IMMUNE DISEASES CLASSIFICATION

A Guide to Immunologic Health – 2026 Edition

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Introduction

The human immune system is a marvel of biological engineering, a sophisticated network designed to distinguish "self" from "non-self." However, when this precision fails, the resulting pathologies — ranging from debilitating autoinflammation to life-threatening immunodeficiencies — present some of the most complex challenges in modern medicine. For clinicians, researchers, and policymakers, the primary challenge is not just treating these diseases but **defining and categorizing them.** Historically, immune disorders were scattered across medical specialties based on the organs they affected. A dermatologist saw the skin rash of Lupus, while a nephrologist treated kidney failure. In this book, we provide a comprehensive comparative analysis of the leading frameworks used to organize these conditions:

MedlinePlus / MeSH/ ICD-10 / ICD-11/ SNOMED CT / Gell and Coombs /MedDRA/ IUIS/...

To move beyond abstract theory, this book analyzes the distribution of these diseases within a standardized **10,000-person population**.

By using this consistent denominator, we offer a clear statistical lens through which to view:

1. **High-Frequency Disorders:** Such as seasonal allergies and common autoimmune triggers.
2. **Moderate-Impact Conditions:** Including Rheumatoid Arthritis and Type 1 Diabetes.
3. **Rare and Orphan Diseases:** Such as Severe Combined Immunodeficiency (SCID) and rare autoinflammatory syndromes.

Content

Limitations of Medline, MeSH, and MedlinePlus in Immunologic Classification

While Medline, MeSH, and MedlinePlus are cornerstone resources in the medical information ecosystem, they serve distinct purposes that are often misaligned with the requirements of formal immunologic classification. For researchers and clinicians needing a rigorous, hierarchy-based framework, these tools present significant structural challenges.

The Problem with Retrieval-Based Systems (MeSH & Medline)

Medline and its controlled vocabulary, MeSH (Medical Subject Headings), are primarily bibliographic tools. Their primary objective is to facilitate the search and retrieval of articles across one of the world's largest databases of medical terminology.

- Broad Indexing vs. Pathogenetic Precision: MeSH uses a "tree structure" optimized for discovery. It often groups diseases by broad organ systems or clinical presentation to ensure researchers find as many relevant papers as possible. However, in modern immunology, classification depends on specific genetic mutations and molecular pathways (such as those defined by the IUIS).
- Poly-hierarchical Ambiguity: In MeSH, a single term like "Lupus" may appear under "Skin Diseases" and "Immune System Diseases" simultaneously. While excellent for finding articles, this lack of a singular, definitive structure makes it unsuitable for formal classification purposes.

MedlinePlus: Consumer Education vs. Clinical Classification

MedlinePlus is an invaluable resource for patients and the general public, providing easy-to-read health information. However, its structure is even further removed from clinical classification needs:

- Consumer-Centric Organization: MedlinePlus organizes information by "Health Topics" designed for accessibility. It prioritizes common names and symptoms over the complex, mechanism-based hierarchies required for immunologic health.
- Simplified Categories: To remain user-friendly, MedlinePlus often collapses distinct immunologic disorders into broad categories like "Autoimmune Diseases" or "Immune System Disorders," obscuring the granular differences necessary for clinical or research-level classification.

> Important
> Key Distinction: Medline, MeSH, and MedlinePlus are aggregators and educators, not classifiers. They are designed to collect, retrieve, and explain information, whereas a true immunologic classification system must define the strict biological and clinical boundaries of a disease.

Why a Specialized Classification is Necessary

This ebook, "Immune Diseases Classification: A Guide to Immunologic Health," fills the gap left by these general indexing and consumer services. By prioritizing clinical accuracy and the latest IUIS standards over broad bibliographic indexing or consumer-level summaries, this classification provides:

1. Mechanistic Hierarchy: Grouping diseases by their underlying immunologic failure rather than just symptom clusters or search-friendly terms.
2. Clinical Precision: A structure designed for definitive diagnosis and research categorization rather than library management or patient education.
3. Specific Granularity: Detailed breakdowns of inborn errors of immunity and specific cytokine pathways that broader indexing systems often overlook.

In summary, while MeSH and Medline are essential for navigating the vast volume of medical literature, and MedlinePlus is vital for patient outreach, they lack the accurate tree structure required for the formal classification of immune diseases. For those who need to understand the precise relationships and categories of immunologic disorders, a specialized, science-led framework is the only reliable choice.

ICD-11 (International Classification of Diseases, 11th Revision)

The transition to ICD-11 brought a massive improvement for immunology. Unlike ICD-10, which scattered immune diseases across different chapters, ICD-11 introduced a dedicated **Chapter 04: Diseases of the Immune System**. This centralizes primary immunodeficiencies, autoinflammatory disorders, and systemic autoimmune diseases into one logical framework.

- ⊟ 04 Diseases of the immune system
  - ⊞ Primary immunodeficiencies
  - ⊞ 4A20 Acquired immunodeficiencies
  - ⊞ Nonorgan specific systemic autoimmune disorders
  - ⊞ Autoinflammatory disorders
  - ⊞ Allergic or hypersensitivity conditions
  - ⊞ Immune system disorders involving white cell lineages
  - ⊞ Certain disorders involving the immune system
  - ⊞ 4B40 Diseases of thymus
  - Organ specific autoimmune disorders
  - Symptoms, signs or clinical findings of blood, blood-forming organs, or the immune system
  - 4B4Y Other specified diseases of the immune system
  - 4B4Z Diseases of the immune system, unspecified

Exclusions

Complications of pregnancy, childbirth and the puerperium(18)
Neoplasms(02)
Developmental anomalies(20)

Summary Table: ICD-10 vs. ICD-11 Structure

Feature	ICD-10	ICD-11
Primary Location	Chapter III (D50-D89)	**Chapter 04 (Entirely dedicated)**
Allergies	Scattered (Skin, Respiratory)	Grouped in Chapter 04
Autoinflammatory	Poorly defined/Mislabeled	Clearly categorized (4A60+)
Logic	Organ-based	**Mechanism-based**

Why the change matters

In ICD-10, if you had a rare autoinflammatory fever, you might have to code it under "Other specified" in a musculoskeletal chapter. In ICD-11, the code **4A60** specifically identifies the immune pathway involved, which helps doctors and researchers track treatments more accurately.

SNOMED CT (Systematized Nomenclature of Medicine—Clinical Terms)

In SNOMED CT immune diseases (immune system disorders) are primarily classified under the **Clinical Finding** hierarchy, specifically as disorders. The main organizing concept is:

414029004 | Disorder of immune function (disorder)

SNOMED CT uses a **polyhierarchy**, so many immune disorders have multiple parents (e.g., also classified by site, etiology, or process). The classification is not a simple single tree but reflects multiple axes.

Parents:

- Disease (disorder)

Concept Details: Disorder of immune function (disorder) SCTID: 414029004

Children (54)

≡ Acute cerebellar ataxia following infectious disease (disorder)
≡ Acute respiratory distress syndrome due to disease caused by severe acute respiratory syndrome coronavirus 2 (disorder)
≡ Allergic bronchospasm caused by dietary substance (disorder)
≡ Allergic diarrhea (disorder)
⊞ Allergic disorder (disorder)
⊞ Allergic headache (disorder)
⊞ Allergic reaction (disorder)
⊞ Allergic urticaria and/or angioedema (disorder)
≡ Alpha-gal syndrome (disorder)
Anti-human leukocyte antigen hyperimmunization (disorder)
≡ Aseptic peritoneal eosinophilia due to and following dialysis (disorder)
⊞ Autoimmune disease (disorder)
⊞ Autoinflammatory disease (disorder)
≡ Bakers' asthma (disorder)

One might expect a clean, nested hierarchy when looking at professional databases like SNOMED CT or MeSH. However, the reality is a ‘semantic chaos’. In SNOMED, for instance, a broad umbrella term like **'Autoimmune disease'** sits on the same hierarchical level as a highly specific trigger like **'Bakers’ asthma.'** > This confirms that these systems are **retrieval architectures**, not biological taxonomies. They are designed to 'tag' and 'retrieve' data across vast databases. SNOMED is designed for **Electronic Health Records (EHR)**. It prioritizes "Clinical Findings" over "Biological Classification."

