IMMUNOLOGY BUZZWORDS

RAPID PATTERN RECOGNITION

Innate • Adaptive • Complement • Cytokines
Hypersensitivity • Autoimmunity • Immunodeficiency

USMLE STEP 1 & STEP 2 BOARD REVIEW

2026 EDUCATIONAL EDITION

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NAME THE IMMUNE EFFECTOR FIRST

IMMUNOLOGY BUZZWORDS

Rapid Pattern Recognition for USMLE Step 1 & Step 2

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Educational Scope Designed for rapid board review and teaching. It is not a substitute for patient-specific evaluation, specialist consultation, current vaccine schedules, prescribing information, or institutional protocols.

How to Use the Buzzword Method

- **1. Name the effector:** antibody, T cell, complement, phagocyte, cytokine, or immune complex.
- **2. Use timing:** minutes suggests Type I; 48-72 hours suggests Type IV; infection age narrows immunodeficiency.
- **3. Match the organism:** encapsulated bacteria suggest humoral/complement/splenic failure; opportunists suggest T-cell failure.
- **4. Read the phenotype:** CD3, CD19/20, CD16/56, immunoglobulins, CH50/AH50, DHR, and vaccine titers.
- **5. Identify the board trap:** a normal cell count does not prove normal function.

Contents

CHAPTER 1

Immune System Roadmap

Separate innate, humoral, cellular, and regulatory failure before naming a disease.

SOURCE-DERIVED CORE: CONSOLIDATED FROM PRIOR SINOE IMMUNOLOGY MATERIALS

IMMUNE SYSTEM RAPID ROADMAP

INNATE	HUMORAL	CELLULAR	REGULATION
TIMING Minutes-hours	**TIMING** Days; memory	**TIMING** Days; memory	**TIMING** Continuous
PLAYERS Neutrophils, macrophages, dendritic cells, NK cells, complement	**PLAYERS** B cells, plasma cells, antibodies	**PLAYERS** CD4 subsets, CD8 T cells	**PLAYERS** Tregs, deletion, anergy, checkpoints
PRIMARY JOB Pattern recognition, inflammation, phagocytosis	**PRIMARY JOB** Neutralization, opsonization, class switching	**PRIMARY JOB** Macrophage activation, coordination, cytotoxicity	**PRIMARY JOB** Maintain self-tolerance and terminate responses
FAILURE PATTERN CGD, LAD, complement defects	**FAILURE PATTERN** XLA, CVID, IgA deficiency	**FAILURE PATTERN** DiGeorge, SCID, HIV	**FAILURE PATTERN** Autoimmunity, allergy, immune dysregulation

EXAM SHORTCUT: ORGANISM + AGE + LYMPHOCYTE PHENOTYPE + FUNCTIONAL TEST

Original immune system roadmap: response arm, timing, primary job, and failure pattern.

Innate immunity "Immediate pattern recognition"

MECHANISM: PRRs recognize conserved microbial and damage patterns; complement, phagocytes, and NK cells act without prior sensitization.
CELL / MOLECULE CLUE: Neutrophils/macrophages, dendritic cells, NK cells, complement; no somatic receptor rearrangement.
BOARD TRAP: Innate immunity can shape adaptive responses through antigen presentation and cytokines.
TREATMENT / PEARL: Defects produce pyogenic/fungal infection, poor inflammation, or impaired oxidative killing.

Adaptive humoral immunity "Antibodies neutralize and opsonize"

MECHANISM: B-cell receptors undergo V(D)J recombination; activated B cells become plasma cells and memory cells.
CELL / MOLECULE CLUE: IgM first response; IgG systemic memory/opsonization; IgA mucosa; IgE allergy/helminths.
BOARD TRAP: A normal B-cell count does not prove normal antibody production.
TREATMENT / PEARL: Poor vaccine titers can reveal functional humoral failure.

Adaptive cellular immunity "CD4 coordinates; CD8 kills"

MECHANISM: TCR recognizes peptide-MHC; costimulation and cytokines determine differentiation.
CELL / MOLECULE CLUE: CD4 uses MHC II; CD8 uses MHC I; NK cells kill low-MHC-I targets without antigen-specific priming.
BOARD TRAP: T cells do not recognize free native antigen.
TREATMENT / PEARL: T-cell failure predisposes to viral, fungal, mycobacterial, and opportunistic infections.

Self-tolerance "Delete, silence, suppress"

MECHANISM: Central tolerance removes strongly self-reactive clones; peripheral anergy, deletion, and Tregs limit escaped clones.
CELL / MOLECULE CLUE: AIRE supports thymic self-antigen display; FOXP3 supports Treg function.
BOARD TRAP: Autoantibody positivity alone is not equivalent to clinical autoimmune disease.
TREATMENT / PEARL: Loss of tolerance may produce infection plus autoimmunity in immune-dysregulation syndromes.

Four Failure Modes in One Table

Failure mode	What is wrong	Clinical result
Too weak	Missing cell, molecule, signaling, or function	Immunodeficiency and opportunistic infection
Too strong	Excessive response to a usually harmless target	Allergy and hypersensitivity
Wrong target	Self-antigen or graft becomes the target	Autoimmunity and rejection
Poor control	Regulation or resolution fails	Immune dysregulation, autoinflammation, cytokine injury

Clinical Clue Hierarchy

Question	Why it matters	Examples
What organism?	Identifies the missing defense arm	Encapsulated, Neisseria, catalase-positive, opportunistic
What age?	Maternal IgG and developmental timing narrow the defect	After 6 months = XLA; early infancy = SCID
Which cells?	Flow cytometry localizes T, B, and NK compartments	CD3, CD19/20, CD16/56
Do the cells work?	Functional defects can occur with normal counts	DHR, vaccine titers, lymphocyte proliferation
What tissue pattern?	Localizes immune-mediated injury	Linear, granular, delayed, granulomatous

Board Habit Do not jump from one infection to a disease name. First classify the immune arm, then use age, organism, phenotype, and a functional test.

CHAPTER 2

Antigens, MHC, and Antigen Presentation

Recognition determines which immune arm is recruited.

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Antigen vs immunogen "Recognized" is not always "response-producing"

MECHANISM: An antigen binds antibody/BCR/TCR; an immunogen reliably elicits an immune response.
MHC / RECEPTOR CLUE: Haptens such as penicillin or nickel become immunogenic when attached to carrier proteins.
BOARD TRAP: TCR recognizes peptide-MHC, not free antigen.
TREATMENT / PEARL: Carrier proteins convert weak small molecules or polysaccharides into stronger T-dependent responses.

MHC class I "All nucleated cells -> CD8"

MECHANISM: Endogenous cytosolic proteins are processed by proteasomes and loaded in the ER through TAP.
MHC / RECEPTOR CLUE: HLA-A, -B, -C; recognized by CD8 cytotoxic T cells.
BOARD TRAP: Beta-2 microglobulin is required; low MHC I can increase NK-cell killing.
TREATMENT / PEARL: Viruses and tumors are classic endogenous-antigen contexts.

MHC class II "Professional APC -> CD4"

MECHANISM: Exogenous material is processed in endosomes; invariant chain/CLIP is exchanged through HLA-DM.
MHC / RECEPTOR CLUE: HLA-DP, -DQ, -DR on dendritic cells, macrophages, B cells.
BOARD TRAP: Bare lymphocyte syndrome type II causes severe CD4 functional deficiency.
TREATMENT / PEARL: CD4 activation requires peptide-MHC II plus costimulation.

Costimulation "B7-CD28 turns on; CTLA-4/PD-1 turn down"

MECHANISM: Signal 1 without signal 2 can produce anergy.
MHC / RECEPTOR CLUE: APC B7 (CD80/86) binds CD28; CTLA-4 competes and inhibits.
BOARD TRAP: Checkpoint blockade can create autoimmune-like toxicity.
TREATMENT / PEARL: CD40-CD40L is essential for macrophage activation and B-cell class switching.

Feature	MHC I	MHC II
Antigen source	Endogenous/cytosolic	Exogenous/endosomal
Expression	All nucleated cells	Professional APCs
T-cell partner	CD8	CD4
Loading site	ER via TAP	Endosome via invariant chain/CLIP
Classic defect	TAP/beta-2 microglobulin	CIITA/RFX bare lymphocyte syndrome

CHAPTER 3

Cytokines and T-Cell Subsets

Use one recurring clinical anchor for each cytokine rather than memorizing an isolated list.

