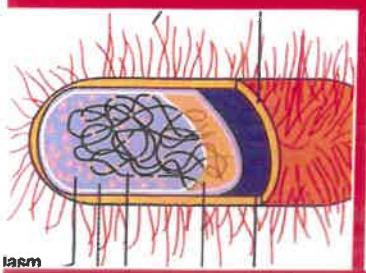
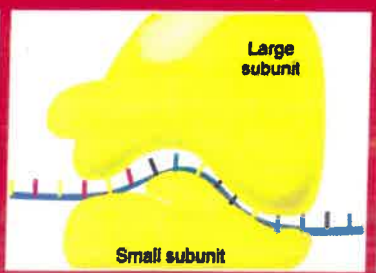
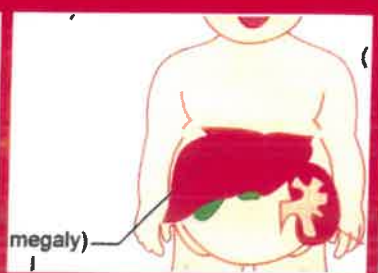
Cerebellum
Get the balance right

# Cerebellum Biochemistry

For the Students
By the Teachers






Cerebellum Biochemistry

# Cerebellum

Get the balance right

# Table of Content



* These chapter are important for FMGE exams

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# Unit 1
# Concepts

# 1 Chapter

# FOUR FORMULAS

Fed state (2 hours after food intake) → Anabolism occurs

Fasting state (12-18 hours without food)

Starvation (1-3 days without food)

## SMILE FORMULA 1

Tells about which pathway/enzyme is Anabolic and which pathway/enzyme is Catabolic?

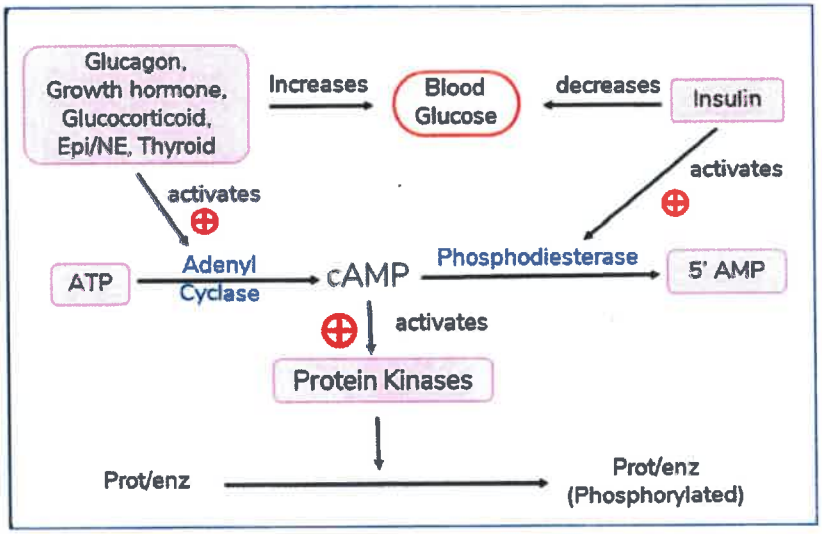
| Anabolic pathways | Catabolic pathways |
|---|---|
| • Glycogenesis<br>• HMP<br>• Fat Synthesis<br>• Lipoprotein Lipase (LPL) enzyme | • Glycolysis<br>• Link Reaction<br>• Glycogenolysis<br>• β-oxidation of fatty acids<br>• Gluconeogenesis<br>• Ketone Body Synthesis<br>• Ketone Body utilization/breakdown<br>• Hormone Sensitive lipase (HSL) enzyme |

**Note:** This division is based on whether pathway occur in catabolic or anabolic state. Pathway occurring in fed state are anabolic while pathways occur in fasting/starvation are considered as catabolic.

## SMILE FORMULA 2

- Related to hormones Insulin and glucagon and their effects on pathways.
- Insulin is released in fed state to cause hypoglycemic action. So, consider insulin as anabolic hormone.
- **Formula:** Insulin activates all anabolic pathways/enzymes especially regulatory enzymes of anabolic pathways.
  - **Exception:** Insulin also activates two catabolic pathway enzymes *i.e.*, Glycolysis and Link Reaction.
- **Formula:** Glucagon activates all catabolic pathway/enzymes
  - **Exception:** glucagon does not activate two catabolic pathway enzymes, *i.e.*, Glycolysis and Link Reaction, as these are activated by Insulin.

