Adopting Best Practice for Infusion Teams

Lori Mayer, DNP, MSN, RN
Shirley O’Leary, APN-BC
Elida Grienel, APN-BC

Infusion Therapies

• Nursing professionals have increasing responsibility in managing multiple sclerosis clinical disease and treatment
• NPs/PAs/RNs play important roles in educating patients about disease-modifying therapy options, decisions on therapy and managing potential adverse effects
Objectives

• Discuss practical applications of infusion therapy
• Framework for professional nursing approach to providing safe infusion care
• Gain an understanding of the approach to patient selection for infusion therapy
• Define recognize monitor and manage infusion related reactions
• Describe a broad understanding in mechanism of action, as well as infusion benefits vs risk
• Discussion

Patient Selection: Managing the Decision

• Is there a magic wand….crystal ball?
• No . . . . then what are the variables for patient selection for any disease modifying therapy, including infusion therapy?
  – Point in disease continuum
  – Aggressiveness of disease course
  – Breakthrough disease
  – Pregnancy, fertility
  – Systemic conditions
  – Congruity of MRI
  – Patient’s desires
  – Health care variables i.e. experience, knowledge, cost, availability

Medications

FDA Approved Infusion Therapies:
• Methylprednisolone
• Mitoxantrone
• Natalizumab
• Alemtuzumab
• Ocrelizumab (currently with the FDA)

Off-label Infusion Therapies:
• Rituximab (Off-label)
• Cyclophosphamide (Off-label)
• Intravenous Immunoglobulin (IVIG, Off-label)

Therapies under investigation:
• Ublituximab
• Anti-lingo

MS and the Immune System

• Etiology of MS, as yet not completely understood, is postulated to be due to immune dysregulation
• Experimental autoimmune encephalomyelitis (EAE), given its many histologic features similar to the MS disease state, is used for study
• MS pathogenesis likely involves activated CD4+ myelin-reactive T cells and involvement of B cells

[Garg & Smith, 2015]
Role of T-Cells in MS

- Peripheral activation of autoreactive T-cells is postulated to be related to a loss of self-tolerance
- CD4+ T-helper 1 (TH1) responsible for pro-inflammatory cytokines
- CD4+ T-helper 2 (TH2) thought to be responsible for antinflammatory cytokines
- CD8+ T-cells are additionally thought to be involved in autoreactivity

B Cells in MS

- B cells are present in the CNS in all forms of MS
- Autoreactive B cells, which form during B-cell development process, exit from the bloodstream to the CNS and accumulate in patients with MS
- Evidence suggest that B cells may contribute to MS disease-state through:
  - Antigen presentation
  - Cytokine production
  - Auto-antibody production
  - Formation of ectopic lymphoid structures in the CNS
Patient Selection for Cyclophosphamide (Cytoxan) Off Label

- Off label use of high-dose cyclophosphamide, a chemotherapy treatment targeted at eradicating autoreactive B and T cells
- Cyclophosphamide has good bioavailability within the CNS
- Generally utilized in patients with aggressive MS, with some data in RR and SPMS in a small (15 pt.) phase II study
- Study by Gladstone et al. looked at a 4 day infusion with median EDSS of 6.5

(Awad & Stuve, 2009; Gladstone et al., 2011)

Cyclophosphamide Benefit vs. Risk

- Patient Selection
  - Not for use in persons with indwelling urinary catheters or recurrent infections
  - Safety issues include bladder cancer and gonadal toxicity
- Risks and side effects
  - Nausea, vomiting, anorexia, hemorrhagic cystitis
  - Infection (febrile neutropenia)
  - Amenorrhea
  - Neoplasia
  - Alopecia

(http://www.accessdata.fda.gov/drugsatfda_docs/label/2013/012141s090,012142s112lbl.pdf, accessed January 18, 2016)
Medication Management: Cyclophosphamide

- Dose calculated based on patient’s BSA
- Must be mixed under a laminar flow hood, using preservative free sterile water as diluent
- All chemo safety protocols and personal protective equipment must be used
- Must be administered with an angiocath of 22 gauge or larger
- Generally the usual MS protocol is monthly for 1 year and then twice monthly for one additional year.


