

Clinical Case - Discussion With Answer

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Case 3

- A 72 years old woman came to hospital with her son. Her son was complaining about her confuse mental status and worsening of her short term memory since few months. She had admitted in hospital for routine check up and examination. After all the investigation, including MRI, and examination , physician diagnosed that it may be degenerative disease like Alzheimer disease (AD)

Question

1. Gives name of proteins involved in pathogenesis of AD.
2. What are differences in structure of amyloid-beta fragment in APP and free amyloid-beta fragment?
3. What are common anatomical findings in MRI of brain of AD patient?
4. Explain role of secretase enzymes in pathogenesis of AD?
5. How does Ca^{2+} and protein phosphorylation play role in pathogenesis of AD.

Case 4

- Early in the morning, 40 years old male patient came in emergency with complain of **chest pain**, perspiration and **altered consciousness** for 4 hours.
- Patient also had **diabetes mellitus** for 10 years. He was taking medicine for diabetes mellitus irregularly. In history, it was found that he was **chronic alcoholic** and a day before chest pain , he also had **heavy alcohol ingestion.**, with no feed intake

Case 4

- Doctor asked for few blood investigations. From ECG finding and abnormal cardiac function test. Diagnosis of **myocardial infarction** was confirmed.
- Following treatment was given
 - loading dose of **anti-platelet drug (Aspirin)**
 - loading dose of **hypocholesterolemic (Statin group) drug**
 - **Fibrinolytic drug (streptokinase)**
 - 50% dextrose saline with Thiamine (Vitamin B1)

Case 4

- After complete management and recovery after 7 days of admission in hospital, at time discharge from hospital, physician advised to take medicines regularly and to take more amount of **fruit and fiber food**.

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Investigation

- Random Blood Sugar = 30 mg%
- HbA1C = 9 %
- S. Cholesterol = 350 mg%
- S. Triglyceride = 250 mg%
- S. HDL Cholesterol = 25 mg%

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Question Case 4

1. What are chronic complication of DM?
2. Why uncontroled diabetic mellitus increase chances of atherosclerosis?
3. What is cardiac function test?
4. Which test will you prefer to do for diagnosis of myocardial infarction, if patient come after 4 day of onset of chest pain?
5. How statin reduce cholesterol level?

Question Case 4

6. What is biochemical explanation of hypoglycemia?
7. Why physician asked to give injectable 50% Dextrose saline with Thiamine (Vitamin B1)?
8. What is role of fruits and fiber in chronic diabetes mellitus and atherosclerosis?
9. Why blood sample for blood sugar estimation is collected in fluoride containing vial?
10. What is re-perfusion injury ? And what is role of allopurinol to prevent it?
11. How will you calculate patient's LDL cholesterol?
12. What is role of fibrinolytic drugs (streptokinase) in myocardial infarction?

What are chronic complication of DM?

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What are chronic complication of DM?

Complications of Diabetes

Macrovascular

Brain

Cerebrovascular disease

- Transient ischemic attack
- Cerebrovascular accident
- Cognitive impairment

Heart

Coronary artery disease

- Coronary syndrome
- Myocardial infarction
- Congestive heart failure

Extremities

Peripheral vascular disease

- Ulceration
- Gangrene
- Amputation

Microvascular

Eye

Retinopathy
Cataracts
Glaucoma

Kidney

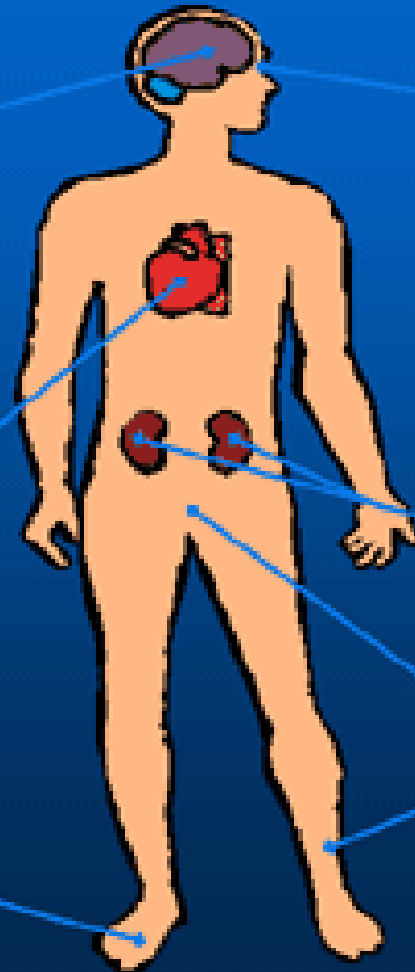
Nephropathy

- Microalbuminuria
- Gross albuminuria
- Kidney failure

Nerves

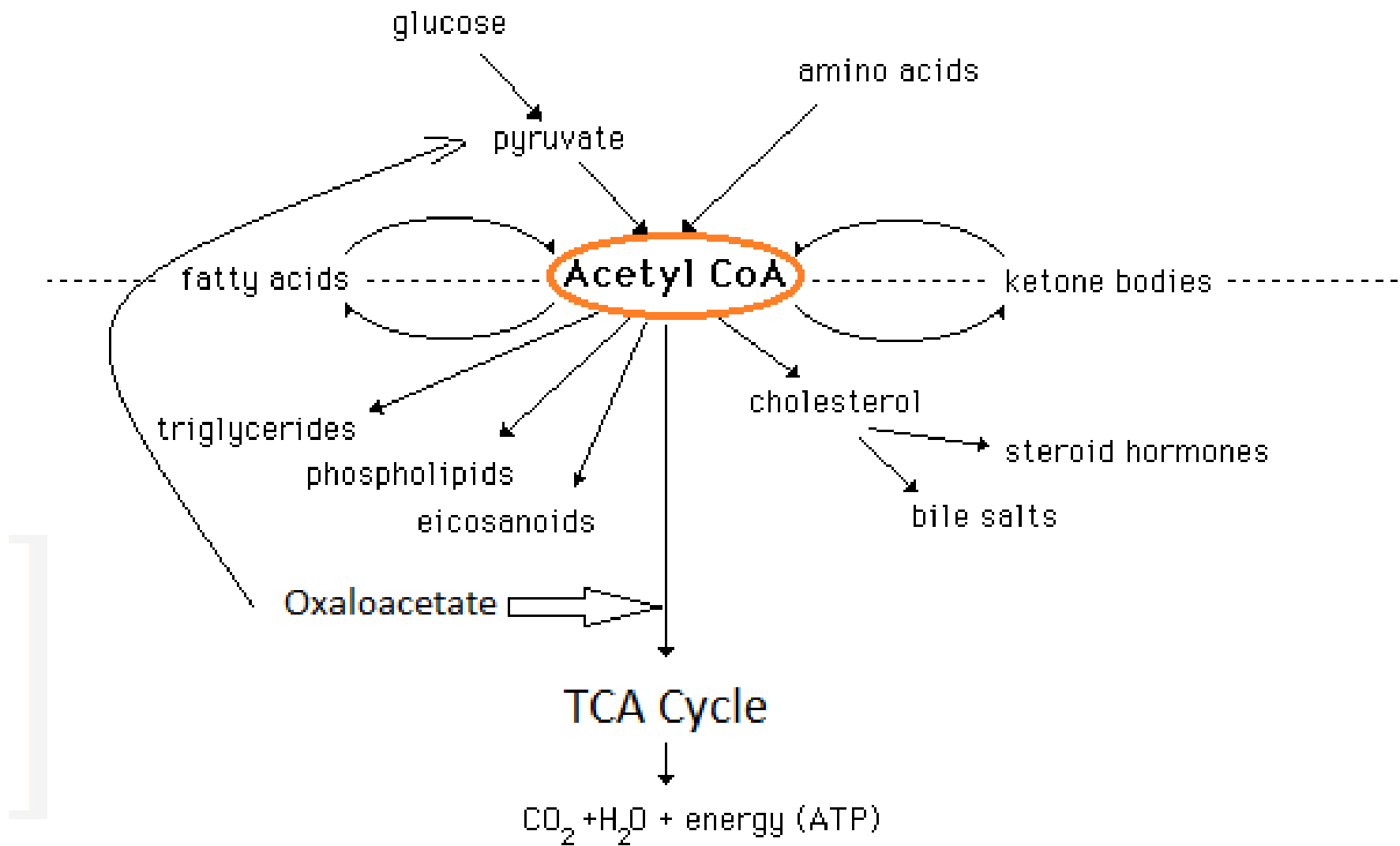
Neuropathy

- Peripheral
- Autonomic



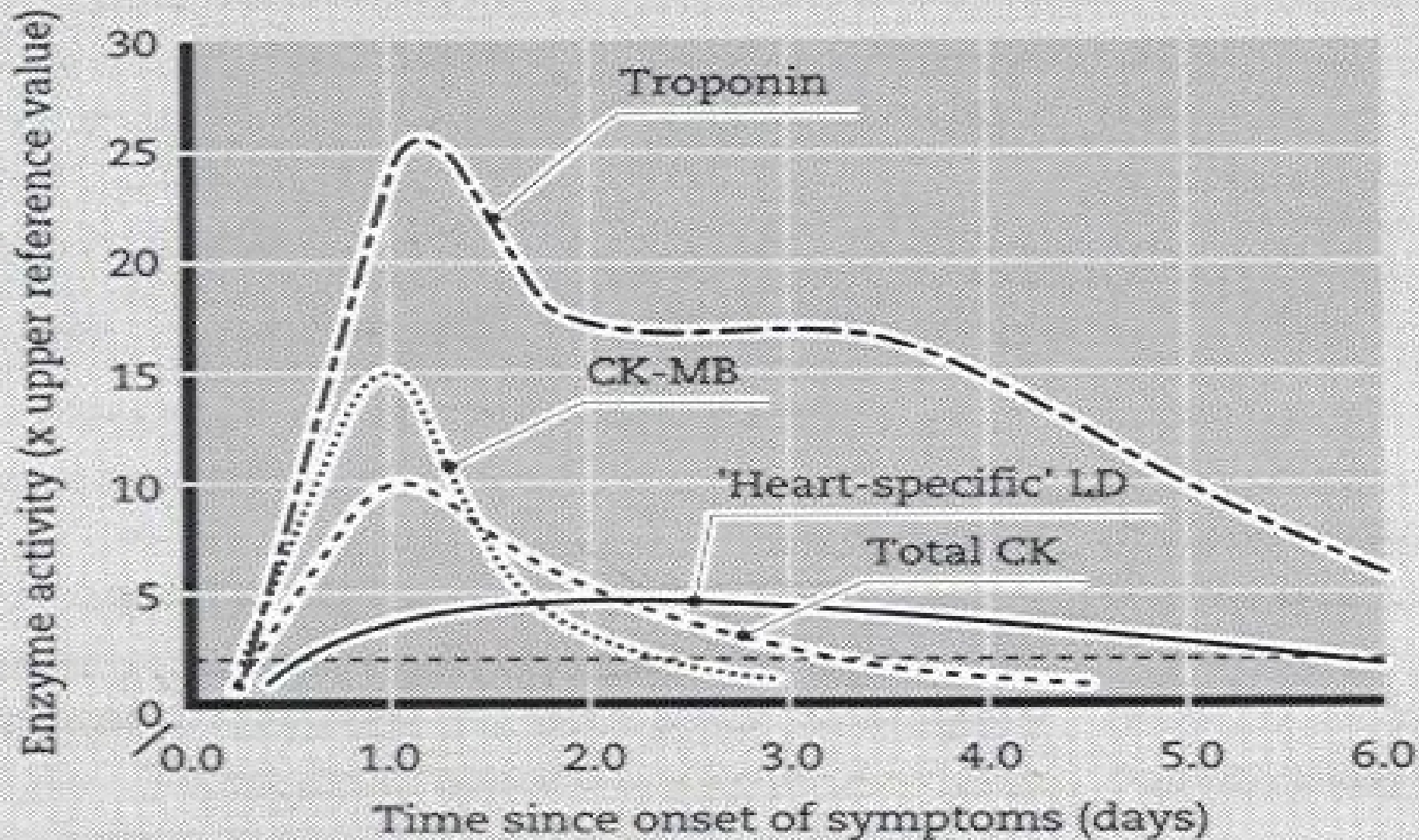
Why uncontrolled diabetic mellitus increase chances of atherosclerosis?

