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## Guidelines for Best Practices for Treatment of Anaphylactic Reaction in the Surgical Patient

### Introduction

The following Guidelines for Best Practices were researched and authored by the AST Education and Professional Standards Committee, and are AST approved.

AST developed the Guidelines to support healthcare delivery organizations (HDO) reinforce best practices in treating *anaphylactic reaction* in the surgical patient as related to the role and duties of the Certified Surgical Technologist (CST®), the credential conferred by the National Board of Surgical Technology and Surgical Assisting. The purpose of the Guidelines is to provide information OR supervisors, risk management, and surgical team members can use in the development and implementation of policies and procedures for treating a surgical patient experiencing anaphylactic reaction in the surgery department. The Guidelines are presented with the understanding that it is the responsibility of the HDO to develop, approve, and establish policies and procedures for the surgery department regarding treating anaphylactic reaction in surgical patients per HDO protocols.

### Rationale

*Anaphylaxis*, also referred to as an anaphylactic reaction, is a response to an allergen, such as latex, that is classified as a *Type I hypersensitivity reaction*.<sup>1</sup> It is defined “as a serious allergic reaction that is rapid in onset and may cause death.”<sup>2</sup> The onset of anaphylaxis can be rapid, requiring the surgical team to act quickly to provide definitive treatment to stabilize the patient’s condition. The emphasis of this guideline and information contained herein is on treatment of the patient who is experiencing anaphylaxis during surgery. The immediate treatment of the individual in the field varies from the treatment the patient receives in the operating room (OR). Therefore, surgery personnel are referred to reviewing on a personal basis the basic first-aid treatment of anaphylaxis that occurs outside of the HDO.

Anaphylaxis is a type of *vasogenic shock* that can present a range of signs and symptoms from mild to acute respiratory distress accompanied by circulatory shock and collapse.<sup>3,4</sup> The process actually begins with the patient experiencing an initial exposure to an agent, the allergen, and IgE antibodies are produced that bind to mast cells and basophils.<sup>5-7</sup> Upon re-exposure to the allergen the anaphylactic response is mediated by a Type I hypersensitivity reaction in which the *IgE antibodies* cause the release of the inflammatory mediators BK-A, *histamine*, leukotrienes and platelet-activating factor

from the mast cells and basophils.<sup>5,8,9</sup> These mediators are responsible for producing the signs and symptoms of anaphylaxis.<sup>10</sup> Symptoms usually occur in 20 – 30 minutes.<sup>9,10</sup>

Histamine, in combination with additional vasodilator substances, causes systemic vasodilation, pooling of the blood in the peripheral circulatory system, and increased capillary permeability.<sup>11</sup> The peripheral and visceral edema produce hypovolemia and shock, whereas arteriolar vasodilation dramatically decreases the systemic vascular resistance. Due to the peripheral pooling of blood, the blood pressure can dramatically decrease in a very short span of time.

The vascular complications are accompanied by respiratory complications, including airway constriction, due to swelling of the smooth muscles in the airway tract, bronchospasm, and angioedema. Angioedema of the pharynx, larynx and trachea produces upper airway obstruction, whereas bronchospasm and mucosal edema produce lower airway obstruction. Histamine tends to cause constriction of the large airway tracts and leukotrienes affect the smaller peripheral airways. The airway obstruction can be just as life threatening because of the laryngeal edema and/or bronchial spasm. Death usually occurs due to asphyxiation and/or circulatory shock.<sup>8</sup>

The estimated incidence of anaphylaxis in patients under anesthesia has wide variation in the literature; based upon the literature review there are reports of 1 in 4,000 to 1 in 25,000 cases and 1 in 10,000 to 1 in 20,000 cases with a mortality of 3% - 10%, and an additional 2% surviving with severe brain damage.<sup>5, 12-16</sup> The occurrence of anaphylaxis is more common among women, most likely due to the number of cosmetic products that are used that sensitize the patient to causative agents, but equal for childhood-aged males and females.<sup>17</sup> Patients with a history of allergies or *atopy* are more prone to experiencing anaphylaxis.<sup>5</sup> Additionally, patients with a specific comorbid condition or a habit will exhibit signs and symptoms specific to the medical history.<sup>5</sup> For example, a patient with congestive heart failure will be more disposed to cardiovascular complications and a patient with a history of tobacco smoking will be disposed to experiencing bronchospasm.<sup>5</sup>

