Anaphylaxis: What Every Anesthetist Should Know….

John O'Donnell, CRNA, MSN
Director, University of Pittsburgh School of Nursing
Nurse Anesthesia Program
Associate Director, WISER

Participants will:

1. Describe the epidemiology of anaphylactic reactions during anesthesia.
2. Differentiate between anaphylactic and anaphylactoid responses
3. Discuss the clinical presentation of anaphylaxis during anesthesia.
4. Identify agents used during local, regional, or general anesthesia most likely to precipitate an anaphylactic reaction.
5. Prioritize treatment interventions during perioperative anaphylactic reactions according to patient presentation.

Content Outline:

1. Epidemiology of Anaphylactic Reactions
2. Components of the Anaphylactic Reaction
3. Clinical Presentation of Anaphylaxis
4. Differentiation of Anaphylaxis and Anaphylactoid Reactions
5. Important Lab Markers of Anaphylaxis
6. Triggers during the Perioperative Period
7. New and Traditional Treatment of Anaphylaxis
8. Conclusion

Anaphylaxis: What Every Anesthetist Should Know….

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(Winter Institute for Simulation Education and Research

Increasing Incidence of Food Allergy

- Teen Dies from Kissing Boyfriend
  - Ref paper: USA Today, Nov. 29, 2005
- Residual peanut antigen in saliva
- ~ 150-200 anaphylactic food deaths in US
  - Increasingly rapidly
    - Today Show, November 30, 2005

Anaphylaxis

- Multiple medication reactions associated with the term
  - Significant confusion in the literature
- One definition?
  - "a clinical syndrome characterized by acute cardiopulmonary collapse following antigen (foreign substance) exposure"
- Definition is broadening – American Association of Allergists and Immunologists

Levy JH: Anaphylactic Reactions in Anesthesia and Intensive Care. Second Edition. Stoneham, Butterworth-Heinemann Publishers, 1992.

History
Epidemiology & Anaphylaxis
Components of the Reaction
Anaphylactic vs. Anaphylactoid Clinical Presentation
Lab Markers
Perioperative Triggers
Treatment

Why More?? Unknown But Two Possible Explanations

- Exposure theory
  - Modern life has resulted in exposure to many more pollutants and antigens
  - 95% of time for most Americans is indoors
- Sanitized environment theory
  - The world around us and our children is far cleaner than ever before in history
  - We pasteurize and sanitize everything
  - Therefore- reduced exposures- failure of immune system to develop 'desensitization' to some antigens and over-reaction to later exposures

History

- **1st Case??**
  - Tomb of King Menes of Egypt: Wasp sting: 2640 BC
- **1902: Portier/Richet**
  - Sea anemone toxin in dogs
  - Greek: Ana (against), Phylaxis (protection)
- **1913**:
  - Richet receives the Nobel Prize in Physiology for his collaborative research with Portier
- **1967:**
  - **Ishikaza et al.: IgE discovered**
- **1975:**
  - **Coombs/Gell: hypersensitivity reaction classification**

Whiteley SM. The history of immediate hypersensitivity reactions [letter]. [Historical Article. Biography. Letter] Anesthesiology. 82(1):316, 1995 Jan
Brown AFT, Anaphylactic Shock: mechanisms and treatment. Emergency Medicine. 12,1994;89-100.

Classification of Immune Reactions

- Type I:
  - IgE (IgG) reactions: immediate hypersensitivity
- Type II:
  - ATB dependent, cytotoxic
- Type III:
  - Immune complex reactions: complement activated
- Type IV:
  - T-cell mediated: contact dermatitis (glove related)
    - Common
  - Organ rejection: host vs. graft or graft vs. host diseases

Coombs and Gell, 1975: classification of hypersensitivity reactions

Variance in Perioperative Incidence

- Skewing with higher incidence of reaction related to muscle relaxants?
- Sample characteristics/ study design?
  - Size
  - Women > men (as many as 70% of cases- all causes)
  - Age
  - Genetics
- Under-reporting?
- Diagnostic capability?

