TABLE of GENETIC DISORDERS

Disease	Category	Pathogenesis / Heredity	Pathology, Cardinal Symptoms
Cystic Fibrosis		Autosomal Recessive. **CFTR gene** defect on Chrom 7 ------> No Cl^- transport and failure to hydrate mucous secretions (no NaCl transport) ------> excessively viscous mucoid exocrine secretions	Meconium ileus (caused by thick, mucoid meconium), respiratory bronchiectasis,*Pseudomonas* pneumonia, pancreatic insufficiency, hypertonic (high Cl^-concentration) sweat.
Fanconi Anemia		Autosomal Recessive **congenital pancytopenia**.	Normocytic anemia with neutropenia. Short stature, microcephaly, hypogenitalism, strabismus, anomalies of the thumbs, radii, and kidneys, mental retardation, and microphthalmia.
Hartnup's Disease		Autosomal Recessive. Defect in GI uptake of neutral amino acids ------> malabsorption of**tryptophan** (niacin precursor) ------> **niacin deficiency** among other things.	**Pellagra**-like syndrome (diarrhea, dementia, dermatitis), light-sensitive skin rash, temporary cerebellar ataxia.
Kartagener's Syndrome		Autosomal Recessive. Defect in **dynein arms** ------> lost motility of **cilia**	**Recurrent sinopulmonary infections** (due to impaired ciliary tract). ***Situs inversus***, due to impaired ciliary motion during embryogenesis: lateral transposition of lungs, abdominal and thoracic viscera are on opposite sides of the body as normal. Possible dextrocardia, male sterility.
Pyruvate Dehydrogenase Deficiency		Autosomal Recessive. **Pyruvate Dehydrogenase** deficiency ------> buildup of lactate and pyruvate ------> **lactic acidosis.**	Neurologic defects. Treatment: Increase intake of **ketogenic** nutrients (**leucine, lysine**) ------> increase

			formation of Acetyl-CoA from other sources.
Xeroderma Pigmentosum		Autosomal Recessive. Defect in DNA repair, inability to repair **thymine dimers** resulting from**UV-light** exposure ------> excessive skin damage and skin cancer.	Dry skin, melanomas, pre-malignant lesions, other cancers. Ophthalmic and neurologic abnormalities.
Familial Hypercholesterolemia	Autosomal Dominant Disorders	Autosomal Dominant. **LDL-Receptor** defect.	Heterozygous: accelerated atherosclerosis. Homozygous: accelerated atherosclerosis, MI by age 35, **xanthomas**.
Hereditary Hemorrhagic Telangiectasia (Osler-Weber-Rendu Syndrome)	Autosomal Dominant Disorders	Autosomal Dominant.	**Telangiectasias** of skin and mucous membranes.
Hereditary Spherocytosis	Autosomal Dominant Disorders	Autosomal Dominant. **Band-3** deficiency in RBC membrane ------> spherical shape to cells. Other RBC structural enzyme deficiencies can cause it, too.	Sequestration of spherocytes in spleen ------> hemolytic anemia.
Huntington's Disease	Autosomal Dominant Disorders	Autosomal Dominant, *100% penetrance*. Genetic defect on Chrom 4 -----> atrophy of caudate nuclei, putamen, frontal cortex.	Progressive dementia with onset in adulthood, choreiform movements, athetosis.
Marfan's Syndrome	Autosomal Dominant Disorders	Autosomal Dominant. **Fibrillin** deficiency ------> faulty scaffolding in connective tissue (elastin has no anchor).	Arachnodactyly, dissecting aortic aneurysms, **ectopia lentis** (subluxation of lens), mitral valve prolapse.
Neurofibromatosis (Von Recklinghausen Disease)	Autosomal Dominant Disorders	Autosomal Dominant. **NF1 gene** defect (no GTPase protein) ------> dysregulation of *Ras* tumor-suppressor protein.	Multiple neurofibromas (Café au Lait spots) which may become malignant,**Lisch nodules** (pigmented hamartomas of the iris). Increased risk for tumors:

			pheochromocytoma, Wilms tumor, Rhabdomyosarcoma, leukemias.
Tuberous Sclerosis	Autosomal Dominant Disorders	Autosomal Dominant.	**Tubers** (glial nodules), seizures, mental retardation. Associated with adenoma sebaceum (facial lesion), myocardial rhabdomyomas, **renal angiomyolipomas**.
Von Hippel-Lindau Syndrome	Autosomal Dominant Disorders	Autosomal Dominant, short arm of chromosome 3. Same genetic region is associated with incidence of **renal cell carcinoma**.	(1) Hemangioblastomas of cerebellum, medulla, or retina, (2) adenomas, (3) cysts in visceral organs. High risk for renal cell carcinoma.
Congenital Fructose Intolerance	Carbohydrate Metabolism Defect	Autosomal Recessive. **Aldolase B** deficiency ------> buildup of **Fructose-1-Phosphate** in tissues ------> inhibit glycogenolysis and gluconeogenesis.	Severe **hypoglycemia**. Treatment: *Remove fructose from diet.*
Galactosemia	Carbohydrate Metabolism Defect	Autosomal Recessive. Inability to convert galactose to glucose ------> accumulation of galactose in many tissues.	Failure to thrive, infantile cataracts, mental retardation. Progressive hepatic failure, **cirrhosis**, death.
		(1) Classic form: **Galactose-1-phosphate Uridyltransferase** deficiency.	Galactokinase-deficiency: infantile cataracts are prominent.
		(2) Rarer form: **Galactokinase** deficiency.	Treatment: in either case,*remove galactose from diet.*
Angelman Syndrome	Chromosomal	Deletion of part of short arm of **chromosome 15, maternal copy**. An example of **genomic imprinting.**	Mental retardation, ataxic gait, seizures.**Inappropriate laughter**.
Cri du Chat Syndrome	Chromosomal	**5p-**, deletion of the long arm of chromosome 5.	"Cry of the cat." Severe mental retardation, microcephaly, cat-like cry. Low birth-weight, round-face, hypertelorism

			(wide-set eyes), low-set ears, epicanthal folds.
Down Syndrome **(Trisomy 21)**	Chromosomal	**Trisomy 21,** with risk increasing with maternal age. Familial form (no age-associated risk) is translocation **t(21,x)** in a minority of cases.	Most common cause of mental retardation. Will see epicanthal folds, **simian crease**, **brushfield spots** in eyes. Associated syndromes: **congenital heart disease**, **leukemia**,**premature Alzheimer's disease** (same morphological changes).
Edward's Syndrome **(Trisomy 18)**	Chromosomal	**Trisomy 18**	Mental retardation, micrognathia, **rocker-bottom feet**, congenital heart disease, flexion deformities of fingers. Death by 1 year old.
Patau's Syndrome **(Trisomy 13)**	Chromosomal	**Trisomy 13**	Mental retardation, microphthalmia, **cleft lip and palate**, polydactyly, rocker-bottom feet, congenital heart disease. Similar to and more severe than Edward's Syndrome. Death by 1 year old.
Prader-Willi Syndrome	Chromosomal	Deletion of part of short arm of **chromosome 15, paternal copy**. An example of **genomic imprinting.**	Mental retardation, short stature, hypotonia, obesity and huge appetite after infancy. Small hands and feet, hypogonadism.
Fragile-X Syndrome	Chromosomal Sex chromosome	Progressively longer **tandem repeats** on the long arm of the X-chromosome. The longer the number of repeats, the worse the syndrome. Tandem repeats tend to accumulate through generations.	Second most common cause of **mental retardation** next to Down Syndrome. Macro-orchidism (enlarged testes) in males.
Klinefelter's Syndrome (XXY)	Chromosomal Sex chromosome	Non-disjunction of the sex chromosome during Anaphase I of meiosis ------> **Trisomy (47,XXY)**	Hypogonadism, tall stature, gynecomastia. Mild mental retardation. Usually not diagnosed until after puberty. One Barr body seen on buccal smear.

