Fatty acid oxidation → by β oxidation.

Stages and tissue
1. activation of fatty acid → cytosol
2. transport of fatty acid → Mitochondria
3. β-oxidation proper → Mitochondral Matrix.

- Fatty acid not utilized as energy source by :-
→ brain, RBC, adrenal Medulla. (1)

Fatty acid (Long chain carbon)
Thiokinase/ acyl CoA synthetase
ATP → PPi → Pyrophosphatase → 2 Pi [IR]
Acyladenylate
CoA SH → AMP
Acyl CoA
I CYTOSOL

II CARNITINE TRANSPORT SYSTEM

III MITOCHONDRIA
Acyl CoA
Acyl CoA [FAD dependent flavoenzyme] dehydrogenase [Oxidation]
2ATP ← ETC ← $FADH_2$ ← FAD
Δ^2 trans-enoyl CoA
H_2O → enoyl CoA hydratase (Hydration)
β-hydroxyacyl CoA
3ATP ← ETC ← $NADH + H^+$ ← NAD^+
β Hydroxyacyl CoA dehydrogenase [Oxidation]
β ketoacyl CoA
thiolase
Acyl CoA → Acyl CoA (2C) + Acetyl CoA (2C)

Acetyl CoA → liver → Ketone bodies
Acetyl CoA → non liver → TCA
Acetyl CoA → non-liver → krebs cycle → $2CO_2$

II Carnitine transport system:

CYTOSOL | INNER MITO-MEMBRANE [IMM] (Impermeable to fatty acids) | MITOCHONDRIAL MATRIX

Acyl CoA (Fatty acid)
Malonyl CoA ⊖ → carnitin acyl transferase I [CAT-I] (RLE)
(⊕ on outer surface of IMM)
CoA SH
Acyl carnitine
Carrier protein
Carnitine
Acyl carnitine → Acyl - Carnitine
Carnitine acyltransferase II [CAT-2]
(⊕ amines on surface of IMM)
Acyl CoA
CoA SH

OVERALL RXN.

C_n Acyl CoA + FAD + NAD^+ + H_2O + CoA SH
↓
$C_{(n-2)}$ Acyl CoA + Acetyl CoA + $FADH_2$ + NADH + H^+

Malonyl CoA formed in fatty acid synthesis.

RLE → Rate limiting enzyme.

Oxidation of Palmitoyl CoA (16C)

Palmitoyl CoA (16C) + 7 COASH + 7 FAD + 7 NAD^+ + 7 H_2O

↓

8 Acetyl CoA + 7 $FADH_2$ + 7 NADH + 7 H^+

↓ 35 ATP (5 × 7)

TCA cycle → 96 ATP (8 × 12)

Energetics

Standard free energy (palmitate) = 2,340 cal

energy yield by its oxidation → 129 ATP

efficiency of energy conservation by fatty acid oxidation = $\frac{940}{2,340} \times 100 = 40\%$

energetics of palmic acid oxidation

	Mechanism	ATP yield
I.	β oxidation 7 cycles	
•	7 $FADH_2$ (ETC)	
	1 $FADH_2$ → 2 ATP	14 ATP
•	7 NADH (ETC)	
	1 NADH → 3 ATP	21 ATP
II.	From 8 acetyl CoA cytric acid cycle	
	1 Acetyl CoA → 12 ATP	96 ATP
	Total energy (1 mole)	131 ATP
	energy utilized (formation of palmitoyl CoA	−2 ATP
	Total	129 ATP.

Oxidation of odd carbon chain fatty acids.

Propionyl CoA —(CO_2, Propionyl CoA carboxylase; Biotin; ATP → ADP + Pi)→ D-Methylmalonyl CoA

D-Methylmalonyl CoA —(Methyl Melonyl CoA racemase)→ L-Methylmalonyl CoA

L-Methylmalonyl CoA —(Mutase, B_{12})→ (3C) Succinyl CoA → TCA cycle.

L-Methylmalonyl CoA → Methylmalonic acid [accumulation causes Methylmalonic acidemia]

Sudden Infant Death Syndrome (SIDS)

- 10% due to deficiency of Medium chain alyl CoA dehydrogenase.
- baby feed
  ↓ after fewhours
  glucose level, its utilization level
  ↓es decreases.

so rate of fatty acid oxidation is have to Increase simultaneously to meet the energy needs.

- their is a blockage in fatty acid oxidation pathway.

Jamaican vomiting syndrome.

- Severe hypoglycemia, Vomiting, convulsions, coma and even death.
- CAUSE: eating unripe ackee fruits
- Unripe fruit
  ↓
  contains an unusual toxic amino acids (hypoglycin A)
  ↓
  inhibits acyl CoA dehydrogenase
  ↓
  β oxidation blocked.

Methylmalonic acidemia (2 types)

i) due to deficiency of Vit. B_{12}.
ii) due to defect in enzyme Methylmalonyl CoA Mutase.

- Methylmalonic acid accumulated
  ↓
  Increased excretion in urine.

Problems :-
- Metabolic acidosis
- damage CNS
- retards growth
- fatal in early life.