1. **The Concept of "Is-A" Relationships:** In SNOMED, "Bakers' asthma" is categorized under "Disorder of immune function" because it *is a* disorder of immune function. SNOMED doesn't care if it's a "leaf" or a "branch"—it only cares that the link is logically true.
2. **Granularity for Doctors:** When a doctor types a diagnosis into a computer in Washington Heights, they need to find the specific term quickly. If SNOMED hid "Allergic headache" under four layers of "Allergy" -> "Hypersensitivity" -> "Neurological," it would be too slow to use.
3. **The "Silo" Problem:** You’ll notice **Sepsis** and **Psoriasis** are on your list. In a biological textbook, Psoriasis is a skin disease. In SNOMED, it is elevated to the first level of "Immune Function" because its *mechanism* is immune-mediated.

Gell and Coombs classification

When you are looking for an "official" site for the **Gell and Coombs Classification**, you won't find one in the same way you find a government site for the CDC or the NLM.
This is because the Gell and Coombs system is a **scientific landmark**—a classic medical theory first published in **1963** by British immunologists **Philip George Houthem Gell** and **Robin Coombs**. It isn't a "live" database like MeSH or SNOMED; it is the fundamental **biological framework** upon which all those other messy systems were built.

This system focuses specifically on **hypersensitivity** (overreactions), not the full spectrum of immune disorders (e.g., it excludes primary immunodeficiencies or most pure autoimmune diseases unless they fit these mechanisms). It divides reactions into **four types** based on the immune mechanism, timing, mediators, and pathology. It remains the foundational and most widely taught classification in immunology, allergy, and medical education (e.g., USMLE, textbooks like Abbas' Cellular and Molecular Immunology, Merck Manuals).

Overview of the Gell and Coombs Classification

Type	Name / Alternative Names	Immune Mechanism / Mediators	Timing of Reaction	Key Pathophysiology	Common Clinical Examples
I	Immediate / Anaphylactic / Atopic	IgE-mediated; mast cells, basophils, histamine, leukotrienes	Immediate (minutes)	Allergen cross-links IgE on mast cells → degranulation → release of vasoactive mediators	Anaphylaxis, allergic rhinitis (hay fever), asthma, urticaria (hives), food allergies, atopic dermatitis, angioedema
II	Cytotoxic / Antibody-dependent	IgG or IgM antibodies + complement or Fc receptor cells (phagocytes, NK cells) targeting cell-surface antigens	Minutes to hours	Antibodies bind to cell-bound antigens → complement activation, phagocytosis, or ADCC → cell destruction	Autoimmune hemolytic anemia, Goodpasture syndrome, Graves' disease (type IIb: stimulatory), myasthenia gravis, transfusion reactions, Rh hemolytic disease of newborn
III	Immune complex-mediated	IgG/IgM immune complexes deposit in tissues → complement activation, neutrophil recruitment	6 – 24 Hours	Soluble antigen-antibody complexes deposit in vessels/joints/kidneys → inflammation via complement and Fc receptors	Serum sickness, systemic lupus erythematosus (SLE) flares, post-streptococcal glomerulonephritis, Arthus reaction, some vasculitis (e.g., Henoch-Schönlein purpura)
IV	Delayed-type / Cell-mediated / Tuberculin-type	T-cell mediated (primarily CD4+ Th1 cells, sometimes CD8+); cytokines (IFN-γ, etc.) activate macrophages	Delayed (24–72 hours)	Sensitized T cells release cytokines → macrophage activation, inflammation (no antibodies involved)	Contact dermatitis (e.g., poison ivy, nickel), tuberculin skin test (Mantoux), chronic transplant rejection, some drug rashes (e.g., maculopapular), granulomatous diseases (e.g., tuberculosis, sarcoidosis)

- **Types I–III** are **antibody-mediated** (humoral immunity).
- **Type IV** is **cell-mediated** (no antibodies; T-cell driven).

Recent proposals (e.g., EAACI 2023 position paper) expand to Types V–VII for newer mechanisms like epithelial barrier defects or direct chemical responses, but the original four remain the core.
Limitations: The system is mechanistic rather than clinical; some hypersensitivity (e.g., certain autoinflammatory or pseudo-allergic) don't fit neatly. It's not for immunodeficiencies or non-hypersensitivity autoimmune disorders.
This classification is particularly useful for understanding **allergic** and some **autoimmune** aspects of immune disorders, complementing broader frameworks like the functional classification (immunodeficiency, hypersensitivity, autoimmune, autoinflammatory) or IUIS for primary immunodeficiencies.

Detailed Breakdown of Each Type:

Type I: Immediate Hypersensitivity (Allergy)

This is the most common form of hypersensitivity. When you are exposed to an allergen (like peanuts or pollen), your body produces IgE antibodies. These antibodies sit on mast cells; when the allergen returns, the mast cells "explode" and release histamine.

- The Result: Rapid swelling, itching, or airway constriction.

Type II: Cytotoxic Hypersensitivity

Instead of reacting to an external "fake" threat, the immune system targets actual cells. Antibodies (IgG/IgM) bind to specific antigens on cells (like red blood cells), marking them for destruction by "killer" cells or complement proteins.

- The Result: Specific cell death or organ-specific damage (e.g., destruction of blood cells in Hemolytic Anemia).

Type III: Immune Complex Hypersensitivity

In this type, antibodies bind to antigens floating in the blood, creating "clumps" called immune complexes. These complexes are too large to stay in the blood but too small to be easily cleared, so they get stuck in the linings of small blood vessels, joints, or kidneys.

- The Result: Persistent, widespread inflammation. This is the primary mechanism behind Systemic Lupus Erythematosus (SLE).

Type IV: Delayed Hypersensitivity (Cell-Mediated)

Unlike the first three types, Type IV does not use antibodies. Instead, T-cells recognize an antigen and release cytokines that recruit macrophages to attack the area. Because it takes time for these cells to travel and activate, the reaction is "delayed."

- The Result: Localized tissue damage or chronic autoimmune destruction (e.g., Multiple Sclerosis).

Type IV is subdivided (e.g., IVa: Th1/macrophage, IVb: Th2/eosinophil, IVc: cytotoxic CD8+, IVd: neutrophilic) in modern updates (Pichler et al.).

> *Important*
> *Overlapping Mechanisms: Many complex autoimmune diseases do not stick to just one category. For example, Rheumatoid Arthritis involves both Type III (immune complexes in the joints) and Type IV (T-cells directly attacking cartilage).*

> *Tip*
> *A simple way to remember the types is the acronym ACID:*
> 1. *A - Allergy (Type I)*
> 2. *C - Cytotoxic (Type II)*
> 3. *I - Immune Complex (Type III)*
> 4. *D - Delayed (Type IV)*

In clinical immunology, most autoimmune diseases are technically sub-classified as hypersensitivity reactions.
The two terms describe different aspects of the same problem: "Autoimmune" describes who is being attacked (the self), while "Hypersensitivity" describes how the immune system is carrying out that attack (the biological pathway).

Autoimmune Hemolytic Anemia (AIHA) is the classic example of this overlap:

- Autoimmune Classification: It is autoimmune because the target is your own Red Blood Cells (RBCs).
- Hypersensitivity Classification: It is a Type II (Cytotoxic) Hypersensitivity because the mechanism involves IgG or IgM antibodies binding to the surface of the RBCs and signaling for their destruction.

Common Disorders in Both Groups

The following table matches well-known autoimmune diseases to their corresponding Gell-Coombs Hypersensitivity mechanisms.

Disorder	Autoimmune Target	Hypersensitivity Type	Mechanism
Goodpasture's Syndrome	Kidneys/Lungs	Type II	Antibodies attack the basement membrane.
Myasthenia Gravis	Nerve-Muscle Junction	Type II	Antibodies block acetylcholine receptors.
Lupus (SLE)	Systemic DNA/Proteins	Type III	Antigens and antibodies form "clumps" (complexes) that clog blood vessels.
Post-Strep Glomerulonephritis	Kidneys	Type III	Immune complexes from a previous infection get stuck in kidney filters.
Type 1 Diabetes	Pancreas (Beta Cells)	Type IV	T-cells (not antibodies) directly destroy the insulin-producing cells.
Multiple Sclerosis (MS)	Nerve Insulation (Myelin)	Type IV	T-cells infiltrate the brain and attack the myelin coating.