Cyclophosphamide Nursing Considerations

- Patient preparation:
  - Determine pt’s BSA and calculate dose
  - Baseline CBC, pregnancy test if applicable
  - Give patient prescription for antiemetic
  - Use of mesna, for protection against hemorrhagic cystitis
- Patient Education:
  - Potential side effects of nausea and vomiting, mild alopecia, cystitis, amenorrhea

(Cited from: Gladstone et al., 2011 & Rinaldi et al., 2009)
Cyclophosphamide Nursing Considerations

- Patient Education
  - Need for oral hydration day before, of, and after treatment
  - Mesna administration, a thiol compound, can decrease the risk of hemorrhagic cystitis
  - Need for CBC day of, and 8, 11 and 14 days post treatment
  - Use of oral antiemetic
  - Need for reliable birth control method, category D pregnancy

Intravenous Immunoglobulins (IVIG)
Off Label: Patient Selection

- (IVIG) have been used off label since the 1980’s for a variety of autoimmune diseases
- IVIG MOA is multifaceted, including anti-infective, immunoregulartory, and anti-inflammatory properties
- Overall, well tolerated, severe adverse reactions are rare, usually associated with first dose
- Early studies have reported a consistent benefit to the reduction of relapses
- In a study by Fazekas el al., using 2 doses of IVIG over only 1 year did not show any clinical or MRI benefit
- Thrombosis and renal adverse events

IVIG Medication Management: Off Label Use

- Tolerability
  - Rate of infusion
  - Consider the specific product
  - Comorbidities of the patient i.e. congestive heart failure, renal function

- Reconstitution
  - Lyophilized provides greater flexibility
  - Sterile water for reconstitution provides lower osmolarity
  - Liquid is less time intensive but requires refrigeration
  - Concentration of sugars has an affect on the osmolarity of the solution

(Waterhouse, 2011)

IVIG Nursing Considerations

- Dosing varies; 0.4g/kg to 1g/kg is generally accepted dosing
- Patient preparation:
  - Informed Consent
  - Baseline labs, CBC, CMP
  - (most specifically renal and liver function), IgA level?, hepatitis serology, MRI
  - Pregnancy category C
- Patient education:
  - Rationale
  - Side effects: H/A, chills, rigors, backache, n/v...sometimes flu like symptoms
  - Anaphylactic reactions can occur, but are rare.
- Infusion Protocol

(Elovaara et al., 2008 & Waterhouse, 2011)
High Dose Pulse Methylprednisolone (Solumedrol) Patient Selection

- Anti-inflammatory and immunosuppressive effects
- Steroids are not known to be toxic to the bone marrow
- Use of IV steroids as well as high dose oral steroids are used to treat relapses in MS, widely used in other auto-immune diseases
- Optic neuritis trial, role of postpartum Intravenous steroids, steroids during pregnancy

(Ornelas et al., 2011; Tsoi & Lee, 2011)

Methylprednisolone Administration

- **Tolerability**
  - Rate of infusion
  - Comorbidities of the patient
- **Reconstitution & administration**
  - 1 gram daily over 30 minutes to 4 hours
  - Mix in NS or D5W 100-250 cc
  - May be stored up to 48 hours after mixing

(http://www.accessdata.fda.gov/drugsatfda_docs/label/2011/011856s103s104lbl.pdf accessed January 20, 2016)
Methylprednisolone Nursing Considerations

- Patient preparation
  - Informed Consent
  - Labs? U/A?
  - Hx of DM, Osteoporosis, Vit. D deficiency, frequent UTIs

- Patient education
  - Rationale
  - Side effects: metallic taste, GI upset, insomnia, H/A, mood swings, fluid retention, hyperglycemia.
  - Long-term side effects review
  - Pregnancy category C

- Infusion Protocol

Mitoxantrone Patient Selection: Benefit vs. Risk

- Mitoxantrone, an immunosuppressive approved for treatment of rapidly worsening MS and the only current treatment approved for secondary progressive MS (SPMS)
- Use of this treatment dropped significantly with higher than expected numbers of cardiomyopathy and leukemia in the MS population in postmarketing studies
- Black box warning specific to MS patients; muga is required yearly post last infusion of mitoxantrone to monitor for long-term cardiac effects
- Cardiotoxic events have been seen in patients to whom doses below the current maximum dose of 140mg/m squared have been administered
Mitoxantrone (Novantrone) Administration