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Cytokine	Primary board function	Memory cue / clinical link
IL-1	Fever, endothelial activation	One = hot; inflammasome output
IL-2	T-cell proliferation; Treg survival	Two = T-cell growth; calcineurin pathway
IL-4	Th2 differentiation; IgE switching	Four opens the IgE door
IL-5	Eosinophil growth and activation	Five = eosinophiles survive
IL-6	Acute-phase response; B-cell help	CRP/fibrinogen; cytokine-release syndrome
IL-8/CXCL8	Neutrophil chemotaxis	Eight attracts granulocytes
IL-10	Anti-inflammatory regulation	Treg/macrophage restraint
IL-12	Th1 differentiation; NK activation	Drives IFN-gamma
IL-17	Neutrophil recruitment at barriers	Defect -> mucocutaneous Candida
IL-23	Maintains Th17	Inflammatory bowel/psoriasis pathway
IFN-gamma	Macrophage activation; granulomas	Th1/NK signal
TNF-alpha	Inflammation; granuloma maintenance	Anti-TNF -> TB/reactivation risk

Th1 "IL-12 -> IFN-gamma"

MECHANISM: Th1 activates macrophages and supports cell-mediated defense against intracellular organisms.
CYTOKINE / CLINICAL CLUE: Granulomatous inflammation; mycobacterial defense.
BOARD TRAP: Th1 is not the dominant helminth/allergy pathway.
TREATMENT / PEARL: Defects in IL-12/IFN-gamma signaling predispose to disseminated mycobacterial infection.

Th2 "IL-4, IL-5, IL-13"

MECHANISM: Th2 promotes IgE, eosinophils, mucus, and alternative macrophage activation.
CYTOKINE / CLINICAL CLUE: Allergy, asthma, helminths.
BOARD TRAP: IgE is not the main opsonizing antibody.
TREATMENT / PEARL: IL-5/eosinophils are major tissue-injury effectors in late allergic responses.

Th17 "Barrier neutrophils"

MECHANISM: IL-17 recruits neutrophils and strengthens mucocutaneous defense.
CYTOKINE / CLINICAL CLUE: Chronic mucocutaneous Candida with STAT3/Th17 defects.
BOARD TRAP: Th17 is distinct from oxidative burst defects.
TREATMENT / PEARL: Hyper-IgE syndrome classically combines eczema, cold abscesses, retained teeth, and high IgE.

Treg "FOXP3 + IL-10/TGF-beta"

MECHANISM: Tregs suppress autoreactive cells and maintain peripheral tolerance.
CYTOKINE / CLINICAL CLUE: IPEX: immune dysregulation, polyendocrinopathy, enteropathy, X-linked.
BOARD TRAP: Tregs are CD4 cells with high CD25 expression.
TREATMENT / PEARL: Loss of Treg function causes severe early autoimmunity rather than a simple infection-only syndrome.

T-Cell Subset Compression Table

Subset	Driver / product	Dominant job	Failure clue
Th1	IL-12 / IFN-gamma	Macrophage activation	Disseminated mycobacteria
Th2	IL-4, IL-5, IL-13	IgE and eosinophils	Allergy/helminths
Th17	IL-6, TGF-beta, IL-23 / IL-17	Barrier neutrophils	Mucocutaneous Candida
Treg	FOXP3 / IL-10, TGF-beta	Tolerance	IPEX/autoimmunity
CD8	MHC I / perforin-granzyme	Cytotoxic killing	Viral/tumor control failure

Cytokine-to-Therapy Board Links

Pathway	Therapeutic concept	Risk / exam clue
IL-2 transcription	Calcineurin inhibition	Reduced T-cell activation; nephrotoxicity
IL-6 receptor	Tocilizumab-type blockade	Cytokine-release/inflammatory pathway
TNF-alpha	Anti-TNF therapy	Loss of granuloma maintenance; TB risk
IL-4/IL-13	Type 2 inflammation blockade	Asthma/atopic disease pathway
IL-5	Eosinophil-targeted therapy	Eosinophilic asthma pathway

Cytokine Shortcut The toxic effect of a biologic often follows the normal job of the blocked cytokine. Block granuloma maintenance and latent granulomatous infection can reappear.

CHAPTER 4

B Cells, Immunoglobulins, and Class Switching

Antibody isotype predicts location, effector function, and clinical failure.

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IgM "First, pentamer, fixes complement"

MECHANISM: Naive B cells express IgM/IgD; secreted IgM is pentameric and efficiently activates classical complement.
IMMUNOGLOBULIN CLUE: Primary response; intravascular; ABO natural antibodies are often IgM.
BOARD TRAP: IgM generally does not cross the placenta.
TREATMENT / PEARL: High IgM with low IgG/A/E suggests class-switch failure.

IgG "Placenta + opsonization + memory"

MECHANISM: IgG neutralizes, opsonizes, activates complement, and mediates ADCC.
IMMUNOGLOBULIN CLUE: Only major isotype crossing placenta; dominant secondary response.
BOARD TRAP: Maternal IgG can mask infant antibody deficiency for months.
TREATMENT / PEARL: FcRn prolongs IgG half-life and transports maternal antibody.

IgA "Mucosal dimer"

MECHANISM: Secretory IgA neutralizes pathogens on mucosal surfaces and in breast milk.
IMMUNOGLOBULIN CLUE: J chain and secretory component; GI/respiratory defense.
BOARD TRAP: Selective IgA deficiency may be asymptomatic; transfusion reactions occur only in a subset with anti-IgA.
TREATMENT / PEARL: Giardia and recurrent mucosal infection are classic clues.

IgE "Mast cells and helminths"

MECHANISM: IgE binds Fc-epsilon-RI on mast cells/basophils; cross-linking triggers degranulation.
IMMUNOGLOBULIN CLUE: Type I hypersensitivity, eosinophils, parasite defense.
BOARD TRAP: Serum IgE concentration is low despite potent receptor-bound function.
TREATMENT / PEARL: Epinephrine is first-line for anaphylaxis.

Class switching "CD40L + cytokines"

MECHANISM: Tfh cells provide CD40L-CD40 signaling; AID mediates class-switch recombination and somatic hypermutation.
IMMUNOGLOBULIN CLUE: Hyper-IgM syndrome: high/normal IgM, low other isotypes, opportunistic infection.
BOARD TRAP: Class switching changes the heavy-chain constant region, not antigen specificity.
TREATMENT / PEARL: Absent germinal centers and Cryptosporidium/Pneumocystis are classic CD40L clues.

Affinity Maturation Somatic hypermutation plus selection in germinal centers increases affinity. It is different from class switching, which changes effector function while preserving antigen specificity.

CHAPTER 5

Complement and Opsonization

C3 is the central amplifier; C5b-C9 is the membrane attack complex.

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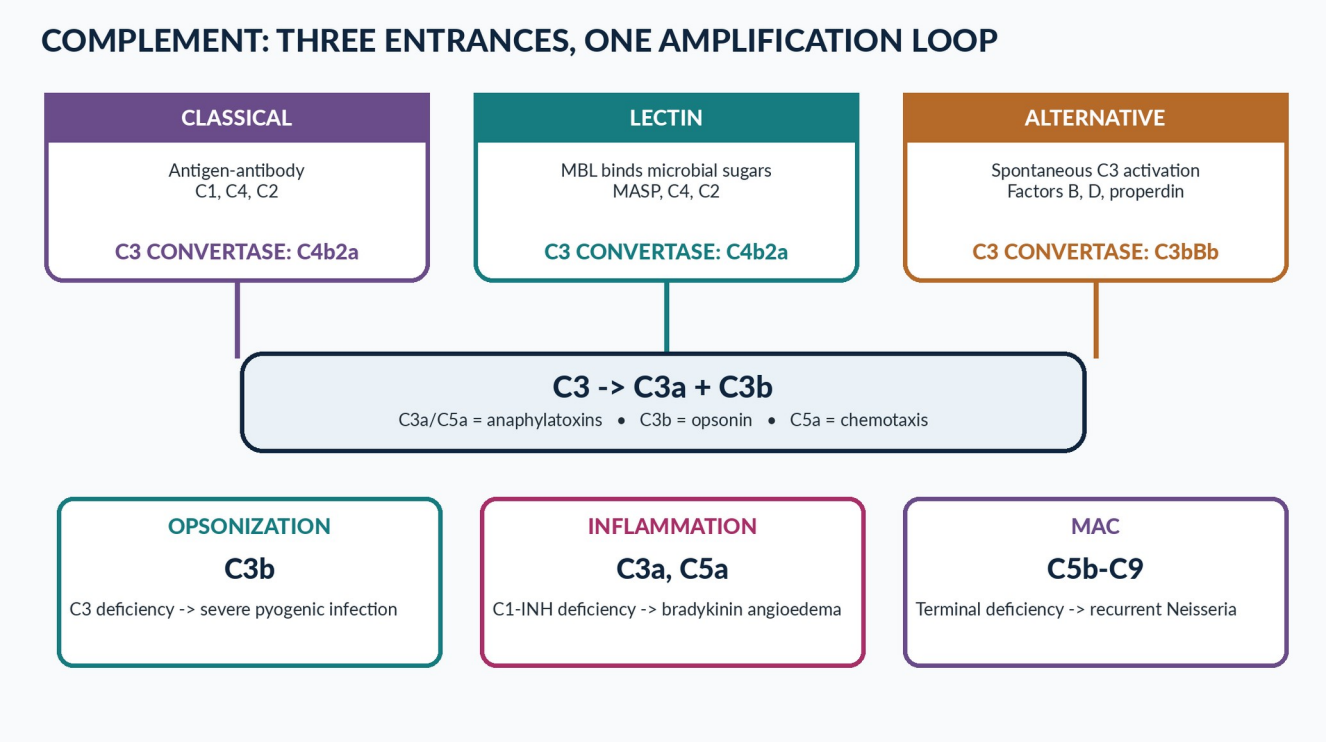

Original complement map: pathway entry, C3 convergence, and the three major outputs.

