Can Any One Guess
Todays Topic Of Discussion?

Biochemistry Of Starvation

What Is Starvation?

- Starvation is **complete stoppage of eating food** by a human body.

What Is Total Starvation?

- Total starvation is **complete stoppage of Food and Water**.

Conditions Developing Starvation

- **Food Scarcity**

(Natural Calamities , Draughts Floods and ,Famines)

- **Extreme Poverty**
- **Lost in Sea routes for long durations**
- **Clinical Conditions:** Major Surgeries, Severe Burns.
- **Desire to loose rapid weight**
- **Political Issues**: Hunger Strikes

Features Of Starved Body

- **No entry of exogenous food constituents**
- **Body in starvation is deprived of:**

  - **Calories** (Carbs and Lipids)
  - **Building blocks** (Proteins)
  - **Growth Factors**(Vitamins and Minerals)
  - **Protectors** (Antioxidants)

During Starvation the body is under Metabolic Stress

- **During Starvation** the body is in an **emergency condition**
- **Starved body has to get adapted**
- **And Manage with Endogeneous reserve**

Survival Period During Starvation

- **Survival period** during Starvation depends upon **the:**
- **Reserve Fat stores in Adiposecytes.**
  - **More content of TAG in Adiposecytes**
  - **More is the duration of survival in Starvation and vice a versa.**

Length Of Survival In Starvation

- **Due to deprivation of only Food:**
  - **3 to 4 Weeks**
  - **Longer up to 65 days**
- **Deprivation of water alone then survival is only for few days**
  - **Less than a week**

Effects Of Starvation

OR

Human Body Adaptation In Starvation

Biochemical Alterations In Starvation

During Starvation

- **No exogenous Food** source ingested
- Food **Nutrients get deprived**
- Body is in an **emergency condition**
- **Metabolic stress is developed**
- Body **manages and adapts to live on the endogenous fuel stores.**
- **Alterations in metabolic/biochemical processes**

- The biochemical alterations during Starvation are influenced by **hormonal actions.**
- **Glucagon and Epinephrine** in starvation act upon the target organs
- **Stimulate metabolic pathways** which **supply fuels** and
- **Improve survival phase during Starvation.**

Different Modes
To Study Biochemical Adaptations
During Starvation Phases

Study Of Biochemistry Of Starvation
With Respect To

- Stages
- Metabolism
- Organs

Occurrence Of Four Stages During Starvation OR Metabolic Alterations During Starvation

Stages	Metabolic Process
First Stage	Increased Glycogenolysis
Second Stage	Increased Gluconeogenesis
Third Stage	Increased Lipolysis/Fatty acid Beta Oxidation
Fourth Stage	Increased Ketogenesis

Alternative Adaptations In Different Metabolic Processes During Starvation

Hormonal Alterations In Starvation

- **Insulin secretion decreased**
- **Glucagon and Epinephrine increased**

Hormonal Influences In Starvation

Hormone	Source	Change in Secretion
Norepinephrine	Sympathetic Nervous System	↓↓↓
Norepinephrine	Adrenal Gland	↑
Epinephrine	Adrenal Gland	↑
Thyroid Hormone T4	Thyroid Gland (changes to T3 peripherally)	↓↓↓

- When **food is in Short supply**
- Metabolic activity decreases to spare fuel.
- **Conservation of energy** is one of the basic adaptive responses to calorie reduction

- **The Hormones influences the utilization of endogenous reserve stores and**
- **Supply fuels to body organs during starvation phase.**

- **Norepinephrine and T3 participate to**

- **Decrease in metabolic activity** when calorie intake decreases.

Biochemical Adaptations Of Carbohydrate Metabolism During Starvation Phase

Carbohydrate Metabolism In Liver During Starvation Phase

- **Glycogenolysis Increased**
- **Glycogenesis Decreased**
- **Gluconeogenesis Increased**
- **Glycolysis Decreased**
- **TCA operation Decreased**
- **HMP Shunt Decreased**
- **Blood Glucose level Decreases** (later stages)
- **Cellular Glucose Deprivation** (In Muscle Cells)

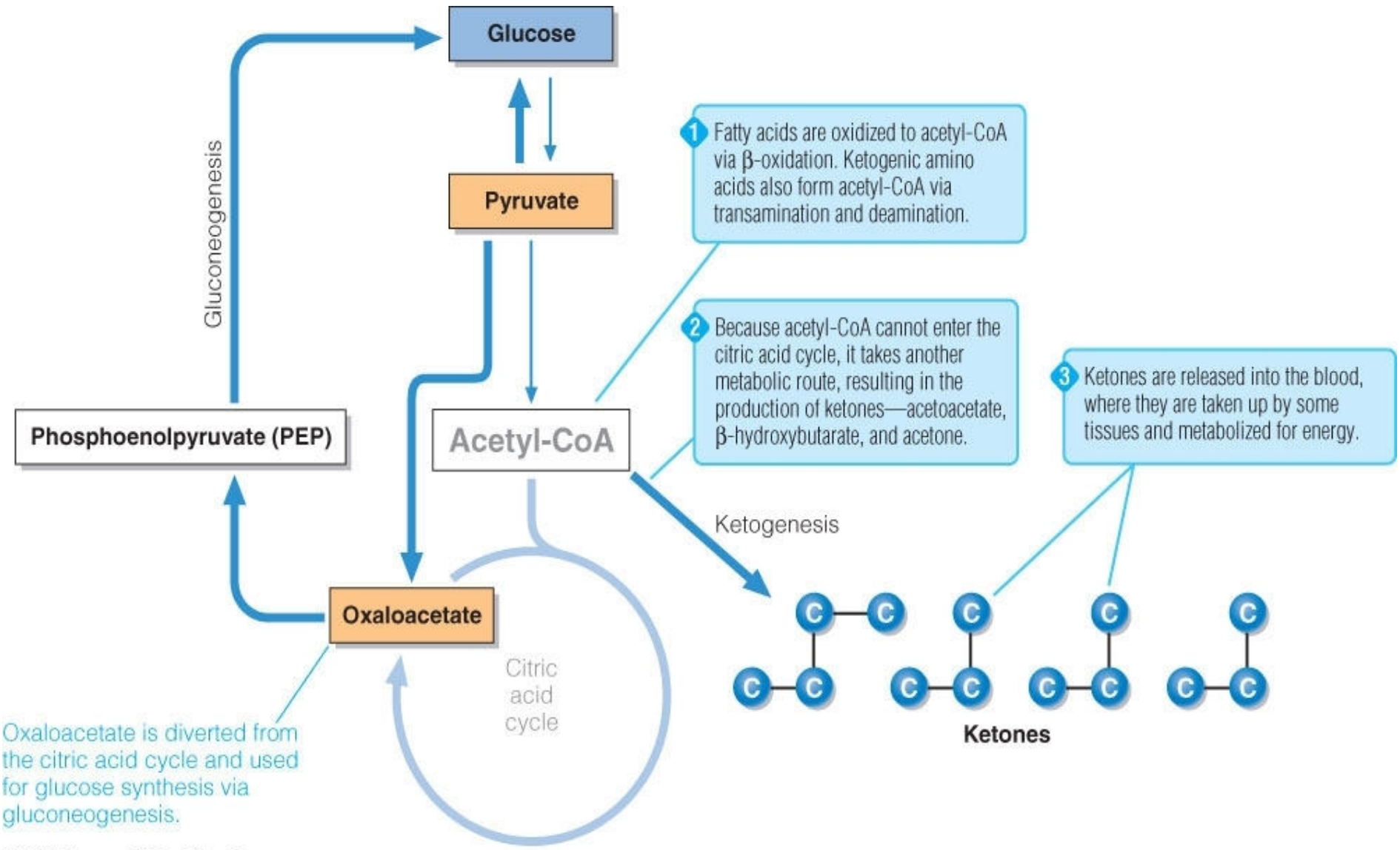
- **PDH a Multi Enzyme Complex** is **inhibited during Starvation**.

