Wondershare EdrawMind

- **hypersensitivity**
  - type 1
    - i.e., immediate hypersensitivity reactions, allergy, atopy
    - mehcanism
      - reaction first requires sensitization to the specific allergen and occurs in geneto-environmental factors predisposed individuals (those having certain MHC haplotype).
      - is then processed by the dendritic cell The antigen-presenting cells then migrate to lymph nodes, where they prime naive TH cells to be TH2
      - TH2 cells then bind activated B cells by same allergen to promote production of IGE
      - in reexposure to the antigen IGE binds to mast cells and basophils(sensitization phase)
      - IGE binds antigens by crosslinking which is the binding of 2 IGE with one allergen
    - phases
      - early phase
        - with in 5 min
        - immediate wheal-and-flare reaction
        - Preformed mediators
          - Tryptase : its exact role is uncertain,
          - Proteoglycans : Proteoglycans include heparin.
          - histamine
            - has two receptors
              - histamine 1 (H1)
                - H1 receptor antagonists (commonly called antihistamines) can inhibit the allergy response
              - histamine 2 (H2)
                - H2 antagonist inhibit gastric secretions
            - cause contraction of smooth muscles of the airway and GI tract, increased vasopermeability and vasodilation, enhanced mucus production, pruritus (itching) , cutaneous vasodilation
        - Newly formed mediators
          - lipid metabolites
            - Leukotrienes cause prolonged bronchoconstriction
            - prostaglandin D2 (PGD2).
              - acts on smooth muscle cells and acts as a vasodilator and a bronchoconstrictor
            - Platelet-activating factor (PAF): Adenosine: Bradykinin (all function as histamine)
      - late phase
        - 2 to 4 hours after early phase
        - accumulation of inflammatory leukocytes
          - including neutrophils,eosinophils, basophils, and helper T cells
        - cytokines produced by TH2
          - IL-4,IL-13
            - Stimulates and maintains TH2 cell proliferation and switches B cells to IgE synthesis.
          - IL-5
            - This cytokine is key in the maturation, chemotaxis, activation, and survival of eosinophils.
          - IL-6: promotes mucus production
          - Tumor necrosis factor-alpha
            - This activates neutrophils, increases monocyte chemotaxis
    - Allergen
      - they are prtoeins with low molecular wight
      - Pollens, house dust mite (most common allergen), cat or dog hair flakes
      - Some are ingested like, egg, milk, peanuts and fish
      - Drugs like penicillin and cephalosporin
    - clinical manifistation
      - Urticaria (Eczema. Atopic dermatitis) and wheals formation:
        - in the superficial layers of the skin can cause pruritic wheals (suface swelling in the skin) with surrounding erythema. If deeper layers of the dermis and subcutaneous tissues are involved, angioedema results.
      - Allergic rhinitis (nasal inflammation, called hay fever,): Sneezing, itching, nasal congestion, rhinorrhea, and itchy or watery eyes.
      - Allergic conjunctivitis with itchy eyes
      - anaphylaxis
        - systemic vasodilation and vasopermeability can result in significant hypotension and edema and is referred to as anaphylactic shock. Anaphylactic shock is one of the two most common causes for death in anaphylaxis; the other is throat swelling and asphyxiation (suffocation)
      - GIT
        - Food allergy; It can also be affected with nausea, abdominal cramping (stomach ache) , bloating (swelling of abdomen), and diarrhea
    - Diagnostic tests
      - Skin test (prick and intradermal
        - Induction of very low amount of extract allergen and see the reaction in 15 mins.Extracavation of serum, pruritis and erythema (wheal and flare ; itchy flaming sweling of skin).
      - Skin patch test; allergen patch
        - followed by biopsy of the skin 24 or 48hrs after putting the patch, eczema, spongiosis (formation of sponge-like layer in the skin) of the epidermis and cell infiltrate are checked for.
      - Serum assay of IgE antibodies RAST
    - treatment
      - Anti-histamine, leukotrienes antagonists, corticosteroids
      - For anaphylactic shock; IM adrenaline, IV anti-histamine and corticosteroids.
      - Humanized monoclonal Anti-IgE
      - by immunotherapy
      - IL12

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- **hypersensitivety**
  - Type 2
    - i.e., antibody- mediated hypersensitivity reactions
    - mechanism
      - Ab bind antigens present on the cell surface (self or foreign; like RBCs) or tissue surface
      - leading to
        - Activation of the complement pathway.lysis
        - Antibody dependent cellular cytotoxicity ⇧ lysis
        - Opsonization and phagocytosis
    - diseases
      - Abs target RBCs
        - Transfusion rejection and hyper acute graft rejection
          - lead to intravascular hemolysis, No need to pre-exposure
          - Pre-formed IgM Ab
        - Hemolytic anemia of newborn (RH system antigen
          - IgG Ab against RH+
          - need pre-exposure.
        - Autoimmune hemolytic anemia
          - can be either spontaneous or drug induced
          - Warm reactive auto-Ab (IGG) unknown cause, destruction in spleen
          - Cold reactive auto-Ab (against certain carbohydrates on the RBCs , mainly IgM) destruction intravascular
          - Auto-Ab caused by allergy to drugs (penicillin ,methyldopa, quinine)
            - The drug –Ab is adsorbed on the erythrocytes surface
      - The target may be neutrophils (DNA, cytoplasm protein and mitochondria) expressed on the surface of the cells in SLE then bound to auto-Ab,
      - platelet in ITP (idiopathic thrombocytopenic purpura)
      - Good pasture,: renal and lung basement membrane (IgG)
      - Myasthenia gravis: Acetylcholine receptors in muscle (IgG),muscle weakness
      - Pemphigus: adhesion molecules in skin, HLA-dr4 related (IgG4)
      - Antibodies specific for thyroid stimulating hormone receptor in graves' disease. hyperthyroidism, Ab attacks the thyroid and causes it to make more thyroid hormone than your body needs
    - tests
      - coombs test
        - direct
          - detect the presence of Ab on surface of cell(sensitized RBC)
          - usewd for
            - autoimmune hemolytic anemia
            - hemolytic disease of the newborn
            - sensitization of red blood cells caused by the presence of drugs, or a transfusion reaction
        - indirect
          - indirect agglutination test for looking for specific antibodies in serum
          - used for
            - Of recipient for presence of Ab against donor blood in Preparation for blood transfusion
            - screening mothers who are susceptible to have baby with hemolytic anemia of newborn.
      - biopsy
        - by immunofluorescence; the presence of antibody and complement in the lesion. The staining pattern is normally smooth and linear
        - used for
          - Goodpasture's nephritis (renal and lung basement membrane) and pemphigus (skin intercellular protein, desmosome
    - treatment
      - anti-inflammatory and immunosuppressive agents
    - importance in treating tumors
      - Anti-CD20 Ab in B cell lymphoma
      - Anti-CD52 Ab in B, T cell leukemia