ALLERGY

altered state of reactivity to common environmental and food antigens causing clinical reactions.

Elements:

allergens, t cells th2 cytokine release il4,5,13 causes IgE & eosinophilia (local + systemic). the antibodies are allergen specific. IgE mediated hyperresponsiveness in target organs: lung, skin, gastrointestinal tract, and nose

allergens are almost always proteins -> antigen: depend on stimulation capacity, stability in tissues + dose & time of stay. there is a role of antigen presenting cells e.g. dendritic+ Langerhans -> *sensitization phase* monocytes and macrophages in re-exposure: *elicitation phase* on t helper.

low-MWs moieties, such as drugs, can become allergens by reacting with serum proteins & increasingly carbohydrates are recognized as allergens: galactose?

Eosinophils releases proteins bind to M2 receptors, releases Ach causing airway hyperresponsiveness e.g. narrowing. + leukotrienes, PGs released increase vascular permeability. While the cytokines: il5,3 GM-CSF regulates the eosinophils function.

mast cells are local cells, don't circulate, often in epithelial of: git, rs, skin, can release lipid mediators like COX & LOX -> pro inflammatory.

Phases:

so early phase = was cello degranulation: swelling, itching, sneezing, wheezing, cramps.

late-phase response can occur within hours of allergen exposure, reaching a maximum at 6-12 hr can cause blockade: mass effect secondary to circulatory cell recruit.

chronic allergic disease, tissue inflammation can persist for days to years. -> repeated stimulation of allergic effector: tissue remodeling e.g. in asthma

Etiology:

atopy is genetic, due to defective genes that control barrier function in specific target organs + genes encoding pattern-recognition receptors of the innate immune system that engage microbial pathogens and influence the adaptive immune

+ have a strong familial predisposition, ~ 60% heritability found in twin studies of asthma and atopic dermatitis.

+ barrier dysfunction has a key role in the pathogenesis of allergic diseases. eg. hepatitis A virus) correlate with asthma? as dysregulation of these frontline immune defense systems due to infection? also S.aereus? would permit abnormal response to common environmental allergens.

Diagnosing:

history & exam: timing of exposure: duration? consistent with phases? past history? of the same/ other kind of allergies? + previous therapies. + family history: 50% when 1 parent is allergic, 66% for both. maternal > paternal hx.

timing: dust, pollen, morning, animal dander, pets? fungal spores? + aeroallergens, such as pollens and fungal spores, the concentrations of which in outdoor air fluctuate seasonally, with indoor sources being year round

food allergies are more common in infants and young children, resulting primarily in cutaneous, gastrointestinal, and, less frequently respiratory symptoms. if IgE involved its around 2 hr. after ingestion of the offending. more than that think of other kind of allergies.

find source and eliminate that is the definitive management of allergies.

chronic corticosteroids/ other med. always crosscheck hx of side effect of medication if on treatment, e.g. growth suppression. steroid induced hypertension?

systemic manifestation:

children feature? rhinorrhea + pruritus ->allergic salute (cup nose up)->nasal crease: horizontal wrinkle over nasal bridge, eye grinding, allergic cluck by tongue on palate, eventually nasal polyps can develop: impaired smelling, snoring, apnea? sinusitis?

r/o fever, purulent discharge, unilateral siting.

pulsus paradoxus, defined as a drop in systolic blood pressure during inspiration >10 mm Hg can occur with asthma: as hyperinflated lungs blocks the venous return.

blue-gray to purple discolorations beneath their child's lower eyelids, venous stasis (allergic shiners) not too sensitive though (40% of non-allergic populationn. have it) instead morgan folds are typical for atopic dermatitis: infraorbital skin folds from inner cants to lower lid margin.

conjunctivitis? injection, lacrimation, edema, chemises, edema? and with repeated rubbing risk for keratoconus.

earlobe skin too + otitis media with effusion is common in children with allergic rhinitis, + lip lickers dermatitis. + dermatitis). Tonsillar and adenoidal hypertrophy + snoring raises the possibility of obstructive

chest findings depend on duration, severity + activity. in acute: hyper inflated, tachypnea, use accessory muscles, wheezing with prolonged expiatory time. decreased airflow + wheezes: bilateral unilateral rule out foreign body ingestion.

digital clubbing as a sign of chronic hypoxia (often in chronic bronchitis/ cystic fibrosis for kids) is rarely seen in patients with uncomplicated asthma, so rule them out

xerosis, or dry skin, is the most common skin abnormality of allergic children + urticaria/angioedema for attic dermatitis. thickened skin and exaggerated palmar and plantar creases (hyper linearity) if there is atopic dermatitis? keratosis pillars.

