İmmün yetmezlikler

	Affected components	Main causes[6]	Main pathogens of resultant infections[6]
Humoral immune deficiency **B cell deficiency**	B cells, plasma cells or antibodies	• Primary humoral • Multiple myeloma • Chronic lymphoid leukemia • AIDS	• *Streptococcus pneumoniae* • *Hemophilus influenzae* • *Pneumocystis jirovecii* • *Giardia intestinalis* • *Cryptosporidium parvum*
T cell deficiency	T cells	• Marrow and other transplantation • AIDS • Cancer chemotherapy • Lymphoma • Glucocorticoid therapy	Intracellular pathogens, including *Herpes simplex virus*, *Mycobacterium*, *Listeria*,[7] and intracellular fungal infections.[6]
Neutropenia	Neutrophil granulocytes	• Chemotherapy • Bone marrow transplantation • Dysfunction, such as chronic granulomatous disease	• *Enterobacteriaceae* • Oral *Streptococci* • *Pseudomonas aeruginosa* • *Enterococcus* species • *Candida* species • *Aspergillus* species

Asplenia	Spleen	• Splenectomy
		• Trauma
		• Sickle-cell anemia
			• Polysaccharide encapsulated bacteria,[8] particularly:
			  • *Streptococcus pneumoniae*[8]
			  • *Haemophilus influenzae*[8]
			  • *Neisseria meningitidis*[8]
			• *Plasmodium* species
			• *Babesia* species

Complement deficiency	Complement system	• Congenital deficiencies	• *Neisseria* species • *Streptococcus pneumoniae*

https://en.wikipedia.org/wiki/Immunodeficiency

Disease	Genetic defect	Inheritance	OMIM	T cells	B cells	Ig
1. T-B+ severe combined immune deficiency (SCID)						
γc deficiency (common gamma chain SCID, CD132 deficiency)	*IL2RG*	XL	308380	Very low	Normal to high	Low
JAK3 deficiency	*JAK3*	AR	600173	Very low	Normal to high	Low
IL7Rα deficiency	*IL7R*	AR	146661	Very low	Normal to high	Low
CD45 deficiency	*PTPRC*	AR	151460	Very low	Normal	Low
CD3δ deficiency	*CD3D*	AR	186790	Very low	Normal	Low
CD3ε deficiency	*CD3E*	AR	186830	Very low	Normal	Low
CD3ζ deficiency	*CD3Z*	AR	186780	Very low	Normal	Low
Coronin-1A deficiency	*CORO1A*	AR	605000	Very low	Normal	Low
LAT deficiency	*LAT*	AR	602354	Normal to low	Normal to low	High

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2. T-B- SCID						
RAG deficiency	*RAG1* *RAG2*	AR	179615 179616	Very low	Very low	Decreased
DCLRE1C (Artemis) deficiency	*DCLRE1C*	AR	605988	Very low	Very low	Decreased
DNA PKcs deficiency	*PRKDC*	AR	615966	Very low	Very low	Variable
Cernunnos/XLF deficiency	*NHEJ1*	AR	611290	Very low	Very low	Decreased
DNA ligase IV deficiency	*LIG4*	AR	601837	Very low	Very low	Decreased
Adenosine deaminase (ADA) deficiency	*ADA*	AR	608958	Very low	Low, decreasing	Low, decreasing
AK2 defect	*AK2*	AR	103020	Very low	Very Low	Decreased

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AK2 defect	*AK2*	AR	103020	Very low	Very Low	Decreased
Activated RAC2 defect	*RAC2*	AD GOF	602049	Very low	Very Low	Low, poor specific antibody responses
3. Combined immunodeficiency (CID), generally less profound than SCID						
CD40 ligand (CD154) deficiency	*CD40LG*	XL	308230	Normal to low	$sIgM^+IgD^+$ naïve B cells present; IgG^+, IgA^+, IgE^+ memory B cells absent	IgM normal or high, Ig isotypes low