Biochemical Alterations of Lipid Metabolism In Starvation

Lipid Metabolism During Starvation

- **Lipolysis is Increased**
- **Mobilization of Free Fatty acids increased**
- **Beta oxidation of Fatty acids increased**
- **Incomplete Fatty acid Oxidation increased**
- **Ketogenesis Increased**
- **Ketolysis Decreased**
- **Ketosis Noted** (Ketoacidosis)-**Rotheras Test +ve**
- **Lipogenesis is Decreased**
- **Enzyme Acetyl Carboxylase** is **inhibited during Starvation**.

Increased Ketogenesis In Starvation



What Happens? When Ketone body production Exceeds than the Ketone body Utilization?

– When?

– Cellular Glucose deprivations occurs in

- Uncontrolled Diabetes
- Prolonged Starvation

- Ketosis
  – High levels of Ketone Bodies in blood and urine
- Ketoacidosis
  – Severe ketosis
  – Lowered blood pH,
  – Nausea ,Acetone breath
  – Coma, Death

Cure For Ketosis

- Ketosis Cured by **infusion of Glucose**.

Alterations In Protein Metabolism During Starvation

During Starvation

- **Catabolism** Of **Muscle Proteins increased**
- **Transdeamination** reaction of Amino acids is **increased**
- **To release Glucogenic amino acids**

- Ammonia Detoxification and **Urea production increased initially** and **decreased as Starvation phase prolongs**.
- Body is in **negative Nitrogen Balance.**
- Concentration of **Functional Proteins Decreases**.

Glucose Nitrogen Ratio Increased In Starvation

⑦ GLUCOSE - NITROGEN RATIO (GN - Ratio)
OR
DEXTROSE - NITROGEN RATIO (DN - ratio)

GN ratio "is" - Ratio of Glucose (Dextrose) to Urea Nitrogen in Urine From Proteins.

$$\text{GN ratio} = \frac{\text{Glucose in gm}}{\text{Urea Nitrogen in Urine in gm}} = \frac{3.65 \text{ gm of Glucose}}{1 \text{ gm of Urea Nitrogen From Proteins}}$$

GN ratio = 3.65

Since Proteins contains 16 % Nitrogen
What is the amount of Glucose produced by 100 gm of Proteins?

$$3.65 = \frac{G}{16}$$

GN ratio indicates the rate of Muscle protein breakdown & Gluconeogenesis during Starvation Phase.

∴ G = 58.4 % of Protein is Glucogenic.

GN RATIO ↑ed in STARVATION
Diabetes Mellitus
CANCER
HYPERTHYROIDISM.

During Starvation Alterations Occur In Water and Electrolyte And Acid Base Balance

- **Reduction in Body Water**
- **Reduction of Potassium ions**
- **Acidic blood pH** due to increased Ketone bodies

- **On prolonged phase of Starvation there results**

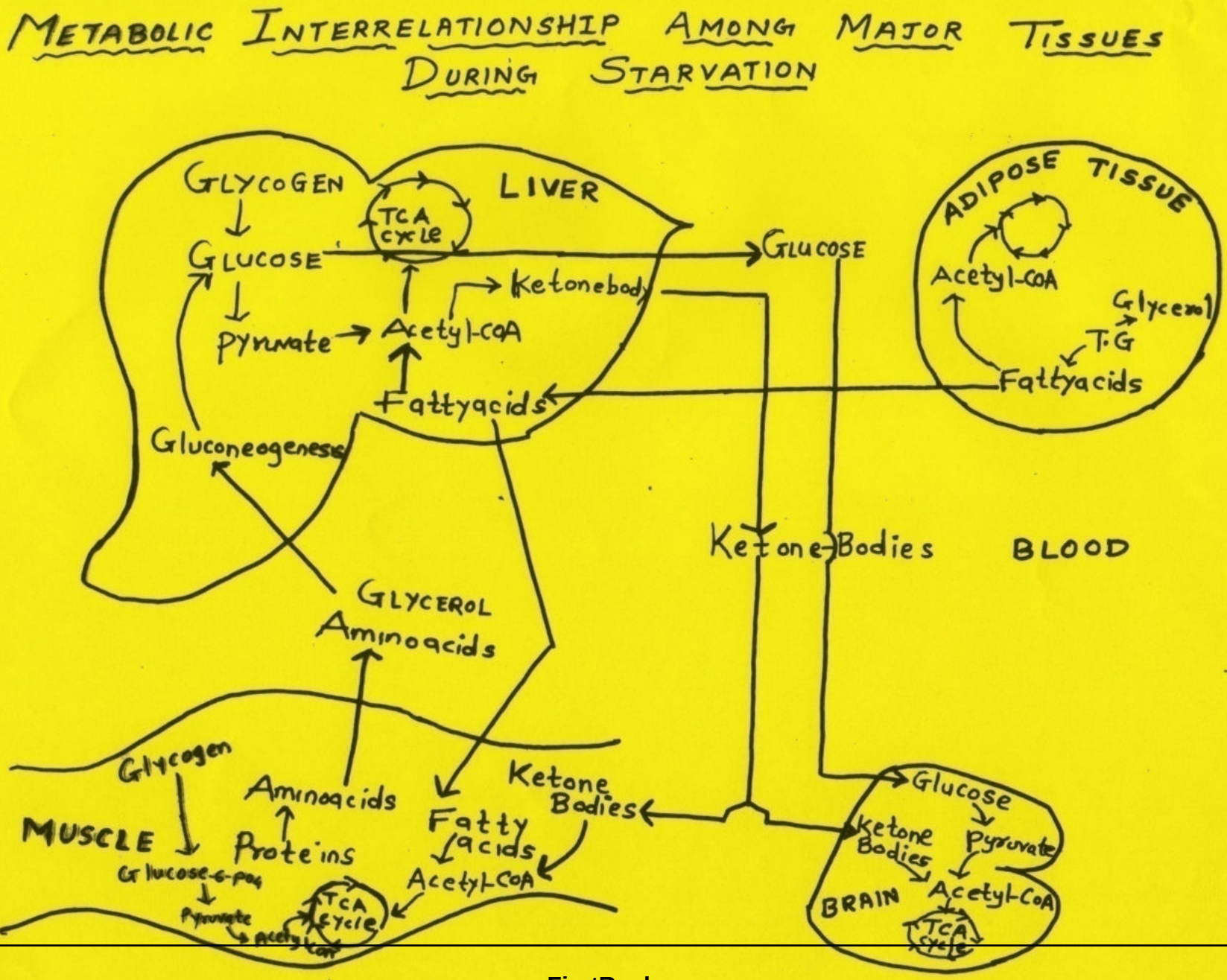
- **Severe dehydration and Acid Base imbalance**

