Clinical immunology PhD Microbiology(2022-2023)

Prof. Dr. Ikram Abbas Aboud Al-Samarraae

The Clinical Hypersensitivity:

The clinical signs of type I hypersensitivity result from the abrupt and excessive release of inflammatory mediators from mast cells, eosinophils, and basophiles. The severity and location of these responses depend on the number; location of these cells; degree of sensitization of an animal; and the amount of antigen involved, finally its route of administration. All these causes generalized mast cell degranulation and massive mediator release; that exceeds the ability of mast cell to respond to the rapid changes in the vascular system, an animal will undergo allergic anaphylaxis and may die.

Allergic anaphylaxis is severe, systemic hypersensitivity reaction. The clinical signs are determined by organ system involvement, which differs among the major domestic animals. Many of the symptoms are result of vasoactive molecules making smooth muscle contract in the bronchi, gastrointestinal tract, uterus, and bladder.

The major shock organs of horses are the lung and the intestine .Bronchial and bronchiolar constriction leads to coughing, dyspnea, and eventually apnea. Severe pulmonary emphysema and bronchiolar edema are commonly seen, also edematous hemorrhagic enterocolitis may cause severe diarrhea. The major mediators of anaphylaxis in horses are histamine and serotonin.

In cattle the major shock organ is the lung that characterized by profound systemic hypotension and pulmonary hypertension which resulting by constriction of the pulmonary vein and leads to pulmonary edema and severe dyspnea. The smooth muscle of the bladder and intestine contract, causing urination, defecation and bloating . The main mediators in cattle are serotonin, kinins and leukotrienes. Dopamine acts in bovine anaphylaxis by enhancing histamine and leukotrienes release from the lung, thus exerting a form of positive feedback. Because of the anticoagulant properties of heparin from mast cells, blood from animals experiencing anaphylaxis may fail to coagulate.

In sheep, pulmonary signs predominate in allergic anaphylaxis as a result of constriction of the bronchi and pulmonary vessels. Smooth muscle constriction also occurs in the bladder and intestine, and the mediators of type I hypersensitivity in sheep are histamine, serotonin, leukotrienes and kinins.

Specific Allergic Conditions:-

Allergic anaphylaxis is the most dramatic and severe type I Hypersensitivity reaction. It is more common to observe local allergic reactions, the sites of which are preferable to the route of administration of antigens. Example, inhaled antigens (allergens) provoke inflammation in the upper respiratory tract, trachea, and bronchi, resulting in fluid exudation from the nasal mucosa (hay fever) and tracheobronchial constriction (Asthma). Aerosolized antigen will also contact the eyes and provoke conjunctivitis and intense lacrimation. Ingested antigens may provoke diarrhea and colic as intestinal smooth muscle contracts violently. If sufficiently severe, the resulting diarrhea may be hemorrhagic. The antigen reaching the skin causes local dermatitis. The reaction

is erythematous and edematous and is described as an urticarial type, their lesions are extremely irritating because of the histamine released; consequently, scratching may mask the true nature of the lesion.

Milk Allergy:

Jersey cattle may become allergic to the α casein of their own milk. Normally, this protein is synthesized in the udder, and the animals are milked regularly, nothing untoward occurs. If milking is delayed, however, the increased intramammary pressure forces milk proteins into blood stream. In allergic cattle, this may result in reactions ranging from mild discomfort with urticarial skin lesions to acute anaphylaxis and death. Prompt milking can treat the condition, and affected animals may have to go for several lactations without drying –off because of the severe reactions that occur on cessation of milking.

Food Allergy:

About 2% of ingested protein is absorbed as peptide fragments large enough to be recognized as foreign. This antigen may travel in the blood and reach mast cells in the skin within a few minutes. It has been claimed that up to 30% of skin diseases in dogs are due to allergic dermatitis and that responses to ingested allergens may account for 1% of cutaneous disease in dogs and cats, although true prevalence is unknown. The clinical consequences of food allergies are seen both in the digestive tract and on the skin. It is important not to confuse '' food allergy '' an immunologically mediated reaction to food allergens, with ''food intolerance '' The American Academy of Allergy and Immunology has defined ''food intolerance '' as those adverse reactions to foods that are not immunologically mediated.