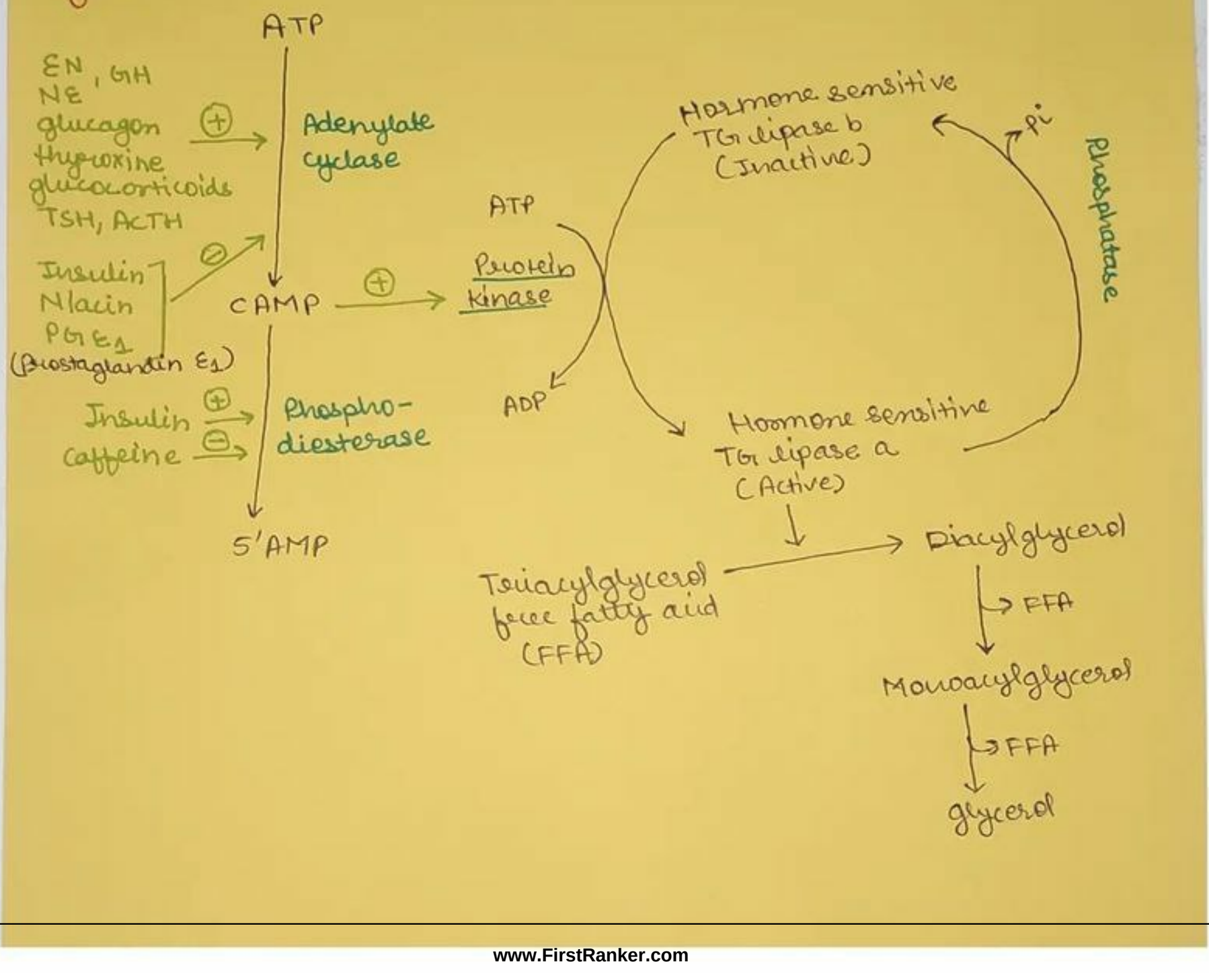
Refsum's disease (α oxidation)

- defect in α-oxidation due to deficiency of phytanic acid (α-oxidase enzyme).
- accumulated unusual fatty acids
  ↓
  Phytanic acid.
- severe neurological disorders
  - cerebral ataxia, peripheral neuropathy
- (Rx)
  Patient should not be given green leafy vegitables (chlorophyll).

Zellweger syndrome (2) as called e cerebrohepatorenal syndrome

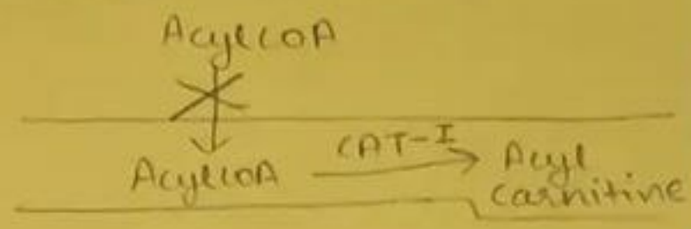
- absence of peroxisomes in all tissues.
- accumulated in
  - brain
  - liver
  - kidney.
- long chain fatty acids
  ↓
  not oxidized.

Regulation



Fatty acids	location
• Short/Medium chain (2-12C) • long chain (14-20 C) • Very long chain (>20C)	diffuse freely in Mitochondria use carnitine transport in Mito. oxidized in a peroxisome.

Systemic primary carnitine deficiency.
- No transport into Mito. Membrane.
- Hypoketotic Hypoglycemia.



Myopathic CAT-II Deficiency
- Myoglobinuria
- Hypotonic, Weak Muscles
- ↑ Triglycerides in Muscles.

Medium chain AcylCoA Dehydrogenase deficiency.
- Hepatic Dysfunction
- Hyperammonemia

Rx avoid fasting.