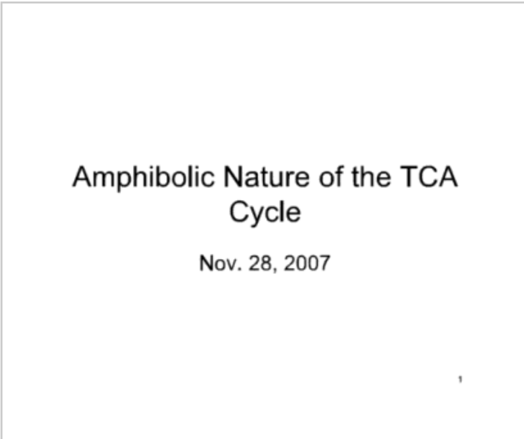
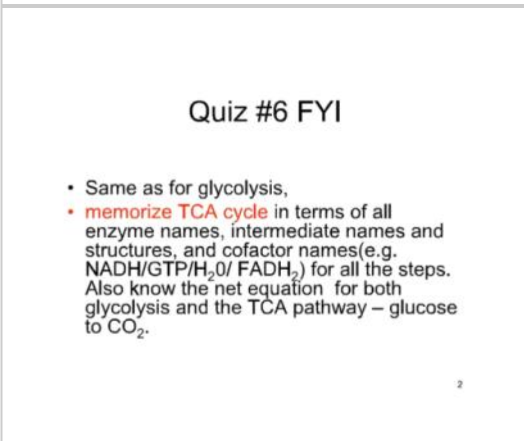
Notes 11/28

Wednesday, November 28, 2007
10:04 AM

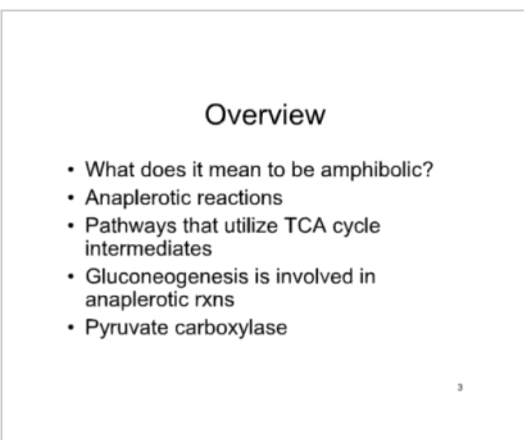
Notes 1128

Audio recording started: 10:05 AM Wednesday, November 28, 2007

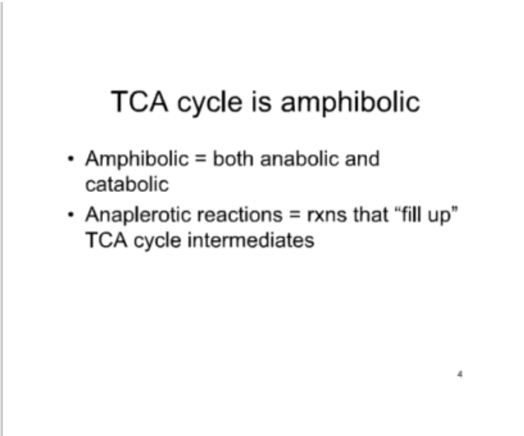




Slide 3: Overview
- What does it mean to be ampbolic



- Slide 4: TCA Cycle is amphibolic
    - Amphibolic = both anabolic and catabolic
    - Anaplerotic reactions = reactions that "fill up" TCA cycle intermediates
        - TCA cycle intermediates can be shuttled off to other reactions. Intermediates must be replenished... these reactions are referred to as anaplerotic



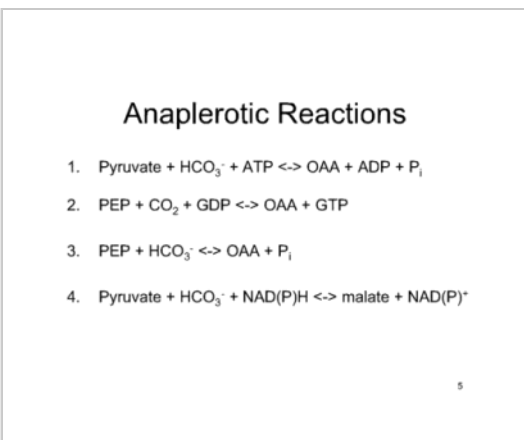
- Slide 5: Anaplerotic Reactions
  a. Pyruvate + HCO_3^- + ATP <-> OAA + ADP + P_i
     - Pyruvate isn't involved in creating energy directly and must undergo TCA cycle
     - Pyruvate can be used to directly make OAA
     - Enzyme: Pyruvate Carboxylase
     - Commonly happens in liver and kidneys

  b. PEP + CO_2 +GDP <-> OAA + GTP
     - Enzyme: PEP (phosphylenolpyruvate) carboxykinase
     - Occurs in heart and skeletal muscle