Laxenaire MC, Mertes PM, Moss J. *Anaphylactic and Anaphylactoid Reactions During Anesthesia*: Advancing Knowledge in Healthcare & McMahon Publishing; 2004

Anaphylaxis in the 'World'

- Anaphylaxis reported to represent 0.02% of all ER admissions
  - Idiopathic event: ~ 50% of cases
  - Food: peanuts and shellfish
    - ~30,000 events
  - Drugs:
    - Antibiotics and NSAIDs
  - Bee or wasp stings
  - Radiocontrast media
  - Latex

- Incidence in ALL inpatients of ~ 1: 3000

Liebowicz P. *Anaphylactic and Anaphylactoid Reactions* in Adkinson NF, Middleton E. *Middleton's allergy: principles & practice*. 6th ed. St. Louis: Mosby; 2003.
Sampson HA. Anaphylaxis and emergency treatment. Pediatrics. 2003;111(6):1601-1608

What is the *true* incidence of perioperative anaphylaxis?

Acta Anaesthesiol Scand 2001; 45: 1196–1203
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ISSN 0001-5172

Review Article

Rocuronium and anaphylaxis – a statistical challenge

J. H. LAAKE[1] and J.-A. RØTTINGEN[2]
[1]*Department of Anaesthesiology, National Hospital (Rikshospitalet), and* [2]*Foundation for Health Services Research (HELTEF), Central Hospital of Akershus, Norway*

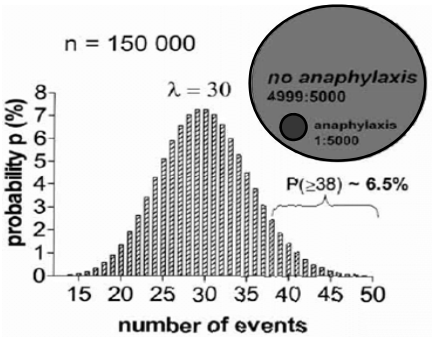
Perioperative Anaphylaxis

- Represents ~10% of anesthetic complications
- Incidence reported as 1:1,000 to 1:25,000 anesthetics…

Why the disparity?

•Laxenaire MC, Mertes PM, Moss J. *Anaphylactic and Anaphylactoid Reactions During Anesthesia*: Advancing Knowledge in Healthcare & McMahon Publishing; 2004.
•Lieberman P. Anaphylactic reactions during surgical and medical procedures. *J Allergy Clin Immunol.* Aug 2002;110:S64-69.
•Hepner DL, Castells MC, Goldstein S, Amar D. Anaphylaxis During the Perioperative Period. Pharmacotherapeutic Considerations in Anesthesia. 2003;5(1):1381-1395.
•Naguib M, Magboul MM. Adverse effects of neuromuscular blockers and their antagonists. *Middle East Journal of Anesthesiolology.* 1998;14(5):341-373

Statistical Problem With Rare Events



Laake JH, Rottingen JA. Rocuronium and anaphylaxis--a statistical challenge. *Acta Anaesthesiologica Scandinavica.* 2001;45(10):1196-1203

Annual Mortality Estimates for Specific Agents: Overall US

- **Anaphylactic**
  - **Food:**
    - **150-200/yr**
  - **IV PCN:**
    - **100-500/yr**
  - **Stinging insects**
    - **40-100/yr.**
- **Anaphylactoid**
  - **RCM:**
    - **< 500/yr**
  - **NSAIDS?**

Brown AFT, Anaphylactic Shock: mechanisms and treatment. *Emergency Medicine.* 12,1994;89-100.
Sampson HA. Anaphylaxis and emergency treatment. *Pediatrics.* 2003;111(6):1601-1608

Components of Reaction

- **Antigen**
  - **Protein, large, MW>8000**
    - **Regularly occuring molecular groupings**
  - **Hapten**
    - **Smaller molecules (drugs, chemicals, etc)**
    - **Attached to endogenous protein**
- **Leukocytes = Basis of intrinsic immunity**
- **Lymphocytes = Basis of acquired immunity**
- **Antibodies**

Perioperative Mortality Rate?

