PATHOPHYSIOLOGY OF PRIMARY IMMUNE DEFICIENCIES

Disorder	Etiology	Pathophysiology and Presentation	Lab Findings and Diagnosis	Treatment
GENERAL FEATURES Gingivitis and periodontits are common in all immunodeficiencies: phagocytic, AMI, neutropenia DDx: asplenia, anatomic defect, malnutrition, CF, Kartagener's syndrome, allergies				
ANTIBODY DEFICIENCIES				
LIMITED ANTIBODY DEFICIENCIES	**Selective IgA deficiency** **IgG subclass deficiency** **Impaired Polysaccharide Responsiveness (IPR)**	Recurrent sinusitis Recurrent AOM Pneumonias Responds to ABx	Quantitate Immunoglobulins IgG subclass levels Ab titre response to vaccination	Prophylactic ABx Empiric ABx therapy
SELECTIVE IgA DEFICIENCY	**Anti-epileptic drugs** **Familial**	25% are asymptomatic **25% have recurrent RTIs** 25% are **atopic** + 25% with **autoimmune disorder** Anaphylaxis to blood and IVIG transfusions (if contains IgA)	IgA is absent in serum and RT secretions Autoantibodies (indirect Coombs) to RBCs IgG2 subclass deficiency	ABx Avoid IVIG and blood transfusions Immunization
IMPAIRED POLYSACCHARIDE RESPONSIVENESS		Typically normal until 2 yrs Commonly occurs > 60 yrs due to natural senescence of AMI	**Poor Ab response to most serotypes in the Pneumovax** NML IgG and subclasses AMI response to protein Ags is intact	Continuous ABx therapy Conjugate vaccination IVIG (rare)
TRANSIENT HYPOGAMMAGLOBULINEMIA of INFANCY	**Latency in Ig synthesis** **RF:** prematurity	Recurrent bacterial infections 4 – 24 mos. Chronic diarrhea FTT Eczema Food intolerance	Global depression in all immunoglobulins IgE > 100 IU/mL Neutropenia	ABx Steroids IVIG

X-LINKED AGGAMAGLOBULINEMIA	Absent B-cells Absent Ig	Pyogenic infections occurring ? 6 mos. Absent tonsils and lymph nodes Bronchiectasis, enteroviral encephalitis, OPV polio reversion	Ig < 200 md/dL No functional Abs Absent B cells NML T-cells	IVIG ABx **No vaccination!**
COMMON VARIABLE IMMUNODEFICIENCY	Intrinsic B-cell deficit T-cell deficits are variable	Onset > 10 yrs Frequent URT infections Sinusitis, pneumonia, bronchiectasis Diarrhea Autoimmunity, blood dyscrasias, malignancy	Ig < 400 mg/dL No Abs NML B-cell count Variable T-cell count and Fx	IVIG ABx
CMI DEFICIENCIES				
DiGeorge syndrome (22q11)	Thymic aplasia	**Complete DiGeorge Syndrome**: this is RARE! Classic facies Neonatal tetany Cardiac outflow tract defects Microcephaly MR **Partial DiGeorge Syndrome (22q11 deletion)** **CATCH-22 Syndrome** Results in velo-cardio-facial syndrome Clef-palate, velopharyngeal defect, cardiac outflow tract malformation, GE reflux Hypocalcemia URI infections (may have aspiration) Selective Ab deficits	Absence of thymus T-cell depletion Ig NML Hypocalcemia	Cardiac repair Ca2+ and VitD supplementation Marrow and thymus transplant
ISOLATED T-CELL DEFICIENCY (including HIV)	Low T-cell count **HIV** **APECED Syndrome** **Chronic Mucocutaneous Candidiasis**	Non-specific rash FTT Chronic diarrhea Opportunistic Infections	Cutaneous anergy (candida Ag) SelectiveCD4+ depletion (HIV) Depressed T-cell response to mitogens	Tx infections Prophylactic antifungals + Abx

SEVERE COMBINED IMMUNODEFICIENCY (SCID)	Genetic defects: AR, X-linked, and sporadic	Early dermatologic, respiratory, GI infection FTT PCP pneumonia, candidiasis, rashes Absent tonsils and lymph nodes	**T-cell depletion** **Absence of thymus** Variable B cell count Abnormal TRECS	Allogenic marrow transplant Gene therapy (X-linked variants only)
FUNCTIONAL DEFICIENCIES				
LEUKOCYTE ADHESION DEFECT TYPE I	AR inheritance Defective CD18/CD11b (Mac-1) adhesion complex	Soft-tissue infections Dermatitis Periodontitis Delayed detachment of umbilical cord	**Leukocytosis** **Decreased CD11b expression** on granulocytes Deficient phagocytosis and chemotaxis	ABx GM-CSF Allogenic Marrow Transplant
CHRONIC GRANULOMATOUS DISEASE	Genetic defects: X-linked, AR Defective NADPH oxidase	Skin, bone, lung abscesses *S. aureus, Serratia*, *Aspergillus* Splenomegaly Hepatomegaly Lymphadenopathy Delayed wound healing	**Abnormal oxidation tests (DHR)** Elevated Ig NML T-cells	ABx Antifungals IFN-γ Steroids (if granulomatous lesion is obstructive)
COMPLEMENT DEFICIENCIES				
LATE COMPLEMENT DEFECT (C6 – C9)	AR	Recurrent infection with *Neisseria* (meningitis, gonorrhea) Onset in early adulthood Collagen-vascular disorders Angioneurotic edema	**Absent CH50** May have some activity with C9 deficiency **Absence of enzyme on immunoassay**	Prophylactic ABx Conjugate vaccination (encapsulated organisms)