ESID Registry – Working Definitions for Clinical Diagnosis of PID

These criteria are only for patients with **no genetic diagnosis***.
*Exceptions: Atypical SCID, DiGeorge syndrome – a known genetic defect and confirmation of criteria is mandatory.

Available entries (Please click on an entry to see the criteria.) **Page**

Disease and OMIM number for disease entry (examples)	IUIS category	OMIM number for disease-associated genes (examples)	ORPHA number for disease entry (examples)	HPO terms (examples)	Contributors	Clinical criteria for a probable diagnosis (= working definitions for clinical diagnosis classification)	Suggestions for alternative diagnosis (i.e., if the criteria are not completely fulfilled)
Acquired angioedema	9. Phenocopies of inborn errors of immunity		ORPHA:91385	Acquired angioedema	Sofia Grigoriadou, Matthew Buckland	At least one of the following - Recurrent angioedema without urticarial rash - History of predisposing disorder (e.g. autoimmune, lymphoreticular malignancy) **AND** No family history to suggest HAE or an alternative diagnosis **AND** Low complement C4 (< 2.S.D of the mean) between or during angioedema attacks **AND** absent C1 esterase protein or absent C1 esterase inhibitor function **AND** (Low C1q level **OR** anti-C1Q antibodies **OR** anti-C1E antibodies)	
Agammaglobulinemia 300310, 300755, 601495, 613500, 612692, 613501, 613502, 613506, 616941, 615214	3. Predominantly antibody deficiencies	300300, 147020, 146770, 112205, 147245, 604515, 171833, 147141, *608360*	ORPHA:33110 ORPHA:47	Agammaglobulinemia	Annarosa Soresina, Nizar Mahlaoui, Hans Ochs, Isabella Quinti	Fewer than 2% circulating B cells (CD19 and CD20), preferably in two separate determinations and a normal number of T cells (CD3, CD4 and CD8) **AND** serum IgG levels below: -200 mg/dl in infants aged < 12 months -500 mg/dl in children aged > 12 months **OR** normal IgG levels with IgA and IgM below 2SD **AND** onset of recurrent infections before 5 years of age	For patients with normal B cells and agammaglobulinaemia, please consider **"Unclassified antibody deficiency"**

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						OR positive maternal family history of agammaglobulinemia	
Asplenia syndrome (Ivemark syndrome) 208530	6. Defects in intrinsic and innate immunity	*602880*	ORPHA:97548	Asplenia syndrome (Ivemark syndrome)	Nizar Mahlaoui, David Edgar, Stephan Ehl, Capucine Picard, Jean-Laurent Casanova	Asplenia or hyposplenia **AND** Documentation of Howell-Jolly bodies on blood smears **AND** radiological findings evidencing asplenia (US, CT scan, scintigraphy) **AND** heterotaxia defects (dextrocardia, situs inversus, other…) or other heart and great vessel defects	
Ataxia telangiectasia (ATM) 208900	2. Combined immunodeficiencies with associated or syndromic features	607585	ORPHA:100	Ataxia telangiectasia (ATM)	Nizar Mahlaoui, David Edgar, Stephan Ehl, Richard Gatti, Dominique Stoppa-Lyonnet	Ataxia **AND at least two of the following :** • Oculocutaneous telangiectasia • Elevated alpha-fetoprotein (tenfold the upper limit of normal) • Lymphocyte A-T karyotype (translocation 7;14) • Cerebellum hypoplasia on MRI	
Atypical Severe Combined Immunodeficiency (Atypical SCID)	1. Immunodeficiencies affecting cellular and humoral immunity	*179615.0016*, *608958.0031*, *308380.0010*, *308380.0013*		Atypical SCID	Stephan Ehl, Alain Fischer	Mutation in a SCID-causing gene **AND** >100 T cells/µl **AND** Absence of characteristic SCID-associated infections (PCP, symptomatic CMV, persistent respiratory or gastrointestinal virus infection) ***in the first year of life*** **AND**	Combined immunodeficiency

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						Does not fulfil the criteria for Omenn syndrome	

Autoimmune lymphoproliferative syndrome (ALPS)
 	
601859, 603909, 607271, 616100, 615559, 614470
	4. Diseases of immune dysregulation	134637, 134638, 601762, 601763, 602457, *123890, 176977, 164790*	ORPHA:3261
			ORPHA:436159
			ORPHA:275517
				ALPS	David Edgar, Stephan Ehl, Frederic Rieux-Laucat, Benedicte Neven	**At least one of the following:**
						• splenomegaly
						• lymphadenopathy (>3 nodes, >3 months, non-infectious, non-malignant)
						• autoimmune cytopenia (>/= 2 lineages)
						• history of lymphoma
						• affected family member
						AND at least one of the following:
						• TCRab+CD3+CD4-CD8- of TCRab+CD3+ T cells > 6%
						• elevated biomarkers (at least 2 of the following):
						  • sFASL > 200pg/ml
						  • Vitamin B12 > 1500ng/L
						  • IL-10 > 20pg/ml
						  • Impaired FAS mediated apoptosis
							For patients with lymphoproliferation and/or autoimmunity who do not fulfil these criteria, please consider the following diagnoses:
							• CVID
							• Combined immunodeficiencies
							• Unclassified disorders of immune dysregulation

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APECED / APS1 with CMC - Autoimmune polyendocrinopathy candidiasis ectodermal dystrophy (APECED) 240300	4. Diseases of immune dysregulation	607358	ORPHA:3453	APECED / APS1 with CMC - Autoimmune polyendocrinopathy candidiasis ectodermal dystrophy (APECED)	Nizar Mahlaoui, Frank van de Veerdonk, Desa Lilic	**Look for at least 2 of the following:** • chronic mucocutaneous candidiasis (oral, oesophageal (difficulty swallowing) genital, skin, nails) – confirm with culture • autoimmune hypoparathyroidism / hypocalcemia • autoimmune adrenocortical failure (Addison's disease) • other autoimmune: hypergonadotropic hypogonadism, alopecia, vitiligo, autoimmune hepatitis, type 1 diabetes, gastrointestinal dysfunction • other: ectodermal dystrophy: dental enamel hypoplasia, nail dystrophy **Diagnostic tests (specific for APECED / APS1):** • organ-specific autoantibodies (parathyroid, adrenal, gonads, islet cell) • anti-cytokine autoantibodies (IFNα & ω and/or IL17A /IL17F/ IL22) [comment: sensitivity & specificity >95% (*Kisand et al, Eur J Immunol 2011*), can replace AIRE genotyping as >70 known mutations]	

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Barth syndrome 302060	5. Congenital defects of phagocyte number or function	300394	ORPHA:111	Barth syndrome	Nizar Mahlaoui, Jean Donadieu, Christoph Klein	Male **AND** Cardiac features (heart failure, dilated cardiomyopathy, left ventricular non-compaction, endocardial fibroelastosis, and serious disturbances of heart rhythm such as ventricular fibrillation or tachycardia) **AND** Chronic Neutropenia **AND at least one of the following** • Neuromuscular features such as skeletal myopathy, hypotonia, delayed motor milestones, exercise intolerance, and abnormal fatigability. • Distinctive facial gestalt (most evident in infancy) • Growth delay is common in childhood	

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Bloom syndrome 210900	2. Combined immunodeficiencies with associated or syndromic features	604610	ORPHA:125	Bloom syndrome	Markus Seidel, Beata Wolska, Corry Weemaes, Andy Gennery	Short stature **AND** • immunodeficiency (hypogammaglobulinemia, variably reduced lymphocyte proliferation, lower respiratory tract infections) • Cytogenetics: high sister-chromatid exchange rate, chromosomal breaks **AND at least one of the following** • Skin: photosensitivity, butterfly erythema, café-au-lait maculae • Head: microcephaly, dolichocephaly, prominent ears and nose • Hands: syndactyly, polydactyly, fifth finger clinodactyly • Malignoma: leukemia, lymphoma, adenocarcinoma, squamous cell carcinoma	
Cartilage hair hypoplasia (CHH) 250250	2. Combined immunodeficiencies with associated or syndromic features	157660	ORPHA:175	Cartilage hair hypoplasia (CHH)	Nizar Mahlaoui, Bobby Gaspar, Andrew Gennery	Short stature **AND** immunodeficiency (combined immunodeficiency (variable T and B cell lymphopenia), **AND AT LEAST one of the following:** • radiographical manifestations of CHH (metaphyseal chondrodysplasia,	

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						• light-coloured hypoplastic hair / fine silky hair • gastrointestinal malabsorption or Hirschsprung's , • hematological abnormalities (bone marrow dysplasia, pure red cell aplasia), • granulomatous inflammation (skin lesions,…), • EBV driven lymphoproliferative disease • Malignancies **AND** no sign of other immune-osseous dysplasia (Schimke disease)	
CD8 deficiency 608957	1. Immunodeficiencies affecting cellular and humoral immunity	186910	ORPHA:169085	CD8 deficiency	Nizar Mahlaoui, Matthew Buckland, Sofia Grigoriadou	**CD8+ cells:** less than 350/µl if age less than 2 years less than 250/µl if age betweeen 2 and 4 years less than 150/µl if age greater than 4 years **AND** Recurrent and/or severe infections **AND** Normal or increased CD4, CD19 and CD56 **AND** normal class HLA-class 1 expression **AND** Other primary causes of lymphopenia excluded	

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Chronic mucocutaneous candidiasis (CMC)	9. Phenocopies of inborn errors of immunity	607358	ORPHA:1334	Chronic mucocutaneous candidiasis (CMC)	Nizar Mahlaoui, Frank van de Veerdonk, Desa Lilic	**Look for:** • chronic, persistent or recurrent non-invasive mucocutaneous Candida or dermatophyte infections (oral, esophageal (difficulty swallowing, esophageal cancer) genital, skin, nails) – confirm with culture • other infections: skin (boils, abscesses, eczema, rosacea) lungs (chest infections, bronchiectasis) eyes (stye, blepharitis, conjunctivitis) • autoimmunity: hypothyroidism, vitiligo, alopecia, autoimmune hepatitis • vasculopathy (intracranial aneurisms, brain vascular anomalies) • family history / early age of onset **Exclude secondary causes:** • predisposing conditions: HIV, diabetes, iron deficiency, neutropenia, dentures	

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						• predisposing treatments: antibiotics, immunosuppressive drugs, inhaled steroids, PPIs • exclude isolated recurrent vulvo-vaginal candidiasis (RVVC) [Comment: Informative tests (where available): i. Th-17 & Th-22 cells and production ii. Low CD4 and B cell counts (combined immune deficiency) iii. Low iron]	
Complement component 1q deficiency (C1q deficiency) 613652	8. Complement deficiencies	120550, 120570, 120575	ORPHA:169147	Complement component 1q deficiency	Matthew Buckland, Ania Manson, Sofia Grigoriadou	**At least one of the following;** • Increased susceptibility to infections with encapsulated organisms • SLE like syndrome • Family history of symptomatic C1q deficiency **AND** CH50/CH100 activity less than 10% of control value with normal AP50/AP100 activity	
Complement component 1r deficiency (C1r deficiency)	8. Complement deficiencies	613785	ORPHA:169147	Complement component 1r deficiency	Matthew Buckland, Ania Manson, Sofia Grigoriadou	**At least one of the following;** • Increased susceptibility to infections with encapsulated organisms • SLE like syndrome • Ehler's Danlos Phenotype	

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216950						• Family history of symptomatic C1r deficiency **AND** CH50/CH100 activity less than 10% of control value with normal AP50/AP100 activity	
Complement component 1s deficiency (C1s deficiency) 613783	8. Complement deficiencies	120580	ORPHA:169147	Complement component 1s deficiency	Matthew Buckland, Ania Manson, Sofia Grigoriadou	**At least one of the following;** • Increased susceptibility to infections with encapsulated organisms • SLE like syndrome • Multiple autoimmune diseases • Ehler's Danlos Phenotype • Family history of symptomatic C1s deficiency **AND** CH50/CH100 activity less than 10% of control value with normal AP50/AP100 activity	
Complement component 2 deficiency 217000	8. Complement deficiencies	*613927*	ORPHA:169147	Complement component 2 deficiency	Matthew Buckland, Ania Manson, Sofia Grigoriadou	**At least one of the following;** • Increased susceptibility to infections (recurrent pyogenic) • Discoid lupus • SLE • Family history of symptomatic C2 Deficiency **AND** CH50 or CH100 activity less than 10% of control activity **AND**	

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						Absent C2 with normal C3 and C4 complement levels	
Complement component 3 deficiency (C3) 613779	8. Complement deficiencies	120700	ORPHA:280133	Complement component 3 deficiency (C3)	Matthew Buckland, Ania Manson, Sofia Grigoriadou	**At least one of the following;** • Increased susceptibility to infections (Neisseria or streptococcal) • Glomerulonephritis • Family history of symptomatic C3 Deficiency **AND** CH50/CH100 and AP50/AP100 less than 10% of control activity **AND** Absent immunochemical C3 with normal Factor H and I levels	
Complement component 4 deficiency (C4A, C4B) 614380, 614379	8. Complement deficiencies	120810, *120820*	ORPHA:169147	Complement component 4 deficiency (C4A, C4B)	Matthew Buckland, Ania Manson, Sofia Grigoriadou	**At least one of the following;** • Increased susceptibility to infections (Neisserial) • Family history of recurrent Neisserial disease **AND** CH50 (or CH100) and AP50 (or AP100) activity less than 5% of control activity **AND** Low immunochemical C4 protein or reduced bactericidal activity	

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Complement component 5 deficiency 609536	8. Complement deficiencies	120900	ORPHA:169150	Complement component 5 deficiency	Matthew Buckland, Ania Manson, Sofia Grigoriadou	**At least one of the following;** • Increased susceptibility to infections (Neisserial) • Family history of recurrent Neisserial disease **AND** CH50 (or CH100) and AP50 (or AP100) activity less than 5% of control activity **AND** Low immunochemical C5 protein or reduced bactericidal activity	
Complement component 6 deficiency 612446	8. Complement deficiencies	217050	ORPHA:169150	Complement component 6 deficiency	Matthew Buckland, Ania Manson, Sofia Grigoriadou	**At least one of the following;** • Increased susceptibility to infections (Neisserial) • Family history of recurrent Neisserial disease **AND** CH50 (or CH100) and AP50 (or AP100) activity less than 5% of control activity **AND** Low immunochemical C6 protein or reduced bactericidal activity	
Complement component 7 deficiency 610102	8. Complement deficiencies	217070	ORPHA:169150	Complement component 7 deficiency	Matthew Buckland, Ania Manson, Sofia Grigoriadou	**At least one of the following;** • Increased susceptibility to infections (Neisserial) • Family history of recurrent Neisserial disease **AND**	

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						CH50 (or CH100) and AP50 (or AP100) activity less than 5% of control activity **AND** Low immunochemical C7 protein or reduced bactericidal activity	
Complement component 8 deficiency (C8A, C8B, C8G) 613790, 613789	8. Complement deficiencies	120950, 120960, 120930	ORPHA:169150	Complement component 8 deficiency (C8A, C8B, C8G)	Matthew Buckland, Ania Manson, Sofia Grigoriadou	**At least one of the following;** • Increased susceptibility to infections (Neisserial) • Family history of recurrent Neisserial disease **AND** CH50 (or CH100) and AP50 (or AP100) activity less than 5% of control activity **AND** Low immunochemical C8 protein or reduced bactericidal activity	
Complement component 9 deficiency 613825	8. Complement deficiencies	120940	ORPHA:169150	Complement component 9 deficiency	Matthew Buckland, Ania Manson, Sofia Grigoriadou	**At least one of the following;** • Increased susceptibility to infections (Neisserial) • Family history of recurrent Neisserial disease **AND** CH50 (or CH100) and AP50 (or AP100) activity less than 5% of control activity **AND** Absent immunochemical C9 protein or reduced bactericidal activity	

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CSR defects and HIGM syndrome 608106, 605258, 608184	3. Predominantly antibody deficiencies	600678, *191525*, *605257*		CSR defects and HIGM syndrome	Stephan Ehl, Anne Durandy, Teresa Espanol	**At least one of the following:** • increased susceptibility to infections (recurrent and/or opportunistic, including cryptosporidium) • immune dysregulation (autoimmunity, lymphoproliferation, sclerosing cholangitis) • cytopenia (neutropenia or autoimmune) • malignancy (lymphoma) • affected family member **AND** marked decrease of IgG (measured at least twice) **AND** normal or elevated IgM (measured at least twice) **AND** defined causes of hypogammaglobulinemia have been excluded **AND** no evidence of profound T-cell deficiency, defined as 2/3 of the following (mo=month, y=year of life): • CD4 numbers/microliter: 0-6mo <1000, 6mo-1y <800, 1-2y <500, 2-6y <300, 6-12y <250, >12y <200 • % naive CD4: 0-2y <30%, 2-6y <25%, 6-16y <20%, >16y 10% • T cell proliferation absent	

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						AND no evidence of Ataxia telangiectasia (cafe-au lait spots, ataxia, telangiectasia, raised AFP)	
Chediak Higashi syndrome (CHS) 214500	4. Diseases of immune dysregulation	606897	ORPHA:167	Chediak Higashi syndrome (CHS)	Nizar Mahlaoui, David Edgar, Stephan Ehl, Genevieve de Saint Basile, Despina Moshous	**At least one of:** • recurrent bacterial infections • episode of hemophagocytic lymphohistiocytosis (HLH) • Neutropenia • reduced lymphocyte degranulation/cytotoxicity • affected family member **AND one of:** • Typical hair shaft abnormalities • Presence of intracytoplasmic typical giant granules on blood or bone marrow smears	Immunodeficiency with partial albinism
Chronic granulomatous disease (CGD) 306400, 233700, 233690, 233710, 613960	5. Congenital defects of phagocyte number or function	300481, 608508, 608512, 608515, 601488	ORPHA:379	Chronic granulomatous disease (CGD)	Maria Kanariou, Reinhard Seger	**At least one of the following:** • deep seated infection due to bacteria and/or fungi (abscesses, osteomyelitis, lymphadenitis) • recurrent pneumonia • lymphadenopathy and/or hepatomegaly and/or splenomegaly • obstructing/diffuse granulomata (gastrointestinal or urogenital tract) • chronic inflammatory manifestations (colitis, liver abscess and fistula formation)	

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						• failure to thrive • affected family member **AND** absent/significantly decreased respiratory burst (NBT or DHR, measured at least twice)	
Clericuzio-type poikiloderma with neutropenia syndrome 604173	5. Congenital defects of phagocyte number or function	613276	ORPHA:221046	Clericuzio-type poikiloderma with neutropenia syndrome	Nizar Mahlaoui, Jean Donadieu, Christoph Klein	Chronic neutropenia, **AND** Poikiloderma, **AND** Recurrent infections, **AND** Pachyonychia, **OR** Palmo-plantar hyperkeratosis	
COHEN syndrome 216550	5. Congenital defects of phagocyte number or function	607817	ORPHA:193	COHEN syndrome	Nizar Mahlaoui, Jean Donadieu, Christoph Klein	Chronic neutropenia. **AND at least 2 of the followings:** • intellectual deficiency (ID), • microcephaly, • facial dysmorphism, • slender extremities, • obesity, • progressive chorioretinal dystrophy	

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Combined immunodeficiency (CID) 616433, 615607, 615897, 312863, 615468, 614172, 616098, 616740, 618131, 233600	1. Immunodeficiencies affecting cellular and humoral immunity	603122, 300386, 109535, 186740, 186910, 176947, 170260, 170261, 601962, 109700, 600005, 603200, 601863, 601861, 602037, 604655, 604758, *300715*, *153390*, *604011*, *611432*, *604965*, *309845*, *186880*, *606558*, *600315*, *602354*, *607210*, *603517*, *603258*,	ORPHA:169082 ORPHA:169090 ORPHA:217390 ORPHA:505227 ORPHA:357329 ORPHA:445018 ORPHA:397964 ORPHA:504530 ORPHA:317428 ORPHA:431149 ORPHA:317430 ORPHA:314689 ORPHA:476113 ORPHA:911 ORPHA:231154		Stephan Ehl, Maria Kanariou, Alain Fischer	**At least one of:** • at least one severe infection (requiring hospitalization) • one manifestation of immune dysregulation (autoimmunity, IBD, severe eczema, lymphoproliferation, granuloma) • malignancy • affected family member **AND** 2 of 4 T cell criteria fulfilled: • reduced CD3 or CD4 or CD8 T cells (using age-related reference values) • reduced naïve CD4 and/or CD8 T cells • elevated g/d T cells • reduced proliferation to mitogen or TCR stimulation **AND** HIV excluded **AND** exclusion of a clinical diagnosis associated with CID (e.g., defined syndromic diseases, DKC, AT, CHH)	

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		190010, *605383*, *604860*, *308380*					
Common variable immunodeficiency disorders (CVID) 607594, 240500, 613493, 613494, 613495, 613496, 614699, 614700, 615577, 615767, 616576, 616873, 617765	3. Predominantly antibody deficiencies	*604558*, *604907*, *107265*, *606269*, *112210*, *186845*, *120650*, *606453*, *164012*, *605384*, *164011*, *603023*, *615332*	ORPHA:1572	Common variable immunodeficiency disorders (CVID)	Vojtech Thon, Natalia Martinez, Maria Kanariou, Klaus Warnatz, Isabella Quinti, Helen Chapel	**At least one of the following:** • increased susceptibility to infection • autoimmune manifestations • granulomatous disease • unexplained polyclonal lymphoproliferation • affected family member with antibody deficiency **AND** marked decrease of IgG and marked decrease of IgA with or without low IgM levels (measured at least twice; <2SD of the normal levels for their age); **AND** at least one of the following: • poor antibody response to vaccines (and/or absent isohemagglutinins); i.e., absence of protective levels despite vaccination where defined • low switched memory B cells (<70% of age-related normal value) **AND** secondary causes of hypogammaglobulinemia have been excluded (e.g., infection, protein loss, medication, malignancy)	For patients <4 years old or patients with incomplete criteria please consider "**Unclassified antibody deficiency"**. For patients with evidence of profound T-cell deficiency, please consider **Combined immunodeficiencies**.

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						AND diagnosis is established after the 4th year of life (but symptoms may be present before) **AND** no evidence of profound T-cell deficiency, defined as 2 out of the following (y=years of life): • CD4 numbers/microliter: 2-6y <300, 6-12y <250, >12y <200 • % naive of CD4: 2-6y <25%, 6-16y <20%, >16y <10% T cell proliferation absent	
Congenital neutropenia 202700, 613107, 610738, 612541, 615285, 616022, 617014, 300392	5. Congenital defects of phagocyte number or function	130130, 600871, 605998, 611045, 610035, 602671, 300392, 610389, *604592*, *138971*, *146928*, *616012*	ORPHA:486 ORPHA:439849 ORPHA:420702 ORPHA:420699 ORPHA:331176 ORPHA:423384 ORPHA:99749 ORPHA:42738 ORPHA:86788	Congenital neutropenia	Nizar Mahlaoui, Jean Donadieu	Neutropenia below 0.5 g/L measured on at least 3 occasions **OR** Neutropenia below 1 g/L measured on at least 3 occasions with at least one of the following: • deep seated infection due to bacteria and/or fungi • recurrent pneumonia • buccal and/or genital aphtous lesions or ulcerations • omphalitis • affected family member **AND e**xclusion of secondary causes of neutropenia	For other patients with chronic neutropenia, please consider **Unclassified phagocytic disorders**.

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Cyclic neutropenia 162800	5. Congenital defects of phagocyte number or function	130130	ORPHA:2686	Cyclic neutropenia	Nizar Mahlaoui, David Edgar, Stephan Ehl, Jean Donadieu	Cyclic fluctuation of Neutrophil counts (every 16 to 28 days) During these neutropenic episodes, symptoms are **at least one of the following**: • Increased susceptibility to infections • Oral aphthae • Abdominal pain episodes	
Defects of TLR/NFkappa-B signaling 610799, 607676, 300640, 300584, 300636, 300301, 618204, 615592, 612132	6. Defects in intrinsic and innate immunity; *OR* categories 2, 3, 7.	*602170*, *606883*, *300248*, *603258*, *164008*, *603029*, *608204*, *601896*, *604834*	ORPHA:70592 ORPHA:69088 ORPHA:98813	Defects of TLR/NFkappa-B signaling	Nizar Mahlaoui, Capucine Picard, Jacinta Bustamante	Recurrent and/or severe infections **AND at least 2 of the following:** • normal T- and B-cell responses • mild inflammatory reaction • polysaccharide-specific serum antibodies deficiency • anhidrotic ectodermal dysplasia features in some patients	
Defects with susceptibility to mycobacterial infection (MSMD) 614891, 614890, 209950, 615978, 614889, 614892,	6. Defects in intrinsic and innate immunity	601604, 161561, 107470, 147569, 600555, 300481, 601565, 176941, 147571,	ORPHA:748 ORPHA:319552 ORPHA:319558 ORPHA:319569 ORPHA:99898 ORPHA:319581 ORPHA:319574 ORPHA:319547 ORPHA:319595 ORPHA:319605		Nizar Mahlaoui, Capucine Picard, Jacinta Bustamante	Infections caused by weakly virulent mycobacteria, such as BCG vaccines and environmental mycobacteria, tuberculosis, salmonellosis, candidiasis, other intramacrophagic bacteria, fungi, or parasites, **AND** Altered IFN-γ mediated immunity tests or Altered IL-12 mediated immunity tests **AND**	

Disease and OMIM number for disease entry (examples)	IUIS category	OMIM number for disease-associated genes (examples)	ORPHA number for disease entry (examples)	HPO terms (examples)	Contributors	Clinical criteria for a probable diagnosis (= working definitions for clinical diagnosis classification)	Suggestions for alternative diagnosis (i.e., if the criteria are not completely fulfilled)
613796, 300645, 614893, 611521, 616126, 616622		602943, 147795,	ORPHA:319623 ORPHA:319600 ORPHA:319563 ORPHA:477857 ORPHA:319543 ORPHA:319589 ORPHA:319535 ORPHA:319539 ORPHA:319612			no IFN-γ auto-antibodies	
Deficiency of specific IgG (Specific antibody deficiency - SPAD)	3. Predominantly antibody deficiencies	102582	ORPHA:169443		Nizar Mahlaoui, David Edgar, Stephan Ehl, Helen Chapel, Isabella Quinti, Esther de Vries	Infections (recurrent or severe bacterial) **AND** normal serum/plasma IgG, A and M and IgG subclass levels **AND** Profound alteration of the antibody responses to *S.* pneumoniae (or other polysaccharide vaccine) either after documented invasive infection or after test immunization. **AND** Exclusion of T cell defect	**Unclassified antibody deficiencies**
DiGeorge syndrome 188400	2. Combined immunodeficiencies with associated or syndromic features	602054, *602269*, *138720*, *116790*, *600237*, *601754*	ORPHA:567	DiGeorge syndrome	Nizar Mahlaoui, David Edgar, Stephan Ehl	Documented microdeletion 22q11 or 10p **AND** signs of immunodeficiency, i.e. infections (recurrent or severe bacterial) and/or immune dysregulation	

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Dyskeratosis congenital 305000, 127550, 613989, 613990, 615190, 616553, 613987, 224230, 613988, 616353	2. Combined immunodeficiencies with associated or syndromic features	300126, *612661*, *604319*, *187270*, *602322*, *608833*, *604212*, *606471*, *606470*, *609377*	ORPHA:1775	Dyskeratosis congenita	Nizar Mahlaoui, David Edgar, Stephan Ehl, Inderjeet Dokal	**At least two of the following:** • Skin pigmentation abnormalities • Nail dystrophy • Mucosal leucoplakia • Bone marrow failure **AND** Very short telomeres	
Early-onset inflammatory bowel disease 615767, 613148, 612567	Categories 1, 4, 7.	*605384*, *124092*, *146933*, *123889*	ORPHA:477661 ORPHA:238569	Early-onset inflammatory bowel disease	Joris van Montfrans, Christoph Klein, Nicolette Moes	Histologically proven inflammatory bowel disease (IBD) diagnosed with an onset at pediatric age. The following differentiation in age of onset applies (Uhlig et al Gastroenterologie 2014, PMID 25058236): - Infant Onset IBD: onset < 0-2 yrs - Neonatal onset IBD: onset < 28 days **AND** exclusion of infectious cause (bacterial, viral, parasitic) **AND at least one of the following:** • Failure to thrive • Increased values of calprotectine in stool	

Disease and OMIM number for disease entry (examples)	IUIS category	OMIM number for disease-associated genes (examples)	ORPHA number for disease entry (examples)	HPO terms (examples)	Contributors	Clinical criteria for a probable diagnosis (= working definitions for clinical diagnosis classification)	Suggestions for alternative diagnosis (i.e., if the criteria are not completely fulfilled)
Early-onset multi-organ autoimmune disease 615952, 617006, 613385	Categories 1, 4, 7.	*102582*, *176947*, *606409*	ORPHA:438159 ORPHA:228426	Early-onset multi-organ autoimmune disease	Joris van Montfrans, Andrew Cant, Mario Abinun	This disease is featured by a variable set of presenting symptoms. These presenting symptoms may be "ALPS like" or "IPEX like". **At least:** The onset of at least 2 separate auto immune diseases <18 yrs (such as: autoimmune cytopenias, IDDM, autoimmune thyroiditis, or organ specific autoimmunity including lung-, gastrointestinal-, hepatic- autoimmune disease, and/or other endocrine dysfunction) **AND at least one of the following:** • Lymphadenopathy > 6 months in >1 region • Hepatosplenomegaly • Recurrent viral infections / reactivations such as mollusca and zoster reactivations • Skin features (eczema or vasculopathy) • Auto immune arthritis	
Epidermodysplasia verruciformis 226400, 618231, 305350	6. Defects in intrinsic and innate immunity	605828, 605829, 162643	ORPHA:302	Epidermodysplasia verruciformis	Joris van Montfrans, Jean-Laurent Casanova, Capucine Picard	Extensive flat wart-like papules, usually on extremities, trunk or neck **AND at least one of the following:** • pityriasis versicolor-like macules on skin	

Disease and OMIM number for disease entry (examples)	IUIS category	OMIM number for disease-associated genes (examples)	ORPHA number for disease entry (examples)	HPO terms (examples)	Contributors	Clinical criteria for a probable diagnosis (= working definitions for clinical diagnosis classification)	Suggestions for alternative diagnosis (i.e., if the criteria are not completely fulfilled)
						• development of cutaneous carcinomas	
Factor B Deficiency 615561	8. Complement deficiencies	138470		Factor B Deficiency	Matthew Buckland, Ania Manson, Sofia Grigoriadou	**At least one of the following;** • Increased susceptibility to infections (recurrent pyogenic including Neisseria) • Family History of symptomatic Factor B Deficiency **AND** AP50/AP100 activity less than 10% of control value with normal CH50/CH100 activity **Or** Absent Factor B activity in serum in functional or immunochemical assessment	
Factor D deficiency 613912	8. Complement deficiencies	134350	ORPHA:169467	Factor D deficiency	Matthew Buckland, Ania Manson, Sofia Grigoriadou	**At least one of the following;** • Increased susceptibility to infections (recurrent pyogenic including Neisseria) • Family History of symptomatic Factor D Deficiency **AND** AP50/AP100 activity less than 10% of control value with normal CH50/CH100 activity **Or** Absent Factor D activity in serum in functional or immunochemical assessment	

Disease and OMIM number for disease entry (examples)	IUIS category	OMIM number for disease-associated genes (examples)	ORPHA number for disease entry (examples)	HPO terms (examples)	Contributors	Clinical criteria for a probable diagnosis (= working definitions for clinical diagnosis classification)	Suggestions for alternative diagnosis (i.e., if the criteria are not completely fulfilled)
Factor H Deficiency 609814	8. Complement deficiencies	134370	ORPHA:200421	Factor H deficiency	Matthew Buckland, Ania Manson, Sofia Grigoriadou	**At least one of the following;** • Increased susceptibility to infections (recurrent pyogenic including Neisseria) • Family History of symptomatic Factor H Deficiency (Recessive or Dominant Inheritance) • Pre-eclampsia **AND** Reduced serum C3 (due to spontaneous activation) **AND/OR** Reduced AP50/AP100 and CH50/CH100 due to reduced serum C3 **Or** Absent Factor H by immunochemical assessment	
Factor H Related Protein Deficiency 235400, 614809	8. Complement deficiencies	134371, 600889, 605336, 605337, 608593		Factor H Related Protein Deficiency	Matthew Buckland, Ania Manson, Sofia Grigoriadou	**At least one of the following;** • Increased susceptibility to infections (recurrent pyogenic including Neisseria) • Family History of symptomatic Factor H Deficiency (Recessive or Dominant Inheritance) **AND/OR** Normal AP50/AP100 and CH50/CH100 **And** Antibodies to Factor H	
Factor I Deficiency 610984	8. Complement deficiencies	217030	ORPHA:200418	Factor I deficiency	Matthew Buckland, Ania	**At least one of the following;** • Increased susceptibility to infections (recurrent pyogenic including Neisseria)	

Disease and OMIM number for disease entry (examples)	IUIS category	OMIM number for disease-associated genes (examples)	ORPHA number for disease entry (examples)	HPO terms (examples)	Contributors	Clinical criteria for a probable diagnosis (= working definitions for clinical diagnosis classification)	Suggestions for alternative diagnosis (i.e., if the criteria are not completely fulfilled)
					Manson, Sofia Grigoriadou	• Family History of symptomatic Factor I Deficiency (Recessive or Dominant Inheritance) • Pre-eclampsia **AND** Reduced serum C3 (due to spontaneous activation) **AND/OR** Reduced AP50/AP100 and CH50/CH100 due to reduced serum C3 **Or** Absent Factor I by immunochemical assessment	
Ficolin 3 Deficiency (FC3RN) 613860	8. Complement deficiencies	604973	ORPHA:331190	Ficolin 3 deficiency	Matthew Buckland, Ania Manson, Sofia Grigoriadou	**At least one of the following;** • Increased susceptibility to infections • Glomerulonephritis • Multiple Abscesses **AND** Absent Ficollin dependent complement activation **AND/OR** Absent FC3RN	
Familial hemophagocytic lymphohistiocytosis syndromes (FHLH)	4. Diseases of immune dysregulation	170280, 608897, 605014, 601717, 610884,	ORPHA:540	Familial hemophagocytic lymphohistiocytosis syndromes (FHLH)	Stephan Ehl, Genevieve de Saint Basile, Gritta Janka	**At least one of the following:** • at least 1 episode of HLH (at least 5/8 criteria as defined by the Histiocyte Society) • affected family member **AND at least one of the following:**	For patients with incomplete criteria, please consider **Unclassified disorders of**

Disease and OMIM number for disease entry (examples)	IUIS category	OMIM number for disease-associated genes (examples)	ORPHA number for disease entry (examples)	HPO terms (examples)	Contributors	Clinical criteria for a probable diagnosis (= working definitions for clinical diagnosis classification)	Suggestions for alternative diagnosis (i.e., if the criteria are not completely fulfilled)
267700, 603553, 608898, 603552, 613101						• recurrent disease (>4 weeks after initiating treatment for first episode) • persistent disease (no full remission can be achieved) • partial albinism • absent or significantly decreased Perforin expression in flow cytometry • at least one assay with absent degranulation (NK or CTL) or two assays with reduced degranulation • at least 2 assays with absent NK cell cytotoxicity	**immune dysregulation**.
FOXP3 deficiency (IPEX) 304790	4. diseases of immune dysregulation	300292	ORPHA:37042	FOXP3 deficiency (IPEX)	Nizar Mahlaoui, David Edgar, Stephan Ehl, Hans Ochs, Benedicte Neven	**At least one of** • Severe and protracted enteropathy with villous atrophy in a male infant • Severe, often multiple endocrinopathies **AND** Exclusion of hypogammaglobulinaemia **AND at least one of the following:** • Low or absent Foxp3 expression by CD4+CD25+ on flow analysis • No overt T cell defect (proliferations are normal) • Elevated IgA and IgE levels • Normal CD25 expression	Combined immunodeficiency

Disease and OMIM number for disease entry (examples)	IUIS category	OMIM number for disease-associated genes (examples)	ORPHA number for disease entry (examples)	HPO terms (examples)	Contributors	Clinical criteria for a probable diagnosis (= working definitions for clinical diagnosis classification)	Suggestions for alternative diagnosis (i.e., if the criteria are not completely fulfilled)
Glycogen storage disease type 1b (GS1b) 232220	5. Congenital defects of phagocyte number or function	602671	ORPHA:79259	Glycogen storage disease type 1b (GS1b)	Nizar Mahlaoui, David Edgar, Stephan Ehl, Jean Donadieu	Recurrent infections **AND** Fasting intolerance **AND** Hypoglycaemic attacks **AND** Hyperlactacidemia **AND** Glycogen accumulation in the liver **AND** colitis mimicking Crohn's disease **AND one of:** • neutrophil function alterations • neutropenia	
Griscelli syndrome type 2 607624	4. Diseases of immune dysregulation	603868	ORPHA:79477	Griscelli syndrome type 2	Nizar Mahlaoui, David Edgar, Stephan Ehl, Genevieve de Saint Basile, Despina Moshous	**At least one of the following:** • episode of hemophagocytic lymphohistiocytosis (HLH) • reduced lymphocyte degranulation/cytotoxicity • affected family member **AND** Typical hair shaft abnormalities **AND** Absence of giant granules on blood smear	Immunodeficiency with partial albinism

Disease and OMIM number for disease entry (examples)	IUIS category	OMIM number for disease-associated genes (examples)	ORPHA number for disease entry (examples)	HPO terms (examples)	Contributors	Clinical criteria for a probable diagnosis (= working definitions for clinical diagnosis classification)	Suggestions for alternative diagnosis (i.e., if the criteria are not completely fulfilled)
Hereditary Angioedema (C1inh) 106100, 610618	8. Complement deficiencies	606860, 610619	ORPHA:100050 ORPHA:100051 ORPHA:91378	Hereditary angioedema	Matthew Buckland, Ania Manson, Sofia Grigoriadou	**At least one of the following;** • Recurrent angioedema without urticaria • Recurrent abdominal pain and vomiting • Laryngeal oedema • Family history of angioedema **AND** Low complement C4 (< 2.S.D of the mean) between or during angioedema attacks **AND** Absent C1 esterase protein (Type 1 HAE) or absent C1 esterase inhibitor function (Type 2 HAE) **AND** Normal C1q level	
Herpetic encephalitis (HSE) 613002, 610551, 614849, 614850, 617900, 616532, 608033	6. Defects in intrinsic and innate immunity	603029, 608204, 601896, 607601, 604834, 603734, *601181*, *600650*	ORPHA:1930	Herpetic encephalitis (HSE)	Nizar Mahlaoui, Jean-Laurent Casanova, Isabelle Meyts, Shen-Yin Zhang	Sporadic Herpes Simplex virus 1 (HSV-2 are excluded) encephalitis in otherwise healthy individuals, wide spectrum of clinical features ranging from necrosis of brain tissue (of the forebrain in 95%, of the brainstem in 5%), fever, altered behavior and disturbed consciousness, with brain image data suggesting brain lesions, and with **at least one of the four following virological criteria fulfilled:** 1) HSV-1 PCR positive in CSF, OR 2) HSV-1 antigen positive in CSF OR,	

Disease and OMIM number for disease entry (examples)	IUIS category	OMIM number for disease-associated genes (examples)	ORPHA number for disease entry (examples)	HPO terms (examples)	Contributors	Clinical criteria for a probable diagnosis (= working definitions for clinical diagnosis classification)	Suggestions for alternative diagnosis (i.e., if the criteria are not completely fulfilled)
						3) anti-HSV-1 antibodies in CSF, OR **4)** sero-conversion of anti-HSV-1 antibodies in blood.	
Hermansky-Pudlak syndrome (type 2) 608233	4. Diseases of immune dysregulation	603401	ORPHA:183678	Hermansky-Pudlak syndrome (type 2)	Nizar Mahlaoui, Stephan Ehl	Oculocutaneous albinism **AND** Chronic neutropenia **AND at least one of the following:** • bleeding diathesis • recurrent infections • hemophagocytic lymphohistiocytosis (HLH) **AND** Defective cytotoxicity caused by impaired degranulation	
HLA class I deficiency 604571	1. Immunodeficiencies affecting cellular and humoral immunity	170260, 170261, 601962, 109700	ORPHA:34592	HLA class I deficiency	Matthew Buckland, Ania Manson, Sofia Grigoriadou	**At least one of the following:** • Predisposition to recurrent and/or opportunistic infections • Granulomatous skin lesions **AND at least one of the following:** • Predisposition to recurrent and/or opportunistic infections • Necrotizing granulomatous skin lesions • Low T-CD8 or lymphopenia • Absence of Ab production in response to antigens • Absence of T cell proliferation in response to antigens	

Disease and OMIM number for disease entry (examples)	IUIS category	OMIM number for disease-associated genes (examples)	ORPHA number for disease entry (examples)	HPO terms (examples)	Contributors	Clinical criteria for a probable diagnosis (= working definitions for clinical diagnosis classification)	Suggestions for alternative diagnosis (i.e., if the criteria are not completely fulfilled)
						AND Reduced or absent HLA A,B,C expression at the surface of resting and PHA/Cytokine activated T-cells	
HLA class II deficiency (MHC2) 209920	1. Immunodeficiencies affecting cellular and humoral immunity	600005, 603200, 601863, 601861	ORPHA:572	HLA class II deficiency (MHC2)	Nizar Mahlaoui, David Edgar, Stephan Ehl, Capucine Picard, Amos Etzioni	**One of the following:** • Recurrent and/or opportunistic infections • Autoimmunity **AND one of the following:** • Hypogammaglobulinaemia • Lymphopenia • Low T-CD4 count • absence of Ab production in response to antigens or absence of T cell proliferations in response to antigens **AND** Reduced or absent HLA DR expression at the surface of B cells and/or monocytes	Combined immunodeficiency
Hoyeraal-Hreidarsson syndrome 305000	2. Combined immunodeficiencies with associated or syndromic features	300126, *609377*, *604212*, *608833*, *187270*, *604319*	ORPHA:3322	Hoyeraal-Hreidarsson syndrome	Nizar Mahlaoui, David Edgar, Stephan Ehl, Inderjeet Dokal	**At least four of the following criteria:** • Microcephaly and/or neurocognitive impairment • Cerebellar hypoplasia • Bone marrow failure • Immune deficiency including B cell lymphopenia • Severe enteropathy • Severe failure to thrive This can be substantiated by undertaking telomere length analysis (usually very short)	

Disease and OMIM number for disease entry (examples)	IUIS category	OMIM number for disease-associated genes (examples)	ORPHA number for disease entry (examples)	HPO terms (examples)	Contributors	Clinical criteria for a probable diagnosis (= working definitions for clinical diagnosis classification)	Suggestions for alternative diagnosis (i.e., if the criteria are not completely fulfilled)
Hyper IgE syndrome (HIES) 147060, 243700, 611521	2. Combined immunodeficiencies with associated or syndromic features	102582, *611432*, *176941*	ORPHA:2314 ORPHA:331223	Hyper IgE syndrome (HIES)	Beata Wolska, David Edgar, Bodo Grimbacher, Steven Holland	IgE > 10 times the norm for age **AND** pathologic susceptibility to infectious diseases **AND** no evidence of T-cell deficiency (low T cell numbers, low naive T cells, reduced proliferation) **AND** no evidence of B cell deficiency (low B cell numbers, hypogammaglobulinaemia)	For patients with evidence of T-cell deficiency, please consider: **Combined immunodeficiencies**. For patients with evidence of B-cell deficiency, please consider **Unclassified antibody deficiency**. For other patients, please consider **Unclassified immunodeficiencies**.