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- What is cardiac function test?
- Which test will you prefer to do for diagnosis of myocardial infarction, if patient come after 5 day of onset of chest pain?

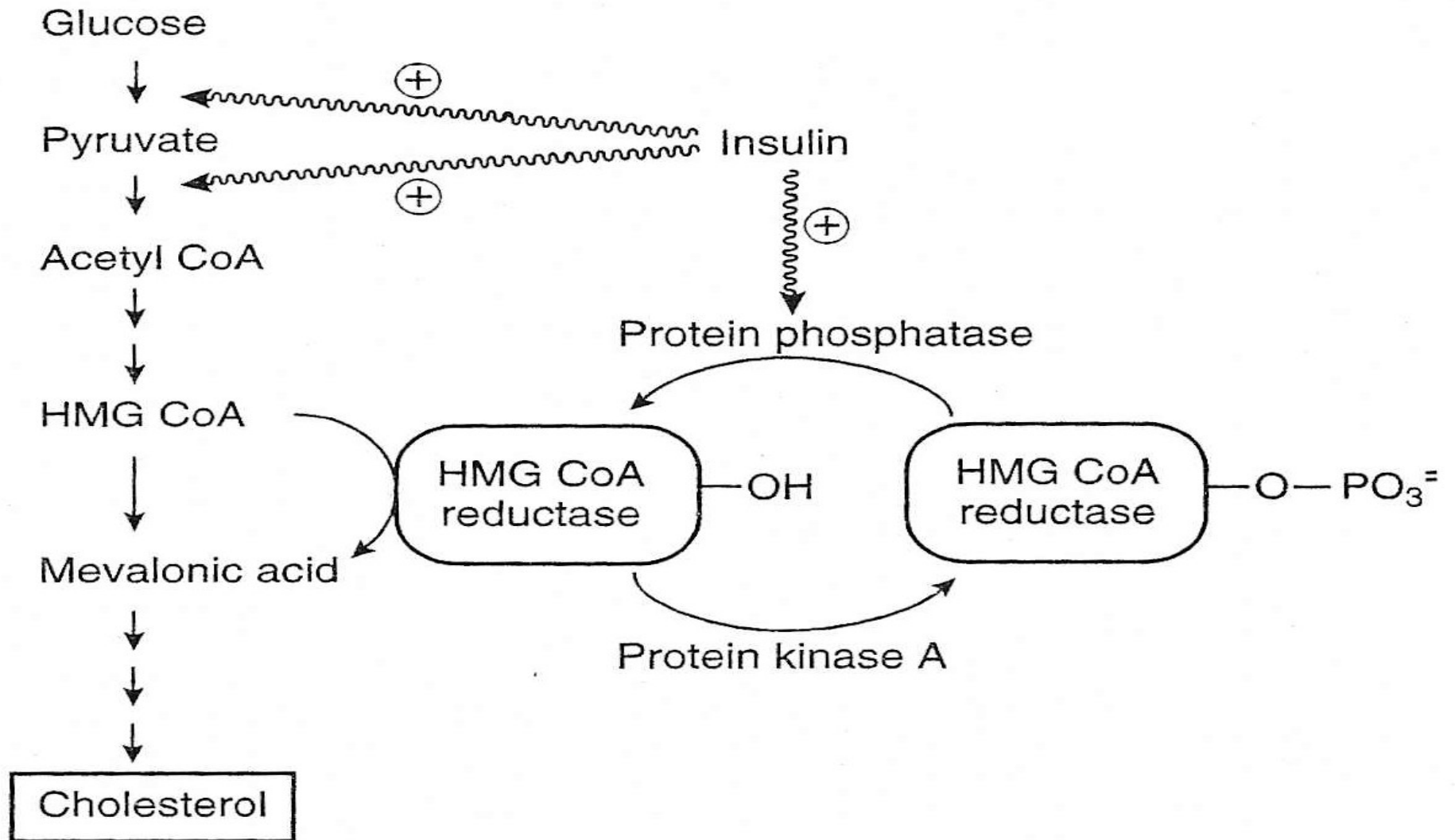
ENZYME ACTIVITY AFTER MYOCARDIAL INFARCTION



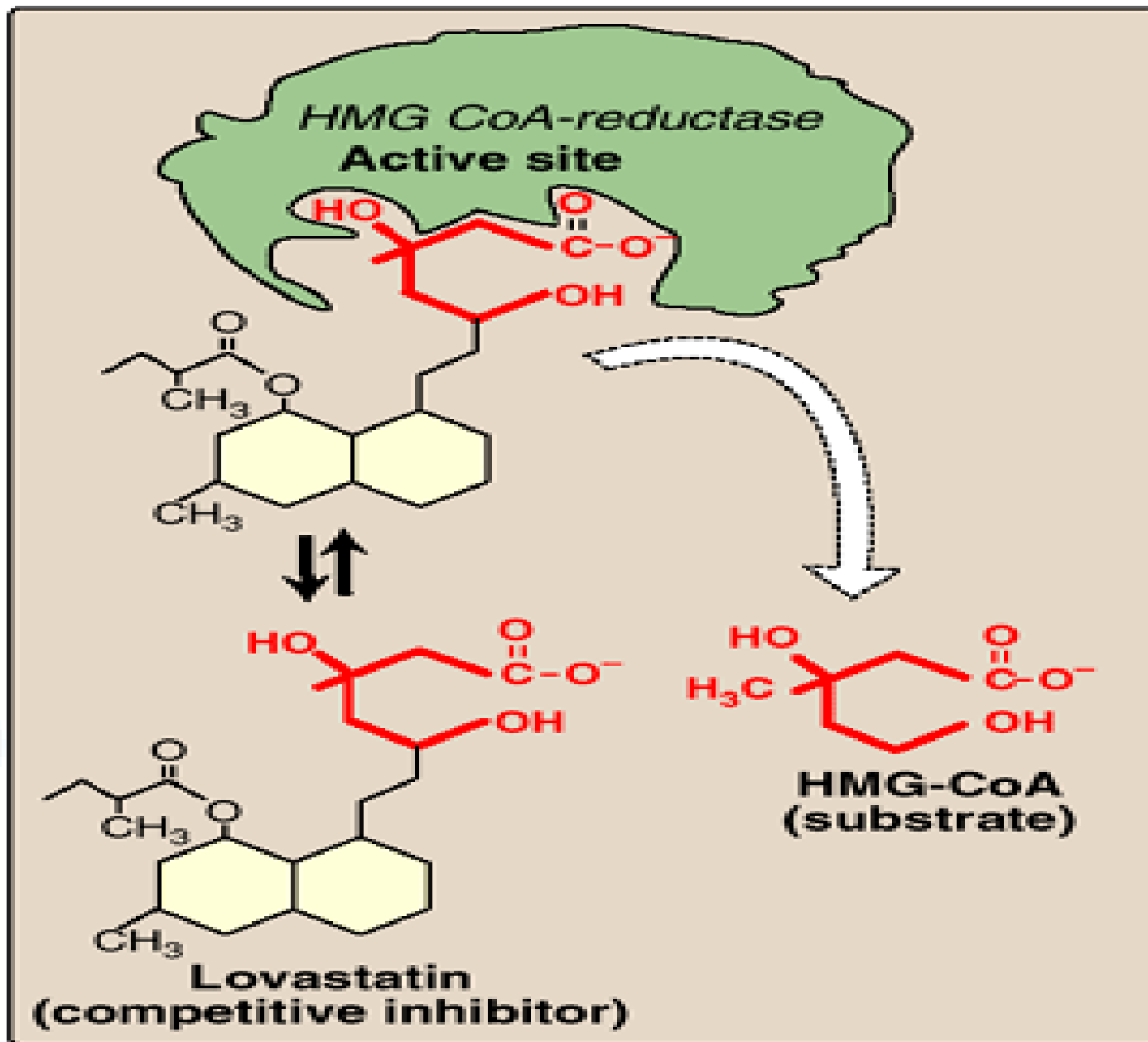
- How statin reduce cholesterol level?

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Cholesterol Regulation



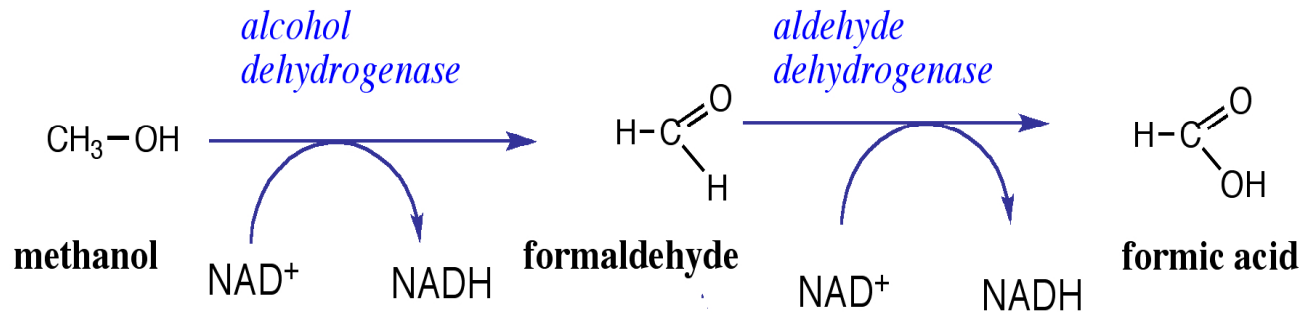
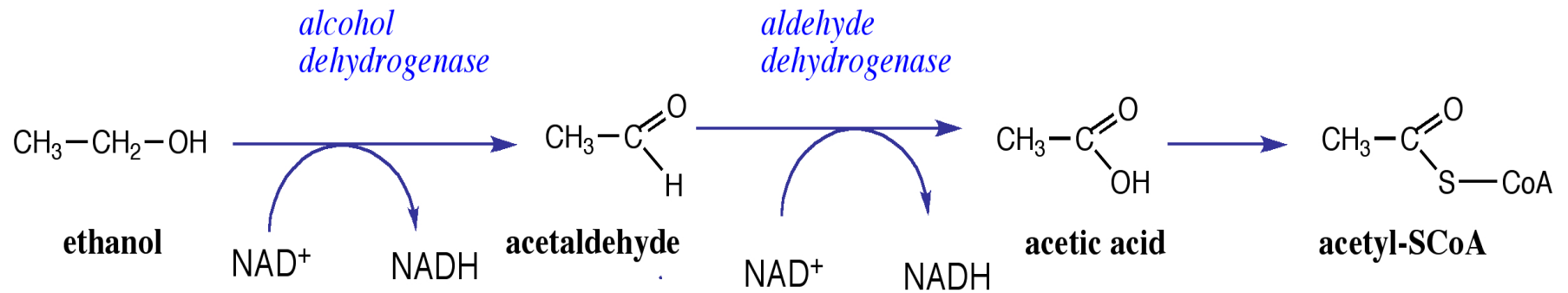
Competitive Inhibition