Alterations In BMR

- **BMR is first affected in starvation.**

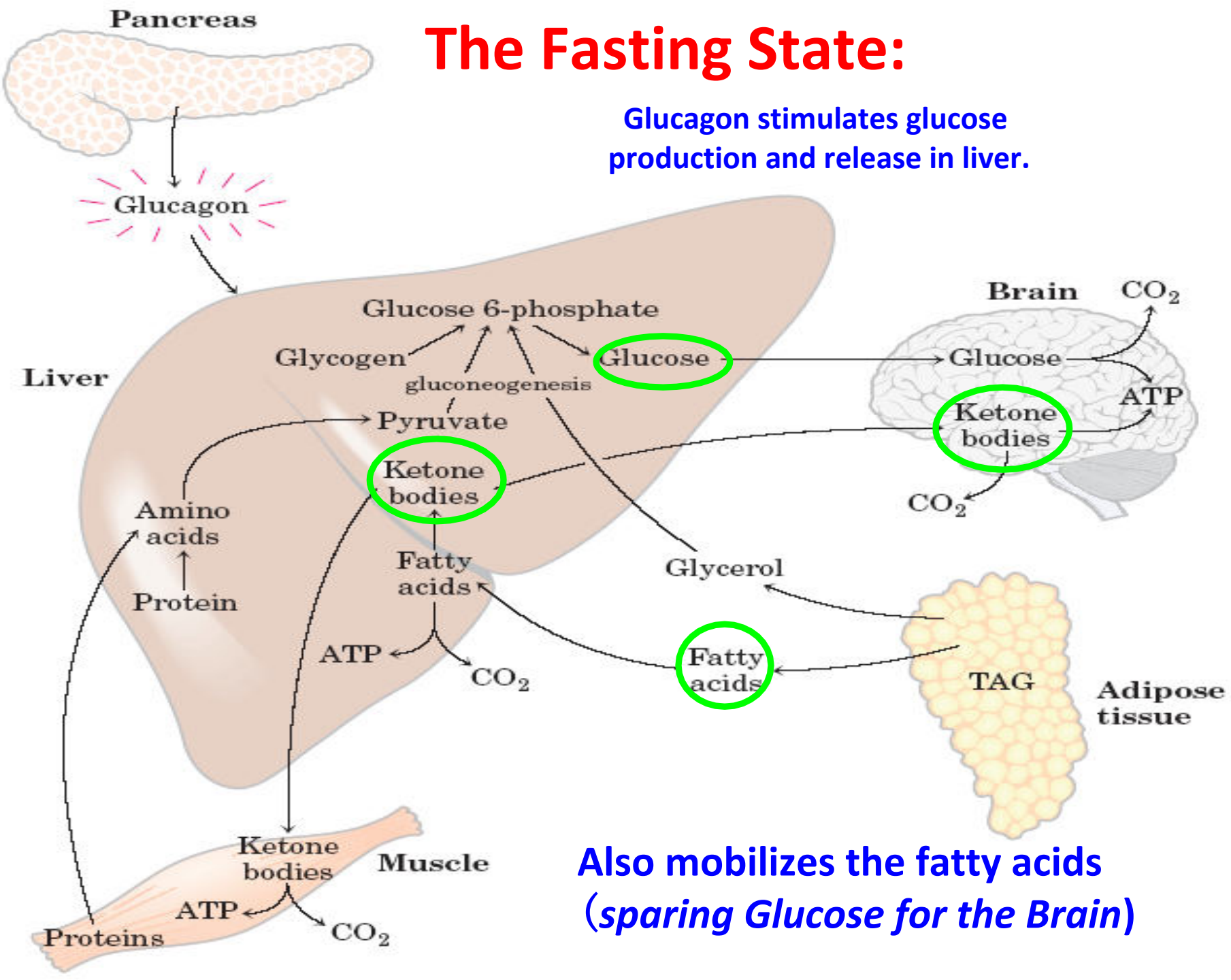
- In starvation **BMR is Decreased.**

Biochemical Adaptations By Organs During Starvation



The Fasting State:

Glucagon stimulates glucose production and release in liver.