Disease and OMIM number for disease entry (examples)	IUIS category	OMIM number for disease-associated genes (examples)	ORPHA number for disease entry (examples)	HPO terms (examples)	Contributors	Clinical criteria for a probable diagnosis (= working definitions for clinical diagnosis classification)	Suggestions for alternative diagnosis (i.e., if the criteria are not completely fulfilled)
IgA with IgG subclass deficiency	3. Predominantly antibody deficiencies				Nizar Mahlaoui, David Edgar, Stephan Ehl, Helen Chapel, Isabella Quinti, Esther de Vries	Infections (recurrent or severe bacterial) **AND** Undetectable serum/plasma IgA level (with normal/lowish IgG and IgM levels) **AND** Low levels in one or more IgG subclass (documented twice) **AND** normal IgG antibody response to some vaccinations **AND** Exclusion of T cell defect	**Unclassified antibody deficiencies**
Immunodeficiency centromeric instability facial anomalies syndrome (ICF) 242860, 614069, 616910, 616911	2. Combined immunodeficiencies with associated or syndromic features	602900, 614064, 609937, 603946	ORPHA:2268	Immunodeficiency-centromeric instability-facial anomalies syndrome (ICF)	Markus Seidel, Beata Wolska, Corry Weemaes, Capucine Picard	Immunodeficiency (variable hypogammaglobulinemia, variably reduced T, B, and NK cells, bacterial and opportunistic infections) **AND** • Head: microcephaly, hypertelorism, epicanthal folds, flat face, micrognathia, macroglossia, tongue protrusion, small upturned nose • Cytogenetics: Centromeric instability of chromosomes 1, 9 and 16 with increased somatic recombination and formation of multibranched/-radial configurations **AND at least two of the following** • Short stature • Neurologic: variable mental retardation	

Disease and OMIM number for disease entry (examples)	IUIS category	OMIM number for disease-associated genes (examples)	ORPHA number for disease entry (examples)	HPO terms (examples)	Contributors	Clinical criteria for a probable diagnosis (= working definitions for clinical diagnosis classification)	Suggestions for alternative diagnosis (i.e., if the criteria are not completely fulfilled)
						• Malabsorption, diarrhea • Sinusitis, upper and lower respiratory tract infections	
IPEX-like disease 614162	4. Diseases of immune dysregulation	*600555*	ORPHA:391487	IPEX-like disease	Nizar Mahlaoui, David Edgar, Stephan Ehl, Hans Ochs, Benedicte Neven	**At least one of** • Severe and protracted enteropathy with villous atrophy in a male infant • Severe, often multiple endocrinopathies **AND** Exclusion of hypogammaglobulinaemia **AND at least one of the following:** • Normal Foxp3 expression by CD4+CD25+ on flow analysis • No overt T cell defect (proliferations are normal) • Elevated IgA and IgE levels	Combined immunodeficiency
Isolated IgG subclass deficiency	3. Predominantly antibody deficiencies	*147110*	ORPHA:183675		Nizar Mahlaoui, David Edgar, Stephan Ehl, Helen Chapel, Isabella Quinti, Esther de Vries	Infections (recurrent or severe bacterial) **AND** normal IgG, A and M serum/plasma levels **AND** Low levels in one or more IgG subclass (documented twice) **AND** Normal IgG antibody response to some vaccinations **AND**Exclusion of T cell defect	**Unclassified antibody deficiencies**

Disease and OMIM number for disease entry (examples)	IUIS category	OMIM number for disease-associated genes (examples)	ORPHA number for disease entry (examples)	HPO terms (examples)	Contributors	Clinical criteria for a probable diagnosis (= working definitions for clinical diagnosis classification)	Suggestions for alternative diagnosis (i.e., if the criteria are not completely fulfilled)
Isolated congenital asplenia 271400	6. Defects in intrinsic and innate immunity	150370, 141250	ORPHA:101351	Isolated congenital asplenia	Nizar Mahlaoui, David Edgar,Stephan Ehl, Capucine Picard, Jean-Laurent Casanova	Asplenia or hyposplenia **AND** Documentation of Howell-Jolly bodies on blood smears **AND** radiological findings evidencing asplenia (US, CT scan, scintigraphy) **AND** exclusion of any over developmental defect such as heterotaxia (dextrocardia, situs inversus, other…) or other heart and great vessel defects	
Mannose-binding lectin deficiency (MBL) 614372	6. Defects in intrinsic and innate immunity	*154545*		Mannose-binding lectin deficiency (MBL)	Matthew Buckland, Sofia Grigoriadou, Ania Manson	Infections (severe recurrent bacterial) **AND one of the following:** Mannose binding lectin <75 µg/L: Correlates with homozygous variant alleles and non-functional MBL which is associated with the greatest risk of infection. **OR** 75 - 399.9 µg/L: Correlates with functional MBL deficiency associated with increased risk of infection. **OR** 400 - 1300 µg/L: Correlates with heterozygous varient alleles and may show mild deficiency associated with some increased risk of infection. note: patients should be classified as homozygous, functional or heterozygous deficient as appropriate.	

Disease and OMIM number for disease entry (examples)	IUIS category	OMIM number for disease-associated genes (examples)	ORPHA number for disease entry (examples)	HPO terms (examples)	Contributors	Clinical criteria for a probable diagnosis (= working definitions for clinical diagnosis classification)	Suggestions for alternative diagnosis (i.e., if the criteria are not completely fulfilled)
Membrane CoFactor Protein (CD46) Deficiency	8. Complement deficiencies	120920			Matthew Buckland, Ania Manson, Sofia Grigoriadou	**At least one of the following;** Increased susceptibility to infections • Glomerulonephritis • Recurrent pyogenic infections • Pre-eclampsia **AND** AP50/AP100 activity less than 10% of control value with normal CH50/CH100 activity **AND/OR** Evidence of absent C3b binding by competitive immunoassay	
MonoMAC (WILD) 614172	5. Congenital defects of phagocyte number or function	137295	ORPHA:228423	MonoMAC (WILD)	Isabella Quinti, Andrew Cant	**At least one of the following:** • disseminated non-tubercolous mycobacterial infections • opportunistic fungal, and viral infections • familial myelodysplastic syndrome / acute myelogenous leukemia • pulmonary alveolar proteinosis • erythema nodosum • lymphedema • disseminated warts • anogenital dysplasia **AND** Monocytopenia, dendritic cell, B and NK lymphocytes lymphopenia **AND** Bone marrow hypocellularity, fibrosis, and multilineage dysplasia	

Disease and OMIM number for disease entry (examples)	IUIS category	OMIM number for disease-associated genes (examples)	ORPHA number for disease entry (examples)	HPO terms (examples)	Contributors	Clinical criteria for a probable diagnosis (= working definitions for clinical diagnosis classification)	Suggestions for alternative diagnosis (i.e., if the criteria are not completely fulfilled)
Netherton syndrome 256500	2. Combined immunodeficiencies with associated or syndromic features	605010	ORPHA:634	Netherton syndrome	Joris van Montfrans Ellen Renner, Hans Ochs, Nizar Mahlaoui	**At least two of the following:** • generalized ichthyosis (erythroderma covered by fine scales) with an onset < 2 months of age • short hair due to broken off distal shaft, specific hair shaft abnormality called trichorrhexis invaginata or "bamboo hair" • atopic manifestations, including food allergies or elevated serum levels of IgE. **AND at least one of the following:** • failure to thrive in the first years of life • recurrent infections (skin and other locations) • intermittent diarrhea	
Nijmegen breakage syndrome 251260	2. Combined immunodeficiencies with associated or syndromic features	602667	ORPHA:647	Nijmegen breakage syndrome	Markus Seidel, Beata Wolska, Corry Weemaes, Andy Gennery	Microcephaly **AND** reduced T cell number and/or elevated percentage of memory CD4 and CD8 cells and/or reduced T cell function **AND at least two of the following** • Typical facial appearance • Variable hypogammaglobulinemia, dysgammaglobulinemia and/or reduction of B cells - opportunistic and/or chronic, recurrent infections,	

Disease and OMIM number for disease entry (examples)	IUIS category	OMIM number for disease-associated genes (examples)	ORPHA number for disease entry (examples)	HPO terms (examples)	Contributors	Clinical criteria for a probable diagnosis (= working definitions for clinical diagnosis classification)	Suggestions for alternative diagnosis (i.e., if the criteria are not completely fulfilled)
						predominantly of the respiratory tract • Skin: Café-au-lait spots and/or hypopigmented areas and/or skin granulomas • lymphoma/leukemia or other malignancy • Chromosomal instability (especially chrom. 7 and 14), increased sensitivity towards ionizing radiation and alkylating agents	
Omenn syndrome 603554	Categories 1, 2, 4.	*605988*, *179615*, *179616*, *607210*, *601837*, *146661*	ORPHA:39041	Omenn syndrome	Nizar Mahlaoui, Annarosa Soresina, Anna Villa, Alain Fischer	Desquamating erythroderma in the first year of life **AND** one of the following: • lymphoproliferation • failure to thrive • chronic diarrhoea • recurrent pneumonia **AND** eosinophilia or elevated IgE **AND** T-cell deficiency (low naïve cells, reduced proliferation, oligoclonality) **AND** maternal engraftment excluded **AND** HIV excluded	For other patients with severe erythroderma, please consider: -SCID -IPEX -Unclassified disorders of immune dysregulation -Unclassified defects in innate immunity.

Disease and OMIM number for disease entry (examples)	IUIS category	OMIM number for disease-associated genes (examples)	ORPHA number for disease entry (examples)	HPO terms (examples)	Contributors	Clinical criteria for a probable diagnosis (= working definitions for clinical diagnosis classification)	Suggestions for alternative diagnosis (i.e., if the criteria are not completely fulfilled)
Papillon-Lefevre syndrome 245000	5. Congenital defects of phagocyte number or function	602365	ORPHA:678	Papillon-Lefèvre syndrome	Isabella Quinti, Steven Holland, Nizar Mahlaoui	Palmoplantar hyperkeratosis **AND** severe early onset periodontitis affecting both the deciduous and permanent teeth **AND at least one of the following:** • mild mental retardation • pyogenic infections • hyperhidrosis • intracranial calcifications • abnormal neutrophil function tests Differential diagnosis includes: allelic variants of PLS, such as Haim-Munk syndrome and prepubertal/aggressive periodontitis. Other diseases with similar dermatologic features include localized epidermolytic palmoplantar keratoderma, Howel-Evans syndrome, Greither's disease, and keratosis punctate.	
Partial albinism and immunodeficiency syndrome	4. Diseases of immune dysregulation				Nizar Mahlaoui, Stephan Ehl	Partial oculo-cutaneous albinism **AND at least one of the following:** • recurrent bacterial infections • episode of hemophagocytic lymphohistiocytosis (HLH) • reduced lymphocyte degranulation/cytotoxicity • affected family member **AND**	

Disease and OMIM number for disease entry (examples)	IUIS category	OMIM number for disease-associated genes (examples)	ORPHA number for disease entry (examples)	HPO terms (examples)	Contributors	Clinical criteria for a probable diagnosis (= working definitions for clinical diagnosis classification)	Suggestions for alternative diagnosis (i.e., if the criteria are not completely fulfilled)
						Exclusion of Chediak Higashi Syndrome, Griscelli Syndrome type 2, and Hermansky-Pudlak Syndrome type 2	
Properdin P factor complement deficiency (PFC) 312060	8. Complement deficiencies	300383	ORPHA:2966	Properdin P factor complement deficiency (PFC)	Matthew Buckland, Ania Manson, Sofia Grigoriadou	**At least one of the following;** • Increased susceptibility to infections (recurrent pyogenic including Neisseria) • Family History (X-linked inheritance pattern **AND** AP50/AP100 activity in at least the bottom 10% of control value with normal CH50/CH100 activity **AND** Absent Properdin (type I/II) or activity (type III) in serum in functional or immunochemical assessment	
Schimke disease 242900	2. Combined immunodeficiencies with associated or syndromic features	606622	ORPHA:1830	Schimke disease	Nizar Mahlaoui, David Edgar, Stephan Ehl	Predominantly T cell defects (low T cell counts, low T cell proliferations) **AND** osseous dysplasia (metaphyseal usually) **AND** kidney dysfunction	

Disease and OMIM number for disease entry (examples)	IUIS category	OMIM number for disease-associated genes (examples)	ORPHA number for disease entry (examples)	HPO terms (examples)	Contributors	Clinical criteria for a probable diagnosis (= working definitions for clinical diagnosis classification)	Suggestions for alternative diagnosis (i.e., if the criteria are not completely fulfilled)
Seckel syndrome 210600, 606744, 613676, 613529, 614728, 614851, 615807, 616777, 617253		*606605*, *601215*, *601810*, *604124*, *613529*, *609279*, *605925*, *605958*, *614724*, *608684*, *617246*	ORPHA:808	Seckel syndrome	Markus Seidel, Beata Wolska, Corry Weemaes, Andy Gennery	Short stature (pre- and postnatal growth retardation), severe microcephaly **AND at least three of the following:** • Head: downward slanting palpebral fissures, sloping forehead, face asymmetry, prominent beaked nose, selective tooth agenesis • Hematology: pancytopenia • Cytogenetics: increased sister chromatid exchange • Neurology: mental retardation, seizures, and CNS structural abnormalities • Skeletal: fifth finger clinodactyly, hip and radius head dislocation, hypoplasia of proximal radius and proximal fibula, 11 ribs, scoliosis	
Selective CD4 cell deficiency 615518		*604011*		Selective CD4 cell deficiency	Matthew Buckland, Ania Manson, Sofia Grigoriadou	$CD4^+$ T cell less than 350/µl (patient more than 4 years of age) or less than 20% of circulating T-lymphocytes at any age **AND** OKT4 Deficiency Excluded **AND** Normal or increased CD8, CD19 and CD56 **AND** HIV Negative **And** Other primary causes of lymphopenia excluded	

Disease and OMIM number for disease entry (examples)	IUIS category	OMIM number for disease-associated genes (examples)	ORPHA number for disease entry (examples)	HPO terms (examples)	Contributors	Clinical criteria for a probable diagnosis (= working definitions for clinical diagnosis classification)	Suggestions for alternative diagnosis (i.e., if the criteria are not completely fulfilled)
Selective IgA deficiency *137100*, 609529	3. Predominantly antibody deficiencies	*604907*		Selective IgA deficiency	Vojtech Thon, Natalia Martinez, Maria Kanariou, Klaus Warnatz, Isabella Quinti	**At least one of the following:** • increased susceptibility to infection • autoimmune manifestations • affected family member **AND** diagnosis after 4th year of life **AND** undetectable serum IgA (when measured with nephelometry less than 0.07 g/L) but normal serum IgG and IgM (measured at least twice) **AND** secondary causes of hypogammaglobulinemia have been excluded. **AND** normal IgG antibody response to all vaccinations **AND** Exclusion of T-cell defect	For patients with abnormal vaccine responses, please consider **Deficiency of specific IgG (SPAD)**. For other patients, please consider **Unclassified antibody deficiency**.
Selective IgM deficiency	3. Predominantly antibody deficiencies		ORPHA:331235	Selective IgM deficiency	Nizar Mahlaoui, David Edgar, Stephan Ehl, Helen Chapel, Isabella Quinti, Esther de Vries	Infections (either invasive or recurrent, usually bacterial) **AND** Low IgM serum/plasma level (with normal IgG and IgG subclasses and IgA plasma level) **AND** Normal IgG antibody response to all vaccinations **AND** Exclusion of T-cell defect	**Unclassified antibody deficiencies**

Disease and OMIM number for disease entry (examples)	IUIS category	OMIM number for disease-associated genes (examples)	ORPHA number for disease entry (examples)	HPO terms (examples)	Contributors	Clinical criteria for a probable diagnosis (= working definitions for clinical diagnosis classification)	Suggestions for alternative diagnosis (i.e., if the criteria are not completely fulfilled)
Severe combined immunodeficiency (SCID) 300400, 600802, 608971, 102700, 601457, 602450, 611291, 615617, 615615, 615617, 617237	1. Immunodeficiencies affecting cellular and humoral immunity	308380, 600173, 146661, 151460, 186790, 186830, 186780, 605000, 602354, 179615, 179616, 605988, 611290, 601837, 103020, 608958, *600899*, *600838*, *176947*, *607210*	ORPHA:276 ORPHA:35078 ORPHA:169160 ORPHA:169157 ORPHA:169154 ORPHA:277 ORPHA:331206 ORPHA:275 ORPHA:183660 ORPHA:357237 ORPHA:228003 ORPHA:420573 ORPHA:317425 ORPHA:397787 ORPHA:504523 ORPHA:280142 ORPHA:317416 ORPHA:317419	Severe combined immunodeficiency (SCID)	Stephan Ehl, Alain Fischer	**At least one of the following:** • invasive bacterial, viral or fungal/opportunistic infection • persistent diarrhoea and failure to thrive • affected family member **AND** manifestation in the first year of life **AND** HIV excluded **AND** 2 of 4 T cell criteria fulfilled: • low or absent CD3 or CD4 or CD8 T cells • reduced naive CD4 and/or CD8 T cells • elevated g/d T cells • reduced or absent proliferation to mitogen or TCR stimulation	For other (e.g. older) patients with T-cell deficiency, consider **Combined IDs**.
Shwachman-Diamond-syndrome 260400, 617941	5. Congenital defects of phagocyte number or function	607444, *617048*, *617538*, *604857*	ORPHA:811	Shwachman-Diamond syndrome	Nizar Mahlaoui, Jean Donadieu	Neutropenia **AND** Exocrine pancreatic failure **AND at least one of the following:** • enlargement of metaphyseal zones on bone X-rays • cognitive retardation or behavioural problems	

Disease and OMIM number for disease entry (examples)	IUIS category	OMIM number for disease-associated genes (examples)	ORPHA number for disease entry (examples)	HPO terms (examples)	Contributors	Clinical criteria for a probable diagnosis (= working definitions for clinical diagnosis classification)	Suggestions for alternative diagnosis (i.e., if the criteria are not completely fulfilled)
Thymoma with immunodeficiency			ORPHA:169105	Thymoma with immunodeficiency	David Edgar, Helen Chapel	Presence of thymoma **AND** reduced serum IgG (< 2SD below the mean reference for age)	
Transient hypogammaglobulinaemia of infancy	3. Predominantly antibody deficiencies		ORPHA:169139		David Edgar, Maria Kanariou, Esther de Vries	IgG below age-related normal value detected in the first three years of life (measured at least twice) **AND** defined causes of hypogammaglobulinaemia have been excluded **AND** spontaneous resolution approx. after the 4th birthday NB: Patients will initially be registered as **Unclassified antibody deficiency,** in the registry and moved to **THI**, if there is spontaneous resolution before age 4.	
Warts hypogammaglobulinemia infections and myelokathexis (WHIM) 193670	6. Defects in intrinsic and innate immunity	162643	ORPHA:51636	Warts hypogammaglobulinemia infections and myelokathexis (WHIM)	Jean Donadieu, Sarah, Beaussant Cohen, Bodo Grimbacher	Neutropenia **AND** lymphopenia **AND** monocytopenia **AND** Evidence of myelokathexis on bone marrow smear; **AND at least one of the following:** • Recurrent and severe HPV infections • Recurrent bacterial infections	

Disease and OMIM number for disease entry (examples)	IUIS category	OMIM number for disease-associated genes (examples)	ORPHA number for disease entry (examples)	HPO terms (examples)	Contributors	Clinical criteria for a probable diagnosis (= working definitions for clinical diagnosis classification)	Suggestions for alternative diagnosis (i.e., if the criteria are not completely fulfilled)
						• Mycobacterial infection(s) • Mild hypogammagobulinemia	
Wiskott-Aldrich syndrome (XLT/WAS) 301000, 614493	2. Combined immunodeficiencies with associated or syndromic features	300392, *602357*	ORPHA:906	Wiskott-Aldrich-syndrome	Annarosa Soresina, Natalia Martinez, Michael Albert, Adrian Thrasher	**At least one of the following:** • eczema • recurrent bacterial or viral infections • autoimmune diseases (incl. vasculitis) • malignancy • reduced WASP expression in a fresh blood sample • abnormal antibody response to polysaccharide antigens and/or low isohemagglutinins • positive maternal family history of XLT/WAS **AND** male patient with thrombocytopenia (less than 100,000 platelets/mm3) (measured at least twice) **AND** small platelets (platelet volume < 7,5 fl)	
X-linked lymphoproliferative syndrome (XLP) 308240, 300635	4. Diseases of immune dysregulation	300490, 300079	ORPHA:2442	X-linked lymphoproliferative syndrome (XLP)	Nizar Mahlaoui, Stephan Ehl	Male individual (or female with severely skewed X-chromosome inactivation) **AND two of the following:** • at least 1 episode of HLH (according to the Histiocyte Society criteria) • affected family member • abnormal EBV response • Hypogammaglobulinemia • Inflammatory Bowel Disease • Vasculitis	

Disease and OMIM number for disease entry (examples)	IUIS category	OMIM number for disease-associated genes (examples)	ORPHA number for disease entry (examples)	HPO terms (examples)	Contributors	Clinical criteria for a probable diagnosis (= working definitions for clinical diagnosis classification)	Suggestions for alternative diagnosis (i.e., if the criteria are not completely fulfilled)
						• Lymphoid Neoplasm, especially if EBV-associated **AND at least one of the following minor criteria:** • decreased or absent SAP (for XLP1) or XIAP (for XLP2) expression assessed by Flow Cytometry • reduced frequency of iNKT cells (< 0.02% of T cells) • Normal Perforin expression in flow cytometry • Normal degranulation (NK or CTL) assays or Normal NK cell cytotoxicity assays **AND** No partial albinism **AND** Normal work-up for metabolic diseases	
Unclassified antibody deficiency					Esther de Vries, Nizar Mahlaoui, David Edgar, Isabella Quinti, Helen Chapel	**At least one of the following:** • Recurrent or severe bacterial infections • Autoimmune phenomena (especially cytopenias) • Polyclonal lymphoproliferation • Affected family member **AND at least one of the following**: • marked decrease of at least one of total IgG, IgG1, IgG2, IgG3, IgA or IgM levels	

Disease and OMIM number for disease entry (examples)	IUIS category	OMIM number for disease-associated genes (examples)	ORPHA number for disease entry (examples)	HPO terms (examples)	Contributors	Clinical criteria for a probable diagnosis (= working definitions for clinical diagnosis classification)	Suggestions for alternative diagnosis (i.e., if the criteria are not completely fulfilled)
						• failure of IgG antibody response(s) to vaccines **AND** secondary causes of hypogammaglobulinemia have been excluded (e.g., infection, protein loss, medication, malignancy) **AND** no clinical signs of T-cell related disease **AND** does not fit **any** of the other working definitions (**ex**cluding 'unclassified immunodeficiencies')	
Unclassified phagocytic disorders					Nizar Mahlaoui, Capucine Picard, Jacinta Bustamante	**At least one of the following:** • deep seated infection due to bacteria and/or fungi • recurrent severe pneumonia • buccal and/or genital aphtous lesions or ulcerations • omphalitis • chronic inflammatory manifestations (e.g. colitis, fistula formation) • affected family member • BCGitis or BCGosis **AND** normal to subnormal respiratory burst (NBT or DHR, assessed at least twice)	
Unclassified disorders of immune dysregulation					Stephan Ehl, Maria Kanariou	**At least one of the following:** • autoimmune manifestations • lymphoproliferation • severe eczema • inflammatory bowel disease	For patients with evidence of profound T-cell deficiency, please register

Disease and OMIM number for disease entry (examples)	IUIS category	OMIM number for disease-associated genes (examples)	ORPHA number for disease entry (examples)	HPO terms (examples)	Contributors	Clinical criteria for a probable diagnosis (= working definitions for clinical diagnosis classification)	Suggestions for alternative diagnosis (i.e., if the criteria are not completely fulfilled)
						• granuloma • vasculitis • HLH-like disease **AND** at least one numeric or functional abnormal finding upon immunological investigation **AND** no evidence of profound T-cell deficiency, defined as 2 out of the following (y=year of life): • CD4 numbers/microliter: 0-6mo <1000, 6mo-1y <800, 1-2y <500, 2-6y <300, 6-12y <250, >12y <200 • % naïve CD4: 0-2y <30%, 2-6y <25%, 6-16y <20%, >16y 10% • T cell proliferation absent **AND** no evidence of B-cell deficiency (low B cell numbers, hypogammaglobulinemia)	these as **Combined immunodeficiencies**. For patients with evidence of B-cell deficiency, please register as **Unclassified antibody deficiency**.
Unclassified defects in innate immunity					Nizar Mahlaoui, Maria Kanariou, Capucine Picard, Jacinta Bustamante	**At least one of the following:** • onset of disease before 5 y of age • pyogenic bacterial infections • unusual infections and/or atypical clinical course **AND** the dominant abnormal immunological finding concerns the innate immune system (excluding defects in phagocyte number or function) i.e. NF-κB-dependent TLR and IL-1R immunity	For patients with evidence of profound defect of phagocytes, please consider **Unclassified phagocytic disorders**.

Disease and OMIM number for disease entry (examples)	IUIS category	OMIM number for disease-associated genes (examples)	ORPHA number for disease entry (examples)	HPO terms (examples)	Contributors	Clinical criteria for a probable diagnosis (= working definitions for clinical diagnosis classification)	Suggestions for alternative diagnosis (i.e., if the criteria are not completely fulfilled)
						AND functional spleen (no Howell-Jolly bodies on blood smears)	
Unclassified complement deficiencies					Annarosa Soresina, Matthew Buckland, David Edgar	**At least one of the following:** • one episode of bacteraemia, meningitis or systemic Neisserial infection • recurrent respiratory infections **AND** persistent defect of CH50 or AP50 (in three determinations in 6 months) **AND** no evidence of other conventional immunological defects	
Unclassified autoinflammatory diseases					David Edgar, Beata Wolska, Helen Lachmann	Recurrent fever (temperature >38 degrees Celsius) having occurred on at least 6 occasions. **AND** exclusion of other known infective / inflammatory autoimmune disorders **AND** documented evidence of increased inflammatory markers (ESR/CRP) **AND** age of onset under 40 years **AND** predominantly but not exclusively systemic symptoms	

Disease and OMIM number for disease entry (examples)	IUIS category	OMIM number for disease-associated genes (examples)	ORPHA number for disease entry (examples)	HPO terms (examples)	Contributors	Clinical criteria for a probable diagnosis (= working definitions for clinical diagnosis classification)	Suggestions for alternative diagnosis (i.e., if the criteria are not completely fulfilled)
Unclassified syndromic immunodeficiencies					Stephan Ehl, Alain Fischer	**At least one of the following:** • dysmorphic features such as short stature, facial abnormalities, microcephaly, skeletal abnormalities • other organ manifestations such as albinism, hair or tooth abnormalities, heart or kidney defects, hearing abnormalities, primary neurodevelopmental delay, seizures **AND** at least one numeric or functional abnormal finding upon immunological investigation **AND** exclusion of secondary causes for immunological abnormalities (infection, malignancy)	
Unclassified immunodeficiencies					Stephan Ehl, Alain Fischer	**At least one of the following:** • at least one major infection • abnormal course or frequency of minor infections • at least one manifestation of immune dysregulation • failure to thrive • affected family member **AND** at least one numeric or functional abnormal finding upon immunological investigation **AND** exclusion of secondary causes for immunological abnormalities	For patients with syndromic manifestations, consider **Unclassified syndromic IDs**.

Disease and OMIM number for disease entry (examples)	IUIS category	OMIM number for disease-associated genes (examples)	ORPHA number for disease entry (examples)	HPO terms (examples)	Contributors	Clinical criteria for a probable diagnosis (= working definitions for clinical diagnosis classification)	Suggestions for alternative diagnosis (i.e., if the criteria are not completely fulfilled)
						(infection, protein loss, medication, malignancy) **AND** does not fit **any** of the other working definitions (**in**cluding 'unclassified syndromic immunodeficiencies')	

Acquired angioedema

Very frequent

Term Identifier	Term Name	Definition
HP:0002027	Abdominal pain	An unpleasant sensation characterized by physical discomfort (such as pricking, throbbing, or aching) and perceived to originate in the abdomen.
HP:0100665	Angioedema	Rapid swelling (edema) of the dermis, subcutaneous tissue, mucosa and submucosal tissues of the skin of the face, normally around the mouth, and the mucosa of the mouth and/or throat, as well as the tongue during a period of minutes to several hours. The swelling can also occur elsewhere, typically in the hands. Angioedema is similar to urticaria, but the swelling is subcutaneous rather than on the epidermis.
HP:0000969	Edema	An abnormal accumulation of fluid beneath the skin, or in one or more cavities of the body.

Occasional

Term Identifier	Term Name	Definition
HP:0001541	Ascites	Accumulation of fluid in the peritoneal cavity.
HP:0000282	Facial edema	
HP:0005225	Intestinal edema	Accumulation of cell free, noninflammatony fluid within the wall of the intestinal tract producing uniform thickening of the mucosal folds.
HP:0005214	Intestinal obstruction	Blockage or impairment of the normal flow of the contents of the intestine towards the anal canal.
HP:0012027	Laryngeal edema	An abnormal accumulation of fluid and swelling in the tissues of the larynx.
HP:0001025	Urticaria	Raised, well-circumscribed areas of erythema and edema involving the dermis and epidermis. Urticaria is intensely pruritic, and blanches completely with pressure.

Source: HPO-ORDO Ontological Module - Validation association date: 01.06.2016 - PMID:20667117, PMID:8438855

Agammaglobulinemia

X – linked agammaglobulinemia

Very frequent

Term Identifier	Term Name	Definition
HP:0100763	Abnormality of lymphatic system	An anomaly of the lymphatic system, a network of lymphatic vessels that carry a clear fluid called lymph unidirectionally towards either the right lymphatic duct or the thoracic duct, which in turn drain into the right and left subclavian veins respectively.
HP:0100765	Abnormality of the tonsils	An abnormality of the tonsils.
HP:0004432	Agammaglobulinemia	Absence or extremely low level of IgA, IgM, and IgM in the circulation.
HP:0002028	Chronic diarrhea	The presence of chronic diarrhea, which is usually taken to mean diarrhea that has persisted for over 4 weeks.
HP:0000389	Chronic otitis media	Chronic otitis media refers to fluid, swelling, or infection of the middle ear that does not heal and may cause permanent damage to the ear.
HP:0000509	Conjunctivitis	Inflammation of the conjunctiva.
HP:0001508	Failure to thrive	Failure to thrive (FTT) refers to a child whose physical growth is substantially below the norm.
HP:0012378	Fatigue	A subjective feeling of tiredness characterized by a lack of energy and motivation.
HP:0001945	Fever	Elevated body temperature due to failed thermoregulation.
HP:0000162	Glossoptosis	Posterior displacement of the tongue into the pharynx, i.e., a tongue that is mislocalised posteriorly.
HP:0002721	Immunodeficiency	Failure of the immune system to protect the body adequately from infection, due to the absence or insufficiency of some component process or substance.
HP:0100838	Recurrent cutaneous abscess formation	An increased susceptibility to cutaneous abscess formation, as manifested by a medical history of recurrent cutaneous abscesses.
HP:0006532	Recurrent pneumonia	An increased susceptibility to pneumonia as manifested by a history of recurrent episodes of pneumonia.
HP:0004322	Short stature	A height below that which is expected according to age and gender norms. Although there is no universally accepted definition of short stature, many refer to "short stature" as height more than 2 standard deviations below the mean for age and gender (or below the 3rd percentile for age and gender dependent norms).
HP:0000246	Sinusitis	Inflammation of the paranasal sinuses owing to a viral, bacterial, or fungal infection, allergy, or an autoimmune reaction.
HP:0000988	Skin rash	A red eruption of the skin.
HP:0200042	Skin ulcer	A discontinuity of the skin exhibiting complete loss of the epidermis and often portions of the dermis and even subcutaneous fat.

Frequent

Term Identifier	Term Name	Definition
HP:0002088	Abnormality of lung morphology	Any structural anomaly of the lung.
HP:0001369	Arthritis	Inflammation of a joint.
HP:0100658	Cellulitis	A bacterial infection and inflammation of the skin und subcutaneous tissues.
HP:0002901	Hypocalcemia	An abnormally decreased calcium concentration in the blood.
HP:0001287	Meningitis	Inflammation of the meninges.
HP:0001875	Neutropenia	An abnormally low number of neutrophils in the peripheral blood.
HP:0000407	Sensorineural hearing impairment	A type of hearing impairment in one or both ears related to an abnormal functionality of the cochlear nerve.
HP:0100806	Sepsis	Systemic inflammatory response to infection.

Occasional

Term Identifier	Term Name	Definition
HP:0001596	Alopecia	Loss of hair from the head or body.
HP:0001903	Anemia	A reduction in erythrocytes volume or hemoglobin concentration.
HP:0002960	Autoimmunity	The occurrence of an immune reaction against the organisms own cells or tissues.
HP:0012115	Hepatitis	Inflammation of the liver.
HP:0001053	Hypopigmented skin patches	
HP:0002024	Malabsorption	Impaired ability to absorb one or more nutrients from the intestine.
HP:0002664	Neoplasm	An organ or organ-system abnormality that consists of uncontrolled autonomous cell-proliferation which can occur in any part of the body as a benign or malignant neoplasm (tumour).
HP:0002754	Osteomyelitis	Osteomyelitis is an inflammatory process accompanied by bone destruction and caused by an infecting microorganism.
HP:0001873	Thrombocytopenia	A reduction in the number of circulating thrombocytes.
HP:0001824	Weight loss	Reduction in existing body weight.

Autosomal agammaglobulinemia

Very frequent

Term Identifier	Term Name	Definition
HP:0004432	Agammaglobulinemia	Absence or extremely low level of IgA, IgM, and IgM in the circulation.

HP:0000389	Chronic otitis media	Chronic otitis media refers to fluid, swelling, or infection of the middle ear that does not heal and may cause permanent damage to the ear.
HP:0000509	Conjunctivitis	Inflammation of the conjunctiva.
HP:0012735	Cough	A sudden, audible expulsion of air from the lungs through a partially closed glottis, preceded by inhalation.
HP:0002014	Diarrhea	Abnormally increased frequency of loose or watery bowel movements.
HP:0012378	Fatigue	A subjective feeling of tiredness characterized by a lack of energy and motivation.
HP:0001945	Fever	Elevated body temperature due to failed thermoregulation.
HP:0002721	Immunodeficiency	Failure of the immune system to protect the body adequately from infection, due to the absence or insufficiency of some component process or substance.
HP:0002719	Recurrent infections	Increased susceptibility to infections.
HP:0002205	Recurrent respiratory infections	An increased susceptibility to respiratory infections as manifested by a history of recurrent respiratory infections.
HP:0001581	Recurrent skin infections	Infections of the skin that happen multiple times.
HP:0000246	Sinusitis	Inflammation of the paranasal sinuses owing to a viral, bacterial, or fungal infection, allergy, or an autoimmune reaction.
HP:0000988	Skin rash	A red eruption of the skin.

Frequent

Term Identifier	Term Name	Definition
HP:0001369	Arthritis	Inflammation of a joint.
HP:0001508	Failure to thrive	Failure to thrive (FTT) refers to a child whose physical growth is substantially below the norm.
HP:0002754	Osteomyelitis	Osteomyelitis is an inflammatory process accompanied by bone destruction and caused by an infecting microorganism.

Occasional

Term Identifier	Term Name	Definition
HP:0002110	Bronchiectasis	Persistent abnormal dilatation of the bronchi owing to localized and irreversible destruction and widening of the large airways.
HP:0100658	Cellulitis	A bacterial infection and inflammation of the skin und subcutaneous tissues.
HP:0001944	Dehydration	
HP:0000286	Epicanthus	A fold of skin starting above the medial aspect of the upper eyelid and arching downward to cover, pass in front of and lateral to the medial canthus.
HP:0008572	External ear malformation	A malformation of the auricle of the ear.
HP:0012115	Hepatitis	Inflammation of the liver.

HP:0000218	High palate	Height of the palate more than 2 SD above the mean (objective) or palatal height at the level of the first permanent molar more than twice the height of the teeth (subjective).
HP:0000316	Hypertelorism	Interpupillary distance more than 2 SD above the mean (alternatively, the appearance of an increased interpupillary distance or widely spaced eyes).
HP:0002024	Malabsorption	Impaired ability to absorb one or more nutrients from the intestine.
HP:0001287	Meningitis	Inflammation of the meninges.
HP:0001875	Neutropenia	An abnormally low number of neutrophils in the peripheral blood.
HP:0100806	Sepsis	Systemic inflammatory response to infection.
HP:0200043	Verrucae	Warts, benign growths on the skin or mucous membranes that cause cosmetic problems as well as pain and discomfort. Warts most often occur on the hands, feet, and genital areas.

Source: HPO-ORDO Ontological Module - Validation association date: 01.06.2016

Asplenia syndrome (Ivemark syndrome)

Rare

Term Identifier	Term Name	Definition
HP:0031834	Aortopulmonary collateral arteries	Small ectopic arteries or arterial branches that connect the aorta, aortic branches and/or subclavian artery regions directly to the lung parenchyma, usually seen in conjunction with pulmonary atresia, ventricular septal defect (VSD) and/or closed ductus arteriosus.
HP:0001746	Asplenia	Absence (aplasia) of the spleen.
HP:0011565	Common atrium	Complete absence of the interatrial septum with common atrioventricular valve and two atrioventricular connections.
HP:0000023	Inguinal hernia	Protrusion of the contents of the abdominal cavity through the inguinal canal.
HP:0001696	Situs inversus totalis	A left-right reversal (or "mirror reflection") of the anatomical location of the major thoracic and abdominal organs.
HP:0001636	Tetralogy of Fallot	A congenital cardiac malformation comprising pulmonary stenosis, overriding aorta, ventricular septum defect, and right ventricular hypertrophy. The diagnosis of TOF is made if at least three of the four above mentioned features are present.
HP:0005160	Total anomalous pulmonary venous return	Total anomalous pulmonary venous return refers to a congenital malformation in which all four pulmonary veins do not connect normally to the left atrium, but instead drain abnormally to the right atrium.
HP:0001669	Transposition of the great arteries	A complex congenital heart defect in which the aorta arises from the morphologic right ventricle and the pulmonary artery arises from the morphologic left ventricle.

No frequency available

Term Identifier	Term Name	Definition
HP:0031565	Abdominal situs ambiguus	An abnormality in which the abdominal organs are positioned in such a way with respect to each other and the left-right axis as to be not clearly lateralised and thus have neither the usual, or normal (situs solitus), nor the mirror-imaged (situs inversus) arrangements.
HP:0002101	Abnormal lung lobation	Defects in the formation of pulmonary lobules.
HP:0001274	Agenesis of corpus callosum	Absence of the corpus callosum as a result of the failure of the corpus callosum to develop, which can be the result of a failure in any one of the multiple steps of callosal development including cellular proliferation and migration, axonal growth or glial patterning at the midline.
HP:0001631	Atrial septal defect	Atrial septal defect (ASD) is a congenital abnormality of the interatrial septum that enables blood flow between the left and right atria via the interatrial septum.

HP:0001674	Complete atrioventricular canal defect	A congenital heart defect characteizred by a specific combination of heart defects with a common atrioventricular valve, primum atrial septal defect and inlet ventricular septal defect.
HP:0001748	Polysplenia	Polysplenia is a congenital disease manifested by multiple small accessory spleens.
HP:0004935	Pulmonary artery atresia	A congenital anomaly with a narrowing or complete absence of the opening between the right ventricle and the pulmonary artery.
HP:0001642	Pulmonic stenosis	A narrowing of the right ventricular outflow tract that can occur at the pulmonary valve (valvular stenosis) or just below the pulmonary valve (infundibular stenosis).
HP:0011536	Right atrial isomerism	Right atrial isomerism is characterized by bilateral triangular, morphologically right atrial, appendages, both joining the atrial chamber along a broad front with internal terminal crest.
HP:0001750	Single ventricle	The presence of only one working lower chamber in the heart, usually with a virtual absence of the ventricular septum and usually present in conjunction with double inlet left or right ventricle.
HP:0001629	Ventricular septal defect	A hole between the two bottom chambers (ventricles) of the heart. The defect is centered around the most superior aspect of the ventricular septum.