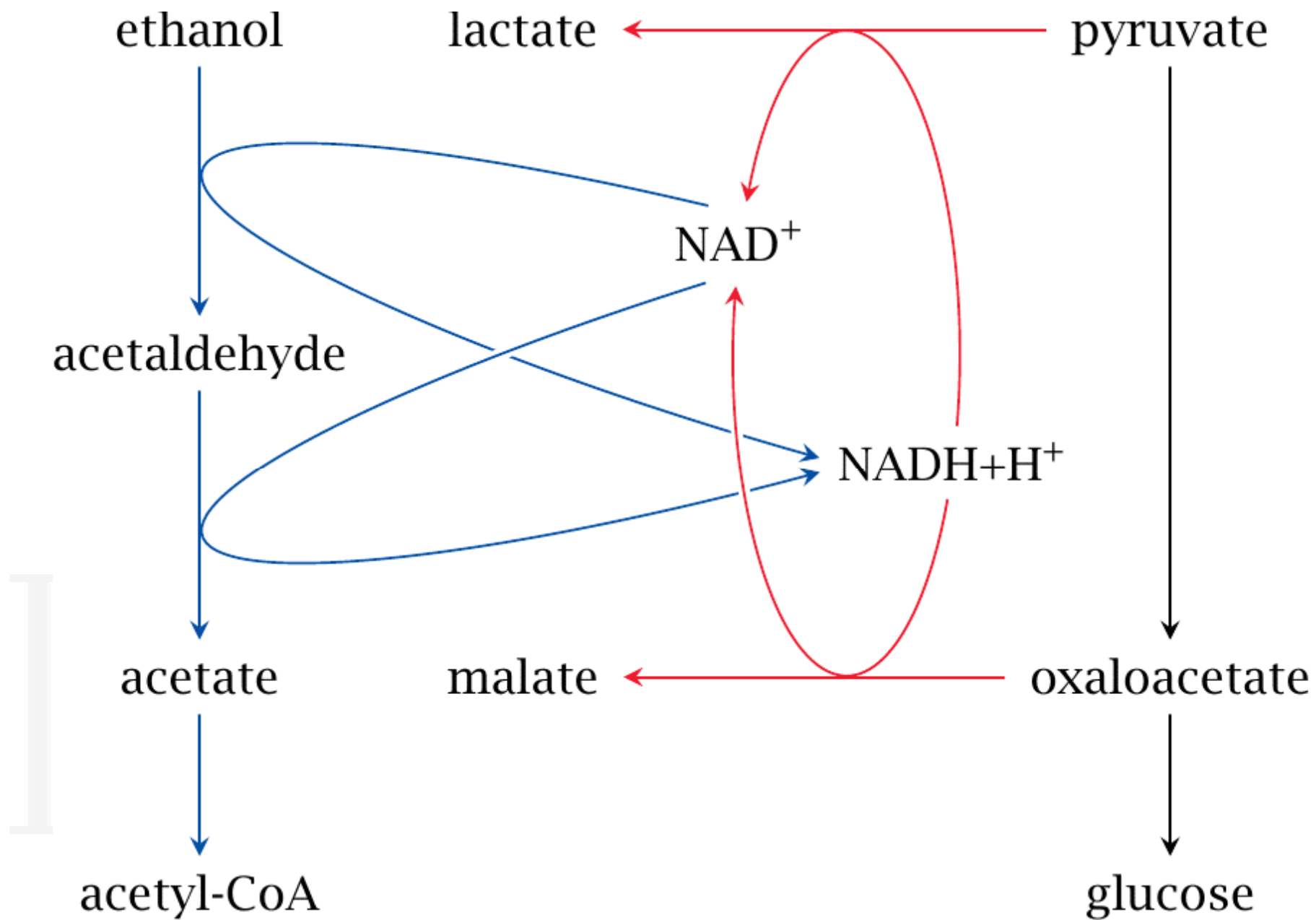


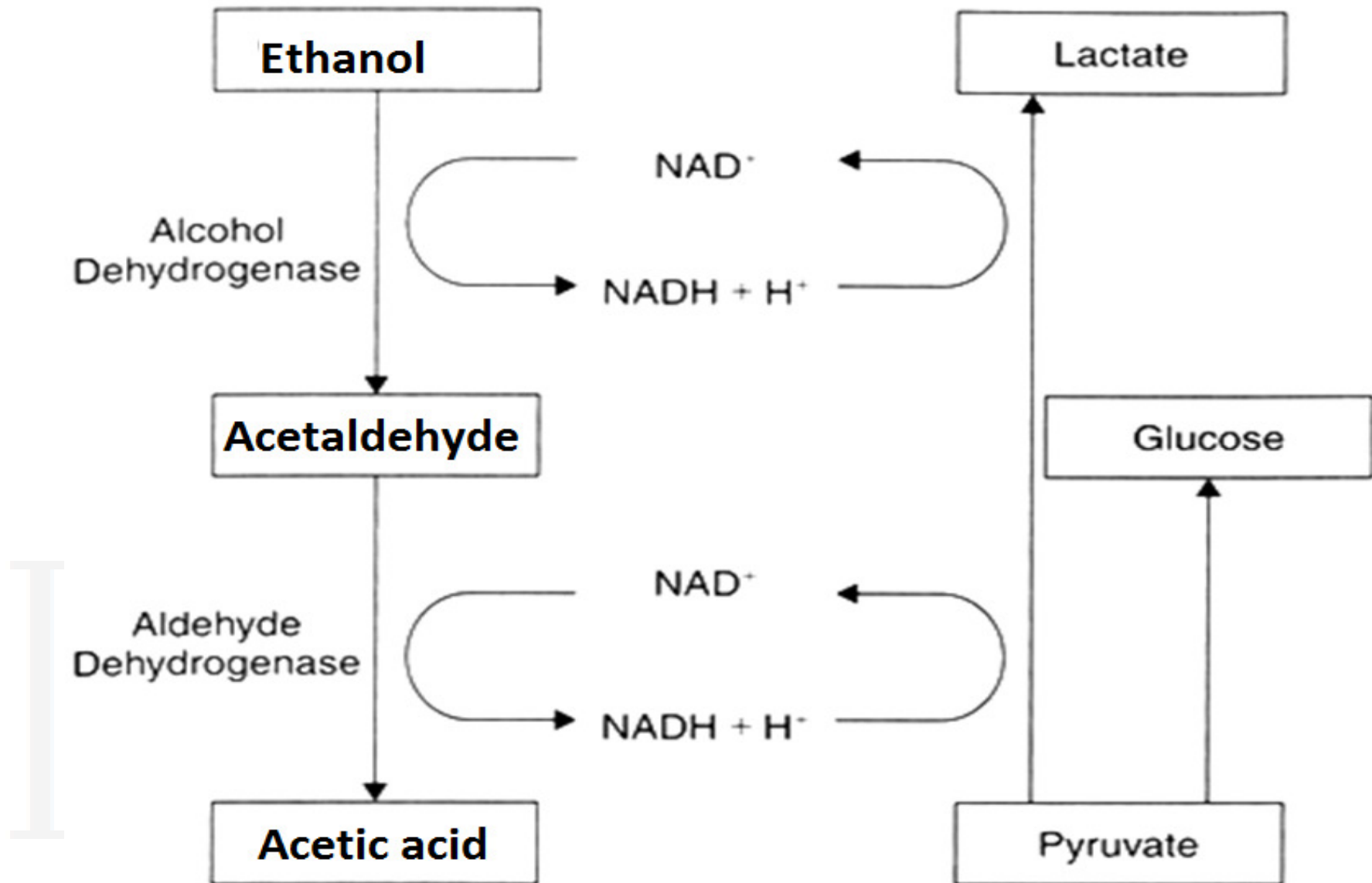
- What is biochemical explanation of hypoglycemia?

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Alcohol Metabolism

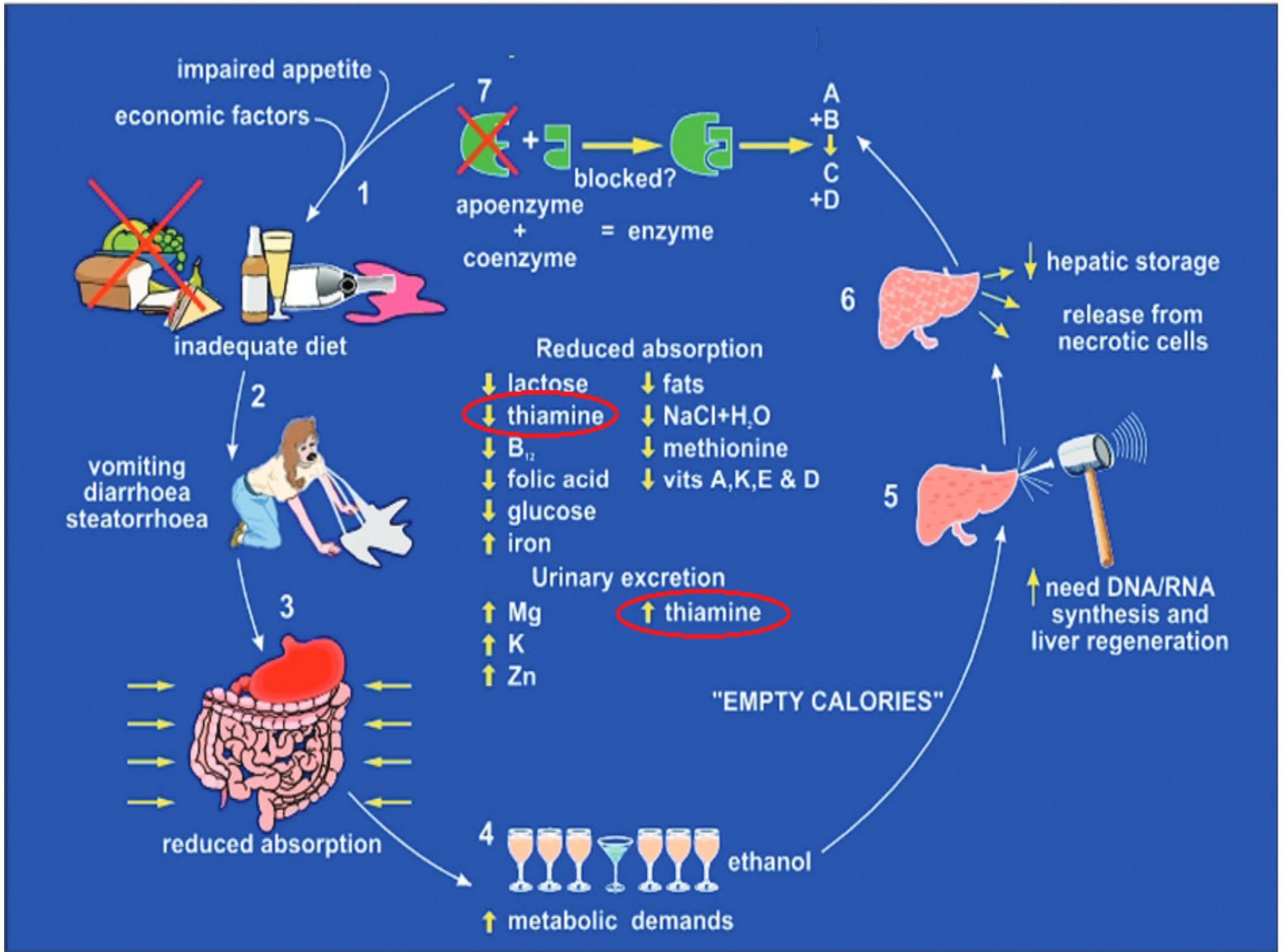






- Why physician asked to give injectable 50% Dextrose saline with Thiamine (Vitamin B1)?

