Anaphylaxis

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Background: Anaphylaxis has been a recognized entity dating back over four centuries. The first reported case of anaphylaxis dates back to 2600 B.C.E., and continues to cause medical emergencies up to the present day.

While anaphylaxis can be triggered by several agents such as drugs, food, and insect venom, for anesthesiologists, the major triggering agents are drugs and natural rubber latex. In relationship to anesthesia, while the data is limited, the incidence of anaphylactic reactions during anesthesia and surgery appears to be between 1:5000 to 1:25,000. Even under the close supervision that occurs in an operating room, the morbidity and mortality associated with an anaphylactic reaction remains high. (5, 7).

In term of diagnosis, it can be useful to differentiate anaphylactic from anaphylactoid reaction. The former is defined as IgE mediated while the latter can be through non-immune mechanisms. However, on clinical presentation the two are indistinguishable and are treated the same.

Allergic Cascade: On the first presentation of an allergen, the body produces IgE antibodies in response. These IgE molecules become attached to the surface of mast cells and basophiles. When the body is presented on a subsequent occasion with the allergen, these allergens cross-link the IgE antibodies on the mast cells and basophiles and causes degranulation and release of allergic mediators. It is this abnormal release of an excessive amount of these mediators that leads to an anaphylactic reaction. There are several types of mediators released over time. Initially, degranulation causes immediate release of preformed mediators such as histamine, TNF-α, proteases, and heparin. Then over the next few minutes, lipid mediators such as prostaglandins and leukotrienes are released. Then over the subsequent hour cytokine are produced such as IL-4 and IL-13. Currently, there is research on the potential for reducing the severity and extent of an anaphylactic reaction through removal of total IgE in the body (11).

In order to diagnosis an anaphylactic reaction it is important to know the signs and symptoms of a reaction. All organ systems of the body can be affected including the skin (hives, erythema, urticaria, and pruritis, which may be localized or general), the eyes (redness, itching, and angioedema), the upper respiratory tract (stuffy or runny nose), the lower respiratory tract (shortness of breath, cough, and wheezing) the gastrointestinal system (cramps, nausea, vomiting, and diarrhea), and the cardiovascular system (hypotension, tachycardia, and cardiovascular collapse).

Treatment:
Immediate treatment of any life-threatening reaction is always the A, B, C's of basic life support. In addition, for an anaphylactic reaction it is important to stop the exposure (if possible by determining the causative agent), manage the airway, give volume with balanced salt solution, and administer epinephrine (titrate as needed), and transfer to a monitored area after the patient is stabilized.

Diagnosis:
The diagnosis of an anaphylactic reaction is usually made using several methods. First, a history of a reaction that is consistent with an anaphylactic reaction in term of the timing of events and any previous reactions (5, 7) is useful. There are also nonspecific markers in the blood that can be measured after a presumed reaction has occurred, such as serum mast cell tryptase (a marker of mast cell as opposed to basophile activation, peaks at 30-60, half-life 2 hrs) and compliment C3 and C4, that suggest an IgE mediated anaphylactic reaction. There are also more specific serology test such as IgE specific antibody tests that are available for some drugs and latex. Finally there is skin testing, however this should only be performed by an experienced person with proper resuscitation equipment immediately available (1, 6).

Agents causing anaphylactic reactions in the perioperative period:
The two common agents causing anaphylactic reactions in the perioperative period are neuromuscular agents and natural rubber latex (10, 12), with a decreasing incidence of reactions to neuromuscular agents and an increasing incidence of reactions to natural rubber latex over the last two decades. However, other agents commonly used in the perioperative period have also been associated with anaphylactic reaction albeit at a lower incidence. These include antibiotics, blood products, colloids, protamine, hypnotics, and opioids.

Natural Rubber Latex:
There are frequent latex exposures in the OR which include gloves (both examination and sterile), foley catheters, tourniquets, injection ports in IV tubing and fluid bags, pulmonary artery balloon catheters, prepackaged kits (latex gloves).

Between 1996-1997 there were 435 cases of reactions to latex allergies reported to the FDA. Using this number of reported cases, the FDA estimated that the true total number of case in the United States to be around 43,500. Of the reported cases, 100 were cases of anaphylaxis. Therefore, currently in the U.S. it is believed that latex induced reaction represents approximately10% of all anaphylactic reactions reported under anesthesia (13).

Epidemiology:
Several groups have increased prevalence of latex sensitization including children with spina bifida and congenital GU abnormalities (prevalence 18-73%), Health care workers (3-17%), Rubber industry workers (11%), and patients with atopy- asthma, rhinitis, eczema (6.8%). Furthermore physicians in general have a reported prevalence of 5-10%, while anesthesiologists have a significantly higher rate of 11.6-15.8% (2, 4, 9).

Clinical History:
Clinical history specific to a latex allergy can include swelling, hives, itching with dental or pelvic exam, swelling or wheezing with blowing up balloons, hives or itching with household rubber gloves, elastic in underwear or bathing suit, sensitivity to condoms, food allergies, especially to banana, avocado, kiwi, chestnuts, or any unexplained reactions under anesthesia. From previous work it is clear that several factors clearly identify individuals predisposed to the risk of sensitization to natural rubber latex (atopy, food allergies, and skin symptoms) (4).

Recommendations:
Individuals who are sensitized to latex should observe strict latex avoidance procedures. Furthermore, personal avoidance of latex by a sensitized individual may be sufficient to prevent progression to symptomatic disease. (8).

Aerosol Exposure:
Aerosol latex exposure can trigger an allergic reaction. Current preliminary work in our laboratory suggests that while certain sterile powdered latex surgeon gloves generate significant amounts of latex aeroallergen, the particle are large (> 10 micron), are therefore less likely to be respired. Latex gloves that generate lower amounts of respired particles should be less likely to contribute to symptomatic allergic disease than gloves that generate a high level of respired particles such as examination gloves.

Who is at risk?
Preliminary work in our laboratory has also been undertaken to identify potential genetic markers for latex allergy based on phenotype, and a positive serology (latex-specific IgE). Initial candidate genes were chosen from genes associated atopy, asthma and allergy. We studied operating room personnel (anesthesiologists, surgeons, & nurses) at Johns Hopkins Medical Institutions Anesthesiologists attending the annual American Society of Anesthesiologists meeting (1999 & 2000). We collected a clinical history through a questionnaire, and drew blood for serum for RAST testing (latex specific IgE, Pharmacia CAP). We also extracted DNA from cells for candidate genes analysis using PCR analysis for polymorphisms. We found a significant association between a polymorphism on the IL13 gene and the development of latex allergy (3).

Conclusion:
Prevention of latex allergies requires identification of "at risk" individuals and decreased "exposure" to natural rubber latex. The current management of a latex allergic individual consists of avoidance.

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