Source: National Center for Advancing Translational Sciences – GARD (last updated 01.08.2019)

Ataxia telangiectasia (ATM)

Very frequent

Term Identifier	Term Name	Definition
HP:0003220	Abnormality of chromosome stability	A type of chromosomal aberration characterised by reduced resistance of chromosomes to change or deterioration.
HP:0000496	Abnormality of eye movement	An abnormality in voluntary or involuntary eye movements or their control.
HP:0100022	Abnormality of movement	An abnormality of movement with a neurological basis characterized by changes in coordination and speed of voluntary movements.
HP:0002715	Abnormality of the immune system	An abnormality of the immune system.
HP:0010515	Aplasia/Hypoplasia of the thymus	Absence or underdevelopment of the thymus.
HP:0001251	Ataxia	Cerebellar ataxia refers to ataxia due to dysfunction of the cerebellum. This causes a variety of elementary neurological deficits including asynergy (lack of coordination between muscles, limbs and joints), dysmetria (lack of ability to judge distances that can lead to under- oder overshoot in grasping movements), and dysdiadochokinesia (inability to perform rapid movements requiring antagonizing muscle groups to be switched on and off repeatedly).
HP:0005374	Cellular immunodeficiency	An immunodeficiency characterized by defective cell-mediated immunity or humoral immunity.
HP:0004313	Decreased antibody level in blood	An abnormally decreased level of immunoglobulin in blood.
HP:0000823	Delayed puberty	Passing the age when puberty normally occurs with no physical or hormonal signs of the onset of puberty.
HP:0002910	Elevated hepatic transaminases	Elevations of the levels of SGOT and SGPT in the serum. SGOT (serum glutamic oxaloacetic transaminase) and SGPT (serum glutamic pyruvic transaminase) are transaminases primarily found in the liver and heart and are released into the bloodstream as the result of liver or heart damage. SGOT and SGPT are used clinically mainly as markers of liver damage.
HP:0001288	Gait disturbance	The term gait disturbance can refer to any disruption of the ability to walk. In general, this can refer to neurological diseases but also fractures or other sources of pain that is triggered upon walking. However, in the current context gait disturbance refers to difficulty walking on the basis of a neurological or muscular disease.
HP:0002721	Immunodeficiency	Failure of the immune system to protect the body adequately from infection, due to the absence or insufficiency of some component process or substance.
HP:0001888	Lymphopenia	A reduced number of lymphocytes in the blood.
HP:0100579	Mucosal telangiectasiae	Telangiectasia of the mucosa, the mucous membranes which are involved in absorption and secretion that line

		cavities that are exposed to the external environment and internal organs.
HP:0002167	Neurological speech impairment	
HP:0000639	Nystagmus	Rhythmic, involuntary oscillations of one or both eyes related to abnormality in fixation, conjugate gaze, or vestibular mechanisms.
HP:0000147	Polycystic ovaries	
HP:0002216	Premature graying of hair	Development of gray hair at a younger than normal age.
HP:0007495	Prematurely aged appearance	
HP:0002205	Recurrent respiratory infections	An increased susceptibility to respiratory infections as manifested by a history of recurrent respiratory infections.
HP:0000486	Strabismus	A misalignment of the eyes so that the visual axes deviate from bifoveal fixation. The classification of strabismus may be based on a number of features including the relative position of the eyes, whether the deviation is latent or manifest, intermittent or constant, concomitant or otherwise and according to the age of onset and the relevance of any associated refractive error.
HP:0100585	Telangiectasia of the skin	Presence of small, permanently dilated blood vessels near the surface of the skin, visible as small focal red lesions.
HP:0001337	Tremor	An unintentional, oscillating to-and-fro muscle movement about a joint axis.

Frequent

Term Identifier	Term Name	Definition
HP:0000819	Diabetes mellitus	A group of abnormalities characterized by hyperglycemia and glucose intolerance.
HP:0001260	Dysarthria	Dysarthric speech is a general description referring to a neurological speech disorder characterized by poor articulation. Depending on the involved neurological structures, dysarthria may be further classified as spastic, flaccid, ataxic, hyperkinetic and hypokinetic, or mixed.
HP:0005599	Hypopigmentation of hair	
HP:0002664	Neoplasm	An organ or organ-system abnormality that consists of uncontrolled autonomous cell-proliferation which can occur in any part of the body as a benign or malignant neoplasm (tumour).
HP:0001250	Seizures	Seizures are an intermittent abnormality of the central nervous system due to a sudden, excessive, disorderly discharge of cerebral neurons and characterized clinically by some combination of disturbance of sensation, loss of consciousness, impairment of psychic function, or convulsive movements. The term epilepsy is used to describe chronic, recurrent seizures.
HP:0004322	Short stature	A height below that which is expected according to age and gender norms. Although there is no universally accepted

		definition of short stature, many refer to "short stature" as height more than 2 standard deviations below the mean for age and gender (or below the 3rd percentile for age and gender dependent norms).
HP:0003202	Skeletal muscle atrophy	The presence of skeletal muscular atrophy (which is also known as amyotrophy).
HP:0001257	Spasticity	A motor disorder characterized by a velocity-dependent increase in tonic stretch reflexes with increased muscle tone, exaggerated (hyperexcitable) tendon reflexes.

Occasional

Term Identifier	Term Name	Definition
HP:0000035	Abnormality of the testis	An anomaly of the testicle (the male gonad).
HP:0008065	Aplasia/Hypoplasia of the skin	
HP:0100543	Cognitive impairment	Abnormality in the process of thought including the ability to process information.
HP:0001508	Failure to thrive	Failure to thrive (FTT) refers to a child whose physical growth is substantially below the norm.
HP:0007565	Multiple cafe-au-lait spots	The presence of six or more cafe-au-lait spots.
HP:0005978	Type II diabetes mellitus	A type of diabetes mellitus initially characterized by insulin resistance and hyperinsulinemia and subsequently by glucose interolerance and hyperglycemia.

Source: HPO-ORDO Ontological Module - Validation association date: 01.06.2016

Atypical SCID

No frequency available

Term Identifier	Term Name	Definition
HP:0002014	Diarrhea	Abnormally increased frequency of loose or watery bowel movements.
HP:0000976	Eczematoid dermatitis	
HP:0001508	Failure to thrive	Failure to thrive (FTT) refers to a child whose physical growth is substantially below the norm.
HP:0002240	Hepatomegaly	Abnormally increased size of the liver.
HP:0005401	Recurrent candida infections	An increased susceptibility to candida infections, as manifested by a history of recurrent episodes of candida infections.
HP:0001744	Splenomegaly	Abnormal increased size of the spleen.
HP:0003139	Panhypogammaglobulinemia	A reduction in the circulating levels of all the major classes of immunoglobulin. is characterized by profound decreases in all classes of immunoglobulin with an absence of circulating B lymphocytes.
HP:0002090	Pneumonia	Inflammation of any part of the lung parenchyma.

Source: National Center for Advancing Translational Sciences – GARD (last updated 01.08.2019)

Autoimmune lymphoproliferative syndrome (ALPS)

Very frequent

Term Identifier	Term Name	Definition
HP:0002960	Autoimmunity	The occurrence of an immune reaction against the organism's own cells or tissues.
HP:0002730	Chronic noninfectious lymphadenopathy	A chronic form of lymphadenopathy that is not related to infection.
HP:0002716	Lymphadenopathy	Enlargment (swelling) of a lymph node.
HP:0001744	Splenomegaly	Abnormal increased size of the spleen.

Frequent

Term Identifier	Term Name	Definition
HP:0001892	Abnormal bleeding	An abnormal susceptibility to bleeding, often referred to as a bleeding diathesis. A bleeding diathesis may be related to vascular, platelet and coagulation defects.
HP:0030782	Abnormal serum interleukin level	An abnormal amount of any of the interleukins, a class of cytokines, in the circulation.
HP:0001890	Autoimmune hemolytic anemia	An autoimmune form of hemolytic anemia.
HP:0001973	Autoimmune thrombocytopenia	The presence of thrombocytopenia in combination with detection of antiplatelet antibodies.
HP:0000978	Bruising susceptibility	An ecchymosis (bruise) refers to the skin discoloration caused by the escape of blood into the tissues from ruptured blood vessels. This term refers to an abnormally increased susceptibility to bruising. The corresponding phenotypic abnormality is generally elicited on medical history as a report of frequent ecchymoses or bruising without adequate trauma.
HP:0002851	Elevated proportion of CD4-negative, CD8-negative, alpha-beta regulatory T cells	An abnormally increased proportion of CD4-negative, CD8-negative (double negative or DN) alpha-beta regulatory T cells (Tregs) as compared to total number of T cells.
HP:0002240	Hepatomegaly	Abnormally increased size of the liver.
HP:0001971	Hypersplenism	A malfunctioning of the spleen in which it prematurely destroys red blood cells.
HP:0005404	Increased B cell count	An abnormal increase from the normal count of B cells.
HP:0003237	Increased circulating IgG level	An abnormally increased level of immunoglobulin G in blood.
HP:0010702	Increased antibody level in blood	An increased level of gamma globulin (immunoglobulin) in the blood.
HP:0001904	Neutropenia in presence of anti-neutropil antibodies	A type of neutropenia that is observed in the presence of granulocyte-specific antibodies.

Occasional

Term Identifier	Term Name	Definition

HP:0031392	Abnormal proportion of CD4 T cells	Any abnormality in the proportion of CD4 T cells relative to the total number of T cells.
HP:0031393	Abnormal proportion of CD8 T cells	Any abnormality in the proportion of CD8 T cells relative to the total number of T cells.
HP:0040126	Abnormal vitamin B12 level	A deviation from the normal concentration of cobalamin (vitamin B12) in the blood. Vitamin B12 is one of the eight B vitamins.
HP:0003453	Antineutrophil antibody positivity	The presence of autoantibodies in the serum that react against neutrophils.
HP:0003493	Antinuclear antibody positivity	The presence of autoantibodies in the serum that react against nuclei or nuclear components.
HP:0003613	Antiphospholipid antibody positivity	The presence of circulating autoantibodies to phospholipids.
HP:0012191	B-cell lymphoma	A type of lymphoma that originates in B-cells.
HP:0030080	Burkitt lymphoma	A form of undifferentiated malignant lymphoma commonly manifested as a large osteolytic lesion in the jaw or as an abdominal mass.
HP:0004844	Coombs-positive hemolytic anemia	A type of hemolytic anemia in which the Coombs test is positive.
HP:0004315	Decreased circulating IgG level	An abnormally decreased level of immunoglobulin G (IgG) in blood.
HP:0002850	Decreased circulating total IgM	An abnormally decreased level of immunoglobulin M (IgM) in blood.
HP:0005407	Decreased proportion of CD4-positive T cells	A decreased proportion of circulating CD4-positive helper T cells relative to total T cell count.
HP:0001880	Eosinophilia	Increased count of eosinophils in the blood.
HP:0000099	Glomerulonephritis	Inflammation of the renal glomeruli.
HP:0012115	Hepatitis	Inflammation of the liver.
HP:0012189	Hodgkin lymphoma	A type of lymphoma characterized microscopically by multinucleated Reed-Sternberg cells.
HP:0003261	Increased circulating IgA level	An abnormally increased level of immunoglobulin A in blood.
HP:0003212	Increased circulating total IgE level	An abnormally increased overall level of immunoglobulin E in blood.
HP:0100827	Lymphocytosis	Increase in the number or proportion of lymphocytes in the blood.
HP:0001888	Lymphopenia	A reduced number of lymphocytes in the blood.
HP:0012539	Non-Hodgkin lymphoma	A type of lymphoma characterized microscopically by the absence of multinucleated Reed-Sternberg cells.
HP:0001923	Reticulocytosis	An elevation in the number of reticulocytes (immature erythrocytes) in the peripheral blood circulation.
HP:0002923	Rheumatoid factor positive	The presence in the serum of an autoantibody directed against the Fc portion of IgG.
HP:0002848	Specific anti-polysaccharide antibody deficiency	The presence of normal overall immunoglobulin levels with deficiency of specific immunoglobulins directed against bacterial polysaccharides.
HP:0012190	T-cell lymphoma	A type of lymphoma that originates in T-cells.
HP:0100646	Thyroiditis	Inflammation of the thyroid gland.
HP:0001025	Urticaria	Raised, well-circumscribed areas of erythema and edema involving the dermis and epidermis. Urticaria

		is intensely pruritic, and blanches completely with pressure.
HP:0002633	Vasculitis	Inflammation of blood vessel.

Rare

Term Identifier	Term Name	Definition
HP:0002725	Systemic lupus erythematosus	A chronic, relapsing, inflammatory, and often febrile multisystemic disorder of connective tissue, characterized principally by involvement of the skin, joints, kidneys, and serosal membranes.
HP:0001369	Arthritis	Inflammation of a joint.
HP:0002671	Basal cell carcinoma	The presence of a basal cell carcinoma of the skin.
HP:0031020	Bone marrow hypercellularity	A larger than normal amount or percentage of hematopoietic cells relative to marrow fat.
HP:0005528	Bone marrow hypocellularity	A reduced number of hematopoietic cells present in the bone marrow relative to marrow fat.
HP:0002583	Colitis	Colitis refers to an inflammation of the colon and is often used to describe an inflammation of the large intestine (colon, cecum and rectum). Colitides may be acute and self-limited or chronic, and broadly fit into the category of digestive diseases.
HP:0010619	Fibroadenoma of the breast	A benign biphasic tumor of the breast with epithelial and stromal components.
HP:0005263	Gastritis	The presence of inflammation of the gastric mucous membrane.
HP:0002315	Headache	Cephalgia, or pain sensed in various parts of the head, not confined to the area of distribution of any nerve.
HP:0001402	Hepatocellular carcinoma	A kind of neoplasm of the liver that originates in hepatocytes and presents macroscopically as a soft and hemorrhagic tan mass in the liver.
HP:0001789	Hydrops fetalis	The abnormal accumulation of fluid in two or more fetal compartments, including ascites, pleural effusion, pericardial effusion, and skin edema.
HP:0008069	Neoplasm of the skin	A tumor (abnormal growth of tissue) of the skin.
HP:0100648	Neoplasm of the tongue	A tumor (abnormal growth of tissue) of the tongue.
HP:0012490	Panniculitis	Inflammation of adipose tissue.
HP:0008209	Premature ovarian insufficiency	Amenorrhea due to loss of ovarian function before the age of 40. Primary ovarian inssuficiency (POI) is a state of female hypergonadotropic hypogonadism. It can manifest as primary amenorrhea with onset before menarche or secondary amenorrhea.
HP:0002206	Pulmonary fibrosis	Replacement of normal lung tissues by fibroblasts and collagen.
HP:0002113	Pulmonary infiltrates	
HP:0011107	Recurrent aphthous stomatitis	Recurrent episodes of ulceration of the oral mucosa, typically presenting as painful, sharply circumscribed fibrin-covered mucosal defects with a hyperemic border.

HP:0000083	Renal insufficiency	A reduction in the level of performance of the kidneys in areas of function comprising the concentration of urine, removal of wastes, the maintenance of electrolyte balance, homeostasis of blood pressure, and calcium metabolism.
HP:0001250	Seizures	Seizures are an intermittent abnormality of the central nervous system due to a sudden, excessive, disorderly discharge of cerebral neurons and characterized clinically by some combination of disturbance of sensation, loss of consciousness, impairment of psychic function, or convulsive movements. The term epilepsy is used to describe chronic, recurrent seizures.
HP:0000854	Thyroid adenoma	The presence of a adenoma of the thyroid gland.
HP:0002890	Thyroid carcinoma	The presence of a carcinoma of the thyroid gland.
HP:0000554	Uveitis	Inflammation of one or all portions of the uveal tract.

Source: HPO-ORDO Ontological Module - Validation association date: 29.04.2019 – PMID:15767081; PMID:11418480; PMID:9028957; PMID:8929361; PMID:7540117; PMID: 1386609; PMID:4165068; PMID:20301287; PMID:30958694

APECED / APS1 with CMC - Autoimmune polyendocrinopathy candidiasis ectodermal dystrophy (APECED)

Very frequent

Term Identifier	Term Name	Definition
HP:0100530	Abnormality of calcium-phosphate metabolism	
HP:0100659	Abnormality of the cerebral vasculature	
HP:0001231	Abnormality of the fingernails	An abnormality of the fingernails.
HP:0008221	Adrenal hyperplasia	Enlargement of the adrenal gland.
HP:0002960	Autoimmunity	The occurrence of an immune reaction against the organism's own cells or tissues.
HP:0002728	Chronic mucocutaneous candidiasis	Recurrent or persistent superficial Candida infections of the skin, mucous membranes, and nails.
HP:0003118	Increased circulating cortisol level	Overproduction of the hormone of cortisol by the adrenal cortex, resulting in a characteristic combination of clinical symptoms termed Cushing syndrome, with truncal obesity, a round, full face, striae atrophicae and acne, muscle weakness, and other features.
HP:0004319	Decreased circulating aldosterone level	Abnormally reduced levels of aldosterone.
HP:0000829	Hypoparathyroidism	A condition caused by a deficiency of parathyroid hormone characterized by hypocalcemia and hyperphosphatemia.
HP:0007759	Opacification of the corneal stroma	Reduced transparency of the stroma of cornea.
HP:0000613	Photophobia	Excessive sensitivity to light with the sensation of discomfort or pain in the eyes due to exposure to bright light.
HP:0008207	Primary adrenal insufficiency	Insufficient production of steroid hormones (primarily cortisol) by the adrenal glands as a result of a primary defect in the glands themselves.
HP:0000505	Visual impairment	Visual impairment (or vision impairment) is vision loss (of a person) to such a degree as to qualify as an additional support need through a significant limitation of visual capability resulting from either disease, trauma, or congenital or degenerative conditions that cannot be corrected by conventional means, such as refractive correction, medication, or surgery.

Frequent

Term Identifier	Term Name	Definition
HP:0000518	Cataract	A cataract is an opacity or clouding that develops in the crystalline lens of the eye or in its capsule.

Occasional

Term Identifier	Term Name	Definition
HP:0001596	Alopecia	Loss of hair from the head or body.
HP:0002514	Cerebral calcification	The presence of calcium deposition within brain structures.
HP:0001053	Hypopigmented skin patches	

Source: HPO-ORDO Ontological Module - Validation association date: 01.06.2016

Barth syndrome

Very frequent

Term Identifier	Term Name	Definition
HP:0001644	Dilated cardiomyopathy	Dilated cardiomyopathy (DCM) is defined by the presence of left ventricular dilatation and left ventricular systolic dysfunction in the absence of abnormal loading conditions (hypertension, valve disease) or coronary artery disease sufficient to cause global systolic impairment. Right ventricular dilation and dysfunction may be present but are not necessary for the diagnosis.

Frequent

Term Identifier	Term Name	Definition
HP:0008322	Abnormal mitochondrial morphology	Any structural anomaly of the mitochondria.
HP:0001874	Abnormality of neutrophils	A neutrophil abnormality.
HP:0001706	Endocardial fibroelastosis	Diffuse thickening of the ventricular endocardium and by associated myocardial dysfunction

Occasional

Term Identifier	Term Name	Definition
HP:0001875	Neutropenia	An abnormally low number of neutrophils in the peripheral blood.
HP:0001992	Organic aciduria	Excretion of non-amino organic acids in urine.
HP:0001762	Talipes equinovarus	Talipes equinovarus (also called clubfoot) typically has four main components: inversion and adduction of the forefoot; inversion of the heel and hindfoot; equinus (limitation of extension) of the ankle and subtalar joint; and internal rotation of the leg.

Source: HPO-ORDO Ontological Module - Validation association date: 01.06.2016

Bloom syndrome

Very frequent

Term Identifier	Term Name	Definition
HP:0003220	Abnormality of chromosome stability	A type of chromosomal aberration characterised by reduced resistance of chromosomes to change or deterioration.
HP:0000366	Abnormality of the nose	An abnormality of the nose.
HP:0000951	Abnormality of the skin	An abnormality of the skin.
HP:0002750	Delayed skeletal maturation	A decreased rate of skeletal maturation. Delayed skeletal maturation can be diagnosed on the basis of an estimation of the bone age from radiographs of specific bones in the human body.
HP:0002014	Diarrhea	Abnormally increased frequency of loose or watery bowel movements.
HP:0000268	Dolichocephaly	An abnormality of skull shape characterized by a increased anterior-posterior diameter, i.e., an increased antero-posterior dimension of the skull. Cephalic index less than 76%. Alternatively, an apparently increased antero-posterior length of the head compared to width. Often due to premature closure of the sagittal suture.
HP:0010783	Erythema	Redness of the skin, caused by hyperemia of the capillaries in the lower layers of the skin.
HP:0005598	Facial telangiectasia in butterfly midface distribution	Telangiectases (small dilated blood vessels) located near the surface of the skin in a butterfly midface distribution.
HP:0001511	Intrauterine growth retardation	An abnormal restriction of fetal growth with fetal weight below the tenth percentile for gestational age.
HP:0000272	Malar flattening	Underdevelopment of the malar prominence of the jugal bone (zygomatic bone in mammals), appreciated in profile, frontal view, and/or by palpation.
HP:0000275	Narrow face	Bizygomatic (upper face) and bigonial (lower face) width are both more than 2 standard deviations below the mean (objective); or, an apparent reduction in the width of the upper and lower face (subjective).
HP:0002664	Neoplasm	An organ or organ-system abnormality that consists of uncontrolled autonomous cell-proliferation which can occur in any part of the body as a benign or malignant neoplasm (tumour).
HP:0008897	Postnatal growth retardation	Slow or limited growth after birth.
HP:0002205	Recurrent respiratory infections	An increased susceptibility to respiratory infections as manifested by a history of recurrent respiratory infections.
HP:0004322	Short stature	A height below that which is expected according to age and gender norms. Although there is no universally accepted definition of short stature, many refer to "short stature" as height more than 2 standard deviations below the mean for age and gender (or below the 3rd percentile for age and gender dependent norms).

HP:0000246	Sinusitis	Inflammation of the paranasal sinuses owing to a viral, bacterial, or fungal infection, allergy, or an autoimmune reaction.
HP:0005585	Spotty hyperpigmentation	

Frequent

Term Identifier	Term Name	Definition
HP:0000271	Abnormality of the face	An abnormality of the face.
HP:0010669	Cheekbone underdevelopment	Underdevelopment of the zygomatic bone [UBERON_0001683]. That is, a reduction in size of the zygomatic bone, including the zygomatic process of the temporal bone of the skull, which forms part of the zygomatic arch.
HP:0000992	Cutaneous photosensitivity	An increased sensitivity of the skin to light. Photosensitivity may result in a rash upon exposure to the sun (which is known as photodermatosis). Photosensitivity can be diagnosed by phototests in which light is shone on small areas of skin.
HP:0001620	High pitched voice	An abnormal increase in the pitch (frequency) of the voice.
HP:0003196	Short nose	Distance from nasion to subnasale more than two standard deviations below the mean, or alternatively, an apparently decreased length from the nasal root to the nasal tip.
HP:0100585	Telangiectasia of the skin	Presence of small, permanently dilated blood vessels near the surface of the skin, visible as small focal red lesions.

Occasional

Term Identifier	Term Name	Definition
HP:0002488	Acute leukemia	A clonal (malignant) hematopoietic disorder with an acute onset, affecting the bone marrow and the peripheral blood. The malignant cells show minimal differentiation and are called blasts, either myeloid blasts (myeloblasts) or lymphoid blasts (lymphoblasts).
HP:0000027	Azoospermia	Absence of any measurable level of sperm in his semen.
HP:0004313	Decreased antibody level in blood	An abnormally decreased level of immunoglobulin in blood.
HP:0000868	Decreased fertility in females	
HP:0006101	Finger syndactyly	Webbing or fusion of the fingers, involving soft parts only or including bone structure. Bony fusions are referred to as "bony" Syndactyly if the fusion occurs in a radio-ulnar axis. Fusions of bones of the fingers in a proximo-distal axis are referred to as "Symphalangism".
HP:0001161	Hand polydactyly	A kind of polydactyly characterized by the presence of a supernumerary finger or fingers.
HP:0000975	Hyperhidrosis	Abnormal excessive perspiration (sweating) despite the lack of appropriate stimuli like hot and humid weather.

HP:0001053	Hypopigmented skin patches	
HP:0008064	Ichthyosis	An abnormality of the skin characterized the presence of excessive amounts of dry surface scales on the skin resulting from an abnormality of keratinization.
HP:0002720	Decreased circulating IgA level	Decreased levels of immunoglobulin A (IgA).
HP:0004315	Decreased circulating IgG level	An abnormally decreased level of immunoglobulin G (IgG) in blood.
HP:0002850	Decreased circulating total IgM	An abnormally decreased level of immunoglobulin M (IgM) in blood.
HP:0001256	Intellectual disability, mild	Mild intellectual disability is defined as an intelligence quotient (IQ) in the range of 50-69.
HP:0002665	Lymphoma	A cancer originating in lymphocytes and presenting as a solid tumor of lymhpoid cells.
HP:0000252	Microcephaly	Occipito-frontal (head) circumference (OFC) less than -3 standard deviations compared to appropriate, age matched, normal standards (Ross JJ, Frias JL 1977, PMID:9683597). Alternatively, decreased size of the cranium.
HP:0007378	Neoplasm of the gastrointestinal tract	A tumor (abnormal growth of tissue) of the gastrointestinal tract.
HP:0000411	Protruding ear	Angle formed by the plane of the ear and the mastoid bone greater than the 97th centile for age (objective); or, outer edge of the helix more than 2 cm from the mastoid at the point of maximum distance (objective).
HP:0009804	Reduced number of teeth	The presence of a reduced number of teeth as in Hypodontia or as in Anodontia.
HP:0000960	Sacral dimple	A subtype of skin dimples presenting as an indentation in the skin of the intergluteal cleft .
HP:0002860	Squamous cell carcinoma	The presence of squamous cell carcinoma of the skin.

Source: HPO-ORDO Ontological Module - Validation association date: 01.06.2016

Cartilage hair hypoplasia (CHH)

Very frequent

Term Identifier	Term Name	Definition
HP:0011849	Abnormal bone ossification	Any anomaly in the formation of bone or of a bony substance, or the conversion of fibrous tissue or of cartilage into bone or a bony substance.
HP:0000940	Abnormal diaphysis morphology	An abnormality of the structure or form of the diaphysis, i.e., of the main or mid-section (shaft) of a long bone.
HP:0003312	Abnormal form of the vertebral bodies	Abnormal morphology of vertebral body.
HP:0100569	Abnormal vertebral ossification	An abnormality of the formation and mineralization of one or more vertebrae.
HP:0005930	Abnormality of epiphysis morphology	An anomaly of epiphysis, which is the expanded articular end of a long bone that developes from a secondary ossification center, and which during the period of growth is either entirely cartilaginous or is separated from the shaft by a cartilaginous disk.
HP:0007703	Abnormality of retinal pigmentation	
HP:0001671	Abnormality of the cardiac septa	An anomaly of the intra-atrial or intraventricular septum.
HP:0009832	Abnormality of the distal phalanx of finger	Any anomaly of distal phalanx of finger.
HP:0000944	Abnormality of the metaphysis	An abnormality of one or more metaphysis, i.e., of the somewhat wider portion of a long bone that is adjacent to the epiphyseal growth plate and grows during childhood.
HP:0001732	Abnormality of the pancreas	An abnormality of the pancreas.
HP:0004625	Biconvex vertebral bodies	Presence of abnormal convexity of the upper and lower end plates of the vertebrae, i.e., an exaggerated bulging out of the upper and lower vertebral end plates.
HP:0000592	Blue sclerae	An abnormal bluish coloration of the sclera.
HP:0006487	Bowing of the long bones	A bending or abnormal curvature of a long bone.
HP:0001638	Cardiomyopathy	A myocardial disorder in which the heart muscle is structurally and functionally abnormal, in the absence of coronary artery disease, hypertension, valvular disease and congenital heart disease sufficient to cause the observed myocardial abnormality.
HP:0000444	Convex nasal ridge	Nasal ridge curving anteriorly to an imaginary line that connects the nasal root and tip. The nose appears often also prominent, and the columella low.
HP:0005019	Diaphyseal thickening	
HP:0008873	Disproportionate short-limb short stature	A type of disproportionate short stature characterized by a short limbs but an average-sized trunk.

HP:0002353	EEG abnormality	Abnormality observed by electroencephalogram (EEG), which is used to record of the brain's spontaneous electrical activity from multiple electrodes placed on the scalp.
HP:0001508	Failure to thrive	Failure to thrive (FTT) refers to a child whose physical growth is substantially below the norm.
HP:0008499	High-grade hypermetropia	A severe form of hypermetropia with over +5.00 diopters.
HP:0003307	Hyperlordosis	Abnormally increased cuvature (anterior concavity) of the lumbar or cervical spine.
HP:0002901	Hypocalcemia	An abnormally decreased calcium concentration in the blood.
HP:0100729	Large face	
HP:0001377	Limited elbow extension	Limited ability to straighten the arm at the elbow joint.
HP:0003027	Mesomelia	Shortening of the middle parts of the limbs (forearm and lower leg) in relation to the upper and terminal segments.
HP:0005871	Metaphyseal chondrodysplasia	An abnormality of skeletal development characterized by a disturbance of the metaphysis and its histological structure with relatively normal epiphyses and vertebrae.
HP:0100255	Metaphyseal dysplasia	The presence of dysplastic regions in metaphyseal regions.
HP:0002983	Micromelia	The presence of abnormally small extremities.
HP:0001252	Muscular hypotonia	Muscular hypotonia is an abnormally low muscle tone (the amount of tension or resistance to movement in a muscle), often involving reduced muscle strength. Hypotonia is characterized by a diminished resistance to passive stretching.
HP:0001875	Neutropenia	An abnormally low number of neutrophils in the peripheral blood.
HP:0002093	Respiratory insufficiency	
HP:0008905	Rhizomelia	Disproportionate shortening of the proximal segment of limbs (i.e. the femur and humerus).
HP:0002650	Scoliosis	The presence of an abnormal lateral curvature of the spine.
HP:0000470	Short neck	Diminished length of the neck.
HP:0004279	Short palm	Short palm.
HP:0002652	Skeletal dysplasia	A general term describing features characterized by abnormal development of bones and connective tissues.
HP:0000535	Sparse eyebrow	Decreased density/number and/or decreased diameter of eyebrow hairs.
HP:0008070	Sparse hair	Reduced density of hairs.
HP:0010301	Spinal dysraphism	A heterogeneous group of congenital spinal anomalies that result from defective closure of the neural tube early in fetal life.
HP:0000486	Strabismus	A misalignment of the eyes so that the visual axes deviate from bifoveal fixation. The classification of strabismus may be based on a number of features including the relative position of the eyes, whether the deviation is latent or manifest, intermittent or constant, concomitant or otherwise and according to the age of onset and the relevance of any associated refractive error.
HP:0002982	Tibial bowing	A bending or abnormal curvature of the tibia.

HP:0002777	Tracheal stenosis	
HP:0000505	Visual impairment	Visual impairment (or vision impairment) is vision loss (of a person) to such a degree as to qualify as an additional support need through a significant limitation of visual capability resulting from either disease, trauma, or congenital or degenerative conditions that cannot be corrected by conventional means, such as refractive correction, medication, or surgery.

Frequent

Term Identifier	Term Name	Definition
HP:0003272	Abnormality of the hip bone	An abnormality of the hip bone.
HP:0000174	Abnormality of the palate	Any abnormality of the palate, i.e., of roof of the mouth.
HP:0005280	Depressed nasal bridge	Posterior positioning of the nasal root in relation to the overall facial profile for age.
HP:0006589	Flaring of lower rib cage	
HP:0000212	Gingival overgrowth	Hyperplasia of the gingiva (that is, a thickening of the soft tissue overlying the alveolar ridge. The degree of thickening ranges from involvement of the interdental papillae alone to gingival overgrowth covering the entire tooth crown.
HP:0000368	Low-set, posteriorly rotated ears	Ears that are low-set (HP:0000369) and posteriorly rotated (HP:0000358).
HP:0002024	Malabsorption	Impaired ability to absorb one or more nutrients from the intestine.
HP:0008155	Mucopolysaccharidurıa	Excessive amounts of mucopolysaccharide in the urine.
HP:0000545	Myopia	An abnormality of refraction characterized by the ability to see objects nearby clearly, while objects in the distance appear blurry.
HP:0000774	Narrow chest	Reduced width of the chest from side to side, associated with a reduced distance from the sternal notch to the tip of the shoulder.
HP:0011220	Prominent forehead	Forward prominence of the entire forehead, due to protrusion of the frontal bone.
HP:0001315	Reduced tendon reflexes	Diminution of tendon reflexes, which is an invariable sign of peripheral nerve disease.

Occasional

Term Identifier	Term Name	Definition
HP:0003220	Abnormality of chromosome stability	A type of chromosomal aberration characterised by reduced resistance of chromosomes to change or deterioration.
HP:0002644	Abnormality of pelvic girdle bone morphology	An abnormality of the bony pelvic girdle, which is a ring of bones connecting the vertebral column to the femurs.
HP:0000772	Abnormality of the ribs	An anomaly of the rib.

HP:0005616	Accelerated skeletal maturation	An abnormally increased rate of skeletal maturation. Accelerated skeletal maturation can be diagnosed on the basis of an estimation of the bone age from radiographs of specific bones in the human body.
HP:0002251	Aganglionic megacolon	An abnormality resulting from a lack of intestinal ganglion cells (i.e., an aganglionic section of bowel) that results in bowel obstruction with enlargement of the colon.
HP:0001903	Anemia	A reduction in erythrocytes volume or hemoglobin concentration.
HP:0000463	Anteverted nares	Anteriorly-facing nostrils viewed with the head in the Frankfurt horizontal and the eyes of the observer level with the eyes of the subject. This gives the appearance of an upturned nose (upturned nasal tip).
HP:0008056	Aplasia/Hypoplasia affecting the eye	
HP:0010318	Aplasia/Hypoplasia of the abdominal wall musculature	Absence or underdevelopment of the abdominal musculature.
HP:0000248	Brachycephaly	An abnormality of skull shape characterized by a decreased anterior-posterior diameter. That is, a cephalic index greater than 81%. Alternatively, an apparently shortened anteroposterior dimension (length) of the head compared to width.
HP:0100543	Cognitive impairment	Abnormality in the process of thought including the ability to process information.
HP:0004313	Decreased antibody level in blood	An abnormally decreased level of immunoglobulin in blood.
HP:0002750	Delayed skeletal maturation	A decreased rate of skeletal maturation. Delayed skeletal maturation can be diagnosed on the basis of an estimation of the bone age from radiographs of specific bones in the human body.
HP:0000457	Depressed nasal ridge	Lack of prominence of the nose resulting from a posteriorly-placed nasal ridge.
HP:0000286	Epicanthus	A fold of skin starting above the medial aspect of the upper eyelid and arching downward to cover, pass in front of and lateral to the medial canthus.
HP:0012722	Heart block	Impaired conduction of cardiac impulse occurring anywhere along the conduction pathway.
HP:0002240	Hepatomegaly	Abnormally increased size of the liver.
HP:0005692	Joint hyperflexibility	Increased mobility and flexibility in the joint due to the tension in tissues such as ligaments and muscles.
HP:0000400	Macrotia	Median longitudinal ear length greater than two standard deviations above the mean and median ear width greater than two standard deviations above the mean (objective); or, apparent increase in length and width of the pinna (subjective).
HP:0000768	Pectus carinatum	A deformity of the chest caused by overgrowth of the ribs and characterized by protrusion of the sternum.
HP:0000960	Sacral dimple	A subtype of skin dimples presenting as an indentation in the skin of the intergluteal cleft.

HP:0010306	Short thorax	Reduced inferior to superior extent of the thorax.
HP:0200055	Small hand	Disproportionately small hand.
HP:0000431	Wide nasal bridge	Increased breadth of the nasal bridge (and with it, the nasal root).

Source: HPO-ORDO Ontological Module - Validation association date: 01.06.2016

CD8 deficiency

No frequency available

Term Identfier	Term Name	Definition
HP:0000007	Autosomal recessive inheritance	A mode of inheritance that is observed for traits related to a gene encoded on one of the autosomes (i.e., the human chromosomes 1-22) in which a trait manifests in individuals with two pathogenic alleles, either homozygotes (two copies of the same mutant allele) or compound heterozygotes (whereby each copy of a gene has a distinct mutant allele).
HP:0002205	Recurrent respiratory infections	An increased susceptibility to respiratory infections as manifested by a history of recurrent respiratory infections.
HP:0002110	Bronchiectasis	Persistent abnormal dilatation of the bronchi owing to localized and irreversible destruction and widening of the large airways.
HP:0002718	Recurrent bacterial infections	Increased susceptibility to bacterial infections, as manifested by recurrent episodes of bacterial infection.
HP:0004429	Recurrent viral infections	Increased susceptibility to viral infections, as manifested by recurrent episodes of viral infection.
HP:0005422	Absence of CD8-positive T cells	Lack of detectible CD8-positive T cells

Source: OMIM Clinical synopsis - #608957; Creation date: 30.09.2004, Cassandra L. Kniffin

Chronic mucocutaneous candidiasis (CMC)

Very frequent

Term Identifier	Term Name	Definition
HP:0008388	Abnormal toenail morphology	An anomaly of the toenail.
HP:0001231	Abnormality of the fingernails	An abnormality of the fingernails.
HP:0002715	Abnormality of the immune system	An abnormality of the immune system.
HP:0000159	Abnormal lip morphology	An abnormality of the lip.
HP:0000153	Abnormality of the mouth	An abnormality of the mouth.
HP:0001597	Abnormality of the nail	Abnormality of the nail.
HP:0000951	Abnormality of the skin	An abnormality of the skin.
HP:0001821	Broad nail	Increased width of nail.
HP:0100825	Cheilitis	Inflammation of the lip.
HP:0010783	Erythema	Redness of the skin, caused by hyperemia of the capillaries in the lower layers of the skin.
HP:0000962	Hyperkeratosis	Hyperkeratosis is thickening of the outer layer of the skin, the stratum corneum, which is composed of large, polyhedral, plate-like envelopes filled with keratin which are the dead cells that have migrated up from the stratum granulosum.
HP:0002719	Recurrent infections	Increased susceptibility to infections.
HP:0000988	Skin rash	A red eruption of the skin.
HP:0200042	Skin ulcer	A discontinuity of the skin exhibiting complete loss of the epidermis and often portions of the dermis and even subcutaneous fat.

Frequent

Term Identifier	Term Name	Definition
HP:0000142	Abnormal vagina morphology	Any structural abnormality of the vagina.
HP:0030016	Dyspareunia	Recurrent or persistent genital pain associated with sexual intercourse.
HP:0200034	Papule	A circumscribed, solid elevation of skin with no visible fluid, varying in size from a pinhead to less than 10mm in diameter at the widest point.

Occasional

Term Identifier	Term Name	Definition
HP:0000682	Abnormality of dental enamel	An abnormality of the dental enamel.

HP:0004370	Abnormality of temperature regulation	An abnormality of temperature homeostasis.
HP:0004306	Abnormal endocardium morphology	An abnormality of the endocardium.
HP:0000478	Abnormality of the eye	Any abnormality of the eye, including location, spacing, and intraocular abnormalities.
HP:0000504	Abnormality of vision	*Abnormality of eyesight (visual perception).*
HP:0012735	Cough	A sudden, audible expulsion of air from the lungs through a partially closed glottis, preceded by inhalation.
HP:0008872	Feeding difficulties in infancy	Impaired feeding performance of an infant as manifested by difficulties such as weak and ineffective sucking, brief bursts of sucking, and falling asleep during sucking. There may be difficulties with chewing or maintaining attention.
HP:0000790	Hematuria	The presence of blood in the urine. Hematuria may be gross hematuria (visible to the naked eye) or microscopic hematuria (detected by dipstick or microscopic examination of the urine).
HP:0002105	Hemoptysis	Coughing up (expectoration) of blood or blood-streaked sputum from the larynx, trachea, bronchi, or lungs.
HP:0012115	Hepatitis	Inflammation of the liver.
HP:0000103	Polyuria	An increased rate of urine production.
HP:0000989	Pruritus	Pruritus is an itch or a sensation that makes a person want to scratch. This term refers to an abnormally increased disposition to experience pruritus.
HP:0002205	Recurrent respiratory infections	An increased susceptibility to respiratory infections as manifested by a history of recurrent respiratory infections.
HP:0000010	Recurrent urinary tract infections	Repeated infections of the urinary tract.
HP:0001250	Seizures	Seizures are an intermittent abnormality of the central nervous system due to a sudden, excessive, disorderly discharge of cerebral neurons and characterized clinically by some combination of disturbance of sensation, loss of consciousness, impairment of psychic function, or convulsive movements. The term epilepsy is used to describe chronic, recurrent seizures.

Source: HPO-ORDO Ontological Module - Validation association date: 01.06.2016

Complement component 1q deficiency (C1q deficiency)

No frequency available

Term Identifier	Term Name	Definition
HP:0000007	Autosomal recessive inheritance	A mode of inheritance that is observed for traits related to a gene encoded on one of the autosomes (i.e., the human chromosomes 1-22) in which a trait manifests in individuals with two pathogenic alleles, either homozygotes (two copies of the same mutant allele) or compound heterozygotes (whereby each copy of a gene has a distinct mutant allele).
HP:0000793	Membranoproliferative glomerulonephritis	A type of glomerulonephritis characterized by diffuse mesangial cell proliferation and the thickening of capillary walls due to subendothelial extension of the mesangium. The term membranoproliferative glomerulonephritis is often employed to denote a general pattern of glomerular injury seen in a variety of disease processes that share a common pathogenetic mechanism, rather than to describe a single disease entity
HP:0002725	Systemic lupus erythematosus	A chronic, relapsing, inflammatory, and often febrile multisystemic disorder of connective tissue, characterized principally by involvement of the skin, joints, kidneys, and serosal membranes.
HP:0002960	Autoimmunity	The occurrence of an immune reaction against the organism's own cells or tissues.
HP:0005356	Decreased serum complement factor I	A reduced level of the complement component Factor I in circulation.
HP:0002719	Recurrent infections	Increased susceptibility to infections.

Source: OMIM Clinical synopsis - #613652; Creation date: 05.03.2012, Joanna S. Amberger

Complement component 1r deficiency (C1r deficiency)

No frequency available

Term Identifier	Term Name	Definition
HP:0004431	Complement deficiency	An immunodeficiency defined by the absent or suboptimal functioning of one of the complement system proteins.
HP:0002960	Autoimmunity	The occurrence of an immune reaction against the organism's own cells or tissues.
HP:0007417	Discoid lupus rash	Cutaneous lesion that develops as a dry, scaly, red patch that evolves to an indurated and hyperpigmented plaque with adherent scale. Scarring may result in central white patches (loss of pigmentation) and skin atrophy.
HP:0000123	Nephritis	The presence of inflammation affecting the kidney.
HP:0002837	Recurrent bronchitis	An increased susceptibility to bronchitis as manifested by a history of recurrent bronchitis.
HP:0001369	Arthritis	Inflammation of a joint.
HP:0002829	Arthralgia	Joint pain.
HP:0002719	Recurrent infections	Increased susceptibility to infections.
HP:0000007	Autosomal recessive inheritance	A mode of inheritance that is observed for traits related to a gene encoded on one of the autosomes (i.e., the human chromosomes 1-22) in which a trait manifests in individuals with two pathogenic alleles, either homozygotes (two copies of the same mutant allele) or compound heterozygotes (whereby each copy of a gene has a distinct mutant allele).

Source: OMIM Clinical synopsis - %216950

Complement component 1s deficiency (C1s deficiency)

No frequency available

Term Identifier	Term Name	Definition
HP:0012115	Hepatitis	Inflammation of the liver.
HP:0002725	Systemic lupus erythematosus	A chronic, relapsing, inflammatory, and often febrile multisystemic disorder of connective tissue, characterized principally by involvement of the skin, joints, kidneys, and serosal membranes.
HP:0005339	Abnormality of complement system	An abnormality of the complement system.
HP:0000872	Hashimoto thyroiditis	A chronic, autoimmune type of thyroiditis associated with hypothyroidism.
HP:0002719	Recurrent infections	Increased susceptibility to infections.