Also mobilizes the fatty acids (*sparing Glucose for the Brain*)

Differentiation In Well Fed And Fasting States Of Human Body

	WELL-FED STATE	FASTING STATE
Hormones	↑ Insulin	↑ Glucagon, Adrenaline, Cortisol
Response of the body	Hyperglycemia ↑ Glycogenesis ↑ Lipogenesis ↑ Protein synthesis	Hypoglycemia ↑ Lipolysis ↑ Ketogenesis ↑ Proteolysis

	WELL-FED STATE	FASTING STATE
Source of Glucose	from food	from stores (Glycogen) Gluconeogenesis
Fate of Glucose	Glycolysis formation of Glycogen and TAG stores	Glycolysis

	WELL-FED STATE	FASTING STATE
Source of Fatty acids	from food TAG	from storage TAG
Fate of Fatty acids	β-oxidation synthesis of TAG and Store as Depot Fat	↑ β-oxidation (Incomplete one) Ketogenesis

	WELL-FED STATE	FASTING STATE
Source of Amino acids	from food	From muscle Proteins
Fate of Amino acids	Protein synthesis	Glucogenic amino acids Produce Glucose via Gluconeogenesis

Preferred fuels By Human body In the Well-Fed and Fasting States

Organs	Well-Fed	Fasting
Liver	Glucose & Fatty acids	Fatty acids
Resting skeletal Muscle	Glucose & Fatty acids	Fatty acids & KB
Cardiac muscle	Fatty acids	FA,AA & KB
Adipose tissue	Glucose	Fatty acids
Brain	Glucose	Glucose ,Later KB
RBCs	Glucose	Glucose

BIOCHEMICAL PROFILE OF EARLY FASTING STATE

- Blood Glucose levels decreases
  - 65 mg/dl
- Active Glycogenolysis
  - Muscle and Liver
- Shift of metabolic fuel from Glucose to fatty acids
  - Fatty acid mobilization from adipose tissues
- Gluconeogenesis
  - Glucose Alanine cycle

BIOCHEMICAL PROFILE OF STARVED STATE

- GLUCOSE levels more decreased
  - 40 mg/dL
- PROTEIN CATABOLISM increased
  - Sequesters Nitrogen as urea
  - Excretes 20 to 30 grams daily
- Gluconeogenesis taking place using precursors as
  - Amino acids
  - Lactate
  - Glycerol
- KETONE BODIES increased
  - Acetyl CoA converted to ketone bodies via Ketogenesis

In Prolonged Starvation

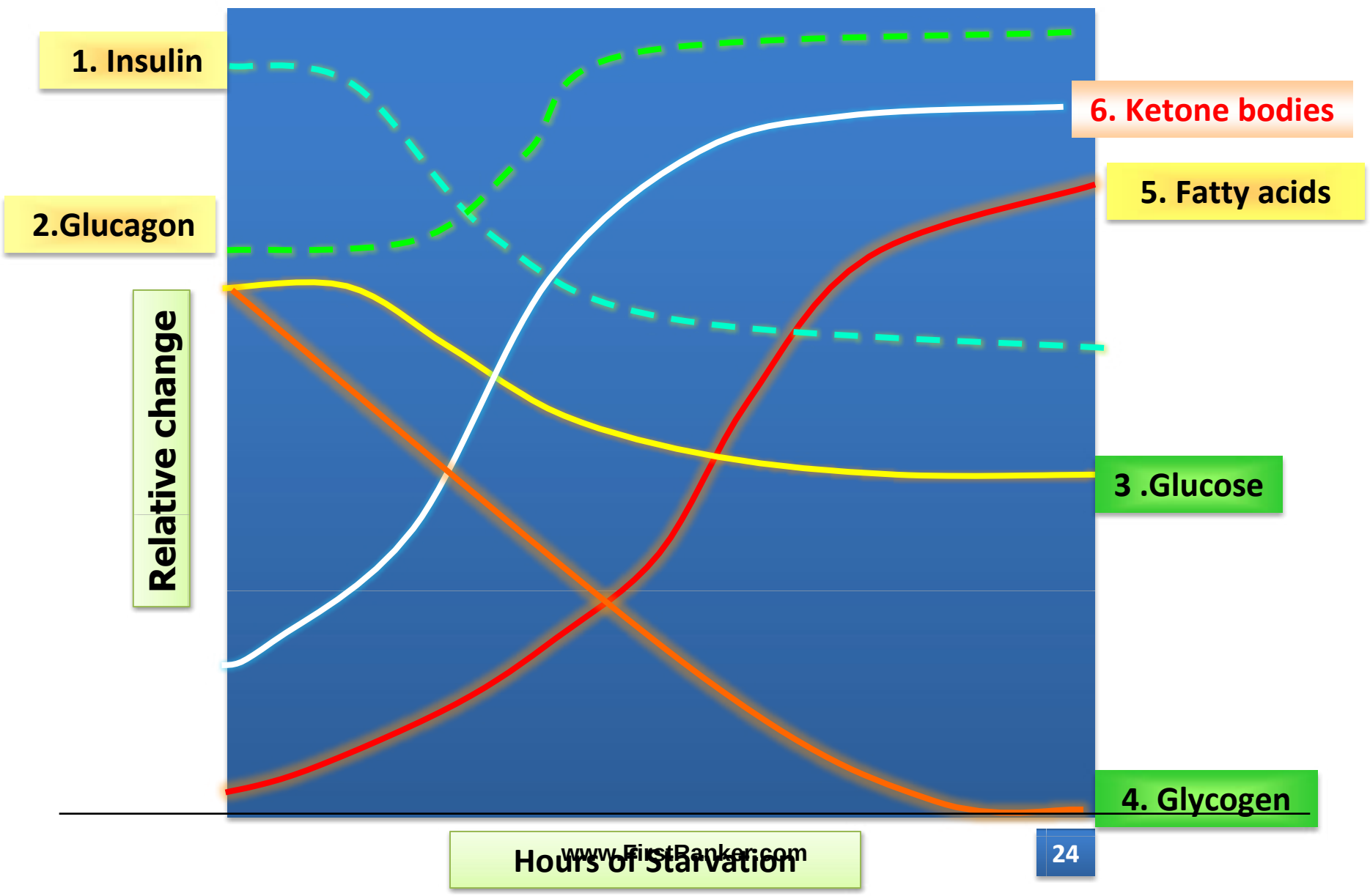
- **After 3 days of Starvation ->** Liver forms large amounts of Ketone bodies

  (Due to shortage of Oxaloacetate)
- Ketone Bodies -> released into blood
- **Brain and Heart start to use ketone bodies as fuel during phase of Starvation.**