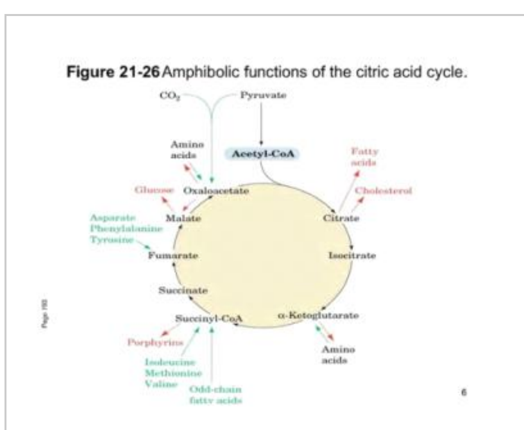
  c. PEP + HCO_3^- <-> OAA + P_i
     - PEP is high energy compound and this energy is harness for reaction
     - Enzyme: PEP Carboxylase

  - Anaplerotic Reactions tend to form OAA
     - Because it is starting molecule of TCA cycle

  d. Pyruvate + HCO_3^- + NAD(P)H <-> malate + $NAD(P)^+$
     - Enzyme: malic enzyme
     - Similar to reaction 1
     - Malate can be transported from mitochondria to cytosol (OAA cannot do this)



- Slide 6: Figure 21-26 Amphibolic functions of the citric acid cycle
  - Outlines amphibolic reactions
  - Many of the reactions are not committed only to TCA cycle
  - Porphyrins: used to make heme
  - Oxaloacetate is precursor to gluconeogenisis



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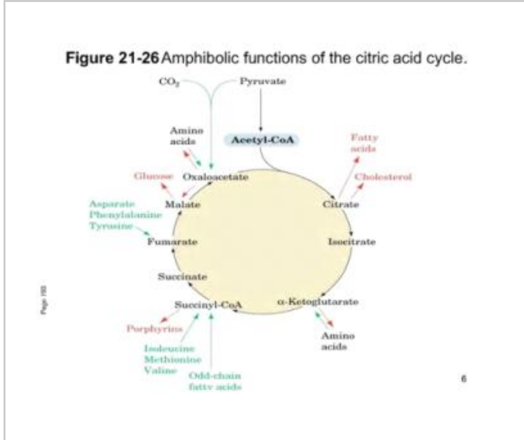
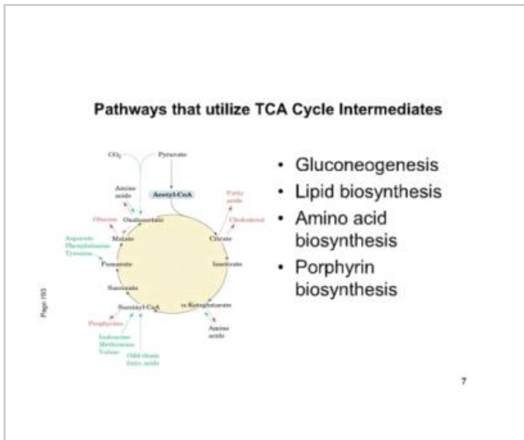
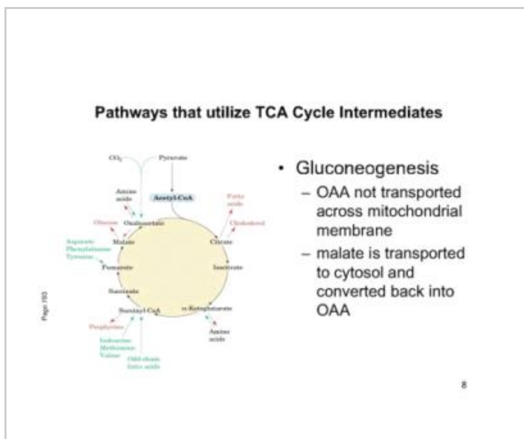