C3 deficiency "Central opsonin missing"

MECHANISM: Loss of C3b impairs opsonization and complement amplification.
CH50 / AH50 / CLINICAL CLUE: Severe recurrent pyogenic/encapsulated infections; immune-complex disease can occur.
BOARD TRAP: C3 deficiency is broader than terminal MAC deficiency.
TREATMENT / PEARL: CH50 and AH50 are both often abnormal when C3 is absent.

C5-C9 deficiency "Recurrent Neisseria"

MECHANISM: Terminal complement cannot form an effective membrane attack complex.
CH50 / AH50 / CLINICAL CLUE: Recurrent meningococcal or gonococcal infection.
BOARD TRAP: Opsonization can remain relatively intact.
TREATMENT / PEARL: Vaccination and infection-prevention planning are key clinical considerations.

Early classical deficiency "SLE-like immune-complex disease"

MECHANISM: C1q/C2/C4 defects impair clearance of apoptotic debris and immune complexes.
CH50 / AH50 / CLINICAL CLUE: Autoimmunity plus infection; low classical-pathway function.
BOARD TRAP: Not all complement deficiencies present primarily with infection.
TREATMENT / PEARL: CH50 low with relatively preserved AH50 localizes to classical pathway.

C1 inhibitor deficiency "Angioedema without urticaria"

MECHANISM: Uncontrolled kallikrein-bradykinin signaling increases vascular permeability.
CH50 / AH50 / CLINICAL CLUE: Low C4; normal tryptase; swelling without pruritic hives.
BOARD TRAP: Antihistamines/epinephrine may not reliably control bradykinin-mediated attacks.
TREATMENT / PEARL: Differentiate from histamine-mediated anaphylaxis.

DAF/CD59 loss "PNH + complement hemolysis"

MECHANISM: PIGA mutation prevents GPI anchoring of complement regulators CD55 and CD59.
CH50 / AH50 / CLINICAL CLUE: Intravascular hemolysis, thrombosis, cytopenias; flow cytometry/FLAER testing.
BOARD TRAP: The classic "morning urine" clue is neither required nor specific.
TREATMENT / PEARL: Complement inhibition is a targeted-treatment concept.

CH50	AH50	Interpretation
Low	Normal	Classical-pathway defect: C1, C2, C4
Normal	Low	Alternative-pathway defect: factor B, D, properdin
Low	Low	C3 or terminal/common-pathway defect; consumption also possible
Normal	Normal	Major complement pathway deficiency less likely

Complement Regulators and Board Traps

Regulator	Main action	Disease link
C1 inhibitor	Limits classical pathway and kallikrein	Hereditary/acquired bradykinin angioedema
Factor H / I	Inactivate alternative-pathway C3b	Atypical HUS / C3 glomerulopathy patterns
CD55 / DAF	Accelerates convertase decay	Lost in PNH
CD59	Blocks MAC assembly	Lost in PNH

Consumption Trap Low complement can reflect inherited deficiency or active consumption. Pair CH50/AH50 with individual components, clinical timing, infection history, and immune-complex disease.

CHAPTER 6

Neutrophils, Phagocytosis, and Innate Killing

Recognize -> adhere -> migrate -> ingest -> fuse -> kill.

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Leukocyte recruitment "Selectins roll; integrins stick; PECAM crosses"

MECHANISM: Inflammation causes margination, rolling, chemokine activation, firm adhesion, diapedesis, and chemotaxis.
FUNCTIONAL TEST / ORGANISM CLUE: LAD-1: CD18 beta-2 integrin defect -> delayed cord separation, no pus, neutrophilia.
BOARD TRAP: Neutrophilia can reflect failure to leave blood, not excessive tissue recruitment.
TREATMENT / PEARL: C5a, IL-8, LTB4, and bacterial N-formyl peptides are chemotactic signals.

Opsonization "C3b and IgG make microbes easier to eat"

MECHANISM: Fc-gamma receptors and complement receptors bind opsonized organisms and trigger phagocytosis.
FUNCTIONAL TEST / ORGANISM CLUE: Encapsulated organisms depend heavily on antibody/complement/splenic clearance.
BOARD TRAP: Direct pattern recognition exists but is less efficient for slippery capsules.
TREATMENT / PEARL: Asplenia, antibody deficiency, and C3 deficiency converge on encapsulated-bacteria risk.

Oxidative burst "NADPH oxidase -> superoxide -> peroxide"

MECHANISM: NADPH oxidase generates superoxide; MPO uses hydrogen peroxide and chloride to form hypochlorous acid.
FUNCTIONAL TEST / ORGANISM CLUE: CGD: abnormal DHR; catalase-positive abscesses/granulomas.
BOARD TRAP: MPO deficiency is usually milder and DHR is normal.
TREATMENT / PEARL: Catalase-positive organisms destroy their own peroxide, removing a potential substrate source.

Granules and NETosis "Primary granules contain MPO"

MECHANISM: Azurophilic granules contain MPO/defensins/proteases; secondary granules contain lactoferrin/lysozyme; NETs trap microbes.
FUNCTIONAL TEST / ORGANISM CLUE: Chediak-Higashi: giant granules, partial albinism, neuropathy from LYST trafficking defect.
BOARD TRAP: NETs can contribute to thrombosis and autoantigen exposure.
TREATMENT / PEARL: Phagosome ingestion can be intact while intracellular killing fails.

Failure point	Prototype	Buzzword
Rolling	LAD-2	Absent sialyl-Lewis X; developmental delay
Firm adhesion	LAD-1	CD18; delayed cord; no pus; neutrophilia
Phagolysosome trafficking	Chediak-Higashi	Partial albinism; giant granules; neuropathy
Oxidative burst	CGD	Catalase-positive infections; abnormal DHR
MPO reaction	MPO deficiency	Candida risk; normal DHR

CHAPTER 7

Hypersensitivity Types I-IV

Identify the mediator, timing, and tissue pattern before memorizing the disease list.

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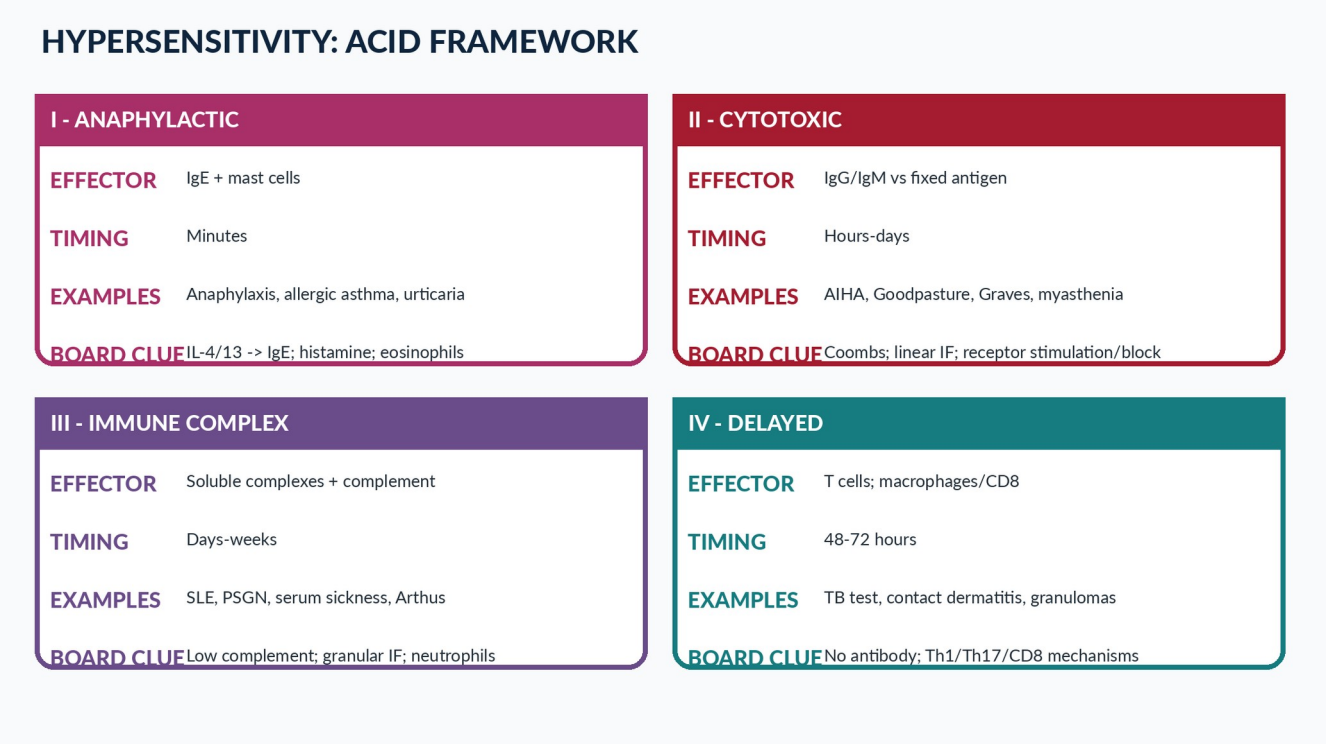

Original ACID hypersensitivity map: effector, timing, examples, and diagnostic clue.