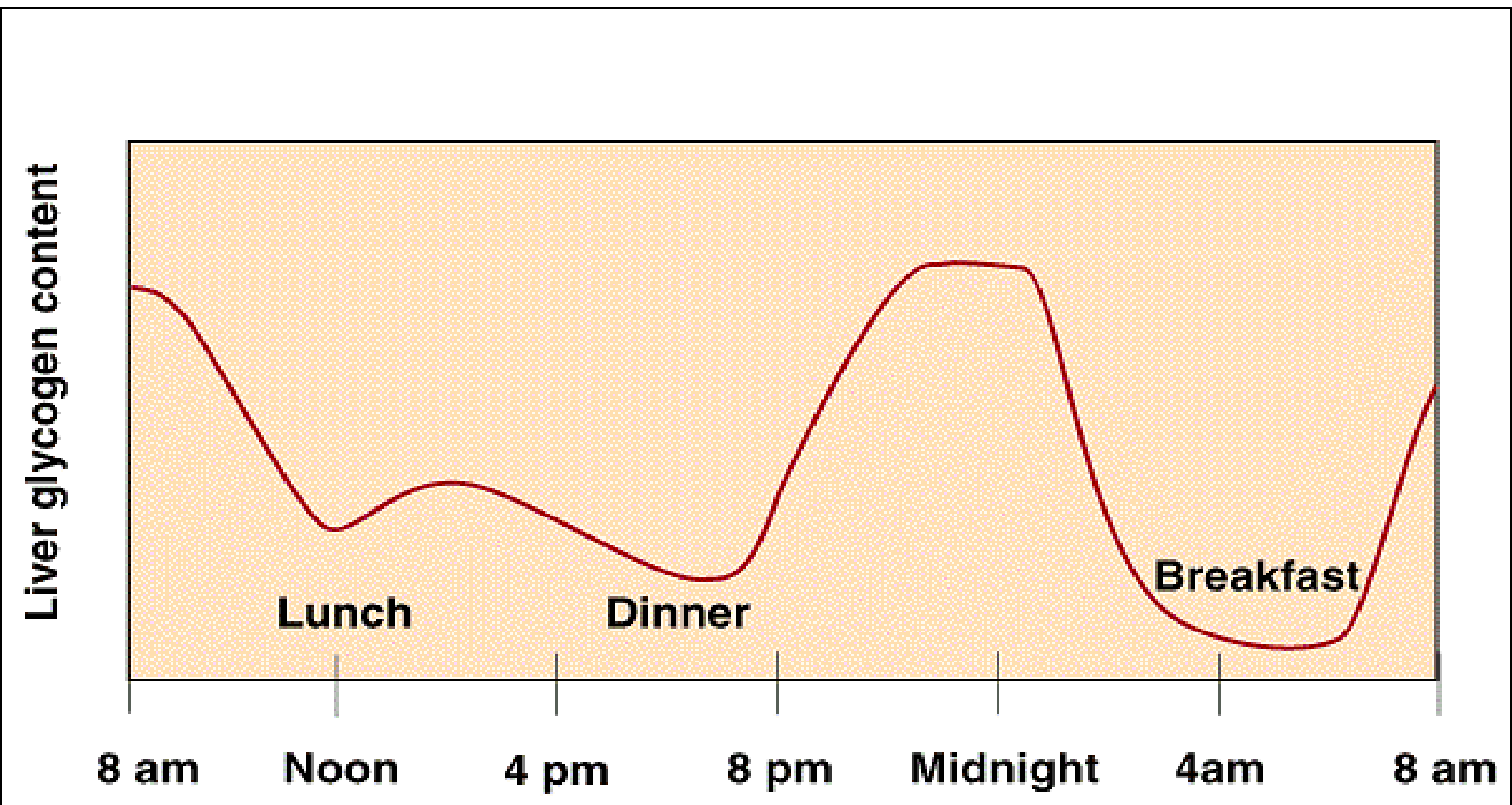
Starvation Of Several Weeks

- After several weeks of starvation -> Ketone bodies become major fuel of Brain
- After depletion of TAG stores
- Proteins degradation accelerates
- Death due to loss of Heart, Liver, and Kidney function.

