MEDICAL EDUCATION RESOURCE

Citric Acid Cycle

? CITRIC ACID CYCLE (TCA CYCLE)

The final common oxidative pathway of carbohydrates, fats, and proteins.

Occurs in the **mitochondrial matrix**.

? OVERVIEW OF THE CYCLE

Acetyl-CoA (2C) + Oxaloacetate (4C) ? Citrate (6C) ? series of oxidative decarboxylations ? regeneration of oxaloacetate.

Produces **NADH, FADH?, GTP, CO?** ? used for ATP generation in ETC.

? REACTIONS OF THE TCA CYCLE (STEPWISE)

1. Acetyl-CoA + Oxaloacetate ? Citrate

- **Enzyme:** Citrate synthase
- Key regulated step
- Highly exergonic

2. Citrate ? Isocitrate

- **Enzyme:** Aconitase
- Requires **iron ($Fe^{2?}$)**

- Reversible isomerization

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3. Isocitrate ? ?-Ketoglutarate

- **Enzyme:** Isocitrate dehydrogenase
- **NADH formed**
- **CO? released**
- First rate-limiting oxidative step

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4. ?-Ketoglutarate ? Succinyl-CoA

- **Enzyme:** ?-Ketoglutarate dehydrogenase complex
- Requires **TPP, lipoic acid, FAD, NAD?, CoA**
- **NADH formed**
- **CO? released**

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5. Succinyl-CoA ? Succinate

- **Enzyme:** Succinyl-CoA synthetase
- **GTP formed**
- Substrate-level phosphorylation

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6. Succinate ? Fumarate

- **Enzyme:** Succinate dehydrogenase
- **FADH? formed**
- Only TCA enzyme located in **inner mitochondrial membrane**

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7. Fumarate ? Malate

- **Enzyme:** Fumarase
- Hydration reaction

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8. Malate ? Oxaloacetate

- **Enzyme:** Malate dehydrogenase
- **NADH formed**
- Regenerates oxaloacetate ? cycle continues

? ENERGETICS OF TCA CYCLE

From **1 molecule of acetyl-CoA**:

- **3 NADH ? 3 × 3 ATP = 9 ATP**
- **1 FADH? ? 2 ATP**
- **1 GTP ? 1 ATP**
- **Total = 12 ATP per acetyl-CoA**

(Modern value using P/O ratios ? approx. **10 ATP**)

? SIGNIFICANCE OF TCA CYCLE

- Final common pathway for oxidation of **carbohydrates, fats, and proteins**
- Produces reducing equivalents **NADH, FADH?** for ATP production
- Generates intermediates for **biosynthesis**
- Provides **GTP** (substrate-level phosphorylation)
- Essential for neuronal and cardiac energy metabolism

? AMPHIBOLIC ROLE (Dual Anabolic + Catabolic)

TCA cycle serves **both**:

Catabolic functions

- Oxidation of acetyl-CoA ? CO?
- Formation of NADH/FADH? for oxidative phosphorylation

Anabolic functions

Intermediates act as precursors for synthesis of:

- **Citrate ? fatty acids / cholesterol**
- **?-KG ? glutamate ? amino acids**

- **Succinyl-CoA ? heme**
- **Malate ? gluconeogenesis**
- **Oxaloacetate ? aspartate ? amino acids**

? ANAPLEROTIC REACTIONS (Refilling TCA intermediates)

- **Pyruvate ? Oxaloacetate**
  - Enzyme: Pyruvate carboxylase
  - Requires **biotin**
- **Pyruvate ? Malate**
- **Amino acids ? ?-KG, Succinyl-CoA, Fumarate, Oxaloacetate**

These reactions maintain cycle flow during high demand.

? REGULATION OF TCA CYCLE

Regulated at **three irreversible steps**:

1. Citrate Synthase

- Inhibited by: **ATP, NADH, citrate, succinyl-CoA**

2. Isocitrate Dehydrogenase

- Activated by: **ADP, $Ca^{2?}$**

- Inhibited by: **ATP, NADH**

3. ?-Ketoglutarate Dehydrogenase

- Activated by: **Ca²?**
- Inhibited by: **Succinyl-CoA, NADH**

Overall inhibitors:

- **High ATP**
- **High NADH**
- **High succinyl-CoA**

Overall activators:

- **ADP**
- **Ca²? (muscle contraction)**
- **High NAD?**

? INTEGRATION OF METABOLISM WITH TCA CYCLE

Carbohydrates

- Glucose ? pyruvate ? acetyl-CoA ? enters TCA.

