Unit II – Problem 3 – Biochemistry: Mobilization of Stored Fats and β-Oxidation

- **Oxidation of 1 g of fat will provide energy equal to 9 kcal.**
- **Release of fatty acids from TAG:**
  - **Activation of Hormone Sensitive Lipase (HSL):**
    - ✓ Epinephrine → cyclic AMP → phosphrylated HSL (active form).
    - ✓ Insulin → produces dephosphorylated HSL (inactive form).
  - **Fate of glycerol:**
    - ✓ It goes back to the liver to:
      - ❖ Be phosphorylated again to synthesize TAG.
      - ❖ Be converted to DHAP by dehydrogenase and enter the process of glycolysis.
  - **Fate of fatty acids:**
    - ✓ Free (un-esterified) fatty acids bind with albumin and transported to tissues (except erythrocytes and brain) to be oxidized for energy.
- **β-oxidation of fatty acids (occurring in the mitochondria and producing NADH, $FADH_2$ and acetyl CoA):**
  - **Transport of Long Chain Fatty Acids (LCFA) into the mitochondria:**
    - ✓ LCFA translocation:
      - ❖ Fatty acyl CoA → via CPT-1 → Acyl carnitine → via CPT-II (and releasing free carnitine) → fatty acyl CoA.
    - ✓ Inhibitor of carnitine shuttle → malonyl CoA
    - ✓ Sources of carnitine:
      - ❖ Meat products.
      - ❖ Lysine + Methionine (in liver and kidneys).
    - ✓ Carnitine deficiencies occur because of:
      - ❖ Liver diseases.
      - ❖ Hemodialysis.
      - ❖ Malnutrition.
      - ❖ Increased requirement for carnitine.
  - **CPT-I deficiency:**
    - ✓ There is no use of LCFA as source of energy → leading to hypoglycemia.
    - ✓ Treatment:
      - ❖ Avoid prolonged fasting.
      - ❖ Eat diet high in carbohydrates and low in LCFA.
      - ❖ Take supplements of Medium Chain Fatty Acids (MCFA) and carnitine.
  - **Entry of Small Chain Fatty Acid (SCFA) and MCFA into the mitochondria:**
    - ✓ They are composed of less than 12 carbons thus passing into mitochondria without CPT-I aid.
  - **Reactions of β-oxidation:**
    - ✓ Oxidation (which releases $FADH_2$) → hydration → oxidation (releasing NADH) → thiolytic cleavage.
  - **Energy yield from fatty acid oxidation:**
    - ✓ Example: palmatic acid (containing 16 carbons):
      - ❖ 8 acetyl CoA x 12 = 96 ATP
      - ❖ 7 NADH x 3 = 21 ATP
      - ❖ 7 $FADH_2$ x 2 = 14 ATP

        = total of 131 ATP → subtract 2 ATP (which are used for fatty acid activation) = 129 ATP

- **MCFA dehydrogenase (MCAD) deficiency:**
  - ✓ There are four dehydrogenases for short, medium, long and very long fatty acids.
  - ✓ MCAD deficiency is an inborn error of metabolism in which medium chain fatty acids are not oxidized. This condition is managed by avoiding prolonged fasting.
- **Oxidation of fatty acids with an odd number of carbons:**
  - ✓ Same steps of β-oxidation of even number fatty acids until the last three carbons remaining (this will be known as propionyl CoA):
    - ❖ *Synthesis of D-methylmalonyl CoA:*
      - ➢ Propionyl CoA → via carboxylase (and use of biotin) → D-methylmalonyl CoA.
    - ❖ *Formation of L-methylmalonyl CoA:*
      - ➢ L-methylmalonyl CoA → via mutase (and use of vitamin B12) → succinyl CoA.
- **Oxidation of unsaturated fatty acids provides less amount of energy.**
- **β-oxidation in peroxisome:**
  - ✓ It occurs with VLCFA (≥ 22 carbons).
  - ✓ Zellweger syndrome: peroxisomal biogenesis disorder.
  - ✓ Adrenoleukodystrophy: VLCFA cannot across peroxisome.