Investigations:

<u>in vitro tests></u>

500 eosinophils/μL in peripheral blood, >1500 without an identifiable etiology should suggest 1 of the 2 hyper eosinophilic syndromes

nasal and bronchial secretions may be examined for eosinophils: Hansel stain

elevated IgE value: IgE values are measured in international units (IU), with 1 IU equal to 2.4 ng of IgE. diagnostic value of a total IgE level is poor as they are often elevated in all allergic patient. + infestation /IgE myeloma, and other disease/ meds can rise it

allergen-specific IgE (sIgE) levels in the serum

<u>in vivo</u>

the skin prick test/ intradermal patch
provocation testing is performed to examine the association between allergen exposure? methacholine & food challenges
endoscopy eosinophilic esophagitis.

Management Principles:

<u>environmental</u> control measures: cat, mites, cockroaches, animal dander, mood, pollens,

<u>pharmacological</u>

adrenergic agonists alpha -> vasoconstriction eg nasal decongestant pseudoephedrine, & antihistamine, + beta -> bronchodilation treatment of asthma. specifically, a1-2. b1-3 with specific tissue distribution!

epinephrine remains the drug of choice for the treatment of anaphylaxis because of its combined α- and β-adrenergic effects.

note side effect of a agonists: vasoconstrictors-> metabolic disorders, such as diabetes and hyperthyroidism as HPA axis is stimulated. + adverse effects of excitability, headache, nervousness, palpitations, tachycardia, arrhythmias, hypertension,
nausea, vomiting, and urinary retention. use them topically.

selective for the β2-adrenergic receptor, such as albuterol, levalbuterol, and pirbuterol, have the advantage of producing significant bronchodilation with less cardiac stimulation.

LABA with an inhaled corticosteroid have had significant impact on treatment of moderate persistent asthma. as it also improves mucocilliary clearance, decrease vascular permeability and low Act stimulation. Can be delivered orally, by inhalation, or by injection.

adverse effects of β-adrenergic agents include tremor, palpitations, tachycardia, arrhythmias, central nervous system stimulation, hyperglycemia, hypokalemia, hypomagnesemia, and a transient increase in hypoxia, which is attributed to an increase in perfusion to inadequately ventilated areas of the asthmatic lung.

Anticholinergic drugs inhibit vagally mediated reflexes by antagonizing action of acetylcholine at muscarinic receptors. ipratropium bromide is the most. therapy using ipratropium bromide and β-agonist therapy in more severe asthma exacerbations. Ipratropium is available by prescription as a metered dose inhaler delivering/ nasal spray.

Histamine effects triggered through H1-receptor binding are those most relevant to allergic inflammation, and include pain, pruritus, vasodilation, increased vascular permeability, smooth muscle contraction, mucus production, and stimulation of parasympathetic nerve and reflexes

H1-type antihistamines are traditionally divided into 6 classes. antihistamines are further divided into first generation antihistamines, which, because of their lipophilicity, cross the blood–brain barrier to exert effects on the central nervous system like sedative and anticholinergic effects: drying of the mouth and eyes, urinary retention, constipation, excitation, nervousness, palpitations, and tachycardia and second-generation antihistamines, which exert minimal.

Orally administered antihistamines are well absorbed and reach peak serum concentrations within ∼2 hr and removed by hepatic clearance.

Chromones: Cromolyn sodium and nedocromil sodium: inhibit mast cell degranulation and mediator release. Cromolyn and nedocromil prevent early- and late-phase allergic responses when administered before allergen exposure. they lack of bronchodilator properties, neither drug is useful for the treatment of acute asthma,

Glucocorticoids are widely used in the treatment of allergic disorders because of their potent anti-inflammatory properties. sprays, creams and ointments, metered-dose inhalers, and as a solution for nebulization.

<u>Other meds</u>

1. of its bronchodilation effects, theophylline (1,3- dimethylxanthine)
2. inhibiting leukotriene production or by blocking receptor binding.
3. Monoclonal ant immunoglobulin E antibodies (anti-IgE) bind to circulating IgE (omalizumab)
4. Irrigation with nasal saline can improve symptoms for those with mild
5. Allergen immunotherapy involves administering gradually increasing doses of allergens to a person with allergic disease for the purpose of reducing or eliminating the patient's adverse clinical response