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CD40 deficiency	*CD40*	AR	606843	Normal		
ICOS deficiency	*ICOS*	AR	604558	Normal	Normal	Low
ICOSL deficiency	*ICOSLG*	AR	605717	Low	Low	Low
CD3γ deficiency	*CD3G*	AR	186740	Normal number, but low TCR expression	Normal	Normal
CD8 deficiency	*CD8A*	AR	186910	Absent CD8, Normal CD4	Normal	Normal
ZAP-70 deficiency (ZAP70 LOF)	*ZAP70*	AR	269840	Low CD8 number, normal CD4 number but with poor function	Normal	Normal
ZAP-70 combined hypomorphic and activating mutations	*ZAP70*	AR (LOF/GOF)	617006	Decreased CD8, normal or decreased CD4 cells	Normal or decreased	Normal IgA, low IgM low/normal IgG; protective Ab respon vaccines

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MHC class II deficiency group A, B, C, D	*CIITA*	AR	600005	Low CD4+ T cells, reduced MHC II expression on lymphocytes	Normal	Normal to low
	RFXANK	AR	603200			
	RFX5	AR	601863			
	RFXAP	AR	601861			
IKAROS deficiency	*IKZF1*	AD DN	603023	no memory T cells	no memory B cells	Low Ig,
DOCK8 deficiency	*DOCK8*	AR	243700	T cell lymphopenia, reduced naïve CD8 T cells, increased exhausted CD8+ T_{EM} cells, reduced MAIT, NKT cells, increased γδ T cells; poor proliferation; few Treg with poor function	increased total B cells, reduced memory B cells Poor peripheral B cell tolerance.	Low IgM, normal/hig IgG and IgA, very hi IgE, poor antibody responses
DOCK2 deficiency	*DOCK2*	AR	603122	Low	Normal	IgG normal or low, p antibody responses