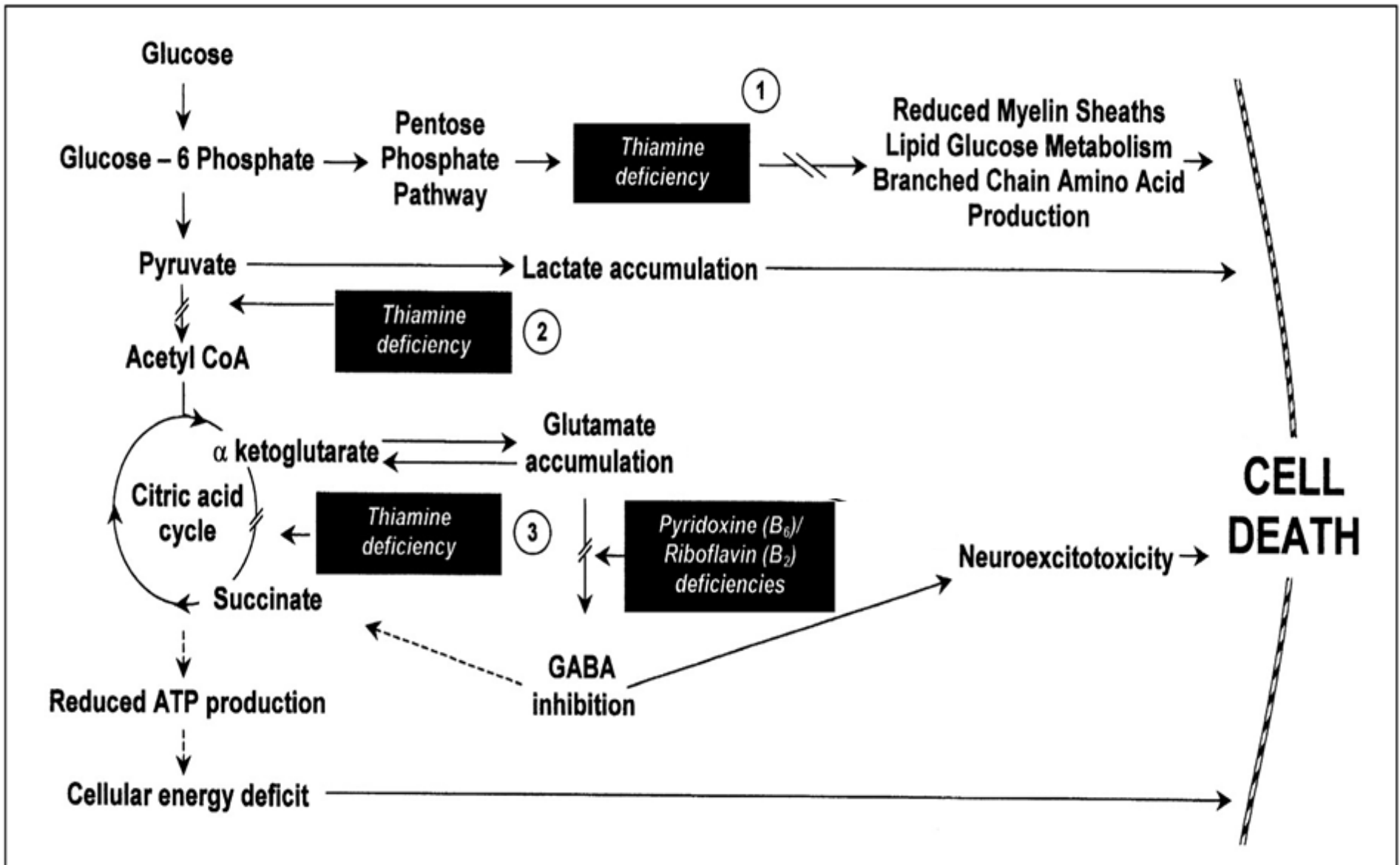
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Thiamine Deficiency Due to Alcoholism

- Reduce GI Absorption
- Inadequate Diet
- Hepatic Damage
- Decrease Hepatic Storage
- Increase Diuresis
- Increase Metabolic demand

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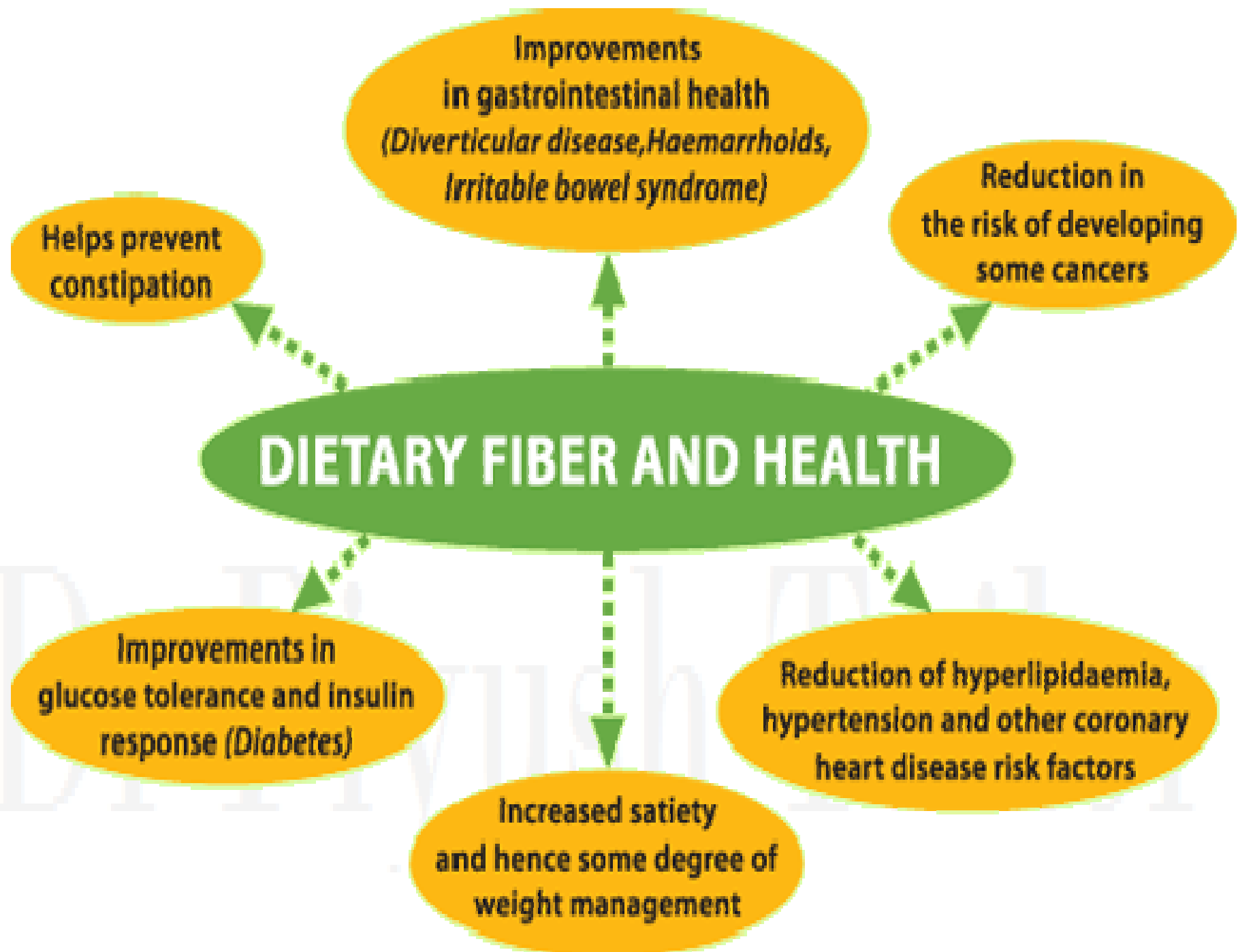


Thiamine dependent enzymes:-

- ① Transketolase
- ② Pyruvate dehydrogenase complex
- ③ α-Ketoglutarate dehydrogenase complex

- What is role of fruits and fiber in chronic diabetes mellitus and atherosclerosis?

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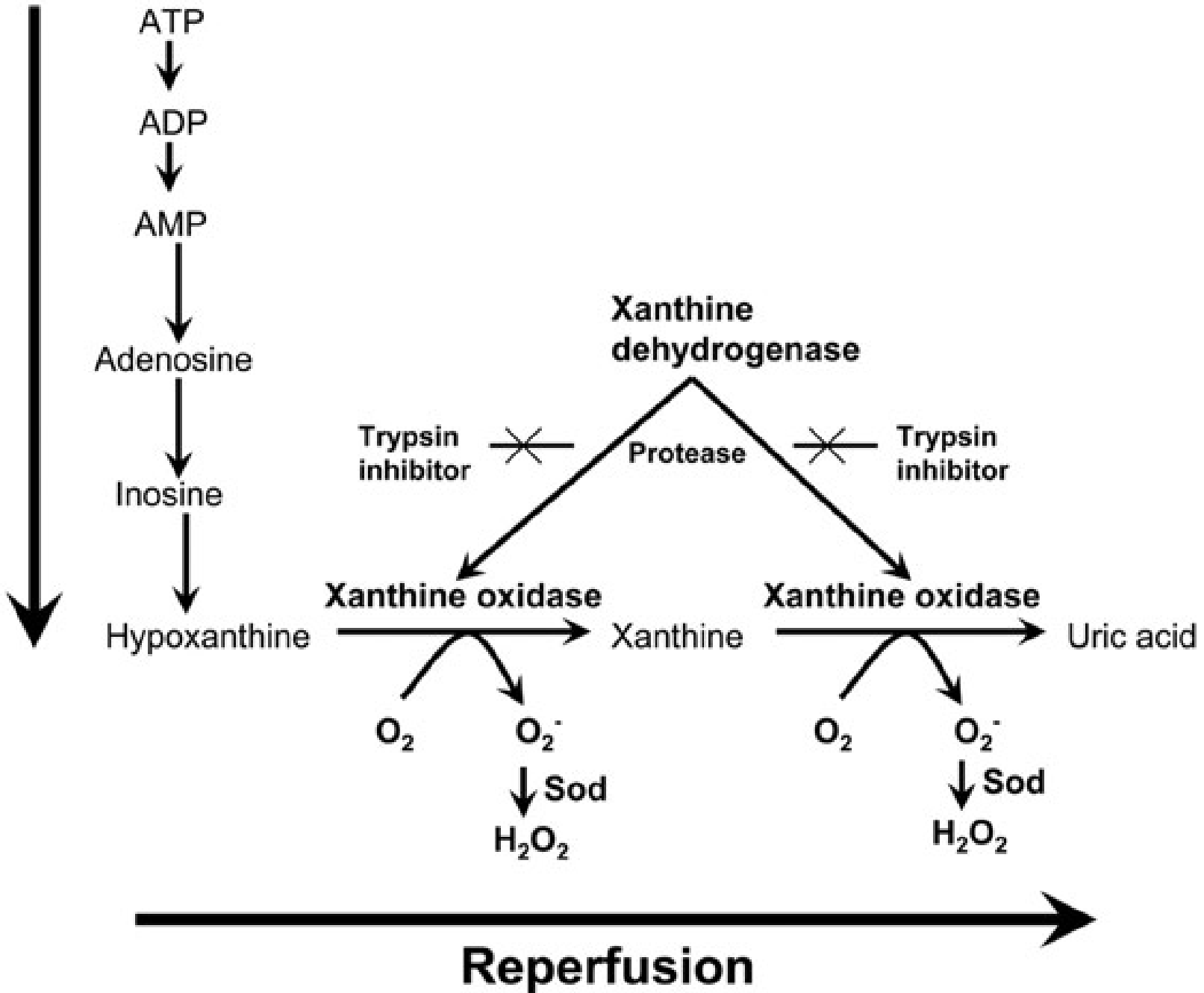


- Why blood sample for blood sugar estimation is collected in fluoride containing vial?
- Inhibit Enolase
- Glycolysis
- Inhibit utilization of Glucose by cells
- Get actual blood sugar even after few hours.

- What is re-perfusion injury ? And what is role of allopurinol to prevent it?

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Ischemia



- How will you calculate patient's LDL cholesterol?