Source: OMIM - #613783; Creation date: 01.03.2011, Carol A.Bocchini

Complement component 2 deficiency

No frequency available

Term Identifier	Term Name	Definition
HP:0000979	Purpura	Purpura (from Latin: purpura, meaning "purple") is the appearance of red or purple discolorations on the skin that do not blanch on applying pressure. They are caused by bleeding underneath the skin. This term refers to an abnormally increased susceptibility to developing purpura. Purpura are larger than petechiae.
HP:0002725	Systemic lupus erythematosus	A chronic, relapsing, inflammatory, and often febrile multisystemic disorder of connective tissue, characterized principally by involvement of the skin, joints, kidneys, and serosal membranes.
HP:0007417	Discoid lupus rash	Cutaneous lesion that develops as a dry, scaly, red patch that evolves to an indurated and hyperpigmented plaque with adherent scale. Scarring may result in central white patches (loss of pigmentation) and skin atrophy.
HP:0005339	Abnormality of complement system	An abnormality of the complement system.
HP:0000007	Autosomal recessive inheritance	A mode of inheritance that is observed for traits related to a gene encoded on one of the autosomes (i.e., the human chromosomes 1-22) in which a trait manifests in individuals with two pathogenic alleles, either homozygotes (two copies of the same mutant allele) or compound heterozygotes (whereby each copy of a gene has a distinct mutant allele).
HP:0002960	Autoimmunity	The occurrence of an immune reaction against the organism's own cells or tissues.

Source: OMIM - #217000; Creation date: 15.06.1995, John F. Jackson

Complement component 3 deficiency (C3)

No frequency available

Term Identifier	Term Name	Definition
HP:0000100	Nephrotic syndrome	Nephrotic syndrome is a collection of findings resulting from glomerular dysfunction with an increase in glomerular capillary wall permeability associated with pronounced proteinuria. Nephrotic syndrome refers to the constellation of clinical findings that result from severe renal loss of protein, with Proteinuria and hypoalbuminemia, edema, and hyperlipidemia.
HP:0000083	Renal insufficiency	A reduction in the level of performance of the kidneys in areas of function comprising the concentration of urine, removal of wastes, the maintenance of electrolyte balance, homeostasis of blood pressure, and calcium metabolism.
HP:0000793	Membranoproliferative glomerulonephritis	A type of glomerulonephritis characterized by diffuse mesangial cell proliferation and the thickening of capillary walls due to subendothelial extension of the mesangium. The term membranoproliferative glomerulonephritis is often employed to denote a general pattern of glomerular injury seen in a variety of disease processes that share a common pathogenetic mechanism, rather than to describe a single disease entity.
HP:0005421	Decreased serum complement C3	A reduced level of the complement component C3 in circulation.
HP:0002725	Systemic lupus erythematosus	A chronic, relapsing, inflammatory, and often febrile multisystemic disorder of connective tissue, characterized principally by involvement of the skin, joints, kidneys, and serosal membranes.
HP:0002718	Recurrent bacterial infections	Increased susceptibility to bacterial infections, as manifested by recurrent episodes of bacterial infection.
HP:0005430	Reccurent Neisserial infections	Recurrent infections by bacteria of the genus Neisseria, including N. meningitidis (one of the most common causes of bacterial meningitis).

Source: OMIM Clinical synopsis- #613779; Creation date: 15.06.1995, John F. Jackson; revised: 20.04.2011, Cassandra L. Kniffin

Complement component 4 deficiency (C4a, C4b)

No frequency available

Term Identifier	Term Name	Definition
HP:0000979	Purpura	Purpura (from Latin: purpura, meaning "purple") is the appearance of red or purple discolorations on the skin that do not blanch on applying pressure. They are caused by bleeding underneath the skin. This term refers to an abnormally increased susceptibility to developing purpura. Purpura are larger than petechiae.
HP:0002633	Vasculitis	Inflammation of blood vessel.
HP:0004431	Complement deficiency	An immunodeficiency defined by the absent or suboptimal functioning of one of the complement system proteins.
HP:0002725	Systemic lupus erythematosus	A chronic, relapsing, inflammatory, and often febrile multisystemic disorder of connective tissue, characterized principally by involvement of the skin, joints, kidneys, and serosal membranes.
HP:0000099	Glomerulonephritis	Inflammation of the renal glomeruli.
HP:0000992	Cutaneous photosensitivity	An increased sensitivity of the skin to light. Photosensitivity may result in a rash upon exposure to the sun (which is known as photodermatosis). Photosensitivity can be diagnosed by phototests in which light is shone on small areas of skin.
HP:0005430	Recurrent Neisserial infections	Recurrent infections by bacteria of the genus Neisseria, including N. meningitidis (one of the most common causes of bacterial meningitis).
HP:0045043	Decreased serum complement C4a	A reduced level of the complement component C4a in circulation.
HP:0045044	Decreased serum complement C4b	A reduced level of the complement component C4b in circulation.
HP:0200120	Chronic active hepatitis	Chronic hepatitis associated with recurrent clinical exacerbations, extrahepatic manifestations, and progression to cirrhosis.
HP:0001287	Meningitis	Inflammation of the meninges.

Source: OMIM Clinical synopsis- #614380; Creation date: 15.06.1995, John F. Jackson; reviewed: 15.05.2000, Ada Hamosh
OMIM # 614379; Creation date: 06.12.2011, Matthew B. Gross; updated: 29.03.2012, Cassandra L. Kniffin

Complement component 5 deficiency

No frequency available

Term Identifier	Term Name	Definition
HP:0002719	Recurrent infections	Increased susceptibility to infections.
HP:0007569	Generalized seborrheic dermatitis	Seborrheic dermatitis that is not localized to any one particular region.
HP:0004431	Complement deficiency	An immunodeficiency defined by the absent or suboptimal functioning of one of the complement system proteins.
HP:0000007	Autosomal recessive inheritance	A mode of inheritance that is observed for traits related to a gene encoded on one of the autosomes (i.e., the human chromosomes 1-22) in which a trait manifests in individuals with two pathogenic alleles, either homozygotes (two copies of the same mutant allele) or compound heterozygotes (whereby each copy of a gene has a distinct mutant allele).
HP:0002041	Intractable diarrhea	
HP:0006946	Recurrent meningitis	An increased susceptibility to meningitis as manifested by a medical history of recurrent episodes of meningitis.

Source: OMIM #609536; Creation date: 17.08.2005, Victor A. McKusick; updated: 23.03.2011, Paul J. Converse

Complement component 6 deficiency

No frequency available

Term Identifier	Term Name	Definition
HP:0004431	Complement deficiency	An immunodeficiency defined by the absent or suboptimal functioning of one of the complement system proteins.
HP:0005381	Recurrent meningococcal disease	Recurrent infections by Neisseria meningitidis (one of the most common causes of bacterial meningitis), which is also known as meningococcus.
HP:0000007	Autosomal recessive inheritance	A mode of inheritance that is observed for traits related to a gene encoded on one of the autosomes (i.e., the human chromosomes 1-22) in which a trait manifests in individuals with two pathogenic alleles, either homozygotes (two copies of the same mutant allele) or compound heterozygotes (whereby each copy of a gene has a distinct mutant allele).

Source: OMIM #612446; Creation date: 01.12.2008, Matthew B. Gross; updated: 23.03.2011, Paul J. Converse

Complement component 7 deficiency

No frequency available

Term Identifier	Term Name	Definition
HP:0004431	Complement deficiency	An immunodeficiency defined by the absent or suboptimal functioning of one of the complement system proteins.
HP:0005381	Recurrent meningococcal disease	Recurrent infections by Neisseria meningitidis (one of the most common causes of bacterial meningitis), which is also known as meningococcus.
HP:0000007	Autosomal recessive inheritance	A mode of inheritance that is observed for traits related to a gene encoded on one of the autosomes (i.e., the human chromosomes 1-22) in which a trait manifests in individuals with two pathogenic alleles, either homozygotes (two copies of the same mutant allele) or compound heterozygotes (whereby each copy of a gene has a distinct mutant allele).

Source: OMIM #610102; Creation date: 10.05.2006, Victor A. McKusick; updated: 23.03.2011, Paul J. Converse

Complement component 8 deficiency (C8A, C8B, C8G)

No frequency available

Term Identifier	Term Name	Definition
HP:0000007	Autosomal recessive inheritance	A mode of inheritance that is observed for traits related to a gene encoded on one of the autosomes (i.e., the human chromosomes 1-22) in which a trait manifests in individuals with two pathogenic alleles, either homozygotes (two copies of the same mutant allele) or compound heterozygotes (whereby each copy of a gene has a distinct mutant allele).
HP:0001287	Meningitis	Inflammation of the meninges.
HP:0004434	C8 deficiency	A reduced level of the complement component C8 in circulation.
HP:0002725	Systemic lupus erythematosus	A chronic, relapsing, inflammatory, and often febrile multisystemic disorder of connective tissue, characterized principally by involvement of the skin, joints, kidneys, and serosal membranes.
HP:0005430	Recurrent Neisserial infections	Recurrent infections by bacteria of the genus Neisseria, including N. meningitidis (one of the most common causes of bacterial meningitis).

Source: OMIM Clinical synopsis #613790 – Creation date: 15.06.1995, John F. Jackson
OMIM Clinical synopsis #613789 – Creation date: 05.03.2012, Joanna S. Amberger

Complement component 9 deficiency

No frequency available

Term Identifier	Term Name	Definition
HP:0012308	Decreased serum complement C9	A reduced level of the complement component C9 in circulation.
HP:0005430	Recurrent Neisserial infections	Recurrent infections by bacteria of the genus Neisseria, including N. meningitidis (one of the most common causes of bacterial meningitis).

Source: OMIM #613825 – Creation date: 23.03.2011, Matthew B. Gross

CSR defects and HIGM syndrome

No frequency available

Term Identifier	Term Name	Definition
HP:0000007	Autosomal recessive inheritance	A mode of inheritance that is observed for traits related to a gene encoded on one of the autosomes (i.e., the human chromosomes 1-22) in which a trait manifests in individuals with two pathogenic alleles, either homozygotes (two copies of the same mutant allele) or compound heterozygotes (whereby each copy of a gene has a distinct mutant allele).
HP:0200117	Recurrent upper and lower respiratory tract infections	Increased susceptibility to upper and lower respiratory tract infections, as manifested by recurrent episodes of upper and lower respiratory tract infections.
HP:0000031	Epididymitis	The presence of inflammation of the epididymis.
HP:0002716	Lymphadenopathy	Enlargment (swelling) of a lymph node.
HP:0003496	Increased circulating IgM level	An abnormally increased level of immunoglobulin M in blood.
HP:0002720	Decreased circulating IgA level	Decreased levels of immunoglobulin A (IgA).
HP:0004315	Decreased circulating IgG level	An abnormally decreased level of immunoglobulin G (IgG) in blood.
HP:0002959	Impaired Ig class switch recombination	An impairment of the class-switch recombination process that normally leads B lymphocytes to produce IgG, IgA, or IgE.
HP:0002718	Recurrent bacterial infections	Increased susceptibility to bacterial infections, as manifested by recurrent episodes of bacterial infection.
HP:0002721	Immunodeficiency	Failure of the immune system to protect the body adequately from infection, due to the absence or insufficiency of some component process or substance.
HP:0002110	Bronchiectasis	Persistent abnormal dilatation of the bronchi owing to localized and irreversible destruction and widening of the large airways.
HP:0004798	Recurrent infection of the gastrointestinal tract	Recurrent infection of the gastrointestinal tract.
HP:0002754	Osteomyelitis	Osteomyelitis is an inflammatory process accompanied by bone destruction and caused by an infecting microorganism.
HP:0001890	Autoimmune hemolytic anemia	An autoimmune form of hemolytic anemia.
HP:0001973	Autoimmune thrombocytopenia	The presence of thrombocytopenia in combination with detection of antiplatelet antibodies.
HP:0002849	Absence of lymph node germinal center	Absence of germinal centers in lymph nodes. Germinal centers are the parts of lymph nodes in which B lymphocytes proliferate, differentiate, mutate through somatic hypermutation and class switch during antibody responses.
HP:0002863	Myelodysplasia	Clonal hematopoietic stem cell disorders characterized by dysplasia (ineffective production) in one or more

		hematopoietic cell lineages, leading to anemia and cytopenia.

Source: OMIM Clinical synopsis #608106 – Creation date: 08.10.2004, Kelly A. Przylepa;
OMIM Clinical synopsis #608184 – Creation date: 20.01.2004, Kelly A. Przylepa;
OMIM Clinical synopsis #605258 – Creation date: 06.10.2004, Kelly A. Przylepa

Chédiak Higashi syndrome (CHS)

Very frequent

Term Identifier	Term Name	Definition
HP:0001881	Abnormal leukocyte morphology	An abnormality of leukocytes.
HP:0012145	Abnormality of multiple cell lineages in the bone marrow	
HP:0000504	Abnormality of vision	Abnormality of eyesight (visual perception).
HP:0001903	Anemia	A reduction in erythrocytes volume or hemoglobin concentration.
HP:0001284	Areflexia	Absence of neurologic reflexes such as the knee-jerk reaction.
HP:0000978	Bruising susceptibility	An ecchymosis (bruise) refers to the skin discoloration caused by the escape of blood into the tissues from ruptured blood vessels. This term refers to an abnormally increased susceptibility to bruising. The corresponding phenotypic abnormality is generally elicited on medical history as a report of frequent ecchymoses or bruising without adequate trauma.
HP:0001945	Fever	Elevated body temperature due to failed thermoregulation.
HP:0007513	Generalized hypopigmentation	
HP:0011358	Generalized hypopigmentation of hair	Reduced pigmentation of hair diffusely.
HP:0000225	Gingival bleeding	Hemorrhage affecting the gingiva.
HP:0001263	Global developmental delay	A delay in the achievement of motor or mental milestones in the domains of development of a child, including motor skills, speech and language, cognitive skills, and social and emotional skills. This term should only be used to describe children younger than five years of age.
HP:0002240	Hepatomegaly	Abnormally increased size of the liver.
HP:0002721	Immunodeficiency	Failure of the immune system to protect the body adequately from infection, due to the absence or insufficiency of some component process or substance.
HP:0007730	Iris hypopigmentation	An abnormal reduction in the amount of pigmentation of the iris.
HP:0002716	Lymphadenopathy	Enlargment (swelling) of a lymph node.
HP:0001875	Neutropenia	An abnormally low number of neutrophils in the peripheral blood.
HP:0003401	Paresthesia	Abnormal sensations such as tingling, pricking, or numbness of the skin with no apparent physical cause.
HP:0000704	Periodontitis	Inflammation of the periodontium.
HP:0009830	Peripheral neuropathy	Peripheral neuropathy is a general term for any disorder of the peripheral nervous system. The main clinical features used to classify peripheral neuropathy are

		distribution, type (mainly demyelinating versus mainly axonal), duration, and course.
HP:0100838	Recurrent cutaneous abscess formation	An increased susceptibility to cutaneous abscess formation, as manifested by a medical history of recurrent cutaneous abscesses.
HP:0002205	Recurrent respiratory infections	An increased susceptibility to respiratory infections as manifested by a history of recurrent respiratory infections.
HP:0200042	Skin ulcer	A discontinuity of the skin exhibiting complete loss of the epidermis and often portions of the dermis and even subcutaneous fat.
HP:0001744	Splenomegaly	Abnormal increased size of the spleen.
HP:0011364	White hair	Hypopigmented hair that appears white.
HP:0001873	Thrombocytopenia	A reduction in the number of circulating thrombocytes.

Frequent

Term Identifier	Term Name	Definition
HP:0000646	Amblyopia	Reduced visual acuity that is uncorrectable by lenses in the absence of detectable anatomic defects in the eye or visual pathways.
HP:0000969	Edema	An abnormal accumulation of fluid beneath the skin, or in one or more cavities of the body.
HP:0000421	Epistaxis	Epistaxis, or nosebleed, refers to a hemorrhage localized in the nose.
HP:0002665	Lymphoma	A cancer originating in lymphocytes and presenting as a solid tumor of lymhpoid cells.
HP:0000639	Nystagmus	Rhythmic, involuntary oscillations of one or both eyes related to abnormality in fixation, conjugate gaze, or vestibular mechanisms.
HP:0000613	Photophobia	Excessive sensitivity to light with the sensation of discomfort or pain in the eyes due to exposure to bright light.
HP:0001250	Seizures	Seizures are an intermittent abnormality of the central nervous system due to a sudden, excessive, disorderly discharge of cerebral neurons and characterized clinically by some combination of disturbance of sensation, loss of consciousness, impairment of psychic function, or convulsive movements. The term epilepsy is used to describe chronic, recurrent seizures.
HP:0001337	Tremor	An unintentional, oscillating to-and-fro muscle movement about a joint axis.

Occasional

Term Identifier	Term Name	Definition
HP:0002071	Abnormality of extrapyramidal motor function	A neurological condition related to lesions of the basal ganglia leading to typical abnormalities including akinesia (inability to initiate changes in activity and perform volitional movements rapidly and easily), muscular rigidity (continuous contraction of muscles with constant resistance to passive movement), chorea (widespread arrhythmic movements of a forcible, rapid, jerky, and restless nature), athetosis (inability to sustain the muscles

		of the fingers, toes, or other group of muscles in a fixed position), and akathisia (inability to remain motionless).
HP:0100022	Abnormality of movement	An abnormality of movement with a neurological basis characterized by changes in coordination and speed of voluntary movements.
HP:0001251	Ataxia	Cerebellar ataxia refers to ataxia due to dysfunction of the cerebellum. This causes a variety of elementary neurological deficits including asynergy (lack of coordination between muscles, limbs and joints), dysmetria (lack of ability to judge distances that can lead to under- oder overshoot in grasping movements), and dysdiadochokinesia (inability to perform rapid movements requiring antagonizing muscle groups to be switched on and off repeatedly).
HP:0001631	Atrial septal defect	Atrial septal defect (ASD) is a congenital abnormality of the interatrial septum that enables blood flow between the left and right atria via the interatrial septum.
HP:0002067	Bradykinesia	Bradykinesia literally means slow movement, and is used clinically to denote a slowness in the execution of movement (in contrast to hypokinesia, which is used to refer to slowness in the initiation of movement).
HP:0001272	Cerebellar atrophy	Atrophy (wasting) of the cerebellum.
HP:0002376	Developmental regression	Loss of developmental skills, as manifested by loss of developmental milestones.
HP:0002239	Gastrointestinal hemorrhage	Hemorrhage affecting the gastrointestinal tract.
HP:0007440	Generalized hyperpigmentation	
HP:0000995	Melanocytic nevus	A oval and round, colored (usually medium-to dark brown, reddish brown, or flesh colored) lesion. Typically, a melanocytic nevus is less than 6 mm in diameter, but may be much smaller or larger.
HP:0002063	Rigidity	Continuous involuntary sustained muscle contraction. When an affected muscle is passively stretched, the degree of resistance remains constant regardless of the rate at which the muscle is stretched. This feature helps to distinguish rigidity from muscle spasticity.

Source: HPO-ORDO Ontological Module - Validation association date: 01.06.2016

Chronic granulomatous disease (CGD)

Very frequent

Term Identifier	Term Name	Definition
HP:0001874	Abnormality of neutrophils	A neutrophil abnormality.
HP:0006510	Chronic obstructive pulmonary disease	An anomaly that is characterized progressive airflow obstruction that is only partly reversible, inflammation in the airways, and systemic effects or comorbities.
HP:0000992	Cutaneous photosensitivity	An increased sensitivity of the skin to light. Photosensitivity may result in a rash upon exposure to the sun (which is known as photodermatosis). Photosensitivity can be diagnosed by phototests in which light is shone on small areas of skin.
HP:0001945	Fever	Elevated body temperature due to failed thermoregulation.
HP:0002240	Hepatomegaly	Abnormally increased size of the liver.
HP:0001034	Hypermelanotic macule	A hyperpigmented circumscribed area of change in normal skin color without elevation or depression of any size.
HP:0012733	Macule	A flat, distinct, discolored area of skin less than 1 cm wide that does not involve any change in the thickness or texture of the skin.
HP:0002024	Malabsorption	Impaired ability to absorb one or more nutrients from the intestine.
HP:0100721	Mediastinal lymphadenopathy	Swelling of lymph nodes within the mediastinum, the central compartment of the thoracic cavities that contains the heart and the great vessels, the esophagus, and trachea and other structures including lymph nodes.
HP:0000388	Otitis media	Inflammation or infection of the middle ear.
HP:0002021	Pyloric stenosis	An abnormal narrowing of the pylorus.
HP:0002205	Recurrent respiratory infections	An increased susceptibility to respiratory infections as manifested by a history of recurrent respiratory infections.
HP:0000246	Sinusitis	Inflammation of the paranasal sinuses owing to a viral, bacterial, or fungal infection, allergy, or an autoimmune reaction.
HP:0002575	Tracheoesophageal fistula	An abnormal connection (fistula) between the esophagus and the trachea.

Occasional

Term Identifier	Term Name	Definition
HP:0000964	Eczema	Eczema is a form of dermatitis. The term eczema is broadly applied to a range of persistent skin conditions and can be related to a number of underlying conditions. Manifestations of eczema can include dryness and recurring skin rashes with redness, skin edema, itching and dryness, crusting, flaking, blistering, cracking, oozing, or bleeding.
HP:0000230	Gingivitis	Inflammation of the gingiva.

HP:0100533	Inflammatory abnormality of the eye	Inflammation of the eye, parts of the eye or the periorbital region.
HP:0100523	Liver abscess	The presence of an abscess of the liver.
HP:0001287	Meningitis	Inflammation of the meninges.
HP:0100806	Sepsis	Systemic inflammatory response to infection.
HP:0200042	Skin ulcer	A discontinuity of the skin exhibiting complete loss of the epidermis and often portions of the dermis and even subcutaneous fat.
HP:0001744	Splenomegaly	Abnormal increased size of the spleen.

Source: HPO-ORDO Ontological Module - Validation association date: 01.06.2016

Clericuzio-type poikiloderma with neutropenia syndrome

Occasional

Term Identifier	Term Name	Definition
HP:0000316	Hypertelorism	Interpupillary distance more than 2 SD above the mean (alternatively, the appearance of an increased interpupillary distance or widely spaced eyes).
HP:0000272	Malar flattening	Underdevelopment of the malar prominence of the jugal bone (zygomatic bone in mammals), appreciated in profile, frontal view, and/or by palpation.

Rare

Term Identifier	Term Name	Definition
HP:0003236	Elevated serum creatine kinase	An elevation of the level of the enzyme creatine kinase (also known as creatine phosphokinase, CPK; EC 2.7.3.2) in the blood. CPK levels can be elevated in a number of clinical disorders such as myocardial infarction, rhabdomyolysis, and muscular dystrophy.
HP:0025435	Increased lactate dehydrogenase activity	An elevated activity of the enzyme lactate dehydrogenase in serum.
HP:0011800	Midface retrusion	Posterior positions and/or vertical shortening of the infraorbital and perialar regions, or increased concavity of the face and/or reduced nasolabial angle.
HP:0001875	Neutropenia	An abnormally low number of neutrophils in the peripheral blood.
HP:0007556	Plantar hyperkeratosis	Hyperkeratosis affecting the sole of the foot.
HP:0001029	Poikiloderma	Poikiloderma refers to a patch of skin with (1) reticulated hypopigmentation and hyperpigmentation, (2) wrinkling secondary to epidermal atrophy, and (3) telangiectasias.
HP:0000403	Recurrent otitis media	Increased susceptibility to otitis media, as manifested by recurrent episodes of otitis media.
HP:0006532	Recurrent pneumonia	An increased susceptibility to pneumonia as manifested by a history of recurrent episodes of pneumonia.
HP:0011108	Recurrent sinusitis	A recurrent form of sinusitis.
HP:0004322	Short stature	A height below that which is expected according to age and gender norms. Although there is no universally accepted definition of short stature, many refer to "short stature" as height more than 2 standard deviations below the mean for age and gender (or below the 3rd percentile for age and gender dependent norms).
HP:0001744	Splenomegaly	Abnormal increased size of the spleen.

No frequency available

Term Identifier	Term Name	Definition

HP:0000007	Autosomal recessive inheritance	A mode of inheritance that is observed for traits related to a gene encoded on one of the autosomes (i.e., the human chromosomes 1-22) in which a trait manifests in individuals with two pathogenic alleles, either homozygotes (two copies of the same mutant allele) or compound heterozygotes (whereby each copy of a gene has a distinct mutant allele).
HP:0000498	Blepharitis	Inflammation of the eyelids.
HP:0000509	Conjunctivitis	Inflammation of the conjunctiva.

Source: National Center for Advancing Translational Sciences – GARD (last updated 01.08.2019);
OMIM Clinical synopsis #604173 – Creation date: 02.11.2011, Marla J.F. O´Neill

COHEN syndrome

Very frequent

Term Identifier	Term Name	Definition
HP:0000164	Abnormality of the dentition	Any abnormality of the teeth.
HP:0000499	Abnormal eyelash morphology	An abnormality of the eyelashes.
HP:0000492	Abnormal eyelid morphology	An abnormality of the eyelids.
HP:0010295	Aplasia/Hypoplasia of the tongue	Absence or underdevelopment of the tongue.
HP:0001166	Arachnodactyly	Abnormally long and slender fingers ("spider fingers").
HP:0010669	Hypoplasia of the zygomatic bone	Underdevelopment of the zygomatic bone [UBERON_0001683]. That is, a reduction in size of the zygomatic bone, including the zygomatic process of the temporal bone of the skull, which forms part of the zygomatic arch.
HP:0001135	Chorioretinal dystrophy	
HP:0000494	Downslanted palpebral fissures	The palpebral fissure inclination is more than two standard deviations below the mean.
HP:0000212	Gingival overgrowth	Hyperplasia of the gingiva (that is, a thickening of the soft tissue overlying the alveolar ridge. The degree of thickening ranges from involvement of the interdental papillae alone to gingival overgrowth covering the entire tooth crown.
HP:0001263	Global developmental delay	A delay in the achievement of motor or mental milestones in the domains of development of a child, including motor skills, speech and language, cognitive skills, and social and emotional skills. This term should only be used to describe children younger than five years of age.
HP:0002705	High, narrow palate	The presence of a high and narrow palate.
HP:0000327	Hypoplasia of the maxilla	Abnormally small dimension of the Maxilla. Usually creating a malocclusion or malalignment between the upper and lower teeth or resulting in a deficient amount of projection of the base of the nose and lower midface region.
HP:0001249	Intellectual disability	Subnormal intellectual functioning which originates during the developmental period. Intellectual disability, previously referred to as mental retardation, has been defined as an IQ score below 70.
HP:0000527	Long eyelashes	Mid upper eyelash length >10 mm or increased length of the eyelashes (subjective).
HP:0000294	Low anterior hairline	Distance between the hairline (trichion) and the glabella (the most prominent point on the frontal bone above the root of the nose), in the midline, more than two SD below the mean. Alternatively, an apparently decreased distance between the hairline and the glabella.
HP:0000252	Microcephaly	Head circumference below 2 standard deviations below the mean for age and gender.
HP:0000347	Micrognathia	Developmental hypoplasia of the mandible.

HP:0001252	Muscular hypotonia	Muscular hypotonia is an abnormally low muscle tone (the amount of tension or resistance to movement in a muscle), often involving reduced muscle strength. Hypotonia is characterized by a diminished resistance to passive stretching.
HP:0000545	Myopia	An abnormality of refraction characterized by the ability to see objects nearby clearly, while objects in the distance appear blurry.
HP:0002167	Neurological speech impairment	
HP:0001875	Neutropenia	An abnormally low number of neutrophils in the peripheral blood.
HP:0000194	Open mouth	A facial appearance characterized by a permanently or nearly permanently opened mouth.
HP:0000426	Prominent nasal bridge	Anterior positioning of the nasal root in comparison to the usual positioning for age.
HP:0009804	Reduced number of teeth	The presence of a reduced number of teeth as in Hypodontia or as in Anodontia.
HP:0001852	Sandal gap	A widely spaced gap between the first toe (the great toe) and the second toe.
HP:0000322	Short philtrum	Distance between nasal base and midline upper lip vermilion border more than 2 SD below the mean. Alternatively, an apparently decreased distance between nasal base and midline upper lip vermilion border.
HP:0011308	Slender toe	Toes that are disproportionately narrow (reduced girth) for the hand/foot size or build of the individual.
HP:0001182	Tapered finger	The gradual reduction in girth of the finger from proximal to distal.
HP:0000574	Thick eyebrow	Increased density/number and/or increased diameter of eyebrow hairs.

Frequent

Term Identifier	Term Name	Definition
HP:0001000	Abnormality of skin pigmentation	An abnormality of the pigmentation of the skin.
HP:0200046	Cat cry	The presence of a characteristic high-pitched cry that sounds similar to the meowing of a kitten.
HP:0004209	Clinodactyly of the 5th finger	Clinodactyly refers to a bending or curvature of the fifth finger in the radial direction (i.e., towards the 4th finger).
HP:0002967	Cubitus valgus	Abnormal positioning in which the elbows are turned out.
HP:0001558	Decreased fetal movement	An abnormal reduction in quantity or strength of fetal movements.
HP:0000823	Delayed puberty	Passing the age when puberty normally occurs with no physical or hormonal signs of the onset of puberty.
HP:0001531	Failure to thrive in infancy	
HP:0008872	Feeding difficulties in infancy	Impaired feeding performance of an infant as manifested by difficulties such as weak and ineffective sucking, brief bursts of sucking, and falling asleep during sucking. There may be difficulties with chewing or maintaining attention.

HP:0006101	Finger syndactyly	Webbing or fusion of the fingers, involving soft parts only or including bone structure. Bony fusions are referred to as "bony" Syndactyly if the fusion occurs in a radio-ulnar axis. Fusions of bones of the fingers in a proximo-distal axis are referred to as "Symphalangism".
HP:0002857	Genu valgum	The legs angle inward, such that the knees are close together and the ankles far apart.
HP:0001511	Intrauterine growth retardation	An abnormal restriction of fetal growth with fetal weight below the tenth percentile for gestational age.
HP:0005692	Joint hyperflexibility	Increased mobility and flexibility in the joint due to the tension in tissues such as ligaments and muscles.
HP:0001572	Macrodontia	Increased size of the teeth, which can be defined as a mesiodistal tooth diameter (width) more than 2 SD above mean for age. Alternatively, an apparently increased maximum width of the tooth.
HP:0004283	Narrow palm	For children from birth to 4 years of age, the palm width is more than 2 SD below the mean; for children from 4 to 16 years of age the palm width is below the 5th centile; or, the width of the palm appears disproportionately narrow for its length.
HP:0001513	Obesity	Accumulation of substantial excess body fat.
HP:0004322	Short stature	A height below that which is expected according to age and gender norms. Although there is no universally accepted definition of short stature, many refer to "short stature" as height more than 2 standard deviations below the mean for age and gender (or below the 3rd percentile for age and gender dependent norms).
HP:0100874	Thick hair	Increased density of hairs, i.e., and elevated number of hairs per unit area.
HP:0001612	Weak cry	

Occasional

Term Identifier	Term Name	Definition
HP:0007703	Abnormality of retinal pigmentation	
HP:0003272	Abnormality of the hip bone	An abnormality of the hip bone.
HP:0009906	Aplasia/Hypoplasia of the earlobes	Absence or underdevelopment of the ear lobes.
HP:0000028	Cryptorchidism	Testis in inguinal canal. That is, absence of one or both testes from the scrotum owing to failure of the testis or testes to descend through the inguinal canal to the testis.
HP:0000612	Iris coloboma	A coloboma of the iris.
HP:0002808	Kyphosis	Exaggerated anterior convexity of the thoracic vertebral column.
HP:0000568	Microphthalmia	A developmental anomaly characterized by abnormal smallness of one or both eyes.
HP:0001634	Mitral valve prolapse	One or both of the leaflets (cusps) of the mitral valve bulges back into the left atrium upon contraction of the left ventricle.

HP:0000639	Nystagmus	Rhythmic, involuntary oscillations of one or both eyes related to abnormality in fixation, conjugate gaze, or vestibular mechanisms.
HP:0000648	Optic atrophy	Atrophy of the optic nerve. Optic atrophy results from the death of the retinal ganglion cell axons that comprise the optic nerve and manifesting as a pale optic nerve on fundoscopy.
HP:0000767	Pectus excavatum	A defect of the chest wall characterized by a depression of the sternum, giving the chest ("pectus") a caved-in ("excavatum") appearance.
HP:0000384	Preauricular skin tag	A rudimentary tag of skin often containing ear tissue including a core of cartilage and located just anterior to the auricle (outer part of the ear).
HP:0002650	Scoliosis	The presence of an abnormal lateral curvature of the spine.
HP:0001250	Seizures	Seizures are an intermittent abnormality of the central nervous system due to a sudden, excessive, disorderly discharge of cerebral neurons and characterized clinically by some combination of disturbance of sensation, loss of consciousness, impairment of psychic function, or convulsive movements. The term epilepsy is used to describe chronic, recurrent seizures.
HP:0000407	Sensorineural hearing impairment	A type of hearing impairment in one or both ears related to an abnormal functionality of the cochlear nerve.
HP:0000486	Strabismus	A misalignment of the eyes so that the visual axes deviate from bifoveal fixation. The classification of strabismus may be based on a number of features including the relative position of the eyes, whether the deviation is latent or manifest, intermittent or constant, concomitant or otherwise and according to the age of onset and the relevance of any associated refractive error.
HP:0001629	Ventricular septal defect	A hole between the two bottom chambers (ventricles) of the heart. The defect is centered around the most superior aspect of the ventricular septum.

Source: HPO-ORDO Ontological Module - Validation association date: 01.06.2016

Common variable immunodeficiency disorders (CVID)

Very frequent

Term Identifier	Term Name	Definition
HP:0001973	Autoimmune thrombocytopenia	The presence of thrombocytopenia in combination with detection of antiplatelet antibodies.
HP:0000248	Brachycephaly	An abnormality of skull shape characterized by a decreased anterior-posterior diameter. That is, a cephalic index greater than 81%. Alternatively, an apparently shortened anteroposterior dimension (length) of the head compared to width.
HP:0000389	Chronic otitis media	Chronic otitis media refers to fluid, swelling, or infection of the middle ear that does not heal and may cause permanent damage to the ear.
HP:0002721	Immunodeficiency	Failure of the immune system to protect the body adequately from infection, due to the absence or insufficiency of some component process or substance.
HP:0001888	Lymphopenia	A reduced number of lymphocytes in the blood.
HP:0000388	Otitis media	Inflammation or infection of the middle ear.
HP:0002090	Pneumonia	Inflammation of any part of the lung parenchyma.
HP:0002205	Recurrent respiratory infections	An increased susceptibility to respiratory infections as manifested by a history of recurrent respiratory infections.
HP:0002837	Recurrent bronchitis	An increased susceptibility to bronchitis as manifested by a history of recurrent bronchitis.

Frequent

Term Identifier	Term Name	Definition
HP:0001392	Abnormality of the liver	An abnormality of the liver.
HP:0002023	Anal atresia	Congenital absence of the anus, i.e., the opening at the bottom end of the intestinal tract.
HP:0002110	Bronchiectasis	Persistent abnormal dilatation of the bronchi owing to localized and irreversible destruction and widening of the large airways.
HP:0002910	Elevated hepatic transaminase	Elevations of the levels of SGOT and SGPT in the serum. SGOT (serum glutamic oxaloacetic transaminase) and SGPT (serum glutamic pyruvic transaminase) are transaminases primarily found in the liver and heart and are released into the bloodstream as the result of liver or heart damage. SGOT and SGPT are used clinically mainly as markers of liver damage.
HP:0001878	Hemolytic anemia	A type of anemia caused by premature destruction of red blood cells (hemolysis).
HP:0002716	Lymphadenopathy	Enlargment (swelling) of a lymph node.
HP:0000979	Purpura	Purpura (from Latin: purpura, meaning "purple") is the appearance of red or purple discolorations on the skin that do not blanch on applying pressure. They are caused by bleeding underneath the skin. This term refers to an

		abnormally increased susceptibility to developing purpura. Purpura are larger than petechiae.
HP:0001744	Splenomegaly	Abnormal increased size of the spleen.

Occasional

Term Identifier	Term Name	Definition
HP:0002829	Arthralgia	Joint pain.
HP:0002097	Emphysema	
HP:0001531	Failure to thrive in infancy	
HP:0100723	Gastrointestinal stroma tumor	
HP:0002665	Lymphoma	A cancer originating in lymphocytes and presenting as a solid tumor of lymhpoid cells.
HP:0006783	Posterior pharyngeal cleft	
HP:0002091	Restrictive ventilatory defect	A functional defect characterized by reduced total lung capacity (TLC) not associated with abnormalities of expiratory airflow or airway resistance. Restrictive lung disease may be caused by alterations in lung parenchyma or because of a disease of the pleura, chest wall, or neuromuscular apparatus.
HP:0002633	Vasculitis	Inflammation of blood vessel.

Source: HPO-ORDO Ontological Module - Validation association date: 01.06.2016

Congenital neutropenia

Always present

Term Identifier	Term Name	Definition
HP:0001875	Neutropenia	An abnormally low number of neutrophils in the peripheral blood.

Very fequent

Term Identifier	Term Name	Definition
HP:0002718	Recurrent bacterial infections	Increased susceptibility to bacterial infections, as manifested by recurrent episodes of bacterial infection.
HP:0004429	Recurrent viral infections	Increased susceptibility to viral infections, as manifested by recurrent episodes of viral infection.

Frequent

Term Identifier	Term Name	Definition
HP:0002027	Abdominal pain	An unpleasant sensation characterized by physical discomfort (such as pricking, throbbing, or aching) and perceived to originate in the abdomen.
HP:0002014	Diarrhea	Abnormally increased frequency of loose or watery bowel movements.
HP:0001945	Fever	Elevated body temperature due to failed thermoregulation.
HP:0000230	Gingivitis	Inflammation of the gingiva.
HP:0001888	Lymphopenia	A reduced number of lymphocytes in the blood.
HP:0012311	Monocytosis	An increased number of circulating monocytes.
HP:0000155	Oral ulcer	Erosion of the mucous mebrane of the mouth with local excavation of the surface, resulting from the sloughing of inflammatory necrotic tissue.
HP:0000704	Periodontitis	Inflammation of the periodontium.
HP:0025439	Pharyngitis	Inflammation (due to infection or irritation) of the pharynx.
HP:0002090	Pneumonia	Inflammation of any part of the lung parenchyma.
HP:0011107	Recurrent aphthous stomatitis	Recurrent episodes of ulceration of the oral mucosa, typically presenting as painful, sharply circumscribed fibrin-covered mucosal defects with a hyperemic border.
HP:0410018	Recurrent ear infections	Increased susceptibility to ear infections, as manifested by recurrent episodes of ear infections.
HP:0001581	Recurrent skin infections	Infections of the skin that happen multiple times.
HP:0005425	Recurrent sinopulmonary infections	An increased susceptibility to infections involving both the paranasal sinuses and the lungs, as manifested by a history of recurrent sinopulmonary infections.
HP:0004798	Recurrent infection of the gastrointestinal tract	Recurrent infection of the gastrointestinal tract.
HP:0012384	Rhinitis	Inflammation of the nasal mucosa with nasal congestion.

Occasional

Term Identifier	Term Name	Definition
HP:0006721	Acute lymphoblastic leukemia	A form of acute leukemia characterized by excess lympoblasts.
HP:0004808	Acute myeloid leukemia	A form of leukemia characterized by overproduction of an early myeloid cell.
HP:0003453	Antineutrophil antibody positivity	The presence of autoantibodies in the serum that react against neutrophils.
HP:0001915	Aplastic anemia	Aplastic anemia is defined as pancytopenia with a hypocellular marrow.
HP:0100658	Cellulitis	A bacterial infection and inflammation of the skin und subcutaneous tissues.
HP:0001880	Eosinophilia	Increased count of eosinophils in the blood.
HP:0001028	Hemangioma	A hemangioma is a benign tumor characterized by blood-filled spaces lined by benign endothelial cells. A hemangioma characterized by large endothelial spaces (caverns) is called a cavernous hemangioma (in contrast to a hemangioma with small endothelial spaces, which is called capillary hemangioma).
HP:0001909	Leukemia	A cancer of the blood and bone marrow characterized by an abnormal proliferation of leukocytes.
HP:0002863	Myelodysplasia	Clonal hematopoietic stem cell disorders characterized by dysplasia (ineffective production) in one or more hematopoietic cell lineages, leading to anemia and cytopenia.
HP:0000938	Osteopenia	Osteopenia is a term to define bone density that is not normal but also not as low as osteoporosis. By definition from the World Health Organization osteopenia is defined by bone densitometry as a T score -1 to -2.5.
HP:0006480	Premature loss of teeth	Premature loss of teeth not related to trauma or neglect.
HP:0025452	Pyoderma gangrenosum	A deep skin ulcer with a well defined border, which is usually violet or blue. The ulcer edge is often undermined (worn and damaged) and the surrounding skin is erythematous and indurated. The ulcer often starts as a small papule or collection of papules, which break down to form small ulcers with a so called cat's paw appearance. These coalesce and the central area then undergoes necrosis to form a single ulcer.

Source: HPO-ORDO Ontological Module - Validation association date: 16.04.2019 - PMID:28593997, PMID:28875503

*applies only to autosomal dominant congenital neutropenia

Cyclic neutropenia

Very frequent

Term Identifier	Term Name	Definition
HP:0001903	Anemia	A reduction in erythrocytes volume or hemoglobin concentration.
HP:0012378	Fatigue	A subjective feeling of tiredness characterized by a lack of energy and motivation.
HP:0001875	Neutropenia	An abnormally low number of neutrophils in the peripheral blood.
HP:0000155	Oral ulcer	Erosion of the mucous mebrane of the mouth with local excavation of the surface, resulting from the sloughing of inflammatory necrotic tissue.
HP:0001845	Overlapping toe	Describes a foot digit resting on the dorsal surface of an adjacent digit when the foot is at rest.
HP:0001581	Recurrent skin infections	Infections of the skin that happen multiple times.
HP:0100806	Sepsis	Systemic inflammatory response to infection.

Frequent

Term Identifier	Term Name	Definition
HP:0000704	Periodontitis	Inflammation of the periodontium.