• Tolerability
  – Hydration
  – Antiemetics

• Reconstitution and Administration
  – Understanding of chemo administration
  – Considered a extravasation hazard as is the case with all chemotherapies
  – Should be mixed under sterile conditions, contains no preservatives, requires dilution with NS or 5% Dextrose
  – Administered after dilution via a port into a free flowing infusion of NS or 5% dextrose over no less than 3 minutes, generally 10 to 15 minutes
  – Those HCP administering should wear appropriate gowns, goggles, and gloves; Chemo disposal is required
  – IV antiemetic administered after mitoxantrone administration

Mitoxantrone Nursing Considerations

• Patient preparation
  – Rationale
  – Informed Consent
  – Hx. of previous chemo and infectious disease hx. i.e. TB, HIV, UTIs.
    Baseline labs including U/A, CBC (ANC > 1500, platelets > 100,000, nl liver function) CMP, pregnancy
  – Pregnancy category D

• Patient education
  – Labs required baseline and 10-14 days post treatment
  – Muga required prior to each treatment; and yearly post treatment
  – Suggest immunizations, dental work at least 4-6 weeks prior to first tx
  – Risk vs benefit
  – Administration of mitoxantrone can cause the urine and sclera of the eye to have a blue-green color for the first 24 hours after treatment

• Infusion Protocol

(http://www.accessdata.fda.gov/drugsatfda_docs/label/2012/019297s035lbl.pdf accessed January 15, 2016)
Allergic and Hypersensitivity Reactions

• Potentially severe or life-threatening allergic reaction that can occur very quickly—as fast as within a couple of minutes of exposure to the allergen
• Does not occur with first infusion
  – Timing related to infusion, can occur within minutes or be delayed: can occur anywhere from 10-12 hours to days post exposure
  – Symptoms may include:
    • Urticaria, angioedema, hypotension, dyspnea, hoarseness, wheezing, bronchospasm
    • Shock, rigors, nausea, vomiting, abdominal cramps
  – Mediated by IgE, generally this initial exposure does not produce symptoms, but becomes apparent with repetitive exposure - the immune system is over-reacting to a perceived danger
An Allergic Reaction - Overview

Anaphylaxis Protocol

• If emergent, proceed as follows:
  – If suspected and the patient experiences shortness of breath or shock syndrome call 911 plan transfer to nearest medical treatment facility
  – Administer Epinephrine 1/100 (1mg/ml) 0.2 ml to 0.5 ml IV, IM or SQ, may repeat once in 5 minutes
  – Give diphenhydramine 25-50mg IVP
  – Methylprednisolone 125mg IVP
  – May initiate a continuous infusion of Sodium Chloride 0.9% 500mls
  – Any patient receiving Epinephrine must go to ER
Cytokine Release Reactions

Non-Allergic Cytokine Release Infusion-Related Reactions

- Monoclonal antibodies have potential for a non-allergic infusion reaction caused by cytokine release
- Recognition and expert management may enable patients to be re-challenged with the monoclonal antibody, potentially improving clinical outcome (Vogel, 2010)
- May occur anytime after the start of the infusion
  - non-immune mediated and overlap with allergic symptoms
  - Rash, headache, nausea, fatigue, tachycardia, weakness, pruritis
  - Causes: i.e. drugs, rate of infusion
  - Typically mild to moderate in severity, may appear as a complex of symptoms include: chill, fever, nausea, headache, rash itching
- Vasovagal reactions

(Chung, 2008; Namey et al., 2010)
Cytokine Release Reaction

- Binding of monoclonal antibody to the antigen on target cell
- Causes an initiation of events with chemokine mediated recruitment of immune cells and complement to the area
- Then cell lysis occurs via binding to immune effector cells to the antibody which targets the cell for destruction
- Results in cytokine release generating cytokine related reactions

Treating Infusion/Hypersensitivity

- Have your protocol in place, this should cover your initial actions
  - Stopping the infusion
  - Starting NS and maintaining access
  - Placing the patient in a modified Trendelenburg and assessing the ABCs (airway, breathing, circulation, defibrillation)
- Notify your supervising physician
- Help to keep the patient calm and obtain assistance

(Chung, 2008; Namey et al., 2010)
What is your Pharmacologic Therapy?

- Diphenhydramine 25-50mg IV, Ranitidine 50 mg IV, Cimetidine 300mg IV, Oxygen, Short acting bronchodilator inhaler i.e. Albuterol, Corticosteroids PO or IV
- EPINEPHRINE 1:1000, 0.15 to 0.3ml IM
  - Immediately if severe reaction, may repeat every 5-15 minutes as needed
  - When to call 911
  - Follow-up

(Peperen, 2009; Chung, 2008; Lenz, 2007; Namey et al., 2010)

Premedication and Re-challenge?