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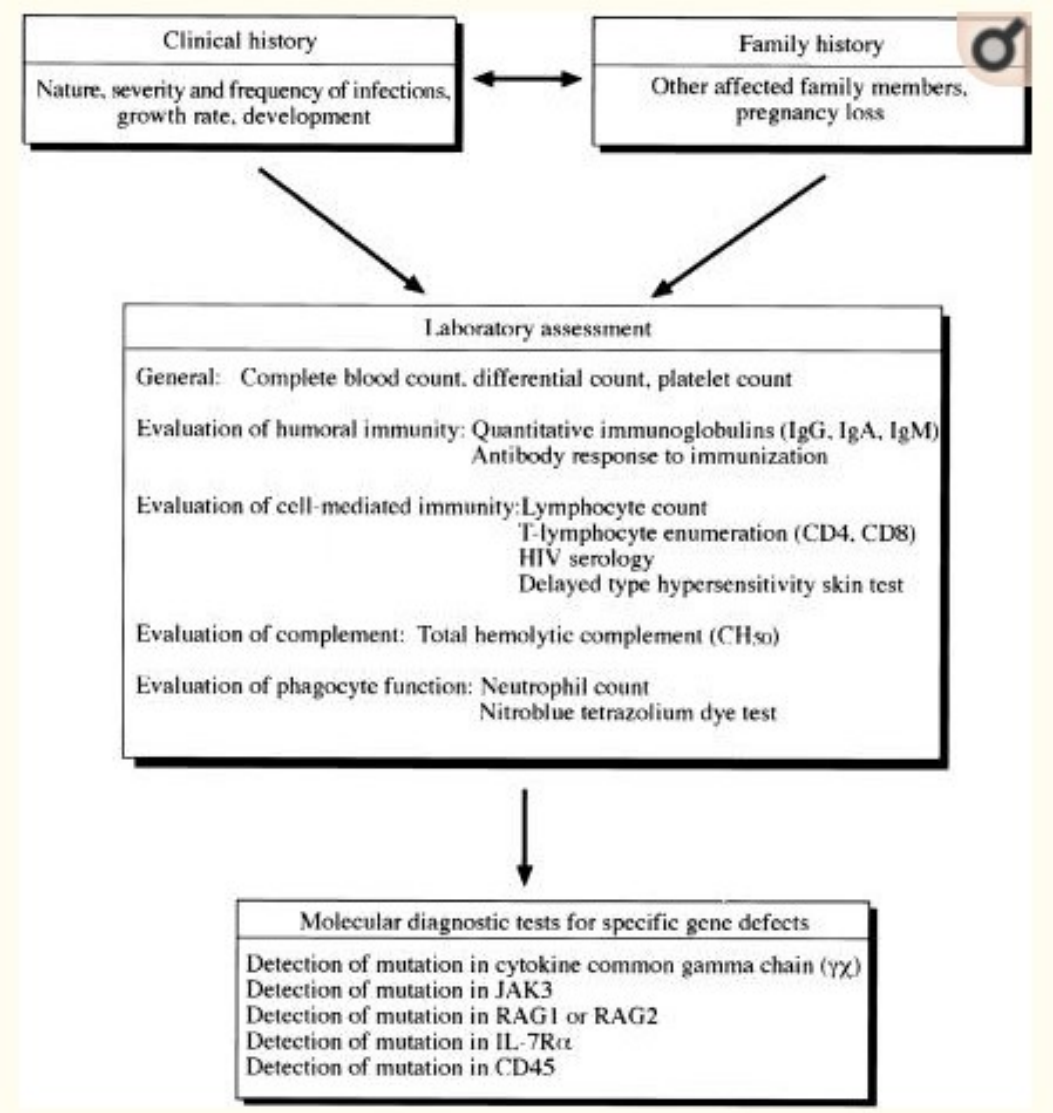
Disease	Genetic defect	Inheritance	OMIM	Ig	Associated features
1. Severe reduction in all serum immunoglobulin isotypes with profoundly decreased or absent B cells, agammaglobulinemia					
BTK deficiency, X-linked agammaglobulinemia (XLA)	*BTK*	XL	300300	All isotypes decreased in majority of patients, some patients have detectable immunoglobulins	Severe bacterial infections, normal numbers of pro-B cells
μ heavy chain deficiency	*IGHM*	AR	147020	All isotypes decreased	Severe bacterial infections, normal numbers of pro-B cells
λ5 deficiency	*IGLL1*	AR	146770		
Igα deficiency	*CD79A*	AR	112205		
Igβ deficiency	*CD79B*	AR	147245		
BLNK deficiency	*BLNK*	AR	604515		
p110δ deficiency	*PIK3CD*	AR	602839		Severe bacterial infections; autoimmune complications (IBD)
p85 deficiency	*PIK3R1*	AR	615214		Severe bacterial infections, cytopenias, decreased or absent pro-B cells
E47 transcription factor deficiency	*TCF3*	AD	616941		Recurrent bacterial infections
	TCF3	AR	147141		Severe, recurrent bacterial infections, failure to thrive
SLC39A7 (ZIP7) deficiency	*SLC39A7*	AR	601416		Early onset infections, blistering dermatosis, failure to thrive, thrombocytopenia
Hoffman syndrome/TOP2B deficiency	*TOP2B*	AD	126431		Recurrent infections, facial dysmorphism, limb anomalies

2. Severe reduction in at least 2 serum immunoglobulin isotypes with normal or low number of B cells, CVID phenotype

Common variable immune deficiency with no gene defect specified (CVID)	Unknown	Variable		Low IgG and IgA and/or IgM	Clinical phenotypes vary: most have recurrent infections, some have polyclonal lymphoproliferation, autoimmune cytopenias and/or granulomatous disease
Activated p110δ syndrome (APDS)	*PIK3CD* GOF	AD	615513 (APDS1)	Normal/increased IgM, reduced IgG and IgA	Severe bacterial infections; reduced memory B cells and increased transitional B cells, EBV ± CMV viremia, lymphadenopathy/splenomegaly, autoimmunity, lymphoproliferation, lymphoma
	PIK3R1	AD	616005 (APDS2)		Severe bacterial infections, reduced memory B cells and increased transitional B cells, lymphadenopathy/splenomegaly, lymphoproliferation, lymphoma; developmental delay
PTEN deficiency (LOF)	*PTEN*	AD	158350	Normal/Decreased	Recurrent infections, Lymphoproliferation, Autoimmunity; developmental delay
CD19 deficiency	*CD19*	AR	107265	Low IgG and IgA and/or IgM	Recurrent infections, may have glomerulonephritis (CD81 mutation abolishes expression of CD19, thereby phenocopying CD19 mutations)
CD81 deficiency	*CD81*	AR	186845	Low IgG, low or normal IgA and IgM	
CD20 deficiency	*CD20*	AR	112210	Low IgG, normal or elevated IgM and IgA	Recurrent infections
CD21 deficiency	*CD21*	AR	120650	Low IgG, impaired anti-pneumococcal response	Recurrent infections
TACI deficiency[#]	*TNFRSF13B*	AR or AD	604907	Low IgG and IgA and/or IgM	Variable clinical expression and penetrance for