Distinction: Autoimmune vs. Allergic Hypersensitivity
While most autoimmune diseases are hypersensitivities, not all hypersensitivities are autoimmune. The difference lies in the antigen (the trigger):

- Allergic Hypersensitivity (Type I): The mechanism is hypersensitive, but the target is External (e.g., Peanuts, Pollen). This is not autoimmune.
- Autoimmune Hypersensitivity (Types II, III, IV): The mechanism is hypersensitive, and the target is Internal/Self (e.g., DNA, Joint Tissue). This is autoimmune.

> *Important*
> *Complex Overlap: Some diseases like Rheumatoid Arthritis are so aggressive that they use multiple hypersensitivity pathways. RA involves Type III (immune complexes in joint fluid) and Type IV (T-cells destroying cartilage).*

> *Tip*
> *If you are a student or patient trying to distinguish these, remember that Type I is almost never autoimmune (it's always an allergy), whereas Types II, III, and IV are the primary "engine rooms" behind almost all autoimmune diseases.*

Functional / Mechanistic Classification

(Most Widely Taught and Used Clinically)

Immunodeficiencies — Immune system too weak/underactive → increased infections.
Primary (genetic/congenital) vs. Secondary (acquired, e.g., HIV, medications, malnutrition).

Hypersensitivities / Allergic Disorders
— Immune system overreacts to harmless antigens → allergies, asthma, anaphylaxis.
Often uses the classic Gell and Coombs classification (Types I–IV hypersensitivity).

Autoimmune Diseases — Immune system attacks self-tissues → chronic inflammation/damage.
Subdivided into:
Organ-specific (targets one organ/tissue, e.g., type 1 diabetes, Hashimoto's thyroiditis, multiple sclerosis).
Systemic (affects multiple organs, e.g., systemic lupus erythematosus, rheumatoid arthritis, Sjögren's

Autoinflammatory Disorders — Dysregulated innate immunity (e.g., periodic fever syndromes like FMF, cryopyrin-associated periodic syndromes).

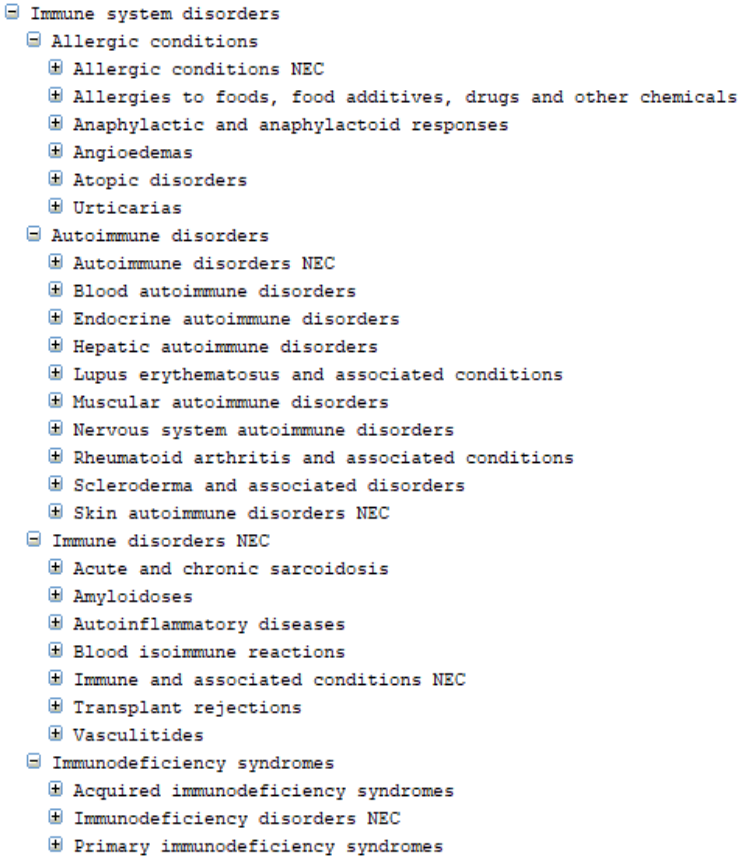
Other / Overlapping — e.g., transplant rejection, graft-versus-host disease, cytokine release syndrome.

Why is it recommended:
Clear, practical, and aligns with how clinicians think about pathogenesis and treatment.
Used in resources like NIAID, Hopkins Medicine, Merck Manuals, and consumer sites.

MedDRA Classification of Immune Disorders

MedDRA (Medical Dictionary for Regulatory Activities) is a standardized medical terminology developed by the International Council for Harmonisation (ICH) for use in pharmacovigilance, clinical trials, and regulatory reporting (e.g., adverse event coding for drugs, biologics, and vaccines). It is hierarchical, multi-axial (terms can link to multiple System Organ Classes/SOCs for flexibility), and focuses on grouping terms for safety data analysis. Within MedDRA, at the first level of the children hierarchy, we can find

- Immune system disorders
  - Allergic conditions
  - Autoimmune disorders
  - Immune disorders NEC
  - Immunodeficiency syndromes



Immune disorders are primarily classified under the **SOC Immune system disorders** (MedDRA code 10021428 or similar, depending on version; often listed as concept 10021428 in browsers).

This SOC groups' terms by **disease process** (pathologic mechanism) rather than strict anatomy or etiology alone. It uses a multi-axial structure, so many terms (e.g., autoimmune connective tissue diseases) have primary links here but secondary links to site-specific SOCs (e.g., Musculoskeletal and connective tissue disorders) or others.

MedDRA Hierarchy Levels (Relevant to Immune Disorders)

MedDRA has 5 levels (from general to specific):

- **SOC** (System Organ Class): Highest level — e.g., Immune system disorders.
- **HLGT** (High Level Group Term): Major groupings under the SOC.
- **HLT** (High Level Term): Subgroupings (pathologic or anatomic).
- **PT** (Preferred Term): The core coded concept (single medical idea used for analysis).
- **LLT** (Lowest Level Term): Synonyms, variants, or more granular entries linked to one PT.

Main Structure in SOC Immune system disorders

Based on MedDRA Introductory Guides (Versions 23.0–28.1, consistent across recent releases):

The SOC is divided into these key **HLGTs** (High Level Group Terms):

- ## HLGT Allergic conditions

  (10001708) Covers hypersensitivity and allergic reactions (overlaps with Gell-Coombs Type I–IV in some cases).
  - Includes HLTs like Allergic conditions NEC, Anaphylactic reactions, Angioedema and urticaria, etc.
  - Examples: PT Anaphylactic reaction, PT Allergic rhinitis, PT Drug hypersensitivity, PT Food allergy.

- ## HLGT Autoimmune disorders

  (10003816) The largest and most detailed for autoimmune diseases (immune attacking self).
  - Sub-classified at HLT level by anatomic site/pathology (e.g., Blood autoimmune disorders, Endocrine autoimmune disorders, Hepatic autoimmune disorders, Muscular autoimmune disorders, Nervous system autoimmune disorders, Skin autoimmune disorders NEC, etc.).
  - Examples:
    - PT Systemic lupus erythematosus
    - PT Rheumatoid arthritis
    - PT Autoimmune thyroiditis
    - PT Autoimmune hepatitis
    - PT Multiple sclerosis
    - PT Autoimmune haemolytic anaemia (often multi-axial to Blood and lymphatic system disorders)

- ## HLGT Immunodeficiency syndromes (10021460) Focuses on immunodeficiencies.
  - Primarily well-defined primary and some secondary immunodeficiencies (to avoid overly broad grouping).
  - Examples: PT Acquired immunodeficiency syndrome (AIDS), PT Common variable immunodeficiency, PT Severe combined immunodeficiency, PT Complement deficiency.

- ## HLGT Immune disorders NEC

  (10027665) "Not Elsewhere Classified" — catches miscellaneous or unspecified immune issues.
  - Includes some transplant-related (e.g., graft-versus-host disease, rejection — primary here, secondary in Injury/poisoning or site SOCs).

