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**Allergy**

**Definition**

Allergy is an abnormal or hypersensitive response of the immune system to a substance introduced into the body.

Allergic diseases are increasing in prevalence and are contributing significantly to health care costs. For example, the number of children with allergies has recently doubled. One of the most common medical emergencies that can occur in the dental office is that of **an acute allergic reaction**.

**Incidence and prevalence:**

* About a 1- 3% risk for an allergic reaction is associ­ated with administration of any drug.
* Fatal drug reac­tions occur in about 0.01% of surgical inpatients and 0.1% of medical inpatients.
* Drugs are the most common cause of urticarial reac­tion in adults, and food and infection are the most common causes of these lesions in children. The most common causes of anaphylactic death are penicillin, bee stings, and wasp stings.

**Component of immune system:**

1. **Non-specific immunity**:
2. Mechanical and Mechanical reflexes: like skin, mucosa, coughing and sneezing.
3. Secretion of bactericidal substances: Stomach acid, Earwax (cerumen), Enzymes in tears or saliva.
4. Phagocytic cells: Neutrophils, Monocytes, Macrophages.
5. Circulating chemicals: Complement, Interferon.
6. **Specific immunity:**
7. **Humoral immunity**:

(1) Protection against bacterial infection

(2) Clones of B lymphocytes

(3) Recognition of chemical configuration

(4) Production of antibodies by plasma cells

(5)Eradication of antigen

B-lymphocyte recognize specific antigens that were processed by T-lymphocyte and macrophage. After recognition, B-cells multiply and differentiate to plasma cells and memory cells. Memory cells remain inactive until exposure to the same antigen later on. Once activated, memory cell differentiate to plasma cells that would start productions of immunoglobulins. Different immunoglobulins have different functions (IgA, IgE, IgM, IgG, IgD).

1. **Cellular immune:**

(1) Protection against viral infection, tuberculosis, leprosy

(2) Transplant rejection

(3) Production of cytokines by T lymphocytes

(4) Eradication of antigen

In the cellular or delayed immune system, T lymphocytes play the central role. The primary function of this system is to recognize and eradi­cate antigens that are fixed in tissues or within cells. This system is involved in protection against viruses, tubercu­losis, and leprosy. Antibodies are not operative in the cell-mediated immune system. Effector T lymphocytes produce various cytokines that serve as active agents of this system.

**Type I Hypersensitivity Reactions:** Type I hypersen­sitivity reactions commonly are caused by food sub­stances (e.g., shellfish, nuts, eggs, and milk), antibiotics, and insect bites (e.g., bee stings). They are related to the humoral immune system and usually occur soon after second contact with an antigen; however, many people have repeated contacts with a specific drug or material before they become allergic to it. Dif­ferent types of type I hypersensitivity reactions could occur:

* **Anaphylaxis**is an acute reaction involving the smooth muscle of the bronchi in which antigen–IgE antibody complexes form on the surface of mast cells which causes sudden histamine release from these cells. The release of histamine, as well as other vasoactive mediators, leads to smooth muscle contraction and increased vascular permeability. The potential end result is acute respiratory compromise and cardiovascular collapse.
* **Atopy**is a hypersensitivity state that is influenced by hereditary factors. Hay fever, asthma, urticaria, and angioedema are examples of atopic reactions. Lesions most commonly associated with atopic reactions include **urticaria***,* which is a superficial lesion of the skin, and **angioedema***,* which is a lesion that occurs in the deep dermis or subcutaneous tissues and often involves diffuse enlargement of the lips, infraorbital tissues, larynx, or tongue. In true allergic reactions, these lesions result from the effects of antigens and their antibodies on mast cells in various locations in the body. As is typical for type I hypersensitivity, the antigen–antibody complex causes the release of mediators (histamine) from mast cells. These mediators then produce an increase in the permeability of adjacent vascular structures, resulting in loss of intravascular fluid into surrounding tissue spaces—seen clinically as urticaria, angioedema, and secretions associated with hay fever.