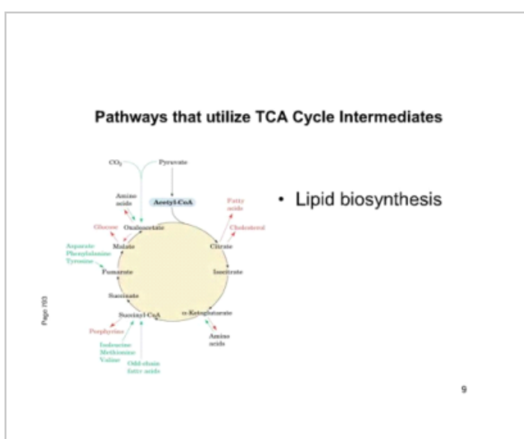
- Slide 7: Pathways that utilize TCA cycle Intermediates
  - Gluconeogenesis
  - Lipid boisynthesis
  - Amino acid biosynthesis
  - Porphyrin biosynthesis



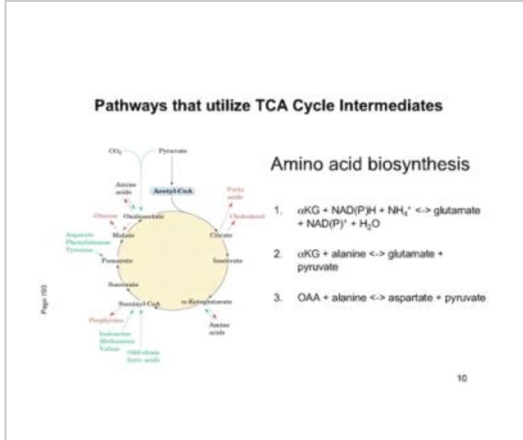
- Slide 8: Pathways that utilize TCA cycle intermedites
  - Gluconeogenesis
    - OAA not transported across mitochondrial membrane
    - Malate is transported to cytosol and converted back into OAA



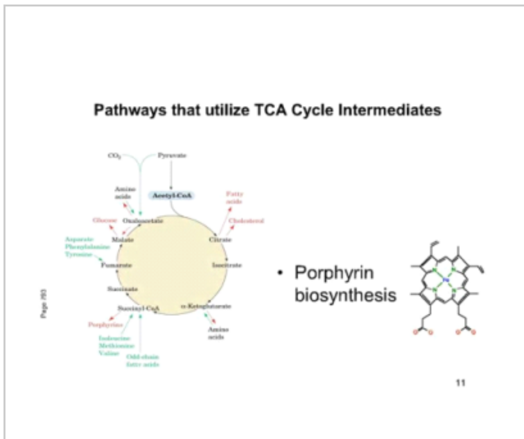
- Slide 9: Pathways that utilize Tca Cycle Intermediates
  - Lipid



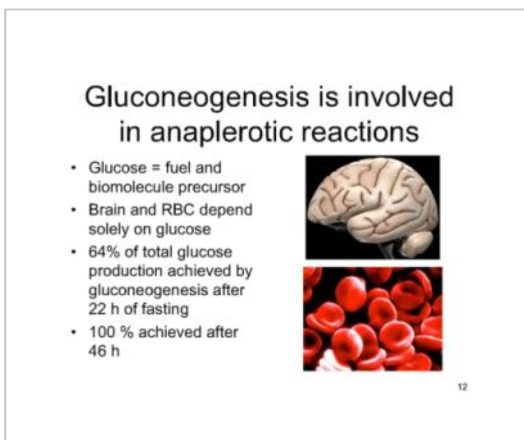
- Slide 10: Amino Acid biosynthesis
    a. αKG + NAD(P)H + NH_4^+ <-> glutamate + $NAD(P)^+$ + H_2O
        - Dehydration reaction results in water
        - Not covering specific enzyme
        - Referred to as deamination (named for reverse reaction)
    b. αKG + alanine <-> glutamate + pyruvate
        - Referred to as transamination because it transfers amino group from alanine to αKG
    c. OAA + alanine <-> aspartate + pyruvate
        - Also transamination



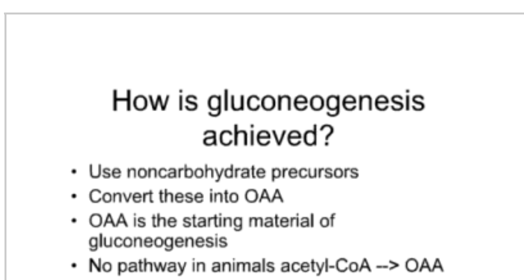
- Slide 11: Pathways toat utilize TCA Cycle Intermediates
    - Porphyrin biosynthesis (chem 153C)
        - We won't get into detail or study mechanism