Turner's Syndrome (XO)	Chromosomal Sex chromosome	Non-disjunction of the sex chromosome during Anaphase I of meiosis ------> **Monosomy (45,X)**	Streak gonads, primary amenorrhea, webbed neck, short stature, **coarctation of Aorta**, infantile genitalia. *No mental retardation.* No Barr bodies visible on buccal smear.
XXX Syndrome	Chromosomal Sex chromosome	**Trisomy (47,XXX)** and other multiple X-chromosome abnormalities.	Usually phenotypically normal. May see menstrual abnormalities or mild mental retardation in some cases.
Ehlers-Danlos Syndrome	Connective Tissue disease	Various defects in collagen synthesis. • **Type-I**: Autosomal dominant, mildest form. • **Type-IV**: autosomal dominant. Defect in reticular collagen (type-III) • **Type-VI**: autosomal-recessive. • **Type-VII**: Defect in collagen type I • **Type-IX**: X-linked recessive	Laxity of joints, hyperextensibility of skin, poor wound healing, aneurysms. • **Type-I**: Diaphragmatic hernia. Common, normal life-expectancy. • **Type-IV**: Ecchymoses, arterial rupture. *Dangerous*due to rupture aneurysms. • **Type-VI**: Retinal detachment, corneal rupture
Osteogenesis Imperfecta	Connective tissue disease	Defects in **Collagen Type I** formation.	Multiple fractures after birth, **blue sclerae**, thin skin, progressive deafness in some types (due to abnormal middle ear ossicles). **Type-I** is most common;**Type-II** is most severe;**Type-IV** is mildest form.
Cori's Disease **(Glycogen Storage Disease Type III)**	Glycogen Storage Disease	Autosomal Recessive. **Debranching enzyme** deficiency (can only break down linear chains of glycogen, not at branch points) ------> accumulate glycogen in	Stunted growth, hepatomegaly, hypoglycemia.

		liver, heart, skeletal muscle.	
McArdle's Disease **(Glycogen Storage Disease Type V)**	Glycogen Storage Disease	Autosomal Recessive. **muscle phosphorylase** deficiency (cannot utilize glycogen in skeletal muscle) ------> accumulation of glycogen in skeletal muscle.	Muscle cramps, muscle weakness, easy fatigability. Myoglobinuria with strenuous exercise.
Pompe's Disease **(Glycogen Storage Disease Type II)**	Glycogen Storage Disease	Autosomal Recessive. **alpha-1,4-Glucosidase** deficiency (cannot break down glycogen) ------> accumulate glycogen in liver, heart, skeletal muscle.	Cardiomegaly, hepatomegaly, and systemic findings, leading to early death.
Von Gierke's Disease **(Glycogen Storage Disease Type I)**	Glycogen Storage Disease	Autosomal Recessive. **Glucose-6-Phosphatase** deficiency (cannot break down glycogen) ------> accumulate glycogen in liver and kidney.	Severe fasting**hypoglycemia**, hepatomegaly from lots of glycogen in liver.
Hemophilia A (Factor VIII Deficiency)	Hemophilia	X-Linked Recessive. **Factor VIII** deficiency	Hemorrhage, hematuria, hemarthroses. Prolonged PTT.
Hemophilia B (Factor IX Deficiency)	Hemophilia	X-Linked Recessive. **Factor IX** deficiency.	Milder than Hemophilia A. Hemorrhage, hematuria, hemarthroses. Prolonged PTT.
Von Willebrand Disease	Hemophilia	Autosomal dominant and recessive varieties. **Von Willebrand Factor** deficiency ------> defect in initial formation of platelet plugs, and shorter half-life of Factor VIII in blood.	Hemorrhage, similar to hemophilia. **Type-I**: Most mild. **Type-II**: Intermediate. **Type-III**: most severe, with recessive inheritance (complete absence).
Ataxia-Telangiectasia	Immune deficiency Combined Deficiency	Autosomal Recessive. Unknown. Numerous chromosomal breaks and elevated AFP is found. Symptomatic by age 2 years.	Cerebellar ataxia, telangiectasia (enlarged capillaries of face and skin), **B and T-Cell deficiencies**, IgA deficiency.
Chédiak-Higashi Syndrome	Immune deficiency	Defect in polymerization of microtubules in neutrophils ----> failure	Recurrent pyogenic infections, *Staphylococcus, Streptococcus.*