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Friedewald formula

Total Cholesterol =

(VLDL chole) + (HDL chole) + (LDL chole)

VLDL-cholesterol =

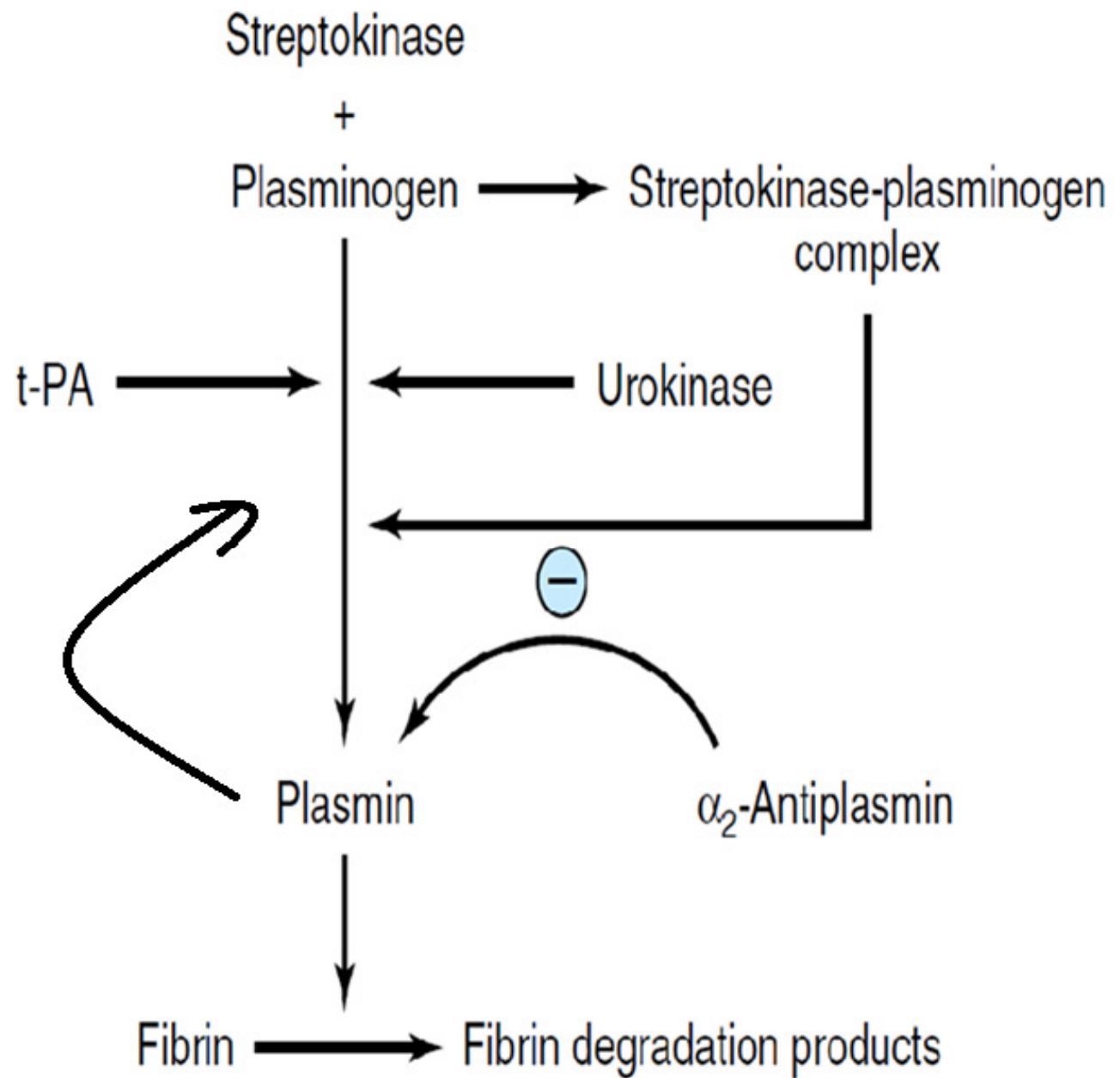
S. Triglyceride / 5

LDL-cholesterol =

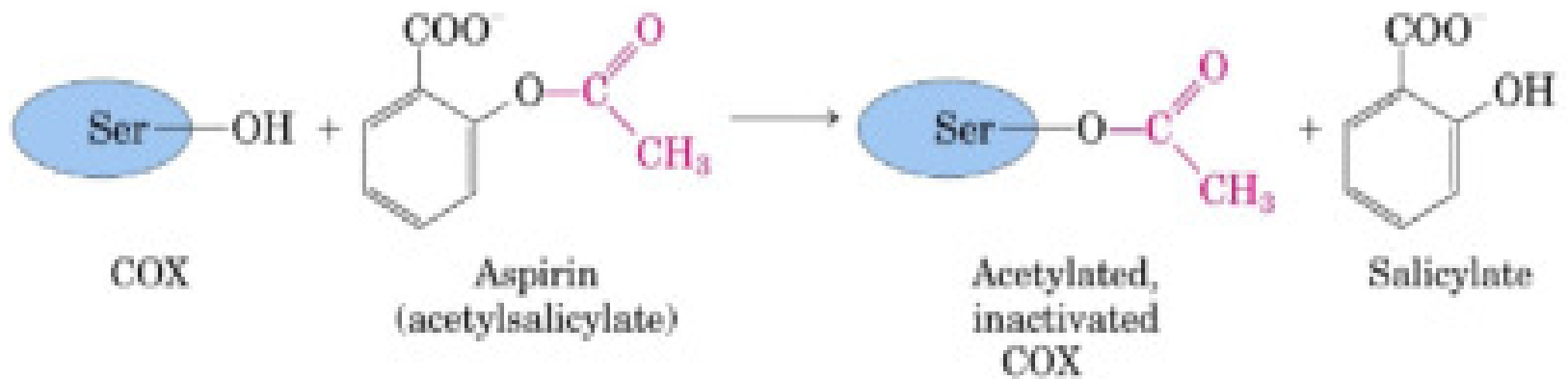
Total cholesterol – (TG/5) – HDL

- What is role of fibrinolytic drugs (streptokinase) in myocardial infarction?

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- Give biochemical explanation of antiplatelet drug- Aspirin.



(1)

Phospholipids

(Phospholipase
A-2)



Arachidonic Acid

Cyclooxygenase

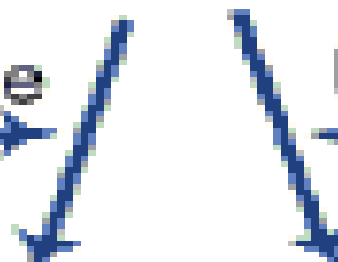


Prostaglandins
Thromboxanes

Lipoxygenase



Leukotrienes



D

r

Phospholipids

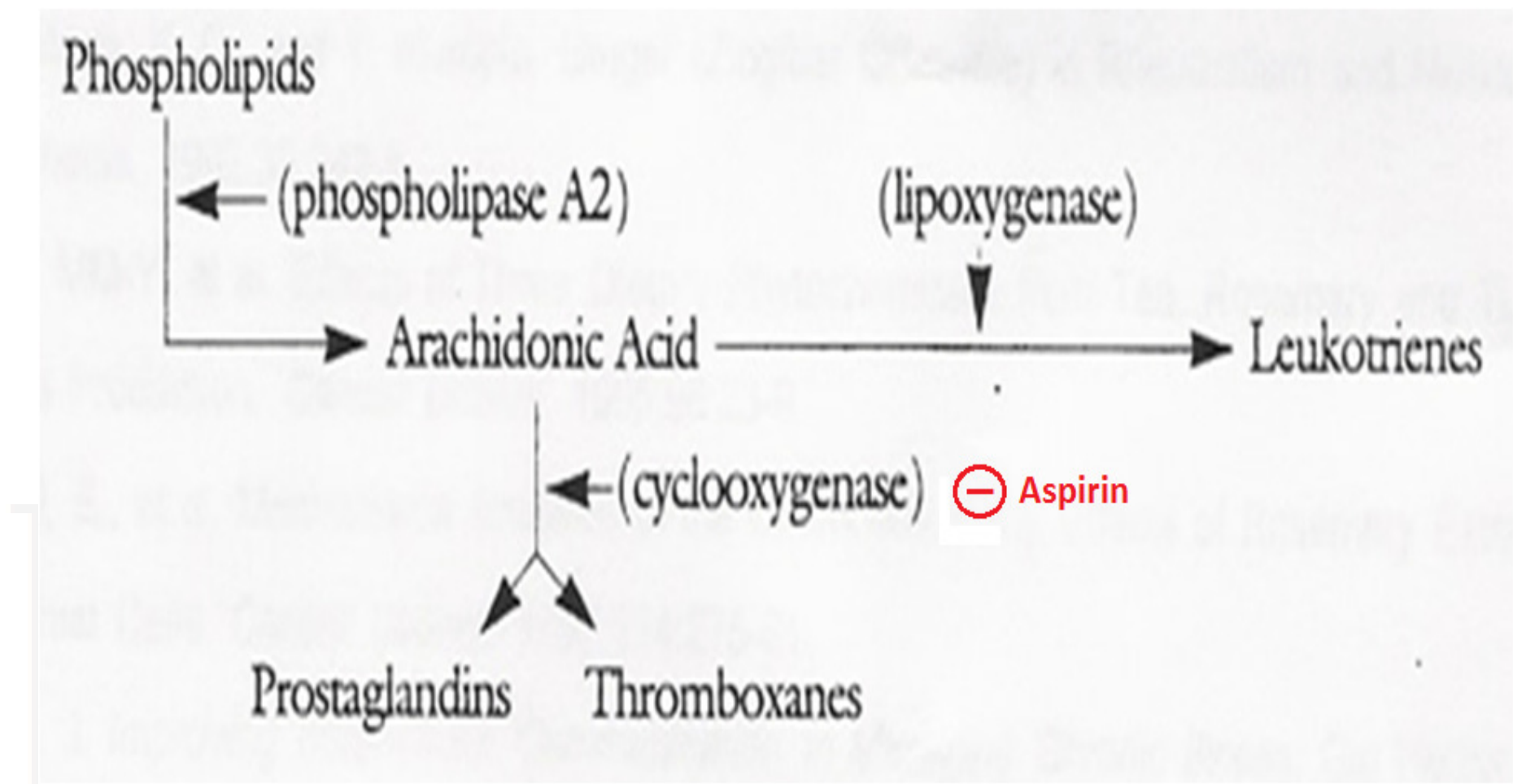
← (phospholipase A2)

(lipoxygenase)

→ Arachidonic Acid → Leukotrienes

← (cyclooxygenase) ⊖ Aspirin

Prostaglandins Thromboxanes



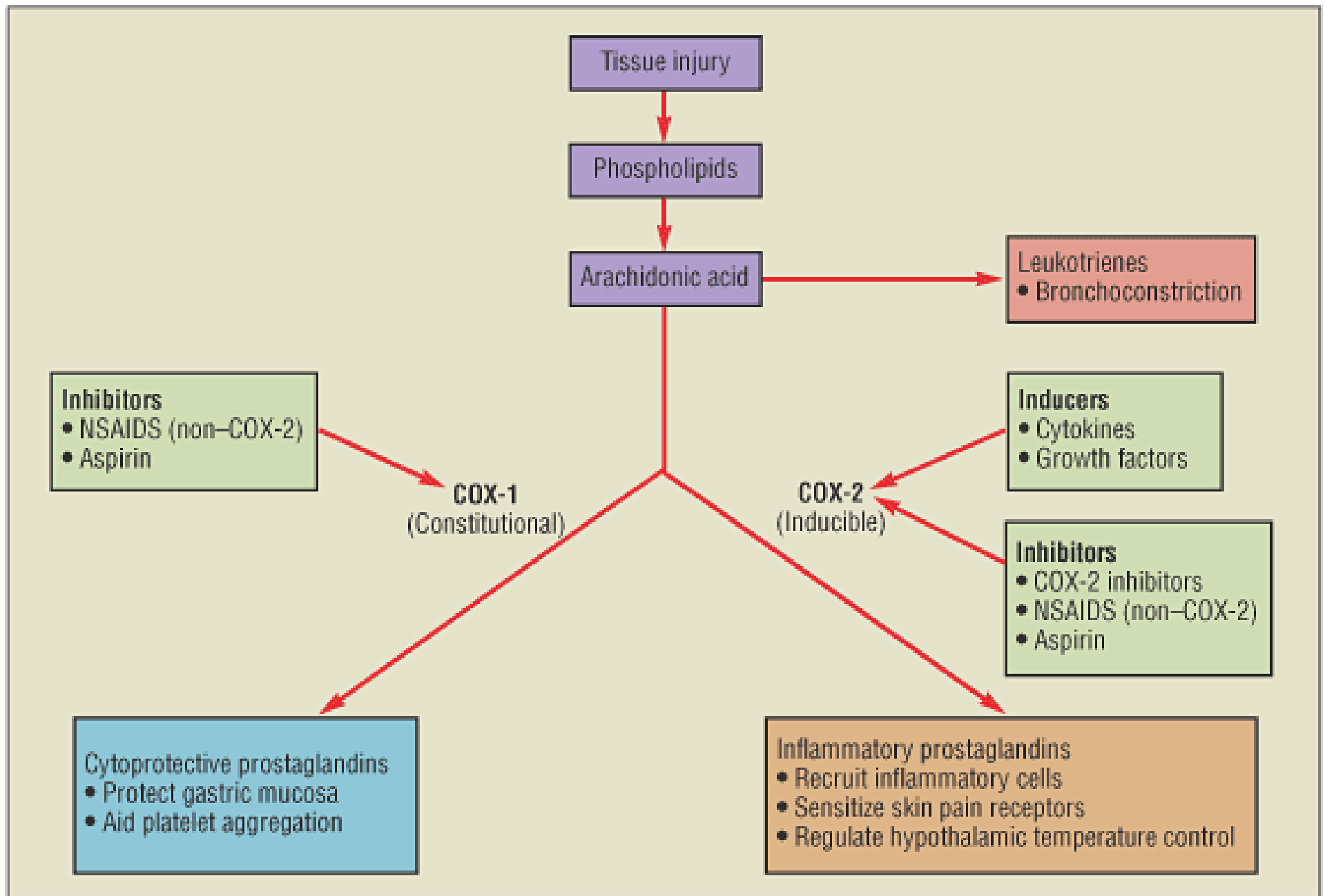


FIGURE 1. Algorithm of the biochemical pathway shows that the formation of prostaglandins occurs via both cyclooxygenase enzymes (COX-1 and COX-2).