Key Conventions and Notes in MedDRA for Immune Disorders

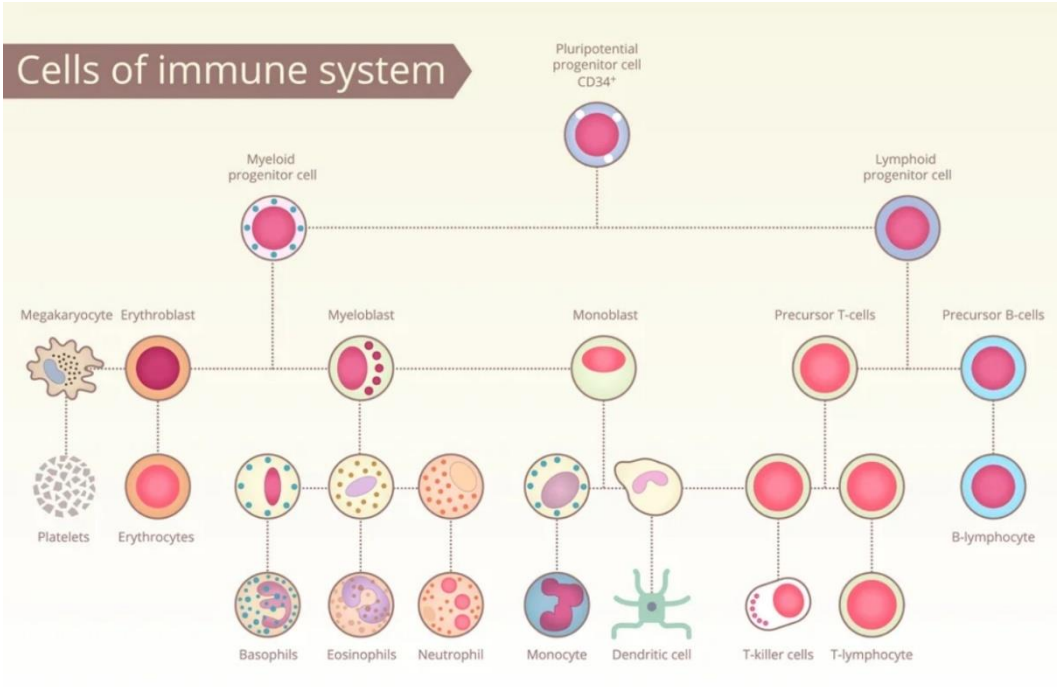
- **Multi-axiality** is common due to systemic nature → e.g., PT Rheumatoid arthritis has primary SOC Immune system disorders (HLGT Autoimmune disorders) but secondary in Musculoskeletal and connective tissue disorders.
- Transplant rejection/graft-vs-host: Primary in Immune system disorders (immune-mediated), secondary in Injury, poisoning and procedural complications + anatomic site.
- Secondary immunodeficiencies: Only specific/well-defined ones grouped here (e.g., medication-induced); broad acquired ones (e.g., due to cancer) often primary elsewhere.
- Overlaps: Allergic/hypersensitivity terms may link to Skin/respiratory SOCs secondarily; some autoimmune cytopenias primary in Blood and lymphatic system disorders.

Comparison to Previous Classifications

Aspect	MedDRA (SOC Immune system disorders)	SNOMED CT (e.g., 414029004 Disorder of immune function)	Gell-Coombs (Hypersensitivity)	MedlinePlus (Consumer Grouping)
Primary Focus	Pharmacovigilance / adverse events coding	Clinical EHR / detailed ontology	Mechanisms of hypersensitivity	Patient education / broad buckets
Structure	5-level hierarchy; multi-axial; 4 main HLGTs	Polyhierarchical; deep subtypes	4 types (I–IV)	Loose topics (autoimmune, immunodeficiency, allergies)
Autoimmune	Dedicated HLGT with anatomic HLTs	Under autoimmune disease (85828009) + multi-parent	Types II/III often	Separate topic with >80 examples
Immunodeficiency	HLGT Immunodeficiency syndromes (limited secondary)	Deep hierarchy (primary/secondary, combined, etc.)	Not covered	Encyclopedia list of examples
Allergies/Hypersensitivity	HLGT Allergic conditions	Under allergic/hypersensitivity conditions	Core (Types I–IV)	Separate allergy/asthma topics
Granularity	High for regulatory needs (thousands of PTs/LLTs)	Extremely high (clinical precision)	Mechanistic only	Broad / representative
Best For	Safety reporting, signal detection, regulatory submissions	EHR interoperability, detailed clinical coding	Understanding allergic mechanisms	Consumer understanding

MedDRA is the standard for drug safety databases (e.g., FDA, EMA, WHO VigiBase) and often used with Standardized MedDRA Queries (SMQs) like "Immune-mediated/autoimmune disorders" for aggregated analysis.
For the most current/exact hierarchy (as MedDRA updates biannually), check official sources:

- MedDRA website (meddra.org) Introductory Guide or browser.
- NCI EVS Explore: Search "Immune system disorders" under MedDRA.
- BioPortal: MEDDRA ontology viewer.



IUIS Classification for Inborn Errors of Immunity (IEI) / Primary Immunodeficiencies

The **International Union of Immunological Societies (IUIS)** provides the gold-standard categorizing Inborn Errors of Immunity (IEI), formerly known as Primary Immunodeficiency Diseases (PIDs).

Download the Classification table: Updated IEI classification table (October, 2024)

Human inborn errors of immunity: 2024 update on the classification from the International Union of Immunological Societies Expert Committee This updated report classifies 508 genes and 17 phenocopies linked to inborn errors of immunity, including 67 new monogenic defects and 2 phenocopies. The additions were reviewed and confirmed by the IUIS Expert Committee using established criteria.

- **Genotypic classification** — Lists gene defects (508 genes + variants in some cases).
- **Phenotypic classification** — Describes 559 IEI phenotypes, including 67 novel monogenic defects and 2 new phenocopies (e.g., due to autoantibodies or somatic mutations).

Phenocopies are conditions that *look* exactly like a genetic immune disease but are not inherited.

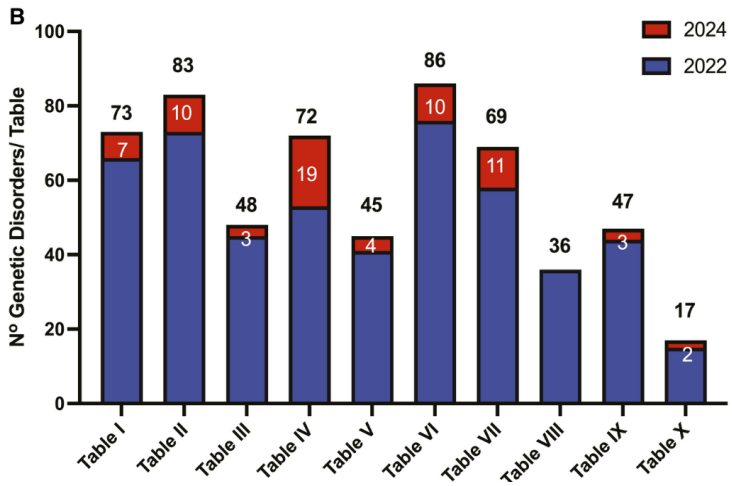
Table 10. Phenocopies of IEIs

Associated with somatic mutations

Example: **Autoimmune lymphoproliferative syndrome (ALPS-SFAS)** Somatic mutation in *TNFRSF6*

Associated with autoantibodies

Example: **Recurrent staphylococcal skin infection** AutoAb to IL-6



The classification organizes IEI into **10 main tables** (with sub-tables for overlapping phenotypes). Each table groups disorders by affected immune compartment or predominant clinical/manifestation, with associated genes, inheritance patterns, key immunological features, and clinical presentations.

While the general population may see 'immune disease' as a single category, the IUIS classification reveals a landscape of over 550 distinct molecular battles, where a single letter change in a patient's DNA can dictate the difference between a mild allergy and a total lack of defense.

Gene-First Approach: While the ICD-10 might just say "Combined Immunodeficiency," the IUIS identifies the exact gene (e.g. RAG1, ADA, or IL2RG) and the inheritance pattern (Autosomal Recessive, X-linked, etc.).

Frequent Updates: Because genomic science moves so fast, the IUIS Expert Committee updates these tables every two years to include newly discovered "experiments of nature."

In your IUIS Excel sheet, you likely saw a column titled "OMIM." In the complex world of clinical informatics, **OMIM (Online Mendelian Inheritance in Man)** serves as the definitive "Encyclopedia of Human Genes and Genetic Phenotypes." Every entry in OMIM is assigned to a unique **six-digit MIM number** like **600000 and above:** Newer entries (post-1994). While systems like MeSH and SNOMED are designed to help you *find* articles or *bill* for a doctor's visit, OMIM is designed to link a specific **Genotype** (the DNA mutation) to a specific **Phenotype** (the clinical disease). OMIM is a continuously updated digital catalog of human genes and genetic disorders. It focuses on the relationship between a genetic locus and its corresponding clinical features.

