverse Events

- Viral transmission
  - Gammagard™ implicated in Hep C transmission
  - Prevention
    - Products re-evaluated for antiviral treatment
      - Solvent detergent added to many preparations
      - Pasteurization added to Gammar-PIV™(discontinued)
      - Chromatography,
      - nanofiltration

Nanofiltration

Nanofiltration





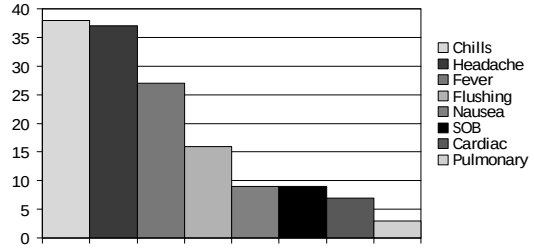
Caprylate Treatment

- Gamunex® is the first product worldwide using caprylate to reduce viral load as part of a new integrated manufacturing process
- Caprylate is a saturated medium-chained (8) fatty acid
- Plant origin
- Non-toxic
- Caprylate precipitation/cloth filtration
- Caprylate incubation

What is the rate of IVIG ADRs

- Ohio State University Medical Center
- Data base 1992-2002
- Number of patients = 1280
- Number of infusions = 7490
- Overall ADR rate (all IGIVs)
  - 29% of all patients
  - 7.6% of all infusions

OSUMC Frequency of Adverse Reactions by Type



Management of Adverse Events

Prevention

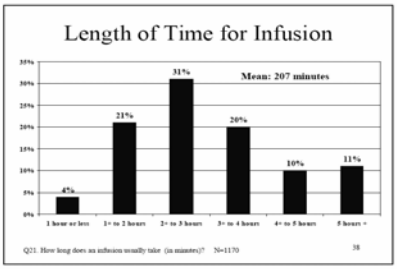
- Exercise caution in patients with:
  - Pre-existing renal problems
  - Diabetes mellitus
  - Volume depletion
  - Concomitant nephrotoxic medications
  - Paraproteinema
  - Age older than 65 years
  - Sepsis
- IVIG administration points
  - Use lower concentrations
  - Minimize sugars and saline
  - Administer slowly

Management of Adverse Events

Thromboembolic events

- Pulmonary embolism
- Deep Vein Thrombosis
- Myocardial infarction
- Hemolytic anemia
- Causes
  - Coagulation Factor XI
  - Increased plasma viscosity
  - Risk factors
  - ? Role of salt vs sugar content
- IVIG administration points
  - Use lower concentrations
  - Minimize sugars and saline
  - Administer slowly

Figure 5: Length of IGIV Infusion in PID Patients



Immune Deficiency Foundation. Treatment experiences and preferences of patients with primary immune deficiency diseases: First national survey, 2003. Available at http://www.primaryimmune.org/pid/2003_idf_survey_complete.pdf. Accessed July 2005.

Volume
Rate of Infusion

- Adverse events:
  - Rapid infusion - anaphylactoid reactions
    - Chills, flushing, tachycardia, back/chest pain, shortness of breath, nausea/vomiting, headache
  - Proposed mechanisms
    - Complement activation
    - Presence of kinins
    - Stimulation of monocytes, cytokine release
  - More common with first infusion, higher doses
  - Premedications?

Sekul EA, et al. Ann Intern Med 1994;121:259-62.

Volume and Rate of Infusion

- Volume for an 80-g dose
  - 5% = 1600 mL
  - 6% = 1333 mL
  - 10% = 800 mL
- Minimum infusion times for an 80-g dose
  - IGIV 6% = 8.3 h
  - IGIV 10% = 3.5 h
- Patient populations at risk
  - Renal dysfunction, heart failure, volume overload

1. Carimune® PI. Kankakee, Ill: ZLB Behring LLC; 2005; 2. Gamunex ® PI. Research Triangle Park, NC: Talecris Biotherapeutics; 2005.