- Slide 12: Gluconeogenesis is involved in anaplerotic reactions
    - Glucose fuel and biomolecule precursor
    - Brain and RBC depend solely on glucose as energy
    - 64% of total glucose production achieved by gluconeogenesis after 22h of fasting
    - 100% achieved after 46h



- Slide 13: How is gluconeogenesis achieved?
    - Use noncarbohydrate precursors
    - Convert non carbohydrate precursors into OAA
    - OAA is starting material of gluconeogenesis
    - No pathway in animals: acetyl-CoA --> OAA
    - Fatty acid -> acetyl-CoA
        - Animals can't use fatty acids to make glucose
        - Plants can do this via glyoxylate pathway.
            - Plant seeds are rich in oil (fatty acids)
            - Plant embryo inside seed uses these fatty acids as energy



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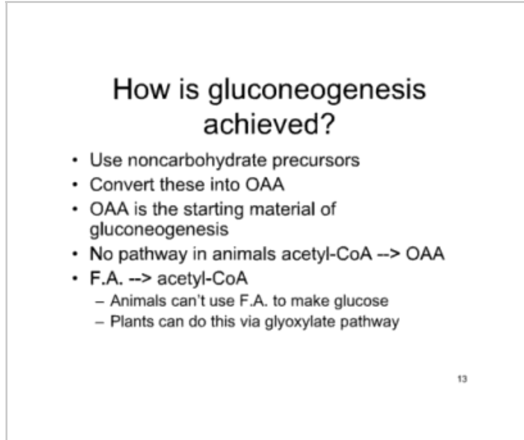
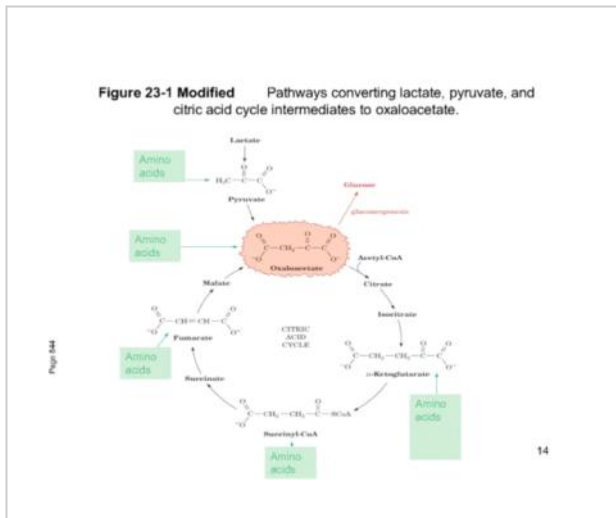
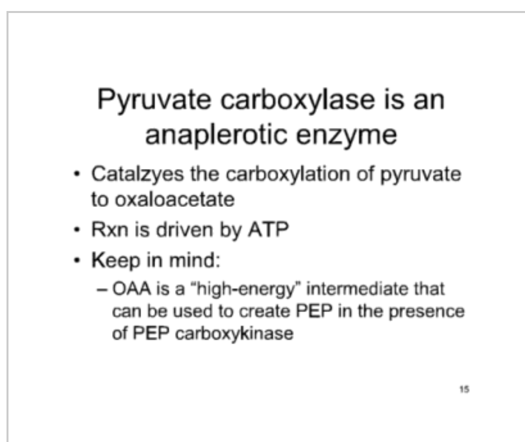


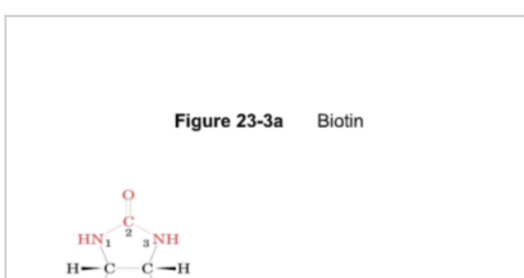
- Slide 14: Figure 23-1 Modified: Pathways converting lactate, pyruvate, and citric acid cycle intermediates to oxaloacetate
  - Lactate can be converted to pyruvate which can be converted to OAA



- Slide 15: Pyruvate carboxylase is an anaplerotic enzyme
  - Catalyzes the carboxylation of pyruvate to oxaloacetate
  - Reaction is driven by ATP
  - Keep in mind:
    - OAA is a "high-energy" intermediate that can be used to create PEP in the presence of PEP carboxykinase



- Slide 16: Figure 23-3a Biotin
  - Biotin is a cofactor
  - Need to recognize structure of biotin (not draw from scratch)
  - Function of biotin: CO_2 carrier
  - Biotin has a valerate side chain.