## Phosphorylation and Dephosphorylation by cAMP




- cAMP causes phosphorylation
- Why many hormones increase blood glucose while only one hormone decreases blood glucose?
  - Because hypoglycaemia is more dangerous than hyperglycaemia.
- Insulin activates phosphodiesterase so ↓ cAMP and causes dephosphorylation
- Glucagon and epi/NE, GH, Glucocorticoid and thyroid hormones activates adenyl cyclase so ↑ cAMP and cause phosphorylation

## SMILE FORMULA 3

- Related to Phosphorylation and Dephosphorylation states of enzymes
  - Any Pathway or Enzyme which is activated by Insulin will be active in its Dephosphorylated state. It includes all anabolic pathways and glycolysis and Link reaction.
  - Any pathway or Enzyme which is activated by Glucagon (Catabolic enzymes) is active in Phosphorylated state.

**Exception:** ATP Citrate Lyase that is an anabolic enzyme (activated by insulin) but it is active in phosphorylated state

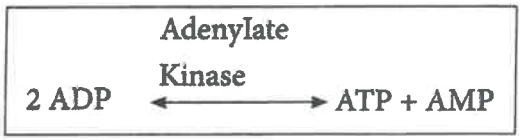
## SMILE FORMULA 4

- Tells Which pathway occurs in which compartment of the cell?
  - All Anabolic Pathways occur in Cytoplasm
  - All Catabolic Pathways occur in Mitochondria
  - Exception: Two catabolic pathways also occur in cytoplasm.
    1. Glycolysis
    2. Glycogenolysis
- Pathways which occur in both Mitochondria and Cytoplasm
  - Urea cycle
  - Haem synthesis
  - Gluconeogenesis
- Whenever a pathway occurs in both, it starts in mitochondria and finishes in cytoplasm
- TCA, ETC → vital pathways that occur in mitochondria and do not depend on fed or fasting state

**Note:** There are some other pathways such as urea cycle, nucleotide, DNA, RNA, Protein and AA synthesis which are neither regulated by hormones and do not depend on fed and fasting state. So, don't use formulas for these pathways.

## ADENYL KINASE

- It's a phosphotransferase and perform conversion of 2ADP to AMP and ATP




- Used for interconversion of nucleotides ADP, ATP and AMP which are required for different functions in the cell.

# 2 Chapter

# THE TWO LIPASES

| Lipoprotein Lipase (LPL) | Hormone Senstitive Lipase (HSL) |
|---|---|
| • Present in the endothelium of blood vessels | • Pre sent in the adipose tissues |
| • Breaks down fats (TG) travelling in the blood to FA and Glycerol | • Breaks down fats (TG) stored in adipose tissue to FA and Glycerol during fasting and starvation |
| • FA and Glycerol are absorbed into adipose tissue and get stored as TG | • Released FA and Glycerol is passed into blood and used for energy by liver and other organs |
| • Helps to store fats, hence considered as anabolic enzyme | • Helps to break fats, hence considered as catabolic enzyme |
| • Activated by anabolic hormone insulin and inhibited by glucagon | • Activated by catabolic hormone glucagon and inhibited by insulin |

# 3 Chapter

# HOW TO USE FORMULAS

**Q1. Which of the following does not occur in mitochondria?** *(AIIMS Nov 2016)*

(a) Beta oxidation
(b) Fatty acid synthesis
(c) DNA synthesis
(d) Protein synthesis

**Ans.** (b) Fatty acid synthesis

| Pathway | Nature | Compartment |
|---|---|---|
| **Beta oxidation** | Catabolic | Mitochondria |
| **Fatty acid synthesis** | Anabolic | Cytoplasm |
| **DNA synthesis** | Mitochondrial DNA and protein synthesis | Mitochondria |
| **Protein synthesis** | | |

**Q2. Which of the following is active in dephosphorylated state?** *(PGI May 2017)*

(a) Glycogen Synthase
(b) Pyruvate Carboxylase
(c) Glycogen phosphorylase
(d) Acetyl CoA Carboxylase
(e) Pyruvate dehydrogenase