The most common clinical features of anaphylaxis during anesthesia are cardiovascular and cutaneous signs and symptoms.<sup>8</sup> However, cutaneous signs can be difficult to identify, because the patient is draped. Additionally, with a patient under anesthesia, there is the obvious absence of the patient to be able to communicate with the surgical team.<sup>5</sup> Most cases of surgical anaphylaxis occur within minutes during the induction period when muscle relaxants, sedatives, and opiates are administered intravenously.<sup>10,18</sup> The primary target body systems are cardiorespiratory, gastrointestinal (GI) tract, and skin and mucous membranes; the first indicators to likely be identified are cardiovascular compromise and bronchospasm.<sup>5,10</sup> The life-threatening symptoms are swelling of the airway (edema), severe bronchospasm, cardiac dysrhythmias and eventual cardiac collapse.<sup>10</sup> Ring and Messmer developed a grading system that is still current<sup>19</sup>:

- Grade I: Cutaneous and mucous membrane signs and symptoms.
- Grade II: Cutaneous and mucous membrane signs and symptoms accompanied by cardiovascular and/or respiratory signs.
- Grade III: Cardiovascular collapse with signs and symptoms indicating involvement of other body systems – GI tract, genitourinary tract.
- Grade IV: Cardiac arrest.

Approximately 80% of anaphylactic reactions are grade II or III.<sup>5</sup>

Table 1 lists the clinical signs and symptoms of anaphylaxis. The bolded words indicate the primary signs for patients under general anesthesia.

**Table 1: Clinical Signs and Symptoms of Anaphylaxis<sup>10, 20</sup>**

<b>Body System</b>	<b>Signs and Symptoms</b>
Integumentary	<b>Urticaria</b> , pruritus, facial edema
Cardiovascular	<b>Dysrhythmias, Hypotension, tachycardia</b>
Respiratory	<b>Bronchospasm, increased respiratory rate</b> , dyspnea, hypoxia, pulmonary edema,
Genitourinary	<b>Decreased urine output</b>
Hematologic	<b>Disseminated intravascular coagulation</b>

### **Evidence-based Research and Key Terms**

The research of articles, letters, nonrandomized trials, and randomized prospective studies is conducted using the Cochrane Database of Systematic Reviews and MEDLINE®, the U.S. National Library of Medicine® database of indexed citations and abstracts to medical and healthcare journal articles.

The key terms used for the research of the guidelines include: anaphylactic reaction; anaphylaxis; atopy; histamine; IgE antibodies; latex allergy; Type I hypersensitivity reaction; vasogenic shock. Key terms used in the Guidelines are italicized and included in the glossary.

### **Guideline I**

**CSTs should know the agents, drugs and solutions that can cause an anaphylactic reaction in the surgical patient so as to be aware that a reaction can occur any time these are used and be prepared to assist the surgical team in treating the patient. The time for the reaction to occur is proportional to the type of causative agent.**

1. The primary cause of anaphylaxis in the patient under anesthesia is neuromuscular blocking drugs (NMBD); it has been identified as the cause of anaphylaxis in 50% - 70% of cases and one in 6,500 patients.<sup>5,21-26</sup> Allergy to NMBDs is more common in women than men with 3:4 reactions occurring in females.<sup>17,27</sup> This is thought to be due to sensitization to agents that are in both a variety of topical cosmetics and NMBDs.<sup>28,29</sup> The female can experience an allergic reaction to NMBDs upon initial exposure, likely from exposure to topical agents.<sup>30</sup> Clinical signs and symptoms usually occur within minutes of use of the NMBD; often 30 minutes or less.<sup>30</sup> All NMBDs can cause anaphylaxis; however, the NMBDs indicated in clinical studies most responsible for reactions include atracurium, pancuronium, succinylcholine and vecuronium with succinylcholine posing the greatest risk.<sup>18,31</sup>
2. The second most common cause of anaphylaxis during anesthesia is *latex allergy*.<sup>21,32</sup> The reactions involve a direct IgE-mediated immune response to the polypeptides in natural latex. Because the latex exposure is primarily through the skin or mucosa, clinical signs and symptoms may not appear for 15 – 60 minutes.<sup>5,30</sup> Patients with congenital abnormalities of the GU tract, spina bifida and spinal