- **Mortality remains significant- as high as 3.4-6.0% of cases of anaphylaxis...Why?**
- **Perhaps simulation science can provide some clues….**
  - **In one study, *none* of 42 anesthesiologists tested on a high fidelity simulator made the correct diagnosis within the first ten minutes**
- **Upon recognition, the majority did not implement a structured plan of treatment**

Jacobsen J, Lindekaer AL, Ostergaard HT, et al. Management of anaphylactic shock evaluated using a full-scale anaesthesia simulator. Acta Anaesthesiol Scand 2001;45:315–9

Leukocytes: Intrinsic Immunity

Types	#/ml (plasma)	%	Comment
Granulocyte: • Neutrophils	3000-6000	55-65	Bacteria/virus defense. Phagocytes
Granulocyte: • Eosinophils	0-300	1-3	Parasite defense
Granulocyte: • Basophil • Mast cell	0-100	0-1	Concentrated in perivascular tissues. Granules: mediators
Monocyte	300-500	3-6	Phagocytes. R-E system.
Lymphocyte (B &T)	1500-3500	25-35	Humoral/cellular immunity.
Plasma cell	?	?	ATB factories. From B lymphocytes.

How Common is Allergy to Anesthetic Agents Overall- August 2006?

- Tomayo E et al. *Allergy* 2006;61:952-953
  - Prospective trial- N=424
  - Skin prick testing for 30 anesthetics
  - 4.7% had at least one positive
  - Muscle relaxants were #1
  - Previous history of drug allergy was the only predictor

Lymphocytes: Acquired Immunity

B Cells	T cells
Humoral Immunity(Blood)	Tissue Immunity/Cellular
Origin: Stem cells	Origin: Stem cells
Processed: Bursal equivalent	Processed: Thymus
Stored: Lymph tissue sites	Stored: Lymph tissue sites

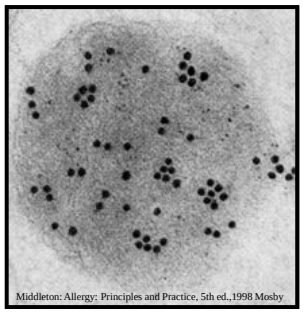
Antigen contact:
• Activated: T helper.
• Plasma Cell :
  • Makes antigen specific antibodies
  • Clones: amplification
  • Clones: become B memory cells that remain in lymph tissue.
	Antigen Contact:
	• Helper T gives off lymphokines, activates B cells.
	• Cytotoxic and suppresser T's are activated .
	• T's develop antigen specific receptors.
	• T memory cells stored in lymph tissues.

Anaphylactic Response & Antibody Formation

- **Initial contact**
  - **Sensitization of cellular/humoral components**
- **2nd exposure = ↑ degranulation of mast cells….. Why?**
  - **Mast cells have 40-100,000 IgE attachment sites**
  - **Antigen must cross bridge two adjacent IgE antibodies to degranulate**
  - **↑ allergy history = vast ↑ IgE sites**

Are all mast cells alike?

Are they essentially the same cells as basophils aside from location?



High magnification view of grating/lattice structure in granules of MC_{TC} cell. In humans, a nomenclature is used based on neutral protease composition, MC_T for mast cells with tryptase alone, and MC_{TC} for those with tryptase, chymase, mast cell carboxypeptidase, and cathepsin G

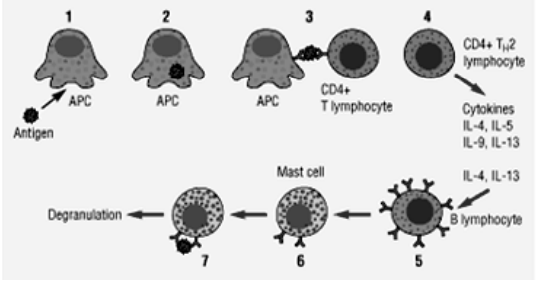
Antibodies

- **Serum glycoproteins produced by plasma cells(humoral)**
- **Attach to immune cells and spray antigen with contents**
- **Activate the complement system**
  - Cascade: amplifies the response
  - C3A, C4A, C5A

Yoshino A. Nagashima S. Uchiyama M. **Anesthesia** & **Analgesia**. 81(4).1995:878-9

- *Anaphylactoid reaction in a surgeon to surgical rubber*
  - Do not differentiate the terminology
  - No previous symptoms
  - Full blown reaction requiring resuscitation

Antigen Presenting Cell to Degranulation



Why the Confusion of Terms?