Type I "Minutes + IgE + mast cell"

MECHANISM: Sensitization induces Th2 IL-4/13 and IgE; re-exposure cross-links mast-cell-bound IgE.
TIMING / PATHOLOGY CLUE: Histamine/tryptase early; leukotrienes and eosinophils late.
BOARD TRAP: Serum tryptase supports mast-cell activation but does not replace clinical diagnosis.
TREATMENT / PEARL: Intramuscular epinephrine is first-line for anaphylaxis.

Type II "Antibody against a fixed target"

MECHANISM: IgG/IgM causes complement injury, opsonization, ADCC, or receptor stimulation/blockade.
TIMING / PATHOLOGY CLUE: Coombs-positive hemolysis; linear GBM IF; Graves stimulation; myasthenia blockade.
BOARD TRAP: Not all Type II disease destroys cells; receptors can be functionally altered.
TREATMENT / PEARL: Maternal IgG can cross placenta and cause neonatal disease.

Type III "Complexes travel and lodge"

MECHANISM: Soluble antigen-antibody complexes deposit in glomeruli, joints, skin, or vessels and activate complement/neutrophils.
TIMING / PATHOLOGY CLUE: Low complement; granular IF; serum sickness; Arthus reaction.
BOARD TRAP: The antigen is not fixed in the tissue at the start.
TREATMENT / PEARL: Timing is often days to weeks after exposure.

Type IV "T cells take time"

MECHANISM: Th1/Th17 cytokines activate macrophages/neutrophils; CD8 cells directly kill targets.
TIMING / PATHOLOGY CLUE: TB skin test, contact dermatitis, granulomas, type 1 diabetes, many drug eruptions.
BOARD TRAP: No antibody is required.
TREATMENT / PEARL: Patch testing and delayed timing distinguish from immediate allergy.

Type IV Subtypes

Subtype	Dominant effector	Classic example
IVa	Th1 + macrophages	TB skin test, granulomatous inflammation
IVb	Th2 + eosinophils	Eosinophilic drug reactions
IVc	CD8 cytotoxic T cells	Type 1 diabetes, SJS/TEN patterns
IVd	T cells + neutrophils	Selected pustular drug eruptions

Transplant Link Hyperacute rejection is mainly antibody mediated; acute rejection can be cellular or antibody mediated; chronic rejection is progressive vascular and fibrotic injury with important T-cell participation.

Hypersensitivity Diagnostic Patterns

Pattern	Mechanism	Classic clue
Positive direct Coombs	Type II antibody-coated cells	Autoimmune hemolysis/transfusion reaction
Linear basement-membrane IF	Type II fixed antigen	Anti-GBM disease
Granular or lumpy-bumpy IF	Type III immune complexes	SLE/PSGN
Low C3/C4 during inflammation	Complement consumption	Active immune-complex disease
Delayed patch or skin test	Type IV T cells	Contact dermatitis/TB response

Anaphylaxis Emergency Minutes plus urticaria, wheeze, hypotension, or airway swelling is a clinical diagnosis. Intramuscular epinephrine is first-line; laboratory confirmation must not delay treatment.

CHAPTER 8

Tolerance and Autoimmunity

Autoimmunity is a failure of deletion, anergy, regulation, clearance, or checkpoint control.

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Systemic lupus erythematosus "Anti-dsDNA + low complement + nephritis"

MECHANISM: Defective clearance and immune-complex formation produce multisystem Type III injury.
AUTOANTIBODY / PATHOLOGY CLUE: ANA sensitive; anti-dsDNA and anti-Smith specific; full-house renal IF.
BOARD TRAP: Antihistone is more associated with drug-induced lupus; renal/CNS disease is less common there.
TREATMENT / PEARL: Complement can track immune-complex consumption during active disease.

Rheumatoid arthritis "Anti-CCP + symmetric inflammatory small joints"

MECHANISM: Autoantibodies and T-cell/macrophage cytokines drive synovitis and pannus formation.
AUTOANTIBODY / PATHOLOGY CLUE: RF is less specific; anti-CCP is more specific; TNF/IL-6 pathways are therapeutic targets.
BOARD TRAP: Osteoarthritis is not an autoimmune synovitis.
TREATMENT / PEARL: Extra-articular nodules and lung disease can occur.

Sjogren syndrome "Dry eyes, dry mouth, SSA/SSB"

MECHANISM: Lymphocytic destruction of lacrimal and salivary glands produces sicca symptoms.
AUTOANTIBODY / PATHOLOGY CLUE: Parotid enlargement, dental caries, lymphoma risk.
BOARD TRAP: SSA can also occur in SLE and neonatal lupus.
TREATMENT / PEARL: Evaluate systemic features rather than treating dryness as isolated.

Systemic sclerosis "CREST vs diffuse"

MECHANISM: Vascular injury and fibroblast activation cause fibrosis.
AUTOANTIBODY / PATHOLOGY CLUE: Anti-centromere -> limited/PAH; anti-Scl-70 -> diffuse/ILD; anti-RNA polymerase III -> renal crisis association.
BOARD TRAP: High-dose glucocorticoids can increase renal-crisis risk.
TREATMENT / PEARL: Raynaud often precedes other manifestations.

Organ-specific antibody disease "Receptor stimulation or blockade"

MECHANISM: Antibodies can alter receptor function without cell destruction.
AUTOANTIBODY / PATHOLOGY CLUE: Graves stimulates TSH receptor; myasthenia blocks AChR; pernicious anemia targets intrinsic factor.
BOARD TRAP: Type II does not always mean cytolysis.
TREATMENT / PEARL: Match antibody mechanism to physiologic direction.

CHAPTER 9

B-Cell and Antibody Deficiencies

The age when maternal IgG wanes is a major mechanistic clue.

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X-linked agammaglobulinemia "Boy + absent tonsils + infections after 6 months"

MECHANISM: BTK mutation arrests pre-B-cell maturation.
IMMUNOGLOBULIN / FLOW CLUE: Very low all isotypes; absent/very low CD19/20 B cells; small lymphoid tissue.
BOARD TRAP: Maternal IgG can protect early infancy.
TREATMENT / PEARL: Immunoglobulin replacement and infection prevention are central management principles.

Common variable immunodeficiency "Adult infections + Giardia + autoimmunity"

MECHANISM: B cells are present but fail to differentiate effectively into plasma cells and produce antibody.
IMMUNOGLOBULIN / FLOW CLUE: Low IgG plus low IgA and/or IgM; poor vaccine response; lymphoma/granulomatous disease risk.
BOARD TRAP: Do not diagnose solely from one low immunoglobulin value; exclude secondary causes.
TREATMENT / PEARL: Presentation can occur in adolescence or adulthood.

Selective IgA deficiency "Mucosal infection or asymptomatic"

MECHANISM: Isolated low IgA impairs mucosal neutralization.
IMMUNOGLOBULIN / FLOW CLUE: Recurrent respiratory/GI infection, Giardia, allergy, autoimmunity; possible transfusion anaphylaxis in anti-IgA subset.
BOARD TRAP: Most patients are not continuously ill.
TREATMENT / PEARL: Use washed or IgA-reduced products when clinically indicated for sensitized patients.

Hyper-IgM syndrome "High IgM + opportunists + no class switching"

MECHANISM: CD40L deficiency blocks T-cell help to B cells and macrophages; AID defects produce a different phenotype.
IMMUNOGLOBULIN / FLOW CLUE: Low IgG/A/E, absent germinal centers, Pneumocystis/Cryptosporidium risk.
BOARD TRAP: IgM may be normal rather than dramatically high.
TREATMENT / PEARL: Neutropenia can occur in CD40L deficiency.

Transient hypogammaglobulinemia of infancy "Delayed endogenous IgG production"

MECHANISM: Physiologic IgG nadir is prolonged but improves with age.
IMMUNOGLOBULIN / FLOW CLUE: B cells present; vaccine response and clinical severity guide evaluation.
BOARD TRAP: Do not confuse with XLA, where B cells are absent.
TREATMENT / PEARL: Longitudinal follow-up distinguishes transient from persistent deficiency.