Lipids

- ?-oxidation ? acetyl-CoA ? enters TCA.
- Odd-chain fatty acids ? succinyl-CoA.

Proteins

- Glucogenic amino acids ? TCA intermediates (oxaloacetate, ?-KG, fumarate).
- Ketogenic amino acids ? acetyl-CoA/acetoacetate.

Gluconeogenesis & TCA

- Malate shuttles oxaloacetate out of mitochondria.
- Oxaloacetate is key link between TCA and glucose formation.

Urea Cycle Link

- Fumarate ? aspartate shuttle connects TCA and urea cycle.

Fatty Acid Synthesis Link

- Citrate transported out ? acetyl-CoA for lipogenesis.

? HIGH-YIELD CLINICAL CORRELATIONS

- **Thiamine deficiency** ? inhibits ?-KG dehydrogenase ? neurological symptoms (Wernicke's).
- **Arsenite** inhibits lipoic acid ? blocks ?-KG dehydrogenase.
- **Fluoroacetate poisoning** inhibits aconitase ? TCA block.

- **Inherited fumarase deficiency** ? severe encephalopathy.

? IMPORTANT POINTS TO REMEMBER — CITRIC ACID CYCLE

? Basics & Location

- TCA cycle occurs in the **mitochondrial matrix**.
- Common oxidative pathway for **carbohydrates, fats, and proteins**.
- Each turn of the cycle oxidizes **acetyl-CoA ? CO? + NADH + FADH? + GTP**.

? Key Steps & Enzymes

- First step: **Citrate synthase** condenses oxaloacetate + acetyl-CoA.
- Only membrane-bound enzyme: **Succinate dehydrogenase** (Complex II of ETC).
- Two oxidative decarboxylations release **CO?**:
    - **Isocitrate dehydrogenase**
    - **?-Ketoglutarate dehydrogenase**

? Cofactor Requirements

- **?-Ketoglutarate dehydrogenase** uses:
  TPP, FAD, NAD?, CoA, and lipoic acid (same as PDH complex).

- **Aconitase** requires **Fe²?**.
- **Succinate dehydrogenase** uses **FAD**.

? Energy Yield

From **1 acetyl-CoA**, TCA produces:

- **3 NADH** ? 9 ATP
- **1 FADH?** ? 2 ATP
- **1 GTP** ? 1 ATP
- **Total ? 12 ATP** (classic) or **10 ATP** (modern P/O ratio).

? Rate-Limiting & Regulatory Points

Major regulatory enzymes:

- **Isocitrate dehydrogenase** ? activated by **ADP, Ca²?**; inhibited by **ATP, NADH**.
- **Citrate synthase** ? inhibited by **ATP, NADH, citrate, succinyl-CoA**.
- **?-Ketoglutarate dehydrogenase** ? activated by **Ca²?**; inhibited by **NADH, succinyl-CoA**.

Overall inhibitors:
High **ATP**, high **NADH**.

Overall activators:
High **ADP**, high **NAD?**, high **Ca²?** (muscle contraction).

? Amphibolic Nature (Dual Role)

TCA cycle is both **catabolic** and **anabolic**.

Catabolic roles

- Oxidizes acetyl-CoA to **CO?**.
- Produces NADH/FADH? for ATP formation.

Anabolic roles

Cycle intermediates form precursors for:

- **Citrate ? fatty acids / cholesterol**
- **?-Ketoglutarate ? glutamate ? amino acids**
- **Succinyl-CoA ? heme**
- **Oxaloacetate ? aspartate ? pyrimidines**
- **Malate ? gluconeogenesis**

? Anaplerotic Reactions (Refilling TCA Pool)

- **Pyruvate ? oxaloacetate** (pyruvate carboxylase ? biotin dependent).
- **Pyruvate ? malate**.
- Amino acids ? TCA intermediates (e.g., valine/isoleucine ? succinyl-CoA).

These reactions keep the cycle running when intermediates are diverted for biosynthesis.