FUEL CHOICE DURING STARVATION

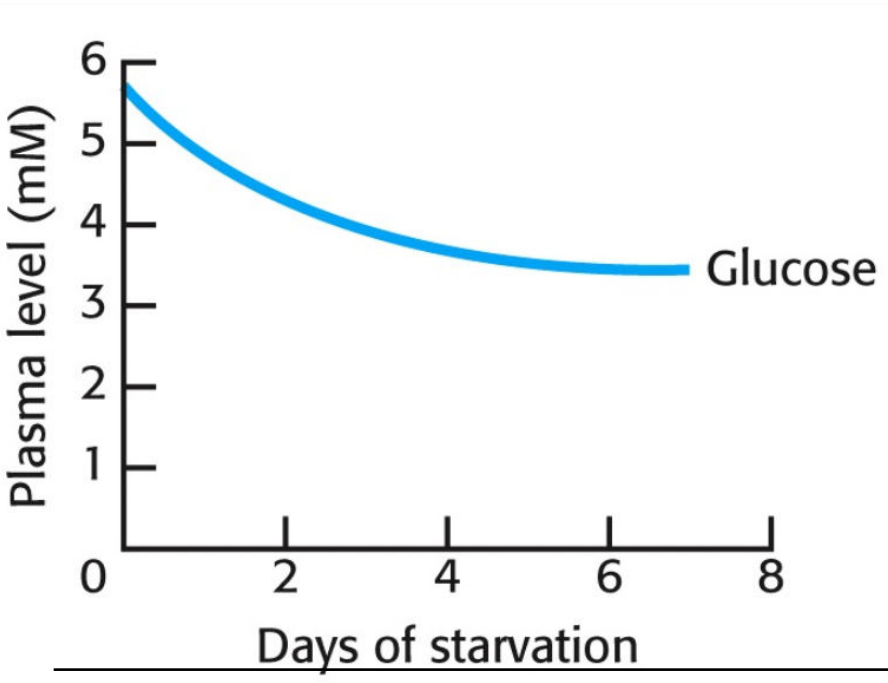


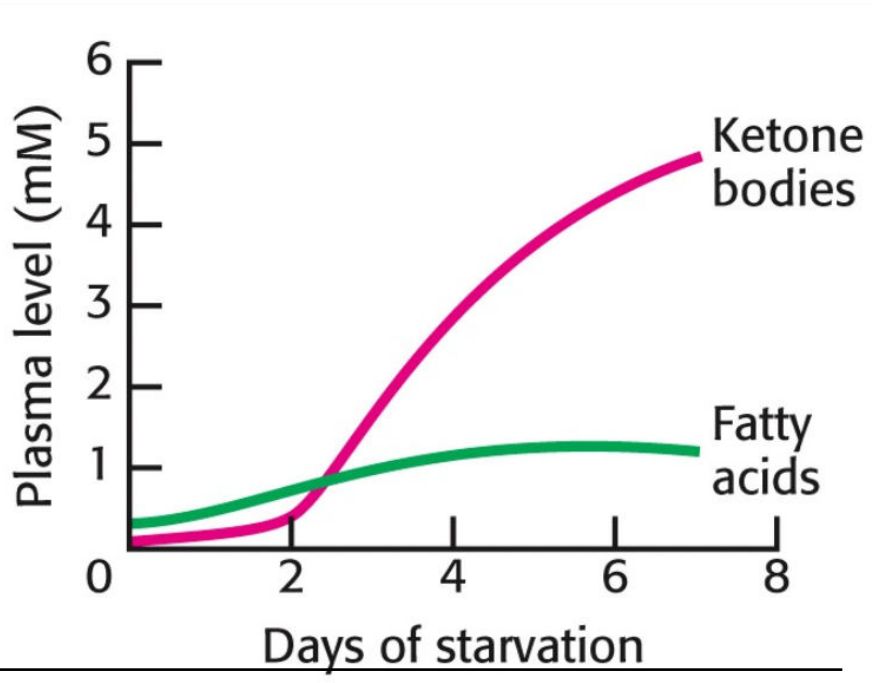
Changes Of Liver Glycogen Content



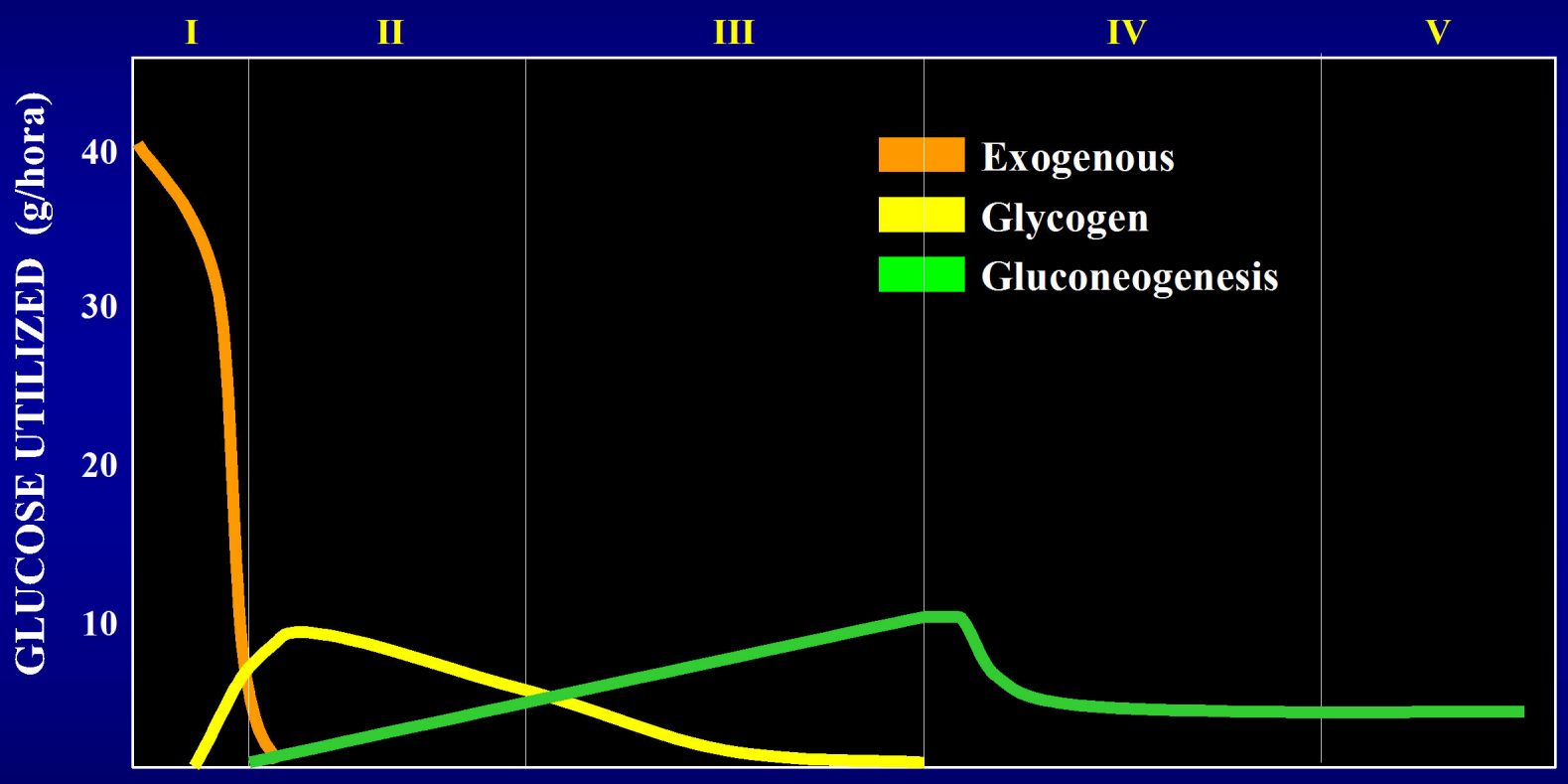
During Starvation