OMIM uses a specific symbol system to tell you exactly what is known about a disease:

- **Number alone (#):** The phenotype is caused by mutations in two or more genes (e.g., #209950 for certain SCID types).
- **Asterisk (*):** The entry describes a specific gene (e.g., *300300 for the *BTK* gene).
- **Percent (%):** The disease is confirmed as Mendelian, but the specific molecular cause is not yet known.

Clinical databases often use intermediate identifiers (like UMLS MTHU codes) to map generalized findings such as : C5543054|ENG|P|L17170832|PF|S20755257|Y|A33219662|||MTHU072802|OMIM|PTCS|MTHU072802|Abnormal immune activation|0|N|256|

The "Missing" 6-Digit Number: In many database exports, if a clinical term is a *general finding* (like "Abnormal immune activation") rather than a *specific Mendelian disease* (like "Wiskott-Aldrich Syndrome"), the system uses a placeholder or a broader mapping code because there isn't a single "Inborn" gene for "activation" in general.

The 10 Main Tables of the IUIS IEI Classification

Table	Category	Description / Key Features	Sub-tables (if applicable)	Examples of Disorders / Genes
I	Immunodeficiencies affecting cellular and humoral immunity	Severe combined immunodeficiencies (SCID) and combined immunodeficiencies (CID) without syndromic features; profound T ± B cell defects.	3 sub-tables (e.g., SCID, CID with less profound defects).	SCID (e.g., IL2RG, ADA), CID (e.g., RAG1/2, ZAP70).
II	Combined immunodeficiencies with associated or syndromic features	Combined defects plus extra-immune features (e.g., ectodermal dysplasia, cartilage-hair hypoplasia).	9 sub-tables (e.g., with facial dysmorphism, metabolic issues, etc.).	DiGeorge syndrome (TBX1), Cartilage-hair hypoplasia (RMRP), Wiskott-Aldrich (WAS).
III	Predominantly antibody deficiencies	B-cell or antibody production defects; often normal T cells but recurrent bacterial infections.	3 sub-tables (e.g., agammaglobulinemia, hypogammaglobulinemia).	X-linked agammaglobulinemia (BTK), Common variable immunodeficiency (many genes).
IV	Diseases of immune dysregulation	Autoimmunity, lymphoproliferation, or autoinflammation with immunodeficiency overlap.	7 sub-tables (e.g., hemophagocytic syndromes, autoimmune polyendocrinopathy).	ALPS (FAS), IPEX (FOXP3), CTLA4 haploinsufficiency.
V	Congenital defects of phagocyte number or function	Neutropenia, defects in neutrophil/monocyte function → bacterial/fungal infections.	4 sub-tables (e.g., severe congenital neutropenia, chronic granulomatous disease).	CGD (CYBB, etc.), Kostmann syndrome (HAX1).
VI	Defects in intrinsic and innate immunity	Susceptibility to specific pathogens (e.g., mycobacteria, viruses, bacteria) due to innate pathway defects.	9 sub-tables (e.g., MSMD, viral/bacterial/fungal susceptibility).	Mendelian susceptibility to mycobacterial disease (IFNGR1/2), TLR defects.
VII	Autoinflammatory disorders	Recurrent fevers/inflammation without clear autoimmunity; innate immune dysregulation.	3 sub-tables (e.g., IL-1 mediated, NF-κB mediated).	Familial Mediterranean fever (MEFV), Cryopyrin-associated periodic syndromes (NLRP3).
VIII	Complement deficiencies	Defects in complement cascade → infections (esp. encapsulated bacteria) or autoimmunity (e.g., SLE-like).	None (single table).	C3 deficiency, Properdin deficiency.
IX	Bone marrow failure	IEI presenting primarily as pancytopenia or marrow failure syndromes.	None.	Fanconi anemia (some genes), Dyskeratosis congenita.
X	Phenocopies of inborn errors of immunity	Non-germline mimics (somatic mutations, autoantibodies) that phenocopy monogenic IEI.	None.	VEXAS (somatic UBA1), Autoantibodies to IFN-γ or IL-6.

Comparison of Major Immune Disease Families (per 10,000 people)

The following chart compares the expected number of cases for the three primary categories of immune dysfunction as of March 2026.

Immune Disease Family	Estimated Cases	Primary Mechanism
Hypersensitivities	~3,800 cases	Overreaction to external, harmless substances.
Autoimmune Diseases	~850 cases	Misdirection of attack against self-tissue.
Immunodeficiencies	~45 cases	Absence or weakness of immune defense.

Visualizing the Scale Difference

1. Hypersensitivities (38%) (~3,800 people)
    - This group is the "giant" of immune diseases. It includes:
        - Allergic Rhinitis (Hay Fever): ~2,000 people.
        - Atopic Dermatitis (Eczema): ~1,000 people.
        - Asthma: ~800 people.
2. Autoimmune Diseases (8.5%) (~850 people)
    - The second-largest group, primarily driven by:
        - Autoimmune Thyroid Disease: ~500 people.
        - Celiac Disease: ~100 people.
        - Rheumatoid Arthritis: ~100 people.
3. Immunodeficiencies (0.45%) (~45 people)
    - This group is the smallest but often represents the most severe medical complexity:
        - Acquired (Secondary): ~39 people (includes HIV and drug-induced deficiency).
        - Primary (Inborn): ~6 people (includes CVID and SCID).

Key Comparisons

- Prevalence Gap: You are nearly 85 times more likely to have an allergy or asthma than you are to be born with a primary immunodeficiency.
- The "Treatment Paradox": While Hypersensitivities affect almost 4,000 out of 10,000 people, their treatment is often over-the-counter (antihistamines). In contrast, the 45 people with immunodeficiencies may require monthly hospital-based infusions (IVIG) that cost thousands of dollars per dose.
- The Overlap: Many of the 850 people with autoimmunity also fall into the 3,800 people with hypersensitivity. Having one immune dysfunction often predisposes an individual to others.

Important
Diagnostic Focus: In a standard medical practice, a doctor will see dozens of patients for allergies (Hypersensitivity) every week, but they might only encounter a new case of Primary Immunodeficiency once every few years. This rarity is why PIDs are often diagnosed late.

Tip
If you fall into the largest group (Hypersensitivity) and your symptoms are not controlled by standard medications, it may be worth screening for the smaller Autoimmune group, as conditions like Eosinophilic Esophagitis can overlap both categories.

Top 30 Hypersensitivity Diseases (per 10,000 people)

Rank	Disease / Condition	Gell-Coombs Type	Est. Cases
1	**Allergic Rhinitis (Hay Fever)**	**Type I** (Immediate)	**2,000**
2	**Allergic Contact Dermatitis**	**Type IV** (Delayed)	**1,500**
3	**Atopic Dermatitis (Eczema)**	**Type I** (Immediate)	**1,000**
4	**Asthma**	**Type I** (Immediate)	**800**
5	**Hashimoto's Thyroiditis**	**Type IV** (Cell-mediated)	**500**
6	**Psoriasis**	**Type IV** (Cell-mediated)	**250**
7	**Graves' Disease**	**Type II** (Cytotoxic)	**150**
8	**Shellfish Allergy**	**Type I** (Immediate)	**130**
9	**Celiac Disease**	**Type IV** (Cell-mediated)	**100**
10	**Rheumatoid Arthritis (RA)**	**Type III / IV** (Mixed)	**100**
11	**Vitiligo**	**Type IV** (Cell-mediated)	**75**
12	**Peanut Allergy**	**Type I** (Immediate)	**60**
13	**Type 1 Diabetes Mellitus**	**Type IV** (Cell-mediated)	**55**
14	**Sjögren's Syndrome**	**Type IV** (Cell-mediated)	**50**
15	**Ulcerative Colitis**	**Type IV** (Cell-mediated)	**40**
16	**Crohn's Disease**	**Type IV** (Cell-mediated)	**30**
17	**Ankylosing Spondylitis**	**Type IV** (Cell-mediated)	**25**
18	**Alopecia Areata**	**Type IV** (Cell-mediated)	**20**
19	**Psoriatic Arthritis**	**Type IV** (Cell-mediated)	**15**
20	**Pernicious Anemia**	**Type II** (Cytotoxic)	**12**
21	**Multiple Sclerosis (MS)**	**Type IV** (Cell-mediated)	**10**
22	**Lupus (SLE)**	**Type III** (Immune Complex)	**10**
23	**Polymyalgia Rheumatica**	**Type IV** (Cell-mediated)	**10**
24	**Drug Hypersensitivity (confirmed)**	**Type I / IV** (Mixed)	**8**
25	**IgA Nephropathy**	**Type III** (Immune Complex)	**5**
26	**Autoimmune Uveitis**	**Type IV** (Cell-mediated)	**5**
27	**Giant Cell Arteritis**	**Type IV** (Cell-mediated)	**3**
28	**Myasthenia Gravis**	**Type II** (Cytotoxic)	**2**
29	**Autoimmune Hepatitis**	**Type II / IV** (Mixed)	**2**
30	**Immune Thrombocytopenia (ITP)**	**Type II** (Cytotoxic)	**1.5**

Cancers

Cancers are generally not classified as immune diseases in formal medical terminology, but there is a significant and complex overlap between the two fields.