	Phagocyte Deficiency	in **neutrophil** migration and phagocytosis. Also results in failure in **lysosomal function** in neutrophils.	
Chronic Granulomatous Disease	Immune deficiency Phagocyte Deficiency	X-Linked (usually) **NADPH Oxidase** deficiency ------> no formation of peroxides and superoxides ------> no oxidative burst in phagocytes.	Failure of phagocytes leads to susceptibility to infections, especially *Staph Aureus* and *Aspergillus* spp. B and T cells usually remain normal.
Chronic Mucocutaneous Candidiasis	Immune deficiency T-Cell Deficiency	T-Cell deficiency specific to *Candida*.	Selective recurrent*Candida* infections. Treat with anti-fungal drugs.
Job's Syndrome	Immune deficiency Phagocyte Deficiency	A failure to produce **gamma-Interferon** by T-Helper cells, leading to an increase in T_H2 cells (no negative feedback) ------> excessively high levels of **IgE**.	High histamine levels, eosinophilia. Recurrent**cold** (non-inflammatory) Staphylococcal **abscesses**(resulting from high histamine), eczema.
Selective IgA Deficiency	Immune deficiency B-Cell Deficiency	IgA deficiency may be due to a failure of heavy-chain gene switching.	*The most common congenital immune deficiency.* There also exists selective IgM and IgG deficiencies, but they are less common.
Severe Combined Immunodeficiency (SCID)	Immune deficiency Combined Deficiency	Autosomal Recessive. **Adenosine Deaminase** deficiency ------> accumulation of **dATP** ------> inhibit ribonucleotide reductase ------> decrease in DNA precursors	Severe deficiency in both humoral and cellular immunity, due to impaired DNA synthesis. Bone marrow transplant may be helpful in treatment.
Thymic Aplasia (DiGeorge Syndrome)	Immune deficiency T-Cell Deficiency	Failure of development of the **3rd and 4th Pharyngeal Pouches** ------> agenesis of the thymus and parathyroid glands.	**T-Cell deficiency** from no thymus. **Hypocalcemic tetany** from primary parathyroid deficiency.

Wiskott-Aldrich Syndrome	Immune deficiency Combined Deficiency	Inability to mount initial **IgM** response to the capsular polysaccharides of pyogenic bacteria.	In infancy, recurrent pyogenic infections, eczema, thrombocytopenia, excessive bleeding. IgG levels remain normal.
X-Linked Agammaglobulinemia (Bruton's Disease)	Immune deficiency B-Cell Deficiency	X-Linked. Mutation in gene coding for **tyrosine kinase** causes failure of Pre-B cells to differentiate into B-Cells.	Recurrent pyogenic infections after 6 months (when maternal antibodies wear off). Can treat with polyspecific gamma globulin preparations.
Fabry's Disease	Lysosomal Storage Disease	X-Linked Recessive. **alpha-Galactosidase A** deficiency ----> buildup of **ceramide trihexoside**in body tissues.	**Angiokeratomas** (skin lesions) over lower trunk, fever, severe burning pain in extremities, cardiovascular and cerebrovascular involvement.
Gaucher's Disease	Lysosomal Storage Disease	Autosomal Recessive. **Glucocerebrosidase** deficiency ------> accumulation of glucocerebrosides (gangliosides, sphingolipids) in lysosomes throughout the body.	• **Type-I**: Adult form. 80% of cases, retain partial activity. Hepatosplenomegaly, erosion of femoral head, mild anemia. Normal lifespan with treatment. • **Type-II**: Infantile form. Severe CNS involvement. Death before age 1. • **Type-III**: Juvenile form. Onset in early childhood, involving both CNS and viscera, but less severe than Type II.
Niemann-Pick Lipidosis	Lysosomal Storage Disease	Autosomal Recessive. **Sphingomyelinase** deficiency ------> accumulation of sphingomyelin in phagocytes.	Sphingomyelin-containing**foamy histiocytes** in reticuloendo-thelial system and spleen. Hepatosplenomegaly, anemia, fever, sometimes CNS deterioration. Death by age 3.
Hunter's Syndrome	Lysosomal Storage	**X-Linked Recessive**. **L-iduronosulfate**	Similar to but less severe than Hurler Syndrome.

	Disease	**sulfatase** deficiency ------> buildup of**mucopolysaccharides** (heparan sulfate and dermatan sulfate)	Hepatosplenomegaly, micrognathia, retinal degeneration, joint stiffness, mild retardation, cardiac lesions.
Hurler's Syndrome	Lysosomal Storage Disease	Autosomal Recessive. **alpha-L-iduronidase** deficiency ------> accumulation of**mucopolysaccharides** (heparan sulfate, dermatan sulfate) in heart, brain, liver, other organs.	Gargoyle-like facies, progressive mental deterioration, stubby fingers, death by age 10. Similar to Hunter's Syndrome.
Tay-Sachs Disease	Lysosomal Storage Disease	Autosomal Recessive. **Hexosaminidase A** deficiency ------> accumulation of G_{M2} ganglioside in neurons.	CNS degeneration, retardation, **cherry red-spot** of macula, blindness (amaurosis). Death before age 4.
Albinism	Nitrogen Metabolism Defect	Autosomal Recessive. **Tyrosinase** deficiency ------> inability to synthesize melanin from tyrosine. Can result from a lack of migration of neural crest cells.	Depigmentation, pink eyes, increased risk of skin cancer.
Alkaptonuria	Nitrogen Metabolism Defect	Autosomal Recessive. **Homogentisic Oxidase** deficiency (inability to metabolize Phe and Tyr) ------> buildup and urinary excretion of **homogentisic acid**.	Urine turns dark and black on standing, **ochronosis**(dark pigmentation of fibrous and cartilage tissues), ochronotic arthritis, cardiac valve involvement. Disease is generally *benign*.
Homocystinuria	Nitrogen Metabolism Defect	Autosomal Recessive. **Cystathionine synthase** defect (either deficiency, or lost affinity for pyridoxine, Vit. B_6) ------> buildup of homocystine and deficiency of cysteine.	Mental retardation, ectopia lentis, sparse blond hair, genu valgum, failure to thrive, thromboembolic episodes, fatty changes of liver. Treatment: Cysteine supplementation, give excess pyridoxine to compensate for lost pyridoxine affinity.
Lesch-Nyhan Syndrome	Nitrogen Metabolis	X-Linked Recessive. **Hypoxanthine-**	**Hyperuricemia** (gout), mental retardation, self-mutilation