**Type II Hypersensitivity Reactions*.*** The key ele­ments involved in type II hypersensitivity are shown in Box 19-9. These reactions are IgG-or IgM-mediated. The classic example of type II (cytotoxic) hypersensitiv­ity is transfusion reaction caused by mismatched blood.

**Type III Hypersensitivity Reactions**These reactions take place in blood vessels and involve soluble immune complexes. They constitute what is referred to as *immune complex–mediated hypersensitivity.* Their key feature is vasculitis. Clinical examples include systemic lupus ery­thematosus and streptococcal glomerulonephritis.

**Type IV Hypersensitivity Reactions**

* Type IV hyper­sensitivity reactions, which involve the cellular immune system, include infectious contact dermatitis, transplant rejection, and graft-versus-host disease. Events in type IV hypersensitivity (contact dermatitis), which may involve dendritic cells and Langerhans cells, present the antigen to undifferentiated T lymphocytes. Some of the more common antigens that cause contact dermatitis include metal jewelry, perfumes, rubber prod­ucts, chemicals such as formaldehyde, and medicines such as topical anesthetics.
* Type IV hypersensitivity reac­tions usually are delayed and appear about 48 to 72 hours after contact has been made with the antigen.
* Infectious-type allergic reactions are exemplified by the tuberculin skin test, in which a person who has previ­ously been exposed to *Mycobacterium tuberculosis* develops a delayed response, usually within 48 to 72 hours after a second exposure to components of the bacteria. This response is characterized by induration, erythema, swelling, and sometimes ulceration at the site of injection.
* **Contact allergy** occurs when a substance of low molecular weight that is not antigenic by itself comes in contact with a tissue component (primarily a protein) and forms an antigenic complex. This small molecule is called a **hapten**(or one half of an antigen), and the result­ing complex causes sensitization of T lymphocytes. Poison ivy is an example of a contact allergy wherein the reaction is delayed (with response occurring 48 to 72 hours after contact is made with the allergen).
* **Graft rejection** occurs when organs or tissues from one body are transplanted into another body. Cellular rejection of transplanted tissue occurs, unless the donor and recipient are genetically identical or the host immune response has been suppressed.
* **Graft-versus-host** reaction is an unusual phenomenon that occurs in bone marrow transplant recipients whose cellular immune system has been rendered deficient by whole body irradiation. Lymphocytes transferred to the host attempt to destroy host tissue.

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| Hypersensitivity reactions | | | |
| Type | **Alternative**  **nomenclature** | **Mechanisms** | **Examples** |
| I | Immediate  (anaphylactic) | IgE-mediated  via mast cell  degranulation | Atopic disorders  Anaphylaxis |
| II | Cytotoxic | Antibody against  membranebound  surface  antigens | Pemphigus  Idiopathic thrombocytopenic  purpura  Blood transfusion  reactions |
| III | Immune  complex | Immune complexes  deposited  in tissues | Systemic lupus  erythematosus  Rheumatoid arthritis |
| IV | Cell mediated | T-lymphocyte  mediated | Contact allergies  Graft rejection |

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| **Common allergens** | | |
| **Source of**  **allergen** | **Hypersensitivity** | **Examples** |
| Food products | I | Milk, nuts, egg, shellfish |
| Drugs | I, III | Aspirin, penicillins, sulfonamides |
| Environmental | I, IV | Animal hair, dust mite, pollen |
| Latex | IV, I (rare) | Condoms, dressings, elastic, bands, gloves |
| Dental materials | IV | Amalgam alloy, gold, mercury |

**Local Anesthetics**

The reaction most often associated with local anesthetics is a toxic reaction, which usually results from inadvertent intravenous injection of the anesthetic solution. Excessive amounts of an anesthetic also can cause a toxic reaction or a reac­tion to the vasoconstrictor.