Occasional

Term Identifier	Term Name	Definition
HP:0002027	Abdominal pain	An unpleasant sensation characterized by physical discomfort (such as pricking, throbbing, or aching) and perceived to originate in the abdomen.
HP:0001879	Abnormal eosinophil morphology	An abnormal count or structure of eosinophils.
HP:0000670	Carious teeth	Caries is a multifactorial bacterial infection affecting the structure of the tooth. This term has been used to describe the presence of more than expected dental caries.
HP:0002716	Lymphadenopathy	Enlargment (swelling) of a lymph node.
HP:0002205	Recurrent respiratory infections	An increased susceptibility to respiratory infections as manifested by a history of recurrent respiratory infections.
HP:0011107	Recurrent aphthous stomatitis	Recurrent episodes of ulceration of the oral mucosa, typically presenting as painful, sharply circumscribed fibrin-covered mucosal defects with a hyperemic border.
HP:0001873	Thrombocytopenia	A reduction in the number of circulating thrombocytes.

Source: HPO-ORDO Ontological Module - Validation association date: 01.06.2016

Defects in TLR/NFkappa-B signalling

Very frequent

Term Identifier	Term Name	Definition
HP:0002721	Immunodeficiency	Failure of the immune system to protect the body adequately from infection, due to the absence or insufficiency of some component process or substance.
HP:0001875	Neutropenia	An abnormally low number of neutrophils in the peripheral blood.
HP:0002718	Recurrent bacterial infections	Increased susceptibility to bacterial infections, as manifested by recurrent episodes of bacterial infection.
HP:0007499	Recurrent staphylococcal infections	Increased susceptibility to staphylococcal infections, as manifested by recurrent episodes of staphylococcal infections.
HP:0005366	Recurrent streptococcus pneumoniae infections	Increased susceptibility to streptococcus pneumoniae infections as manifested by a history of recurrent infections by streptococcus pneumoniae.

Source: HPO-ORDO Ontological Module - Validation association date: 01.06.2016

*applies only to Immunodeficiency due to interleukin-1 receptor-associated kinase-4 deficiency

DiGeorge syndrome

Very frequent

Term Identifier	Term Name	Definition
HP:0001999	Abnormal facial shape	An abnormal morphology (form) of the face or its components.
HP:0012303	Abnormal aortic arch morphology	An anomaly of the arch of aorta.
HP:0000600	Abnormality of the pharynx	An anomaly of the pharynx, i.e., of the tubular structure extending from the base of the skull superiorly to the esophageal inlet inferiorly.
HP:0001641	Abnormal pulmonary valve morphology	Any structural abnormality of the pulmonary valve.
HP:0001631	Atrial septal defect	Atrial septal defect (ASD) is a congenital abnormality of the interatrial septum that enables blood flow between the left and right atria via the interatrial septum.
HP:0000414	Bulbous nose	Increased volume and globular shape of the anteroinferior aspect of the nose.
HP:0000175	Cleft palate	Cleft palate is a developmental defect of the palate resulting from a failure of fusion of the palatine processes and manifesting as a separation of the roof of the mouth (soft and hard palate).
HP:0000405	Conductive hearing impairment	An abnormality of vibrational conductance of sound to the inner ear leading to impairment of sensory perception of sound.
HP:0002357	Dysphasia	
HP:0000286	Epicanthus	A fold of skin starting above the medial aspect of the upper eyelid and arching downward to cover, pass in front of and lateral to the medial canthus.
HP:0000778	Hypoplasia of the thymus	Underdevelopment of the thymus.
HP:0002721	Immunodeficiency	Failure of the immune system to protect the body adequately from infection, due to the absence or insufficiency of some component process or substance.
HP:0000369	Low-set ears	Upper insertion of the ear to the scalp below an imaginary horizontal line drawn between the inner canthi of the eye and extending posteriorly to the ear.
HP:0001252	Muscular hypotonia	Muscular hypotonia is an abnormally low muscle tone (the amount of tension or resistance to movement in a muscle), often involving reduced muscle strength. Hypotonia is characterized by a diminished resistance to passive stretching.
HP:0001611	Nasal speech	A type of speech characterized by the presence of an abnormally increased nasal airflow during speech.
HP:0002691	Platybasia	A developmental malformation of the occipital bone and upper end of the cervical spine, in which the latter appears to have pushed the floor of the occipital bone upward such that there is an abnormal flattening of the skull base.
HP:0000426	Prominent nasal bridge	Anterior positioning of the nasal root in comparison to the usual positioning for age.

HP:0000506	Telecanthus	Distance between the inner canthi more than two standard deviations above the mean (objective); or, apparently increased distance between the inner canthi.
HP:0001636	Tetralogy of Fallot	A congenital cardiac malformation comprising pulmonary stenosis, overriding aorta, ventricular septum defect, and right ventricular hypertrophy. The diagnosis of TOF is made if at least three of the four above mentioned features are present.
HP:0001660	Truncus arteriosus	A single arterial trunk arises from the cardiac mass. The pulmonary arteries, aorta and coronary arteries arise from this single trunk with no evidence of another outflow tract.
HP:0000582	Upslanted palpebral fissure	The palpebral fissure inclination is more than two standard deviations above the mean for age (objective); or, the inclination of the palpebral fissure is greater than typical for age.
HP:0001629	Ventricular septal defect	A hole between the two bottom chambers (ventricles) of the heart. The defect is centered around the most superior aspect of the ventricular septum.
HP:0000431	Wide nasal bridge	Increased breadth of the nasal bridge (and with it, the nasal root).
HP:0030680	Abnormality of cardiovascular system morphology	Any structural anomaly of the heart and great vessels.

Frequent

Term Identifier	Term Name	Definition
HP:0000164	Abnormality of the dentition	Any abnormality of the teeth.
HP:0000492	Abnormal eyelid morphology	An abnormality of the eyelids.
HP:0000929	Abnormal skull morphology	An abnormality of the skull, the bony framework of the head which is comprised of eight cranial and fourteen facial bones.
HP:0100765	Abnormality of the tonsils	An abnormality of the tonsils.
HP:0001061	Acne	A skin condition in which there is an increase in sebum secretion by the pilosebaceous apparatus associated with open comedones (blackheads), closed comedones (whiteheads), and pustular nodules (papules, pustules, and cysts).
HP:0012732	Anorectal anomaly	An abnormality of the anus or rectum.
HP:0001166	Arachnodactyly	Abnormally long and slender fingers ("spider fingers").
HP:0007018	Attention deficit hyperactivity disorder	Attention deficit hyperactivity disorder (ADHD) manifests at age 2-3 years or by first grade at the latest. The main symptoms are distractibility, impulsivity, hyperactivity, and often trouble organizing tasks and projects, difficulty going to sleep, and social problems from being aggressive, loud, or impatient.
HP:0000670	Carious teeth	Caries is a multifactorial bacterial infection affecting the structure of the tooth. This term has been used to

		describe the presence of more than expected dental caries.
HP:0000389	Chronic otitis media	Chronic otitis media refers to fluid, swelling, or infection of the middle ear that does not heal and may cause permanent damage to the ear.
HP:0002019	Constipation	Infrequent or difficult evacuation of feces.
HP:0011496	Corneal neovascularization	Ingrowth of new blood vessels into the cornea.
HP:0001263	Global developmental delay	A delay in the achievement of motor or mental milestones in the domains of development of a child, including motor skills, speech and language, cognitive skills, and social and emotional skills. This term should only be used to describe children younger than five years of age.
HP:0000365	Hearing impairment	A decreased magnitude of the sensory perception of sound.
HP:0002901	Hypocalcemia	An abnormally decreased calcium concentration in the blood.
HP:0000829	Hypoparathyroidism	A condition caused by a deficiency of parathyroid hormone characterized by hypocalcemia and hyperphosphatemia.
HP:0005435	Impaired T cell function	Abnormally reduced ability of T cells to perform their functions in cell-mediated immunity.
HP:0001256	Intellectual disability, mild	Mild intellectual disability is defined as an intelligence quotient (IQ) in the range of 50-69.
HP:0000276	Long face	Facial height (length) is more than 2 standard deviations above the mean (objective); or, an apparent increase in the height (length) of the face (subjective).
HP:0000343	Long philtrum	Distance between nasal base and midline upper lip vermilion border more than 2 SD above the mean. Alternatively, an apparently increased distance between nasal base and midline upper lip vermilion border.
HP:0000272	Malar flattening	Underdevelopment of the malar prominence of the jugal bone (zygomatic bone in mammals), appreciated in profile, frontal view, and/or by palpation.
HP:0002435	Meningocele	Protrusion of the meninges through a defect of the vertebral column.
HP:0003326	Myalgia	Pain in muscle.
HP:0007271	Occipital myelomeningocele	
HP:0000396	Overfolded helix	A condition in which the helix is folded over to a greater degree than normal. That is, excessive curling of the helix edge, whereby the free edge is parallel to the plane of the ear.
HP:0000627	Posterior embryotoxon	A posterior embryotoxon is the presence of a prominent and anteriorly displaced line of Schwalbe.
HP:0000508	Ptosis	The upper eyelid margin is positioned 3 mm or more lower than usual and covers the superior portion of the iris (objective); or, the upper lid margin obscures at least part of the pupil (subjective).
HP:0000089	Renal hypoplasia	Hypoplasia of the kidney.

HP:0001051	Seborrheic dermatitis	Seborrheic dermatitis is a form of eczema which is closely related to dandruff. It causes dry or greasy peeling of the scalp, eyebrows, and face, and sometimes trunk.
HP:0000470	Short neck	Diminished length of the neck.
HP:0004322	Short stature	A height below that which is expected according to age and gender norms. Although there is no universally accepted definition of short stature, many refer to "short stature" as height more than 2 standard deviations below the mean for age and gender (or below the 3rd percentile for age and gender dependent norms).
HP:0000385	Small earlobe	Reduced volume of the earlobe.
HP:0001328	Specific learning disability	Impairment of certain skills such as reading or writing, coordination, self-control, or attention that interfere with the ability to learn. The impairment is not related to a global deficiency of intelligence.
HP:0001281	Tetany	A condition characterized by intermittent involuntary contraction of muscles (spasms) related to hypocalcemia or occasionally magnesium deficiency.

Occasional

Term Identifier	Term Name	Definition
HP:0000682	Abnormality of dental enamel	An abnormality of the dental enamel.
HP:0001646	Abnormal aortic valve morphology	Any abnormality of the aortic valve.
HP:0000765	Abnormality of the thorax	Any abnormality of the thorax (the region of the body formed by the sternum, the thoracic vertebrae and the ribs).
HP:0000130	Abnormality of the uterus	An abnormality of the uterus.
HP:0001872	Abnormal thrombocyte morphology	An abnormality of platelets.
HP:0002251	Aganglionic megacolon	An abnormality resulting from a lack of intestinal ganglion cells (i.e., an aganglionic section of bowel) that results in bowel obstruction with enlargement of the colon.
HP:0002023	Anal atresia	Congenital absence of the anus, i.e., the opening at the bottom end of the intestinal tract.
HP:0000739	Anxiety	Intense feelings of nervousness, tenseness, or panic, often in reaction to interpersonal stresses; worry about the negative effects of past unpleasant experiences and future negative possibilities; feeling fearful, apprehensive, or threatened by uncertainty; fears of falling apart or losing control.
HP:0002139	Arrhinencephaly	
HP:0001369	Arthritis	Inflammation of a joint.
HP:0002099	Asthma	Asthma is characterized by increased responsiveness of the tracheobronchial tree to multiple stimuli, leading to narrowing of the air passages with resultant dyspnea, cough, and wheezing.

HP:0100750	Atelectasis	Collapse of part of a lung associated with absence of inflation (air) of that part.
HP:0000717	Autism	Autism is a neurodevelopmental disorder characterized by impaired social interaction and communication, and by restricted and repetitive behavior. Autism begins in childhood. It is marked by the presence of markedly abnormal or impaired development in social interaction and communication and a markedly restricted repertoire of activity and interest. Manifestations of the disorder vary greatly depending on the developmental level and chronological age of the individual (DSM-IV).
HP:0002960	Autoimmunity	The occurrence of an immune reaction against the organism's own cells or tissues.
HP:0000708	Behavioral abnormality	An abnormality of mental functioning including various affective, behavioural, cognitive and perceptual abnormalities.
HP:0007302	Bipolar affective disorder	
HP:0002607	Bowel incontinence	Involuntary fecal soiling in adults and children who have usually already been toilet trained.
HP:0000518	Cataract	A cataract is an opacity or clouding that develops in the crystalline lens of the eye or in its capsule.
HP:0000453	Choanal atresia	Absence or abnormal closure of the choana (the posterior nasal aperture).
HP:0001081	Cholelithiasis	Hard, pebble-like deposits that form within the gallbladder.
HP:0006510	Chronic obstructive pulmonary disease	An anomaly that is characterized progressive airflow obstruction that is only partly reversible, inflammation in the airways, and systemic effects or comorbities.
HP:0000028	Cryptorchidism	Testis in inguinal canal. That is, absence of one or both testes from the scrotum owing to failure of the testis or testes to descend through the inguinal canal to the testis.
HP:0000716	Depressivity	Frequent feelings of being down, miserable, and/or hopeless; difficulty recovering from such moods; pessimism about the future; pervasive shame; feeling of inferior self-worth; thoughts of suicide and suicidal behavior.
HP:0000494	Downslanted palpebral fissures	The palpebral fissure inclination is more than two standard deviations below the mean.
HP:0001508	Failure to thrive	Failure to thrive (FTT) refers to a child whose physical growth is substantially below the norm.
HP:0008872	Feeding difficulties in infancy	Impaired feeding performance of an infant as manifested by difficulties such as weak and ineffective sucking, brief bursts of sucking, and falling asleep during sucking. There may be difficulties with chewing or maintaining attention.
HP:0001829	Foot polydactyly	A kind of polydactyly characterized by the presence of a supernumerary toe or toes.
HP:0002020	Gastroesophageal reflux	A condition in which the stomach contents leak backwards from the stomach into the esophagus through the lower esophageal sphincter.
HP:0002239	Gastrointestinal hemorrhage	Hemorrhage affecting the gastrointestinal tract.

HP:0000501	Glaucoma	Glaucoma refers loss of retinal ganglion cells in a characteristic pattern of optic neuropathy usually associated with increased intraocular pressure.
HP:0001161	Hand polydactyly	A kind of polydactyly characterized by the presence of a supernumerary finger or fingers.
HP:0000238	Hydrocephalus	Hydrocephalus is an active distension of the ventricular system of the brain resulting from inadequate passage of CSF from its point of production within the cerebral ventricles to its point of absorption into the systemic circulation.
HP:0000316	Hypertelorism	Interpupillary distance more than 2 SD above the mean (alternatively, the appearance of an increased interpupillary distance or widely spaced eyes).
HP:0100735	Hypertensive crisis	
HP:0000836	Hyperthyroidism	An abnormality of thyroid physiology characterized by excessive secretion of the thyroid hormones thyroxine (i.e., T4) and/or 3,3',5-triiodo-L-thyronine zwitterion (i.e., triiodothyronine or T3).
HP:0000821	Hypothyroidism	Deficiency of thyroid hormone.
HP:0001053	Hypopigmented skin patches	
HP:0000047	Hypospadias	Abnormal position of urethral meatus on the ventral penile shaft (underside) characterized by displacement of the urethral meatus from the tip of the glans penis to the ventral surface of the penis, scrotum, or perineum.
HP:0000023	Inguinal hernia	Protrusion of the contents of the abdominal cavity through the inguinal canal.
HP:0001249	Intellectual disability	Subnormal intellectual functioning which originates during the developmental period. Intellectual disability, previously referred to as mental retardation, has been defined as an IQ score below 70.
HP:0002566	Intestinal malrotation	An abnormality of the intestinal rotation and fixation that normally occurs during the development of the gut. This can lead to volvulus, or twisting of the intestine that causes obstruction and necrosis.
HP:0001511	Intrauterine growth retardation	An abnormal restriction of fetal growth with fetal weight below the tenth percentile for gestational age.
HP:0005692	Joint hyperflexibility	Increased mobility and flexibility in the joint due to the tension in tissues such as ligaments and muscles.
HP:0001601	Laryngomalacia	Laryngomalacia is a congenital abnormality of the laryngeal cartilage in which the cartilage is floppy and prolapses over the larynx during inspiration.
HP:0000252	Microcephaly	Head circumference below 2 standard deviations below the mean for age and gender.
HP:0000347	Micrognathia	Developmental hypoplasia of the mandible.
HP:0000568	Microphthalmia	A developmental anomaly characterized by abnormal smallness of one or both eyes.
HP:0005562	Multiple renal cysts	The presence of many cysts in the kidney.
HP:0011324	Multiple suture craniosynostosis	Craniosynostosis involving at least 2 cranial sutures, where the exact pattern of sutures fused has not been precisely specified.

HP:0000160	Narrow mouth	Distance between the commissures of the mouth more than 2 SD below the mean. Alternatively, an apparently decreased width of the oral aperture (subjective).
HP:0001513	Obesity	Accumulation of substantial excess body fat.
HP:0000648	Optic atrophy	Atrophy of the optic nerve. Optic atrophy results from the death of the retinal ganglion cell axons that comprise the optic nerve and manifesting as a pale optic nerve on fundoscopy.
HP:0002999	Patellar dislocation	The kneecap normally is located within the groove termed trochlea on the distal femur and can slide up and down in it. Patellar dislocation occurs if the patella fully dislocates out of the groove.
HP:0001643	Patent ductus arteriosus	In utero, the ductus arteriosus (DA) serves to divert ventricular output away from the lungs and toward the placenta by connecting the main pulmonary artery to the descending aorta. A patent ductus arteriosus (PDA) in the first 3 days of life is a physiologic shunt in healthy term and preterm newborn infants, and normally is substantially closed within about 24 hours after bith and completely closed after about three weeks. Failure of physiologcal closure is referred to a persistent or patent ductus arteriosus (PDA). Depending on the degree of left-to-right shunting, PDA can have clinical consequences.
HP:0000113	Polycystic kidney dysplasia	The presence of multiple cysts in both kidneys.
HP:0001561	Polyhydramnios	The presence of excess amniotic fluid in the uterus during pregnancy.
HP:0000979	Purpura	Purpura (from Latin: purpura, meaning "purple") is the appearance of red or purple discolorations on the skin that do not blanch on applying pressure. They are caused by bleeding underneath the skin. This term refers to an abnormally increased susceptibility to developing purpura. Purpura are larger than petechiae.
HP:0001136	Retinal arteriolar tortuosity	The presence of an increased number of twists and turns of the retinal arterioles.
HP:0100753	Schizophrenia	A mental disorder characterized by a disintegration of thought processes and of emotional responsiveness. It most commonly manifests as auditory hallucinations, paranoid or bizarre delusions, or disorganized speech and thinking, and it is accompanied by significant social or occupational dysfunction. The onset of symptoms typically occurs in young adulthood, with a global lifetime prevalence of about 0.3-0.7%.
HP:0002650	Scoliosis	The presence of an abnormal lateral curvature of the spine.
HP:0001250	Seizures	Seizures are an intermittent abnormality of the central nervous system due to a sudden, excessive, disorderly discharge of cerebral neurons and characterized clinically by some combination of disturbance of sensation, loss of consciousness, impairment of psychic function, or convulsive movements. The term epilepsy is used to describe chronic, recurrent seizures.

HP:0000322	Short philtrum	Distance between nasal base and midline upper lip vermilion border more than 2 SD below the mean. Alternatively, an apparently decreased distance between nasal base and midline upper lip vermilion border.
HP:0002414	Spina bifida	Incomplete closure of the embryonic neural tube, whereby some vertebral arches remain unfused and open. The mildest form is spina bifida occulta, followed by meningocele and meningomyelocele.
HP:0001744	Splenomegaly	Abnormal increased size of the spleen.
HP:0000486	Strabismus	A misalignment of the eyes so that the visual axes deviate from bifoveal fixation. The classification of strabismus may be based on a number of features including the relative position of the eyes, whether the deviation is latent or manifest, intermittent or constant, concomitant or otherwise and according to the age of onset and the relevance of any associated refractive error.
HP:0001762	Talipes equinovarus	Talipes equinovarus (also called clubfoot) typically has four main components: inversion and adduction of the forefoot; inversion of the heel and hindfoot; equinus (limitation of extension) of the ankle and subtalar joint; and internal rotation of the leg.
HP:0001873	Thrombocytopenia	A reduction in the number of circulating thrombocytes.
HP:0011662	Tricuspid atresia	Failure to develop of the tricuspid valve and thus lack of the normal connection between the right atrium and the right ventricle.
HP:0000262	Turricephaly	Tall head relative to width and length.
HP:0001537	Umbilical hernia	Protrusion of abdominal contents through a defect in the abdominal wall musculature around the umbilicus. Skin and subcutaneous tissue overlie the defect.
HP:0002619	Varicose veins	Enlarged and tortuous veins.
HP:0000076	Vesicoureteral reflux	Abnormal (retrograde) movement of urine from the bladder into ureters or kidneys related to inadequacy of the valvular mechanism at the ureterovesicular junction or other causes.

Source: HPO-ORDO Ontological Module - Validation association date: 01.06.2016

Dyskeratosis congenita

Very frequent

Term Identifier	Term Name	Definition
HP:0008066	Abnormal blistering of the skin	The presence of one or more bullae on the skin, defined as fluid-filled blisters more than 5 mm in diameter with thin walls.
HP:0001874	Abnormality of neutrophils	A neutrophil abnormality.
HP:0001231	Abnormal fingernail morphology	An abnormality of the fingernails.
HP:0001903	Anemia	A reduction in erythrocytes volume or hemoglobin concentration.
HP:0001034	Hypermelanotic macule	A hyperpigmented circumscribed area of change in normal skin color without elevation or depression of any size.
HP:0012733	Macule	A flat, distinct, discolored area of skin less than 1 cm wide that does not involve any change in the thickness or texture of the skin.
HP:0008404	Nail dystrophy	Onychodystrophy (nail dystrophy) refers to nail changes apart from changes of the color (nail dyschromia) and involves partial or complete disruption of the various keratinous layers of the nail plate.
HP:0002745	Oral leukoplakia	A thickened white patch on the oral mucosa that cannot be rubbed off.
HP:0001873	Thrombocytopenia	A reduction in the number of circulating thrombocytes.

Frequent

Term Identifier	Term Name	Definition
HP:0001928	Abnormality of coagulation	An abnormality of the process of blood coagulation. That is, altered ability or inability of the blood to clot.
HP:0000008	Abnormality of female internal genitalia	An abnormality of the female internal genitalia.
HP:0000164	Abnormality of the dentition	Any abnormality of the teeth.
HP:0000600	Abnormality of the pharynx	An anomaly of the pharynx, i.e., of the tubular structure extending from the base of the skull superiorly to the esophageal inlet inferiorly.
HP:0012732	Anorectal anomaly	An abnormality of the anus or rectum.
HP:0008065	Aplasia/Hypoplasia of the skin	
HP:0010624	Aplastic/hypoplastic toenail	Absence or underdevelopment of the toenail.
HP:0005528	Bone marrow hypocellularity	A reduced number of hematopoietic cells present in the bone marrow relative to marrow fat.
HP:0000670	Carious teeth	Caries is a multifactorial bacterial infection affecting the structure of the tooth. This term has been used to describe the presence of more than expected dental caries.

HP:0005374	Cellular immunodeficiency	An immunodeficiency characterized by defective cell-mediated immunity or humoral immunity.
HP:0010450	Esophageal stenosis	An abnormal narrowing of the lumen of the esophagus.
HP:0001263	Global developmental delay	A delay in the achievement of motor or mental milestones in the domains of development of a child, including motor skills, speech and language, cognitive skills, and social and emotional skills. This term should only be used to describe children younger than five years of age.
HP:0000975	Hyperhidrosis	Abnormal excessive perspiration (sweating) despite the lack of appropriate stimuli like hot and humid weather.
HP:0001053	Hypopigmented skin patches	
HP:0001511	Intrauterine growth retardation	An abnormal restriction of fetal growth with fetal weight below the tenth percentile for gestational age.
HP:0000668	Hypodontia	A developmental anomaly characterized by a reduced number of teeth, whereby up to 6 teeth are missing.
HP:0002024	Malabsorption	Impaired ability to absorb one or more nutrients from the intestine.
HP:0000704	Periodontitis	Inflammation of the periodontium.
HP:0002757	Recurrent fractures	The repeated occurrence of bone fractures (implying an abnormally increased tendency for fracture).
HP:0002205	Recurrent respiratory infections	An increased susceptibility to respiratory infections as manifested by a history of recurrent respiratory infections.
HP:0100670	Rough bone trabeculation	
HP:0004322	Short stature	A height below that which is expected according to age and gender norms. Although there is no universally accepted definition of short stature, many refer to "short stature" as height more than 2 standard deviations below the mean for age and gender (or below the 3rd percentile for age and gender dependent norms).
HP:0008070	Sparse hair	Reduced density of hairs.
HP:0200042	Skin ulcer	A discontinuity of the skin exhibiting complete loss of the epidermis and often portions of the dermis and even subcutaneous fat.
HP:0000679	Taurodontia	Increased volume of dental pulp of permanent molar.
HP:0100585	Telangiectasia of the skin	Presence of small, permanently dilated blood vessels near the surface of the skin, visible as small focal red lesions.
HP:0002575	Tracheoesophageal fistula	An abnormal connection (fistula) between the esophagus and the trachea.
HP:0008661	Urethral stenosis	Abnormal narrowing of the urethra.

Occasional

Term Identifier	Term Name	Definition
HP:0000499	Abnormal eyelash morphology	An abnormality of the eyelashes.

HP:0000534	Abnormal eyebrow morphology	An abnormality of the eyebrow.
HP:0000035	Abnormal testis morphology	An anomaly of the testicle (the male gonad).
HP:0001596	Alopecia	Loss of hair from the head or body.
HP:0010885	Avascular necrosis	A disease where there is cellular death (necrosis) of bone components due to interruption of the blood supply.
HP:0000498	Blepharitis	Inflammation of the eyelids.
HP:0000518	Cataract	A cataract is an opacity or clouding that develops in the crystalline lens of the eye or in its capsule.
HP:0002514	Cerebral calcification	The presence of calcium deposition within brain structures.
HP:0001394	Cirrhosis	A chronic disorder of the liver in which liver tissue becomes scarred and is partially replaced by regenerative nodules and fibrotic tissue resulting in loss of liver function.
HP:0000819	Diabetes mellitus	A group of abnormalities characterized by hyperglycemia and glucose intolerance.
HP:0100627	Displacement of the urethral meatus	A displacement of the external urethral orifice from its normal position (in males normally placed at the tip of glans penis, in females normally placed about 2.5 cm behind the glans clitoridis and immediately in front of that of the vagina).
HP:0000365	Hearing impairment	A decreased magnitude of the sensory perception of sound.
HP:0001399	Hepatic failure	
HP:0002240	Hepatomegaly	Abnormally increased size of the liver.
HP:0000327	Hypoplasia of the maxilla	Abnormally small dimension of the Maxilla. Usually creating a malocclusion or malalignment between the upper and lower teeth or resulting in a deficient amount of projection of the base of the nose and lower midface region.
HP:0002665	Lymphoma	A cancer originating in lymphocytes and presenting as a solid tumor of lymhpoid cells.
HP:0002894	Neoplasm of the pancreas	A tumor (abnormal growth of tissue) of the pancreas.
HP:0000939	Osteoporosis	Osteoporosis is a systemic skeletal disease characterized by low bone density and microarchitectural deterioration of bone tissue with a consequent increase in bone fragility. According to the WHO criteria, osteoporosis is defined as a BMD that lies 2.5 standard deviations or more below the average value for young healthy adults (a T-score below -2.5 SD).
HP:0000982	Palmoplantar keratoderma	Abnormal thickening of the skin of the palms of the hands and the soles of the feet.
HP:0002216	Premature graying of hair	Development of gray hair at a younger than normal age.
HP:0200037	Skin vesicle	A circumscribed, fluid-containing, epidermal elevation generally considered less than 10mm in diameter at the widest point.
HP:0002650	Scoliosis	The presence of an abnormal lateral curvature of the spine.
HP:0001744	Splenomegaly	Abnormal increased size of the spleen.
HP:0011364	White hair	Hypopigmented hair that appears white.

Source: HPO-ORDO Ontological Module - Validation association date: 01.06.2016

Early-onset inflammatory bowel disease

No frequency available

Term Identifier	Term Name	Definition
HP:0025084	Folliculitis	Inflammatory cells within the wall and ostia of the hair follicle, creating a follicular-based pustule.
HP:0004387	Enterocolitis	An inflammation of the colon and small intestine. However, most conditions are either categorized as Enteritis (inflammation of the small intestine) or Colitis (inflammation of the large intestine).
HP:0009789	Perianal abscess	The presence of an abscess located around the anus.
HP:0000007	Autosomal recessive inheritance	A mode of inheritance that is observed for traits related to a gene encoded on one of the autosomes (i.e., the human chromosomes 1-22) in which a trait manifests in individuals with two pathogenic alleles, either homozygotes (two copies of the same mutant allele) or compound heterozygotes (whereby each copy of a gene has a distinct mutant allele).
HP:0005224	Rectal abscess	A collection of pus in the area of the rectum.
HP:0000143	Rectovaginal fistula	The presence of a fistula between the vagina and the rectum.

OMIM Clinical synopsis #612567 – Creation date: 26.02.2015, Marla J.F. O´Neill
OMIM Clinical synopsis #613148 – Creation date: 06.05.2013, Marla J.F. O´Neill

Early-onset multi-organ autoimmune disease

No frequency available

Term Identifier	Term Name	Definition
HP:0000964	Eczema	Eczema is a form of dermatitis. The term eczema is broadly applied to a range of persistent skin conditions and can be related to a number of underlying conditions. Manifestations of eczema can include dryness and recurring skin rashes with redness, skin edema, itching and dryness, crusting, flaking, blistering, cracking, oozing, or bleeding.
HP:0002960	Autoimmunity	The occurrence of an immune reaction against the organism's own cells or tissues.
HP:0002608	Celiac disease	Celiac disease (CD) is an autoimmune condition affecting the small intestine, triggered by the ingestion of gluten, the protein fraction of wheat, barley, and rye. Clinical manifestations of CD are highly variable and include both gastrointestinal and non-gastrointestinal features. The hallmark of CD is an immune-mediated enteropathy. This term is included because the occurence of CD is seen as a feature of a number of other diseases.
HP:0001890	Autoimmune hemolytic anemia	An autoimmune form of hemolytic anemia.
HP:0004313	Decreased antibody level in blood	An abnormally decreased level of immunoglobulin in blood.
HP:0002719	Recurrent infections	Increased susceptibility to infections.
HP:0000821	Hypothyroidism	Deficiency of thyroid hormone.
HP:0000819	Diabetes mellitus	A group of abnormalities characterized by hyperglycemia and glucose intolerance.
HP:0000823	Delayed puberty	Passing the age when puberty normally occurs with no physical or hormonal signs of the onset of puberty.
HP:0004322	Short stature	A height below that which is expected according to age and gender norms. Although there is no universally accepted definition of short stature, many refer to "short stature" as height more than 2 standard deviations below the mean for age and gender (or below the 3rd percentile for age and gender dependent norms).
HP:0000006	Autosomal dominant inheritance	A mode of inheritance that is observed for traits related to a gene encoded on one of the autosomes (i.e., the human chromosomes 1-22) in which a trait manifests in heterozygotes. In the context of medical genetics, an autosomal dominant disorder is caused when a single copy of the mutant allele is present. Males and females are affected equally, and can both transmit the disorder with a risk of 50% for each child of inheriting the mutant allele.
HP:0001973	Autoimmune thrombocytopenia	The presence of thrombocytopenia in combination with detection of antiplatelet antibodies.
HP:0000164	Abnormality of the dentition	Any abnormality of the teeth.
HP:0006515	Interstitial pneumonitis	
HP:0001369	Arthritis	Inflammation of a joint.

HP:0000100	Nephrotic syndrome	Nephrotic syndrome is a collection of findings resulting from glomerular dysfunction with an increase in glomerular capillary wall permeability associated with pronounced proteinuria. Nephrotic syndrome refers to the constellation of clinical findings that result from severe renal loss of protein, with Proteinuria and hypoalbuminemia, edema, and hyperlipidemia.
HP:0012579	Minimal change glomerulonephritis	The presence of minimal changes visible by light microscopy but flattened and fused podocyte foot processes on electron microscopy in a person with nephrotic range proteinuria.
HP:0000093	Proteinuria	Increased levels of protein in the urine.

OMIM Clinical synopsis #615952 – Creation date: 20.08.2014, Cassandra L. Kniffin; updated: 23.05.2016, Cassandra L. Kniffin
OMIM Clinical synopsis #617006 – Creation date: 27.06.2016, Cassandra L. Kniffin

Epidermodysplasia verruciformis

Very frequent

Term Identifier	Term Name	Definition
HP:0200034	Papule	A circumscribed, solid elevation of skin with no visible fluid, varying in size from a pinhead to less than 10mm in diameter at the widest point.
HP:0200039	Pustule	A small elevation of the skin containing cloudy or purulent material usually consisting of necrotic inflammatory cells.
HP:0001581	Recurrent skin infections	Infections of the skin that happen multiple times.
HP:0001051	Seborrheic dermatitis	Seborrheic dermatitis is a form of eczema which is closely related to dandruff. It causes dry or greasy peeling of the scalp, eyebrows, and face, and sometimes trunk.
HP:0200035	Skin plaque	A plaque is a solid, raised, plateau-like (flat-topped) lesion greater than 1 cm in diameter.
HP:0200043	Verrucae	Warts, benign growths on the skin or mucous membranes that cause cosmetic problems as well as pain and discomfort. Warts most often occur on the hands, feet, and genital areas.
HP:0002715	Abnormality of the immune system	An abnormality of the immune system.

Frequent

Term Identifier	Term Name	Definition
HP:0001053	Hypopigmented skin patches	
HP:0007565	Multiple cafe-au-lait spots	The presence of six or more cafe-au-lait spots.

Occasional

Term Identifier	Term Name	Definition
HP:0002860	Squamous cell carcinoma	The presence of squamous cell carcinoma of the skin.
HP:0100585	Telangiectasia of the skin	Presence of small, permanently dilated blood vessels near the surface of the skin, visible as small focal red lesions.

Source: HPO-ORDO Ontological Module - Validation association date: 01.06.2016

Factor B deficiency

No frequency available

Term Identifier	Term Name	Definition
HP:0002090	Pneumonia	Inflammation of any part of the lung parenchyma.
HP:0002718	Recurrent bacterial infections	Increased susceptibility to bacterial infections, as manifested by recurrent episodes of bacterial infection.
HP:0005381	Recurrent meningococcal disease	Recurrent infections by Neisseria meningitidis (one of the most common causes of bacterial meningitis), which is also known as meningococcus.
HP:0005416	Decreased serum complement factor B	A reduced level of the complement component factor B in circulation.
HP:0002586	Peritonitis	Inflammation of the peritoneum.

Source: OMIM #615561; Creation date: 12.12.2013, Cassandra L. Kniffin

Factor D Deficiency

No frequency available

Term Identifier	Term Name	Definition
HP:0002718	Recurrent bacterial infections	Increased susceptibility to bacterial infections, as manifested by recurrent episodes of bacterial infection.
HP:0004431	Complement deficiency	An immunodeficiency defined by the absent or suboptimal functioning of one of the complement system proteins.
HP:0000007	Autosomal recessive inheritance	A mode of inheritance that is observed for traits related to a gene encoded on one of the autosomes (i.e., the human chromosomes 1-22) in which a trait manifests in individuals with two pathogenic alleles, either homozygotes (two copies of the same mutant allele) or compound heterozygotes (whereby each copy of a gene has a distinct mutant allele).
HP:0005430	Recurrent Neisserial infections	Recurrent infections by bacteria of the genus Neisseria, including N. meningitidis (one of the most common causes of bacterial meningitis).

OMIM Clinical synopsis #613912 – Creation date: 15.06.1995, John F. Jackson; updated: 20.04.2011, Cassandra L. Kniffin

Factor H deficiency

No frequency available

Term Identifier	Term Name	Definition
HP:0004722	Thickening of the glomerular basement membrane	Increase in thickness of the basal lamina of the glomerulus of the kidney.
HP:0012622	Chronic kidney disease	Functional anomaly of the kidney persisting for at least three months.
HP:0004746	Glomerular subendothelial electron-dense deposits	Electron dense deposits at the glomerular basement membrane,
HP:0002718	Recurrent bacterial infections	Increased susceptibility to bacterial infections, as manifested by recurrent episodes of bacterial infection.
HP:0005369	Decreased serum complement factor H	A reduced level of the complement component Factor H in circulation.
HP:0005389	Depletion of components of the alternative complement pathway	An abnormal reduction in the components of the alternative complement pathway, such as the C3 protein or its cleavage products.
HP:0000007	Autosomal recessive inheritance	A mode of inheritance that is observed for traits related to a gene encoded on one of the autosomes (i.e., the human chromosomes 1-22) in which a trait manifests in individuals with two pathogenic alleles, either homozygotes (two copies of the same mutant allele) or compound heterozygotes (whereby each copy of a gene has a distinct mutant allele).
HP:0000006	Autosomal dominant inheritance	A mode of inheritance that is observed for traits related to a gene encoded on one of the autosomes (i.e., the human chromosomes 1-22) in which a trait manifests in heterozygotes. In the context of medical genetics, an autosomal dominant disorder is caused when a single copy of the mutant allele is present. Males and females are affected equally, and can both transmit the disorder with a risk of 50% for each child of inheriting the mutant allele.
HP:0000790	Hematuria	The presence of blood in the urine. Hematuria may be gross hematuria (visible to the naked eye) or microscopic hematuria (detected by dipstick or microscopic examination of the urine).

OMIM Clinical synopsis #609814 – Creation date: 27.09.2006, Cassandra L. Kniffin

Factor H related protein deficiency

aHUS1

No frequency available

Term Identifier	Term Name	Definition
HP:0100543	Cognitive impairment	Abnormality in the process of thought including the ability to process information.
HP:0001259	Coma	Complete absence of wakefulness and content of conscience, which manifests itself as a lack of response to any kind of external stimuli.
HP:0001269	Hemiparesis	Loss of strength in the arm, leg, and sometimes face on one side of the body. Hemiplegia refers to a complete loss of strength, whereas hemiparesis refers to an incomplete loss of strength.
HP:0001250	Seizures	Seizures are an intermittent abnormality of the central nervous system due to a sudden, excessive, disorderly discharge of cerebral neurons and characterized clinically by some combination of disturbance of sensation, loss of consciousness, impairment of psychic function, or convulsive movements. The term epilepsy is used to describe chronic, recurrent seizures.
HP:0002357	Dysphasia	
HP:0001873	Thrombocytopenia	A reduction in the number of circulating thrombocytes.
HP:0001981	Schistocytosis	The presence of an abnormal number of fragmented red blood cells (schistocytes) in the blood.
HP:0001923	Reticulocytosis	An elevation in the number of reticulocytes (immature erythrocytes) in the peripheral blood circulation.
HP:0001937	Microangiopathic hemolytic anemia	
HP:0003259	Elevated serum creatinine	An increased amount of creatinine in the blood.
HP:0003077	Hyperlipidemia	An elevated lipid concentration in the blood.
HP:0003138	Increased blood urea nitrogen	An increased amount of nitrogen in the form of urea in the blood.
HP:0001945	Fever	Elevated body temperature due to failed thermoregulation.
HP:0005356	Decreased serum complement factor I	A reduced level of the complement component Factor I in circulation.
HP:0005369	Decreased serum complement factor H	A reduced level of the complement component Factor H in circulation.
HP:0005416	Decreased serum complement factor B	A reduced level of the complement component factor B in circulation.
HP:0005421	Decreased serum complement C3	A reduced level of the complement component C3 in circulation.
HP:0100519	Anuria	Absence of urine, clinically classified as below 50ml/day.
HP:0005575	Hemolytic-uremic syndrome	
HP:0001919	Acute kidney injury	Sudden loss of renal function, as manifested by decreased urine production, and a rise in serum creatinine or blood urea nitrogen concentration (azotemia).

HP:0000007	Autosomal recessive inheritance	A mode of inheritance that is observed for traits related to a gene encoded on one of the autosomes (i.e., the human chromosomes 1-22) in which a trait manifests in individuals with two pathogenic alleles, either homozygotes (two copies of the same mutant allele) or compound heterozygotes (whereby each copy of a gene has a distinct mutant allele).
HP:0000006	Autosomal dominant inheritance	A mode of inheritance that is observed for traits related to a gene encoded on one of the autosomes (i.e., the human chromosomes 1-22) in which a trait manifests in heterozygotes. In the context of medical genetics, an autosomal dominant disorder is caused when a single copy of the mutant allele is present. Males and females are affected equally, and can both transmit the disorder with a risk of 50% for each child of inheriting the mutant allele.
HP:0000822	Hypertension	The presence of chronic increased pressure in the systemic arterial system.
HP:0000979	Purpura	Purpura (from Latin: purpura, meaning "purple") is the appearance of red or purple discolorations on the skin that do not blanch on applying pressure. They are caused by bleeding underneath the skin. This term refers to an abnormally increased susceptibility to developing purpura. Purpura are larger than petechiae.
HP:0002014	Diarrhea	Abnormally increased frequency of loose or watery bowel movements.

OMIM Clinical synopsis #235400 – Creation date: 15.06.1995, John F. Jackson; updated: 27.07.2009, Cassandra L. Kniffin

Cfhr5 Deficiency

No frequency available

Term Identifier	Term Name	Definition
HP:0000099	Glomerulonephritis	Inflammation of the renal glomeruli.
HP:0003774	Stage 5 chronic kidney disease	A degree of kidney failure severe enough to require dialysis or kidney transplantation for survival characterized by a severe reduction in glomerular filtration rate (less than 15 ml/min/1.73 m2) and other manifestations including increased serum creatinine.
HP:0000083	Renal insufficiency	A reduction in the level of performance of the kidneys in areas of function comprising the concentration of urine, removal of wastes, the maintenance of electrolyte balance, homeostasis of blood pressure, and calcium metabolism.
HP:0000006	Autosomal dominant inheritance	A mode of inheritance that is observed for traits related to a gene encoded on one of the autosomes (i.e., the human chromosomes 1-22) in which a trait manifests in heterozygotes. In the context of medical genetics, an autosomal dominant disorder is caused when a single copy of the mutant allele is present. Males and females are

		affected equally, and can both transmit the disorder with a risk of 50% for each child of inheriting the mutant allele.
HP:0000790	Hematuria	The presence of blood in the urine. Hematuria may be gross hematuria (visible to the naked eye) or microscopic hematuria (detected by dipstick or microscopic examination of the urine).

