BI/CH 422/622	
OUTLINE: Krebs' Cycle	
Introduction and review Transport Glycogenolysis Glycolysis	How did he figure it out? Overview 8 Steps
Introduction & overview; 2 phases Phase I Phase II Summary: logic, energetics, labeling studie Other sugars Pasteur: Anaerobic vs Aerobic Fermentations: anaerobic fates of pyruvate Lactate-lactate dehydrogenase Exam-1 material Acetoacetate decarboxylase	Citrate Synthase Aconitase Isocitrate dehydrogenase Ketoglutarate dehydrogenase Succinyl-CoA synthetase Succinate dehydrogenase Fumarase Malate dehydrogenase
Exam-2 material Ethanol-pyruvate decarboxylase & alcohol dehydrogenase Pyruvate oxidation: Oxide	Energetics; Regulation Summary ative Phosphorylation
aerobic fates of pyruvate pyruvate dehydrogenase complex	Electron Transport Chemiosmotic theory ATP synthesis



































Clinical Correlations

Glycogen Storage Diseases: Inborn errors in metabolism

Pompe is from a lack of maltase (α -1-4 glucosidase) in liver lysosomes, where glycogen will accumulate. Leads to death in first months after birth.

Cori is from lack of debranching enzyme. Glycogen accumulates and liver enlargens (hepatomegaly). Also have fasting hypoglycemia.

McArdle is from the absence of muscle phosphorylase. Leads to difficulty in muscle use; cramps, fatigue. Less muscle glycolysis leads to lower levels of lactic acid in the blood. Muscles are damaged and patients become debilitated.



Clinical Correlations

GAPDH: Arsenic poisoning and superoxide

Arsenate (HAsO₄^{2–}) can substitute for P_i in biochemical reactions. But, the esters formed from arsenate are unstable and readily hydrolyze.

For the GAPDH reaction, the 1-arsenyl-2-phospho glycerate degrades to 3-phosphoglycerate without production of ATP. Therefore, glycolysis does not net any ATP production.

Arsenite (AsO_2^{-}) is more toxic. It kills any enzyme that contains lipoic acid:

Superoxide $(\bullet O_2^{-})$ overproduction can come from over-exposure to high blood glucose, especially in retina, kidney, and peripheral neurons.* This "reactive-oxygen species" (ROS) activates repair enzymes that end up modifying Cys residues in enzymes; thus killing GAPDH.



*early sites of damage from Type-2 diabetes