CHAPTER 10

T-Cell and Combined Immunodeficiencies

Early severe infection across organism classes is a combined-immune warning.

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FLOW CYTOMETRY AND FUNCTIONAL TEST MAP

T CELLS	B CELLS	NK CELLS	PHAGOCYTES
CD3	**CD19 / CD20**	**CD16 / CD56**	**CD18; DHR**
CD4 / CD8	Surface Ig	Innate cytotoxicity	Adhesion / burst
Low in DiGeorge/SCID/HIV	Absent in XLA; present in CVID	Absent in IL2RG SCID	LAD / CGD

T- B+ NK- IL2RG common gamma-chain
Interpret phenotype with age, infection pattern, immunoglobulins, and genetic testing.

T- B- NK- ADA deficiency
Interpret phenotype with age, infection pattern, immunoglobulins, and genetic testing.

T- B+ NK+ IL-7 receptor / MHC II patterns
Interpret phenotype with age, infection pattern, immunoglobulins, and genetic testing.

T- B- NK+ RAG/JAK3-pattern differential
Interpret phenotype with age, infection pattern, immunoglobulins, and genetic testing.

Original flow-cytometry map: major lymphocyte markers, functional assays, and SCID phenotypes.

DiGeorge syndrome "CATCH-22"

MECHANISM: 22q11.2 deletion disrupts third/fourth pharyngeal pouch development.
T/B/NK PHENOTYPE: Thymic hypoplasia, low T cells, hypocalcemia, conotruncal cardiac defects, absent thymic shadow.
BOARD TRAP: B-cell numbers can be normal but T-dependent antibody responses impaired.
TREATMENT / PEARL: Severity varies; live-vaccine decisions require immune assessment.

X-linked SCID "T- B+ NK-"

MECHANISM: IL2RG common gamma-chain defect disrupts multiple cytokine receptors.
T/B/NK PHENOTYPE: Early thrush, diarrhea, failure to thrive, opportunistic infection, absent thymic shadow.
BOARD TRAP: B cells may be numerically present but function poorly without T-cell help.
TREATMENT / PEARL: Newborn screening uses T-cell receptor excision circles; definitive therapy is urgent specialist-directed immune reconstitution.

ADA-SCID "T- B- NK- + toxic purines"

MECHANISM: Adenosine deaminase deficiency causes dATP accumulation and lymphotoxicity.
T/B/NK PHENOTYPE: Profound combined lymphopenia; skeletal abnormalities may occur.
BOARD TRAP: Do not confuse with PNP deficiency, which more selectively affects T cells.
TREATMENT / PEARL: Enzyme replacement/gene or stem-cell approaches are specialist therapies.

Wiskott-Aldrich syndrome "Eczema + infections + small platelets"

MECHANISM: WASP cytoskeletal defect impairs immune synapse and platelet formation.
T/B/NK PHENOTYPE: X-linked; low/abnormal IgM, high IgA/IgE, autoimmunity and malignancy risk.
BOARD TRAP: Platelets are small, unlike many other thrombocytopenias.
TREATMENT / PEARL: Stem-cell transplantation is potentially curative.

Ataxia-telangiectasia "Ataxia + telangiectasia + high AFP"

MECHANISM: ATM DNA double-strand-break response defect causes radiosensitivity and immune dysfunction.
T/B/NK PHENOTYPE: Low IgA, recurrent sinopulmonary infection, malignancy risk.
BOARD TRAP: Avoid unnecessary ionizing radiation exposure.
TREATMENT / PEARL: Neurologic progression is a central clue.

Bare lymphocyte syndrome "Low MHC expression"

MECHANISM: MHC I defects impair CD8 development; MHC II defects impair CD4 activation and resemble combined immunodeficiency.
T/B/NK PHENOTYPE: Flow and HLA-expression testing; severe infections with normal immunoglobulin interpretation requiring context.
BOARD TRAP: The lymphocyte may be present but unable to present/recognize antigen normally.
TREATMENT / PEARL: MHC II deficiency is sometimes called bare lymphocyte syndrome type II.

SCID Phenotype Quick Table

Phenotype	First mechanism to consider	Key distinction
T- B+ NK-	IL2RG common gamma-chain	X-linked; B cells present but poorly functional
T- B- NK-	ADA deficiency	Toxic purine metabolites affect all lymphocytes
T- B- NK+	RAG recombination defects	Absent antigen-receptor rearrangement
T- B+ NK+	IL-7 receptor / MHC II-related differential	Use CD4/CD8, HLA expression, and genetics

Live-Vaccine Red Flag Severe T-cell or combined immunodeficiency can allow disseminated disease from a vaccine strain. Do not use a generic schedule without immune assessment in a suspected SCID infant.

Combined Immunodeficiency Checklist

- **Age:** first months of life.
- **Organisms:** bacterial, viral, fungal, and opportunistic.
- **Clinical course:** persistent thrush, diarrhea, failure to thrive, severe vaccine infection.
- **Laboratory emergency:** infant lymphopenia or abnormal newborn TREC screening.
- **Next step:** urgent immunology evaluation, protective infection precautions, and definitive workup.

CHAPTER 11

Phagocyte, Complement, and Splenic Defects

The infection organism and inflammatory response reveal where innate defense fails.

SOURCE-DERIVED CORE: CONSOLIDATED FROM PRIOR SINOE IMMUNOLOGY MATERIALS

Chronic granulomatous disease "Catalase-positive abscesses + abnormal DHR"

MECHANISM: NADPH oxidase deficiency prevents superoxide generation and effective oxidative killing.
DHR / FLOW / SMEAR CLUE: Staphylococcus, Serratia, Burkholderia, Nocardia, Aspergillus; granuloma formation.
BOARD TRAP: DHR is preferred over the older nitroblue tetrazolium test.
TREATMENT / PEARL: Ingestion is intact; intracellular killing fails.

Leukocyte adhesion deficiency type 1 "Delayed cord + no pus + neutrophilia"

MECHANISM: CD18 beta-2 integrin deficiency prevents firm adhesion and extravasation.
DHR / FLOW / SMEAR CLUE: Recurrent bacterial skin/mucosal infection; poor wound healing; high circulating neutrophils.
BOARD TRAP: The problem is migration, not antibody production.
TREATMENT / PEARL: Flow cytometry for CD18/CD11 supports diagnosis.

Chediak-Higashi syndrome "Partial albinism + giant granules + neuropathy"

MECHANISM: LYST mutation disrupts lysosomal trafficking and phagolysosome fusion.
DHR / FLOW / SMEAR CLUE: Recurrent pyogenic infections; giant granules; accelerated hemophagocytic phase can occur.
BOARD TRAP: Do not confuse with Griscelli syndrome, which has different molecular defects.
TREATMENT / PEARL: Neuropathy and pigment dilution are discriminating clues.

Hyper-IgE syndrome "Cold abscesses + retained teeth + fractures"

MECHANISM: STAT3-related Th17 deficiency impairs neutrophil recruitment at epithelial barriers.
DHR / FLOW / SMEAR CLUE: Very high IgE, eczema, coarse facies, pneumatoceles.
BOARD TRAP: Abscesses may lack inflammatory warmth.
TREATMENT / PEARL: Differentiate from Wiskott-Aldrich by platelet size/count and skeletal/dental clues.

Asplenia "Howell-Jolly bodies + encapsulated bacteria"

MECHANISM: Spleen removes opsonized organisms and abnormal blood cells.
DHR / FLOW / SMEAR CLUE: S. pneumoniae, H. influenzae, N. meningitidis; severe babesiosis risk.
BOARD TRAP: Normal antibody and complement do not replace splenic filtration.
TREATMENT / PEARL: Vaccination and fever action planning are essential clinical concepts.

CHAPTER 12

Immune Dysregulation Syndromes

Inborn errors of immunity can present with autoimmunity, inflammation, allergy, or malignancy - not only infection.

SOURCE-DERIVED CORE: CONSOLIDATED FROM PRIOR SINOE IMMUNOLOGY MATERIALS

IPEX "Enteropathy + eczema + early diabetes"

MECHANISM: FOXP3 mutation causes Treg failure and severe systemic autoimmunity.
GENETIC / INFLAMMATORY CLUE: X-linked infant with chronic diarrhea, dermatitis, endocrinopathy, high IgE.
BOARD TRAP: This is immune dysregulation, not isolated food allergy.
TREATMENT / PEARL: Urgent immunology evaluation and definitive immune therapy are required.

APECED / APS-1 "Chronic Candida + endocrine autoimmunity"

MECHANISM: AIRE defect impairs thymic presentation of tissue-specific self-antigens.
GENETIC / INFLAMMATORY CLUE: Chronic mucocutaneous candidiasis, hypoparathyroidism, adrenal insufficiency.
BOARD TRAP: Candida occurs from IL-17-related autoantibodies, not classic neutrophil oxidative failure.
TREATMENT / PEARL: Monitor for multiple evolving autoimmune organs.