Factor I deficiency

No frequency available

Term Identifier	Term Name	Definition
HP:0005356	Decreased serum complement factor I	A reduced level of the complement component Factor I in circulation.
HP:0005376	Recurrent Haemophilus influenzae infections	Increased susceptibility to Haemophilus influenzae infections as manifested by recurrent episodes of infection by Haemophilus influenzae.
HP:0000403	Recurrent otitis media	Increased susceptibility to otitis media, as manifested by recurrent episodes of otitis media.
HP:0005381	Recurrent meningococcal disease	Recurrent infections by Neisseria meningitidis (one of the most common causes of bacterial meningitis), which is also known as meningococcus.
HP:0005369	Decreased serum complement factor H	A reduced level of the complement component Factor H in circulation.
HP:0005366	Recurrent streptococcus pneumoniae infections	Increased susceptibility to streptococcus pneumoniae infections as manifested by a history of recurrent infections by streptococcus pneumoniae.
HP:0000246	Sinusitis	Inflammation of the paranasal sinuses owing to a viral, bacterial, or fungal infection, allergy, or an autoimmune reaction.
HP:0005416	Decreased serum complement factor B	A reduced level of the complement component factor B in circulation.
HP:0001581	Recurrent skin infections	Infections of the skin that happen multiple times.
HP:0005421	Decreased serum complement C3	A reduced level of the complement component C3 in circulation.
HP:0011108	Recurrent sinusitis	A recurrent form of sinusitis.
HP:0000010	Recurrent urinary tract infections	Repeated infections of the urinary tract.
HP:0000083	Renal insufficiency	A reduction in the level of performance of the kidneys in areas of function comprising the concentration of urine, removal of wastes, the maintenance of electrolyte balance, homeostasis of blood pressure, and calcium metabolism.
HP:0012330	Pyelonephritis	An inflammation of the kidney involving the parenchyma of kidney, the renal pelvis and the kidney calices.
HP:0000099	Glomerulonephritis	Inflammation of the renal glomeruli.
HP:0000007	Autosomal recessive inheritance	A mode of inheritance that is observed for traits related to a gene encoded on one of the autosomes (i.e., the human chromosomes 1-22) in which a trait manifests in individuals with two pathogenic alleles, either homozygotes (two copies of the same mutant allele) or compound heterozygotes (whereby each copy of a gene has a distinct mutant allele).
HP:0002633	Vasculitis	Inflammation of blood vessel.
HP:0006946	Recurrent meningitis	An increased susceptibility to meningitis as manifested by a medical history of recurrent episodes of meningitis.
HP:0001369	Arthritis	Inflammation of a joint.

OMIM Clinical synopsis #610984 – Creation date: 30.04.2007, Cassandra L. Kniffin

Ficolin 3 Deficiency (FC3RN)

No frequency available

Term Identifier	Term Name	Definition
HP:0002722	Recurrent abscess formation	An increased susceptibility to abscess formation, as manifested by a medical history of recurrent abscesses.
HP:0002721	Immunodeficiency	Failure of the immune system to protect the body adequately from infection, due to the absence or insufficiency of some component process or substance.
HP:0002783	Recurrent lower respiratory tract infections	An increased susceptibility to lower respiratory tract infections as manifested by a history of recurrent lower respiratory tract infections.
HP:0000007	Autosomal recessive inheritance	A mode of inheritance that is observed for traits related to a gene encoded on one of the autosomes (i.e., the human chromosomes 1-22) in which a trait manifests in individuals with two pathogenic alleles, either homozygotes (two copies of the same mutant allele) or compound heterozygotes (whereby each copy of a gene has a distinct mutant allele).
HP:0200043	Verrucae	Warts, benign growths on the skin or mucous membranes that cause cosmetic problems as well as pain and discomfort. Warts most often occur on the hands, feet, and genital areas.

OMIM Clinical synopsis #613860 – Creation date: 02.06.2016, Cassandra L. Kniffin

Familial hemophagocytic lymphohistiocytosis syndromes (FHLH)

FHLH 1

No frequency available

Term Identifier	Term Name	Definition
HP:0002516	Increased intracranial pressure	An increase of the pressure inside the cranium (skull) and thereby in the brain tissue and cerebrospinal fluid.
HP:0000737	Irritability	
HP:0001263	Global developmental delay	A delay in the achievement of motor or mental milestones in the domains of development of a child, including motor skills, speech and language, cognitive skills, and social and emotional skills. This term should only be used to describe children younger than five years of age.
HP:0002301	Hemiplegia	Paralysis (complete loss of muscle function) in the arm, leg, and in some cases the face on one side of the body.
HP:0002445	Tetraplegia	Paralysis of all four limbs, and trunk of the body below the level of an associated injury to the spinal cord. The etiology of quadriplegia is similar to that of paraplegia except that the lesion is in the cervical spinal cord rather than in the thoracic or lumbar segments of the spinal cord.
HP:0002383	Encephalitis	
HP:0001251	Ataxia	Cerebellar ataxia refers to ataxia due to dysfunction of the cerebellum. This causes a variety of elementary neurological deficits including asynergy (lack of coordination between muscles, limbs and joints), dysmetria (lack of ability to judge distances that can lead to under- oder overshoot in grasping movements), and dysdiadochokinesia (inability to perform rapid movements requiring antagonizing muscle groups to be switched on and off repeatedly).
HP:0002922	Increased CSF protein	Increased concentration of protein in the cerebrospinal fluid.
HP:0001250	Seizures	Seizures are an intermittent abnormality of the central nervous system due to a sudden, excessive, disorderly discharge of cerebral neurons and characterized clinically by some combination of disturbance of sensation, loss of consciousness, impairment of psychic function, or convulsive movements. The term epilepsy is used to describe chronic, recurrent seizures.
HP:0001287	Meningitis	Inflammation of the meninges.
HP:0001259	Coma	Complete absence of wakefulness and content of conscience, which manifests itself as a lack of response to any kind of external stimuli.
HP:0012229	CSF pleocytosis	An increased white blood cell count in the cerebrospinal fluid.
HP:0007430	Generalized edema	Generalized abnormal accumulation of fluid beneath the skin, or in one or more cavities of the body.

HP:0003141	Increased LDL cholesterol concentration	An elevated concentration of low-density lipoprotein cholesterol in the blood.
HP:0002155	Hypertriglyceridemia	An abnormal increase in the level of triglycerides in the blood.
HP:0003573	Increased total bilirubin	Increased concentration of total (conjugated and unconjugated) bilirubin in the blood.
HP:0003233	Decreased HDL cholesterol concentration	A decreased concentration of high-density lipoprotein cholesterol in the blood.
HP:0003281	Increased serum ferritin	Abnormal raised concentration of ferritin, a ubiquitous intracellular protein that stores iron, in the blood.
HP:0003075	Hypoproteinemia	A decreased concentration of protein in the blood.
HP:0002902	Hyponatremia	An abnormally decreased sodium concentration in the blood.
HP:0003362	Increased VLDL cholesterol concentration	An increase in the amount of very-low-density lipoprotein cholesterol in the blood.
HP:0003073	Hypoalbuminemia	Reduction in the concentration of albumin in the blood.
HP:0011900	Hypofibrinogenemia	Decreased concentration of fibrinogen in the blood.
HP:0012156	Hemophagocytosis	Phagocytosis by macrophages of erythrocytes, leukocytes, platelets, and their precursors in bone marrow and other tissues.
HP:0008151	Prolonged prothrombin time	Increased time to coagulation in the prothrombin time test, which is a measure of the extrinsic pathway of coagulation. The results of the prothrombin time test are often expressed in terms of the International normalized ratio (INR), which is calculated as a ratio of the patient's prothrombin time (PT) to a control PT standardized for the potency of the thromboplastin reagent developed by the World Health Organization (WHO) using the formula: INR is equal to Patient PT divided by Control PT.
HP:0001882	Leukopenia	An abnormal decreased number of leukocytes in the blood.
HP:0003645	Prolonged partial thromboplastin time	Increased time to coagulation in the partial thromboplastin time (PTT) test, a measure of the intrinsic and common coagulation pathways. Phospholipid, and activator, and calcium are mixed into an anticoagulated plasma sample, and the time is measured until a thrombus forms.
HP:0001873	Thrombocytopenia	A reduction in the number of circulating thrombocytes.
HP:0001903	Anemia	A reduction in erythrocytes volume or hemoglobin concentration.
HP:0000952	Jaundice	Yellow pigmentation of the skin due to bilirubin, which in turn is the result of increased bilirubin concentration in the bloodstream.
HP:0002240	Hepatomegaly	Abnormally increased size of the liver.
HP:0001744	Splenomegaly	Abnormal increased size of the spleen.
HP:0001276	Hypertonia	A condition in which there is increased muscle tone so that arms or legs, for example, are stiff and difficult to move.

HP:0001252	Muscular hypotonia	Muscular hypotonia is an abnormally low muscle tone (the amount of tension or resistance to movement in a muscle), often involving reduced muscle strength. Hypotonia is characterized by a diminished resistance to passive stretching.
HP:0001290	Generalized hypotonia	Generalized muscular hypotonia (abnormally low muscle tone).
HP:0000007	Autosomal recessive inheritance	A mode of inheritance that is observed for traits related to a gene encoded on one of the autosomes (i.e., the human chromosomes 1-22) in which a trait manifests in individuals with two pathogenic alleles, either homozygotes (two copies of the same mutant allele) or compound heterozygotes (whereby each copy of a gene has a distinct mutant allele).
HP:0002716	Lymphadenopathy	Enlargment (swelling) of a lymph node.
HP:0001508	Failure to thrive	Failure to thrive (FTT) refers to a child whose physical growth is substantially below the norm.

OMIM Clinical synopsis %267700 – Creation date: 15.06.1995, John F. Jackson; reviewed: 04.01.2001, Ada Hamosh

FHLH 2

No frequency available

Term Identifier	Term Name	Definition
HP:0002516	Increased intracranial pressure	An increase of the pressure inside the cranium (skull) and thereby in the brain tissue and cerebrospinal fluid.
HP:0001263	Global developmental delay	A delay in the achievement of motor or mental milestones in the domains of development of a child, including motor skills, speech and language, cognitive skills, and social and emotional skills. This term should only be used to describe children younger than five years of age.
HP:0012229	CSF pleocytosis	An increased white blood cell count in the cerebrospinal fluid.
HP:0002301	Hemiplegia	Paralysis (complete loss of muscle function) in the arm, leg, and in some cases the face on one side of the body.
HP:0001287	Meningitis	Inflammation of the meninges.
HP:0002922	Increased CSF protein	Increased concentration of protein in the cerebrospinal fluid.
HP:0001259	Coma	Complete absence of wakefulness and content of conscience, which manifests itself as a lack of response to any kind of external stimuli.
HP:0002445	Tetraplegia	Paralysis of all four limbs, and trunk of the body below the level of an associated injury to the spinal cord. The etiology of quadriplegia is similar to that of paraplegia except that the lesion is in the cervical spinal cord rather than in the thoracic or lumbar segments of the spinal cord.
HP:0002383	Encephalitis	

HP:0001250	Seizures	Seizures are an intermittent abnormality of the central nervous system due to a sudden, excessive, disorderly discharge of cerebral neurons and characterized clinically by some combination of disturbance of sensation, loss of consciousness, impairment of psychic function, or convulsive movements. The term epilepsy is used to describe chronic, recurrent seizures.
HP:0000737	Irritability	
HP:0001251	Ataxia	Cerebellar ataxia refers to ataxia due to dysfunction of the cerebellum. This causes a variety of elementary neurological deficits including asynergy (lack of coordination between muscles, limbs and joints), dysmetria (lack of ability to judge distances that can lead to under- oder overshoot in grasping movements), and dysdiadochokinesia (inability to perform rapid movements requiring antagonizing muscle groups to be switched on and off repeatedly).
HP:0003075	Hypoproteinemia	A decreased concentration of protein in the blood.
HP:0002902	Hyponatremia	An abnormally decreased sodium concentration in the blood.
HP:0002155	Hypertriglyceridemia	An abnormal increase in the level of triglycerides in the blood.
HP:0003073	Hypoalbuminemia	Reduction in the concentration of albumin in the blood.
HP:0003281	Increased serum ferritin	Abnormal raised concentration of ferritin, a ubiquitous intracellular protein that stores iron, in the blood.
HP:0007430	Generalized edema	Generalized abnormal accumulation of fluid beneath the skin, or in one or more cavities of the body.
HP:0003573	Increased total bilirubin	Increased concentration of total (conjugated and unconjugated) bilirubin in the blood.
HP:0001873	Thrombocytopenia	A reduction in the number of circulating thrombocytes.
HP:0011900	Hypofibrinogenemia	Decreased concentration of fibrinogen in the blood.
HP:0001882	Leukopenia	An abnormal decreased number of leukocytes in the blood.
HP:0012156	Hemophagocytosis	Phagocytosis by macrophages of erythrocytes, leukocytes, platelets, and their precursors in bone marrow and other tissues.
HP:0008151	Prolonged prothrombin time	Increased time to coagulation in the prothrombin time test, which is a measure of the extrinsic pathway of coagulation. The results of the prothrombin time test are often expressed in terms of the International normalized ratio (INR), which is calculated as a ratio of the patient's prothrombin time (PT) to a control PT standardized for the potency of the thromboplastin reagent developed by the World Health Organization (WHO) using the formula: INR is equal to Patient PT divided by Control PT.
HP:0001903	Anemia	A reduction in erythrocytes volume or hemoglobin concentration.
HP:0000952	Jaundice	Yellow pigmentation of the skin due to bilirubin, which in turn is the result of increased bilirubin concentration in the bloodstream.
HP:0001744	Splenomegaly	Abnormal increased size of the spleen.
HP:0002240	Hepatomegaly	Abnormally increased size of the liver.

HP:0001276	Hypertonia	A condition in which there is increased muscle tone so that arms or legs, for example, are stiff and difficult to move.
HP:0001290	Generalized hypotonia	Generalized muscular hypotonia (abnormally low muscle tone).
HP:0001252	Muscular hypotonia	Muscular hypotonia is an abnormally low muscle tone (the amount of tension or resistance to movement in a muscle), often involving reduced muscle strength. Hypotonia is characterized by a diminished resistance to passive stretching.
HP:0000007	Autosomal recessive inheritance	A mode of inheritance that is observed for traits related to a gene encoded on one of the autosomes (i.e., the human chromosomes 1-22) in which a trait manifests in individuals with two pathogenic alleles, either homozygotes (two copies of the same mutant allele) or compound heterozygotes (whereby each copy of a gene has a distinct mutant allele).
HP:0002716	Lymphadenopathy	Enlargment (swelling) of a lymph node.
HP:0001508	Failure to thrive	Failure to thrive (FTT) refers to a child whose physical growth is substantially below the norm.

OMIM Clinical synopsis #603553– Creation date: 15.06.1995, John F. Jackson; reviewed: 04.01.2001, Ada Hamosh

FHLH 3

No frequency available

Term Identifier	Term Name	Definition
HP:0001913	Granulocytopenia	An abnormally reduced number of granulocytes in the blood.
HP:0012156	Hemophagocytosis	Phagocytosis by macrophages of erythrocytes, leukocytes, platelets, and their precursors in bone marrow and other tissues.
HP:0011900	Hypofibrinogenemia	Decreased concentration of fibrinogen in the blood.
HP:0001903	Anemia	A reduction in erythrocytes volume or hemoglobin concentration.
HP:0001945	Fever	Elevated body temperature due to failed thermoregulation.
HP:0002155	Hypertriglyceridemia	An abnormal increase in the level of triglycerides in the blood.
HP:0000007	Autosomal recessive inheritance	A mode of inheritance that is observed for traits related to a gene encoded on one of the autosomes (i.e., the human chromosomes 1-22) in which a trait manifests in individuals with two pathogenic alleles, either homozygotes (two copies of the same mutant allele) or compound heterozygotes (whereby each copy of a gene has a distinct mutant allele).
HP:0001433	Hepatosplenomegaly	Simultaneous enlargement of the liver and spleen.
HP:0012178	Reduced natural killer cell activity	Reduced ability of the natural killer cell to function in the adaptive immune response.

Source: OMIM #608898; Creation date: 03.09.2004, Stylianos E. Antonarakis; updated: 12.11.2008 Marla J.F. O'Neill

FHLH 4

No frequency available

Term Identifier	Term Name	Definition
HP:0001875	Neutropenia	An abnormally low number of neutrophils in the peripheral blood.
HP:0001873	Thrombocytopenia	A reduction in the number of circulating thrombocytes.
HP:0011900	Hypofibrinogenemia	Decreased concentration of fibrinogen in the blood.
HP:0001903	Anemia	A reduction in erythrocytes volume or hemoglobin concentration.
HP:0012156	Hemophagocytosis	Phagocytosis by macrophages of erythrocytes, leukocytes, platelets, and their precursors in bone marrow and other tissues.
HP:0002155	Hypertriglyceridemia	An abnormal increase in the level of triglycerides in the blood.
HP:0003281	Increased serum ferritin	Abnormal raised concentration of ferritin, a ubiquitous intracellular protein that stores iron, in the blood.
HP:0001945	Fever	Elevated body temperature due to failed thermoregulation.
HP:0001744	Splenomegaly	Abnormal increased size of the spleen.
HP:0002240	Hepatomegaly	Abnormally increased size of the liver.
HP:0001252	Muscular hypotonia	Muscular hypotonia is an abnormally low muscle tone (the amount of tension or resistance to movement in a muscle), often involving reduced muscle strength. Hypotonia is characterized by a diminished resistance to passive stretching.
HP:0001290	Generalized hypotonia	Generalized muscular hypotonia (abnormally low muscle tone).
HP:0001263	Global developmental delay	A delay in the achievement of motor or mental milestones in the domains of development of a child, including motor skills, speech and language, cognitive skills, and social and emotional skills. This term should only be used to describe children younger than five years of age.
HP:0001250	Seizures	Seizures are an intermittent abnormality of the central nervous system due to a sudden, excessive, disorderly discharge of cerebral neurons and characterized clinically by some combination of disturbance of sensation, loss of consciousness, impairment of psychic function, or convulsive movements. The term epilepsy is used to describe chronic, recurrent seizures.
HP:0000007	Autosomal recessive inheritance	A mode of inheritance that is observed for traits related to a gene encoded on one of the autosomes (i.e., the human chromosomes 1-22) in which a trait manifests in individuals with two pathogenic alleles, either homozygotes (two copies of the same mutant allele) or

		compound heterozygotes (whereby each copy of a gene has a distinct mutant allele).

OMIM Clinical synopsis #603552– Creation date: 03.02.2014, Cassandra L. Kniffin

FHLH 5

No frequency available

Term Identifier	Term Name	Definition
HP:0002155	Hypertriglyceridemia	An abnormal increase in the level of triglycerides in the blood.
HP:0003281	Increased serum ferritin	Abnormal raised concentration of ferritin, a ubiquitous intracellular protein that stores iron, in the blood.
HP:0001954	Recurrent fever	Periodic (episodic or recurrent) bouts of fever.
HP:0000007	Autosomal recessive inheritance	A mode of inheritance that is observed for traits related to a gene encoded on one of the autosomes (i.e., the human chromosomes 1-22) in which a trait manifests in individuals with two pathogenic alleles, either homozygotes (two copies of the same mutant allele) or compound heterozygotes (whereby each copy of a gene has a distinct mutant allele).
HP:0012156	Hemophagocytosis	Phagocytosis by macrophages of erythrocytes, leukocytes, platelets, and their precursors in bone marrow and other tissues.
HP:0001433	Hepatosplenomegaly	Simultaneous enlargement of the liver and spleen.
HP:0012177	Abnormal natural killer cell physiology	A functional anomaly of the natural killer cell.

Source: OMIM #613101; Creation date: 22.10.2009, Marla J.F. O'Neill; updated: 05.01.2011 Marla J.F. O'Neill

FOXP3 deficiency (IPEX)

Very frequent

Term Identifier	Term Name	Definition
HP:0002960	Autoimmunity	The occurrence of an immune reaction against the organism's own cells or tissues.

Frequent

Term Identifier	Term Name	Definition
HP:0002242	Abnormal intestine morphology	An abnormality of the intestine. The closely related term enteropathy is used to refer to any disease of the intestine.
HP:0003111	Abnormal blood ion concentration	Abnormality of the homeostasis (concentration) of a monoatomic ion.
HP:0012393	Allergy	An allergy is an immune response or reaction to substances that are usually not harmful.
HP:0025379	Anti-thyroid peroxidase antibody positivity	The presence of autoantibodies (immunoglobulins) in the serum that react against thyroid peroxidase.
HP:0007473	Crusting erythematous dermatitis	
HP:0000964	Eczema	Eczema is a form of dermatitis. The term eczema is broadly applied to a range of persistent skin conditions and can be related to a number of underlying conditions. Manifestations of eczema can include dryness and recurring skin rashes with redness, skin edema, itching and dryness, crusting, flaking, blistering, cracking, oozing, or bleeding.
HP:0000976	Eczematoid dermatitis	
HP:0001531	Failure to thrive in infancy	
HP:0031401	Reduced proportion of CD4-negative, CD8-negative, alpha-beta regulatory T cells	An abnormally decreased proportion of CD4-negative, CD8-negative (double negative or DN) alpha-beta regulatory T cells (Tregs) as compared to total number of T cells.
HP:0003212	Increased circulating total IgE level	An abnormally increased overall level of immunoglobulin E in blood.
HP:0011123	Inflammatory abnormality of the skin	The presence of inflammation of the skin. That is, an abnormality of the skin resulting from the local accumulation of fluid, plasma proteins, and leukocytes.
HP:0001891	Iron deficiency anemia	
HP:0005208	Secretory diarrhea	Watery voluminous diarrhea resulting from an imbalance between ion and water secretion and absorption.
HP:0100646	Thyroiditis	Inflammation of the thyroid gland.
HP:0100651	Type I diabetes mellitus	A chronic condition in which the pancreas produces little or no insulin. Type I diabetes mellitus is manifested by the sudden onset of severe hyperglycemia with rapid

		progression to diabetic ketoacidosis unless treated with insulin.

Occasional

Term Identifier	Term Name	Definition
HP:0008066	Abnormal blistering of the skin	The presence of one or more bullae on the skin, defined as fluid-filled blisters more than 5 mm in diameter with thin walls.
HP:0030909	Anti-liver cytosolic antigen type 1 antibody positivity	The presence of autoantibodies (immunoglobulins) in the serum that react against a 60-kd peptide contained in the liver cytosolic fraction.
HP:0001890	Autoimmune hemolytic anemia	An autoimmune form of hemolytic anemia.
HP:0001973	Autoimmune thrombocytopenia	The presence of thrombocytopenia in combination with detection of antiplatelet antibodies.
HP:0004326	Cachexia	Severe weight loss, wasting of muscle, loss of appetite, and general debility related to a chronic disease.
HP:0031085	Decreased prealbumin level	A reduced concentration of prealbumin in the blood. Prealbumin, also known as transthyretin, has a half-life in plasma of about 2 days, much shorter than that of albumin. Prealbumin is therefore more sensitive to changes in protein-energy status than albumin, and its concentration closely reflects recent dietary intake rather than overall nutritional status.
HP:0003073	Hypoalbuminemia	Reduction in the concentration of albumin in the blood.
HP:0002901	Hypocalcemia	An abnormally decreased calcium concentration in the blood.
HP:0002917	Hypomagnesemia	An abnormally decreased magnesium concentration in the blood.
HP:0000821	Hypothyroidism	Deficiency of thyroid hormone.
HP:0031104	Insulin receptor antibody positivity	The presence of autoantibodies (immunoglobulins) in the serum that react against the insulin receptor.
HP:0006515	Interstitial pneumonitis	
HP:0002024	Malabsorption	Impaired ability to absorb one or more nutrients from the intestine.
HP:0012578	Membranous nephropathy	A type of glomerulonephropathy characterized by thickening of the basement membrane and deposition of immune complexes in the subepithelial space.
HP:0008404	Nail dystrophy	Onychodystrophy (nail dystrophy) refers to nail changes apart from changes of the color (nail dyschromia) and involves partial or complete disruption of the various keratinous layers of the nail plate.
HP:0001875	Neutropenia	An abnormally low number of neutrophils in the peripheral blood.
HP:0001904	Neutropenia in presence of anti-neutropil antibodies	A type of neutropenia that is observed in the presence of granulocyte-specific antibodies.
HP:0003765	Psoriasiform dermatitis	A skin abnormality characterized by redness and irritation, with thick, red skin that displays flaky, silver-white patches (scales).

HP:0031123	Recurrent gastroenteritis	Increased susceptibility to gastroenteritis, an infectious inflammationof the stomach and small intestines manifested by signs and symptoms such as diarheas and abdominal pain, as manifested by recurrent episodes of gastroenteritis.
HP:0002719	Recurrent infections	Increased susceptibility to infections.
HP:0002205	Recurrent respiratory infections	An increased susceptibility to respiratory infections as manifested by a history of recurrent respiratory infections.
HP:0001581	Recurrent skin infections	Infections of the skin that happen multiple times.
HP:0002098	Respiratory distress	Difficulty in breathing. The physical presentation of respiratory distress is generally referred to as labored breathing, while the sensation of respiratory distress is called shortness of breath or dyspnea.
HP:0001970	Tubulointerstitial nephritis	A form of inflammation of the kidney affecting the interstitium of the kidneys surrounding the tubules.
HP:0001025	Urticaria	Raised, well-circumscribed areas of erythema and edema involving the dermis and epidermis. Urticaria is intensely pruritic, and blanches completely with pressure.
HP:0002013	Vomiting	Forceful ejection of the contents of the stomach through the mouth by means of a series of involuntary spasmic contractions.
HP:0002910	Elevated hepatic transaminase	Elevations of the levels of SGOT and SGPT in the serum. SGOT (serum glutamic oxaloacetic transaminase) and SGPT (serum glutamic pyruvic transaminase) are transaminases primarily found in the liver and heart and are released into the bloodstream as the result of liver or heart damage. SGOT and SGPT are used clinically mainly as markers of liver damage.
HP:0012115	Hepatitis	Inflammation of the liver.

Rare

Term Identifier	Term Name	Definition
HP:0001596	Alopecia	A noncongenital process of hair loss, which may progress to partial or complete baldness.
HP:0002583	Colitis	Colitis refers to an inflammation of the colon and is often used to describe an inflammation of the large intestine (colon, cecum and rectum). Colitides may be acute and self-limited or chronic, and broadly fit into the category of digestive diseases.
HP:0025156	Dependency on intravenous nutrition	Inability to be weaned from intravenous (parenteral) nutrition, as judged by the hydration status (urine output, blood urea nitrogen, creatinine, urine sodium concentration), ability to maintain weight, stool output, and serum electrolyte status.
HP:0005263	Gastritis	The presence of inflammation of the gastric mucous membrane.
HP:0000836	Hyperthyroidism	An abnormality of thyroid physiology characterized by excessive secretion of the thyroid hormones thyroxine (i.e., T4) and/or 3,3',5-triiodo-L-thyronine zwitterion (i.e., triiodothyronine or T3).

HP:0002595	Ileus	Acute obstruction of the intestines preventing passage of the contents of the intestines.
HP:0002716	Lymphadenopathy	Enlargment (swelling) of a lymph node.
HP:0001287	Meningitis	Inflammation of the meninges.
HP:0040288	Nasogastric tube feeding	
HP:0000100	Nephrotic syndrome	Nephrotic syndrome is a collection of findings resulting from glomerular dysfunction with an increase in glomerular capillary wall permeability associated with pronounced proteinuria. Nephrotic syndrome refers to the constellation of clinical findings that result from severe renal loss of protein, with Proteinuria and hypoalbuminemia, edema, and hyperlipidemia.
HP:0002754	Osteomyelitis	Osteomyelitis is an inflammatory process accompanied by bone destruction and caused by an infecting microorganism.
HP:0002090	Pneumonia	Inflammation of any part of the lung parenchyma.
HP:0100806	Sepsis	Systemic inflammatory response to infection.
HP:0001744	Splenomegaly	Abnormal increased size of the spleen.

Source: HPO-ORDO Ontological Module - Validation association date: 23.05.2019 - PMID: 30805323, PMID: 24240290, PMID: 20301297

Glycogen storage disease type 1b (GS1b)

No frequency available

Term Identifier	Term Name	Definition
HP:0000093	Proteinuria	Increased levels of protein in the urine.
HP:0003077	Hyperlipidemia	An elevated lipid concentration in the blood.
HP:0002149	Hyperuricemia	An abnormally high level of uric acid in the blood.
HP:0003128	Lactic acidosis	An abnormal buildup of lactic acid in the body, leading to acidification of the blood and other bodily fluids.
HP:0002149	Hyperuricemia	An abnormally high level of uric acid in the blood.
HP:0002910	Elevated hepatic transaminase	Elevations of the levels of SGOT and SGPT in the serum. SGOT (serum glutamic oxaloacetic transaminase) and SGPT (serum glutamic pyruvic transaminase) are transaminases primarily found in the liver and heart and are released into the bloodstream as the result of liver or heart damage. SGOT and SGPT are used clinically mainly as markers of liver damage.
HP:0001538	Protuberant abdomen	A thrusting or bulging out of the abdomen.
HP:0001733	Pancreatitis	The presence of inflammation in the pancreas.
HP:0002240	Hepatomegaly	Abnormally increased size of the liver.
HP:0000097	Focal segmental glomerulosclerosis	Segmental accumulation of scar tissue in individual (but not all) glomeruli.
HP:0000787	Nephrolithiasis	The presence of calculi (stones) in the kidneys.
HP:0000105	Enlarged kidney	An abnormal increase in the size of the kidney.
HP:0012213	Decreased glomerular filtration rate	An abnormal reduction in the volume of fluid filtered out of plasma through glomerular capillary walls into Bowman's capsules per unit of time.
HP:0000295	Doll-like facies	A characteristic facial appearance with a round facial form, full cheeks, a short nose, and a relatively small chin.
HP:0000155	Oral ulcer	Erosion of the mucous mebrane of the mouth with local excavation of the surface, resulting from the sloughing of inflammatory necrotic tissue.
HP:0000991	Xanthomatosis	The presence of multiple xanthomas (xanthomata) in the skin. Xanthomas are yellowish, firm, lipid-laden nodules in the skin.
HP:0001114	Xanthelasma	The presence of xanthomata in the skin of the eyelid.
HP:0000939	Osteoporosis	Osteoporosis is a systemic skeletal disease characterized by low bone density and microarchitectural deterioration of bone tissue with a consequent increase in bone fragility. According to the WHO criteria, osteoporosis is defined as a BMD that lies 2.5 standard deviations or more below the average value for young healthy adults (a T-score below -2.5 SD).
HP:0001997	Gout	Recurrent attacks of acute inflammatory arthritis of a joint or set of joints caused by elevated levels of uric acid in the blood which crystallize and are deposited in joints, tendons, and surrounding tissues.
HP:0000823	Delayed puberty	Passing the age when puberty normally occurs with no physical or hormonal signs of the onset of puberty.

HP:0004322	Short stature	A height below that which is expected according to age and gender norms. Although there is no universally accepted definition of short stature, many refer to "short stature" as height more than 2 standard deviations below the mean for age and gender (or below the 3rd percentile for age and gender dependent norms).
HP:0000007	Autosomal recessive inheritance	A mode of inheritance that is observed for traits related to a gene encoded on one of the autosomes (i.e., the human chromosomes 1-22) in which a trait manifests in individuals with two pathogenic alleles, either homozygotes (two copies of the same mutant allele) or compound heterozygotes (whereby each copy of a gene has a distinct mutant allele).
HP:0001875	Neutropenia	An abnormally low number of neutrophils in the peripheral blood.
HP:0000822	Hypertension	The presence of chronic increased pressure in the systemic arterial system.
HP:0000660	Lipemia retinalis	A creamy appearance of the retinal blood vessels that occurs when the concentration of lipids in the blood are extremely increased, with pale pink to milky white retinal vessels and altered pale reflexes from choroidal vasculature.
HP:0002718	Recurrent bacterial infections	Increased susceptibility to bacterial infections, as manifested by recurrent episodes of bacterial infection.
HP:0001402	Hepatocellular carcinoma	A kind of neoplasm of the liver that originates in hepatocytes and presents macroscopically as a soft and hemorrhagic tan mass in the liver.

OMIM Clinical synopsis #232220– Creation date: 15.06.1995, John F. Jackson; revised: 20.09.2000, Kelly A. Przylepa

Griscelli syndrome type 2

Very frequent

Term Identifier	Term Name	Definition
HP:0012156	Hemophagocytosis	Phagocytosis by macrophages of erythrocytes, leukocytes, platelets, and their precursors in bone marrow and other tissues.
HP:0002240	Hepatomegaly	Abnormally increased size of the liver.
HP:0005599	Hypopigmentation of hair	
HP:0002721	Immunodeficiency	Failure of the immune system to protect the body adequately from infection, due to the absence or insufficiency of some component process or substance.
HP:0001876	Pancytopenia	An abnormal reduction in numbers of all blood cell types (red blood cells, white blood cells, and platelets).
HP:0007443	Partial albinism	Absence of melanin pigment in various areas, which is found at birth and is permanent. The lesions are known as leucoderma and are often found on the face, trunk, or limbs.
HP:0002216	Premature graying of hair	Development of gray hair at a younger than normal age.
HP:0001744	Splenomegaly	Abnormal increased size of the spleen.

Frequent

Term Identifier	Term Name	Definition
HP:0003077	Hyperlipidemia	An elevated lipid concentration in the blood.
HP:0000952	Jaundice	Yellow pigmentation of the skin due to bilirubin, which in turn is the result of increased bilirubin concentration in the bloodstream.
HP:0002716	Lymphadenopathy	Enlargment (swelling) of a lymph node.
HP:0001875	Neutropenia	An abnormally low number of neutrophils in the peripheral blood.

Occasional

Term Identifier	Term Name	Definition
HP:0001945	Fever	Elevated body temperature due to failed thermoregulation.
HP:0001276	Hypertonia	A condition in which there is increased muscle tone so that arms or legs, for example, are stiff and difficult to move.
HP:0007730	Iris hypopigmentation	An abnormal reduction in the amount of pigmentation of the iris.
HP:0002017	Nausea and vomiting	
HP:0000967	Petechiae	Petechiae are pinpoint-sized reddish/purple spots, resembling a rash, that appear just under the skin or a mucous membrane

		when capillaries have ruptured and some superficial bleeding into the skin has happened. This term refers to an abnormally increased susceptibility to developing petechiae.
HP:0002113	Pulmonary infiltrates	
HP:0001250	Seizures	Seizures are an intermittent abnormality of the central nervous system due to a sudden, excessive, disorderly discharge of cerebral neurons and characterized clinically by some combination of disturbance of sensation, loss of consciousness, impairment of psychic function, or convulsive movements. The term epilepsy is used to describe chronic, recurrent seizures.

Source: HPO-ORDO Ontological Module - Validation association date: 01.06.2016 - PMID: 25315806

Hereditary angioedema (C1Inh)

Very Frequent

Term Identifier	Term Name	Definition
HP:0002027	Abdominal pain	An unpleasant sensation characterized by physical discomfort (such as pricking, throbbing, or aching) and perceived to originate in the abdomen.
HP:0012252	Abnormal respiratory system morphology	A structural anomaly of the respiratory system.
HP:0011971	Dermatographic urticaria	An exaggerated whealing tendency when the skin is stroked, that is, formation of red, itchy bumps and lines on the skin as a result of pressure on the skin (for instance, stroking the skin with a pen or tongue depressor).
HP:0007514	Edema of the dorsum of hands	An abnormal accumulation of fluid beneath the skin on the back of the hands.
HP:0000282	Facial edema	
HP:0005225	Intestinal edema	Accumulation of cell free, noninflammatony fluid within the wall of the intestinal tract producing uniform thickening of the mucosal folds.
HP:0025349	Limbal edema	Swelling of the margin of the cornea overlapped by the sclera.
HP:0003401	Paresthesia	Abnormal sensations such as tingling, pricking, or numbness of the skin with no apparent physical cause.
HP:0040315	Tongue edema	
HP:0001025	Urticaria	Raised, well-circumscribed areas of erythema and edema involving the dermis and epidermis. Urticaria is intensely pruritic, and blanches completely with pressure.

Frequent

Term Identifier	Term Name	Definition
HP:0100755	Abnormality of salivation	
HP:0002014	Diarrhea	Abnormally increased frequency of loose or watery bowel movements.
HP:0002015	Dysphagia	Difficulty in swallowing.
HP:0002094	Dyspnea	Difficult or labored breathing.
HP:0002018	Nausea	A sensation of unease in the stomach together with an urge to vomit.
HP:0002013	Vomiting	Forceful ejection of the contents of the stomach through the mouth by means of a series of involuntary spasmic contractions.

Occasional

Term Identifier	Term Name	Definition
HP:0005483	Abnormal epiglottis morphology	An abnormality of the epiglottis.

HP:0100736	Abnormal soft palate morphology	An abnormality of the soft palate.
HP:0000172	Abnormality of the uvula	Abnormality of the uvula, the conic projection from the posterior edge of the middle of the soft palate.
HP:0001609	Hoarse voice	Hoarseness refers to a change in the pitch or quality of the voice, with the voice sounding weak, very breathy, scratchy, or husky.
HP:0002615	Hypotension	Low Blood Pressure, vascular hypotension.
HP:0005348	Inspiratory stridor	Inspiratory stridor is a high pitched sound upon inspiration that is generally related to laryngeal abnormalities.
HP:0011855	Pharyngeal edema	Abnormal accumulation of fluid leading to swelling of the pharynx.
HP:0002098	Respiratory distress	Difficulty in breathing. The physical presentation of respiratory distress is generally referred to as labored breathing, while the sensation of respiratory distress is called shortness of breath or dyspnea.

Source: HPO-ORDO Ontological Module - Validation association date: 04.07.2017 - PMID: 26661330, PMID: 22299312, PMID: 23283143

*applies only to HAE1

Herpetic encephalitis (HSE)

No frequency available

Term Identifier	Term Name	Definition
HP:0001269	Hemiparesis	Loss of strength in the arm, leg, and sometimes face on one side of the body. Hemiplegia refers to a complete loss of strength, whereas hemiparesis refers to an incomplete loss of strength.
HP:0002171	Gliosis	Gliosis is the focal proliferation of glial cells in the central nervous system.
HP:0001254	Lethargy	A state of disinterestedness, listlessness, and indifference, resulting in difficulty performing simple tasks or concentrating.
HP:0001287	Meningitis	Inflammation of the meninges.
HP:0002353	EEG abnormality	Abnormality observed by electroencephalogram (EEG), which is used to record of the brain's spontaneous electrical activity from multiple electrodes placed on the scalp.
HP:0001289	Confusion	Lack of clarity and coherence of thought, perception, understanding, or action.
HP:0001250	Seizures	Seizures are an intermittent abnormality of the central nervous system due to a sudden, excessive, disorderly discharge of cerebral neurons and characterized clinically by some combination of disturbance of sensation, loss of consciousness, impairment of psychic function, or convulsive movements. The term epilepsy is used to describe chronic, recurrent seizures.
HP:0001249	Intellectual disability	Subnormal intellectual functioning which originates during the developmental period. Intellectual disability, previously referred to as mental retardation, has been defined as an IQ score below 70.
HP:0001268	Mental deterioration	Loss of previously present mental abilities, generally in adults.
HP:0012302	Herpes simplex encephalitis	A severe virus infection of the central nervous system by the herpes simplex virus (HSV).
HP:0005353	Recurrent herpes	Increased susceptibility to herpesvirus, as manifested by recurrent episodes of herpesvirus.

OMIM Clinical synopsis #613002– Creation date: 08.03.2018, Cassandra L. Kniffin
OMIM #610551 – Creation date: 07.11.2006, Ada Hamosh; updated: 09.01.2013, Ada Hamosh

Hermansky-Pudlak syndrome (type 2)

No frequency available

Term Identifier	Term Name	Definition
HP:0000280	Coarse facial features	Absence of fine and sharp appearance of brows, nose, lips, mouth, and chin, usually because of rounded and heavy features or thickened skin with or without thickening of subcutaneous and bony tissues.
HP:0000343	Long philtrum	Distance between nasal base and midline upper lip vermilion border more than 2 SD above the mean. Alternatively, an apparently increased distance between nasal base and midline upper lip vermilion border.
HP:0000431	Wide nasal bridge	Increased breadth of the nasal bridge (and with it, the nasal root).
HP:0000319	Smooth philtrum	Flat skin surface, with no ridge formation in the central region of the upper lip between the nasal base and upper vermilion border.
HP:0000219	Thin upper lip vermilion	Height of the vermilion of the upper lip in the midline more than 2 SD below the mean. Alternatively, an apparently reduced height of the vermilion of the upper lip in the frontal view (subjective).
HP:0000252	Microcephaly	Head circumference below 2 standard deviations below the mean for age and gender.
HP:0000582	Upslanted palpebral fissure	The palpebral fissure inclination is more than two standard deviations above the mean for age (objective); or, the inclination of the palpebral fissure is greater than typical for age.
HP:0000670	Carious teeth	Caries is a multifactorial bacterial infection affecting the structure of the tooth. This term has been used to describe the presence of more than expected dental caries.
HP:0000486	Strabismus	A misalignment of the eyes so that the visual axes deviate from bifoveal fixation. The classification of strabismus may be based on a number of features including the relative position of the eyes, whether the deviation is latent or manifest, intermittent or constant, concomitant or otherwise and according to the age of onset and the relevance of any associated refractive error.
HP:0000639	Nystagmus	Rhythmic, involuntary oscillations of one or both eyes related to abnormality in fixation, conjugate gaze, or vestibular mechanisms.
HP:0000505	Visual impairment	Visual impairment (or vision impairment) is vision loss (of a person) to such a degree as to qualify as an additional support need through a significant limitation of visual capability resulting from either disease, trauma, or congenital or degenerative conditions that cannot be corrected by conventional means, such as refractive correction, medication, or surgery.
HP:0007663	Reduced visual acuity	
HP:0001107	Ocular albinism	An abnormal reduction in the amount of pigmentation (reduced or absent) of the iris and retina.