? Integration with Other Pathways

- **Glucose** enters TCA via pyruvate ? acetyl-CoA.
- **Fatty acids** enter as acetyl-CoA.
- **Amino acids** convert to ?-KG, succinyl-CoA, fumarate, or OAA.
- **Gluconeogenesis** uses malate ? oxaloacetate.
- **Urea cycle** connects via fumarate/aspartate shuttle.
- **Fatty acid synthesis** uses citrate transported out of mitochondria.

? TCA Cycle Inhibitors

- **Fluoroacetate** ? inhibits aconitase.
- **Arsenite** ? inhibits lipoic acid in ?-KG dehydrogenase.
- **Malonate** ? competitive inhibitor of succinate dehydrogenase.

? Clinical Significance

- **Thiamine deficiency** impairs PDH and ?-KG dehydrogenase ? neurological injury.
- **Fumarase deficiency** ? severe developmental delay.

- **Pyruvate accumulation** occurs when entry to TCA is blocked ? lactate formation (lactic acidosis).

? Ultra-Short Exam Capsule

- Occurs in mitochondrial matrix.
- Rate-limiting: **isocitrate dehydrogenase**.
- Produces NADH, FADH?, GTP.
- Amphibolic & anaplerotic roles are exam favorites.
- $Ca^{2?}$ activates, ATP/NADH inhibit.
- Succinate dehydrogenase is only membrane-bound enzyme.

? CLINICAL CASE–BASED QUESTIONS — TCA CYCLE

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1. Severe Thiamine Deficiency with Neurological Symptoms

A chronic alcoholic presents with confusion, ataxia, and ophthalmoplegia.
Labs show elevated **pyruvate and ?-ketoglutarate** in blood.

Diagnosis:

Wernicke’s encephalopathy due to **thiamine deficiency**

Biochemical Basis:

Thiamine is required for **?-ketoglutarate dehydrogenase** and **pyruvate dehydrogenase** ? TCA cycle slows ? accumulation of ?-KG and pyruvate.

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2. Infant with Lactic Acidosis After Minor Infection

A 6-month-old develops severe lactic acidosis after mild viral illness.
Serum pyruvate is high; TCA intermediates are low.

Diagnosis:

Pyruvate dehydrogenase deficiency

Biochemical Link:

Pyruvate cannot convert to acetyl-CoA ? enters lactate ? TCA cycle starved of acetyl-CoA.

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3. Poisoning After Exposure to Rat Killer

A farmer develops vomiting, arrhythmias, and metabolic crisis.
Lab: Profound inhibition of TCA cycle; aconitase activity nearly zero.

Diagnosis:

Fluoroacetate poisoning

Mechanism:

Fluoroacetate ? fluorocitrate ? **inhibits aconitase** ? blocks citrate ? isocitrate step.

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4. Muscle Contraction Increases ATP Turnover

During strenuous exercise, a patient's muscle biopsy shows activated **isocitrate dehydrogenase** and **?-KG dehydrogenase**.

Diagnosis:

This is **normal physiological activation**.

Key Mechanism:

Ca^{2}? released during contraction stimulates both enzymes, increasing TCA cycle flux.

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5. Elderly Patient with Unexplained Hypoglycemia + High Citrate Levels

A 70-year-old woman develops fasting hypoglycemia.
Biochemistry: Elevated **citrate** in mitochondria.

Diagnosis:

TCA cycle slowing due to high ATP/NADH

Reason:

High-energy state inhibits citrate synthase, IDH, and ?-KGDH ? citrate builds up ? exported to cytosol ? inhibits glycolysis (via PFK-1).

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6. Infant Born with Severe Neurodevelopmental Delay + High Fumarate

A newborn shows severe encephalopathy, seizures, and failure to thrive.
Urine shows increased **fumarate**.

Diagnosis:

Fumarase deficiency (rare, severe)

Mechanism:

Block at fumarate ? malate step ? TCA cycle collapse ? low ATP ? neurological deterioration.

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7. Patient with Arsenic Exposure After Well Water Consumption

A farmer presents with garlic odor breath, neuropathy, and vomiting.
Blood tests reveal impaired **?-KG dehydrogenase** complex.

Diagnosis:

Arsenite poisoning

Biochemical Mechanism:

Arsenite binds **lipoic acid**, inhibiting PDH and ?-KGDH ? halts TCA cycle.

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8. Patient with Chronic Hypoxia After COPD Exacerbation

A COPD patient has chronic low O? levels.
Mitochondrial NADH is very **high**.