1. The Key Distinction

In medicine, diseases are grouped by their primary mechanism:

- Immune Diseases: The system itself is malfunctioning (e.g., attacking the body in Autoimmunity or failing to protect it in Immunodeficiency).
- Cancers (Neoplasms): The primary problem is uncontrolled cell growth and the ability of those cells to spread to other parts of the body.

2. Where they Overlap: "Cancers of the Immune System"

While most cancers (like lung or breast cancer) start in organ tissue, some cancers start directly in the cells of the immune system. These are often grouped with immune disorders in educational resources like MedlinePlus because they destroy the body's ability to fight infection.

Cancer Type	Immune Cell Involved	Where it Starts
Leukemia	White Blood Cells (Leukocytes)	Bone Marrow
Lymphoma	Lymphocytes (T-cells & B-cells)	Lymph Nodes / Spleen
Multiple Myeloma	Plasma Cells (Antibody producers)	Bone Marrow

3. The Functional Relationship

Even if cancer is not "of" the immune system, the immune system plays a critical role in every cancer case:

- Immune Surveillance: A healthy immune system constantly patrols the body to find and kill "mutant" cells before they become tumors. Cancer only develops when these cells find a way to evade the immune system.
- Chronic Inflammation: Long-term immune diseases (like Crohn's Disease or Lupus) cause chronic inflammation, which actually increases the risk of developing cancer in those irritated tissues.
- Immunotherapy: This modern field of cancer treatment works by "re-training" or "un-masking" the immune system so it can recognize and destroy cancer cells, essentially treating cancer like an immune problem.

> *Important*
> *Classification Note: If you are looking for information on Leukemia or Lymphoma, you will often find them listed under both "Cancer" and "Immune/Blood Disorders." However, a "Solid Tumor" (like a brain tumor) is almost never referred to as an immune disease.*

> *Tip*
> *Because many treatments for autoimmune diseases suppress the immune system (like Biologics or Methotrexate), patients with those conditions are often monitored more closely for certain types of cancer (like skin cancer or lymphoma) because their "patrol system" is intentionally dampened.*

Autoimmune Disorders

There are over 80 types of autoimmune conditions, and while their causes are not fully understood, they are believed to be a combination of genetic and environmental factors.

Many of them share overlapping symptoms like fatigue, low-grade fever, and inflammation. To make this list easier to navigate, they are categorized by the primary organ system or tissue they affect.

- Version: 2026.1.03
- Primary Classifications: MedlinePlus, ICD-11, and ACR/EULAR 2026 Criteria.
- Scope: 80+ Autoimmune Conditions, FDA-Approved Drug Lists, and Prevalence Statistics.

1. Joints and Muscles (Rheumatic)

These conditions primarily cause inflammation in the connective tissues, joints, and skeletal muscles.

Disease	Estimated Cases (per 10,000 people)	Classification/Notes
Rheumatoid Arthritis (RA)	50 – 100	Most common systemic inflammatory arthritis (~1% of adults).
Polymyalgia Rheumatica	5 – 70	Prevalence increases sharply with age (>50 years).
Ankylosing Spondylitis (AS)	10 – 50	Strongly associated with the HLA-B27 genetic marker.
Psoriatic Arthritis	10 – 25	Affects up to 30% of people who have psoriasis.
Systemic Lupus Erythematosus (SLE)	2 – 15	Significantly higher prevalence in women and certain ethnic groups.
Sjögren's Syndrome	5 – 10	It can occur alone (primary) or with another autoimmune disease.
Systemic Sclerosis (Scleroderma)	0.7 – 7	A rare condition characterized by skin and organ hardening.
Dermatomyositis	0.5 – 1	Rare; involves skin rashes and muscle weakness.
Polymyositis	0.5 – 1	Rare; similar to dermatomyositis but typically without the rash.
Palindromic Rheumatism	0.5 – 5	Rare; characterized by sudden, temporary joint inflammation.
Mixed Connective Tissue Disease (MCTD)	0.1 – 0.5	Extremely rare; features overlap with SLE, Scleroderma, and Myositis.
Relapsing Polychondritis	0.03 – 0.05	Ultra-rare; involves recurring inflammation of cartilage.

2. Endocrine (Hormonal)

These diseases target the glands that produce hormones, most commonly the thyroid and pancreas.

Disease	Est. Cases (per 10,000)	Classification & Clinical Notes
Hashimoto's Thyroiditis	100 – 1200	Most common autoimmune disease; causes hypothyroidism. Primarily affects women (9:1 ratio).
Graves' Disease	50 – 200	Leading cause of hyperthyroidism; characterized by the production of thyroid-stimulating antibodies (TSI).
Type 1 Diabetes Mellitus	50 – 90	Destruction of insulin-producing beta cells in the pancreas. Point prevalence is rising globally due to increased lifespan.
Addison's Disease	1 – 2	Chronic adrenal insufficiency. Requires lifelong replacement of cortisol and aldosterone to prevent adrenal crisis.
Autoimmune Hypophysitis	0.01 – 0.4	Ultra-rare inflammation of the pituitary gland. Often presents with headaches and visual field defects mimicking a tumor.
Autoimmune Oophoritis	0.1 – 1	Inflammation of the ovaries; a common cause of Premature Ovarian Insufficiency (POI) in women with other autoimmune disorders.
Autoimmune Orchitis	0.1 – 0.5	Inflammation of the testes; often secondary to trauma or infection that breaks the blood-testis barrier, leading to infertility.
APS (Types 1, 2, and 3)	0.1 – 0.5	A group of syndromes where multiple endocrine glands fail simultaneously due to a shared autoimmune mechanism.

3. Gastrointestinal (Digestive)

These conditions affect the digestive tract, liver, and biliary system.

Disease	Est. Cases (per 10,000)	Classification & Clinical Notes
Celiac Disease	100 – 130	A permanent gluten intolerance. Unlike a true allergy, it is a T-cell mediated autoimmune response that destroys the villi of the small intestine.
Ulcerative Colitis (UC)	30 – 60	A type of Inflammatory Bowel Disease (IBD) restricted to the colon and rectum. Inflammation is continuous and affects only the inner lining (mucosa).
Crohn's Disease	20 – 50	A type of IBD that can affect any part of the GI tract. Inflammation is "patchy" (skip lesions) and can penetrate the full thickness of the bowel wall.
Microscopic Colitis	5 – 10	Chronic watery diarrhea with a normal-looking colon on endoscopy. Requires a biopsy to see microscopic inflammation (lymphocytic or collagenous).
Primary Biliary Cholangitis (PBC)	2 – 4	Autoimmune destruction of the small bile ducts in the liver. Hallmark: Positive Anti-Mitochondrial Antibodies (AMA) in 95% of cases.
Autoimmune Hepatitis (AIH)	1 – 2	Chronic inflammation of the liver cells (hepatocytes). Often overlaps with other autoimmune diseases like Sjögren's or Celiac.
Primary Sclerosing Cholangitis (PSC)	0.5 – 1	Inflammation and scarring of large bile ducts. Strongly associated with IBD; 70-80% of PSC patients also have Ulcerative Colitis.
Autoimmune Pancreatitis (AIP)	0.2 – 0.5	Often part of a systemic IgG4-related disease. It can mimic pancreatic cancer on imaging but responds dramatically to steroids.