HP:0007513	Generalized hypopigmentation	
HP:0001022	Albinism	An abnormal reduction in the amount of pigmentation (reduced or absent) of skin, hair and eye (iris and retina).
HP:0007384	Aberrant melanosome maturation	
HP:0002286	Fair hair	A lesser degree of hair pigmentation than would otherwise be expected.
HP:0000613	Photophobia	Excessive sensitivity to light with the sensation of discomfort or pain in the eyes due to exposure to bright light.
HP:0001256	Intellectual disability, mild	Mild intellectual disability is defined as an intelligence quotient (IQ) in the range of 50-69.
HP:0001270	Motor delay	A type of Developmental delay characterized by a delay in acquiring motor skills.
HP:0001873	Thrombocytopenia	A reduction in the number of circulating thrombocytes.
HP:0001875	Neutropenia	An abnormally low number of neutrophils in the peripheral blood.
HP:0002240	Hepatomegaly	Abnormally increased size of the liver.
HP:0001744	Splenomegaly	Abnormal increased size of the spleen.
HP:0000358	Posteriorly rotated ears	A type of abnormal location of the ears in which the position of the ears is characterized by posterior rotation (the superior part of the ears is rotated towards the back of the head, and the inferior part of the ears towards the front).
HP:0000369	Low-set ears	Upper insertion of the ear to the scalp below an imaginary horizontal line drawn between the inner canthi of the eye and extending posteriorly to the ear.
HP:0002718	Recurrent bacterial infections	Increased susceptibility to bacterial infections, as manifested by recurrent episodes of bacterial infection.
HP:0000704	Periodontitis	Inflammation of the periodontium.
HP:0001385	Hip dysplasia	The presence of developmental dysplasia of the hip.
HP:0008807	Acetabular dysplasia	The presence of developmental dysplasia of the acetabular part of hip bone.
HP:0002206	Pulmonary fibrosis	Replacement of normal lung tissues by fibroblasts and collagen.

OMIM Clinical synopsis #608233– Creation date: 03.10.2006, Cassandra L. Kniffin

HLA class I deficiency

No frequency available

Term Identifier	Term Name	Definition
HP:0011109	Chronic sinusitis	A chronic form of sinusitis.
HP:0011950	Bronchiolitis	Inflammation of the bronchioles.
HP:0000389	Chronic otitis media	Chronic otitis media refers to fluid, swelling, or infection of the middle ear that does not heal and may cause permanent damage to the ear.
HP:0002097	Emphysema	
HP:0002110	Bronchiectasis	Persistent abnormal dilatation of the bronchi owing to localized and irreversible destruction and widening of the large airways.
HP:0002837	Recurrent bronchitis	An increased susceptibility to bronchitis as manifested by a history of recurrent bronchitis.
HP:0100582	Nasal polyposis	Polypoidal masses arising mainly from the mucous membranes of the nose and paranasal sinuses. They are freely movable and nontender overgrowths of the mucosa that frequently accompany allergic rhinitis.
HP:0001083	Ectopia lentis	Dislocation or malposition of the crystalline lens of the eye. A partial displacement (or dislocation) of the lens is described as a subluxation of the lens, while a complete displacement is termed luxation of the lens. A complete displacement occurs if the lens is completely outside the patellar fossa of the lens, either in the anterior chamber, in the vitreous, or directly on the retina. If the lens is partially displaced but still contained within the lens space, then it is termed subluxation.
HP:0200042	Skin ulcer	A discontinuity of the skin exhibiting complete loss of the epidermis and often portions of the dermis and even subcutaneous fat.
HP:0001000	Abnormality of skin pigmentation	An abnormality of the pigmentation of the skin.
HP:0031949	Recurrent bacterial upper respiratory tract infections	An increased susceptibility to bacterial upper respiratory tract infections as manifested by a history of recurrent bacterial upper respiratory tract infections (running ears - otitis, sinusitis, pharyngitis, tonsillitis).

OMIM Clinical synopsis #604571– Creation date: 07.04.2000, Assil Saleh; reviewed: 19.04.2000, Ada Hamosh

HLA class II deficiency (MHC2)

Always present

Term Identifier	Term Name	Definition
HP:0031390	Reduced MHC II surface expression	A reduction from the normal level of major histocompatibility complex class II molecules expressed at the cell surface.

Very frequent

Term Identifier	Term Name	Definition
HP:0005354	Lack of T cell function	Complete inability of T cells to perform their functions in cell-mediated immunity.
HP:0004798	Recurrent infection of the gastrointestinal tract	Recurrent infection of the gastrointestinal tract.
HP:0002205	Recurrent respiratory infections	An increased susceptibility to respiratory infections as manifested by a history of recurrent respiratory infections.

Frequent

Term Identifier	Term Name	Definition
HP:0005368	Abnormality of humoral immunity	An abnormality of the humoral immune system, which comprises antibodies produced by B cells as well as the complement system.
HP:0200124	Chronic hepatitis due to cryptosporidium infection	Chronic hepatitis associated with infection by cryptosporidia, as demonstrated (for example) by immunohistochemistry of liver tissue.
HP:0002728	Chronic mucocutaneous candidiasis	Recurrent or persistent superficial Candida infections of the skin, mucous membranes, and nails.
HP:0004313	Decreased antibody level in blood	An abnormally decreased level of immunoglobulin in blood.
HP:0025347	Decreased circulating beta-2-microglobulin level	Reduced concentration of beta-2-microglobulin in the blood.
HP:0005407	Decreased proportion of CD4-positive T cells	A decreased proportion of circulating CD4-positive helper T cells relative to total T cell count.
HP:0002014	Diarrhea	Abnormally increased frequency of loose or watery bowel movements.
HP:0001508	Failure to thrive	Failure to thrive (FTT) refers to a child whose physical growth is substantially below the norm.
HP:0004385	Protracted diarrhea	
HP:0002726	Recurrent Staphylococcus aureus infections	Increased susceptibility to Staphylococcus aureus infections, as manifested by recurrent episodes of Staphylococcus aureus infection.
HP:0002718	Recurrent bacterial infections	Increased susceptibility to bacterial infections, as manifested by recurrent episodes of bacterial infection.

HP:0005401	Recurrent candida infections	An increased susceptibility to candida infections, as manifested by a history of recurrent episodes of candida infections.
HP:0002841	Recurrent fungal infections	Increased susceptibility to fungal infections, as manifested by multiple episodes of fungal infection.
HP:0005353	Recurrent herpes	Increased susceptibility to herpesvirus, as manifested by recurrent episodes of herpesvirus.
HP:0005386	Recurrent protozoan infections	Increased susceptibility to protozoan infections, as manifested by recurrent episodes of protozoan infection.
HP:0004429	Recurrent viral infections	Increased susceptibility to viral infections, as manifested by recurrent episodes of viral infection.
HP:0000246	Sinusitis	Inflammation of the paranasal sinuses owing to a viral, bacterial, or fungal infection, allergy, or an autoimmune reaction.
HP:0030991	Sclerosing cholangitis	Cholangitis associated with evident ductal fibrosis that develops as a consequence of long-standing bile duct inflammatory, obstruction, or ischemic injury; it can be obliterative or nonobliterative.
HP:0012384	Rhinitis	Inflammation of the nasal mucosa with nasal congestion.

Occasional

Term Identifier	Term Name	Definition
HP:0031394	Abnormal CD4:CD8 ratio	Any abnormality in the relative amount of CD4+ and CD8+ T lymphocytes.
HP:0000371	Acute otitis media	Acute otitis media is a short and generally painful infection of the middle ear.
HP:0001890	Autoimmune hemolytic anemia	An autoimmune form of hemolytic anemia.
HP:0001973	Autoimmune thrombocytopenia	The presence of thrombocytopenia in combination with detection of antiplatelet antibodies.
HP:0002960	Autoimmunity	The occurrence of an immune reaction against the organism's own cells or tissues.
HP:0005403	Decrease in T cell count	An abnormally low count of T cells.
HP:0001904	Neutropenia in presence of anti-neutropil antibodies	A type of neutropenia that is observed in the presence of granulocyte-specific antibodies.
HP:0031381	Decreased lymphocyte proliferation in response to mitogen	A decreased proliferative response of lymphocytes in vitro or in vivo, when stimulated with mitogens, such as phytohemagglutinin (PHA).
HP:0001875	Neutropenia	An abnormally low number of neutrophils in the peripheral blood.
HP:0001876	Pancytopenia	An abnormal reduction in numbers of all blood cell types (red blood cells, white blood cells, and platelets).
HP:0003139	Panhypogammaglobulinemia	A reduction in the circulating levels of all the major classes of immunoglobulin. is characterized by profound decreases in all classes of immunoglobulin with an absence of circulating B lymphocytes.
HP:0000988	Skin rash	A red eruption of the skin.

Rare

Term Identifier	Term Name	Definition
HP:0001999	Abnormal facial shape	An abnormal morphology (form) of the face or its components.
HP:0002066	Gait ataxia	A type of ataxia characterized by the impairment of the ability to coordinate the movements required for normal walking. Gait ataxia is characteirzed by a wide-based staggering gait with a tendency to fall.
HP:0001260	Dysarthria	Dysarthric speech is a general description referring to a neurological speech disorder characterized by poor articulation. Depending on the involved neurological structures, dysarthria may be further classified as spastic, flaccid, ataxic, hyperkinetic and hypokinetic, or mixed.

Source: HPO-ORDO Ontological Module - Validation association date: 18.04.2019 - PMID: 25001848, PMID: 28676232, PMID: 26634365

Hoyeraal-Hreidarsson syndrome

Very frequent

Term Identifier	Term Name	Definition
HP:0001321	Cerebellar hypoplasia	Underdevelopment of the cerebellum.
HP:0001263	Global developmental delay	A delay in the achievement of motor or mental milestones in the domains of development of a child, including motor skills, speech and language, cognitive skills, and social and emotional skills. This term should only be used to describe children younger than five years of age.
HP:0001249	Intellectual disability	Subnormal intellectual functioning which originates during the developmental period. Intellectual disability, previously referred to as mental retardation, has been defined as an IQ score below 70.
HP:0004334	Dermal atrophy	Partial or complete wasting (atrophy) of the skin.
HP:0001873	Thrombocytopenia	A reduction in the number of circulating thrombocytes.
HP:0000252	Microcephaly	Occipito-frontal (head) circumference (OFC) less than -3 standard deviations compared to appropriate, age matched, normal standards (Ross JJ, Frias JL 1977, PMID:9683597). Alternatively, decreased size of the cranium.
HP:0001508	Failure to thrive	Failure to thrive (FTT) refers to a child whose physical growth is substantially below the norm.
HP:0001511	Intrauterine growth retardation	An abnormal restriction of fetal growth with fetal weight below the tenth percentile for gestational age.
HP:0004322	Short stature	A height below that which is expected according to age and gender norms. Although there is no universally accepted definition of short stature, many refer to "short stature" as height more than 2 standard deviations below the mean for age and gender (or below the 3rd percentile for age and gender dependent norms).
HP:0002721	Immunodeficiency	Failure of the immune system to protect the body adequately from infection, due to the absence or insufficiency of some component process or substance.

Frequent

Term Identifier	Term Name	Definition
HP:0002120	Cerebral cortical atrophy	Atrophy of the cortex of the cerebrum.
HP:0002119	Ventriculomegaly	An increase in size of the ventricular system of the brain.
HP:0011358	Generalized hypopigmentation of hair	Reduced pigmentation of hair diffusely.
HP:0008404	Nail dystrophy	Onychodystrophy (nail dystrophy) refers to nail changes apart from changes of the color (nail dyschromia) and involves partial or complete disruption of the various keratinous layers of the nail plate.
HP:0007392	Excessive wrinkled skin	

HP:0007440	Generalized hyperpigmentation	
HP:0002216	Premature graying of hair	Development of gray hair at a younger than normal age.
HP:0001928	Abnormality of coagulation	An abnormality of the process of blood coagulation. That is, altered ability or inability of the blood to clot.
HP:0001903	Anemia	A reduction in erythrocytes volume or hemoglobin concentration.
HP:0002209	Sparse scalp hair	Decreased number of head hairs per unit area.
HP:0002745	Oral leukoplakia	A thickened white patch on the oral mucosa that cannot be rubbed off.
HP:0001276	Hypertonia	A condition in which there is increased muscle tone so that arms or legs, for example, are stiff and difficult to move.

Occasional

Term Identifier	Term Name	Definition
HP:0001251	Ataxia	Cerebellar ataxia refers to ataxia due to dysfunction of the cerebellum. This causes a variety of elementary neurological deficits including asynergy (lack of coordination between muscles, limbs and joints), dysmetria (lack of ability to judge distances that can lead to under- oder overshoot in grasping movements), and dysdiadochokinesia (inability to perform rapid movements requiring antagonizing muscle groups to be switched on and off repeatedly).
HP:0001265	Hyporeflexia	Reduction of neurologic reflexes such as the knee-jerk reaction.
HP:0005528	Bone marrow hypocellularity	A reduced number of hematopoietic cells present in the bone marrow relative to marrow fat.
HP:0001881	Abnormal leukocyte morphology	An abnormality of leukocytes.
HP:0002514	Cerebral calcification	The presence of calcium deposition within brain structures.
HP:0002664	Neoplasm	An organ or organ-system abnormality that consists of uncontrolled autonomous cell-proliferation which can occur in any part of the body as a benign or malignant neoplasm (tumour).

Source: HPO-ORDO Ontological Module - Validation association date: 01.06.2016

Hyper IgE syndrome (HIES)

Very frequent

Term Identifier	Term Name	Definition
HP:0000989	Pruritus	Pruritus is an itch or a sensation that makes a person want to scratch. This term refers to an abnormally increased disposition to experience pruritus.
HP:0200042	Skin ulcer	A discontinuity of the skin exhibiting complete loss of the epidermis and often portions of the dermis and even subcutaneous fat.
HP:0011354	Generalized abnormality of skin	An abnormality of the skin that is not localized to any one particular region.
HP:0000988	Skin rash	A red eruption of the skin.
HP:0002719	Recurrent infections	Increased susceptibility to infections.
HP:0003212	Increased IgE level	An abnormally increased level of immunoglobulin E in blood.
HP:0000964	Eczema	Eczema is a form of dermatitis. The term eczema is broadly applied to a range of persistent skin conditions and can be related to a number of underlying conditions. Manifestations of eczema can include dryness and recurring skin rashes with redness, skin edema, itching and dryness, crusting, flaking, blistering, cracking, oozing, or bleeding.
HP:0002205	Recurrent respiratory infections	An increased susceptibility to respiratory infections as manifested by a history of recurrent respiratory infections.
HP:0100750	Atelectasis	Collapse of part of a lung associated with absence of inflation (air) of that part.

Frequent

Term Identifier	Term Name	Definition
HP:0000175	Cleft palate	Cleft palate is a developmental defect of the palate resulting from a failure of fusion of the palatine processes and manifesting as a separation of the roof of the mouth (soft and hard palate).
HP:0000271	Abnormality of the face	An abnormality of the face.
HP:0000230	Gingivitis	Inflammation of the gingiva.
HP:0000431	Wide nasal bridge	Increased breadth of the nasal bridge (and with it, the nasal root).
HP:0011220	Prominent forehead	Forward prominence of the entire forehead, due to protrusion of the frontal bone.
HP:0000684	Delayed eruption of teeth	Delayed tooth eruption, which can be defined as tooth eruption more than 2 SD beyond the mean eruption age.
HP:0000164	Abnormality of the dentition	Any abnormality of the teeth.
HP:0001818	Paronychia	The nail disease paronychia is an often-tender bacterial or fungal hand infection or foot infection where the nail and skin

		meet at the side or the base of a finger or toenail. The infection can start suddenly (acute paronychia) or gradually (chronic paronychia).
HP:0200034	Papule	A circumscribed, solid elevation of skin with no visible fluid, varying in size from a pinhead to less than 10mm in diameter at the widest point.
HP:0001595	Abnormality of the hair	An abnormality of the hair.
HP:0008391	Dystrophic fingernails	The presence of misshapen or partially destroyed nail plates, often with accumulation of soft, yellow keratin between the dystrophic nail plate and nail bed, resulting in elevation of the nail plate.
HP:0000389	Chronic otitis media	Chronic otitis media refers to fluid, swelling, or infection of the middle ear that does not heal and may cause permanent damage to the ear.
HP:0005692	Joint hyperflexibility	Increased mobility and flexibility in the joint due to the tension in tissues such as ligaments and muscles.
HP:0002757	Recurrent fractures	The repeated occurrence of bone fractures (implying an abnormally increased tendency for fracture).
HP:0002650	Scoliosis	The presence of an abnormal lateral curvature of the spine.
HP:0012735	Cough	A sudden, audible expulsion of air from the lungs through a partially closed glottis, preceded by inhalation.
HP:0001880	Eosinophilia	Increased count of eosinophils in the blood.
HP:0000490	Deeply set eye	An eye that is more deeply recessed into the plane of the face than is typical.

Occasional

Term Identifier	Term Name	Definition
HP:0001363	Craniosynostosis	Craniosynostosis refers to the premature closure of the cranial sutures. Primary craniosynostosis refers to the closure of one or more sutures due to abnormalities in skull development, and secondary craniosynostosis results from failure of brain growth.
HP:0200037	Skin vesicle	A circumscribed, fluid-containing, epidermal elevation generally considered less than 10mm in diameter at the widest point.
HP:0002754	Osteomyelitis	Osteomyelitis is an inflammatory process accompanied by bone destruction and caused by an infecting microorganism.
HP:0100658	Cellulitis	A bacterial infection and inflammation of the skin und subcutaneous tissues.
HP:0001945	Fever	Elevated body temperature due to failed thermoregulation.
HP:0002617	Dilatation	Abnormal outpouching or sac-like dilatation in the wall of an atery, vein or the heart.
HP:0002665	Lymphoma	A cancer originating in lymphocytes and presenting as a solid tumor of lymhpoid cells.

Source: HPO-ORDO Ontological Module - Validation association date: 01.06.2016

*applies only to autosomal dominant Hyper IgE syndrome

Immunodeficiency-centromeric instability-facial anomalies syndrome (ICF)

Very frequent

Term Identifier	Term Name	Definition
HP:0000347	Micrognathia	Developmental hypoplasia of the mandible.
HP:0002721	Immunodeficiency	Failure of the immune system to protect the body adequately from infection, due to the absence or insufficiency of some component process or substance.
HP:0004313	Decreased antibody level in blood	An abnormally decreased level of immunoglobulin in blood.
HP:0002205	Recurrent respiratory infections	An increased susceptibility to respiratory infections as manifested by a history of recurrent respiratory infections.
HP:0003220	Abnormality of chromosome stability	A type of chromosomal aberration characterised by reduced resistance of chromosomes to change or deterioration.
HP:0004322	Short stature	A height below that which is expected according to age and gender norms. Although there is no universally accepted definition of short stature, many refer to "short stature" as height more than 2 standard deviations below the mean for age and gender (or below the 3rd percentile for age and gender dependent norms).

Frequent

Term Identifier	Term Name	Definition
HP:0005280	Depressed nasal bridge	Posterior positioning of the nasal root in relation to the overall facial profile for age.
HP:0000256	Macrocephaly	Occipitofrontal (head) circumference greater than 97th centile compared to appropriate, age matched, sex-matched normal standards. Alternatively, a apparently increased size of the cranium.
HP:0005374	Cellular immunodeficiency	An immunodeficiency characterized by defective cell-mediated immunity or humoral immunity.
HP:0001888	Lymphopenia	A reduced number of lymphocytes in the blood.
HP:0001903	Anemia	A reduction in erythrocytes volume or hemoglobin concentration.
HP:0001874	Abnormality of neutrophils	A neutrophil abnormality.
HP:0001334	Communicating hydrocephalus	A form of hydrocephalus in which there is no visible obstruction to the flow of the cerebrospinal fluid between the ventricles and subarachnoid space.
HP:0001263	Global developmental delay	A delay in the achievement of motor or mental milestones in the domains of development of a child, including motor skills, speech and language, cognitive skills, and social and emotional skills. This term should only be used to describe children younger than five years of age.
HP:0001249	Intellectual disability	Subnormal intellectual functioning which originates during the developmental period. Intellectual disability, previously

		referred to as mental retardation, has been defined as an IQ score below 70.
HP:0002024	Malabsorption	Impaired ability to absorb one or more nutrients from the intestine.

Occasional

Term Identifier	Term Name	Definition
HP:0000286	Epicanthus	A fold of skin starting above the medial aspect of the upper eyelid and arching downward to cover, pass in front of and lateral to the medial canthus.
HP:0010808	Protruding tongue	Tongue extending beyond the alveolar ridges or teeth at rest.
HP:0012368	Flat face	Absence of concavity or convexity of the face when viewed in profile.
HP:0001537	Umbilical hernia	Protrusion of abdominal contents through a defect in the abdominal wall musculature around the umbilicus. Skin and subcutaneous tissue overlie the defect.
HP:0000369	Low-set ears	Upper insertion of the ear to the scalp below an imaginary horizontal line drawn between the inner canthi of the eye and extending posteriorly to the ear.
HP:0000316	Hypertelorism	Interpupillary distance more than 2 SD above the mean (alternatively, the appearance of an increased interpupillary distance or widely spaced eyes).
HP:0000158	Macroglossia	Increased length and width of the tongue.

Source: HPO-ORDO Ontological Module - Validation association date: 01.06.2016

IPEX-like disease

Very frequent

Term Identifier	Term Name	Definition
HP:0002728	Chronic mucocutaneous candidiasis	Recurrent or persistent superficial Candida infections of the skin, mucous membranes, and nails.
HP:0002788	Recurrent upper respiratory tract infections	An increased susceptibility to upper respiratory tract infections as manifested by a history of recurrent upper respiratory tract infections (running ears - otitis, sinusitis, pharyngitis, tonsillitis).
HP:0002242	Abnormal intestine morphology	An abnormality of the intestine. The closely related term enteropathy is used to refer to any disease of the intestine.
HP:0002750	Delayed skeletal maturation	A decreased rate of skeletal maturation. Delayed skeletal maturation can be diagnosed on the basis of an estimation of the bone age from radiographs of specific bones in the human body.
HP:0001510	Growth delay	A deficiency or slowing down of growth pre- and postnatally.
HP:0004322	Short stature	A height below that which is expected according to age and gender norms. Although there is no universally accepted definition of short stature, many refer to "short stature" as height more than 2 standard deviations below the mean for age and gender (or below the 3rd percentile for age and gender dependent norms).
HP:0000009	Functional abnormality of the bladder	Dysfunction of the urinary bladder.

Frequent

Term Identifier	Term Name	Definition
HP:0005353	Recurrent herpes	Increased susceptibility to herpesvirus, as manifested by recurrent episodes of herpesvirus.
HP:0004387	Enterocolitis	An inflammation of the colon and small intestine. However, most conditions are either categorized as Enteritis (inflammation of the small intestine) or Colitis (inflammation of the large intestine).
HP:0000964	Eczema	Eczema is a form of dermatitis. The term eczema is broadly applied to a range of persistent skin conditions and can be related to a number of underlying conditions. Manifestations of eczema can include dryness and recurring skin rashes with redness, skin edema, itching and dryness, crusting, flaking, blistering, cracking, oozing, or bleeding.
HP:0002958	Immune dysregulation	Altered immune function characterized by lymphoid proliferation, immune activation, and excessive autoreactivity often leading to autoimmune/inflammatory complications.

HP:0002721	Immunodeficiency	Failure of the immune system to protect the body adequately from infection, due to the absence or insufficiency of some component process or substance.
HP:0001890	Autoimmune hemolytic anemia	An autoimmune form of hemolytic anemia.
HP:0002719	Recurrent infections	Increased susceptibility to infections.
HP:0011123	Inflammatory abnormality of the skin	The presence of inflammation of the skin. That is, an abnormality of the skin resulting from the local accumulation of fluid, plasma proteins, and leukocytes.
HP:0004944	Dilatation of the cerebral artery	The presence of a localized dilatation or ballooning of a cerebral artery.
HP:0001920	Renal artery stenosis	The presence of stenosis of the renal artery.
HP:0012163	Carotid artery dilatation	A dilatation (balooning or bulging out of the vessel wall) of a carotid artery.
HP:0100817	Renovascular hypertension	The presence of hypertension related to stenosis of the renal artery.
HP:0001888	Lymphopenia	A reduced number of lymphocytes in the blood.
HP:0010976	B lymphocytopenia	An abnormal decrease from the normal count of B cells.
HP:0002014	Diarrhea	Abnormally increased frequency of loose or watery bowel movements.
HP:0001433	Hepatosplenomegaly	Simultaneous enlargement of the liver and spleen.
HP:0011473	Villous atrophy	The enteric villi are atrophic or absent.
HP:0100646	Thyroiditis	Inflammation of the thyroid gland.
HP:0100651	Type I diabetes mellitus	A chronic condition in which the pancreas produces little or no insulin. Type I diabetes mellitus is manifested by the sudden onset of severe hyperglycemia with rapid progression to diabetic ketoacidosis unless treated with insulin.
HP:0000832	Primary hypothyroidism	A type of hypothyroidism that results from a defect in the thyroid gland.
HP:0000938	Osteopenia	Osteopenia is a term to define bone density that is not normal but also not as low as osteoporosis. By definition from the World Health Organization osteopenia is defined by bone densitometry as a T score -1 to -2.5.
HP:0040160	Generalized osteoporosis	
HP:0000823	Delayed puberty	Passing the age when puberty normally occurs with no physical or hormonal signs of the onset of puberty.
HP:0002110	Bronchiectasis	Persistent abnormal dilatation of the bronchi owing to localized and irreversible destruction and widening of the large airways.
HP:0000818	Abnormality of the endocrine system	An abnormality of the endocrine system.

Occasional

Term Identifier	Term Name	Definition
HP:0012115	Hepatitis	Inflammation of the liver.
HP:0003613	Antiphospholipid antibody positivity	The presence of circulating autoantibodies to phospholipids.

HP:0002724	Recurrent Aspergillus infections	An increased susceptibility to Aspergillus infections, as manifested by a history of recurrent episodes of Aspergillus infections.
HP:0030355	Abnormal serum interferon-gamma level	Abnormal levels of interferon gamma measured in the blood circulation.
HP:0004966	Medial calcification of large arteries	Calcification, that is, pathological deposition of calcium salts in the tunica media of large (conduit) arteries.
HP:0001635	Congestive heart failure	The presence of an abnormality of cardiac function that is responsible for the failure of the heart to pump blood at a rate that is commensurate with the needs of the tissues or a state in which abnormally elevated filling pressures are required for the heart to do so. Heart failure is frequently related to a defect in myocardial contraction.
HP:0001655	Patent foramen ovale	Failure of the foramen ovale to seal postnatally, leaving a potential conduit between the left and right cardiac atria.
HP:0001904	Neutropenia in presence of anti-neutropil antibodies	A type of neutropenia that is observed in the presence of granulocyte-specific antibodies.
HP:0001973	Autoimmune thrombocytopenia	The presence of thrombocytopenia in combination with detection of antiplatelet antibodies.
HP:0001873	Thrombocytopenia	A reduction in the number of circulating thrombocytes.
HP:0002092	Pulmonary arterial hypertension	Pulmonary hypertension is defined mean pulmonary artery pressure of 25mmHg or more and pulmonary capillary wedge pressure of 15mmHg or less when measured by right heart catheterisation at rest and in a supine position.
HP:0011459	Esophageal carcinoma	The presence of a carcinoma of the esophagus.
HP:0012182	Oropharyngeal squamous cell carcinoma	A squamous cell carcinoma that originates in the oropharnyx.
HP:0002383	Encephalitis	

Exclusion criteria

Term Identifier	Term Name	Definition
HP:0005403	Decrease in T cell count	An abnormally low count of T cells.

Source: HPO-ORDO Ontological Module - Validation association date: 25.04.2016 - PMID: 21714643, PMID: 23541320, PMID: 23534974

*applies only to autoimmune enteropathy and endocrinopathy – susceptibility to chronic infections syndrome

Isolated congenital asplenia

No frequency available

Term Identifier	Term Name	Definition
HP:0000006	Autosomal dominant inheritance	A mode of inheritance that is observed for traits related to a gene encoded on one of the autosomes (i.e., the human chromosomes 1-22) in which a trait manifests in heterozygotes. In the context of medical genetics, an autosomal dominant disorder is caused when a single copy of the mutant allele is present. Males and females are affected equally, and can both transmit the disorder with a risk of 50% for each child of inheriting the mutant allele.
HP:0001746	Asplenia	Absence (aplasia) of the spleen.
HP:0001438	Abnormality of abdomen morphology	A structural abnormality of the abdomen ('belly'), that is, the part of the body between the pelvis and the thorax.
HP:0001894	Thrombocytosis	Increased numbers of platelets in the peripheral blood.
HP:0002718	Recurrent bacterial infections	Increased susceptibility to bacterial infections, as manifested by recurrent episodes of bacterial infection.
HP:0005366	Recurrent streptococcus pneumoniae infections	Increased susceptibility to streptococcus pneumoniae infections as manifested by a history of recurrent infections by streptococcus pneumoniae.

Source: OMIM #271400 – Creation date: 04.06.1986, Victor A. McKusick; updated: 08.10.2013, Marla J.F. O´Neill

Mannose-binding Lectin Deficiency

No frequency available

Term Identifier	Term Name	Definition
HP:0031699	Disseminated cryptosporidium infection	Failure to contain infection by a protozoan of the genus Cryptosporidium, leading to spread to many parts of the body.
HP:0001581	Recurrent skin infections	Infections of the skin that happen multiple times.
HP:0005353	Recurrent herpes	Increased susceptibility to herpesvirus, as manifested by recurrent episodes of herpesvirus.
HP:0002742	Recurrent Klebsiella infections	Increased susceptibility to Klebsiella infections, as manifested by recurrent episodes of Klebsiella infection.
HP:0005381	Recurrent meningococcal disease	Recurrent infections by Neisseria meningitidis (one of the most common causes of bacterial meningitis), which is also known as meningococcus.
HP:0001508	Failure to thrive	Failure to thrive (FTT) refers to a child whose physical growth is substantially below the norm.
HP:0000006	Autosomal dominant inheritance	A mode of inheritance that is observed for traits related to a gene encoded on one of the autosomes (i.e., the human chromosomes 1-22) in which a trait manifests in heterozygotes. In the context of medical genetics, an autosomal dominant disorder is caused when a single copy of the mutant allele is present. Males and females are affected equally, and can both transmit the disorder with a risk of 50% for each child of inheriting the mutant allele.

Source: OMIM #614372 – Creation date: 02.12.2011, Matthew B. Gross; updated: 28.11.2016, Cassandra L. Kniffin
PMID: 769701; PMID: 7707811

MonoMAC

No frequency available

Term Identifier	Term Name	Definition
HP:0032283	Disseminated nontuberculous mycobacterial infection	An infection with nontuberculous mycobacteria that affects multiple body sites. Such infections can occur in individuals with immune disease.
HP:0004429	Recurrent viral infections	Increased susceptibility to viral infections, as manifested by recurrent episodes of viral infection.
HP:0001915	Aplastic anemia	Aplastic anemia is defined as pancytopenia with a hypocellular marrow.
HP:0001875	Neutropenia	An abnormally low number of neutrophils in the peripheral blood.
HP:0012312	Monocytopenia	An decreased number of circulating monocytes.
HP:0012176	Abnormal natural killer cell morphology	An anomaly of the natural killer cell, which is a lymphocyte that can spontaneously kill a variety of target cells without prior antigenic activation via germline encoded activation receptors and also regulate immune responses via cytokine release and direct contact with other cells.
HP:0001888	Lymphopenia	A reduced number of lymphocytes in the blood.
HP:0002721	Immunodeficiency	Failure of the immune system to protect the body adequately from infection, due to the absence or insufficiency of some component process or substance.
HP:0002841	Recurrent fungal infections	Increased susceptibility to fungal infections, as manifested by multiple episodes of fungal infection.
HP:0011275	Recurrent mycobacterium avium complex infections	Increased susceptibility to mycobacterial avium complex infections, as manifested by recurrent episodes of mycobacterial infection.
HP:0002863	Myelodysplasia	Clonal hematopoietic stem cell disorders characterized by dysplasia (ineffective production) in one or more hematopoietic cell lineages, leading to anemia and cytopenia.
HP:0012324	Myeloid leukemia	A leukemia that originates from a myeloid cell, that is the blood forming cells of the bone marrow.
HP:0006517	Alveolar proteinosis	Abnormal accumulation of surfactant-like, periodic acid-schiff-positive lipoproteinaceous material in macrophages within the alveolar spaces and distal bronchioles. This results in gas exchange impairment leading to dyspnea and alveolar infiltrates.
HP:0012219	Erythema nodosum	An erythematous eruption commonly associated with drug reactions or infection and characterized by inflammatory nodules that are usually tender, multiple, and bilateral.
HP:0001004	Lymphedema	Localized fluid retention and tissue swelling caused by a compromised lymphatic system.

Source: OMIM #614172 – Creation date: 17.08.2011, Paul J. Converse; updated: 25.11.2014, Ada Hamosh

Netherton syndrome

Very frequent

Term Identifier	Term Name	Definition
HP:0003212	Increased IgE level	An abnormally increased level of immunoglobulin E in blood.
HP:0100326	Immunologic hypersensitivity	Immunological states where the immune system produces harmful responses upon reexposure to sensitising antigens.
HP:0000964	Eczema	Eczema is a form of dermatitis. The term eczema is broadly applied to a range of persistent skin conditions and can be related to a number of underlying conditions. Manifestations of eczema can include dryness and recurring skin rashes with redness, skin edema, itching and dryness, crusting, flaking, blistering, cracking, oozing, or bleeding.
HP:0000956	Acanthosis	A dermatosis characterized by thickened, hyperpigmented plaques, typically on the intertriginous surfaces and neck.
HP:0008064	Ichthyosis	An abnormality of the skin characterized the presence of excessive amounts of dry surface scales on the skin resulting from an abnormality of keratinization.
HP:0002213	Fine hair	Hair that is fine or thin to the touch.
HP:0007479	Congenital nonbullous ichthyosiform erythroderma	The term collodion baby applies to newborns who appear to have an extra layer of skin (known as a collodion membrane) that has a collodion-like quality. It is a descriptive term, not a specific diagnosis or disorder (as such, it is a syndrome). Affected babies are born in a collodion membrane, a shiny waxy outer layer to the skin. This is shed 10-14 days after birth, revealing the main symptom of the disease, extensive scaling of the skin caused by hyperkeratosis. With increasing age, the scaling tends to be concentrated around joints in areas such as the groin, the armpits, the inside of the elbow and the neck. The scales often tile the skin and may resemble fish scales.
HP:0001595	Abnormality of the hair	An abnormality of the hair.
HP:0009886	Trichorrhexis nodosa	Trichorrhexis nodosa is the formation of nodes along the hair shaft through which breakage readily occurs. It is thus a focal defect in the hair fiber that is characterized by thickening or weak points (nodes) that cause the hair to break off easily. The result is defective, abnormally fragile hair.
HP:0007400	Irregular hyperpigmentation	
HP:0002209	Sparse scalp hair	Decreased number of head hairs per unit area.
HP:0002099	Asthma	Asthma is characterized by increased responsiveness of the tracheobronchial tree to multiple stimuli, leading to narrowing of the air passages with resultant dyspnea, cough, and wheezing.

HP:0001025	Urticaria	Raised, well-circumscribed areas of erythema and edema involving the dermis and epidermis. Urticaria is intensely pruritic, and blanches completely with pressure.
HP:0002024	Malabsorption	Impaired ability to absorb one or more nutrients from the intestine.

Frequent

Term Identifier	Term Name	Definition
HP:0002205	Recurrent respiratory infections	An increased susceptibility to respiratory infections as manifested by a history of recurrent respiratory infections.
HP:0004313	Decreased antibody level in blood	An abnormally decreased level of immunoglobulin in blood.
HP:0001263	Global developmental delay	A delay in the achievement of motor or mental milestones in the domains of development of a child, including motor skills, speech and language, cognitive skills, and social and emotional skills. This term should only be used to describe children younger than five years of age.
HP:0001250	Seizures	Seizures are an intermittent abnormality of the central nervous system due to a sudden, excessive, disorderly discharge of cerebral neurons and characterized clinically by some combination of disturbance of sensation, loss of consciousness, impairment of psychic function, or convulsive movements. The term epilepsy is used to describe chronic, recurrent seizures.
HP:0001249	Intellectual disability	Subnormal intellectual functioning which originates during the developmental period. Intellectual disability, previously referred to as mental retardation, has been defined as an IQ score below 70.
HP:0002097	Emphysema	

Occasional

Term Identifier	Term Name	Definition
HP:0002719	Recurrent infections	Increased susceptibility to infections.
HP:0000988	Skin rash	A red eruption of the skin.
HP:0001019	Erythroderma	An inflammatory exfoliative dermatosis involving nearly all of the surface of the skin. Erythroderma develops suddenly. A patchy erythema may generalize and spread to affect most of the skin. Scaling may appear in 2-6 days and be accompanied by hot, red, dry skin, malaise, and fever.
HP:0000958	Dry skin	Skin characterized by the lack of natural or normal moisture.
HP:0000535	Sparse and thin eyebrow	Decreased density/number and/or decreased diameter of eyebrow hairs.
HP:0000653	Sparse eyelashes	Decreased density/number of eyelashes.
HP:0003355	Aminoaciduria	An increased concentration of an amino acid in the urine.
HP:0001944	Dehydration	
HP:0000126	Hydronephrosis	Severe distention of the kidney with dilation of the renal pelvis and calices.

HP:0000086	Ectopic kidney	A developmental defect in which a kidney is located in an abnormal anatomic position.
HP:0004322	Short stature	A height below that which is expected according to age and gender norms. Although there is no universally accepted definition of short stature, many refer to "short stature" as height more than 2 standard deviations below the mean for age and gender (or below the 3rd percentile for age and gender dependent norms).

Source: HPO-ORDO Ontological Module - Validation association date: 01.06.2016

Nijmegen breakage syndrome

Very frequent

Term Identifier	Term Name	Definition
HP:0000252	Microcephaly	Occipito-frontal (head) circumference (OFC) less than -3 standard deviations compared to appropriate, age matched, normal standards (Ross JJ, Frias JL 1977, PMID:9683597). Alternatively, decreased size of the cranium.
HP:0002002	Deep philtrum	Accentuated, prominent philtral ridges giving rise to an exaggerated groove in the midline between the nasal base and upper vermillion border.
HP:0000278	Retrognathia	An abnormality in which the mandible is mislocalised posteriorly.
HP:0000444	Convex nasal ridge	Nasal ridge curving anteriorly to an imaginary line that connects the nasal root and tip. The nose appears often also prominent, and the columella low.
HP:0000294	Low anterior hairline	Distance between the hairline (trichion) and the glabella (the most prominent point on the frontal bone above the root of the nose), in the midline, more than two SD below the mean. Alternatively, an apparently decreased distance between the hairline and the glabella.
HP:0005280	Depressed nasal bridge	Posterior positioning of the nasal root in relation to the overall facial profile for age.
HP:0000340	Sloping forehead	Inclination of the anterior surface of the forehead from the vertical more than two standard deviations above the mean (objective); or apparently excessive posterior sloping of the forehead in a lateral view.
HP:0000470	Short neck	Diminished length of the neck.
HP:0000426	Prominent nasal bridge	Anterior positioning of the nasal root in comparison to the usual positioning for age.
HP:0000271	Abnormality of the face	An abnormality of the face.
HP:0000582	Upslanted palpebral fissure	The palpebral fissure inclination is more than two standard deviations above the mean for age (objective); or, the inclination of the palpebral fissure is greater than typical for age.
HP:0000448	Prominent nose	Distance between subnasale and pronasale more than two standard deviations above the mean, or alternatively, an apparently increased anterior protrusion of the nasal tip.
HP:0002025	Anal stenosis	Abnormal narrowing of the anal opening.
HP:0002023	Anal atresia	Congenital absence of the anus, i.e., the opening at the bottom end of the intestinal tract.
HP:0012732	Anorectal anomaly	An abnormality of the anus or rectum.
HP:0002028	Chronic diarrhea	The presence of chronic diarrhea, which is usually taken to mean diarrhea that has persisted for over 4 weeks.
HP:0006532	Recurrent pneumonia	An increased susceptibility to pneumonia as manifested by a history of recurrent episodes of pneumonia.

HP:0005425	Recurrent sinopulmonary infections	An increased susceptibility to infections involving both the paranasal sinuses and the lungs, as manifested by a history of recurrent sinopulmonary infections.
HP:0002205	Recurrent respiratory infections	An increased susceptibility to respiratory infections as manifested by a history of recurrent respiratory infections.
HP:0001890	Autoimmune hemolytic anemia	An autoimmune form of hemolytic anemia.
HP:0001595	Abnormality of the hair	An abnormality of the hair.
HP:0011362	Abnormal hair quantity	An abnormal amount of hair.
HP:0001268	Mental deterioration	Loss of previously present mental abilities, generally in adults.
HP:0007018	Attention deficit hyperactivity disorder	Attention deficit hyperactivity disorder (ADHD) manifests at age 2-3 years or by first grade at the latest. The main symptoms are distractibility, impulsivity, hyperactivity, and often trouble organizing tasks and projects, difficulty going to sleep, and social problems from being aggressive, loud, or impatient.
HP:0001873	Thrombocytopenia	A reduction in the number of circulating thrombocytes.
HP:0001878	Hemolytic anemia	A type of anemia caused by premature destruction of red blood cells (hemolysis).
HP:0000400	Macrotia	Median longitudinal ear length greater than two standard deviations above the mean and median ear width greater than two standard deviations above the mean (objective); or, apparent increase in length and width of the pinna (subjective).
HP:0000364	Hearing abnormality	An abnormality of the sensory perception of sound.
HP:0004326	Cachexia	Severe weight loss, wasting of muscle, loss of appetite, and general debility related to a chronic disease.
HP:0004322	Short stature	A height below that which is expected according to age and gender norms. Although there is no universally accepted definition of short stature, many refer to "short stature" as height more than 2 standard deviations below the mean for age and gender (or below the 3rd percentile for age and gender dependent norms).
HP:0003220	Abnormality of chromosome stability	A type of chromosomal aberration characterised by reduced resistance of chromosomes to change or deterioration.

Frequent

Term Identifier	Term Name	Definition
HP:0100515	Pollakisuria	Increased frequency of urination.
HP:0002664	Neoplasm	An organ or organ-system abnormality that consists of uncontrolled autonomous cell-proliferation which can occur in any part of the body as a benign or malignant neoplasm (tumour).