What is significant of high HbA1c ?

- HbA** = Adult hemoglobin
- HbA0 = Non-Glycated hemoglobin.
- HbA1 = Glycated hemoglobin
- HbA1a1 = Glycation with Fructose 1-6 diphosphate
- HbA1a2 = Glycation with Glucose 6 phosphate
- HbA1b = Glycation with unknown
- HbA1c** = **Glycation with D glucose**

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Case 5

56 year male patient came in emergency with **alter-conciuosness & haemetemesis** . He was suffering from **chronic cirrhotic liver disease** due to **chronic alcoholism**. On examination , it was found that he has **edema** on both lower limb, fluid collection in peritoneal cavity (**Ascites**), yellowish discolouration of skin & sclera (**icterus**), with **hypotension** (decrease Blood Pressure). On blood investigation following was found.

Case 5 - Investigation

- Blood Glucose : 50 mg%
- Serum Protein : 5.5 gm %
- Serum Albumin : 2.0 gm%
- Serum Ammonia : Very High
- Serum Total Billirubin : 20 mg%
- APTT – Test : 60 second
- APTT – Control : 30 second
- APTT – INR : 2
- Haemoglobin : 6 gm%

- Ultra Sono-Graphy detected
 - Cirrhosis of Liver
 - Fatty Liver

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Case 5 - Investigation

- Physician advise to give Following treatment
- Injection 10% Dextrose
- Injection Thiamine (B1)
- Injection Vitamin K
- Injection 10% Albumin
- Oral Neomycin (Anti-microbial, Antibiotic)
- Liq Lactulose (Laxative)
- Oral Phenylbutarate

1. **Biochemical explanation about following symptoms in chronic alcoholic**
 - Alter consciousness
 - Haemetemesis
2. **Biochemical explanation about following signs in chronic alcoholic**
 - Edeme
 - Ascites
 - Hypotension
3. **What is hepato-renal syndrome?**
4. **Biochemical reason for giving following in patient of chronic alcoholic**
 - Dextrose plus thiamine
 - Vitamin K
 - 10% Albumin
 - Oral Neomycin (Anti-microbial, Antibiotic)
 - Liq Lactulose (Laxative)
 - Oral Phenylbutarate

Case 5 - Question

1. **Biochemical explanation about following symptoms in chronic alcoholic**
 - Alter consciousness
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2. **Biochemical explanation about following signs in chronic alcoholic**
 - Edeme
 - Ascites
 - Hypotension
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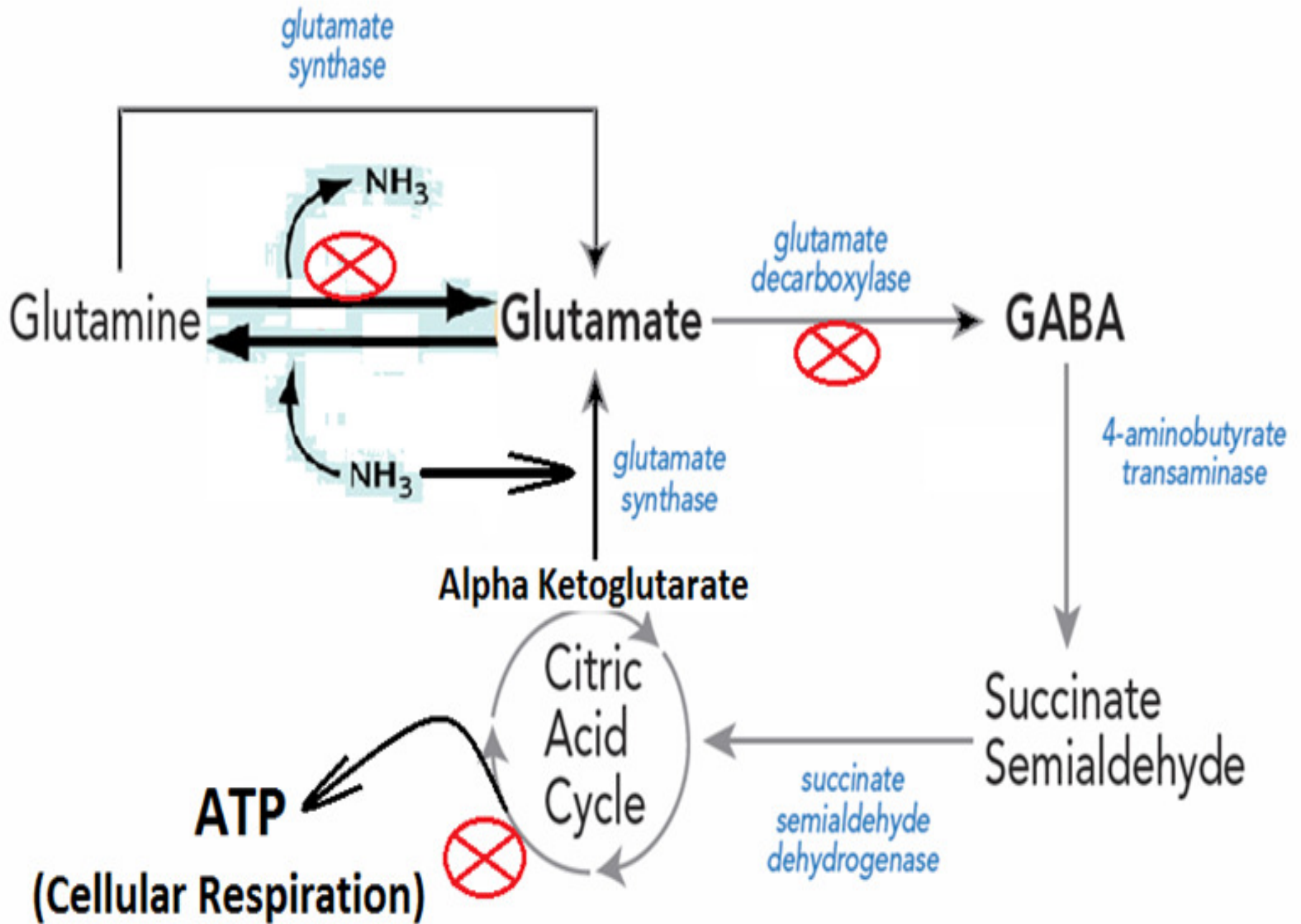
Case 5 - Question

1. **Biochemical reason for giving following in patient of chronic alcoholic**
 - Dextrose plus thiamine
 - Vitamin K
 - 10% Albumin
 - Oral Neomycin (Anti-microbial, Antibiotic)
 - Liq Lactulose (Laxative)
 - Oral Phenylbutarate

Biochemical explanation Alter consciousness in chronic alcoholic

- Hypoglycemia
- Uremic encephalopathy
- Hepatic encephalopathy

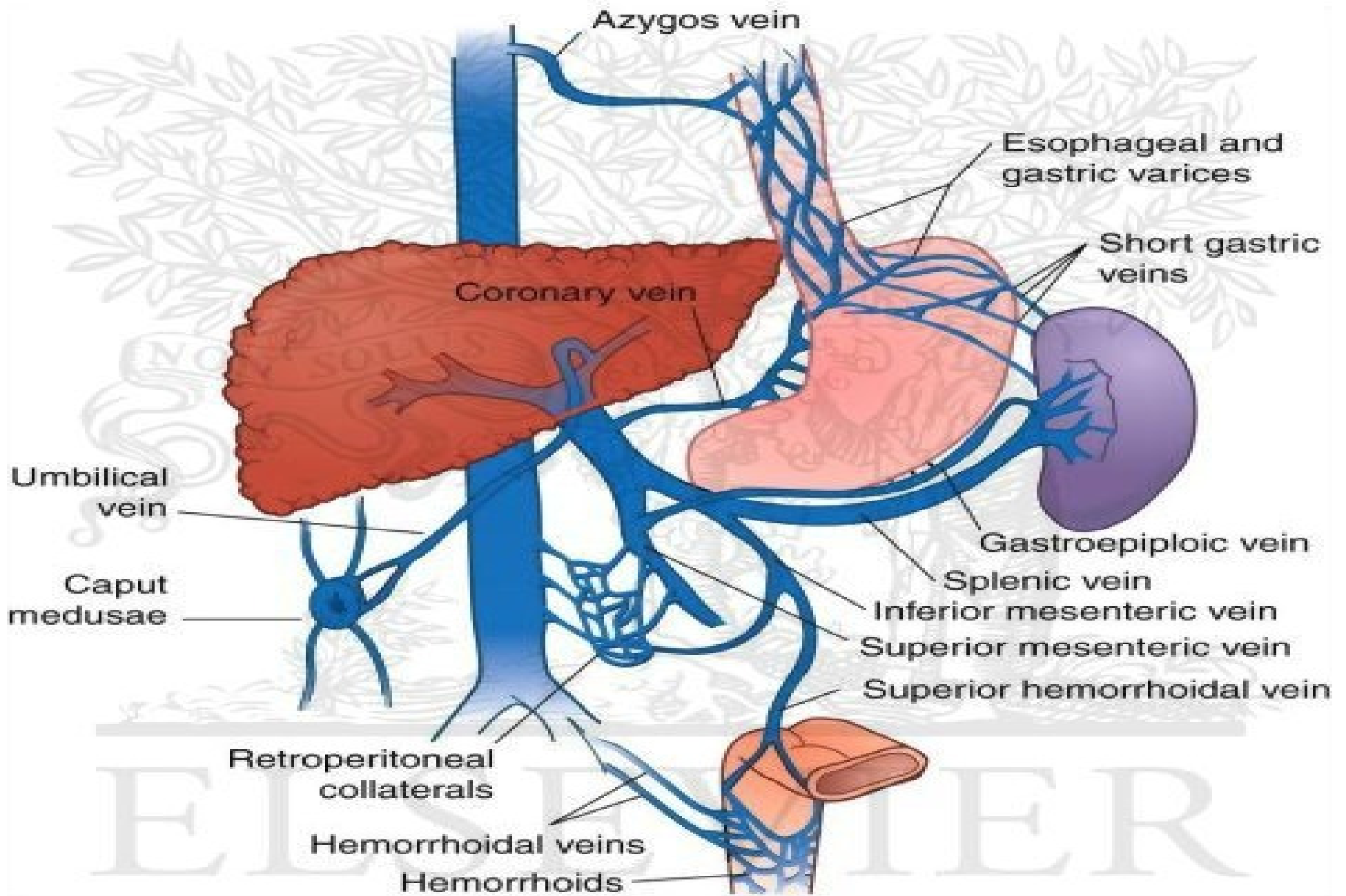
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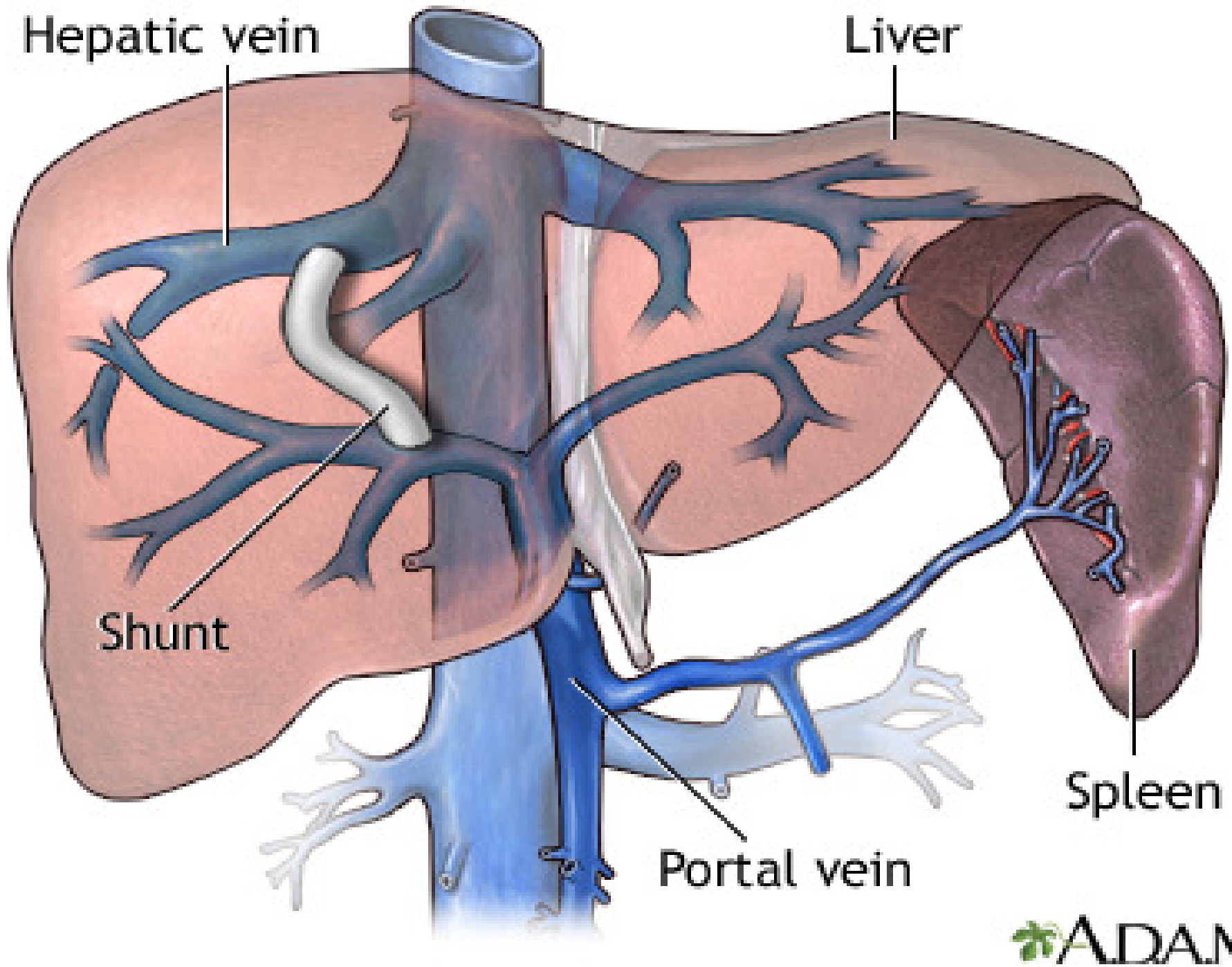