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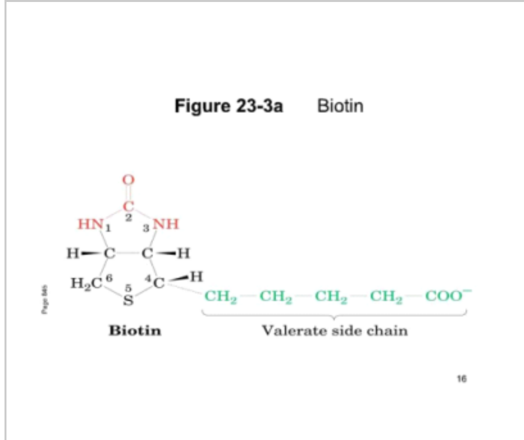
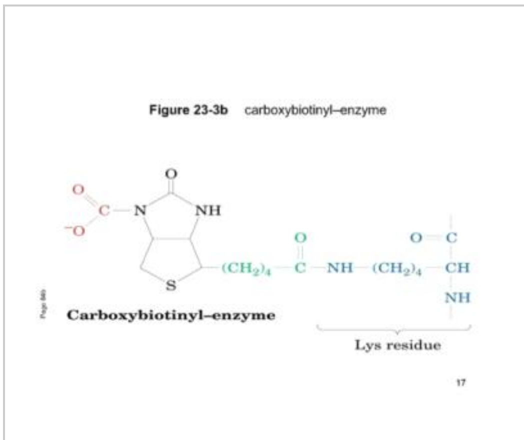
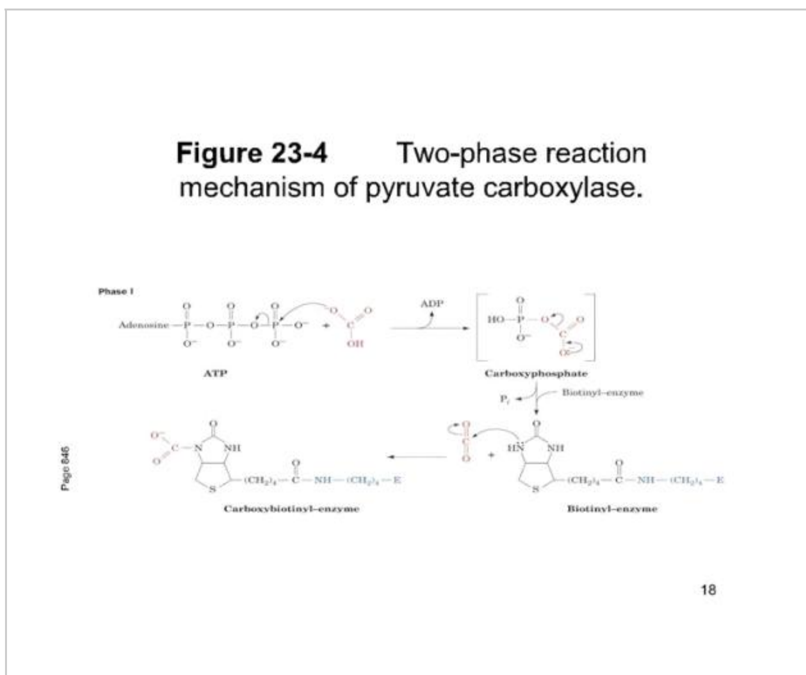


- Slide 17: Figure 23-3b carboxybiotinyl-enzyme



- Slide 18: Figure 23-4 Two-phase reaction mechanism of pyruvate carboxylase
    - Need to know mechanism
    - 2 steps in mechanism
    - Phase 1:
        - ATP and bicarbonate -> carboxyphosphate
        - Carboxyphosphate + biotinyl-enzyme -> carboxybiotinyl-enzyme



- Side 19: figure 23-4 (continued) Two-phase reaction mechanism of pyruvate carboxylase. Phase II
    - Phase 2:
        - Carboxybiotinyl-enzyme + pyruvate ….. -> -> ……