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| **Signs and symptoms associ­ated with toxic reactions to**  **a local anesthetic** |
| Talkativeness  Slurred speech  Dizziness  Nausea  Depression  Euphoria  Excitement   1. Convulsions |

Signs and symptoms of a vaso­constrictor reaction include **tachycardia**, **apprehension**, **sweating**, and **hyperactivity**. Another common reaction to local anesthetics involves an anxious patient who, because of concern about receiving a “shot,” experi­ences **tachycardia**, **sweating**, **paleness**, and **syncope**. True allergic reactions to the local anes­thetics (amides) most often used in dentistry are rare. If the patient’s history supports a toxic or vasocon­strictor reaction, the dentist should:

* Explain the nature of the previous reaction
* Avoid injecting the local anesthetic solution intravenously by aspirating before the injection and limiting the amount of solution to the recommended dose.

If the patient’s history supports an interpretation of fainting and not a toxic or allergic reac­tion, the dentist’s primary task will be **to work with the patient to reduce anxiety during dental visits**.

If the history supports a true allergic reaction to a local anes­thetic, the dentist should try to identify the type of local anesthetic that was used. Once this has been ascertained, **a new anesthetic with a different basic chemical structure** can be used. The two main groups of local anesthetics in dentistry consist of the following:

1. Para-aminobenzoic acid (PABA) esters (procaine and tetracaine)

2. Amides (articaine, bupivacaine, lidocaine, mepivacaine, and prilocaine).

Benzoic acid ester anesthetics may cross-react with each other, whereas amide anesthetics usually do not cross-react. Cross-reaction does not occur between ester and amide local anesthetics.

**Procaine** is the local anesthetic associated with the highest incidence of allergic reactions. Its antigenic compo­nent appears to be PABA, one of the metabolic break­down products of procaine. Lidocaine or another amide local anesthetic should be used for patients with a history of allergy to procaine. Patients who have been allergic to local anesthetics but cannot identify the specific agent to which they reacted present more of a diagnostic problem. The nature of the reaction must be established, and if it is consistent with an allergic reaction, the next step should be to attempt to identify the anesthetic used. When the patient is unable to provide this information, the dentist can attempt to contact the previous dentist involved. If this fails, two additional options are available:

• An antihistamine (e.g., diphenhydramine) can be used as the local anesthetic (discussed later).

• The patient may be referred to an allergist for pro­vocative dose testing.

The dentist may elect to refer the patient to an allergist for evaluation and testing.

When administering an alternative anesthetic to a patient with a history of a local anesthetic allergy, the dentist should follow these steps:

1. Inject slowly, aspirating first to make sure that a vessel is not being injected.

2. Place 1 drop of the solution into the tissues.

3. Withdraw the needle, and wait 5 minutes to see what reaction, if any, occurs. If no allergic reaction occurs, as much anesthetic as is needed for the procedure should be deposited. Be sure to aspirate before giving the second injection.

**Management of patients with history of allergy to penicillin:**

Penicillin is used frequently throughout the world and is a common cause of drug allergy. About 5% to 10% of the population is allergic to penicillin and penicillin-related drugs and about 0.04% to 0.2% of patients treated with penicillin develop an anaphylactic reaction, which is fatal in about 10% of these patients, accounting for some 400 to 800 deaths per year.

**The possi­bility of sensitizing a patient to penicillin varies with different routes of administration, as follow:**

Oraladministration results in sensitization of only about 0.1% of patients.

While Intramuscular injection in about 1% to 2%and for topical application in about 5% to 12%.

Parenteral administration of penicillin evokes a more serious reaction than that typi­cally associated with oral administration**.**

Antibodies produced against penicillin cross-react with the semisyn­thetic penicillins and may cause severe reactions in patients who are allergic to penicillin**.** Patients with a history of penicillin allergy should be given erythromycin or clindamycin for the treatment of oral infection or clindamycin for prophylaxis against infective endocarditis**.** Cephalosporins are often used as alternatives to peni­cillins, however cephalosporins cross-react in 5% to 10% of penicillin-sensitive patients.

Skin testing for allergy to penicillin is much more reliable than is skin testing for allergy to a local anes­thetic.