Pharmaceutical Aspects of IGIV: Sodium Content

Product	Sodium Content
Flebogamma 5% DIF (liquid, 5%)	<3.3 mEq
Gammagard S/D, Polygam® S/D (lyophilized)	0.85% (at 5% concentration)
Gammagard Liquid (liquid, 10%)	Trace
Gamunex (liquid, 10%)	Trace
Privigen (liquid, 10%)	Trace
Carimune NF, Panglobulin® (lyophilized)	0%-0.9%, depending on diluent
Octagam (liquid, 5%)	<30 mmoL/L

Pharmaceutical Aspects of IGIV: Sugar Content

Product	Sugar Content
Flebogamma 5% DIF (liquid, 5%)	Polyol (sugar alcohol)
Gammagard S/D, Polygam S/D (lyophilized)	2% Glucose
Gammagard Liquid (liquid, 10%)	No sugar (glycine-based)
Gamunex (liquid, 10%)	No sugar (glycine-based)
Privigen (liquid, 10%)	No sugar (L-proline–based)
Carimune NF, Panglobulin (lyophilized)	10% Sucrose (at 6% concentration)
Octagam (liquid, 5%)	10% Maltose

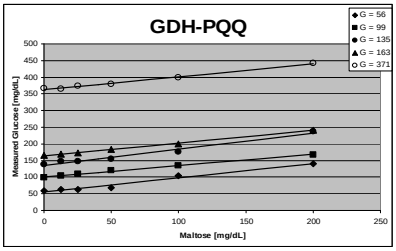
Maltose Warning!

- FDA issued warning about glucose monitoring in patients receiving oral xylose, parenteral maltose, or parenteral galactose
- Several patients died when falsely elevated glucose levels were aggressively treated with insulin. Some patients had been receiving IGIV products containing maltose
- This problem occurs only with the monitoring method that uses an enzyme called GDH-PQQ. This method is employed in some glucose monitoring devices used by diabetics at home and in point-of-care settings
- Caution should be exercised when administering products containing maltose and galactose

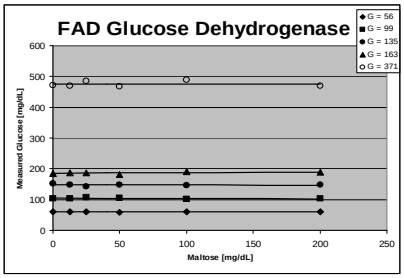
GDH-PQQ = glucose dehydrogenase pyrroloquinolinequinone.

US Food and Drug Administration. Available at: http://www.fda.gov/cber/safety/maltose110405.htm. Accessed November 8, 2007.

Impact of Maltose on Glucose Readings with GDH-PQQ monitors



Impact of Maltose on Glucose Readings with FAD monitors



Pharmaceutical Aspects of IGIV: Osmolality

Product	Osmolality
Flebogamma 5% DIF (liquid, 5%)	342-350 mOsm/kg
Gammagard Liquid (liquid, 10%)	240-300 mOsm/kg
Gammagard S/D, Polygam S/D (lyophilized)	5%: 636 mOsm/L 10%: 1250 mOsm/L
Gamunex (liquid, 10%)	258 mOsm/kg
Privigen (liquid, 10%)	240-440 mOsm/L
Carimune NF, Panglobulin (lyophilized)	In water 3%: 192 mOsm/L; 6%: 384 mOsm/L In saline 6%: 690 mOsm/L; 12%: 1074 mOsm/L
Octagam (liquid, 5%)	310-380 mOsm/kg

IGIV Comparisons: Liquid, 10%

	Gammagard Liquid	Gamunex	Privigen
Process	Cohn-Oncley; cation/anion chromatography	Cohn-Oncley; caprylate/chromatography purified	Cold ethanol, octanoic acid precipitation, anion exchange pH 4
Approved Indications	PID	PID, ITP	PID, ITP
pH	4.6-5.1	4.0-4.5	4.6-5.0
IgG Content	≥98%	≥98%	≥98%
IgA Content	37 µg/mL	46 µg/mL	≤25 µg/mL
Virus Inactivation	Solvent/detergent Low pH	Caprylate precipitation/incubation Low pH	Low pH
Virus Removal	Nanofiltration 35 nm	Depth filtration	Depth filtration, nanofiltration
TSE Labeling	None	Yes	Yes

PID = primary immunodeficiency.

IGIV Comparisons: Liquid, 10% (cont'd)

	Gammagard Liquid	Gamunex	Privigen
PID Study	61 patients	172 patients	80 patients
ADRs: Serious	15 events in 8 patients; 2 aseptic meningitis	8%	20%
ADRs: Nonserious	29%	58%	29% headache, 14% pain
Diluent Used	D5W (not saline)	D5W (not saline)	D5W (infusion line may be flushed with D5W or NS)
Storage	3 years refrigerated	3 years refrigerated	24 months
Room Temperature Storage	9 months	6 months	24 months
Packaging	Latex-free	Latex-free approval pending	Latex-free
Vial Sizes	1 g, 2.5 g, 5 g, 10 g, 20 g	1 g, 2.5 g, 5 g, 10 g, 20 g	5 g, 10 g, 20 g

ADRs = adverse reactions; D5W = 5% dextrose in water; NS = normal saline.