ALPS "Chronic nonmalignant lymphadenopathy + double-negative T cells"

MECHANISM: FAS-pathway apoptosis failure allows autoreactive lymphocytes to persist.
GENETIC / INFLAMMATORY CLUE: Splenomegaly, autoimmune cytopenias, elevated CD3+ TCR-alpha-beta+ CD4-/CD8- cells.
BOARD TRAP: Lymphadenopathy does not automatically mean lymphoma.
TREATMENT / PEARL: Apoptosis defects connect immune accumulation and autoimmunity.

HLH "Fever + splenomegaly + cytopenias + ferritin"

MECHANISM: Uncontrolled macrophage/T-cell activation follows impaired cytotoxic granule function or secondary triggers.
GENETIC / INFLAMMATORY CLUE: High ferritin, triglycerides, low fibrinogen, hemophagocytosis, liver dysfunction.
BOARD TRAP: Hemophagocytosis may be absent early and is not independently diagnostic.
TREATMENT / PEARL: This is a medical emergency requiring protocol-based specialist treatment.

Familial Mediterranean fever "Recurrent serositis + AA amyloid risk"

MECHANISM: MEFV/pyrin inflammasome dysregulation causes autoinflammatory attacks.
GENETIC / INFLAMMATORY CLUE: Fever, peritonitis, pleuritis, erysipelas-like rash; no high-titer autoantibody requirement.
BOARD TRAP: Autoinflammatory disease is innate-immune dysregulation, not classic autoimmunity.
TREATMENT / PEARL: Colchicine prevents attacks and amyloid complications in classic disease.

CHAPTER 13

HIV and Secondary Immunodeficiency

CD4 thresholds predict opportunistic patterns, but modern management is based on prompt diagnosis and antiretroviral therapy.

HIGH-YIELD 2026 EDUCATIONAL SYNTHESIS - VERIFY CLINICAL SCHEDULES AT POINT OF CARE

CD4 pattern	High-yield risk	Classic board clue
<200 cells/µL	Pneumocystis jirovecii	Diffuse bilateral interstitial disease; elevated LDH; exertional hypoxemia
<100	Toxoplasma encephalitis if seropositive; cryptococcosis	Multiple ring-enhancing brain lesions vs high opening pressure
<50	CMV retinitis; disseminated MAC	"Pizza-pie" retina; systemic mycobacterial disease

Acute HIV "Mononucleosis-like illness + high viral load"

MECHANISM: Early widespread viral replication causes fever, rash, pharyngitis, lymphadenopathy, and cytopenias.
CD4 / ACQUIRED CLUE: Fourth-generation antigen/antibody testing; RNA testing can detect very early infection.
BOARD TRAP: A negative antibody-only test may miss acute infection.
TREATMENT / PEARL: Prompt linkage to antiretroviral care is central.

Advanced HIV "Opportunistic infection by CD4 level"

MECHANISM: Progressive CD4 loss impairs macrophage activation, cytotoxic coordination, and mucosal defense.
CD4 / ACQUIRED CLUE: Oral candidiasis, chronic diarrhea, weight loss, PJP, toxoplasmosis, CMV, MAC.
BOARD TRAP: The exact prophylaxis schedule is guideline-dependent and should be verified at point of care.
TREATMENT / PEARL: Viral suppression permits immune recovery and changes risk.

Secondary antibody loss "Protein loss or B-cell-directed therapy"

MECHANISM: Nephrotic syndrome, protein-losing enteropathy, hematologic malignancy, and anti-CD20 therapy can lower effective humoral defense.
CD4 / ACQUIRED CLUE: Low immunoglobulins or poor vaccine responses with an acquired context.
BOARD TRAP: Exclude secondary causes before labeling CVID.
TREATMENT / PEARL: Medication and protein-loss history are diagnostic essentials.

Iatrogenic T-cell suppression "Transplant, chemotherapy, biologics, steroids"

MECHANISM: Different agents impair distinct immune pathways and create characteristic infection risks.
CD4 / ACQUIRED CLUE: Anti-TNF -> granulomatous infection risk; B-cell depletion -> humoral defects; calcineurin blockade -> T-cell effects.
BOARD TRAP: "Immunosuppressed" is not one uniform immune phenotype.
TREATMENT / PEARL: Pre-treatment screening and vaccine planning depend on the specific therapy.

CHAPTER 14

Vaccines and Immune Diagnostic Testing

The schedule changes; the immunologic mechanism remains testable.

HIGH-YIELD 2026 EDUCATIONAL SYNTHESIS - VERIFY CLINICAL SCHEDULES AT POINT OF CARE

Live attenuated vaccine "Strong humoral + cellular memory"

MECHANISM: Replication-limited organisms mimic natural infection and induce durable responses.
TEST / INTERPRETATION: Avoid in severe T-cell/combined immunodeficiency and selected pregnancy contexts.
BOARD TRAP: "Live" does not mean universally prohibited; decisions are patient-specific.
TREATMENT / PEARL: Always verify current schedules and contraindications.

Conjugate vaccine "Polysaccharide linked to protein carrier"

MECHANISM: Protein carrier recruits T-cell help, germinal centers, class switching, and memory in infants.
TEST / INTERPRETATION: Hib and pneumococcal conjugate mechanism.
BOARD TRAP: Pure polysaccharide responses are T-independent and weak in young children.
TREATMENT / PEARL: Conjugation converts a weak polysaccharide response into T-dependent immunity.

Quantitative immunoglobulins "Amount, not function"

MECHANISM: IgG/IgA/IgM levels screen humoral production and must be interpreted by age.
TEST / INTERPRETATION: Low IgG requires repeat/context and assessment of secondary loss.
BOARD TRAP: Normal total IgG can coexist with poor specific-antibody responses.
TREATMENT / PEARL: Use vaccine titers to assess function when appropriate.

Flow cytometry "Count the immune compartments"

MECHANISM: CD3/CD4/CD8, CD19/20, and CD16/56 define T/B/NK phenotype.
TEST / INTERPRETATION: Absent B cells -> XLA; T-/B+/NK- -> IL2RG SCID pattern.
BOARD TRAP: Normal numbers do not prove normal signaling or killing.
TREATMENT / PEARL: Pair phenotype with function and genetics.

DHR testing "Oxidative burst assay"

MECHANISM: Dihydrorhodamine fluorescence rises with neutrophil oxidant production.
TEST / INTERPRETATION: Absent/reduced response supports CGD and can identify carrier patterns.
BOARD TRAP: MPO deficiency generally has a normal oxidative burst signal.
TREATMENT / PEARL: Test the pathway suggested by organism and clinical phenotype.

CH50/AH50 "Screen classical vs alternative"

MECHANISM: Hemolytic assays identify pathway failure or consumption.
TEST / INTERPRETATION: CH50 low only -> classical; AH50 low only -> alternative; both low -> common/terminal/C3 or consumption.
BOARD TRAP: Acute inflammation and immune-complex disease can alter complement levels.
TREATMENT / PEARL: Confirm with individual complement components.

CHAPTER 15

Transplant, Tumor Immunology, and Targeted Therapy

Immune recognition can reject tissue, miss tumors, or be therapeutically redirected.

SOURCE-DERIVED CORE: CONSOLIDATED FROM PRIOR SINOE IMMUNOLOGY MATERIALS

Hyperacute rejection "Minutes-hours + thrombosis"

MECHANISM: Preformed recipient antibodies bind donor ABO/HLA antigens and activate complement/endothelium.
TIMING / PATHOLOGY CLUE: Immediate graft cyanosis, ischemia, fibrinoid necrosis, thrombosis.
BOARD TRAP: This is antibody-mediated and prevented by compatibility testing.
TREATMENT / PEARL: The graft usually cannot be salvaged.

Acute cellular rejection "Days-months + lymphocytes/tubulitis"

MECHANISM: Recipient T cells recognize donor antigen directly/indirectly and attack parenchyma.
TIMING / PATHOLOGY CLUE: Interstitial lymphocytes, endotheliitis, organ-specific injury.
BOARD TRAP: Acute antibody-mediated rejection is a distinct possibility with donor-specific antibodies/C4d.
TREATMENT / PEARL: Treatment depends on cellular vs antibody mechanism and severity.

Chronic rejection "Months-years + fibrosis and vascular narrowing"

MECHANISM: Persistent low-grade immune injury causes intimal thickening, ischemia, and fibrosis.
TIMING / PATHOLOGY CLUE: Progressive loss of function; bronchiolitis obliterans, graft vasculopathy, interstitial fibrosis.
BOARD TRAP: Escalating acute-rejection therapy does not reliably reverse established scarring.
TREATMENT / PEARL: Prevention and long-term risk modification are central.