- cord injury are at a high risk for latex allergy; sensitization to latex occurs up to 75% of patients with spina bifida.<sup>22,32</sup> By 2000, latex was reported to account for approximately 16.6% - 20% of anaphylactic reactions during surgery.<sup>16-18,33</sup> The incidence of latex allergy in pediatric patients is approximately one in 10,000 or 80% of all intraoperative anaphylactic cases.<sup>5,22,32</sup> However, due to the acute awareness of latex allergy, the incidence has dropped as ORs have adopted policies for purchasing non-latex containing products.<sup>30</sup> Treatment of patients under anesthesia who experience anaphylactic reaction to latex is the same as other forms of reaction. For details regarding latex allergy, refer to the *AST Guidelines for Best Practices for Latex Allergy*.
3. Antibiotics are the third leading cause of anaphylactic reaction in the surgical patient.<sup>18,23</sup> According to the French medical studies, antibiotics account for 12% - 15% of identifiable triggers of anaphylaxis.<sup>16,17</sup> The primary antibiotic that causes drug allergies is  $\beta$ -lactam antibiotics including amoxicillin, ampicillin, cephalosporins and penicillin.<sup>5,10</sup> Sulfonamide allergy is also common in surgical patients. Keeping the incidence of drug-allergy-induced anaphylaxis in the surgical patient in perspective, up to 2% of the population is allergic to penicillin, but approximately only 0.01% of penicillin administration results in anaphylactic reaction.<sup>8</sup>
  4. Chlorhexidine (CHL) has been used as an antiseptic and patient skin preparation disinfectant since 1954, and is also used in combination with the topical antibiotic mupirocin to eliminate methicillin-resistant *Staphylococcus aureus* from the nasal vestibule in preparation for nasal surgery.<sup>9,34,35</sup> CHL is poorly reported in the surgical literature as the cause of anaphylaxis, despite warnings by governmental organizations and an increase in recognition, but it is considered a rare occurrence.<sup>9,34-37</sup> The estimation of anaphylaxis caused by CHL is 1 per 10,000 – 20,000 surgical procedures.
    - A. Sharp et al. completed a literature review of thirty-six articles published on surgical patients who experienced anaphylaxis to CHL. The most commonly affected specialty was urology.<sup>34</sup> Six patients required chest compressions and 39.71% of the patient's surgical procedure was not completed with an additional 27.94% of the surgical procedures resulting in unplanned ICU admissions.<sup>34</sup>
    - B. Abreu et al. reported a case of perioperative anaphylaxis to CHL during a septoplasty, turbinectomy and maxillary sinusotomy. CHL was used as the patient skin preparation agent and thirty minutes after the patient had periorbital edema, hives, hypotension and decreased oxygen saturation.<sup>9</sup> Postoperatively, the SPT confirmed CHL as the causative agent and the patient reported experiencing prior lip swelling when mouthwash containing CHL was used.<sup>9</sup>
  5. Although rare and difficult to diagnose, incidences of allergic reactions to hyaluronidase have been reported and the surgical team should be aware of the potential complications including a serious increase in intraocular pressure.<sup>38-42</sup>

6. Methylene blue is an agent that has been used for several years in sentinel node biopsy and fallopian tube procedures that has rare, but potentially life-threatening consequences.<sup>43-45</sup>
  - A. Wahid et al. reported a case of severe anaphylactic shock due to methylene blue in a 6-year old female with a diagnosis of melanoma on her right forearm. The lesion was excised and a sentinel lymph node biopsy was performed. Within five minutes after injection of methylene blue around the lesion the patient experienced bradycardia and immediately progressed into asystole.<sup>46</sup> The patient survived the incident. Postoperative skin prick test (SPT) was performed and the allergist suspected methylene blue to be the causative agent.<sup>46</sup>
  - B. There have only been two other reports of anaphylaxis caused by methylene blue when used for sentinel lymph node biopsy that were confirmed by SPT. In 2010, Jangjoo et al. reported a case and in 2011, Oomah et al. reported the second case.<sup>47,48</sup>
  - C. In 2005, Dewachter et al. reported a case of anaphylaxis when 1% methylene blue was injected intra-uterine to determine fallopian tube patency.<sup>49</sup>
7. Other agents that have been identified as the cause of perioperative anaphylaxis include the following; however, the incidence associated with these agents is rare and account for less than 5% of all episodes.<sup>5,17</sup>
  - A. Polymethyl methacrylate
  - B. Coagulation agents such as heparin.
  - C. Bacitracin used in irrigating solutions.
  - D. Colloids such as albumin, dextran and hetastarch.
  - E. Induction drugs including barbiturates, benzodiazepines, opioids and propofol. Barbiturates are responsible for the majority of reactions.<sup>30</sup>
  - F. Local anesthetics with amino esters such as cocaine, procaine, and tetracaine causing anaphylaxis more commonly than the amino amides.