4. Neurological (Nervous System)

The immune system attacks the protective coating of nerves or the communication between nerves and muscles.

Disorder	Est. Cases (per 10,000)	Classification & Clinical Notes
Multiple Sclerosis (MS)	10 – 30	Most common CNS autoimmune disease. Characterized by demyelination in the brain and spinal cord. Prevalence is highest in northern latitudes.
PANDAS	5 – 20	Pediatric neuropsychiatric syndrome triggered by Strep infections. Characterized by sudden-onset OCD or tics. (*Estimates vary due to evolving diagnostic criteria).
Myasthenia Gravis (MG)	1.5 – 2.5	A disorder of the neuromuscular junction. Causes "fatigable" muscle weakness, often starting with drooping eyelids (ptosis) or double vision.
Guillain-Barré Syndrome	0.1 – 0.2	An acute peripheral nerve attack, often following a viral/bacterial infection. Causes rapid, "ascending" paralysis starting from the feet.
CIDP	0.1 – 0.9	The chronic counterpart to Guillain-Barré. Progressive or relapsing weakness and sensory loss over months rather than days.
ADEM	0.04 – 0.08	An acute, usually one-time inflammatory attack on the brain/spinal cord, most common in children following an infection or vaccine.
Neuromyelitis Optica	0.05 – 0.1	Also known as Devic's Disease. Specifically targets the optic nerves and spinal cord. Hallmark: Positive Aquaporin-4 (AQP4) antibodies.
Lambert-Eaton (LEMS)	0.03 – 0.04	Often paraneoplastic (associated with lung cancer). Weakness typically improves temporarily with repetitive muscle use.
Stiff Person Syndrome	0.01 – 0.02	Ultra-rare; characterized by severe muscle stiffness and painful spasms triggered by noise or stress. Hallmark: Positive Anti-GAD antibodies.

5. Skin (Dermatological)

Conditions that cause skin blistering, discoloration, or chronic scaling.

Disorder	Est. Cases (per 10,000)	Classification & Clinical Notes
Psoriasis	200 – 300	Most common; a chronic papulosquamous disorder. Accelerated skin cell turnover leads to thick, silvery scales.
Vitiligo	50 – 200	Destruction of melanocytes (pigment cells). Classified as non-segmental (generalized) or segmental.
Alopecia Areata	10 – 20	Immune attack on hair follicles. Can range from small patches to total body hair loss (Alopecia Universalis).
Lichen Planus	10 – 100	An interface dermatitis affecting skin and mucous membranes. Characterized by the "6 Ps": Planar, Purple, Polygonal, Pruritic, Papules, and Plaques.
Lichen Sclerosus	10 – 30	Often targets genital skin; characterized by thin, white, "parchment-like" patches. Primarily affects post-menopausal women.
Bullous Pemphigoid	1 – 5	Most common subepidermal blistering disease. Targets the basement membrane; typically affects the elderly.
Dermatitis Herpetiformis	1 – 1.5	The "skin version" of Celiac Disease. Intense, itchy blisters triggered by gluten ingestion.
Pemphigus Vulgaris	0.1 – 0.5	A serious intraepidermal blistering disease. Attacks the "glue" (desmogleins) between skin cells, often starting in the mouth.
Cicatricial Pemphigoid	0.1 – 0.5	Also known as Mucous Membrane Pemphigoid. Focuses on the eyes and mouth, often causing scarring (cicatrix).
Pemphigus Foliaceus	0.05 – 0.1	A more superficial form of pemphigus. Blisters are very fragile and break easily, appearing more like scaly sores.
Epidermolysis Bullosa Acquisita	0.02 – 0.05	Ultra-rare; characterized by extreme skin fragility and blisters at sites of minor trauma (mechanobullous).

6. Blood and Vasculature (Hematologic & Vascular)

These involve attacks on blood cells or the walls of blood vessels (vasculitis).

Disorder	Est. Cases (per 10,000)	Classification & Clinical Notes
Pernicious Anemia	10 – 20	An autoimmune gastritis that prevents B12 absorption. Hallmark: Anti-Intrinsic Factor antibodies.
APS	5 – 10	A thrombophilic disorder where antibodies increase blood clot risk. Also associated with pregnancy complications.
Giant Cell Arteritis	2 – 3	Large-vessel vasculitis primarily affecting the temporal arteries. (*Prevalence is ~20 per 1,000 in those over 50).
ITP	1 – 2	Autoimmune destruction of platelets, leading to bruising and bleeding (purpura).
Henoch-Schönlein (HSP)	0.5 – 2	Small-vessel vasculitis (IgA mediated). Most common in children (*~20 cases per 1,000 in pediatric populations).
Behçet's Disease	0.2 – 4	Systemic vasculitis known for the "triple symptom complex": oral ulcers, genital ulcers, and eye inflammation (uveitis).
Kawasaki Disease	0.1 – 1	Medium-vessel vasculitis in children. Major risk: coronary artery aneurysms.
GPA (Wegener's)	0.3 – 1	Small-vessel vasculitis (ANCA-associated). Primarily affects the respiratory tract and kidneys.
Autoimmune Hemolytic Anemia	0.1 – 0.5	Destruction of red blood cells. Can be "warm" (IgG) or "cold" (IgM) mediated.
Microscopic Polyangiitis	0.1 – 0.4	Small-vessel vasculitis (ANCA-associated). Similar to GPA but without the specialized granuloma formations.
Aplastic Anemia (Immune)	0.02 – 0.05	Bone marrow failure caused by T-cell attack on hematopoietic stem cells.
Polyarteritis Nodosa (PAN)	0.02 – 0.3	Medium-vessel vasculitis. Often associated with Hepatitis B; spares the smallest vessels and the lungs.
EGPA (Churg-Strauss)	0.02 – 0.1	Small-vessel vasculitis (ANCA-associated). Hallmark: Severe asthma and high levels of eosinophils (blood cells).
Takayasu's Arteritis	0.01 – 0.4	Large-vessel vasculitis affecting the aorta and its branches. Often called "Pulseless Disease."
Autoimmune Neutropenia	0.01 – 0.1	Destruction of neutrophils (white blood cells). Often found in infants (primary) or secondary to Lupus or RA.

7. Organ-Specific (Lungs, Kidneys, Eyes, Ears)

Disorder	Est. Cases (per 10,000)	Classification & Clinical Notes
IgA Nephropathy	20 – 50	Most common primary glomerular disease worldwide. Caused by IgA-containing immune complexes lodging in the kidneys.
Autoimmune Uveitis	3.8 – 7	Inflammation of the uveal tract (iris, ciliary body, and choroid). Often associated with HLA-B27 and systemic diseases like Sarcoidosis or IBD.
Autoimmune Myocarditis	1 – 2	Inflammation of the heart muscle. Often triggered by a viral infection (post-viral) or as a side effect of immune checkpoint inhibitors.
Autoimmune Inner Ear (AIED)	1.5	A rare cause of progressive hearing loss. Affects both ears, usually over weeks to months. Responsive to high-dose steroids.
Goodpasture's Syndrome	0.01 – 0.02	A pulmonary-renal syndrome. Caused by antibodies attacking the Type IV collagen found in both the lungs and kidneys.
Cogan's Syndrome	0.01	Ultra-rare; characterized by interstitial keratitis (eye) and vestibuloauditory dysfunction (inner ear). Often associated with vasculitis.
Sympathetic Ophthalmia	0.01	A rare, bilateral granulomatous uveitis occurring after trauma or surgery to one eye (the "inciting eye"), causing the "sympathizing eye" to also be attacked.
Autoimmune Retinopathy	< 0.01	Characterized by the presence of anti-retinal antibodies. Can be paraneoplastic (triggered by a cancer elsewhere) or non-paraneoplastic.

Estimated Autoimmune Distribution (per 10,000 people)

The values below represent the number of individuals expected to have at least one condition in that category. Note that because of "Multiple Autoimmune Syndrome," some individuals may be counted in more than one category.