- We have learned a great deal from Oncology about premedication
  - Antihistamines
  - Acetaminophen
  - Steroids
  - Ranitidine
- Rechallenge?
  - Mild to moderate pending resolution of symptoms with interventional treatment
  - Policies and procedures, prescriber decision

(Lenz, 2007; Joerger, 2012)
Emergency Medications

- Stock epinephrine (e.g., EpiPen)
- Oxygen
- IV fluids
- Diphenhydramine
- Atropine
- Analgesic
- Narcotic analgesic
- Methylprednisolone
- Beta-adrenergic agonist Inhaler

Monoclonal Antibodies/MS Therapies

- Targeted treatment for many different types of cancers and non-malignant disorders
- Engineered with newer biotechnical techniques
- Unique side effect profile
  - potential for non-allergic infusion reactions caused by cytokine release
- Recognition and expert management of cytokine-release reaction
  - enable rechallenging with monoclonal antibody
  - potentially improving outcomes
Monoclonal Antibodies

• Natalizumab (Tysabri)
  – Targets α4-integrin on T-lymphocytes
• Alemtuzumab (Lemtrada)
  – Targets CD52 receptor on T and B lymphocytes
• Ocrelizumab (Ocrevus) (awaiting FDA approval)
  – Targets CD20 on B lymphocytes
• Rituximab (Rituxan) (off label)
  – Targets CD20 on B lymphocyte
Natalizumab (Tysabri) Patient Selection

- Humanized monoclonal antibody
- An $\alpha_4$ integrin antagonist that blocks leukocyte migration from the blood vessels to sites of inflammation by inhibiting the action of cell adhesion molecules-trafficking
- Indicated as monotherapy for the treatment of patients with relapsing forms of multiple sclerosis is generally recommended for patients who have had an inadequate response to, or are unable to tolerate, an alternate MS therapy
- US Food and Drug Administration (FDA) approval placed no restriction for use as a second line therapy in the treatment of MS patients

Natalizumab Benefits & Risks

- Associated with the risk for progressive multifocal leukoencephalopathy (PML)
- Some literature suggests that in patient with aggressive appearing disease, natalizumab may be considered in first 12-24 months regardless of JCV antibody status.
- JCV antibody status considerations
  - Negative antibody status theoretical risk of developing PML (<1:10,000)
  - Positive antibody status stratification: titer < 1.5 and > 1.5 in patients with no previous immunosuppressive treatment
  - Previous immunosuppressive risk
  - Rebound risk with natalizumab discontinuation

[Nicholas et al., 2014; Tur & Montalban, 2014]
Natalizumab Medication Management

• IV infusion given every four weeks

• Tolerability
  – Generally very well tolerated
  – Side effects very comparable to placebo in phase III studies
    • Headache most common side effect
  – Contraindications include persons with a history of PML, or a
    hypersensitivity to natalizumab

• Reconstitution and Administration
  – 300mg 15 ml in 100ml of NS, infuse over 1 hour followed by 1
    hour of observation
  – Does not require a hood for mixing; requires sterile, aseptic
    technique

(O’Leary et al, 2007)

Natalizumab Nursing Considerations

• Patient preparation
  – TOUCH paperwork
  – Baseline lab work, what would you include and how often?
    What does the package insert recommend? CBC, CMP?
  – Current medication list, comorbid conditions
  – Pregnancy category C

• Patient education
  – Risk versus benefit
  – Patient expectations

• Infusion Protocol

Alemtuzumab (Lemtrada) Patient Selection

- Humanized monoclonal antibody directed against CD52 a cell surface antigen expressed on T and B lymphocytes and other immune cells
  - Presumed MoA: Selection/Depletion/Repopulation
  - Depletion antibody-depended cellular cytolysis; complement mediated lysis
  - Contraindication includes persons with a history of HIV

- FDA approved for those patients who have relapsing forms of MS and because of its serious risks it is generally reserved for patients who have had an inadequate response to 2 or more MS treatments
  - Prioritize prognostic factors
    - Suboptimal response, clinical activity
    - Relapse recovery response
    - Neuroimaging activity, Brain MRI, Spinal cord MRI abnormalities
    - Intolerable side effects, abnormal lab values
    - Patient considerations, demographics, genetic, lifestyle