Checkpoint inhibition "Release the T-cell brakes"

MECHANISM: PD-1/PD-L1 or CTLA-4 blockade restores antitumor T-cell activity.
TIMING / PATHOLOGY CLUE: Immune-related adverse events: colitis, dermatitis, hepatitis, endocrinopathy, pneumonitis.
BOARD TRAP: Toxicity can mimic spontaneous autoimmune disease.
TREATMENT / PEARL: Management is organ/severity-specific and may require immunosuppression.

CAR-T and cytokine release "Engineered T cells + fever/hypotension"

MECHANISM: CAR-T recognizes surface antigen independently of MHC; widespread activation can release IL-6 and other cytokines.
TIMING / PATHOLOGY CLUE: Cytokine-release syndrome and neurotoxicity are classic complications.
BOARD TRAP: Target-antigen loss can cause relapse.
TREATMENT / PEARL: IL-6 pathway blockade is a classic treatment concept for severe CRS.

Targeted Immune Therapy Rapid Matrix

Drug/target	Immune effect	Board toxicity clue
Calcineurin inhibitors	Decrease IL-2 transcription and T-cell activation	Nephrotoxicity, hypertension, neurotoxicity
mTOR inhibitors	Block IL-2 signaling/cell-cycle progression	Hyperlipidemia, marrow suppression, impaired wound healing
Anti-TNF	Reduce granuloma maintenance/inflammation	TB and fungal reactivation risk
Anti-CD20	Deplete B cells	Hypogammaglobulinemia, HBV reactivation risk
Checkpoint inhibitors	Increase T-cell activity	Autoimmune-like organ toxicity

Mechanism-to-Toxicity Shortcuts

Mechanism	Expected immune consequence	Clinical clue
Block T-cell activation	Less cellular immunity	Viral/fungal/opportunistic infection risk
Deplete B cells	Reduced antibody production	Low Ig, poor vaccine response, HBV reactivation
Block TNF	Weak granuloma maintenance	TB/endemic fungal reactivation
Release checkpoints	Excess autoreactive T-cell activity	Colitis, hepatitis, endocrinopathy, pneumonitis
Engineer T cells	High-intensity targeted activation	Cytokine-release syndrome and neurotoxicity

Therapy Principle The adverse effect usually follows the normal immune function of the blocked or amplified pathway. Name the pathway first, then predict the infection or inflammatory toxicity.

CHAPTER 16

High-Yield Comparison Matrices

Convert long lists into a small number of diagnostic contrasts.

SOURCE-DERIVED CORE: CONSOLIDATED FROM PRIOR SINOE IMMUNOLOGY MATERIALS

Primary Immunodeficiency Matrix

Disease	Defect / phenotype	Classic trigger	Best board test
XLA	BTK; B cells absent	Boy, infections after 6 months, absent tonsils	CD19/20 flow + immunoglobulins
CVID	B cells present; poor plasma-cell function	Adult sinopulmonary infections, Giardia, autoimmunity	Ig levels + poor vaccine response
Hyper-IgM	CD40L/CD40 or AID pathway	High/normal IgM, low other Ig, opportunists	Ig pattern + genetic/flow evaluation
DiGeorge	22q11; low T cells	Hypocalcemia + conotruncal defect	T-cell flow; anatomy/genetics
SCID	Severe T-cell failure; variable B/NK	Thrush, diarrhea, FTT, opportunists	TREC + flow + genetics
CGD	NADPH oxidase	Catalase-positive abscesses	DHR
LAD-1	CD18	Delayed cord, no pus, neutrophilia	CD18/CD11 flow
C5-C9 deficiency	MAC defect	Recurrent Neisseria	CH50/AH50 + components

Autoantibody Matrix

Disease	Marker	Board clue
SLE	ANA; anti-dsDNA; anti-Smith	Low complement, nephritis, multisystem
Drug-induced lupus	Antihistone	Hydralazine/procainamide/isoniazid; less renal/CNS
RA	Anti-CCP; RF	Symmetric inflammatory small joints
Sjogren	SSA/Ro, SSB/La	Sicca + lymphoma risk
Limited systemic sclerosis	Anti-centromere	CREST + pulmonary hypertension
Diffuse systemic sclerosis	Anti-Scl-70	Skin disease + ILD
Goodpasture	Anti-alpha-3 type IV collagen	Pulmonary hemorrhage + linear GBM IF
Graves	TSH receptor-stimulating Ig	Hyperthyroidism + ophthalmopathy

Organism-to-Immune-Defect Matrix

Organism/pattern	Think first	Prototype
Encapsulated bacteria	Antibody, C3, or splenic clearance	XLA/CVID/C3 deficiency/asplenia
Recurrent Neisseria	Terminal complement	C5-C9 deficiency
Catalase-positive abscesses	Oxidative burst	CGD
No pus + neutrophilia	Adhesion/migration	LAD-1
Viral/fungal/opportunistic infections	T-cell or combined defect	DiGeorge/SCID/HIV
Giardia	Mucosal/humoral deficiency	IgA deficiency/CVID
Disseminated mycobacteria	IL-12/IFN-gamma axis	Mendelian susceptibility pattern
Mucocutaneous Candida	Th17/IL-17 pathway	STAT3-HIES/APECED/IL-17 defects

Hypersensitivity Compression Matrix

Type	Effector	Timing / signature
I	IgE + mast cells	Minutes; tryptase/histamine; anaphylaxis
II	IgG/IgM vs fixed target	Coombs, linear IF, receptor stimulation/block
III	Immune complexes + complement	Days-weeks; low complement; granular IF
IV	T cells/macrophages/CD8	48-72 hours; no antibody required

Complement Compression Matrix

Defect	Signature	Disease clue
C1/C2/C4	Low CH50; normal AH50	SLE-like disease
Alternative factors	Normal CH50; low AH50	Recurrent infection depending component
C3	Both low	Severe pyogenic infection
C5-C9	Both low	Recurrent Neisseria
C1 inhibitor	Low C4	Angioedema without urticaria

CHAPTER 17

Thirty Clinical Buzzword Cases and Final Cheat Sheets

Practice the clue-to-effector-to-diagnosis sequence.

SOURCE-DERIVED CORE: CONSOLIDATED FROM PRIOR SINOE IMMUNOLOGY MATERIALS

CASE 01 A 7-month-old boy has recurrent otitis and pneumonia, absent tonsils, very low immunoglobulins, and no CD19 cells.

Diagnosis: X-linked agammaglobulinemia

Why: Maternal IgG has waned; BTK failure arrests B-cell maturation.

CASE 02 A 28-year-old has recurrent sinusitis, Giardia, autoimmune thrombocytopenia, low IgG/IgA, and normal B-cell numbers.

Diagnosis: Common variable immunodeficiency

Why: B cells are present but fail to produce effective plasma-cell antibody responses.

CASE 03 A patient has recurrent mucosal infections and anaphylaxis after plasma transfusion; IgA is nearly absent.

Diagnosis: Selective IgA deficiency

Why: Anti-IgA antibodies in a sensitized subset can trigger transfusion reactions.

CASE 04 A boy has high IgM, low IgG/IgA, Pneumocystis pneumonia, and absent germinal centers.

Diagnosis: CD40L-deficient hyper-IgM syndrome

Why: T-cell help for class switching and macrophage activation is defective.

CASE 05 An infant has thrush, diarrhea, failure to thrive, T- B+ NK- flow phenotype, and absent thymic shadow.

Diagnosis: X-linked SCID due to IL2RG

Why: Common gamma-chain failure disrupts multiple cytokine receptors.

CASE 06 **An infant has T- B- NK- SCID and accumulated deoxyadenosine metabolites.**

Diagnosis: **ADA deficiency**

Why: Toxic dATP injures all lymphocyte lineages.

CASE 07 **A child has hypocalcemic tetany, truncus arteriosus, low T cells, and no thymic shadow.**

Diagnosis: **DiGeorge syndrome**

Why: Third/fourth pharyngeal pouch failure causes thymic and parathyroid defects.

CASE 08 **A boy has eczema, recurrent infections, and thrombocytopenia with unusually small platelets.**

Diagnosis: **Wiskott-Aldrich syndrome**

Why: WASP cytoskeletal dysfunction produces immune-synapse defects and small platelets.

CASE 09 **A child has progressive ataxia, telangiectasias, recurrent infections, high AFP, and radiosensitivity.**

Diagnosis: **Ataxia-telangiectasia**

Why: ATM DNA-repair failure links neurologic disease, immunodeficiency, and malignancy risk.

CASE 10 **A child has cold staphylococcal abscesses, retained primary teeth, fractures, and very high IgE.**

Diagnosis: **STAT3 hyper-IgE syndrome**

Why: Th17 deficiency impairs epithelial neutrophil recruitment.

CASE 11 **A neonate has delayed umbilical cord separation, neutrophilia, recurrent skin infections, and no pus.**

Diagnosis: **LAD type 1**

Why: CD18 deficiency prevents firm adhesion and tissue extravasation.