Diagnosis:

Impaired oxidative phosphorylation

Explanation:

Low oxygen ? ETC slows ? NADH accumulates ? inhibits TCA cycle (IDH, ?-KGDH inhibited).

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9. Bodybuilder Using High-Protein Diet

In a high-protein diet, blood **alanine and glutamate** are high.
TCA cycle intermediates are elevated.

Diagnosis:

Increased anaplerosis due to amino acids converting to ?-KG, OAA, and fumarate.

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10. Young Woman with Failed Weight Loss Despite Fasting

During prolonged fasting, her TCA cycle intermediate **oxaloacetate** is very low.

Diagnosis:

OAA diverted to **gluconeogenesis**, reducing TCA activity.

Effect:

Acetyl-CoA accumulates ? **ketogenesis increases**.

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11. Patient with Exercise-Induced Muscle Fatigue

A 25-year-old athlete develops early fatigue.
Analysis shows reduced **succinate dehydrogenase** activity.

Diagnosis:

Mitochondrial Complex II defect

Effect:

TCA cycle and ETC both impaired ? decreased ATP production.

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12. Young Man with High Blood Ammonia + Elevated ?-Ketoglutarate

A liver failure patient shows high **ammonia** and elevated **?-KG** depletion in the brain.

Diagnosis:

Ammonia toxicity affecting TCA cycle

Mechanism:

Ammonia + ?-KG ? glutamate
? deprives TCA of ?-KG ? ATP depletion ? cerebral edema.

13. Diabetic Patient with Ketonuria + Low TCA Activity

A type-1 diabetic shows high ketones.
TCA cycle intermediates (OAA, fumarate) are decreased.

Diagnosis:

TCA cycle suppression due to OAA depletion

Reason:

OAA used for gluconeogenesis ? acetyl-CoA enters **ketogenesis** instead of TCA.

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14. Patient with Lipoic Acid Deficiency After Long-Term Antibiotics

A malnourished patient treated long-term with broad-spectrum antibiotics shows reduced PDH and ?-KGDH activity.

Diagnosis:

Microbiome-related lipoic acid deficiency

Mechanism:

Lipoic acid needed for both PDH and ?-KGDH ? TCA cycle slows.

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15. Neonate with Pyruvate Accumulation + Elevated Lactate

Newborn has high blood lactate and normal oxygen levels.
TCA intermediates are markedly low.

Diagnosis:

Pyruvate carboxylase deficiency

Key Insight:

Cannot form **oxaloacetate** ? TCA cycle cannot proceed ? pyruvate ? lactate.

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16. Patient with GTP Deficiency in Liver Injury

In liver disease, **GTP** generation is impaired.

Diagnosis:

Succinyl-CoA synthetase defect

Reason:

This reaction generates GTP ? required for many biosynthetic pathways.

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17. Teenager with Weak Collagen Formation

High levels of **?-KG** in blood; normal TCA but poor collagen cross-linking.

Diagnosis:

Vitamin C deficiency affecting ?-KG-dependent prolyl hydroxylase in collagen synthesis.

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18. Patient with High Citrate in Cytosol + Fatty Liver

Middle-aged man with fatty liver shows high **cytosolic citrate**.

Diagnosis:

Citrate overflow into cytosol ? fatty acid synthesis activation

Mechanism:

Excess citrate ? ATP citrate lyase ? acetyl-CoA ? fatty acid synthesis ? hepatic steatosis.

19. Child with Recurrent Vomiting After Eating High-Carb Meals

Blood tests show spikes in lactate and pyruvate after glucose intake.

Diagnosis:

PDH complex deficiency ? pyruvate cannot enter TCA ? lactate ?

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20. Man with Mitochondrial Disorder + Low ATP

Muscle biopsy shows defective **malate dehydrogenase**.

Diagnosis:

Reduced regeneration of **oxaloacetate** ? TCA cannot proceed ? ATP depression.

? MCQs — Citric Acid Cycle (TCA Cycle)

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1. The TCA cycle occurs in which cellular compartment?

A. Cytosol
B. Nucleus
C. Golgi
D. **Mitochondrial matrix**

Answer: D

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2. Which enzyme of TCA cycle is located in the inner mitochondrial membrane?

A. Aconitase
B. Malate dehydrogenase
C. **Succinate dehydrogenase**
D. Citrate synthase

Answer: C

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3. The rate-limiting enzyme of TCA cycle is:

A. Citrate synthase
B. ?-Ketoglutarate dehydrogenase
C. **Isocitrate dehydrogenase**
D. Malate dehydrogenase

Answer: C

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4. Which reaction of the TCA cycle produces GTP?