Category	Estimated Cases (per 10,000)	Representative Conditions
Endocrine (Hormonal)	850 cases	Hashimoto's, Graves', Type 1 Diabetes
Skin (Dermatological)	375 cases	Psoriasis, Vitiligo, Alopecia Areata
Gastrointestinal (Digestive)	195 cases	Celiac Disease, Crohn's, Ulcerative Colitis
Joints and Muscles (Rheumatic)	120 cases	Rheumatoid Arthritis, Ankylosing Spondylitis
Organ-Specific (Eyes, Ears, Kidneys)	42 cases	IgA Nephropathy, Autoimmune Uveitis
Blood and Vasculature (Hematologic)	22 cases	Pernicious Anemia, ITP, Giant Cell Arteritis
Neurological (Nervous System)	18 cases	Multiple Sclerosis, Myasthenia Gravis

Visualizing the Scale

If you were to look at a stadium filled with 10,000 people:

- Endocrine / Hormonal:  (~850 people)
  - *Nearly 1 in 12 people would have an autoimmune thyroid or pancreatic condition.*
- Dermatological:  (~375 people)
  - *Psoriasis alone accounts for the vast majority of this group.*
- Gastrointestinal:  (~195 people)
  - *Celiac disease is the primary driver of these numbers.*
- Rheumatic:  (~120 people)
  - *Primarily Rheumatoid Arthritis (RA).*
- Rare & Systemic:  (~82 people combined)
  - *This includes all Neurological, Vascular, and Organ-Specific conditions combined.*

Key Takeaways for this Population

- The "Invisible" Majority: Over 8% of this population is living with an endocrine-related autoimmune disorder, though many may not "look sick" because their conditions are managed with hormone replacement (like Insulin or Levothyroxine).
- Specialist Demand: In a city of 10,000, there would be approximately 120 patients requiring a Rheumatologist for joint-destructive diseases, but nearly 400 requiring a Dermatologist for autoimmune skin issues.
- The "Needle in a Haystack": Within these 10,000 people, you might find only one or two individuals with an ultra-rare condition like Stiff Person Syndrome or Goodpasture's Syndrome.

Important

These numbers are estimates based on general population averages. Prevalence can be much higher in specific age groups or genders. For example, in 10,000 women over the age of 50, the number of Endocrine and Rheumatic cases would be significantly higher than in a general mixed population.

Tip

High-prevalence conditions like Hashimoto's and Celiac Disease are often undiagnosed for years. In this group of 10,000, dozens of people likely have these conditions but are currently attributing their fatigue or digestive issues to "stress" or "aging."

Primary Immunodeficiencies

The primary immunodeficiencies (PIDs), now formally known as Inborn Errors of Immunity (IEI), are classified into several categories based on the specific part of the immune system that is failing. According to the latest registry data from organizations like the European Society for Immunodeficiencies (ESID) and the United States Immune Deficiency Network (USIDNET), the distribution remains heavily skewed toward antibody deficiencies.

Primary Immunodeficiency Distribution (Registry Averages)
The following data represents the typical distribution seen in large-scale clinical registries. These percentages can vary slightly by region (e.g., higher rates of combined deficiencies in areas with more consanguinity).

Category	Estimated Percentage (%)
Predominantly Antibody Deficiencies	55%
Combined Immunodeficiencies (CIDs)	18%
Phagocyte Disorders	9%
Immune Dysregulation	7%
Autoinflammatory Disorders	5%
Complement Deficiencies	4%
Innate Immunity Defects	2%

Breakdown of Key Categories
1. Antibody Deficiencies (55%)
This is the most common group. It includes conditions where the body cannot produce enough functional antibodies (immunoglobulins).

- Examples: Common Variable Immunodeficiency (CVID), X-linked Agammaglobulinemia (XLA), and Selective IgA Deficiency.
- Key Symptom: Recurrent bacterial infections, particularly in the sinuses and lungs.

2. Combined Immunodeficiencies (18%)
These are among the most severe PIDs, affecting both T-cells and B-cells.

- Examples: Severe Combined Immunodeficiency (SCID), often known as "Bubble Boy" disease, and Wiskott-Aldrich Syndrome.
- Prognosis: Often considered a medical emergency in infants, requiring a bone marrow transplant for survival.

3. Phagocyte Disorders (9%)
Phagocytes are "eating cells" (like neutrophils) that swallow and destroy invaders.

- Examples: Chronic Granulomatous Disease (CGD) and Leukocyte Adhesion Deficiency (LAD).
- Key Symptom: Deep-seated skin abscesses and internal organ infections.

4. Immune Dysregulation & Autoinflammatory (12% Combined)
These are newer categories where the immune system isn't just "weak," but also "misguided," leading to excessive inflammation or autoimmunity.

- Examples: HLH (Hemophagocytic lymphohistiocytosis) and FMF (Familial Mediterranean Fever).

5. Complement Deficiencies (4%)
The complement system consists of proteins in the blood that help ("complement") antibodies clear pathogens.

- Key Symptom: Increased susceptibility to specific bacteria like *Neisseria meningitidis* (meningitis).

> *Important*
> *Diagnostic Delay: Because many of these conditions (especially antibody deficiencies) present as common infections like ear infections or pneumonia, it often takes years for a patient to be correctly diagnosed with a PID.*

> *Tip*
> *If you or a family member has two or more bouts of pneumonia in one year, or requires IV antibiotics to clear simple infections, consult an immunologist for a screening of immunoglobulin (IgG, IgA, IgM) levels.*

Reference List

This reference list compiles the primary clinical sources, registries, and medical databases used to calculate the prevalence percentages and distribution statistics throughout this guide.

1. General Prevalence & Rheumatic Statistics
Data regarding cases per 10,000 for RA, SLE, AS, and other connective tissue disorders.

- Springer Nature (2026): *Rheumatic Diseases: Clinical Epidemiology and Treatment Targets*. Springer
- BMJ Open (2026): *Population-based Health Trends in Intellectual and Physical Disabilities*. BMJ Open
- Disabled World (2026): *Global Arthritis Prevalence and Comparison Tables*. Disabled World

2. Endocrine & Metabolic Data
Sources for Type 1 Diabetes, Hashimoto's, Graves', and rare glandular conditions.

- Wikipedia / WHO (2026): *Global Status Report on Diabetes and Endocrine Disorders*. Wikipedia
- DovePress (2026): *Comprehensive Management of Hashimoto's Thyroiditis and Associated Autoimmunities*. DovePress
- ResearchGate (2026): *Analytical Phases in Hormonal Evaluation: Incidence of Pituitary and Adrenal Insufficiency*. ResearchGate

3. Gastrointestinal & Liver Registries
Statistics for Celiac Disease, IBD (Crohn's/UC), and biliary conditions.

- MalaCards (2025/2026): *The Human Disease Database: Gastrointestinal System Classifications*. MalaCards
- American College of Gastroenterology (ACG): *2025/2026 Preliminary Program and Global Incidence Hall*. ACG

4. Neurological & Rare Disease Data
Prevalence for Multiple Sclerosis, MG, CIDP, and ultra-rare syndromes like Stiff Person Syndrome.

- ScienceDirect (2026): *Neurotherapeutics and the FcRn Inhibitor Era: Epidemiological Projections*. ScienceDirect
- MDPI (2026): *Acute Disseminated Encephalomyelitis (ADEM): A Population-based View*. MDPI

5. Primary Immunodeficiencies (PID/IEI)
Specific percentages for the distribution of antibody, complement, and phagocyte defects.

- CEJI (2026): *Progress of Primary Immunodeficiency Care: Pattern of Antibody and Combined Deficiencies*. CEJI
- ESID Registry / ResearchGate: *Main Categories of PID based on the IUIS Classification*. ResearchGate
- Frontiers in Immunology (2026): *Building Alliances for Early Detection of Inborn Errors of Immunity*. Frontiers

6. Dermatological & Hypersensitivity Data
Data for the Top 30 ranking, including Psoriasis, Vitiligo, and Allergies.

- Nature (2026): *Multisystemic Associations of Atopic and Inflammatory Skin Diseases*. Nature
- UpToDate (2026): *What's New in Primary Care: Allergy and Immunology Prevalence Worldwide*. UpToDate
- Liv Hospital (2026): *The 80 Rare Autoimmune Diseases: A Complete Guide to Identification*. Liv Hospital

> *Important*
> *Data Methodology: Percentages provided are "point prevalence" estimates (the proportion of people who have the disease at a single point in time). These figures are synthesized from both global averages and specific regional registries (US and Europe) to provide the most accurate representation available as of early 2026.*

> *Tip*
> *For academic research, it is recommended to cross-reference these statistics with the ICD-11 (International Classification of Diseases) coding guide for the most current administrative definitions.*