- Anaphylaxis
  - IgE mediated
    - Indirect mast cell effect
  - Antigen-antibody response results in mast cell/basophil degranulation, mediator release
- Anaphylactoid
  - Direct mast cell degranulation as a result of the chemical structure of drug
  - IgE cannot be implicated
    - *May* be less severe

Which is Which?

An Anaphylactoid reaction *may* be less profound, however, it cannot be clinically distinguished from an Anaphylactic reaction.

Onset, Duration, Severity

- **True anaphylaxis has a *fast onset***
  - Typically < 5 min in the perioperative setting
    - Depends on exposure route and patient
- **Duration and severity of response is multifactorial (can last >24 hr)**
  - **Atopy / anxiety/ other variables**
  - **Time sequence of previous exposure**
- **Does dose matter?**

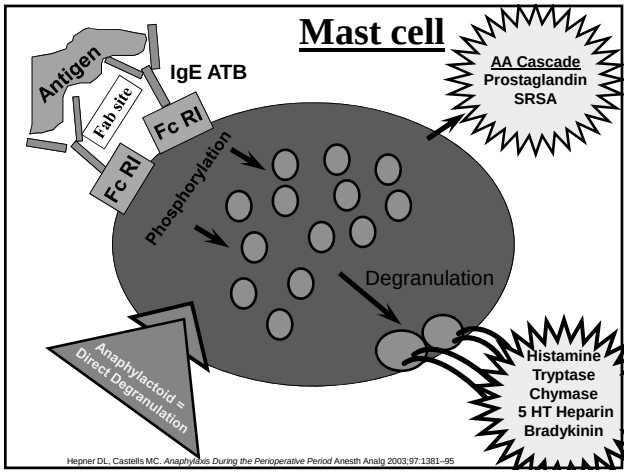
Other Immunologic: Non-Anaphylactic

- Non-IgE mediated but identical symptom complex
- A variety of substances which activate *complement* which then activates neutrophils
  - Complement fragments are considered to be anaphylactoxins
  - Histamine and a variety of other mediators are released from mast cells
- Identical presentation

Symptoms During Anesthesia

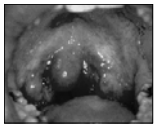
- **Most common: circulatory collapse**
  - Most common symptom during GETA (49%)
  - Sympathoadrenergic responses may be blunted
  - Tachycardia may not be present
- **SAB / Epidural = sympathectomy**
  - Therapy may need to be even *more* aggressive

O'Donnell J. Anaphylactic and Anaphylactoid Responses in the Perioperative Setting. (Abstract) *Proceedings of the American Association of Nurse Anesthetists Annual Meeting*. Aug 2005.



Hepner DL, Castells MC. *Anaphylaxis During the Perioperative Period* Anesth Analg 2003;97:1381–95

Symptoms

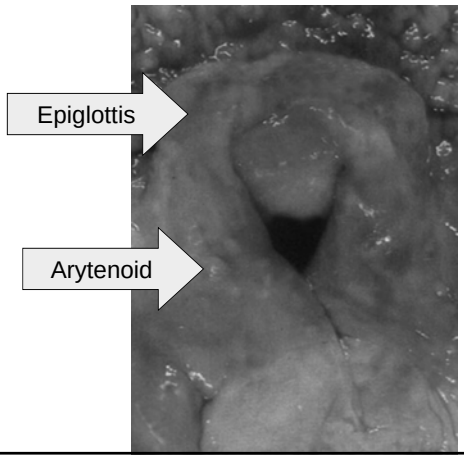


- **Clinical Triad**
  - Hypotension
  - Rash
  - Bronchospasm

Images: How to Recognize Intra-operative Anaphylaxis *Cleveland Clinic Foundation Website* http://www.anes.ccf.org:8080/pilot/latex/DIAG_AN.HTM

Perioperative Diagnosis

- More difficult- why?
  - Loss of subjective complaints (signs)
  - Absence of cutaneous clues (draping)
  - Use of multiple drugs (masking)
- Overdependence on technology??
  - That pressure can't be right- can it??