Occasional

Term Identifier	Term Name	Definition

HP:0100335	Non-midline cleft lip	Clefting of the upper lip affecting the lateral portions of the upper lip rather than the midline/median region.
HP:0000492	Abnormal eyelid morphology	An abnormality of the eyelids.
HP:0000175	Cleft palate	Cleft palate is a developmental defect of the palate resulting from a failure of fusion of the palatine processes and manifesting as a separation of the roof of the mouth (soft and hard palate).
HP:0002859	Rhabdomyosarcoma	
HP:0009733	Glioma	The presence of a glioma, which is a neoplasm of the central nervous system originating from a glial cell (astrocytes or oligodendrocytes).
HP:0002488	Acute leukemia	A clonal (malignant) hematopoietic disorder with an acute onset, affecting the bone marrow and the peripheral blood. The malignant cells show minimal differentiation and are called blasts, either myeloid blasts (myeloblasts) or lymphoid blasts (lymphoblasts).
HP:0002665	Lymphoma	A cancer originating in lymphocytes and presenting as a solid tumor of lymhpoid cells.
HP:0012191	B-cell lymphoma	A type of lymphoma that originates in B-cells.
HP:0012190	T-cell lymphoma	A type of lymphoma that originates in T-cells.
HP:0001480	Freckling	The presence of an increased number of freckles, small circular spots on the skin that are darker than the surrounding skin because of deposits of melanin.
HP:0000992	Cutaneous photosensitivity	An increased sensitivity of the skin to light. Photosensitivity may result in a rash upon exposure to the sun (which is known as photodermatosis). Photosensitivity can be diagnosed by phototests in which light is shone on small areas of skin.
HP:0002269	Abnormality of neuronal migration	An abnormality resulting from an anomaly of neuronal migration, i.e., of the process by which neurons travel from their origin to their final position in the brain.
HP:0001324	Muscle weakness	Reduced strength of muscles.
HP:0003202	Skeletal muscle atrophy	The presence of skeletal muscular atrophy (which is also known as amyotrophy).
HP:0002878	Respiratory failure	A severe form of respiratory insufficiency characterized by inadequate gas exchange such that the levels of oxygen or carbon dioxide cannot be maintained within normal limits.
HP:0003011	Abnormality of the musculature	Abnormality originating in one or more muscles, i.e., of the set of muscles of body.

Source: HPO-ORDO Ontological Module - Validation association date: 01.06.2016

Omenn syndrome

Very frequent

Term Identfier	Term Name	Definition
HP:0004430	Severe combined immunodeficiency	A combined immunodeficiency primary immune deficiency that is characterized by a more severe defect in both the T- and B-lymphocyte systems.
HP:0001019	Erythroderma	An inflammatory exfoliative dermatosis involving nearly all of the surface of the skin. Erythroderma develops suddenly. A patchy erythema may generalize and spread to affect most of the skin. Scaling may appear in 2-6 days and be accompanied by hot, red, dry skin, malaise, and fever.
HP:0002716	Lymphadenopathy	Enlargment (swelling) of a lymph node.
HP:0001596	Alopecia	Loss of hair from the head or body.
HP:0004332	Abnormal lymphocyte morphology	An abnormality of lymphocytes.
HP:0002240	Hepatomegaly	Abnormally increased size of the liver.
HP:0002028	Chronic diarrhea	The presence of chronic diarrhea, which is usually taken to mean diarrhea that has persisted for over 4 weeks.
HP:0001508	Failure to thrive	Failure to thrive (FTT) refers to a child whose physical growth is substantially below the norm.

Frequent

Term Identifier	Term Name	Definition
HP:0002090	Pneumonia	Inflammation of any part of the lung parenchyma.
HP:0001072	Thickened skin	Laminar thickening of skin.
HP:0000958	Dry skin	Skin characterized by the lack of natural or normal moisture.
HP:0000989	Pruritus	Pruritus is an itch or a sensation that makes a person want to scratch. This term refers to an abnormally increased disposition to experience pruritus.
HP:0007549	Desquamation of skin soon after birth	
HP:0001880	Eosinophilia	Increased count of eosinophils in the blood.
HP:0001974	Leukocytosis	An abnormal increase in the number of leukocytes in the blood.
HP:0001744	Splenomegaly	Abnormal increased size of the spleen.
HP:0000969	Edema	An abnormal accumulation of fluid beneath the skin, or in one or more cavities of the body.
HP:0001945	Fever	Elevated body temperature due to failed thermoregulation.
HP:0100840	Aplasia/Hypoplasia of the eyebrow	Absence or underdevelopment of the eyebrow.

Occasional

Term Identifier	Term Name	Definition
HP:0100806	Sepsis	Systemic inflammatory response to infection.

HP:0002960	Autoimmunity	The occurrence of an immune reaction against the organism's own cells or tissues.
HP:0001903	Anemia	A reduction in erythrocytes volume or hemoglobin concentration.
HP:0100646	Thyroiditis	Inflammation of the thyroid gland.
HP:0000821	Hypothyroidism	Deficiency of thyroid hormone.
HP:0001831	Short toe	A toe that appears disproportionately short compared to the foot.
HP:0000100	Nephrotic syndrome	Nephrotic syndrome is a collection of findings resulting from glomerular dysfunction with an increase in glomerular capillary wall permeability associated with pronounced proteinuria. Nephrotic syndrome refers to the constellation of clinical findings that result from severe renal loss of protein, with Proteinuria and hypoalbuminemia, edema, and hyperlipidemia.
HP:0000944	Abnormality of the metaphysis	An abnormality of one or more metaphysis, i.e., of the somewhat wider portion of a long bone that is adjacent to the epiphyseal growth plate and grows during childhood.
HP:0002665	Lymphoma	A cancer originating in lymphocytes and presenting as a solid tumor of lymhpoid cells.

Source: HPO-ORDO Ontological Module - Validation association date: 01.06.2016

Papillon-Lefèvre syndrome

Very frequent

Term Identifier	Term Name	Definition
HP:0000982	Palmoplantar keratoderma	Abnormal thickening of the skin of the palms of the hands and the soles of the feet.
HP:0001231	Abnormality of the fingernails	An abnormality of the fingernails.
HP:0000972	Palmoplantar hyperkeratosis	Hyperkeratosis affecting the palm of the hand and the sole of the foot.
HP:0000166	Severe periodontitis	A severe form of periodontitis.
HP:0000704	Periodontitis	Inflammation of the periodontium.
HP:0200039	Pustule	A small elevation of the skin containing cloudy or purulent material usually consisting of necrotic inflammatory cells.
HP:0009804	Reduced number of teeth	The presence of a reduced number of teeth as in Hypodontia or as in Anodontia.
HP:0000164	Abnormality of the dentition	Any abnormality of the teeth.
HP:0000230	Gingivitis	Inflammation of the gingiva.
HP:0006308	Atrophy of alveolar ridges	
HP:0006323	Premature loss of primary teeth	Loss of the primary (also known as deciduous) teeth before the usual age.

Frequent

Term Identifier	Term Name	Definition
HP:0001597	Abnormality of the nail	Abnormality of the nail.
HP:0008404	Nail dystrophy	Onychodystrophy (nail dystrophy) refers to nail changes apart from changes of the color (nail dyschromia) and involves partial or complete disruption of the various keratinous layers of the nail plate.
HP:0100838	Recurrent cutaneous abscess formation	An increased susceptibility to cutaneous abscess formation, as manifested by a medical history of recurrent cutaneous abscesses.
HP:0002205	Recurrent respiratory infections	An increased susceptibility to respiratory infections as manifested by a history of recurrent respiratory infections.
HP:0001581	Recurrent skin infections	Infections of the skin that happen multiple times.
HP:0011132	Chronic furunculosis	A furuncle (boil) is a skin infection involving an entire hair follicle and nearby skin tissue. Chronic furunculosis refers to recurrent episodes of furuncles, often caused by recurrent staphylococcus infection.
HP:0002514	Cerebral calcification	The presence of calcium deposition within brain structures.

Occasional

Term Identifier	Term Name	Definition
HP:0002231	Sparse body hair	Sparseness of the body hair.
HP:0001073	Cigarette-paper scars	Thin (atrophic) and wide scars.
HP:0000998	Hypertrichosis	Hypertrichosis is increased hair growth that is abnormal in quantity or location.
HP:0001053	Hypopigmented skin patches	
HP:0002230	Generalized hirsutism	Abnormally increased hair growth over much of the entire body.
HP:0002861	Melanoma	The presence of a melanoma, a malignant cancer originating from pigment producing melanocytes. Melanoma can originate from the skin or the pigmented layers of the eye (the uvea).
HP:0008069	Neoplasm of the skin	A tumor (abnormal growth of tissue) of the skin.
HP:0002860	Squamous cell carcinoma	The presence of squamous cell carcinoma of the skin.
HP:0002797	Osteolysis	Osteolysis refers to the destruction of bone through bone resorption with removal or loss of calcium.
HP:0001166	Arachnodactyly	Abnormally long and slender fingers ("spider fingers").
HP:0100523	Liver abscess	The presence of an abscess of the liver.

Source: HPO-ORDO Ontological Module - Validation association date: 01.06.2016

Properdin P factor complement deficiency (PFC)

No frequency available

Term Identifier	Term Name	Definition
HP:0001419	X-linked recessive inheritance	A mode of inheritance that is observed for recessive traits related to a gene encoded on the X chromosome. In the context of medical genetics, X-linked recessive disorders manifest in males (who have one copy of the X chromosome and are thus hemizygotes), but generally not in female heterozygotes who have one mutant and one normal allele.
HP:0005423	Dysfunctional alternative complement pathway	An abnormality of the functioning of any aspect of the alternative complement pathway.
HP:0005381	Recurrent meningococcal disease	Recurrent infections by Neisseria meningitidis (one of the most common causes of bacterial meningitis), which is also known as meningococcus.

Source: OMIM #312060 – Creation date: 04.06.1986, Victor A. McKusick; updated: 14.01.2014, Cassandra L. Kniffin

Schimke disease

Very frequent

Term Identifier	Term Name	Definition
HP:0000926	Platyspondyly	A flattened vertebral body shape with reduced distance between the vertebral endplates.
HP:0005930	Abnormality of epiphysis morphology	An anomaly of epiphysis, which is the expanded articular end of a long bone that developes from a secondary ossification center, and which during the period of growth is either entirely cartilaginous or is separated from the shaft by a cartilaginous disk.
HP:0003300	Ovoid vertebral bodies	When viewed in lateral radiographs, vertebral bodies have a roughly rectangular configuration. This term applies if the vertebral body appears rounded or oval.
HP:0003312	Abnormal form of the vertebral bodies	Abnormal morphology of vertebral body.
HP:0002827	Hip dislocation	Displacement of the femur from its normal location in the hip joint.
HP:0003307	Hyperlordosis	Abnormally increased cuvature (anterior concavity) of the lumbar or cervical spine.
HP:0002843	Abnormal T cell morphology	An abnormality of T cells.
HP:0001903	Anemia	A reduction in erythrocytes volume or hemoglobin concentration.
HP:0001873	Thrombocytopenia	A reduction in the number of circulating thrombocytes.
HP:0001888	Lymphopenia	A reduced number of lymphocytes in the blood.
HP:0000691	Microdontia	Decreased size of the teeth, which can be defined as a mesiodistal tooth diameter (width) more than 2 SD below mean. Alternatively, an apparently decreased maximum width of tooth.
HP:0005280	Depressed nasal bridge	Posterior positioning of the nasal root in relation to the overall facial profile for age.
HP:0000470	Short neck	Diminished length of the neck.
HP:0000414	Bulbous nose	Increased volume and globular shape of the anteroinferior aspect of the nose.
HP:0100820	Glomerulopathy	Inflammatory or noninflammatory diseases affecting the glomeruli of the nephron.
HP:0000100	Nephrotic syndrome	Nephrotic syndrome is a collection of findings resulting from glomerular dysfunction with an increase in glomerular capillary wall permeability associated with pronounced proteinuria. Nephrotic syndrome refers to the constellation of clinical findings that result from severe renal loss of protein, with Proteinuria and hypoalbuminemia, edema, and hyperlipidemia.
HP:0000995	Melanocytic nevus	A oval and round, colored (usually medium-to dark brown, reddish brown, or flesh colored) lesion. Typically, a melanocytic nevus is less than 6 mm in diameter, but may be much smaller or larger.

HP:0003521	Disproportionate short-trunk short stature	A type of disproportionate short stature characterized by a short trunk but a average-sized limbs.
HP:0001511	Intrauterine growth retardation	An abnormal restriction of fetal growth with fetal weight below the tenth percentile for gestational age.
HP:0000093	Proteinuria	Increased levels of protein in the urine.
HP:0005374	Cellular immunodeficiency	An immunodeficiency characterized by defective cell-mediated immunity or humoral immunity.

Frequent

Term Identifier	Term Name	Definition
HP:0007565	Multiple cafe-au-lait spots	The presence of six or more cafe-au-lait spots.

Source: HPO-ORDO Ontological Module - Validation association date: 01.06.2016

Seckel syndrome

Very frequent

Term Identifier	Term Name	Definition
HP:0000252	Microcephaly	Occipito-frontal (head) circumference (OFC) less than -3 standard deviations compared to appropriate, age matched, normal standards (Ross JJ, Frias JL 1977, PMID:9683597). Alternatively, decreased size of the cranium.
HP:0000444	Convex nasal ridge	Nasal ridge curving anteriorly to an imaginary line that connects the nasal root and tip. The nose appears often also prominent, and the columella low.
HP:0000347	Micrognathia	Developmental hypoplasia of the mandible.
HP:0001363	Craniosynostosis	Craniosynostosis refers to the premature closure of the cranial sutures. Primary craniosynostosis refers to the closure of one or more sutures due to abnormalities in skull development, and secondary craniosynostosis results from failure of brain growth.
HP:0000275	Narrow face	Bizygomatic (upper face) and bigonial (lower face) width are both more than 2 standard deviations below the mean (objective); or, an apparent reduction in the width of the upper and lower face (subjective).
HP:0002750	Delayed skeletal maturation	A decreased rate of skeletal maturation. Delayed skeletal maturation can be diagnosed on the basis of an estimation of the bone age from radiographs of specific bones in the human body.
HP:0100543	Cognitive impairment	Abnormality in the process of thought including the ability to process information.
HP:0001249	Intellectual disability	Subnormal intellectual functioning which originates during the developmental period. Intellectual disability, previously referred to as mental retardation, has been defined as an IQ score below 70.
HP:0011342	Mild global developmental delay	Mild global developmental delay
HP:0004322	Short stature	A height below that which is expected according to age and gender norms. Although there is no universally accepted definition of short stature, many refer to "short stature" as height more than 2 standard deviations below the mean for age and gender (or below the 3rd percentile for age and gender dependent norms).
HP:0004326	Cachexia	Severe weight loss, wasting of muscle, loss of appetite, and general debility related to a chronic disease.
HP:0001511	Intrauterine growth retardation	An abnormal restriction of fetal growth with fetal weight below the tenth percentile for gestational age.
HP:0004209	Clinodactyly of the 5th finger	Clinodactyly refers to a bending or curvature of the fifth finger in the radial direction (i.e., towards the 4th finger).
HP:0001852	Sandal gap	A widely spaced gap between the first toe (the great toe) and the second toe.
HP:0007495	Prematurely aged appearance	

Frequent

Term Identifier	Term Name	Definition
HP:0000494	Downslanted palpebral fissures	The palpebral fissure inclination is more than two standard deviations below the mean.
HP:0002209	Sparse scalp hair	Decreased number of head hairs per unit area.
HP:0009804	Reduced number of teeth	The presence of a reduced number of teeth as in Hypodontia or as in Anodontia.
HP:0010579	Cone-shaped epiphysis	Cone-shaped epiphyses (also known as coned epiphyses) are epiphyses that invaginate into cupped metaphyses. That is, the epiphysis has a cone-shaped distal extension resulting from increased growth of the central portion of the epiphysis relative to its periphery.
HP:0000682	Abnormality of dental enamel	An abnormality of the dental enamel.
HP:0001385	Hip dysplasia	The presence of developmental dysplasia of the hip.
HP:0005692	Joint hyperflexibility	Increased mobility and flexibility in the joint due to the tension in tissues such as ligaments and muscles.
HP:0000387	Absent earlobe	Absence of fleshy non-cartilaginous tissue inferior to the tragus and incisura.
HP:0000363	Abnormality of earlobe	An abnormality of the lobule of pinna.
HP:0000501	Glaucoma	Glaucoma refers loss of retinal ganglion cells in a characteristic pattern of optic neuropathy usually associated with increased intraocular pressure.

Occasional

Term Identifier	Term Name	Definition
HP:0002650	Scoliosis	The presence of an abnormal lateral curvature of the spine.

Source: HPO-ORDO Ontological Module - Validation association date: 01.06.2016

Selective CD4 cell deficiency

No frequency available

Term Identifier	Term Name	Definition
HP:0004429	Recurrent viral infections	Increased susceptibility to viral infections, as manifested by recurrent episodes of viral infection.
HP:0002718	Recurrent bacterial infections	Increased susceptibility to bacterial infections, as manifested by recurrent episodes of bacterial infection.
HP:0002841	Recurrent fungal infections	Increased susceptibility to fungal infections, as manifested by multiple episodes of fungal infection.
HP:0410018	Recurrent ear infections	Increased susceptibility to ear infections, as manifested by recurrent episodes of ear infections.
HP:0002837	Recurrent bronchitis	An increased susceptibility to bronchitis as manifested by a history of recurrent bronchitis.
HP:0011108	Recurrent sinusitis	A recurrent form of sinusitis.
HP:0006532	Recurrent pneumonia	An increased susceptibility to pneumonia as manifested by a history of recurrent episodes of pneumonia.
HP:0030885	Recurrent parasitic infections	Increased susceptibility to parasitic infections, as manifested by recurrent episodes of parasitic infection.
HP:0001888	Lymphopenia	A reduced number of lymphocytes in the blood.
HP:0002721	Immunodeficiency	Failure of the immune system to protect the body adequately from infection, due to the absence or insufficiency of some component process or substance.
HP:0002725	Systemic lupus erythematosus	A chronic, relapsing, inflammatory, and often febrile multisystemic disorder of connective tissue, characterized principally by involvement of the skin, joints, kidneys, and serosal membranes.
HP:0001890	Autoimmune hemolytic anemia	An autoimmune form of hemolytic anemia.
HP:0002665	Lymphoma	A cancer originating in lymphocytes and presenting as a solid tumor of lymhpoid cells.

Source: OMIM #615518 – Creation date: 07.11.2013, Marla J.F. O´Neill

Selective IgA deficiency

No frequency available

Term Identifier	Term Name	Definition
HP:0002720	Decreased circulating IgA level	Decreased levels of immunoglobulin A (IgA).
HP:0005425	Recurrent sinopulmonary infections	An increased susceptibility to infections involving both the paranasal sinuses and the lungs, as manifested by a history of recurrent sinopulmonary infections.
HP:0007378	Neoplasm of the gastrointestinal tract	A tumor (abnormal growth of tissue) of the gastrointestinal tract.
HP:0004798	Recurrent infection of the gastrointestinal tract	Recurrent infection of the gastrointestinal tract.
HP:0012393	Allergy	An allergy is an immune response or reaction to substances that are usually not harmful.
HP:0002608	Celiac disease	Celiac disease (CD) is an autoimmune condition affecting the small intestine, triggered by the ingestion of gluten, the protein fraction of wheat, barley, and rye. Clinical manifestations of CD are highly variable and include both gastrointestinal and non-gastrointestinal features. The hallmark of CD is an immune-mediated enteropathy. This term is included because the occurence of CD is seen as a feature of a number of other diseases.
HP:0100280	Crohn's disease	A chronic granulomatous inflammatory disease of the intestines that may affect any part of the gastrointestinal tract from mouth to anus, causing a wide variety of symptoms. It primarily causes abdominal pain, diarrhea which may be bloody, vomiting, or weight loss, but may also cause complications outside of the gastrointestinal tract such as skin rashes, arthritis, inflammation of the eye, tiredness, and lack of concentration. Crohn's disease is thought to be an autoimmune disease, in which the body's immune system attacks the gastrointestinal tract, causing inflammation.
HP:0100279	Ulcerative colitis	A chronic inflammatory bowel disease that includes characteristic ulcers, or open sores, in the colon. The main symptom of active disease is usually constant diarrhea mixed with blood, of gradual onset and intermittent periods of exacerbated symptoms contrasting with periods that are relatively symptom-free. In contrast to Crohn's disease this special form of colitis begins in the distal parts of the rectum, spreads continually upwards and affects only mucose and submucose tissue of the colon.

HP:0002725	Systemic lupus erythematosus	A chronic, relapsing, inflammatory, and often febrile multisystemic disorder of connective tissue, characterized principally by involvement of the skin, joints, kidneys, and serosal membranes.
HP:0001370	Rheumatoid arthritis	Inflammatory changes in the synovial membranes and articular structures with widespread fibrinoid degeneration of the collagen fibers in mesenchymal tissues, as well as atrophy and rarefaction of bony structures.
HP:0002665	Lymphoma	A cancer originating in lymphocytes and presenting as a solid tumor of lymhpoid cells.
HP:0100522	Thymoma	A tumor originating from the epithelial cells of the thymus.
HP:0002099	Asthma	Asthma is characterized by increased responsiveness of the tracheobronchial tree to multiple stimuli, leading to narrowing of the air passages with resultant dyspnea, cough, and wheezing.

Source: OMIM #137100 – Creation date: 04.06.1986, Victor A. McKusick; updated: 24.09.2010, Marla J.F. O´Neill
OMIM #609529 – Creation date: 09.08.2005, Anna M. Stumpf; updated: 04.08.2004, Cassandra L. Kniffin

Selective IgM deficiency

No frequency available

Term Identifier	Term Name	Definition
HP:0004429	Recurrent viral infections	Increased susceptibility to viral infections, as manifested by recurrent episodes of viral infection.
HP:0002718	Recurrent bacterial infections	Increased susceptibility to bacterial infections, as manifested by recurrent episodes of bacterial infection.
HP:0002841	Recurrent fungal infections	Increased susceptibility to fungal infections, as manifested by multiple episodes of fungal infection.
HP:0410018	Recurrent ear infections	Increased susceptibility to ear infections, as manifested by recurrent episodes of ear infections.
HP:0002837	Recurrent bronchitis	An increased susceptibility to bronchitis as manifested by a history of recurrent bronchitis.
HP:0011108	Recurrent sinusitis	A recurrent form of sinusitis.
HP:0006532	Recurrent pneumonia	An increased susceptibility to pneumonia as manifested by a history of recurrent episodes of pneumonia.
HP:0002014	Diarrhea	Abnormally increased frequency of loose or watery bowel movements.
HP:0000988	Skin rash	A red eruption of the skin.
HP:0032163	Molluscum contagiosum	Molluscum contagiosum is a cutaneous viral infection that is commonly observed in both healthy and immunocompromised children. The infection is caused by a member of the Poxviridae family, the molluscum contagiosum virus. Molluscum contagiosum presents as single or multiple small white or flesh-colored papules that typically have a central umbilication. The central umbilication may be difficult to observe in young children and, instead, may bear an appearance similar to an acneiform eruption. The lesions vary in size (from 1 mm to 1 cm in diameter) and are painless, although a subset of patients report pruritus in the area of infection. On average, 11-20 papules appear on the body during the course of infection and generally remains a self-limiting disease. However, in immunosuppressed patients, molluscum contagiosum can be a severe infection with hundreds of lesions developing on the body. Extensive eruption is indicative of an advanced immunodeficiency state.
HP:0001508	Failure to thrive	Failure to thrive (FTT) refers to a child whose physical growth is substantially below the norm.
HP:0004395	Malnutrition	
HP:0002850	Decreased circulating total IgM	An abnormally decreased level of immunoglobulin M (IgM) in blood.

Source: National Center for Advancing Translational Sciences – GARD (last updated 21.12.2017)

Severe combined immunodeficiency (SCID)

Very frequent

Term Identifier	Term Name	Definition
HP:0100806	Sepsis	Systemic inflammatory response to infection.
HP:0002721	Immunodeficiency	Failure of the immune system to protect the body adequately from infection, due to the absence or insufficiency of some component process or substance.
HP:0100763	Abnormality of the lymphatic system	An anomaly of the lymphatic system, a network of lymphatic vessels that carry a clear fluid called lymph unidirectionally towards either the right lymphatic duct or the thoracic duct, which in turn drain into the right and left subclavian veins respectively.
HP:0004430	Severe combined immunodeficiency	A combined immunodeficiency primary immune deficiency that is characterized by a more severe defect in both the T- and B-lymphocyte systems.
HP:0002205	Recurrent respiratory infections	An increased susceptibility to respiratory infections as manifested by a history of recurrent respiratory infections.
HP:0002028	Chronic diarrhea	The presence of chronic diarrhea, which is usually taken to mean diarrhea that has persisted for over 4 weeks.
HP:0001945	Fever	Elevated body temperature due to failed thermoregulation.
HP:0001508	Failure to thrive	Failure to thrive (FTT) refers to a child whose physical growth is substantially below the norm.

Frequent

Term Identifier	Term Name	Definition
HP:0000988	Skin rash	A red eruption of the skin.
HP:0001888	Lymphopenia	A reduced number of lymphocytes in the blood.
HP:0001596	Alopecia	Loss of hair from the head or body.

Occasional

Term Identifier	Term Name	Definition
HP:0000389	Chronic otitis media	Chronic otitis media refers to fluid, swelling, or infection of the middle ear that does not heal and may cause permanent damage to the ear.
HP:0002240	Hepatomegaly	Abnormally increased size of the liver.
HP:0001744	Splenomegaly	Abnormal increased size of the spleen.
HP:0000164	Abnormality of the dentition	Any abnormality of the teeth.
HP:0000252	Microcephaly	Occipito-frontal (head) circumference (OFC) less than -3 standard deviations compared to appropriate, age matched, normal standards (Ross JJ, Frias JL 1977, PMID:9683597). Alternatively, decreased size of the cranium.
HP:0000407	Sensorineural hearing impairment	A type of hearing impairment in one or both ears related to an abnormal functionality of the cochlear nerve.
HP:0000010	Recurrent urinary tract infections	Repeated infections of the urinary tract.

Source: HPO-ORDO Ontological Module - Validation association date: 01.06.2016

Shwachman-Diamond syndrome

Very frequent

Term Identifier	Term Name	Definition
HP:0001875	Neutropenia	An abnormally low number of neutrophils in the peripheral blood.
HP:0001738	Exocrine pancreatic insufficiency	Impaired function of the exocrine pancreas associated with a reduced ability to digest foods because of lack of digestive enzymes.
HP:0001290	Generalized hypotonia	Generalized muscular hypotonia (abnormally low muscle tone).

Frequent

Term Identifier	Term Name	Definition
HP:0000938	Osteopenia	Osteopenia is a term to define bone density that is not normal but also not as low as osteoporosis. By definition from the World Health Organization osteopenia is defined by bone densitometry as a T score -1 to -2.5.
HP:0002750	Delayed skeletal maturation	A decreased rate of skeletal maturation. Delayed skeletal maturation can be diagnosed on the basis of an estimation of the bone age from radiographs of specific bones in the human body.
HP:0000944	Abnormality of the metaphysis	An abnormality of one or more metaphysis, i.e., of the somewhat wider portion of a long bone that is adjacent to the epiphyseal growth plate and grows during childhood.
HP:0001903	Anemia	A reduction in erythrocytes volume or hemoglobin concentration.
HP:0001873	Thrombocytopenia	A reduction in the number of circulating thrombocytes.
HP:0002024	Malabsorption	Impaired ability to absorb one or more nutrients from the intestine.
HP:0001263	Global developmental delay	A delay in the achievement of motor or mental milestones in the domains of development of a child, including motor skills, speech and language, cognitive skills, and social and emotional skills. This term should only be used to describe children younger than five years of age.
HP:0001249	Intellectual disability	Subnormal intellectual functioning which originates during the developmental period. Intellectual disability, previously referred to as mental retardation, has been defined as an IQ score below 70.
HP:0001508	Failure to thrive	Failure to thrive (FTT) refers to a child whose physical growth is substantially below the norm.
HP:0004322	Short stature	A height below that which is expected according to age and gender norms. Although there is no universally accepted definition of short stature, many refer to "short stature" as height more than 2 standard deviations below the mean for age and gender (or below the 3rd percentile for age and gender dependent norms).
HP:0001510	Growth delay	A deficiency or slowing down of growth pre- and postnatally.

HP:0002719	Recurrent infections	Increased susceptibility to infections.
HP:0000964	Eczema	Eczema is a form of dermatitis. The term eczema is broadly applied to a range of persistent skin conditions and can be related to a number of underlying conditions. Manifestations of eczema can include dryness and recurring skin rashes with redness, skin edema, itching and dryness, crusting, flaking, blistering, cracking, oozing, or bleeding.
HP:0008064	Ichthyosis	An abnormality of the skin characterized the presence of excessive amounts of dry surface scales on the skin resulting from an abnormality of keratinization.

Occasional

Term Identifier	Term Name	Definition
HP:0000768	Pectus carinatum	A deformity of the chest caused by overgrowth of the ribs and characterized by protrusion of the sternum.
HP:0002650	Scoliosis	The presence of an abnormal lateral curvature of the spine.
HP:0010306	Short thorax	Reduced inferior to superior extent of the thorax.
HP:0005528	Bone marrow hypocellularity	A reduced number of hematopoietic cells present in the bone marrow relative to marrow fat.
HP:0001915	Aplastic anemia	Aplastic anemia is defined as pancytopenia with a hypocellular marrow.
HP:0000691	Microdontia	Decreased size of the teeth, which can be defined as a mesiodistal tooth diameter (width) more than 2 SD below mean. Alternatively, an apparently decreased maximum width of tooth.
HP:0000670	Carious teeth	Caries is a multifactorial bacterial infection affecting the structure of the tooth. This term has been used to describe the presence of more than expected dental caries.
HP:0011107	Recurrent aphthous stomatitis	Recurrent episodes of ulceration of the oral mucosa, typically presenting as painful, sharply circumscribed fibrin-covered mucosal defects with a hyperemic border.
HP:0002240	Hepatomegaly	Abnormally increased size of the liver.
HP:0001288	Gait disturbance	The term gait disturbance can refer to any disruption of the ability to walk. In general, this can refer to neurological diseases but also fractures or other sources of pain that is triggered upon walking. However, in the current context gait disturbance refers to difficulty walking on the basis of a neurological or muscular disease.
HP:0004808	Acute myeloid leukemia	A form of leukemia characterized by overproduction of an early myeloid cell.
HP:0002863	Myelodysplasia	Clonal hematopoietic stem cell disorders characterized by dysplasia (ineffective production) in one or more hematopoietic cell lineages, leading to anemia and cytopenia.
HP:0001909	Leukemia	A cancer of the blood and bone marrow characterized by an abnormal proliferation of leukocytes.
HP:0100651	Type I diabetes mellitus	A chronic condition in which the pancreas produces little or no insulin. Type I diabetes mellitus is manifested by the sudden onset of severe hyperglycemia with rapid progression to diabetic ketoacidosis unless treated with insulin.

Source: HPO-ORDO Ontological Module - Validation association date: 01.06.2016

Thymoma with immunodeficiency

Very frequent

Term Identifier	Term Name	Definition
HP:0004313	Decreased antibody level in blood	An abnormally decreased level of immunoglobulin in blood.
HP:0100721	Mediastinal lymphadenopathy	Swelling of lymph nodes within the mediastinum, the central compartment of the thoracic cavities that contains the heart and the great vessels, the esophagus, and trachea and other structures including lymph nodes.
HP:0100522	Thymoma	A tumor originating from the epithelial cells of the thymus.

Frequent

Term Identifier	Term Name	Definition
HP:0001581	Recurrent skin infections	Infections of the skin that happen multiple times.
HP:0000246	Sinusitis	Inflammation of the paranasal sinuses owing to a viral, bacterial, or fungal infection, allergy, or an autoimmune reaction.
HP:0001881	Abnormal leukocyte morphology	An abnormality of leukocytes.
HP:0012735	Cough	A sudden, audible expulsion of air from the lungs through a partially closed glottis, preceded by inhalation.
HP:0002094	Dyspnea	Difficult or labored breathing.
HP:0002110	Bronchiectasis	Persistent abnormal dilatation of the bronchi owing to localized and irreversible destruction and widening of the large airways.
HP:0003473	Fatigable weakness	A type of weakness that occurs after a muscle group is used and lessens if the muscle group has some rest. That is, there is diminution of strength with repetitive muscle actions.
HP:0002015	Dysphagia	Difficulty in swallowing.
HP:0000508	Ptosis	The upper eyelid margin is positioned 3 mm or more lower than usual and covers the superior portion of the iris (objective); or, the upper lid margin obscures at least part of the pupil (subjective).
HP:0000010	Recurrent urinary tract infections	Repeated infections of the urinary tract.
HP:0001618	Dysphonia	An impairment in the ability to produce voice sounds.

Occasional

Term Identifier	Term Name	Definition
HP:0002205	Recurrent respiratory infections	An increased susceptibility to respiratory infections as manifested by a history of recurrent respiratory infections.
HP:0001903	Anemia	A reduction in erythrocytes volume or hemoglobin concentration.
HP:0001873	Thrombocytopenia	A reduction in the number of circulating thrombocytes.

HP:0010515	Aplasia/Hypoplasia of the thymus	Absence or underdevelopment of the thymus.
HP:0000819	Diabetes mellitus	A group of abnormalities characterized by hyperglycemia and glucose intolerance.
HP:0002014	Diarrhea	Abnormally increased frequency of loose or watery bowel movements.

Source: HPO-ORDO Ontological Module - Validation association date: 01.06.2016

Warts, hypogammaglobulinemia, infections and myelokathexis (WHIM)

No frequency available

Term Identifier	Term Name	Definition
HP:0005561	Abnormality of bone marrow cell morphology	An anomaly of the form or number of cells in the bone marrow.
HP:0031020	Bone marrow hypercellularity	A larger than normal amount or percentage of hematopoietic cells relative to marrow fat.
HP:0001875	Neutropenia	An abnormally low number of neutrophils in the peripheral blood.
HP:0031160	Myelokathexis	Impaired egress of mature neutrophils from bone marrow causing neutropenia.
HP:0002718	Recurrent bacterial infections	Increased susceptibility to bacterial infections, as manifested by recurrent episodes of bacterial infection.
HP:0004313	Decreased antibody level in blood	An abnormally decreased level of immunoglobulin in blood.
HP:0002788	Recurrent upper respiratory tract infections	An increased susceptibility to upper respiratory tract infections as manifested by a history of recurrent upper respiratory tract infections (running ears - otitis, sinusitis, pharyngitis, tonsillitis).
HP:0004315	Decreased circulating IgG level	An abnormally decreased level of immunoglobulin G (IgG) in blood.
HP:0000055	Abnormality of female external genitalia	An abnormality of the female external genitalia.
HP:0000008	Abnormality of female internal genitalia	An abnormality of the female internal genitalia.
HP:0000006	Autosomal dominant inheritance	A mode of inheritance that is observed for traits related to a gene encoded on one of the autosomes (i.e., the human chromosomes 1-22) in which a trait manifests in heterozygotes. In the context of medical genetics, an autosomal dominant disorder is caused when a single copy of the mutant allele is present. Males and females are affected equally, and can both transmit the disorder with a risk of 50% for each child of inheriting the mutant allele.
HP:0002110	Bronchiectasis	Persistent abnormal dilatation of the bronchi owing to localized and irreversible destruction and widening of the large airways.
HP:0200043	Verrucae	Warts, benign growths on the skin or mucous membranes that cause cosmetic problems as well as pain and discomfort. Warts most often occur on the hands, feet, and genital areas.

Source: OMIM #193670 – Creation date: 06.12.1990, Victor A. McKusick; updated: 06.02.2019, Ada Hamosh
PMID: 25662009

Wiskott-Aldrich-syndrome

Very Frequent

Term Identifier	Term Name	Definition
HP:0011875	Abnormal platelet morphology	An anomaly in platelet form, ultrastructure, or intracellular organelles.
HP:0003010	Prolonged bleeding time	Prolongation of the time taken for a standardized skin cut of fixed depth and length to stop bleeding.
HP:0011029	Internal hemorrhage	The presence of hemorrhage within the body.
HP:0001873	Thrombocytopenia	A reduction in the number of circulating thrombocytes.
HP:0001888	Lymphopenia	A reduced number of lymphocytes in the blood.
HP:0000389	Chronic otitis media	Chronic otitis media refers to fluid, swelling, or infection of the middle ear that does not heal and may cause permanent damage to the ear.
HP:0002205	Recurrent respiratory infections	An increased susceptibility to respiratory infections as manifested by a history of recurrent respiratory infections.
HP:0000246	Sinusitis	Inflammation of the paranasal sinuses owing to a viral, bacterial, or fungal infection, allergy, or an autoimmune reaction.
HP:0002721	Immunodeficiency	Failure of the immune system to protect the body adequately from infection, due to the absence or insufficiency of some component process or substance.
HP:0000388	Otitis media	Inflammation or infection of the middle ear.
HP:0007420	Spontaneous hematomas	Spontaneous development of hematomas (hematoma) or bruises without significant trauma.
HP:0000978	Bruising susceptibility	An ecchymosis (bruise) refers to the skin discoloration caused by the escape of blood into the tissues from ruptured blood vessels. This term refers to an abnormally increased susceptibility to bruising. The corresponding phenotypic abnormality is generally elicited on medical history as a report of frequent ecchymoses or bruising without adequate trauma.
HP:0001945	Fever	Elevated body temperature due to failed thermoregulation.
HP:0002028	Chronic diarrhea	The presence of chronic diarrhea, which is usually taken to mean diarrhea that has persisted for over 4 weeks.

Frequent

Term Identifier	Term Name	Definition
HP:0001879	Abnormal eosinophil morphology	An eosinophil abnormality.
HP:0002248	Hematemesis	The vomiting of blood.
HP:0001903	Anemia	A reduction in erythrocytes volume or hemoglobin concentration.
HP:0002573	Hematochezia	The passage of fresh (red) blood per anus, usually in or with stools. Most rectal bleeding comes from the colon, rectum, or anus.

HP:0001935	Microcytic anemia	A kind of anemia in which the volume of the red blood cells is reduced.
HP:0001878	Hemolytic anemia	A type of anemia caused by premature destruction of red blood cells (hemolysis).
HP:0002960	Autoimmunity	The occurrence of an immune reaction against the organism's own cells or tissues.
HP:0002037	Inflammation of the large intestine	Inflammation, or an inflammatory state in the large intestine.
HP:0000967	Petechiae	Petechiae are pinpoint-sized reddish/purple spots, resembling a rash, that appear just under the skin or a mucous membrane when capillaries have ruptured and some superficial bleeding into the skin has happened. This term refers to an abnormally increased susceptibility to developing petechiae.
HP:0011675	Arrhythmia	Any cardiac rhythm other than the normal sinus rhythm. Such a rhythm may be either of sinus or ectopic origin and either regular or irregular. An arrhythmia may be due to a disturbance in impulse formation or conduction or both.
HP:0001328	Specific learning disability	Impairment of certain skills such as reading or writing, coordination, self-control, or attention that interfere with the ability to learn. The impairment is not related to a global deficiency of intelligence.
HP:0002094	Dyspnea	Difficult or labored breathing.

Occasional

Term Identifier	Term Name	Definition
HP:0011869	Abnormal platelet function	Any anomaly in the function of thrombocytes.
HP:0002170	Intracranial hemorrhage	Hemorrhage occurring within the skull.
HP:0001875	Neutropenia	An abnormally low number of neutrophils in the peripheral blood.
HP:0100806	Sepsis	Systemic inflammatory response to infection.
HP:0001025	Urticaria	Raised, well-circumscribed areas of erythema and edema involving the dermis and epidermis. Urticaria is intensely pruritic, and blanches completely with pressure.
HP:0002633	Vasculitis	Inflammation of blood vessel.
HP:0001645	Sudden cardiac death	The heart suddenly and unexpectedly stops beating resulting in death within a short time period (generally within 1 h of symptom onset).
HP:0000509	Conjunctivitis	Inflammation of the conjunctiva.
HP:0000421	Epistaxis	Epistaxis, or nosebleed, refers to a hemorrhage localized in the nose.
HP:0000225	Gingival bleeding	Hemorrhage affecting the gingiva.
HP:0100820	Glomerulopathy	Inflammatory or noninflammatory diseases affecting the glomeruli of the nephron.
HP:0000140	Abnormality of the menstrual cycle	An abnormality of the ovulation cycle.
HP:0009830	Peripheral neuropathy	Peripheral neuropathy is a general term for any disorder of the peripheral nervous system. The main clinical features

		used to classify peripheral neuropathy are distribution, type (mainly demyelinating versus mainly axonal), duration, and course.
HP:0001287	Meningitis	Inflammation of the meninges.
HP:0006535	Recurrent intrapulmonary hemorrhage	A recurrent hemorrhage occurring within the lung.
HP:0100749	Chest pain	An unpleasant sensation characterized by physical discomfort (such as pricking, throbbing, or aching) localized to the chest.
HP:0100774	Hyperostosis	Excessive growth or abnormal thickening of bone tissue.
HP:0001369	Arthritis	Inflammation of a joint.
HP:0002665	Lymphoma	A cancer originating in lymphocytes and presenting as a solid tumor of lymhpoid cells.
HP:0002488	Acute leukemia	A clonal (malignant) hematopoietic disorder with an acute onset, affecting the bone marrow and the peripheral blood. The malignant cells show minimal differentiation and are called blasts, either myeloid blasts (myeloblasts) or lymphoid blasts (lymphoblasts).
HP:0005558	Chronic leukemia	A slowly progressing leukemia characterized by a clonal (malignant) proliferation of maturing and mature myeloid cells or mature lymphocytes. When the clonal cellular population is composed of myeloid cells, the process is called chronic myelogenous leukemia. When the clonal cellular population is composed of lymphocytes, it is classified as chronic lymphocytic leukemia, hairy cell leukemia, or T-cell large granular lymphocyte leukemia.
HP:0000778	Hypoplasia of the thymus	Underdevelopment of the thymus.
HP:0000491	Keratitis	Inflammation of the cornea.
HP:0200042	Skin ulcer	A discontinuity of the skin exhibiting complete loss of the epidermis and often portions of the dermis and even subcutaneous fat.
HP:0002664	Neoplasm	An organ or organ-system abnormality that consists of uncontrolled autonomous cell-proliferation which can occur in any part of the body as a benign or malignant neoplasm (tumour).

Source: HPO-ORDO Ontological Module - Validation association date: 01.06.2016

X-linked lymphoproliferative syndrome (XLP)

Very frequent

Term Identifier	Term Name	Definition
HP:0005374	Cellular immunodeficiency	An immunodeficiency characterized by defective cell-mediated immunity or humoral immunity.

Frequent

Term Identifier	Term Name	Definition
HP:0004313	Decreased antibody level in blood	An abnormally decreased level of immunoglobulin in blood.
HP:0002665	Lymphoma	A cancer originating in lymphocytes and presenting as a solid tumor of lymhpoid cells.
HP:0002240	Hepatomegaly	Abnormally increased size of the liver.
HP:0002716	Lymphadenopathy	Enlargment (swelling) of a lymph node.
HP:0001744	Splenomegaly	Abnormal increased size of the spleen.

Occasional

Term Identifier	Term Name	Definition
HP:0001903	Anemia	A reduction in erythrocytes volume or hemoglobin concentration.

Source: HPO-ORDO Ontological Module - Validation association date: 01.06.2016