Alemtuzumab Benefits & Risks

- CARE-MS II - Comparison of Alemtuzumab and interferon beta-1a (Rebif)
  - Met co-primary endpoint results
    - 49% reduction ARR vs Rebif®
    - 42% risk reduction in time to confirmed disability progression vs Rebif®

- Boxed warning
  - Risk for serious, sometimes fatal autoimmune conditions and serious, life-threatening infusion reactions, and the drug may cause an increased risk for malignancies, including thyroid cancer, melanoma, and lymphoproliferative disorders

- May cause serious side effects
  - Infusion reactions (Anaphylaxis / Cytokine release)
  - 5 year data infusion reactions most frequent with first course
  - Managed with pretreatment, patient education, systematic medication, monitoring and adjustment of rate of infusion
  - Delayed side effects
    - Autoimmune conditions (ITP, other blood disorders, kidney disorders, thyroid disorders)

- REMS program – available only through a restricted distribution program
Alemtuzumab Medication Management

- Recommended: Two courses of treatment
  - Course Year 1: days 1-5/ dosage 12 mg day/60 mg total
  - Course Year 2: days 1-3/dosage 12 mg day/36 mg total

- Infusion premedication management
  - Given 1000 mg Methylprednisolone IV days days 1-3 both courses
  - Initiate antiviral prophylaxis for herpetic viral infections
  - May consider oral or IV premedications
    - Antihistamines, anti-pyretics

- Infusion preparation
  - Large molecule liquid concentration packaged Alemtuzumab 10 mg/ml in small vial
  - Refrigerate vials at 2-8 degrees centigrade, single use only
  - Requires sterile, aseptic technique, inspect for particulates
  - Use 18 gauge needle draw up 1.2 ml in 3 cc syringe and dilute in 100 ml 9% Sodium Chloride or 5% Dextrose in water, gently invert bad, protect bag from light
  - Deliver infusion over 4 hours with two hour observation period post infusion

Alemtuzumab Nursing Considerations

- Prepare patient for infusion process by educating on possible IAR
  - 92% of alemtuzumab patients experienced infusion reactions
    - Rash, headache, pyrexia, nasopharyngitis, nausea
  - 3% included anaphylaxis in two patients

- Screen for latent or active infection
- Check baseline skin exam done and yearly HPV exam

- Confirm baseline lab evaluations done within 30 days of infusion
  - CBC with differential, Serum creatinine level, Urinalysis with microscopy
  - Thyroid function
  - CD4 count (although not required it may be considered good medical practice. This is not part of the CBC order therefore must be requested)
  - Check updated on vaccines 6 weeks prior to infusion
Nursing Considerations

- May want to consider additional labwork per site protocol
  - HIV, Hep B, Hep C, VZV, Quantaferon Gold (TB screening), Serum pregnancy test, CMP
- During infusion
  - Hourly vital signs
  - Monitor appropriate hydration and nutritional status
- Communicate long-term safety monitoring

Nursing Considerations Post Infusion

- Remind patient to continue antiviral prophylaxis
  - 2 months or CD4 count ≥ 200 cells
- Educate on REMS program long-term safety monitoring
  - Monthly safety labs for up to 48 months post last infusion
    - CBC with differential, Serum creatinine level, Urinalysis with cell counts
    - Quarterly Thyroid function
- Annual skin exams to monitor for melanoma
- Monitor for symptoms of thyroid cancer
Rituximab (Rituxan) Off Label/Benefits and Risks

- Rituximab is a chimeric monoclonal antibody that selectively depletes CD20+ B cells
  - FDA approved for non-Hodgkin’s lymphoma, chronic lymphocytic leukemia
    - Complement-mediated cytotoxicity and antibody-dependent cell-mediated cytotoxicity
- Bar-Or et al, (2008) RRMS trial; 72 week open label phase I
  - Safety and tolerability, primary outcome
  - Two courses both divided doses of 1000mg 6 months apart followed 72 weeks
  - No SAE noted, mild to moderate infusion reactions which decrease with subsequent infusions, fewer T2 lesions and reduction in relapses over 72 weeks
- Hawker et al. primary progressive trial, OLYMPUS Phase II/III was
  - unable to show a difference in time to confirmed disease progression (CDP) against placebo
  - In planned subgroup analysis there was a statistically significant treatment effect by several secondary exploratory endpoints in patients younger than 51 and especially in those with enhancing lesions
  - Patients received 1 gram of IV Rituximab or placebo every 24 weeks for 4 courses