## **Guideline II**

**CSTs in the first scrub and assistant circulator roles should know the measures taken to treat a surgical patient experiencing an anaphylactic reaction to be an effective team member assisting the surgeon, anesthesia care provider and circulator.**

1. After the initial diagnosis is made by the anesthesia provider, rapid, early intervention is critical to successfully treating the patient.<sup>10</sup>
  - A. The five steps that should be immediately performed are<sup>5,10,30,32</sup>:
    - 1) Discontinuing the causative agent.
    - 2) Providing epinephrine to the anesthesia provider or RN circulator for immediate intramuscular injection.
    - 3) Intravascular volume expansion by fully opening the IV.<sup>15</sup>
    - 4) Maintaining the airway and if possible, ventilating with 100% oxygen. If the patient isn't intubated, the anesthesia provider will want to immediately insert an endotracheal tube to secure the airway and may require assistance such as cricoid pressure.<sup>5</sup>

- 5) Requesting additional assistance from surgery personnel who are not working on another surgical procedure including another anesthesia provider. Many of the steps for treatment need to take place simultaneously and extra personnel will be needed.<sup>5</sup>
2. The CST in the first scrub role will be responsible for protecting the sterile field including the back table and Mayo stand.
  - A. The CST may be called upon to break scrub to assist the anesthesia care provider and circulator during emergency call procedures when other OR personnel are not available, e.g. late-night emergency call procedure. In this type of situation, the surgery team may want to draw upon assistance from Emergency Department personnel.
  - B. Depending on the procedure being performed, the CST must be prepared to rapidly assist the surgeon in either packing the surgical wound with sterile sponges and/or wound closure since the immediate steps by the anesthesia provider is to discontinue drug administration and administer 100% oxygen.<sup>50</sup>
3. The CST in the assistant circulator role should be familiar with the surgery department emergency cart and code blue cart with defibrillator including their locations, and drugs that are stocked in the carts.<sup>5</sup>
  - A. The CST should transport the carts into the OR and confirm the defibrillator is ready for use. The CST must know how to administer CPR as well as operating the defibrillator machine for the surgeon to be able to apply the defibrillator pads.
  - B. The CST should know the drugs that are used to treat anaphylaxis to be able to quickly provide them to the anesthesia provider as they are requested.
    - 1) The first drug to be provided to the anesthesia provider or circulating RN should be epinephrine due to its positive effects on blood pressure while providing bronchial smooth muscle relaxation.<sup>10</sup> Additionally, epinephrine inhibits the release of mediators from mast and basophil cells.<sup>51</sup> Table 2 provides the recommended drug therapy and fluids for treating the patient. The protocol remains the same for treating children and adolescents, but the drug dosages are obviously different.<sup>5</sup>

**Table 2: Treatment of Anaphylactic Reactions<sup>5,10,32</sup>**

<b>Drug or Other Treatment</b>	<b>Drug Action</b>
Albuterol <sup>20</sup> (bronchodilator)	Relax bronchial smooth muscles to treat bronchoconstriction
Diphenhydramine (Benadryl® - antihistamine) – requires dilution to avoid vein damage	Antihistamine: H <sub>1</sub> blocker
Epinephrine – administered intramuscularly	Vasoconstriction; relax bronchial smooth muscles
Famotidine (Pepcid® - H <sub>2</sub> blocker) – intravenous	
Hydrocortisone or methylprednisolone (steroids) – intravenous	Anti-inflammatory
IV fluids: crystalloid solution	Treat hypovolemia and prevent circulatory collapse and shock
Ranitidine	Antihistamine: H <sub>2</sub> blocker
Vasopressin <sup>15,52,53</sup>	Reverse vasodilatory shock

4. The anesthesia provider may request the use of transesophageal echocardiography in the intubated patient to assist in the diagnoses of the cause of acute cardiovascular dysfunction.<sup>15</sup> The CST should know where the echo transducer is stored in order to quickly retrieve to provide to the anesthesia provider in the OR.