These reactions can include food idiosyncrasies, in which an animal responds abnormally to a food; metabolic reactions, in which a food component affects the metabolism of the animal; pharmacological reactions, in which some food components may act like drugs; and food poisoning, in which the adverse reaction is caused by a toxin or organism.

About 10% to 15% of dogs with food allergies have gastrointestinal problems. The intestinal reaction may be mild or it may be severe, with vomiting, cramps, and violent, sometimes hemorrhagic, diarrhea occurring soon after feeding. About half of affected dogs have a non seasonal pruritic dermatitis. The skin reactions are usually popular and erythematous may involve the feet, eyes, ears and axillae or perianal area. The lesion itself is highly pruritic and is commonly masked by self - inflicted trauma and secondary bacterial or yeast infections. The foods involved vary but are usually protein- rich such as dairy products, wheat meal, fish, chicken, beef, or eggs and cow's milk showed that they produce IgE against bovine IgG heavy chains .Thus, IgG is the major allergen in cow's milk. It is likely that it triggers hypersensitivity to lamb as a result of cross – reactivity with sheep IgG. A second major antigen in lamb and beef extracts has been identified as phosphoglucomutase. Food allergies have been reported in the horse but are uncommon. The most reliable test for suspected food allergies is to remove all potential allergens and then feed a hypoallergenic diet. These elimination diets usually contain meat and carbohydrates from sources to which the animal is unlikely to have been exposed. Example include mutton, duck, venison, or rabbit with brown rice or potato. The diet may be supplemented by adding other ingredients until

the allergen is identified by a recurrence of clinical signs. Treatment involves elimination the responsible food after correctly identifying it.

Allergies to Vaccines and Drugs:

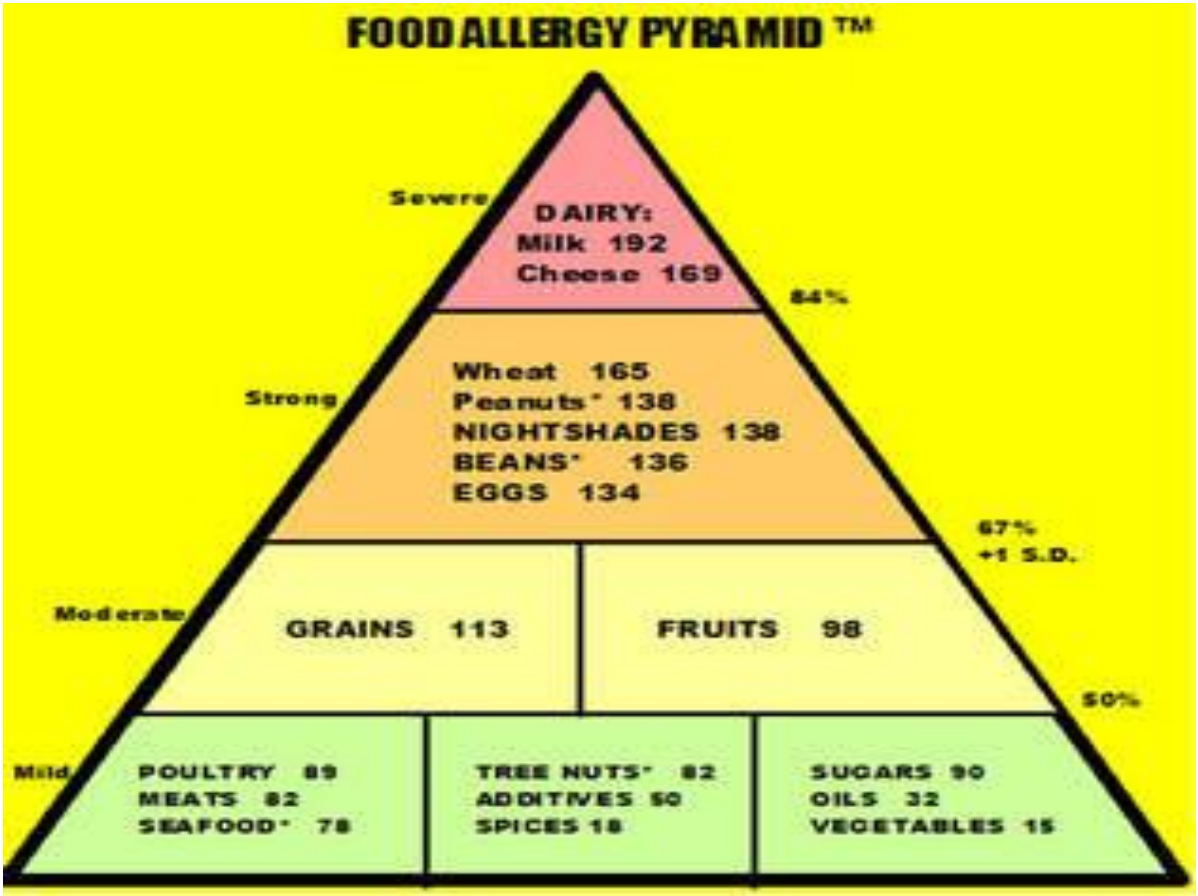
An IgE response may result from the administration of any antigen, including vaccines. It is most likely to occur in vaccines that contain trace amount of fetal calf serum, gelatin, or casein. This must always be taken into account when animals are vaccinated. Severe allergies have been associated with the use of killed foot – and-mouth disease, rabies, and contagious bovine pleuropneumonia vaccines in cattle. IgE responses may also occur following administration of drugs. Most drug molecules are too small to be antigenic, but many can bind to host proteins and then act as haptens. Penicillin allergy, for example, may be induced in animals either by therapeutic exposure or by ingestion of penicillin – contaminated milk.The penicillin molecule is degraded in vivo to several compounds; the most important of these contains a penicilloyl group. This penicilloyl group can bind to proteins and provoke an immune response. In sensitized animals, injection of penicillin may cause a cute systemic anaphylaxis or milder forms of allergy. Feeding of penicillin – contaminated milk to these animals can lead to severe diarrhea. Allergies to many drugs, especially antibiotics and hormones, have been reported in the domestic animals. Even carboxymethylcellulose used as stabilizers in vaccines may provoke allergies.