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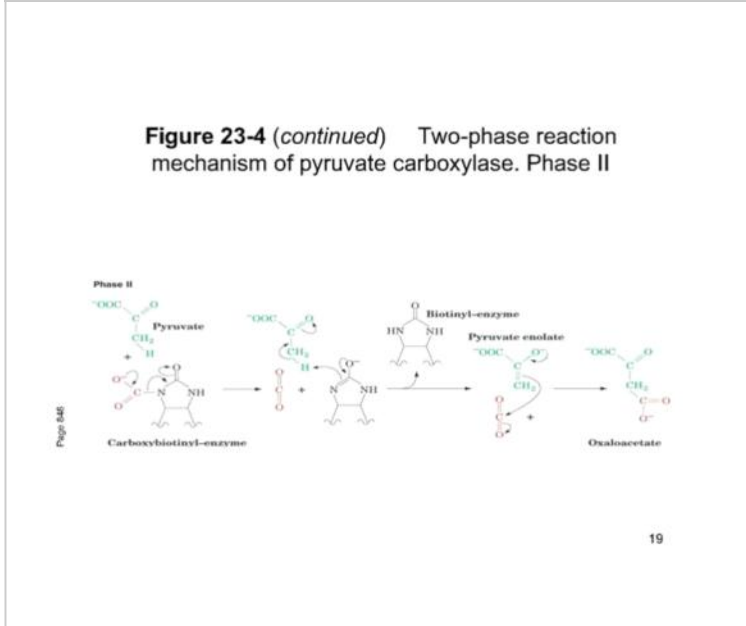
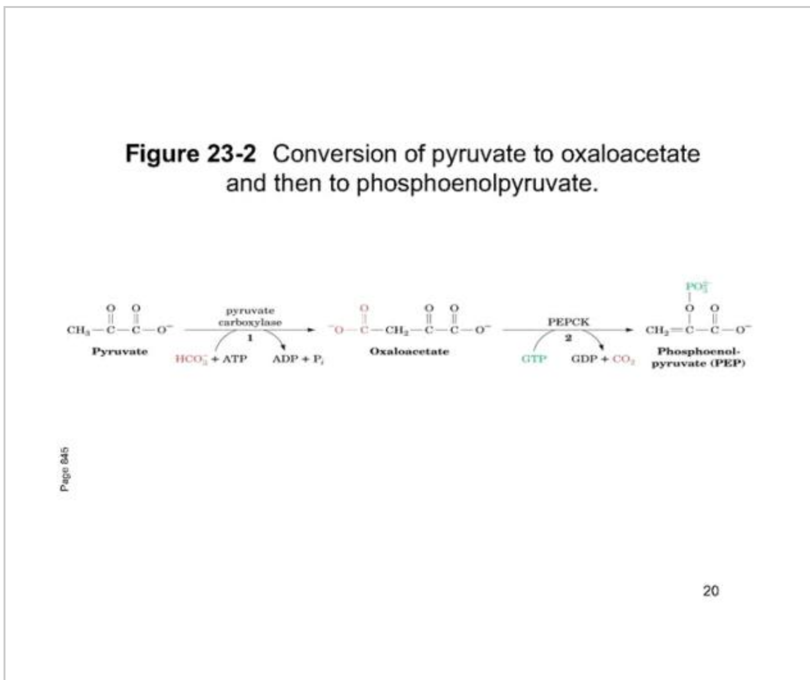
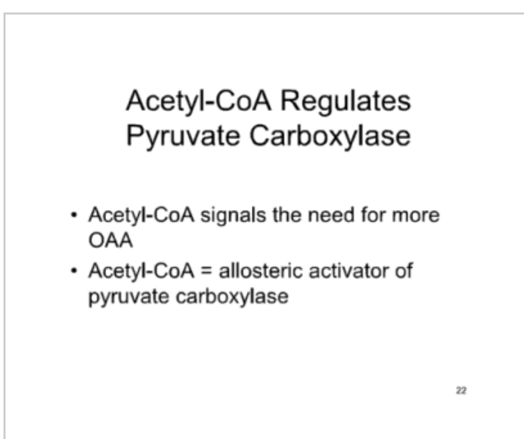


- Slide 20: Figure 23-2 conversion of pyruvate to oxaloacetate and then to phosphoenolpyruvate



- Slide 22: Acetyl-CoA Regulates Pyruvate Carboxylase
  - Acetyl-CoA signals the need for more OAA



- Slide 21: Avidin is a protein that binds to biotin tightly
  - Avidin is found in egg whites (raw; denatured in cooked)