### **Guideline III**

**The surgery department should review the policies and procedures (P&P) regarding treatment of anaphylactic reaction in surgical patients on an annual basis.**

1. The surgery department should include members of the surgical team and administration when reviewing the P&Ps, including CSTs, surgeons, RNs, risk management, and infection control officer.
  - A. The surgery department should document when the P&Ps were reviewed, revision completed (if necessary), and who participated in the review process.
2. CSTs should be familiar with the P&Ps for treatment of anaphylactic reaction in surgical patients. The orientation of new employees should include reviewing the P&Ps.

**Guideline IV****CSTs should complete continuing education to remain current in their knowledge of anaphylactic reaction and treatment of surgical patients.<sup>54</sup>**

1. The continuing education should be based upon the concepts of adult learning, referred to as andragogy. Adults learn best when the information is relevant to their work experience; the information is practical, rather than academic; and the learner is actively involved in the learning process.<sup>55</sup>
2. It is recommended surgery departments use various methods of instruction to facilitate the learning process of CSTs.
  - A. If the education is primarily lecture, methods to engage learners include presentation of case studies for discussion, and audience discussion providing suggestions for reinforcing (subject of Guidelines).
  - B. Other proven educational methods include interactive training videos, and computerized training modules and teleconferences.
  - C. The continuing education should be delivered over short periods of time such as in modules, and not in a one-time lengthy educational session.
3. Continuing education programs should be periodically evaluated for effectiveness including receiving feedback from surgery department personnel.
4. The surgery department should maintain education records for a minimum of three years that include dates of education; names and job titles of employees that completed the continuing education; synopsis of each continuing education session provided; names, credentials, and experience of instructors.



## Competency Statements

Competency Statements	Measurable Criteria
<p>1. CSTs can identify the signs and symptoms of anaphylactic reaction and communicate this information to the surgical team.</p> <p>2. CSTs are qualified to handle and administer medications and solutions in the OR under the direct supervision and order of the surgeon, when treating a patient for anaphylactic reaction.</p> <p>3. CSTs are qualified to participate on the HDO and/or surgery department Latex Allergy Practices Committee as well as any other committees that establish protocols for treating anaphylactic reactions.</p>	<p>1. Educational standards as established by the <i>Core Curriculum for Surgical Technology</i>.<sup>56</sup></p> <p>2. The didactic subject of medications, including calculating dosages and conversions, and preparation and management of medications and solutions, and anesthesia techniques are included in a CAAHEP accredited surgical technology program.</p> <p>3. The didactic subject of anaphylactic reaction and treatment of the surgical patient undergoing a reaction is included in a CAAHEP accredited surgical technology program.</p> <p>4. Students demonstrate knowledge of handling and administering medications and solutions in the lab/mock OR and during clinical rotation.</p> <p>7. CSTs perform patient care duties by assisting the surgical team during emergency situations, including anaphylactic reaction.</p> <p>8. CSTs complete continuing education to remain current in their knowledge of medications and solutions, and OR emergency situations.<sup>54</sup></p>

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## Glossary

*Anaphylactic reaction:* A severe, life-threatening allergic reaction to an allergen such as a drug.

*Anaphylaxis:* See anaphylactic reaction.

*Atopy*: Genetic tendency to develop allergic reactions and produce elevated levels of IgE upon exposure to an allergen(s).

*Histamine*: Body substance that is released by cells in response to injury or allergic reactions causing contraction of smooth muscle and dilation of capillaries.

*IgE antibodies*: Immunoglobulin E antibodies are produced by the immune system. When the immune system overreacts to an allergen the antibodies are produced that travel to cells to stimulate the release of chemicals causing an allergic reaction.