Symptoms: Awake vs. Asleep

System	Manifestation
Cutaneous	Flushing, pruritis, urticaria, angioedema
Cardiovascular	Tachycardia, dysrhythmias, pulmonary hypertension, decreased SVR, cardiovascular collapse, cardiac arrest
Respiratory	Cyanosis, rhinitis, wheezing, shortness of breath, increased $ETCO_2$, respiratory failure, bronchospasm, acute pulmonary edema, increased peak airway pressure
Central Nervous System	Confusion, agitation, decreased level of consciousness, sense of impending doom *(angor animi)*.
Hematologic	DIC
Renal	Decreased renal output secondary to tubular necrosis
Gastrointestinal	Nausea, vomiting, diarrhea, cramping

Table 1: Possible manifestations of anaphylactic reactions in the perioperative setting[1-3,6,8]

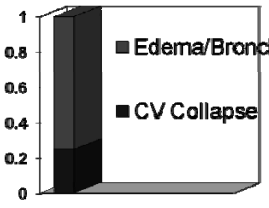
O'Donnell J. Anaphylactic and Anaphylactoid Responses in the Perioperative Setting. (Abstract) *Proceedings of the American Association of Nurse Anesthetists Annual Meeting*. Aug 2005.

Testing for Allergy

- In Vivo
  - *Skin Prick Test* (epidermal)
  - Intradermal test
  - Bronchial challenge
  - Scratch test
  - Patch test
- In Vitro
  - RAST/Elisa
  - Serum IgE assays
  - Complement C3-C5
  - Serum Tryptase levels
    - 40-60 min peak
  - Carboxypeptidase**

Mortality: General vs. Perioperative

In fatalities: > 50% die within the 1st hour



Most common perioperative (recognized) presenting sign is cardiovascular collapse

*Netzel MC, Anaphylaxis: Clinical Presentation, immunologic mechanism, and treatment. *Journal of Emergency Medicine*. 4, 1986; 227-236

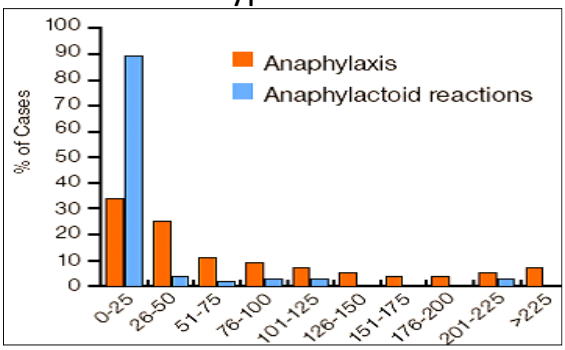
Testing Table

Testing Chart for Allergy Related to Anaphylaxis

Test	Time Frame	Comments
Skin Prick Test (epidermal)	6-8 wks after reaction	Remains 'gold' standard Done as panel on back or forearm
Bronchial challenge	Done as screening for aero-allergens weeks after a reaction	Risk of bronchospasm or airway event
Scratch test/ Patch test	6-8 weeks after reaction	Alternatives to skin prick Patch test for latex allergy might include a 'finger cot'
Histamine	Within the 1st hour due to brief ½ life	Avoid during pregnancy and in patients receiving heparin (false negative) Other reactions release
Tryptase	Measure within 1 hour of reaction (detectable up to 6 hours)	Values above 25 mcg/Liter strongly support anaphylaxis In some cases not detectable
Complement (C3/C5)	Measure within 1 hour	Non- specific, other mechanisms also cause elevation
IgE antibody (RAST) (radioimmunoassay)	Typically weeks post reaction Can be drawn in emergent phase	Easily testing will substantiate IgE mechanism
Carboxypeptidase	Measure within 1 hour	Newest marker Is detectable in cases in which tryptase is not elevated

Table: O'Donnell JM. Current Reviews in Anesthesia- manuscript
Walls A F. Mast Cell Carboxypeptidase Identified as a Blood Marker of Anaphylaxis American Academy of Allergy, Asthma and Immunology (AAAAI) National Meeting 2006. Rausch M. Reuters http://www.medscape.com/viewarticle/524961