IGIV Stability

- How long is reconstituted IGIV stable?
- What does "use immediately" mean?
- How long are the proteins stable?
- Is there risk of microbial contamination in IGIV preparations?
- Can product stability be extended beyond 24 hours?

IGIV Stability

- Pfeifer RW, Siegel J, Ayers LW. Assessment of microbial growth in intravenous immune globulin preparations. *Am J Hosp Pharm.* 1994;51:1676-1679.
  - 11 formulations of 7 products tested with 3 bacteria and 2 fungi at 3 temperatures over 7 days
  - No growth was noted at 7 days at 3 ºC
  - Stability extended to 72 hours refrigerated
  - Experience at OSUMC over 14 years

What does the near future hold?

- Manufacturer's still seek the "Ideal IVIG"
- New products will soon be available
  - Liquid products with new purification processes
  - Higher concentrations with low osmolality may lead to faster and safer infusion rates
- Continuous improvements to safeguard against viral/prion or beyond transmission

What does the distant future predict?

- More precise diagnostic criteria
- Better prognostic indicators
- Combination therapy for more pronounced and long lasting effects
- Monoclonal Ig targeting to improve precision and efficacy
- Gene therapy for permanent improvement

Clinical Consideration: Matching the IGIV with the Patient Profile

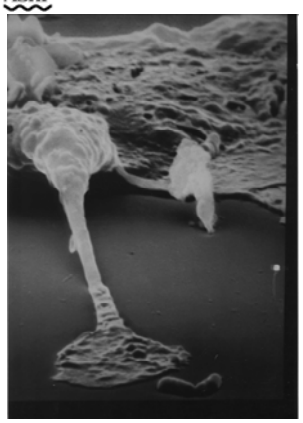
Finding the "right match" for the patient

- IGIV patients are not all the same; nor are IGIV products
- The individual healthcare provider has to make a critical **clinical** decision as to the appropriate product selection

Patient Risk Factors	IGIV Risk Factors					
	Volume load	Sugar content	Sodium content	Osmolality	pH	IgA
Cardiac Impairment	●		●	●		
Renal Dysfunction	●	●	●	●		
Anti-IgA Antibodies						●
Thromboembolic Risk	●		●	●		
(Pre) Diabetic		●				
Elderly Patients	●	●	●	●		
Neonates/Pediatrics	●		●	●	●	

Conclusions

- It is imperative to know the pharmaceutical differences of IGIV products
- Clinical condition of the patient may dictate product selection or modification
- Critical clinical presentation of the patient takes precedent in determining ethical considerations
- All IGIV products are not the same



Questions???

What is the next best course of Action?

1. Discontinue the use of IGIV
2. Give high dose prednisone as pre-medications
3. Increase rate of infusion
4. Consider SCIG
5. Give smaller doses more often
6. Both 4 and 5

Can IGIV be used?

1. Yes… It should be considered because the ITP is severe.
2. No because the patient has renal insufficiency
3. IGIV should not be used because the ITP is severe
4. Platelet transfusion is the best option

What is the best alternatives to IGIV in this case?

- 1. High Dose Steroids
- 2. High Dose Rho(D) antibody
- 3. mycophenolate
- 4. rituximab
- 5 thrombopoetin mimetic
- 1 & 2 could be used in this case

What are the treatment options for this patient?

1. IGIV with high osmolarity and low volume
2. Sucrose stabilized IGIV
3. Plasmaphoresis
4. IVIG with low osmolarity and non-carbohydrate stabilizers
5. 3 & 4 are the best choices

What IGIV dose and infusion guidelines would you recommend?

- 1. Actual body weight of 120 kg with dose 120gm/day for 4 days with rapid infusion protocol
- 2. Ideal Body weight dose of 60 kg and dose of 60grams/day for 4 days
- 3. Adjusted Dosing weight of 90 kg with dose of 45grams for 4 days
- 4. Actual body weight of 120kg with dose of 60 grams for 4 days

The best choice to treat the rigors

- 1. Slow the infusion of IVIG
- 2. Administer meperidine 50mg IVP
- 3. Administer morphine 4mg IVP
- 4. Administer diphenhydramine 100mg IVP

For future treatments

- 1. IGIV can no longer be given
- 2. Change brand to Carimune NF
- 3. Use same product with very slow infusion rate
- 4. Change to SCIG administration
- 5. Use high dose methyl-prednisolone as a pre-medication
- 6. 2, 3 and 4 are reasonable choices