*Latex allergy*: An allergy to the proteins that are present in natural rubber latex. Latex allergy generally develops after repeated exposure to products that contain natural rubber latex such as some types of surgical gloves.

*Type I hypersensitivity reaction*: An immediate hypersensitivity reaction that involves IgE-mediated release of histamine and other mediators from mast cells and basophils causing an anaphylactic reaction.

*Vasogenic shock*: Results from depressed activity of the higher vasomotor centers located in the brainstem and medulla causing vasodilation without loss of fluid.

## References

1. Bochner BS, Lichtenstein LM. Anaphylaxis. *New England Journal of Medicine*. 1991; 324 (25): 1785-1790.
2. Lieberman P, Nicklas RA, Randolph C, Oppenheimer J, Berstein D, Bernstein J, Ellis A, Golden DBK, Greenberger P, Kemp S, Khan D, Ledford D, Lieberman J, Metcalfe D, Nowak-Wegrzyn A, Sicherer S, Wallace D, Blessing-Moore J, Lang D, Portnoy JM, Schuller D, Spector S, Tilles SA. Anaphylaxis – a practice parameter update 2015. *Annals of Allergy, Asthma & Immunology*. 2015; 115: 341-384.
3. Cohn SM, ed. *Complications in Surgery and Trauma*. 2<sup>nd</sup> ed. Boca Rotan, FL: CRC Press; 2014.
4. Levy JH. Anaphylactic and anaphylactoid reactions in the surgical patient. 2010. <https://pdfs.semanticscholar.org/1a552/cbbd1c79c330c6244cb8509d4e5edc79130of.pdf>. Accessed January 5, 2018.
5. Berkeley AV. Anaphylaxis in the operating room. 2017. <https://emedicine.medscape.com/article/2500072-overview#showall>. Accessed January 12, 2018.
6. Kay AB. Allergy and allergic diseases. First of two parts. *New England Journal of Medicine*. 2001; 344: 30-37.
7. Kay AB. Allergy and allergic diseases. Second of two parts. *New England Journal of Medicine*. 2001; 344: 109-113.
8. Butterworth J, Mackey DC, Wasnick J. Morgan and Mikhail's Clinical Anesthesiology. 6<sup>th</sup> ed. New York, NY: McGraw-Hill Education; 2018.

9. de Abreu APT, de Oliveira LRR, de Abreu AFT, de Oliveria ER, de Melo Ireno MS, Aarestrup FM, Aarestrup MF, Aarestrup PF.
10. Rosenberg MB, Phero JC, Giovannitte JA, Jr. Management of allergy and anaphylaxis during oral surgery. *Oral and Maxillofacial Surgery Clinics of North America*. 2013; 25: 401-406.
11. Porth CM. Essentials of Pathophysiology: Concepts of Altered Health States. 4<sup>th</sup> ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2014.
12. Townsend CM, Beauchamp RD, Evers BM, Mattox KL, eds. Sabiston Textbook of Surgery: The Biological Basis of Modern Surgical Practice. 20<sup>th</sup> ed. Philadelphia, PA: Saunders; 2016.
13. Mertes PM, Malinovsky JM, Jouffroy L, Aberer W, Terreehorst I, Brockow K, Demoly P, ENDA, Working Group of the SFAR and SFA, EAACI Interest Group on Drug Allergy. Reducing the risk of anaphylaxis during anesthesia: 2011 updated guidelines for clinical practice. *Journal of Investigational Allergology & Clinical Immunology*. 2011; 21(6): 442-453.
14. Fisher M. Anaphylaxis to anaesthetic drugs. *Novartis Foundation Symposia*. 2004; 257: 193-202.
15. Levy JH, Adkinson NJ, Jr. Anaphylaxis during cardiac surgery: implications for clinicians. *Anesthesia & Analgesia*. 2008; 106: 392-403.
16. Mertes PM, Laxenaire MC, Alla F, Groupe d'Etudes des Reactions Anaphylactoides Peranesthésiques. Anaphylactic and anaphylactoid reactions occurring during anesthesia in France in 1999-2000. *Anesthesiology*. 2003; 99(3): 536-545.
17. Mertes PM, Alla F, Tréchet P, Auroy Y, Jouglu E, Groupe d'Etudes des Reactions Anaphylactoides Peranesthésiques. Anaphylaxis during anesthesia in France : an 8-year national survey. *The Journal of Allergy and Clinical Immunology*. 2011; 128(2): 366-373.
18. Lieberman P. Anaphylactic reactions during surgical and medical procedures. *Journal of Allergy and Clinical Immunology*. 2002; 110(2): S64-S69.
19. Ring J, Messmer K. Incidence and severity of anaphylactoid reactions to colloid volume substitutes. *Lancet*. 1977; 1(8009): 466-469.
20. Snyder K, Keegan C. Pharmacology for the Surgical Technologist. 4<sup>th</sup> ed. Philadelphia, PA: Saunders; 2016.
21. Knowles S R, Weber E, Shear NH. Allergic reactions during general anesthesia [Abstract]. *Journal of Allergy and Clinical Immunology*. 1996; 97(1): 344.
22. Ricci G, Gentili A, Di Lorenzo F. Latex allergy in subjects who had undergone multiple surgical procedures for bladder exstrophy: Relationship with clinical intervention and atopic diseases. *BJU International*, 1999; 84(9): 1058-1062.
23. Dewachter P, Moulton-Faivre C, Emala CW. Anaphylaxis and anesthesia: controversies and new insights. *Anesthesiology*. 2009; 111(5): 1141-1150.
24. Laroche D, Lefrancois C, Gerard JL, Dubois F, Vergnaud MC, Guéant JL, Bricard H. Early diagnosis of anaphylactic reactions to neuromuscular blocking drugs. *British Journal of Anaesthesia*. 1992; 69: 611-614.