Plasma Tryptase as Marker



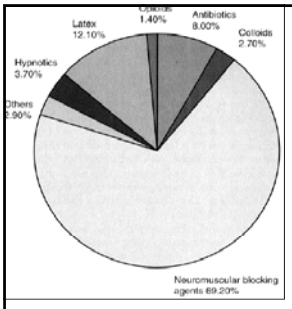
Laxenaire M-C, Mertes PM, Moss J. Special Report: Anaphylactic and Anaphylactoid Reactions During Anesthesia. *Anesthesiology News.* Sept 2004:1-8.
Mertes et al. *Anesthesiology.* 2003;99:536-545

Initiating Perioperative Agents

- **ATB:**
  - **PCN**
    - **Most frequent anaphylactic in general population at ~3%**
  - **Vancomycin**
    - #1 anaphylactoid ATB
  - **Cephalosporins**
- **Hypnotics**
  - **Propofol/STP**

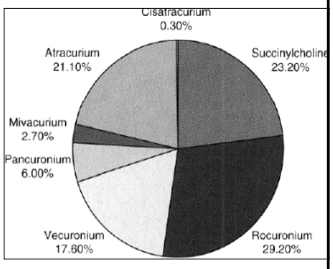
Testing Risks

- Clinical challenges??!!
  - Out on a limb…way out
  - *In vivo* vs. *in vitro* safety
- Novembre E et al. Skin-prick-test-induced anaphylaxis *Allergy.* 50, 6, 1995;511-513



Neuromuscular-blocking agents (%) responsible for anaphylaxis in France (*n* = 336) from January 1997 to December 1998.

Agents involved (%) in anaphylaxis during anesthesia in France (n = 477) from January 1997 to December 1998.



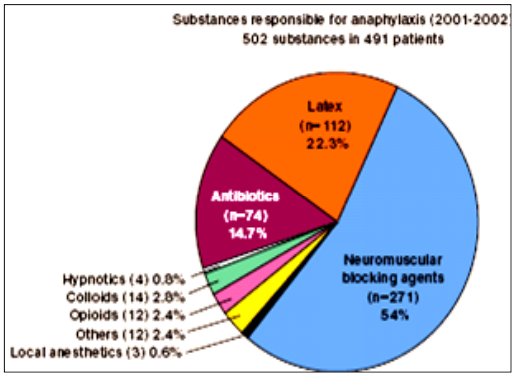
Mertes PM. Laxenaire MC Allergic reactions occurring during anaesthesia. European Journal of Anaesthesioly. 19, 4, 2002;240-262

Initiating Perioperative Agents

- **Muscle relaxants:**
  - **50-70% of cases!**
    - **Also # 1 anaphylactoid**
  - **Quaternary amines**
    - **Soaps, perfumes, makeup sensitize**
- **Latex:**
  - **Special populations**

Hepner DL, Castells MC. Anaphylaxis During the Perioperative Period Anesth Analg 2003;97:1381–95
Vervloet D, Magnan A, Birnbaum J, Pradal M. Allergic emergencies seen in surgical suites. Clinical Reviews in Allergy and Immunology 1999;459-67.

7th French Survey



Laxenaire M-C, Mertes PM, Moss J. Special Report: Anaphylactic and Anaphylactoid Reactions During Anesthesia. *Anesthesiology News.* Sept 2004:1-8.

Muscle Relaxant Anaphylaxis

English and French literature over 25 years (1980-2004): cases	
Muscle relaxants	3,509
Succinylcholine	1,437
Vecuronium	905
Atracurium	475
Pancuronium	251
Rocuronium	387
Mivacurium	40
Cisatracurium	11
Others	3

Laxenaire M-C, Mertes PM, Moss J. Special Report: Anaphylactic and Anaphylactoid Reactions During Anesthesia. *Anesthesiology News.* Sept 2004:1-8.

Contrast Media

- Usually anaphylactoid
- Adverse reactions
  - 1-3 % with non-ionic
  - 5-12% with ionic
- Severe reactions rare
  - Mortality 0.9:100,000

Costa N. Understanding contrast media. *Journal of Infusion Nursing.* Sep-Oct 2004;27(5):302-312.

