Metabolism Final – Lipid Disease Summary

1	G6PD Deficiency	1. a common disease 2. hemolytic anemia 3. highest prevalence in ME, SE Asia, Mediterranean (B-, 2), African Variant (A-, 3) 4. X-linked 5. provides resistance to falciparum malaria 6. precipitating factors (A SPIN F) 7. missense/point mutation.
2	Cystic Fibrosis	1. pancreatic insufficiency (pancreatic lipase deficiency) 2. acid-stable lipases are significant.
3	Orphan Disease	• Combined Pancreatic lipase-colipase Deficiency.
4	Celiac Disease	1. Fat Malabsorption 2. Autoimmune response to gliadin 3. Indicated by the presence of anti-tTG antibodies or absence of villous surface epithelial cells.
5	Steatorrhea-Causing Conditions	1. Short bowel disease 2. Liver or biliary tract disease 3. Pancreatic exocrine insufficiency 4. Cystic fibrosis 5. Celiac Disease
6	Familial Chylomicronemia	1. Type 1 hyperlipoproteinemia 2. Rare autosomal recessive disorder 3. LPL/apo C-II deficiency 4. Results in severe hypertriacylglycerolemia, and can cause pancreatitis.
7	Type 2 Diabetes	• May be caused by failure in regulating glyceroneogenesis due to excess FA and glucose in blood.

8	Carnitine Deficiencies	Primary: - Defective membrane transporter (translocase) - Causes carnitine to be excreted - Treatment: carnitine supplementation.	Secondary: - Valproic acid - Defective FA oxidation - Liver diseases - Carnitine Transferase Deficiencies: - 1: affect liver>>LCFA unusable>> hypoglycemia, coma, death. - 2: affect liver, cardiac muscle, and skeletal muscle. - Treatment: Avoid fasting, diet, and MC TAG supplements.
9	MCAD Deficiency	1. Autosomal recessive 2. Most common inborn B-oxi error 3. Highest in northern European Caucasians 4. Severe hypoglycemia & hypokalemia. 5. Treatment: Avoid fasting, eat frequent meals, diet, w-oxidation is upregulated.	
10	Zellweger Syndrome	• Peroxisomal biogenesis disorder • Impaired beta-oxidation, and ROS detoxification.	
11	X-linked adrenoleukodystrophy	1. A genetic condition 2. Dysfunctional transport of VLCFA across the peroxisomal membrane through defective ABC class D transporters 3. Leads to the accumulation of VLCFAs.	
12	Refsum Disease	1. Autosomal-recessive disorder 2. Caused by a deficiency of peroxisomal PhyH 3. Defective peroxisomal alpha-oxidation of branched-chain FAs.	

13	Respiratory Distress Syndrome (RDS)	1. in preterm infants** 2. Associated with insufficient surfactant production/secretion by type II pneumocytes 3. Treatment: prenatal administration of glucocorticoids shortly before delivery, to induce expression of specific genes.
14	Niemann-Pick Disease	1. Autosomal recessive lysosomal storage disease 2. Caused by a sphingomyelinase deficiency 3. Causes enlarged liver & spleen because of lipid deposits 4. Causes neurodegeneration 5. Occurs in all ethnic groups 6. Type A is more severe and is more frequent in Ashkenazi Jews
15	Lysosomal Storage Diseases	• Caused by defects in the degradation of glycosphingolipids, glycosaminoglycans, and glycoproteins.
16	Sphingolipidoses	1. MOSTLY Autosomal-recessive lysosomal diseases (except fabry) 2. Characterized by mutations in genes that encode lysosomal hydrolases or activator proteins engaged in intralysosomal sphingolipid degradation 3. Progressive diseases that exhibit extensive phenotypic variability (allele/locus) 4. Mostly low incidence except for Gaucher and Tays-Sachs, which are high in Ashkenazi Jews.
17	Tay-Sachs Disease	1. Hexosaminidase A deficiency 2. Ganglioside accumulation 3. Rapid & fatal neurodegeneration 4. Muscle weakness 5. Characterized by bulging lysosomes 6. Affects neurons.

18	Gaucher Disease	1. Glucosidase deficiency 2. Most common lysosomal storage disease 3. Glucocerebroside accumulation 4. Treatment: 5. Recombinant human enzyme replacement therapy 6. Bone marrow transplantation 7. Substrate reduction therapy.
19	Farber Disease	1. Ceramidase deficiency 2. Ceramide accumulation 3. Painful & progressive joint deformity 4. Hoarse cry 5. Tissue granulomas.
20	Fabry disease	1. Galactosidase deficiency 2. X-linked shingolipidose disease 3. Treatment: recombinant human enzyme replacement therapy.
21	Diabetes Mellitus/ Diabetic ketoacidosis	1. High-rate production of ketone bodies (90mg/dl) when the DM is uncontrolled 2. High urinary excretion (5000mg/day) 3. (less insulin>more lipolysis> more FFA in plasma> more ketogenesis) 4. Results in acidemia (ketoacidosis), dehydration, & fruity odor of the breath and urine.
22	Alcoholic ketoacidosis	1. Excess alcohol consumption leading to ketoacidosis 2. 3HB:Ac =~ 3:1 3. Gluconeogenesis is suppressed 4. Pyruvate is converted to lactate = hypovolemia, heart failure, sepsis.

23	Sitosterolemia	1. Defect in cholestrol efflux transporter [from enterocyte into lumen](ABCG5/8) 2. Rare condition 3. Increases MI risk.
24	Cholelithiasis	1. Gallbladder stones 2. Caused by an increase in cholesterol or a decrease in bile acids, another theory is bile oversaturation, causing cholesterol to accumulate 3. Treatment: 4. a cholecystectomy or oral administration of chenodeoxycholic acid for a gradual dissolution of the gallstones.
25	Aspirin-Exacerbated Respiratory Disease	• A response to LT overproduction with NSAID use in ~10% of individuals with asthma. • (LT synthesis is inhibited by cortisol not NSAID!!!!)