**Ans.** (a, d, e)

| | | | | |
|---|---|---|---|---|
| (a) Glycogen Synthase | → | Synthesis | → | Anabolic |
| (b) Pyruvate Carboxylase | → | Gluconeogenesis | → | Catabolic |
| (c) Glycogen phosphorylase | → | Break down | → | Catabolic |
| (d) Acetyl CoA Carboxylase | → | FA Synthesis | → | Anabolic |
| (e) Pyruvate dehydrogenase | → | Link reaction | → | Catabolic |

- **Apply Smile formula 3:** Pathways or Enzymes which are activated by Insulin (Anabolic Enzyme) are always active in Dephosphorylated state with link reaction as an exception.

**Q3. Insulin promotes lipogenesis by all except?**

(a) Decreasing cAMP
(b) Increasing Glucose uptake

(c) Inhibiting Pyruvate Dehydrogenase
(d) Increasing Acetyl CoA

**Ans.** (c) Inhibiting Pyruvate Dehydrogenase

**Q4. Mitochondria are involved in all of the following except:**

(a) ATP Production
(b) Apoptosis
(c) Tri carboxylic Acid Cycle
(d) Cholesterol Synthesis

**Ans.** (d) Cholesterol Synthesis

**Q5. Hormone Sensitive lipase is NOT activated by:**

(a) Insulin
(b) Glucagon
(c) Catecholamines
(d) Thyroid

**Ans:** (a) (Apply Smile formula 1 and 2)

| | | | | |
|---|---|---|---|---|
| (a) Insulin | → | Lipoprotein Lipase | → | Anabolic |
| (b) Glucagon | | | | |
| (c) Catecholamines | → | Hormone Sensitive lipase | → | catabolic |
| (d) Thyroid | | | | |

**Q6. Which of the following is not seen in low insulin-Glucagon Ratio?** *(AIIMS 2019)*

(a) Gluconeogenesis
(b) Glycogen Breakdown
(c) Ketogenesis
(d) Glycogen Storage

**Ans.** (d) (Apply Smile formula 1 and 2) Low Insulin means catabolic state

| | | |
|---|---|---|
| (a) Gluconeogenesis | → | catabolic |
| (b) Glycogen Breakdown | → | catabolic |
| (c) Ketogenesis | → | catabolic |
| (d) Glycogen Storage | → | Anabolic |

**Q7. Which of the following is active in dephosphorylated State?**

(a) Glycogen Synthase
(b) Pyruvate carboxylase
(c) Glycogen Phosphorylase
(d) PEPCK

**Ans.** (a) (Apply Smile formula 3)

| | | |
|---|---|---|
| (a) Glycogen Synthase | → | Anabolic |
| (b) Pyruvate carboxylase | → | catabolic |
| (c) Glycogen Phosphorylase | → | catabolic |
| (d) PEPCK | → | catabolic |