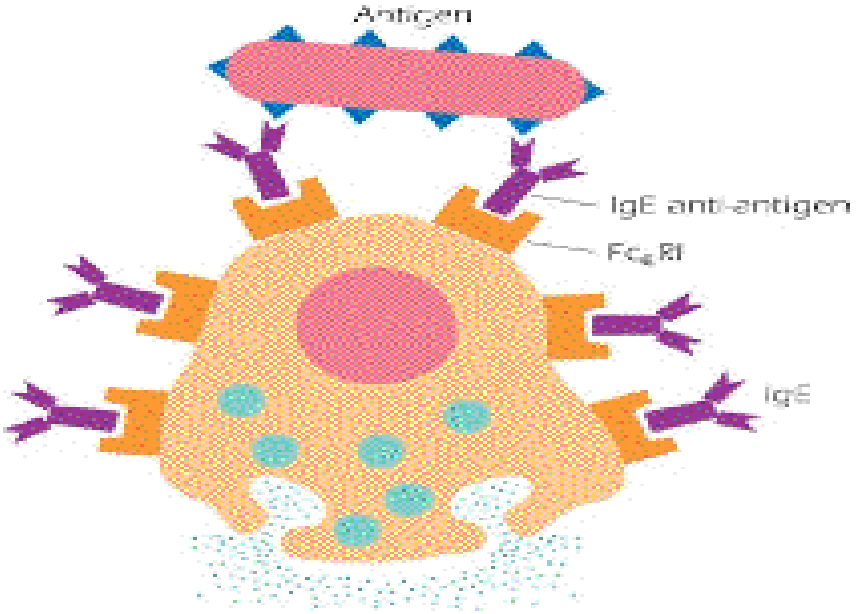
Allergies to Parasites:-

The beneficial role of the IgE mast cell –eosinophil system in immunity to parasitic worms as first observed in the self – cure phenomenon. Helminthes preferentially stimulate IgE responses. Helminthes are commonly associated with many signs of the allergies and anaphylaxis; for example, animals with tapeworms may show respiratory distress or uriticaria. Anaphylaxis may be provoke by rupture of hydatid cyst during surgery or through transfusion of blood from a dog infected with *Dirofilaria immitis* to sensitized animal.

In horse and cattle, Hypersensitivity to insect bites may cause an allergic dermatitis variously called Gulf Coast itch, Queensland itch, or sweet itch. The insects involved include midges (*Culicoides spp*.), black flies (*Simulium spp*.), stable flies (*Stomoxys calcitrans*), mosquitoes, and stick – tight fleas (*Echidnophaga gallinacea*). If animals are allergic to antigens in the saliva of these insects, biting results in the development of uriticaria accompanied by intense pruritus. The itching may provoke severe self – mutilation with subsequent secondary infection that may mask the original allergic nature of the lesion. In mange due to *Sarcoptes scabiei* in dogs and due to *Octodectes cyanotis* in cats, allergies may contribute to the development of skin lesions. The dermis is infiltrated with mast cells, lymphocytes, and plasma cells, and an intradermal injection of mite antigen leads to an immediate wheal – and – flare response. Infested animals may also make precipitating antibodies to mite antigens so that immune complexes may contribute to the development of lesions. Animal do not respond to arthropod allergens with a type I hypersensitivity. Thus, responses to *Demodex* mites and to component of flea saliva may be cell mediated (type IV hypersensitivity). Flea – bite allergic dermatitis is the single most important allergic disease. And continual exposure to fleas at an early age appears to result in a form of hyposensitization. Affected animals, in addition to the characteristic clinical signs, show a reaction

to intradermal injected flea antigen. Most positive animals will respond within a few minutes, but up to 30% may show a delayed reaction at 24 to 48 hours. Hyposensitization therapy has not been shown to be successful in treating flea allergy. Flea allergy can be successfully treated only total flea control.