Patients with True MR Allergy

Possible Choices

- Avoidance when possible
  - Regional anesthesia
- Monovalent hapten therapy
  - Molecules with only 1 quaternary group may be one treatment.
  - Would run as infusion

Watkins J., Adverse reaction to neuromuscular blockers: frequency, investigation, and epidemiology. Acta Anaesth. Scaninavica. 38S, 102,1994;6-10.
Moneret-Vautrin DA, Kanny G, Gueant JL, Widmer S, Laxenaire MC, Prevention by Monovalent Haptens of IgE Dependent Leucocyte Histamine Release to Muscle Relaxants. 107,1995; 172-175.

1^0 Treatment

- **Call for <u>HELP</u>**
- **Terminate or rapidly complete surgery**
- **Stop exposure to possible precipitating agents**

Perioperative Triggers

- **Colloids**
  - **Dextran/ Hetastarch**
  - **T & C blood (~3%)**
- **Opioids**
  - **MSO4 = probably anaphylactoid**
- **Others**
  - **Ester locals (PABA)**
  - **Chymopapain**
  - **Aprotinin**
  - **Protamine (NPH)**
    - Purified pork and humulin have ↓
  - **Radiocontrast media**
    - Ionic vs. non-ionic

Hepner DL, Castells MC. Anaphylaxis During the Perioperative Period Anesth Analg 2003;97:1381–95
Vervloet D, Magnan A, Birnbaum J, Pradal M. Allergic emergencies seen in surgical suites. Clinical Reviews in Allergy and Immunology 1999;459-67.

1^0 Treatment

- **Airway**
  - **100% O2**
  - **Intubate if indicated: Use muscle relaxant?**
- ***Epinephrine***
  - **Dose: Dependent on symptoms**
    - **Mast cell effects, alpha effect, beta effects**
- **Fluids: Aggressively replace**
  - ***Loss of 40-50% of IV volume**
  - **2-4 liters of balanced solution**

Lieberman P. Use of epinephrine in the treatment of anaphylaxis. *Current Opinion in Allergy & Clinical Immunology.* Aug 2003;3(4):313-318.

Choice of Epinephrine Route/Dose

- IV
  - Severe symptoms
  - Dose Range: 0.1mcg/kg to large doses in severe reactions
- SQ vs. IM
  - Emergent reaction...
  - Dose: 100-500 mcg (0.1 to 0.5 mg)

- Sublingual??

Brown AFT, Anaphylactic Shock: mechanisms and treatment. *Emergency Medicine*. 12,1994;89-100.
Wyatt R. Anaphylaxis. *Postgraduate Medicine*. 100, 2, 1996;87-99
Simmons KJ. Sublingual Epinephrine Tablet Promising for Anaphylaxis. American Academy of Allergy, Asthma and Immunology (AAAAI) National Meeting 2006. Rausch M. Reuters ttp://www.medscape.com/viewarticle/524961

Caution IS Warranted...

- CV: MI, heart failure etc…
- Case Report:
  - Horowitz BZ et al. Fatal intracranial bleeding associated with prehospital use of epinephrine. *Annals of Emergency Medicine*. 8,6,1996;725-727.

Vastus Lateralis via Blue-Jean


Figure 2. Use of autoinjectable epinephrine. a. Remove gray safety cap. b. Hold epinephrine as shown, placing black tip at right angle to thigh and pressing hard until autoinjector mechanism functions (there should be a click). Injection may be made through clothing. Hold in place for 10 seconds. Remove injector and massage area.

Courtesy of Elo Elmaa, ALK-Abello, Reading, Berkshire, England.

- IM route has been demonstrated to be clearly superior with respect to efficacy.

Lieberman P. Use of epinephrine in the treatment of anaphylaxis. *Current Opinion in Allergy & Clinical Immunology.* Aug 2003;3(4):313-318.