**Q8. All occur in mitochondria except: [PGMEE 2015]**

(a) Glycolysis
(b) TCA Cycle
(c) ETC
(d) Ketogenesis

**Ans.** (a) (Apply Smile formula 4)

**Q9. The biosynthesis of the enzymes Pyruvate Carboxylase is repressed by:** *(PGMEE 2012-13)*

(a) Insulin
(b) Cortisol
(c) Glucagon
(d) Ketogenesis

**Ans.** (a) (Apply Smile formula 2)

**Q10. Which of the following is active in phosphorylated state?**

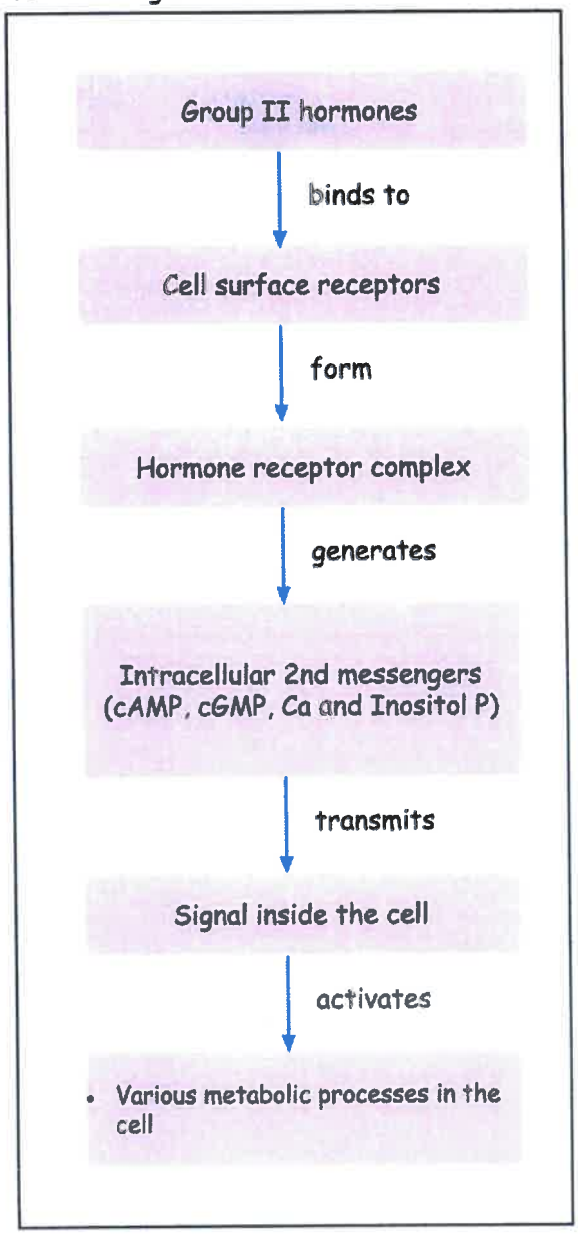
(a) Glycogen Synthase
(b) Glycogen Phosphorylase
(c) Acetyl Co A Carboxylase
(d) G6PD Enzyme

**Ans.** (b) (Apply Smile formula 3)

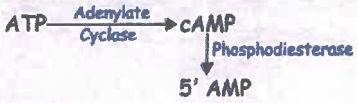
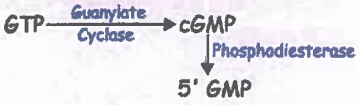
# 4 Chapter

# cAMP and cGMP

- They are 2nd messengers
- Used by group II hormones for their signal transduction



## Differences between cAMP and cGMP

| cAMP | cGMP |
|---|---|
| • More common | • Less common |
| • Less sustained response | • Long term and sustained response |
|  |  <br>• Guanylate cyclase exist in 2 forms:<br>1. Membrane bound form<br>2. Cytoplasmic form |
| • Activate protein kinase A | • Activate protein kinase G |
| • The hormones which use cAMP as second messenger are called as group IIa hormones such as:<br>– Glucagon<br>– LH<br>– FSH<br>– hCG<br>– Calcitonin<br>– Catecholamines | • The hormones which use cGMP as second messenger are called as group IIb hormones<br>• It has role in<br>– Visual cycle<br>– Vasodilatory effect by NO (nitric oxide)<br>– Activation of peptide hormones like ANP and BNP (atrial and brain natriuretic peptides) where membrane bound guanylate cyclase is used. |

# 5 Chapter

# SOURCES OF BLOOD GLUCOSE

**Q1. Sources of Blood Glucose?**

1. Food (till 2 hours of diet)
2. Liver Glycogen [provide glucose for 12-18 Hours]
3. Gluconeogenesis [Requires High Energy]

**Q2. Main/Preferred fuel for the body?**

- In fed state body will use carbohydrates preferably
- In fasting and starvation, body will first use mainly fat and then shift to using proteins.

**Important Information**

Exercise done in morning when body glycogen stores are depleted helps body to consume a lot of energy in gluconeogenesis hence is much more beneficial for reducing weight than exercise done at other times.

# 6 Chapter

# FUEL IN FED, FASTING AND STARVATION

## TABLE: SUBSTRATES UTILIZED FOR ENERGY PRODUCTION

| | Fed | Fasting | Starvation |
|---|---|---|---|
| Brain | Glucose | Glucose | KB |
| Heart | FA | FA | KB |
| Liver | Glucose | FA | Amino Acids |
| Muscle | Glucose | FA | FA and KB |
| Adipose tissue | Glucose | FA | FA |
| RBC | Glucose | Glucose | Glucose |
| Main fuel for body | Carbohydrate | Fat | Amino acids |

## In Fasting

- RBCs cannot use fatty acid or ketone bodies (KB) as fuel even during fasting as they don't have mitochondria where beta-oxidation occurs.
- Brain cannot use FA as FAs cannot cross blood brain barrier.