A. ?-Ketoglutarate ? Succinyl-CoA
B. Malate ? Oxaloacetate
C. Succinyl-CoA ? Succinate
D. Fumarate ? Malate

Answer: C

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5. Which cofactor is required for ?-ketoglutarate dehydrogenase?

A. Biotin
B. Vitamin C
C. **TPP + Lipoic acid + FAD + NAD? + CoA**

D. THF

Answer: C

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6. Which enzyme requires iron (Fe^{2}?)?

A. Citrate synthase
B. **Aconitase**
C. Malate dehydrogenase
D. Succinyl-CoA synthetase

Answer: B

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7. Which step produces FADH??

A. Malate ? Oxaloacetate
B. **Succinate ? Fumarate**
C. Citrate ? Isocitrate
D. ?-KG ? Succinyl-CoA

Answer: B

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8. Total ATP yield from 1 molecule of acetyl-CoA (classic values):

A. 6
B. 8
C. 10
D. **12**

Answer: D

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9. Succinyl-CoA is a precursor for synthesis of:

A. Purines
B. Pyrimidines
C. **Heme**
D. Fatty acids

Answer: C

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10. Which compound inhibits succinate dehydrogenase?

A. Rotenone
B. **Malonate**
C. Cyanide
D. Fluoride

Answer: B

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11. Fluoroacetate inhibits which enzyme?

A. Succinate dehydrogenase
B. Citrate synthase
C. **Aconitase**
D. Malate dehydrogenase

Answer: C

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12. Arsenite inhibits which component of the TCA cycle?

A. Citrate synthase
B. Aconitase
C. **?-Ketoglutarate dehydrogenase**

D. Fumarase

Answer: C

---

13. Which of the following increases TCA cycle activity?

A. High ATP
B. High NADH
C. **High Ca²?**
D. High fatty acids

Answer: C
(Ca²? stimulates IDH and ?-KGDH during muscle contraction)

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14. Which of the following decreases TCA cycle activity?

A. High ADP
B. **High NADH**
C. High Ca²?
D. High pyruvate

Answer: B

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15. Anaplerotic reaction that replenishes oxaloacetate:

A. Pyruvate ? Acetyl-CoA
B. Malate ? Fumarate
C. **Pyruvate ? Oxaloacetate (pyruvate carboxylase)**
D. Fumarate ? Malate

Answer: C

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16. A patient with thiamine deficiency will have impaired:

A. Malate dehydrogenase
B. **?-Ketoglutarate dehydrogenase**
C. Isocitrate dehydrogenase
D. Succinate dehydrogenase

Answer: B

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17. Which is the only substrate-level phosphorylation in the TCA cycle?

A. Succinate ? Fumarate
B. **Succinyl-CoA ? Succinate**
C. Isocitrate ? ?-KG
D. Malate ? OAA

Answer: B

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18. Citrate inhibits which glycolytic enzyme?

A. Hexokinase
B. Pyruvate kinase
C. **PFK-1**
D. Aldolase

Answer: C

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19. High ATP and high NADH will:

A. Activate IDH
B. Activate citrate synthase
C. **Inhibit TCA cycle globally**

D. Increase succinyl-CoA production

Answer: C

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20. Which intermediate can directly participate in gluconeogenesis?

A. Succinyl-CoA
B. Fumarate
C. **Malate**
D. Acetyl-CoA

Answer: C

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21. Which TCA intermediate links to the urea cycle via aspartate?

A. Citrate
B. **Oxaloacetate**
C. Succinate
D. Malate

Answer: B

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22. ?-Ketoglutarate is a precursor for which amino acid?

A. Serine
B. Alanine
C. **Glutamate**
D. Aspartate

Answer: C

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23. Which vitamin deficiency impairs both PDH and ?-KGDH?

A. Vitamin B12
B. Vitamin C
C. Vitamin K
D. **Vitamin B1 (Thiamine)**

Answer: D

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24. In fasting, low oxaloacetate causes:

A. Enhanced glycolysis
B. **Increased ketone body formation**
C. Inhibited ?-oxidation
D. Increased pyruvate carboxylase inhibition

Answer: B

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25. A patient given a drug that inhibits lipoic acid will show elevated:

A. Citrate
B. Succinate
C. **?-Ketoglutarate**
D. Malate

Answer: C

? VIVA VOCE — CITRIC ACID CYCLE

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1. Where does the TCA cycle occur?