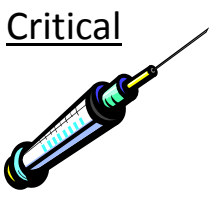
Caution vs Urgency of Giving Epi

- Pumphrey-2000
  - 92-98
    - 168 anaphylaxis deaths in UK from all causes
    - 3 were due to epi overdose
  - Epinephrine was used in 62% of cases but only *14% of the time* before cardiac arrest
    - Compares with 11% in recent US Study
      - (AAAI 2006)

Pumphrey RSH. Lessons for management of **anaphylaxis** from a study of fatal reactions. *Clinical & Experimental Allergy. 30(8):1144-1150, August 2000.*

Epinephrine Is Critical

However……



2^0 Treatment or Pre-Treatment

- **Other inotropes or infusions**
  - **Vasopressin**
- **Albuterol**
  - B_2 agonism
- **Corticosteroids**
- **Glucagon**
- **Atropine**
- **$H_{1/2}$ antagonism**

•Wyatt R. Anaphylaxis. Postgraduate Medicine. 100, 2, 1996;87-99
•Hepner DL, Castells MC, Goldstein S, Amar D. Anaphylaxis During the Perioperative Period. Pharmacotherapeutic Considerations in Anesthesia. 2003;5(1):1381-1395.

Problems With Giving $H_{1,2,3}$ Antagonists During Anaphylaxis?

- Administer both H_1 and H_2 blockers in treating anaphylaxis to balance effect?

Histamine H3 Receptor Blockade Improves Cardiac Function in Canine Anaphylaxis

CARLA CHRUSCH, SATYENDRA SHARMA, HELMUT UNRUH, EDGAR BAUTISTA, KRIKA DUKE, ALLAN BECKER, WAYNE KEPRON, and STEVEN N. MINK

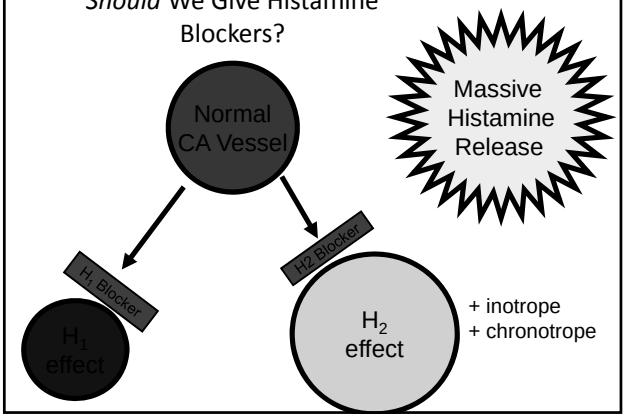
Department of Medicine, Sections of Respiratory Disease and Critical Care Medicine; Department of Medicine, Section of Respiratory Medicine; Department of Allergy and Immunology; Section of Thoracic Surgery; and Department of Pediatrics, University of Manitoba, Winnipeg, Manitoba, Canada

Beta Blockers and Increased Risk?

- Javeed N. etal. 1996:
  - Case analysis:
    - 52 yo male for cardiac cath, on B blockers
    - Pretreated with steroid, Benadryl then RCM given
    - Severe reaction: aggressive therapy, finally responded to glucagon, NE, DA
- B blockers:
  - Theory: may increase mediator release?
  - Interfere with epi effectiveness
  - Consider glucagon and atropine

Javeed N. etal. Refractory Anaphylactic Shock Potentiated by Beta *Blockers Cath. and Cardiovasc. Diagnosis* 39, 1996;383-384

Should We Give Histamine Blockers?



Biphasic Responses/Recurrence

- 1-20% of cases*
  - Lee, 2000, found a 6% incidence in 108 pediatric cases.
  - Occur 1-8 (as far out as 24) hours after symptoms seem to resolve
- Argues for post-response monitoring and admission to ICU

Lee, Joyce M. MD. Greenes, David S. MD. Biphasic Anaphylactic Reactions in Pediatrics. *Pediatrics. 106(4) Part 1 of 2:762-766, October 2000.*

Take Home on Histamine Blockers

- H_1 receptor blockers have demonstrated efficacy
- H_2 receptor blockers are ***not*** recommended in management of acute anaphylaxis
  - If given alone, may precipitate vasoconstriction
  - May have cross reactivity for H_3 – danger of unopposed sympathetic outflow → cardiac ischemia

Nault MA et al. Effects of Selective H1 and H2 Histamine Receptor Antagonists Loratidine and Ranitidine on Autonomic Control of the Heart *Anesthesiology* 2002;96:336-341.

Questions/Comments