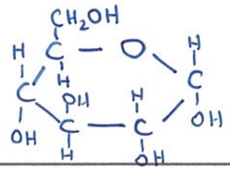
# The Metabolism of Glucose



Date No.

## Glycogenesis

- synthesis of glycogen
- anabolic, requires ATP
- glucose is converted into glucose-6-phosphate (ATP consuming step)
- Through a series of reactions, a chain of α-glucose monomers is formed
- Affected by insulin (↑ glycogenesis), glucagon (↓ glycogenesis) and epinephrine (↓ glycogenesis)

## Glycogenolysis

- breakdown of glycogen
- catabolic
- glucose-6-phosphate initially produced, can be used directly in glycolysis, if low immediate energy demand, it is converted into glucose and released into the blood
- triggered by epinephrine and glucagon, which inhibit glycogenesis enzymes and activate glycogenolysis enzymes

## Gluconeogenesis (Basics)

- generation of glucose from non-sugar substrates
- 90% of starting substrates include pyruvate, lactate, glycerol, alanine and glutamine
- Amino acids undergo deamination or transamination such that the remaining carbon skeleton can enter the pathway (usually as oxaloacetate or pyruvate)
- only odd chain fatty acids can be used to form glucose via a conversion into a precursor of succinyl-CoA
- First, in the mitochondria, pyruvate is converted into oxaloacetate by pyruvate carboxylase, which is stimulated by high acetyl CoA levels and inhibited by high ADP + glucose
- oxaloacetate is then reduced to malate (with NADH → $NAD^+$ + H) for transport out of the matrix
- In the cytosol, the reverse reaction occurs, producing oxaloacetate
- oxaloacetate is then decarboxylated and phosphorylated to form phosphoenolpyruvate
- "Reverse" glycolysis now occurs to produce glucose
- The conversion of glucose-6-phosphate to glucose occurs in the lumen of the ER, by glucose-6-phosphatase.
- Occurs mainly in cortex of kidney and liver
- metformin (diabetes drug) inhibits gluconeogenesis, but during exercise can lead to lactic acidosis as it inhibits hepatic gluconeogenesis, which helps get rid of lactic acid
- The liver and kidneys are the main organs with sufficient enzymes to carry out gluconeogenesis, but astrocytes in the brain can also carry it out

Diagram displaying the gluconeogenesis pathway

mitochondria {
pyruvate
↓ ATP → ADP  Pyruvate carboxylase
oxaloacetate
↓ NADH → NAD
malate
↓ NAD → NADH
oxaloacetate
}

↓

everse, lycolysis' [
phosphoenolpyruvate
⇅
2 phosphoglycerate
⇅ phosphoglycerate mutase
3 phosphoglycerate
⇅
1,3 biphosphoglycerate
⇅ NADH → NAD
glyceraldehyde-3-phosphate
⇅
fructose-1,6-biphosphate
⇅ fructose-1,6-biphosphatase [rate limiting step] [NOTE; NOT phosphofructokinase]
fructose-6-phosphate
⇅ Phosphoglucose isomerase
glucose-6-phosphate
↓ glucose-6-phosphatase (NOT hexokinase)
glucose
]

## Renal Gluconeogenesis

- production of glucose via gluconeogenesis in the kidneys
- mainly in cortex, as cells in the medulla lack glucose-6-phosphatase and other gluconeogenic enzymes
- becomes more pronounced in acidotic conditions or during prolonged fasting
- After liver removal during ~~transport~~ transplant, glucose release only decreases by ~50%
- Comparing [$C_6H_{12}O_6$] in artery v vein shows higher in artery due to use in nephrons
- Calculating renal glucose release (RGR)

Note = $A_G$ = arterial $C_6H_{12}O_6$
$V_G$ = venous $C_6H_{12}O_6$
RBF = renal blood flow
FX = fractional extraction of glucose by kidney

→ Net Renal Glucose Balance (NRGB) = ~~RGR~~ Renal Glucose Uptake (RGU) − RGR

∴ RGR = NRGB + RGU [as RGU is −ve]

$$NRGB = (A_G - V_G) \cdot RBF$$

$$RGU = A_G \times RBF \times FX$$

hence

$$RGR = RBF\left[(A_G - V_G) - A_G FX\right]$$

- Considering that diabetes mellitus can sometimes cause Ketoacidosis (due to breakdown of fat in glucose deficient cells), a positive feedback system may exist, as acidosis of any kind ↑ gluconeogenesis in the kidney

## Cori Cycle

- a.k.a lactic acid cycle, recycles lactic acid to form glucose
- In low oxygen availability, the concentration of $O_2^-$ in the matrix as a terminal electron acceptor becomes a limiting factor for aerobic respiration within muscle cells
- The cells switch to glycolysis, and epinephrine stimulates ~~glucao~~ glycogenolysis to produce glucose for it
- as well as glucose-6-phosphate
- The pyruvate produced is converted by lactate dehydrogenase into lactic acid (up till here 2 ATP produced)
- The lactic acid diffuses out of the ~~blood~~ muscles and into the blood, through which it is transported to the liver
- The lactic acid is then converted into pyruvate for the start of gluconeogenesis
- Gluconeogenesis uses 6ATP to convert the pyruvate into glucose, which is transported back to the muscles
- Can be used in glycolysis immediately or used in glycogenesis
- Generally, with respect to the pyruvate produced in the liver, 1 in every 6 pyruvates produced is converted to acetyl CoA through pyruvate dehydrogenase to produce ATP through OXPHOS to fuel gluconeogenesis