Biochemical explanation of Haemetemesis in chronic alcoholic

- Liver damage
- Less Plasma protein
- Less Albumin
- Less Fibrinogen store
- Less synthesis & store of clotting factor
- Less store of Vitamin K
- Portal Hypertension

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**1. Biochemical explanation
of
Edema
Ascites
Hypotension
in
Chronic alcoholic**

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filtration pressure = hydrostatic pressure - oncotic pressure

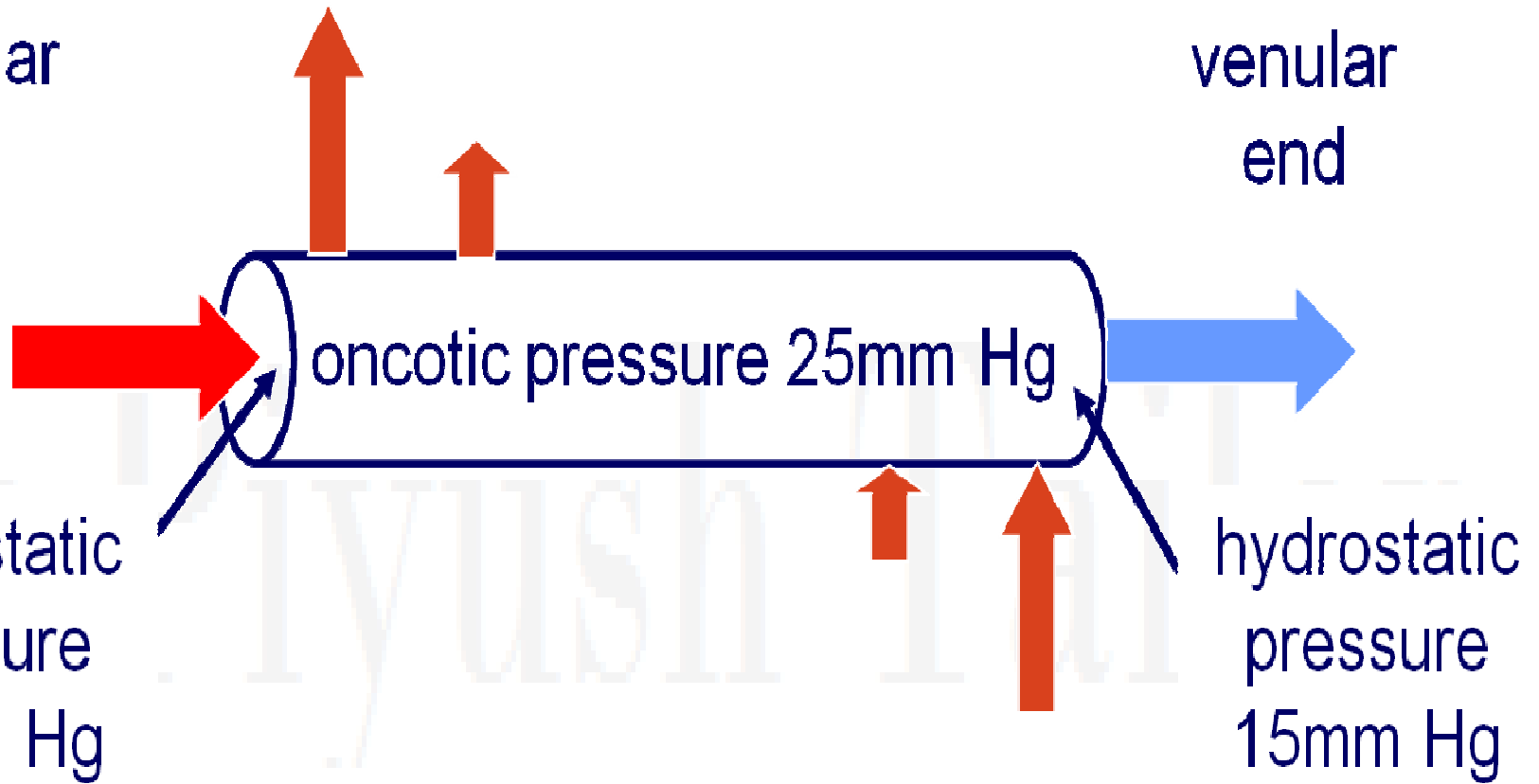
filtration at
arteriolar end

reabsorption at
venular end

arteriolar
end

venular
end

hydrostatic
pressure
35mm Hg



hydrostatic
pressure
15mm Hg

Hepato- Renal Syndrome

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Biochemical reason for giving following in patient of chronic alcoholic

- Dextrose plus thiamine
- Vitamin K
- 10% Albumin

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- Biochemical reason for giving following in patient of chronic alcoholic
 - Oral Neomycin (Anti-microbial, Antibiotic)

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Neomycin

KILL

Intestinal Flora (Lactobacilli)

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Intestinal flora produce Enzymes

➤ Urease

- (Urea - - - - - Ammonia)

➤ Protease & Peptidase

- (RBC – Haemoglobin – Globin – Protein – Amino acid – Ammonia)

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1. Biochemical reason for giving following in patient of chronic alcoholic
 - Liq Lactulose (Laxative)
 - Oral Phenylbutarate

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NDC 0121-0577-16

Lactulose Solution USP

10 g/15 mL


Each 15 mL contains: 10 g lactulose (and less than 1.6 g galactose, less than 1.2 g lactose, and 1.2 g or less of other sugars). Also contains FD&C Yellow No. 6, purified water, and flavoring. Sodium hydroxide used to adjust pH. The pH range is 2.5 to 6.5.

Dispense in original container or tight, light-resistant container with a child-resistant closure.

To the Pharmacist: When ordering this product, include the product number (or NDC) in the description.

Rx ONLY

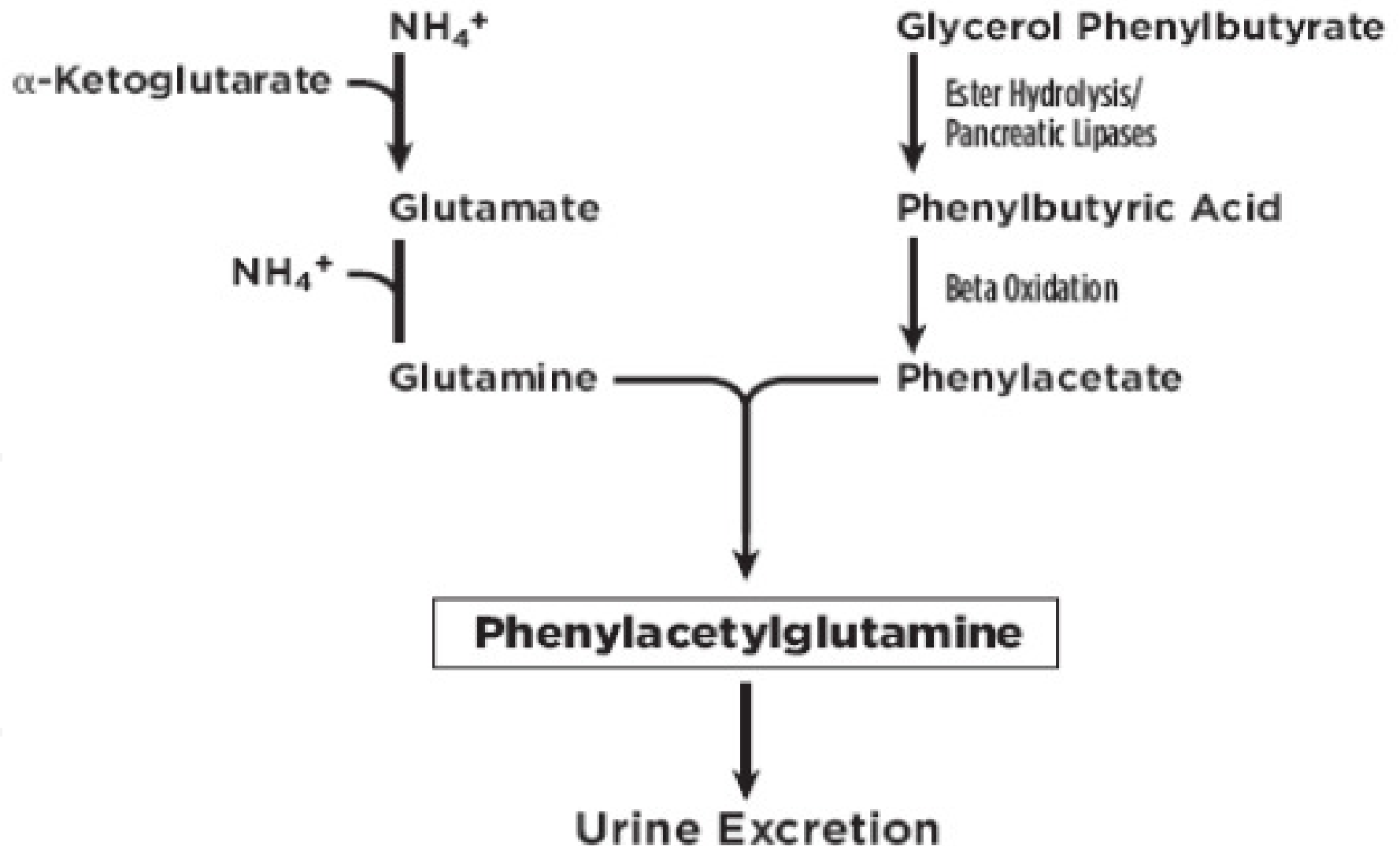
16 fl oz (473 mL)

 **Pharmaceutical
Associates, Inc.**
Greenville, SC 29605

- Lactulose = Synthetic disaccharide
- Each 15 ml of 10 gm Lactulose Solution
 - 1.6 gm Galactose
 - 1.2 gm Lactose
 - 0.1 gm Fructose

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Biochemical reason of **Phenylbutarate** in Hyperammonemia



Case 6

- A 54 year old obese person come in emergency with **altered consciousness level** and **increase respiratory rate (tachypnea)** for last 4 hours.
- He is having history of **uncontrolled diabetes mellitus** since 15 years, as he was not following any medical advice from physician. He was on **insulin therapy** for 3 years, but he was not taking regular dose of insulin. Patient's relative is telling that he is also having complain of **weakness and decrease urine output** for last 2 days.