	m Defect	**Guanine Phosphoribosyltransferase (HGPRT)** deficiency ------> no salvage pathway for purine re-synthesis ------> buildup of purine metabolites	(autistic behavior), choreoathetosis, spasticity.
Maple Syrup Urine Disease	Nitrogen Metabolism Defect	Autosomal Recessive. Deficiency of **branched chain keto-acid decarboxylase** ------> no degradation of branched-chain amino acids ------> buildup of **isoleucine, valine, leucine**.	Severe CNS defects, mental retardation, death. Person smells like maple syrup or burnt sugar. Treatment: *remove the amino acids from diet.*
Phenylketonuria (PKU)	Nitrogen Metabolism Defect	Autosomal Recessive. **Phenylalanine hydroxylase** deficiency (cannot break down Phe nor make Tyr) ------> buildup of phenylalanine, phenyl ketones (phenylacetate, phenyl lactate, phenylpyruvate) in body tissues and CNS.	Symptoms result from accumulation of phenylalanine itself. Mental deterioration, hypopigmentation (blond hair and blue eyes), mousy body odor (from phenylacetic acid in urine and sweat). Treatment: *remove phenylalanine from diet*.
Glucose-6-Phosphate Dehydrogenase (G6PD) Deficiency	RBC Disease	X-Linked Recessive. **Glucose-6-Phosphate Dehydrogenase (G6PD)** deficiency ------> no hexose monophosphate shunt ------> deficiency in NADPH ------> inability to maintain **glutathione** in reduced form, in RBC's	Susceptibility to oxidative damage to RBC's, leading to **hemolytic anemia**. Can be elicited by drugs (primaquine, sulfonamides, aspirin), fava beans (**favism**). More prevalent in blacks.
Glycolytic enzyme deficiencies	RBC Disease	Autosomal Recessive. Defect in hexokinase, glucose-phosphate isomerase, aldolase, triose-phosphate isomerase, phosphate-glycerate kinase, or enolase. Any enzyme in glycolysis pathway.	**Hemolytic anemia** results from any defect in the glycolysis pathway, as RBC's depend on glycolysis for energy.
Autosomal Recessive Polycystic Kidney Disease (ARPKD)	Renal	Autosomal Recessive.	Numerous, diffuse bilateral cysts formed in the collecting ducts. Associated with hepatic fibrosis.

Bartter's Syndrome	Renal	Juxtaglomerular Cell Hyperplasia, leading to **primary hyper-reninemia**.	Elevated renin and aldosterone, hypokalemic alkalosis. *No hypertension.*
Fanconi's Syndrome Type I **(Child-onset cystinosis)**	Renal	Autosomal Recessive. Deficient resorption in proximal tubules.	(1) Cystine deposition throughout body, cystinuria. (2) Defective tubular resorption leads to amino-aciduria, polyuria, glycosuria, chronic acidosis;**Hypophosphatemia** and**Vitamin-D-resistant Rickets**.
Fanconi's Syndrome II **(Adult-onset)**	Renal	Autosomal Recessive. Defective resorption in proximal tubules.	Similar to Fanconi Syndrome Type I, but without the cystinosis. Adult onset **osteomalacia**, amino-aciduria, polyuria, glycosuria.
Autosomal Dominant Polycystic Kidney Disease (ADPKD)	Renal Autosomal Dominant Disorders	Autosomal Dominant.	Numerous, disparate, heterogenous renal cysts occurring bilaterally. Onset in adult life. Associated with liver cysts.