## In Starvation

- Vital organs Brain and heart are adapted to use KB during starvation, so that, if glucose is exhausted by utilization in other organs, death can be avoided as heart and brain can still function by using ketone bodies as an alternative fuel.
- Muscle cells avoid or delay using proteins/AA as fuel to avoid body muscle loss.

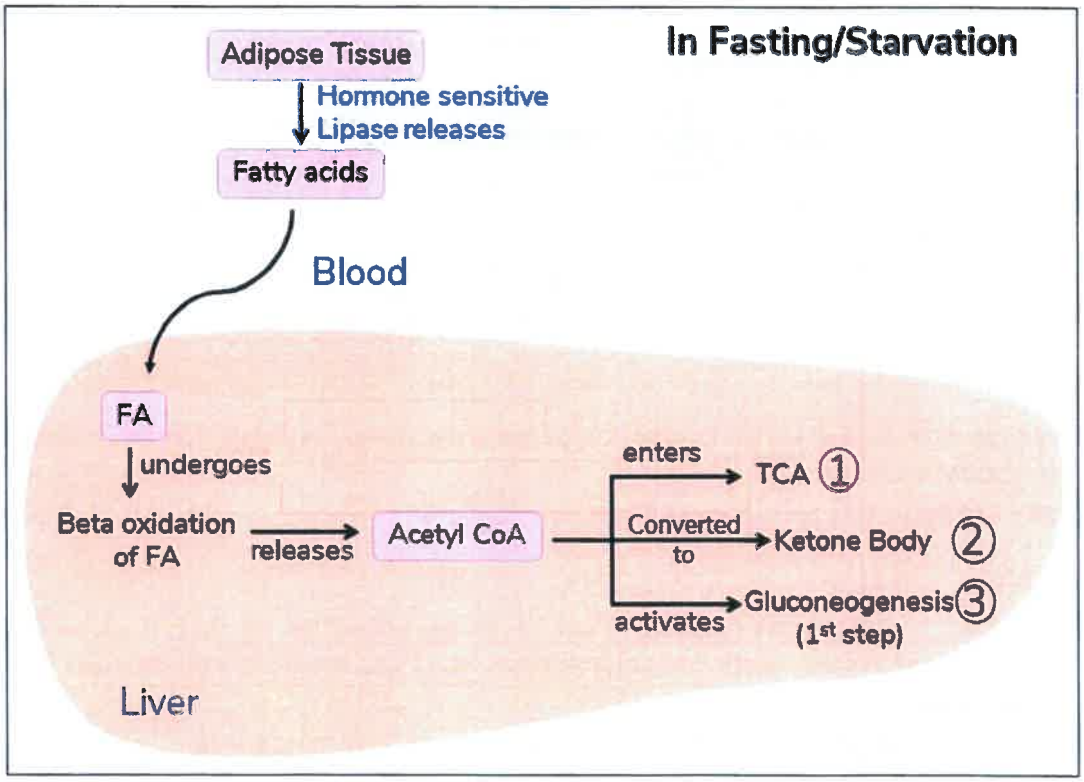
**Important Information**

- Fetal heart and also in case of heart failure, main fuel is Glucose (GLUT-4 allows glucose transport in heart muscles during these conditions)
- Heart is adapted to use FA as main fuel as it works 24 hours and require continuous supply of energy by utilizing energy dense fats as compared to glucose.

7
Chapter

# FASTING STATE

## SCENE IN FASTING STATE




## Sequence of Utilization of Acetyl CoA

1. For use in TCA in liver cells to provide energy to liver cells for ketone bodies synthesis.
2. Once liver has generated enough energy for synthesis, acetyl CoA can now enter KB synthesis.
3. Once KB synthesis is up and running well and supplying the energy to vital organs, then gluconeogenesis will proceed, and acetyl-CoA can now be used for stimulation of 1st step of gluconeogenesis.

**Note:** Any defect of beta-oxidation in liver will lead to non-ketotic hypoglycemia due to non-formation of ketone bodies and no gluconeogenesis.