Rituximab Administration and Nursing Considerations

- Rituximab may only be administered as a intravenous infusion
- Severe infusion reactions can be fatal
- In treatment of RA patients glucocorticoids, mainly methylprednisolone 100mg 30 minutes prior to each infusion is suggested to decrease infusion reactions
- Consider premedications with acetaminophen/antihistamines
- Hepatitis B virus (HBV) reactivation can occur
- Recommendations for CBC and platelet counts every 2-4 months during Rituximab therapy in RA
  - cytopenias can continue beyond the actual treatment period
- Pregnancy category C
Ocrelizumab (Ocrevus) Currently with FDA

• Ocrelizumab is a humanized, monoclonal antibody that selectively targets depletes CD20-expressing B cells (developing and mature B cells), while preserving the capacity for B-cell reconstitution and pre-existing humoral immunity
  — CD20 marker not expressed on stem or mature plasma B cells

• Presumed MoA (Winiarska, 2011)
  — Antibody-dependent cellular cytotoxicity
  — Complement-dependent cytotoxicity
  — Antibody-dependent cellular phagocytosis
  — Direct apoptosis


Ocrelizumab

• Ocrelizumab dosing 600 mg infusion every 24 weeks
  — Cycle 1 (300 mg) divided in two separate infusions 15 days apart
  — Subsequent cycles every 6 months
  — IV methylprednisolone 100mg (optional analgesics/antipyretics/antihistamines) prior to infusion (Hauser et al, ACTRIMS2016)

• Lower immunogenicity risk could improve the safety and efficacy with long-term treatment of chronic diseases Incidence of formation of anti-drug antibodies were very low (Song, et al., 2016)
Ocrelizumab Risks & Benefits

• Opera I and Opera II identical randomized double-blind, double dummy Phase III trials to evaluate efficacy and safety OCR vs interferon B-1a (96 weeks)
  – Primary outcome results showed 46-47% reduction in AAR compared to IFNB-1a at 96 weeks
  – 12 and 24 week confirmed disability progression reduced by 43% and 37% in OCR in the two studies

• Infusion related reactions (IRR) more common in OCR arms; however serious infections similar for OCR and interferon treatment arms

• IRRs (OCR 34.4% vs Rebif 9.7%) were generally mild to moderate in severity, most commonly occurred at first infusion and were manageable with premedication
  – Pruritus, rash, throat irritation and flushing

(Selmaj. et al., 2015 EAN Poster)

Future Therapies Under Investigation

• Ublituximab
  – Third generation Anti-CD20 chimeric monoclonal antibody
    • Targets a unique epitope on B-lymphocyte CD20 antigen
  – Phase II studies have just been initiated

• Anti-LINGO
  – Humanized monoclonal antibody antagonized LINGO-1 receptor
  – In animal modes blocking LINGO-1 promotes myelin repair
  – Phase II RENEW study of anti-LINGO-1 in acute optic neuritis demonstrating remyelination of axons
Infusion Therapy Conclusion

• The future development of infusion monoclonal antibody therapy continues
• Expertise of infusion nursing profoundly impacts the safety and care of MS patients
• Infusion reactions can be managed with pretreatment, patient education, systematic medication, monitoring and adjustment of rate of infusion

References

• Cyclophosphamide package insert. Retrieved January 20, 2016 from
References

- LEMTRADA® (alemtuzumab) [package insert]. Genzyme Corporation, Cambridge MA.
- Selma, et al., EAN2015 [poster presentation] Hoffmann-La Roche Ltd.
- TYSABRI® (natalizumab) [package insert]. Biogen, Cambridge, MA.
Thank You - Questions ??

Anaphylaxis

- Potentially severe or life-threatening allergic reaction that can occur very quickly—as fast as within a couple of minutes of exposure to the allergen
- Requires an initial exposure to an antigen
- Production of IgE antibody
- Antibody residue binds to mast cells/basophils
- Re-exposure, the antigen and antibody bind and receptors activate
- Here comes the histamine.....and other cytokines
- Location of histamine receptors predict type of symptoms
- For all practical purposes, the treatment of all reactions follows the same algorithm
- Have you ever encountered anaphylaxis in your clinic?