

Anaphylaxis in the operating room

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Anaphylaxis is defined as an acute life-threatening systemic event triggered by the sudden release of mediators from basophils and mast cells after exposure to a triggering agent.

The mediators released are numerous and include **tryptase, kinins, leukotrienes, prostaglandin D2, platelet-activating factor (PAF), and histamine**. Histamine is presumed to be the primary mediator of the anaphylactic reaction.¹

Within the OR, anaphylactic reactions have a reported incidence of 1 in 4000 to 1 in 25,000 and have a 3-10% mortality.

Bronchospasm is the most common presenting sign in patients under general anesthesia (78.3%). Other signs and symptoms of anaphylaxis in the OR for patients under general anesthesia include **hypotension** (63.9%), **urticaria** (54.2%), **desaturation** (49.4%), **angioedema** (16.9%) and **cardiovascular collapse** (6%). Patients undergoing neuraxial or regional anesthesia may present with other signs and symptoms (eg, **pruritus or dyspnea**), depending on their level of sedation.

Patients with a history of allergies and atopy are more likely to undergo an anaphylactic reaction. Moreover, the medical history often impacts the clinical presentation during anaphylaxis. For example, a patient with a history of congestive heart failure is more likely to experience cardiovascular collapse, and a patient with a history of smoking tobacco is more likely to experience bronchospasm.

Presentation

The clinical presentation of anaphylaxis in the OR is varied, ranging from **mild to severe** respiratory compromise and including cardiac arrest. Rapid diagnosis of the event is critical for achieving a positive patient outcome. The following four-grade scale, which may be used to classify intraoperative anaphylactic events:

- **Grade 1 – Anaphylaxis with cutaneous signs only**
- **Grade 2 - Anaphylaxis with cutaneous manifestations, as well as hemodynamic instability**

- **Grade 3 – Anaphylaxis with life-threatening reactions, including cardiovascular collapse**
- **Grade 4 – Anaphylaxis with cardiac arrest**

Approximately 80% of anaphylactic reactions are grade 2 or 3.

Etiology

1. Neuromuscular blockers:

The most common cause of anaphylaxis in the OR is the neuromuscular blocking agent, which has been cited as causative in 50-70% of cases. Clinical presentation is often within minutes of induction or other use of the agent.

The mediators of the allergic reaction are IgE antibodies to the tertiary or quaternary ammonium groups to which patients become exposed through prior surgical procedures, other drugs, foods, or household items.

2. Latex

Latex is responsible for another 16.9% of anaphylactic reactions in the general OR. However, for the pediatric population, latex allergy is of particular significance, accounting for 80% of all intraoperative anaphylactic events. Because exposure to latex primarily takes place through the skin or mucosa, presentation is commonly delayed for 15-60 minutes after contact.

Risk factors for latex allergy include the following:

- **History of multiple surgical procedures**
- **Employment within the healthcare field**
- **History of allergy to certain fruit and nuts (eg, kiwi, mango, passion fruit, avocado, strawberry, or chestnut)**

3. Antibiotics

Antibiotics are the third most common causative agent of anaphylactic reactions in the perioperative period (8% incidence).

The beta-lactams, including penicillin, cephalosporins, ampicillin, amoxicillin, carbapenems, and monobactams, account for as many as 75% of all deaths from anaphylaxis in the United States.

The incidence of cross-reactivity between penicillin and cephalosporins is on the order of 10%. However, the cross-reactivity depends on the cephalosporin used; those with beta-lactam side chains (eg, ceftriaxone) are more likely to be implicated. Cephalosporins may also cause allergic reactions through haptens unique to that class.

Other antibiotics, including **vancomycin, bacitracin, gentamycin, metronidazole and clindamycin**, have given rise to multiple reports of hypersensitivity reactions but only rare case reports of perioperative anaphylactic reactions. Allergic reactions to antibiotics are generally more common with IV administration than with oral.

4. **Other agents**

Multiple other agents used in the perioperative period have been implicated in intraoperative anaphylaxis, including the following:

- Bone cement
- Local anesthetics, with esters being more common causes of anaphylaxis than amides
- Colloids (eg, albumin, dextran, and hetastarch [hydroxyethyl starch])
- Cleaning solutions (eg, chlorhexidine and povidone-iodine)
- Coagulation agents (eg, heparin and aprotinin)
- Sugammadex
- Induction drugs (eg, opioids, barbiturates, benzodiazepines, and propofol)

The incidence of anaphylactic reactions with each of these agents is **small**.

Management

Anaphylaxis may present as a biphasic entity. Management of the acute phase of anaphylaxis intraoperatively requires **discontinuing the presumed allergen**, obtaining and **maintaining a secure airway**, and **managing potential cardiovascular compromise**. In most instances, particularly where the anaphylactic reaction is at grade 2 or higher and where the surgical procedure has yet to begin or has just begun, the operation should be canceled and the patient stabilized.

The **drug of choice** in the management of anaphylaxis is **epinephrine**. As many as 80% of deaths related to anaphylaxis generally have been attributed to failure to treat with epinephrine early. As an alpha agonist, epinephrine **decreases the vasodilatory** effects of histamine release, and its beta properties **relax smooth muscle in the airway** and **prevent the release of additional immune mediators**. Epinephrine also has a positive inotropic effect.

For patients with refractory hypotension, additional boluses of epinephrine and even an epinephrine infusion may be required to maintain hemodynamic stability. In some instances, other vasoactive agents (eg, vasopressin), **Trendelenburg position**, and **IV fluids** may be required. Patients who are on beta blockers and are nonresponsive to epinephrine should be treated with IV fluids and glucagon.

Otherwise, the strategy employed intraoperatively is often dictated by the clinical presentation. Bronchospasm is the most common presentation intraoperatively and often necessitates **intubation and ventilation with 100% oxygen**, in addition to the use of epinephrine. Providers may often include **bronchodilators** (eg, albuterol and ipratropium bromide) and inhalation anesthetics to relax airway tone.

Corticosteroids are administered to **decrease edema** and to block the release of immune mediators. Hydrocortisone has a rapid onset of action and is the preferred steroid in this circumstance.

H1 blockers (eg, diphenhydramine) and H2 blockers (eg, ranitidine and famotidine) may be beneficial in both early and late phases of the reaction for as long as 24 hours after the event and should be strongly considered as adjuncts.

Drug dosages

IV adrenaline bolus = 1mcg/kg

IM adrenaline bolus = Adult 500mcg
6-12 years 300mcg
<6 years 150mcg

IV adrenaline infusion = 0.1mcg/kg/min

With 3mg in 50mls dilution, mls/hr = mcg/min. *For an adult commence at 7mls/hr.*

Additional therapy

Aminophylline bolus up to 5mg/kg IV or IM

Hydrocortisone bolus (slow IV or IM)

>12 years.....	200mg
6-12 years.....	100mg
6 months-6 years...	50mg
0-6 months.....	25mg

Chlorpheniramine bolus (slow IV or IM)

>12 years.....	10mg
6-12 years.....	5mg
6 months-6 years...	2.5mg
<6 months ...	250mcg/kg

In the unlikely event that bronchospasm does not respond to adrenaline therapy, alternative treatment is outlined in *Severe Bronchospasm* - see tab 14.