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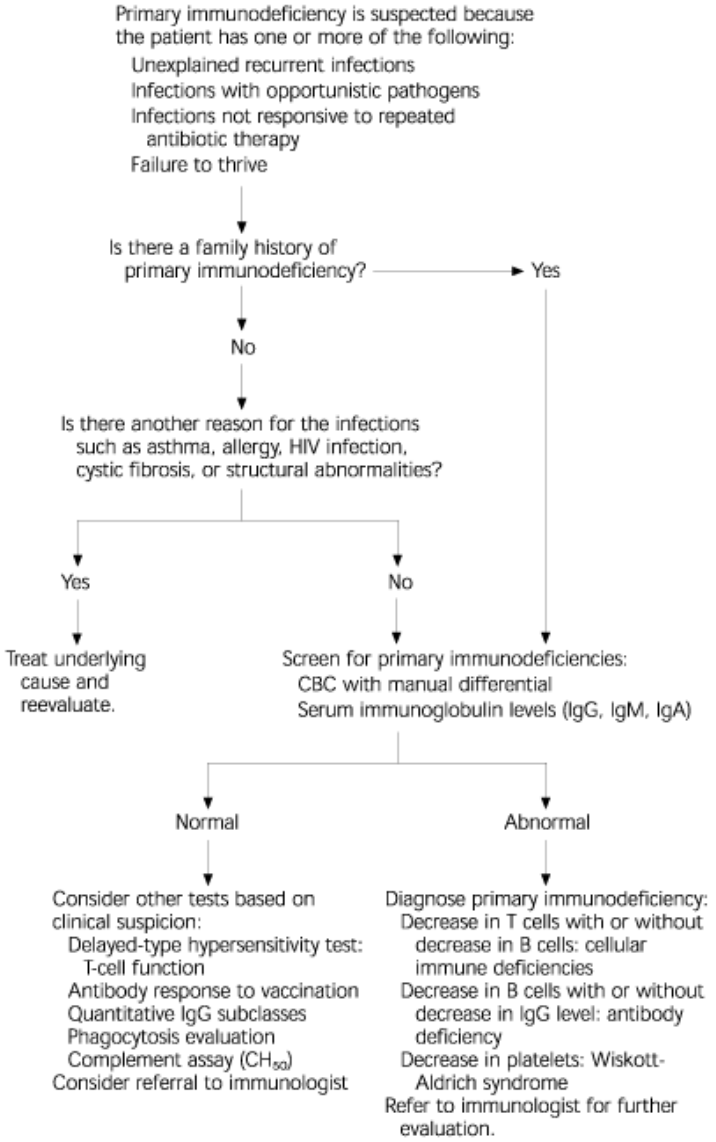
Evaluation for Suspected Primary Immunodeficiency



Primary Immunodeficiencies

MEGAN A. COOPER, PH.D., The Ohio State University College of Medicine and Public Health, Columbus, Ohio
THOMAS L. POMMERING, D.O., Grant Family Practice Residency, Columbus, Ohio
KATALIN KORÁNYI, M.D., Children's Hospital, Columbus, Ohio