CASE 12 **A boy has liver abscesses from Staphylococcus and Aspergillus pneumonia; DHR fluorescence is absent.**

Diagnosis: **Chronic granulomatous disease**

Why: NADPH oxidase failure prevents oxidative killing of catalase-positive organisms.

CASE 13 **A child has partial albinism, recurrent pyogenic infection, giant granules, and neuropathy.**

Diagnosis: **Chediak-Higashi syndrome**

Why: LYST trafficking failure impairs phagolysosome function.

CASE 14 **A college student has recurrent meningococcal meningitis; immunoglobulins and neutrophils are normal.**

Diagnosis: **Terminal complement deficiency**

Why: C5-C9 loss impairs MAC-mediated Neisseria killing.

CASE 15 **A young patient has SLE-like disease and recurrent infection with a low CH50 but normal AH50.**

Diagnosis: **Early classical complement deficiency**

Why: C1/C2/C4 failure impairs classical activation and immune-complex clearance.

CASE 16 **A patient has recurrent swelling without urticaria, low C4, and normal tryptase.**

Diagnosis: **Hereditary angioedema**

Why: C1 inhibitor deficiency causes bradykinin-mediated vascular leak.

CASE 17 **A patient has hemoglobinuria, thrombosis, and loss of CD55/CD59 on blood cells.**

Diagnosis: **Paroxysmal nocturnal hemoglobinuria**

Why: PIGA mutation removes GPI-anchored complement regulators.

CASE 18 **Minutes after a bee sting, a patient develops wheeze, hypotension, and urticaria.**

Diagnosis: **Type I hypersensitivity / anaphylaxis**

Why: IgE cross-linking triggers systemic mast-cell degranulation; epinephrine is first-line.

CASE 19 **A patient has pulmonary hemorrhage and rapidly progressive GN with linear IgG along basement membranes.**

Diagnosis: **Type II hypersensitivity - anti-GBM disease**

Why: Antibody targets fixed type IV collagen antigen.

CASE 20 **A patient develops fever, rash, arthralgias, low complement, and proteinuria 10 days after antiserum.**

Diagnosis: **Type III hypersensitivity - serum sickness**

Why: Circulating immune complexes deposit and activate complement.

CASE 21 **A nickel watch causes an itchy rash that peaks two days after exposure.**

Diagnosis: **Type IV hypersensitivity - contact dermatitis**

Why: Delayed T-cell-mediated inflammation does not require antibody.

CASE 22 **A patient has ptosis and fatigable weakness with antibodies against the acetylcholine receptor.**

Diagnosis: **Type II receptor-blocking hypersensitivity - myasthenia gravis**

Why: Antibody impairs receptor function rather than lysing muscle cells.

CASE 23 **A patient has hyperthyroidism, ophthalmopathy, and TSH receptor-stimulating antibodies.**

Diagnosis: **Graves disease**

Why: Type II antibody stimulates rather than destroys the receptor.

CASE 24 **A young woman has rash, arthritis, cytopenias, proteinuria, anti-dsDNA, and low C3/C4.**

Diagnosis: **Systemic lupus erythematosus**

Why: Immune-complex consumption and nephritis are classic Type III features.

CASE 25 **An infant has severe diarrhea, eczema, diabetes, and a FOXP3 mutation.**

Diagnosis: **IPEX syndrome**

Why: Treg failure causes profound early autoimmune disease.

CASE 26 **A child has chronic candidiasis, hypoparathyroidism, and adrenal insufficiency.**

Diagnosis: **APECED / AIRE deficiency**

Why: Failure of central tolerance plus anti-cytokine autoimmunity produces the triad.

CASE 27 **A patient has fever, splenomegaly, cytopenias, very high ferritin, low fibrinogen, and liver dysfunction.**

Diagnosis: **Hemophagocytic lymphohistiocytosis**

Why: Uncontrolled macrophage/T-cell activation is the core mechanism.

CASE 28 **A transplant becomes cyanotic and thrombosed within minutes of reperfusion.**

Diagnosis: **Hyperacute rejection**

Why: Preformed recipient antibodies trigger complement and vascular thrombosis.

CASE 29 **A kidney transplant develops rising creatinine weeks later with interstitial lymphocytes and tubulitis.**

Diagnosis: **Acute cellular rejection**

Why: Recipient T cells attack graft tubules and endothelium.

CASE 30 **A patient receiving checkpoint inhibition develops diarrhea, hepatitis, rash, and thyroid dysfunction.**

Diagnosis: **Immune-related adverse events**

Why: Releasing T-cell inhibitory checkpoints can produce multisystem autoimmune-like toxicity.

The Twelve Immunology Rules

- **1. Encapsulated bacteria =** antibody, C3, or splenic clearance problem.
- **2. Neisseria =** terminal complement until proven otherwise.
- **3. Catalase-positive abscesses =** CGD and DHR testing.
- **4. Delayed cord + no pus =** LAD-1/CD18.
- **5. Viral/fungal/opportunists =** T-cell or combined defect.
- **6. Absent B cells =** XLA; present B cells with low Ig = consider CVID.
- **7. High IgM + low other isotypes =** class-switch failure.
- **8. Minutes =** Type I; linear fixed-target antibody = Type II; granular complexes = Type III; 48-72 hours = Type IV.
- **9. CH50 low only =** classical pathway; AH50 low only = alternative; both low = common/terminal/C3 or consumption.
- **10. Normal cell numbers do not prove normal function =** use vaccine titers, DHR, proliferation, and pathway assays.
- **11. Autoimmunity + infection =** consider immune dysregulation or CVID, not only "two unrelated diseases."
- **12. Name the effector first =** IgE, IgG/IgM, complex, T cell, complement, phagocyte, B cell, or CD4 cell.

Emergency Red Flags

Finding	Immediate concern
Anaphylaxis with hypotension/bronchospasm	Immediate intramuscular epinephrine and emergency care
Infant lymphopenia + thrush/FTT	SCID emergency; avoid unassessed live vaccines
Fever + severe neutropenia	Life-threatening bacterial/fungal infection
Pulmonary hemorrhage + nephritic urine	Pulmonary-renal immune emergency
Fever + cytopenias + extreme ferritin	HLH/macrophage activation
Angioedema affecting airway	Histamine vs bradykinin mechanism; airway emergency
Post-transplant acute organ dysfunction	Cellular or antibody-mediated rejection/infection
Checkpoint therapy + organ inflammation	Immune-related toxicity

Selected Source and Reference Notes

- High-Yield NBME Immunology & Congenital Immunodeficiencies, Sinoe Medical Association, 2026.
- Opsonization, Neutrophil Phagocytosis, Oxidative Burst, NETosis & Hypersensitivity, Sinoe Medical Association.
- Immunology Lectures - Better Editable 2026 eBook, Sinoe Medical Association.
- Immune System, Inflammation & Immunopathology - 2026 Review, Sinoe Medical Association.
- Congenital Immunodeficiency Buzzwords 2026, Sinoe Medical Association.
- Standard faculty references: Abbas Cellular and Molecular Immunology; Janeway Immunobiology; Robbins & Cotran Pathologic Basis of Disease; major USMLE board-review frameworks.

Edition Note The immune-mechanism, congenital immunodeficiency, flow-cytometry, complement, hypersensitivity, autoimmune, and case frameworks were consolidated from the user's prior Sinoe materials. Current vaccine schedules, prophylaxis thresholds, biologic monitoring, and treatment protocols must be checked against current official guidance at the time of clinical use.

Closing Memory Line

IMMUNOLOGY PATTERN RECOGNITION Organism tells you the missing defense. Age tells you whether maternal antibody was masking the problem. Flow cytometry tells you which cells are present. Functional testing tells you whether they work. Timing and tissue pattern tell you the hypersensitivity mechanism.

Rapid Buzzword Index

Buzzword	Diagnosis / mechanism	Buzzword	Diagnosis / mechanism
Absent tonsils	XLA / absent B cells	Adult + Giardia	CVID
High IgM	Class-switch defect	T- B+ NK-	IL2RG SCID
CATCH-22	DiGeorge	Small platelets	Wiskott-Aldrich
Ataxia + high AFP	Ataxia-telangiectasia	Cold abscesses	STAT3 hyper-IgE
No pus + neutrophilia	LAD-1	Abnormal DHR	CGD
Giant granules	Chediak-Higashi	Recurrent Neisseria	C5-C9 deficiency
Low C4 + no hives	C1-INH deficiency	CD55/CD59 loss	PNH
Linear IF	Type II / anti-GBM	Granular IF	Type III immune complex
Tryptase	Mast-cell activation	48-72 hours	Type IV
FOXP3	IPEX	AIRE	APECED
Double-negative T cells	ALPS	Extreme ferritin	HLH
C4d + DSA	Antibody-mediated rejection	Tubulitis	Acute cellular rejection