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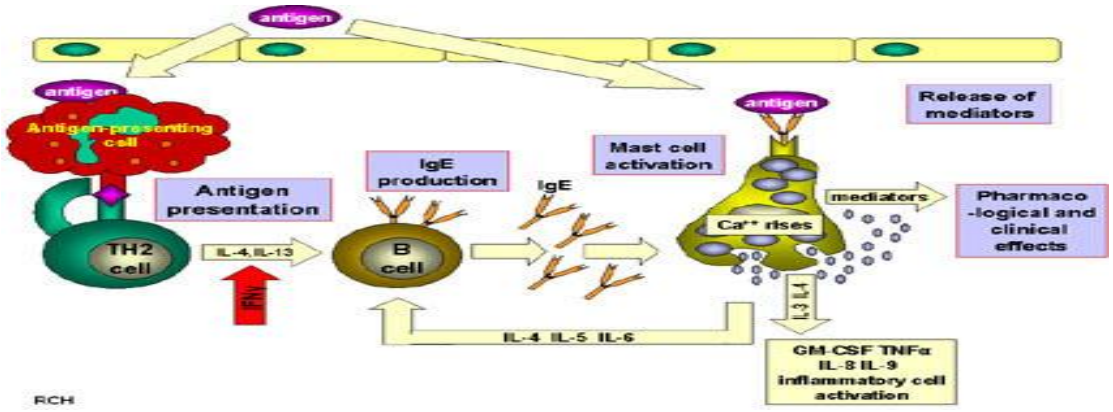
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IFN
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mediators
Release of mediators
Pharmaco -logical and clinical effects
IL-3 IL-4
IL-4 IL-5 IL-6
GM-CSF TNFα IL-8 IL-9 inflammatory cell activation
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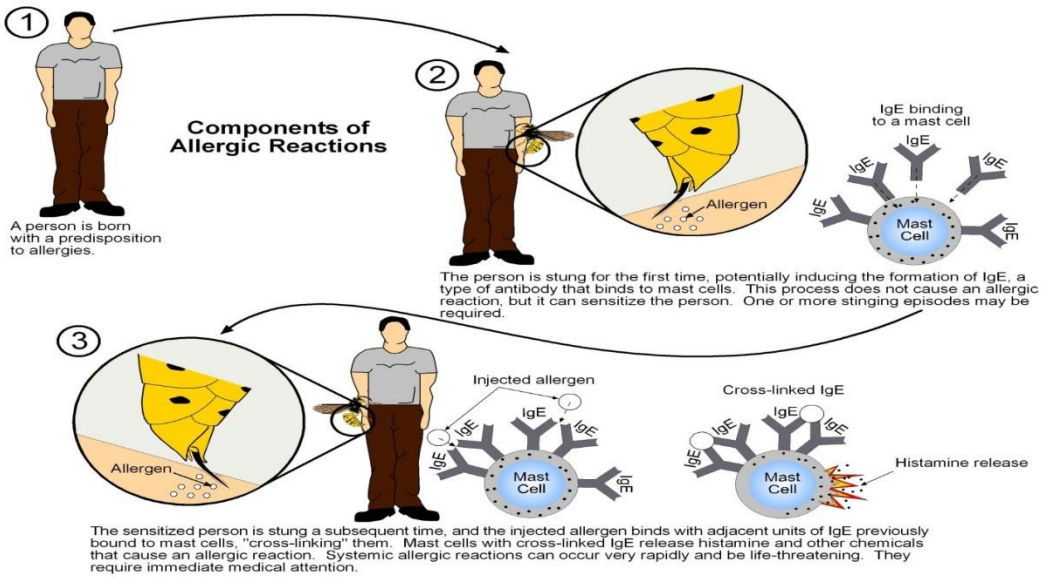
1
Components of Allergic Reactions
A person is born with a predisposition to allergies.
2
Allergen
IgE binding to a mast cell
IgE
Mast Cell
The person is stung for the first time, potentially inducing the formation of IgE, a type of antibody that binds to mast cells. This process does not cause an allergic reaction, but it can sensitize the person. One or more stinging episodes may be required.
3
Allergen
Injected allergen
Mast Cell
Cross-linked IgE
Histamine release
The sensitized person is stung a subsequent time, and the injected allergen binds with adjacent units of IgE previously bound to mast cells, "cross-linking" them. Mast cells with cross-linked IgE release histamine and other chemicals that cause an allergic reaction. Systemic allergic reactions can occur very rapidly and be life-threatening. They require immediate medical attention.

IgE-mediated allergic reactions			
Syndrome	**Common allergens**	**Route of entry**	**Response**
Systemic anaphylaxis	Drugs Serum Venoms	Intravenous	Edema Vasodilation Tracheal occlusion Circulatory collapse Death
Wheal-and-flare	Insect bites Allergy testing	Subcutaneous	Local vasodilation Local edema
Allergic rhinitis (hay fever)	Pollens (ragweed timothy, birch) Dust mite feces	Inhaled	Edema of nasal mucosa Irritation of nasal mucosa
Bronchial asthma	Pollens Dust mite feces	Inhaled	Bronchial constriction Increased mucus production Airway inflammation
Food allergy	Shellfish Milk Eggs Fish Wheat	Oral	Vomiting Diarrhea Pruritis (itching) Urticaria (hives)