When skin testing for penicillin sensitivity is per­formed, both metabolic breakdown products of penicil­lin (the major derivative, penicilloyl polylysine, and the minor derivative mixture) must be tested. 95% of peni­cillin is metabolized to the major determinant and 5% to the minor determinants. If skin test results are nega­tive for **both** breakdown products, the patient is consid­ered not allergic to penicillin.

**Analgesics.** Aspirin may cause gastrointestinal upset, but this problem can be avoided if it is taken with food or a glass of milk**.** Many people (about 2 in 1000) are allergic to salicylates. Allergic reactions to aspirin can be serious, and deaths have been reported. Aspirin provokes a severe reaction in some patients with asthma. They may react in the same way to other nonsteroidal anti-inflammatory drugs (NSAIDs).

**Rubber Products.** A number of reports have demon­strated that certain health care workers and patients are at risk for hypersensitivity reactions to latex or agents used in the production of rubber gloves or related materials (e.g., rubber dam, blood pressure cuff, catheters).Even that in most of time it is of **type IV**, but type I allergic reactions also reported.

**Dental Materials and Products:** Type I, type III, and type IV hypersensitivity reactions have been reported to result from various dental materials and products. Topical anesthetic agents have been reported to cause type I reactions consisting of urticarial swelling. Dental amalgam, acrylic, composite resin, nickel, palladium, chromium, cobalt, eugenol, rubber products, talcum powder, mouthwashes, and toothpastesare examples for reported allergies.

**MANAGEMENT OF SEVERE TYPE I HYPERSENSITIVITY REACTIONS**

• Place the patient in a head-down or supine position.

• Make certain that the airway is patent.

• Administer oxygen.

• Be prepared to send for help and to support respira­tion and circulation. The rate and depth of respiration should be noted, as should the patient’s other vital signs. Most reactions in dental patients consist of simple fainting, which can be well managed by the preceding actions. In addition, the dentist may administer aromatic spirits of ammonia through inha­lation, which encourages breathing through reflex stimulation.

• If these initial steps have not solved the emergency problem, and the cause is highly likely to be allergic, an edematous-type or anaphylactic reaction should be considered.

**If no improvement occur, suggest anaphylactic reaction and:**

* Have someone in the office call emergency ambulance.
  + Place the patient in a supine position.
  + Assess airway, breathing, circulation, and level of consciousness.
  + Establish a patent airway and administer oxygen.
  + Inject 0.3 to 0.5 mL of 1: 1000 epinephrine by an intramuscular (into the tongue) or subcutaneous route.
  + If no pulse is detected, support circulation through closed-chest cardiac massage. Support respiration by mouth-to-mouth breathing.
  + Repeat the injection of epinephrine every 5 minutes as needed to control symptoms and blood pressure.

**DIPHENHYDRAMINE HCl**

Use as a local anesthetic

**Supplies:**

(1) Two 5 mL sterile, disposable syringes with needle

(2) Diphenhydramine is supplied in 1 ml. ampules containing 50 mg/mL

(3) Diluent, such as normal saline, D5W, lactated ringers solution

(4) Epinephrine HCl, 1:1000 concentration, 1 mL ampule

(5) 1 mL tuberculin syringe

Preparation of diphenydramine HCl:

(1) Load contents of 1 mL ampule into syringe

(2) Dilute to a total of 5 mL of fluid by adding 4 mL of diluent

(3) Label syringe “diphenhydramine HCl 10 mg/mL”

**Addition of epinephrine:**

(1) Place 0.05 mL of epinephrine into the tuberculin syringe (this is of one-tenth of an mL)

(2) Carefully inject the epinephrine into the 5 mL syringe of diphenhydramine

(3) Mix the contents well

(4) Label syringe: ‘diphenhydramine HCl 10 mg/mL, epinephrine

1:100,000.

**Technique:**

Administer diphenhydramine HCl in the same manner and volume as any traditional local anesthetic

**Duration of action:**

Pulpal anesthesia: 30 to 60 minutes, Soft tissues: 2 – 4 hours

**Side effects:**

Drowsiness . . . should NOT permit patient to drive automobile

Soreness at injection site . . . inject slowly.