Clinical Findings in the Major Subgroups of Primary Immunodeficiency Disorders

Subgroup	*Onset*	*Pattern of infection*	*Other features*
Disorders of humoral immunity (B-cell differentiation and antibody production)	After 6 months of age; can present in adulthood	Encapsulated bacteria: *Haemophilus influenzae*, pneumococci, streptococci Fungi and parasites: *Giardia lamblia*, Cryptosporidium species Virus: enterovirus (especially with X-linked agammaglobulinemia)	Recurrent infections: sinus infections, otitis media, bronchiectasis Chronic gastrointestinal tract problems, including malabsorption Autoimmunity Postvaccination paralytic polio (with live oral poliovirus vaccine)
T-cell and mixed disorders (combined B-cell and T-cell defects)	Before 6 months of age	Various opportunistic infections: Mycobacterium species, cytomegalovirus, Epstein-Barr virus, varicella virus, enterovirus, Candida species, *Pneumocystis carinii* (pneumonia)	Failure to thrive Oral thrush Graft-versus-host disease from maternal lymphocytes Excess diarrhea Postvaccination disseminated bacille Calmette-Guerin infection or paralytic polio
Phagocytic disorders	Infancy or childhood	Bacteria: *Staphylococcus aureus*, Pseudomonas species, Serratia species Klebsiella species Fungi and parasites: Candida species, Nocardia species, Aspergillus species	Unusually severe infections by common pathogens Granuloma formation, including granulomatous enteritis Poor wound healing Abscesses, skin infections Oral cavity infections Anorectal infections
Complement disorders	Any age	Neisseria infections, including meningococcal and gonococcal infections	Rheumatoid disorders Lupus-like syndrome Scleroderma

Cooper MA, Pommering TL, Korányi K. Primary immunodeficiencies. Am Fam Physician. 2003 Nov 15;68(10):2001-8. PMID: 14655810.

Selected Primary Immunodeficiency Disorders

Disorders (percentage of all primary immunodeficiencies)	*Genetic inheritance pattern*	*Incidence, if known*	*Sex affected*	*Age at diagnosis*
Disorders of humoral immunity: B-cell differentiation and antibody production (~ 50)				
Common variable immunodeficiency	Undetermined	One case per 10,000 to 50,000 persons	Both	>2 years; can be in 20s or 30s
Selective IgA deficiency	Undetermined	About one case per 300 to 700 persons	Both	>4 years
Bruton's or X-linked agammaglobulinemia	X-linked	Undetermined	Males	>6 months
T-cell defects and combined B-cell and T-cell defects (~ 30)				
Severe combined immunodeficiency	X-linked	One case per 100,000 to 500,000 persons	Males	<6 months
T-cell deficient, B-cell competent	Autosomal recessive		Both	<6 months
T-cell deficient, B-cell deficient	Autosomal recessive		Both	<6 months
DiGeorge syndrome	Autosomal dominant or spontaneous	Undetermined	Both	<6 months
Wiskott-Aldrich syndrome	X-linked	Undetermined	Males	<6 months
Ataxia-telangiectasia	Autosomal recessive	Undetermined	Both	>5 years
X-linked hyper IgM	X-linked	Undetermined	Males	Variable
Phagocytic disorders (~ 18)				
Chronic granulomatous disease	X-linked (70% of cases) or autosomal recessive (22% of cases)	One case per 200,000 persons	Males > females	Usually <5 years; diagnosis can be in 20s and 30s
Complement disorders (~ 2)				
Complement deficiencies (at least 16 distinct disorders)	Autosomal recessive, autosomal dominant, or X-linked	Undetermined	Both	Any age

Laboratory Testing for Primary Immunodeficiency Disorders

Laboratory test	*Screens for…*	*What to look for…*
Complete blood cell count with manual differential	T-cell, B-cell, and mixed B-cell and T-cell defects	Decreased numbers of T cells, B cells, or platelets
Delayed-type hypersensitivity skin test	T-cell defects	Negative result signaling possible impaired T-cell response*
Serum IgG, IgM, and IgA levels	Humoral immunodeficiencies	Decrease in any or all of the serum immunoglobulins
Antibody testing to specific antigens after vaccination	Humoral immunodeficiencies	Decreased or absent antibody response to vaccination†
Total hemolytic complement assay (CH_{50})	Complement deficiencies	Decreased or absent proteins if there is a deficiency in the classic pathway
Nitroblue tetrazolium test	Phagocytic disorders	Abnormal test result‡

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