25. Malinovsky JM, Decagny S, Wessel F. Systematic follow-up increases incidence of anaphylaxis during adverse reactions in anesthetized patients. *Acta Anaesthesiologica Scandinavica*. 2008; 52: 175-181.
26. Thong BY, Yeow C. Anaphylaxis during surgical and interventional procedures. *Annals of Allergy, Asthma & Immunology*. 2004; 92: 619-628.
27. Birnbaum J, Porri F, Pradal M, Charpin D, Vervloet D. Allergy during anaesthesia. *Clinical and Experimental Allergy*. 1994; 24(10): 915-921.
28. Baldo BA, Fisher MM. Substituted ammonium as allergenic determinants in drug allergy. *Nature*. 1983; 306: 262.
29. Harboe T, Johansson SG, Florvaag E, Oman H. Pholcodine exposure raises serum IgE in patients with previous anaphylaxis to neuromuscular blocking agents. *Allergy*. 2007; 62(12): 1445-1450.
30. Ledford DK. Perioperative anaphylaxis: clinical manifestations, etiology, and diagnosis. 2011.  
<http://cursoenarm.net/UPTODATE/contents/mobipreview.htm?7/55/8049?view=print>. Accessed January 12, 2018.
31. Fisher MM, Doig GS. Prevention of anaphylactic reactions to anaesthetic drugs. *Drug Safety*. 2004; 27: 393-410.
32. Mali S. Anaphylaxis during the perioperative period. *Anesthesia Essays and Researches*. 2012; 6(2): 124-133.
33. Laxenaire MC. [Epidemiology of anesthetic anaphylactoid reactions. Fourth multicenter survey (July 1994-December 1996)]. *Annales Francaises d'Anesthésie et de Réanimation*. 1999; 18(7): 796-809.
34. Sharp G, Green S, Rose M. Chlorhexidine-induced anaphylaxis in surgical patients: a review of the literature. *ANZ Journal of Surgery*. 2016; 86(4): 237-243.
35. Koch A, Wollina U. Chlorhexidine allergy. *Allergo Journal International*. 2014; 23(3): 85-86.
36. Garvey LH, Kroigaard M, Poulsen LK, Skov PS, Mosbech H, Venemalm L, Degerbeck F, Husum B. IgE-mediated allergy to chlorhexidine. *The Journal of Allergy and Clinical Immunology*. 2007; 120(2): 409-415.
37. Weng M, Zhu M, Chen W, Miao C. Life-threatening anaphylactic shock due to chlorhexidine on the central venous catheter: a case series. *International Journal of Clinical and Experimental Medicine*. 2014; 7(12): 5930-5936.
38. Escolano F, Paré N, Gonzalez I, Castillo J, Valero A, Bartolomé B. Allergic reaction to hyaluronidase in cataract surgery. *European Journal of Anaesthesiology*. 2005; 22(9): 729-730.
39. Szepfalusi Z, Nentwich I, Dobner M, Pillwein K, Urbanek R. IgE-mediated allergic reaction to hyaluronidase in paediatric oncological patients. *European Journal of Pediatrics*. 1997; 156: 199-203.
40. Agrawal A, McLure HA, Dabbs TR. Allergic reaction to hyaluronidase after a peribulbar injection. *Anaesthesia*. 2003; 493-494.
41. Ahluwalia HS, Lukaris A, Lane CM. Delayed allergic reaction to hyaluronidase: a rare sequel to cataract surgery. *Eye*. 2003; 17: 263-266.
42. Kirby B, Butt A, Morrison AM, Beck MH. Type I allergic reaction to hyaluronidase during ophthalmic surgery. *Contact Dermatitis*. 2001; 44(1): 52.