- Fuel changes from Glucose to Fatty acids to Ketone bodies





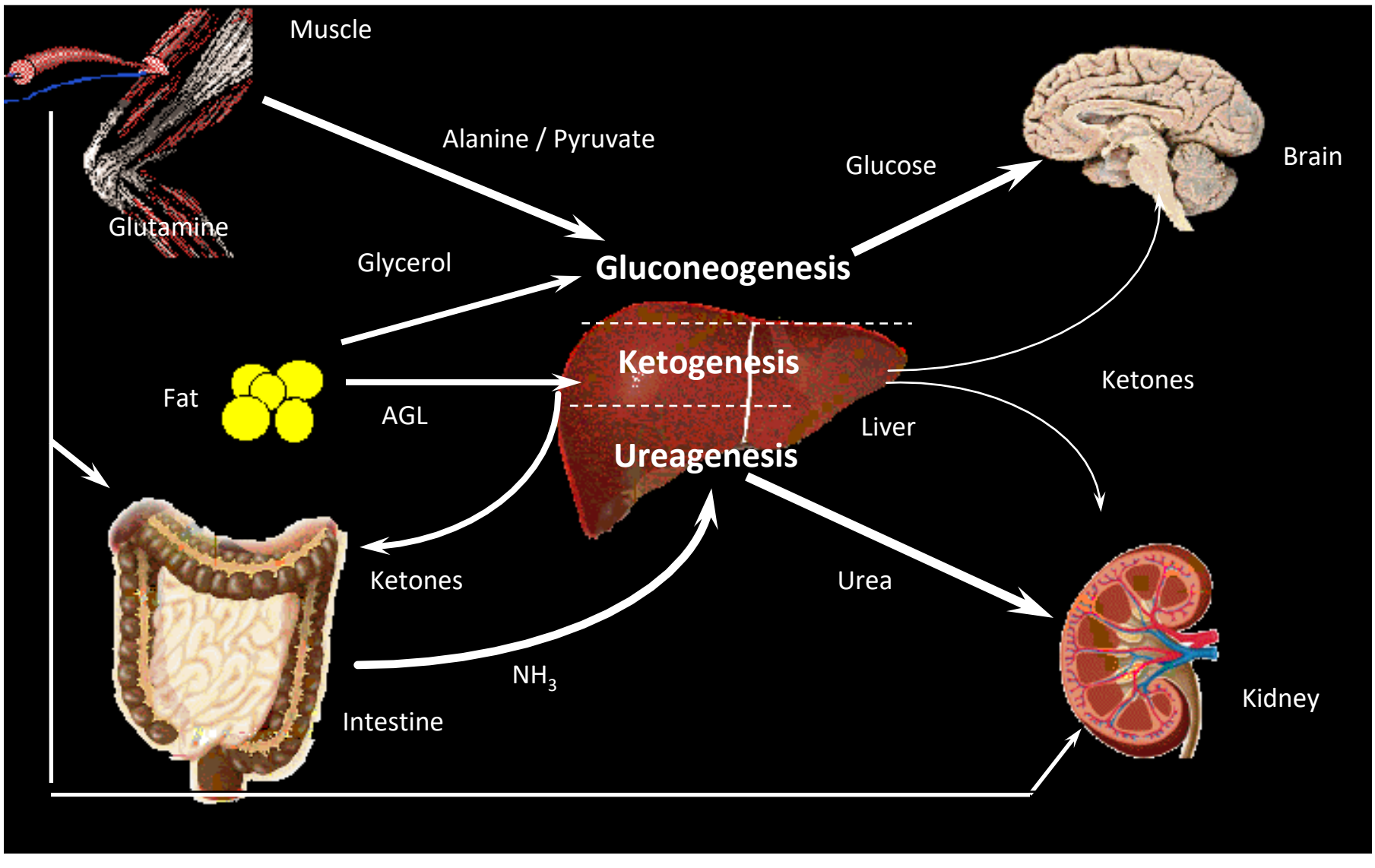
Metabolic Response To Fasting



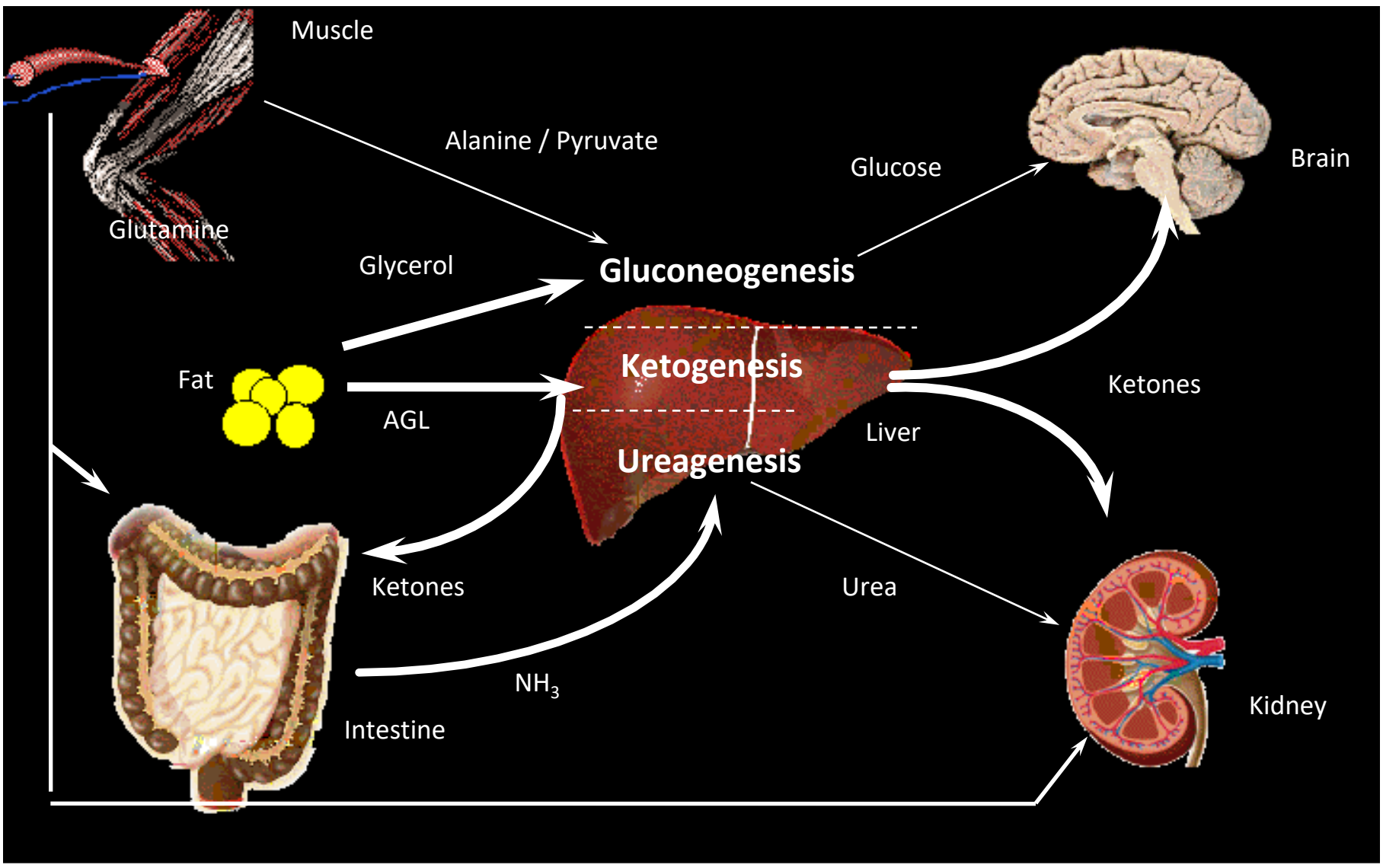
LEGEND	I	II	III	IV	V
FUEL FOR BRAIN	GLUCOSE	GLUCOSE	GLUCOSE	GLUCOSE, KETONES	GLUCOSE, KETONES