In the **mitochondrial matrix**.

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2. What is the common substrate entering the TCA cycle?

Acetyl-CoA.

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3. Name the enzyme for the first step of the cycle.

Citrate synthase.

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4. Which enzyme requires Fe²??

Aconitase.

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5. Which step produces GTP?

Succinyl-CoA ? Succinate (succinyl-CoA synthetase).

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6. What is the only membrane-bound TCA enzyme?

Succinate dehydrogenase (Complex II).

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7. Which TCA enzyme produces FADH??

Succinate dehydrogenase.

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8. Which enzyme produces NADH?

Isocitrate dehydrogenase, ?-ketoglutarate dehydrogenase, and malate dehydrogenase.

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9. Which two steps release CO??

- **Isocitrate ? ?-Ketoglutarate**
- **?-Ketoglutarate ? Succinyl-CoA**

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10. What are the cofactors for ?-ketoglutarate dehydrogenase?

TPP, lipoic acid, FAD, NAD?, CoA.

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11. How many ATP equivalents are produced per acetyl-CoA?

Classically **12 ATP** (modern value ~10).

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12. Why is the cycle called amphibolic?

Because it is **both catabolic and anabolic**.

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13. Which TCA intermediate is precursor for heme synthesis?

Succinyl-CoA.

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14. Which intermediate links TCA and gluconeogenesis?

Malate (via malate shuttle).

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15. Which intermediate forms the amino acid glutamate?

?-Ketoglutarate.

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16. Which vitamin deficiency inhibits TCA cycle most severely?

Vitamin B1 (Thiamine) due to PDH and ?-KGDH impairment.

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17. What activates isocitrate dehydrogenase?

ADP and $Ca^{2?}$.

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18. What inhibits isocitrate dehydrogenase?

ATP and NADH.

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19. What activates ?-ketoglutarate dehydrogenase?

Ca^{2}?.

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20. What inhibits ?-ketoglutarate dehydrogenase?

Succinyl-CoA and NADH.

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21. What is an anaplerotic reaction?

A reaction that **replenishes TCA intermediates**.

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22. Give one anaplerotic reaction.

Pyruvate ? Oxaloacetate (pyruvate carboxylase).

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23. What is the TCA cycle inhibitor found in rat poison?

Fluoroacetate (inhibits aconitase).

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24. What inhibits succinate dehydrogenase competitively?

Malonate.

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25. Why does high NADH inhibit TCA cycle?

High NADH indicates a **high-energy state** ? reduces oxidative steps.

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26. What happens to the TCA cycle during hypoxia?

It **slows down** because NADH cannot be oxidized in ETC.

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27. What metabolic pathway depends directly on TCA cycle NADH/FADH??

Electron transport chain (ETC).

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28. How does TCA link to urea cycle?

Via **fumarate ? aspartate shuttle**.

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29. Why does fasting decrease TCA cycle activity?

Because **oxaloacetate is diverted to gluconeogenesis**, reducing cycle flow.

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30. What happens to acetyl-CoA when OAA is low?

Enters **ketogenesis**.

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31. Which disorder presents with ?-KG buildup and neurological issues?

Thiamine deficiency.

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32. Which TCA enzyme is part of ETC as well?

Succinate dehydrogenase (Complex II).

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33. What is the committed step of TCA?

Citrate synthesis.

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34. Which ion activates two major TCA enzymes during muscle contraction?

Calcium ($Ca^{2?}$).

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35. What inhibits ?-ketoglutarate dehydrogenase in arsenic poisoning?

Arsenite binds **lipoic acid**.

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36. Which intermediate accumulates when citrate synthase is inhibited?

Oxaloacetate.

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37. Name one medical condition where TCA cycle is severely impaired.

Mitochondrial myopathies / **fumarase deficiency** / **PDH deficiency**.

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38. What is the effect of ATP on TCA cycle?

Inhibits major regulatory enzymes.

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39. What ratio controls TCA cycle most strongly?

NAD?/NADH ratio.

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40. What is the overall purpose of the TCA cycle?

To oxidize acetyl-CoA to **CO?** while producing **high-energy reducing equivalents**.