43. Zakaria S, Hoskin TL, Degnim AC. Safety and technical success of methylene blue dye for lymphatic mapping in breast cancer. *American Journal of Surgery*. 2008; 196: 228-233.
44. Masannat Y, Shenoy H, Speirs V, Hanby A, Horgan K. Properties and characteristics of the dyes injected to assist axillary sentinel node localization in breast surgery. *European Journal of Surgical Oncology*. 2006; 32: 381-384.
45. Varghese P, Abdel-Rahman AT, Akberali S, Mostafa A, Gattuso JM, Carpenter R. Methylene blue dye – a safe and effective alternative for sentinel lymph node localization. *The Breast Journal*. 2008; 14: 61-67.
46. Wahid FN, Malkan AD, Pappo A, Wright BB, Adefeyisan S, Sandoval JA. Severe anaphylactic shock due to methylene blue dye. *Journal of Pediatric Surgery*. 2014; 2: 117-118.
47. Jangjoo A, Forghani MN, Mehrabibahar M, Sadeghi R. Anaphylaxis reaction of a breast cancer patient to methylene blue during breast surgery with sentinel node mapping. *Acta Oncologica*. 2010; 49(6): 877-878.
48. Oomah S, Dembinski T, Becker A, Kalicinsky C. Prolonged elevation of serum tryptase resulting from intraoperative anaphylaxis to methylene blue. *Allergy, Asthma, and Clinical Immunology*. 2010; 6(Suppl. 2): P29.
49. Dewachter P, Mouton-Faivre C, Tréchet P, Lieu JC, Mertes PM. Severe anaphylactic shock with methylene blue instillation. *Anesthesia & Analgesia*. 2005; 101: 149-150.
50. Mertes PM, Laxenaire MC. Anaphylaxis during general anesthesia. *CNS Drugs*. 2000; 14(2): 115-133.
51. Hepner DL, Castells MC. Anaphylaxis during the perioperative period. *Anesthesia & Analgesia*. 2003; 97(5): 1381-1395.
52. Landry DW, Oliver JA. The pathogenesis of vasodilatory shock. *New England Journal of Medicine*. 2001; 345: 588-595.
53. Tsuda A, Tanaka KA, Huraux C, Szlam F, Sato N, Yamaguichi K, Levy JH. The in vitro reversal of histamine-induced vasodilation in the human internal mammary artery. *Anesthesia & Analgesia*. 2001; 93: 1453-1459.
54. Association of Surgical Technologists. AST continuing education policies for the CST and CSFA. 2005. Revised June 2017. <http://www.ast.org/webdocuments/CEpolicies/>. Accessed April 20, 2017.
55. Pappas C. The adult learning theory-andragogy-of Malcolm Knowles. May 2013. <https://www.elearningindustry.com/the-adult-learning-theory-andragogy-of-malcolm-knowles>. Accessed April 20, 2017.
56. Association of Surgical Technologists. Core curriculum for surgical technology. 2011. [http://www.ast.org/uploadedFiles/Main\\_Site/Content/Educators/Core%20Curriculum%20v2.pdf](http://www.ast.org/uploadedFiles/Main_Site/Content/Educators/Core%20Curriculum%20v2.pdf). Accessed April 20, 2017.

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