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- PID
  - T-cell deficiency
    - lead to deficient cell-mediated immunity and humoral immunity
    - the main cause of SCID
      - affects both humoral and cell-mediated immunity because of T cell Deficiencies with or without B cells and NK cells
      - types
        - Lymphocyte precursor cell death due to purine metabolism defect
          - ADA (adenosine deaminase) or PNP (purine neucleoside phosphorylase) deficiency results in an accumulation of toxic precursors
          - affects developing T NK and B cells
        - Defective signaling through the common g-chain-dependent cytokine receptors
          - IL-4, IL-7, IL-9, and IL-15 (most common)
          - IL-2R gamma
            - doesnt affect B cells
          - X-linked
        - mutations in the gene encoding the IL-7Rα chain
          - autosomal recessive inheritance
          - pure T-cell deficiency
        - Defective V(D)J recombination; mutation in RAG1 or RAG2 genes, artemis deficiency impair T and B cells
        - Defective pre-TCR/TCR signaling, pure T cell deficiency
        - Reticular dysgenesis (most severe)
          - AKA Aleukocytosis
          - Less than 2% of SCID
          - characteristics
            - total Lack of innate and adaptive humoral and cellular immunity
            - Fatal sepsis within days after birth
            - Myeloid differentiation is blocked at the promyelocytic stage
            - Erythro- and megakaryocytic maturation is normal
          - pathogenesis
            - Mutation in adenylate kinase 2 (AK2), enzyme of mitochondrial energy.
            - Leads to loss of energy required for Differentiation and proliferation of hematopoietic stem cells
          - first from PID that is mitochondoriopathy
    - Digeorse syndrom
      - symptoms
        - Cardiac abnormality (especially tetralogy of Fallot)
        - Abnormal facies
        - Thymic aplasia
        - Cleft palate
        - Hypocalcemia/Hypoparathyroidism
        - abbreviatd as CATCH-22
      - associated with defective development of thymus due to deletion of a small piece in chromosome 22.
    - Defective expression of MHC :
      - AKA Bare lymphocyte syndrome 1&2
      - class 1
        - No or decreased CD8+ T cells
        - Mutations in TAP1, 2
      - class 2
        - No or decreased CD4+ T cells
        - Defective humoral immunity although normal numbers of b cells
    - Ataxia-telangiectasia
      - an autosomal recessive disorder
      - characterized by
        - abnormal gait (ataxia)
        - vascular dilatation (telangiectases) on the whites of the eyes and on sun-exposed areas of skin
        - neurologic deficits
        - increased incidence of tumors, and immunodeficiency and radiation sensitivity.
      - caused by
        - Gene mutation of ATM (ataxia-telangiectasia mutated)
        - which plays in class-switch recombination.
      - may affect both or either B and T cells
        - humoral immune defects is most common
    - Wiskott-Aldrich syndrome
      - X-linked
      - characterized by eczema, thrombocytopenia (reduced blood platelets), and susceptibility to bacterial infection.

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Secondary immune- deficiency

- HIV
  - infects CD4+ T cells , macrophages and dendritic cells. It destroys CD4+ T cells
  - steps of HIV progress
    - Acute HIV infection: flue symptoms + spread of virus
    - clinical latent HIV infection: immune system act (start antibodies and CD8 action) + trapping of virus by dendritic cells in lymph node, more CD4 destruction
    - and later to AIDS, CD4 suppression
  - steps of infection of CD4 T cells
    - gp120 binds CD4
    - gp120 interact with Tcell chemokines
    - conformational change that exposes gp41 called fusion protein
      - enables the viral envelope to fuse with the host T cell membrane.
    - leading to destruction of CD4 T cells.
  - mechanism of immune evasion
    - Very high mutation rate
    - Down regulation of MHC 1
    - Killing CD4
  - transmission
    - Sexual transmission
    - Blood products
    - Mother to fetus
  - tests
    - Serologic tests which detect anti-HIV antibody (IgG and IgM) positive after 1-3 months of infection
    - ELISA; look for the HIV p24 antigen in patient fluids
    - PCR
      - can be detected in the window period so before 1-3 months after infection.
      - some evidence suggest that it can even be detected earlier
  - highly active antiretroviral therapy (HAART)
    - goals
      - improvement in the patient's quality of life, reduction in complications, and reduction of HIV viremia below the limit of detection
    - evene with HAART over the long term HIV-infected patients may experience the disease complications as neurocognitive disorders, cancers, nephropathy, and cardiovascular disease.
    - regimens consist of
      - two nucleoside analogue reverse transcriptase inhibitors (NARTIs or NRTIs) plus either a protease inhibitor or a non -nucleoside reverse transcriptase inhibitor (NNRTI)
      - to inhibit virus from making new DNA for replication.