Ruderman NB. *Annu Rev Med* 1975;26:248

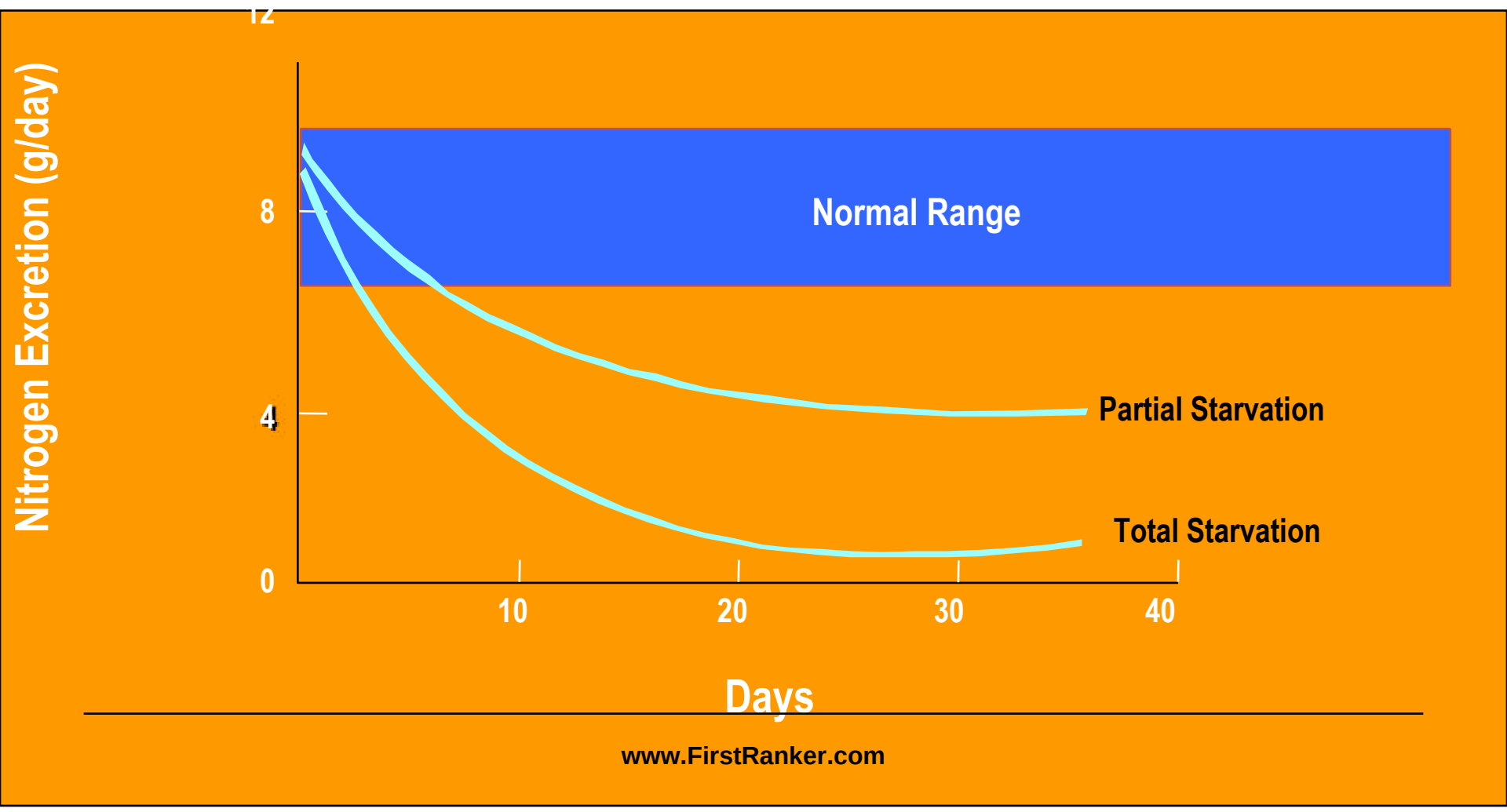
Fasting – Early Stage



Fasting – Late Stage



Energy Expenditure in Starvation



Consequences Of Starvation

- Severe Malnutrition
- Damages and affects vitality of Important Internal Organs
- Decreased BMR
- Night blindness (Vitamin A deficiency)
- Scurvy (Vitamin C deficiency)
- Irregular Menses
- Constipation
- Low Immunity
- Bone Loss
- Anaemia (Iron and Protein deficiency)
- Fatigue
- Dehydration
- Water Electrolyte Imbalance
- High Blood Pressure
- ~~Brain Defects~~
- Death

CONSEQUENCES OF STARVATION : (8)

STARVATION

↓

STOPPAGE OF FODD
NO SUPPLY OF EXOGENOUS SOURCES OF FUEL; BUILDING BLOCKS : GROWTH FACTOR

↓

- ★ METABOLIC STRESS DEVELOPED.
- ★ ENDOGENEOUS RESERVE STORES OF FUEL UTILIZED AND DEPLETED.
- ★ INITIALLY BODY CRAVES FOR FOOD LATER CRAVING FOR FOOD SUBSIDES AND DESIRE FOR FOOD VANISHES.
- ★ PHYSICAL & MENTAL WEAKNESS GRADUALLY ↑s
- ★ IF BODY IS IN GROWING PHASE – GROWTH AFFECTED
- ★ SLEEP INCREASES; PERSON BECOME SEMICONSCIOUS
- ★ MUSCLE WASTING; BODY WT STEADILY LOST.
- ★ RESPIRATION & HEART FUNCTION SLOWS DOWN
- ★ EXCRETION RATE ↓es – AMOUNT OF URINE & UREA CONTENT FALLS
- ★ ANAEMIA; OEDEMA; ACIDOSIS; DEHYDRATION
- ★ IMMUNITY SUPPRESSED; VITAL ORGANS AFFECTED
- ★ COMA & DEATH → LIFE ENDS

Questions

- Explain the different stages of starvation & biochemical alterations in the body during these stages.

OR

- **Biochemical alterations/adaptations during starvation**.

- Describe the role of following organs during various stages of starvation
- Liver
- Brain
- Muscles
- Adipose tissues

THANK YOU