On **General examination**, physician noted

- Dryness of mouth
- Pale & dry conjunctive
- Shrunken eye ball.
- Low volume pulse
- Tachypnea (increase respiratory rate)
- Tachycardia (increase heart rate)
- Very low blood pressure (70/40 mm Hg).

Doctor makes admission in ICU and asked immediately for blood investigation.

Laboratory Investigation

Parameter	Value	Reference range
RBS	500 mg/dl	140 mg/dl
Serum Acetone	10 mg/dl	<1 mg/dl
Serum Creatinine	2.5 mg/dl	0.4 - 1.4 mg/dl
Blood Urea	150 mg/dl	15 - 45 mg/dl
Serum Na ⁺	120 mmol/l	135 - 145 mmol/l
Serum K ⁺	6.0 mmol/l	3.5 - 5.0 mmol/l
pH	7.1	7.35 - 7.45
pO ₂	95 mmHg	90 - 100 mmHg
pCO ₂	24 mmHg	32 - 40 mmHg
HCO ₃ ⁻ (Bicarbonate)	12 mmol/l	24 - 32 mmol/l

Diagnosed = “**Diabetic ketoacidosis with acute renal failure**”

Advised to following **treatment**.

- **Inj normal saline** fast I.V. (4-5 litre in 1st 24 hrs)
Until systolic blood pressure reaches to normal
- **Inj Human Insulin** injection slow infusion I.V.
As per blood sugar level
- **Inj Bicarbonate** 200 ml I.V.
- **K⁺ Binding resin** Sachets Orally.
- Urinary catheterization done.
- But urine output is nil

- To follow below **protocol for treatment** of this patient.
- If RBS > 200 mg/dl ---> Give Normal Saline + Human Insulin
- If RBS < 200 mg/dl ---> Give Dextrose Saline + Human Insulin

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Doctor asked to

repeat following investigation

during management

- RBS every 2 hourly.
- Serum K⁺ level after 4 hours.
- Arterial Blood Gas analysis after 6 hours (if require)

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24 hours after admission and intensive care

He get consciousness, normal respiration ,
normal blood pressure & 1200 ml of urine output.

- RBS = 150 mg% with Human insulin infusion
- Serum acetone = 2 mg/dl
- Electrolyte and ABG = Normal.

He shifted to ward & remained admitted for 5
days in hospital.

On discharge, physician advises to take prescribe
insulin dose regularly as well as regular follow up
with FBS & PP2BS.

Question Case 6

1. Give explanation for altered consciousness and increase respiratory rate in this case.
2. What metabolic and functional abnormality can occur due to increase acetone level?
3. Why after 24 hours serum acetone came down nearer to normal level?
4. What is patho-physiology behind decrease urine output in this patient?
5. Give comment on patient ABG report.
6. Give biochemical reason for increase K^+ level in this case.
7. What is biochemical reason for giving dextrose saline plus human insulin infusion if RBS is below 200 mg%?
8. How bicarbonate, insulin and K^+ binding resin reduce serum potassium level?

Answer Case 6

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Give explanation for altered consciousness and increase respiratory rate in this case.

➤ **Reason of Unconsciousness in DKA**

- Dehydration
- Shock

➤ **Reason of Tachypnea in DKA**

- Metabolic acidosis
- Due to compensatory response after carotid receptor stimulation

What metabolic and functional abnormality can occur due to increase acetone level?

Decrease Blood pressure

Decrease cardiac contractility

Alteration in cardiac rhythm

Arterial vasodilation and hypotension

Increase insulin resistance

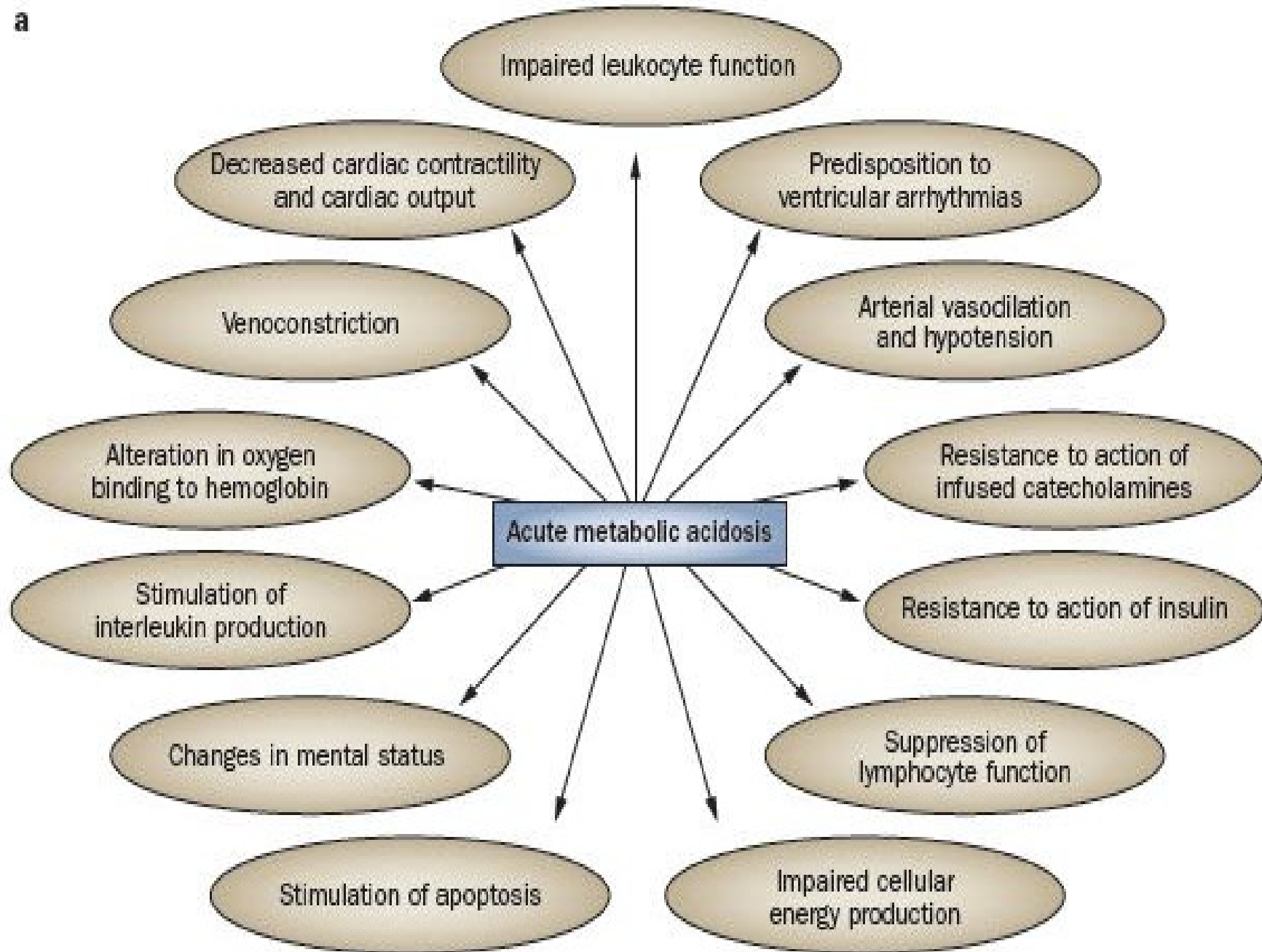
Alteration in Oxygen binding capacity

Impair consciousness level

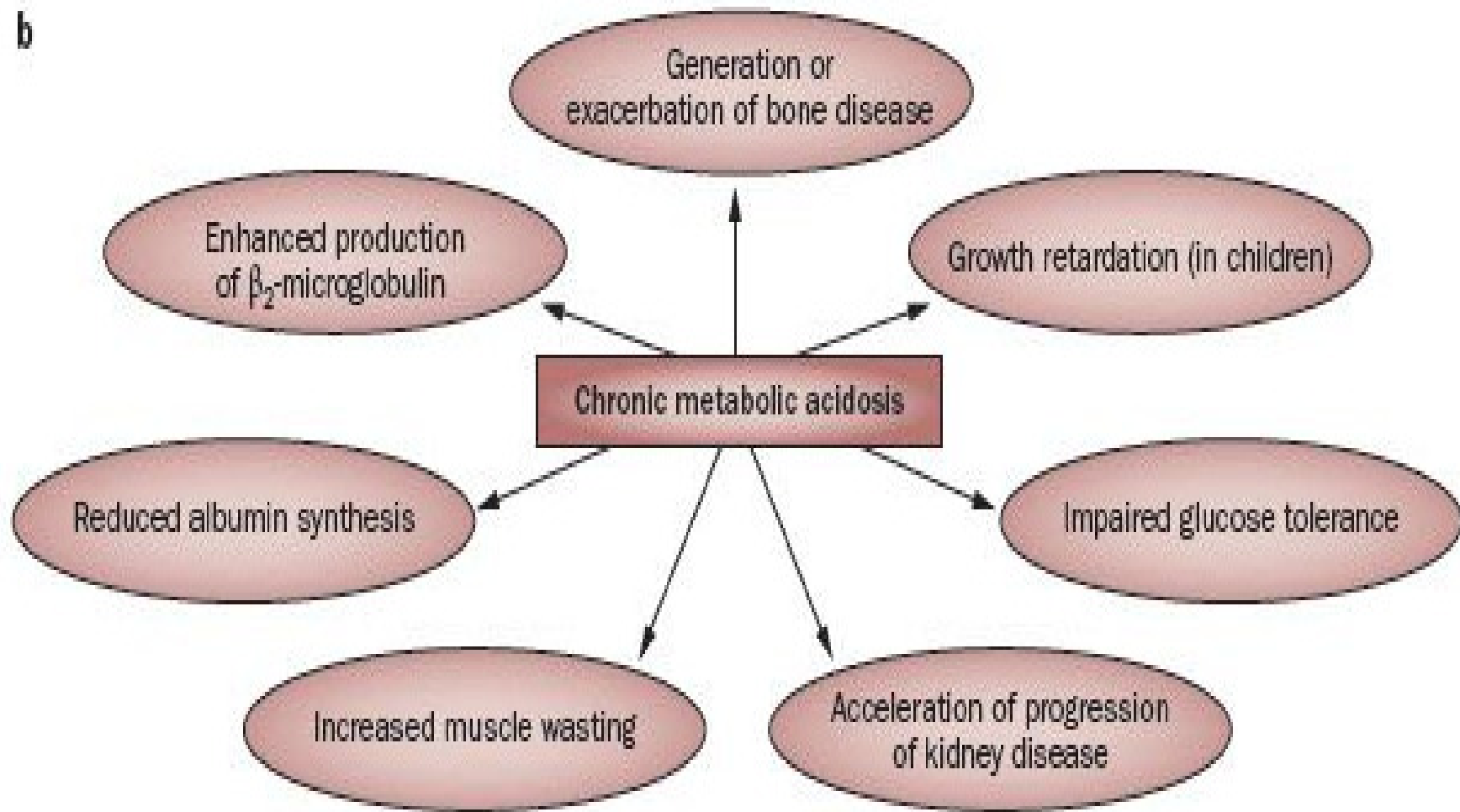
Suppressed lymphocyte function

Impaired cellular energy production

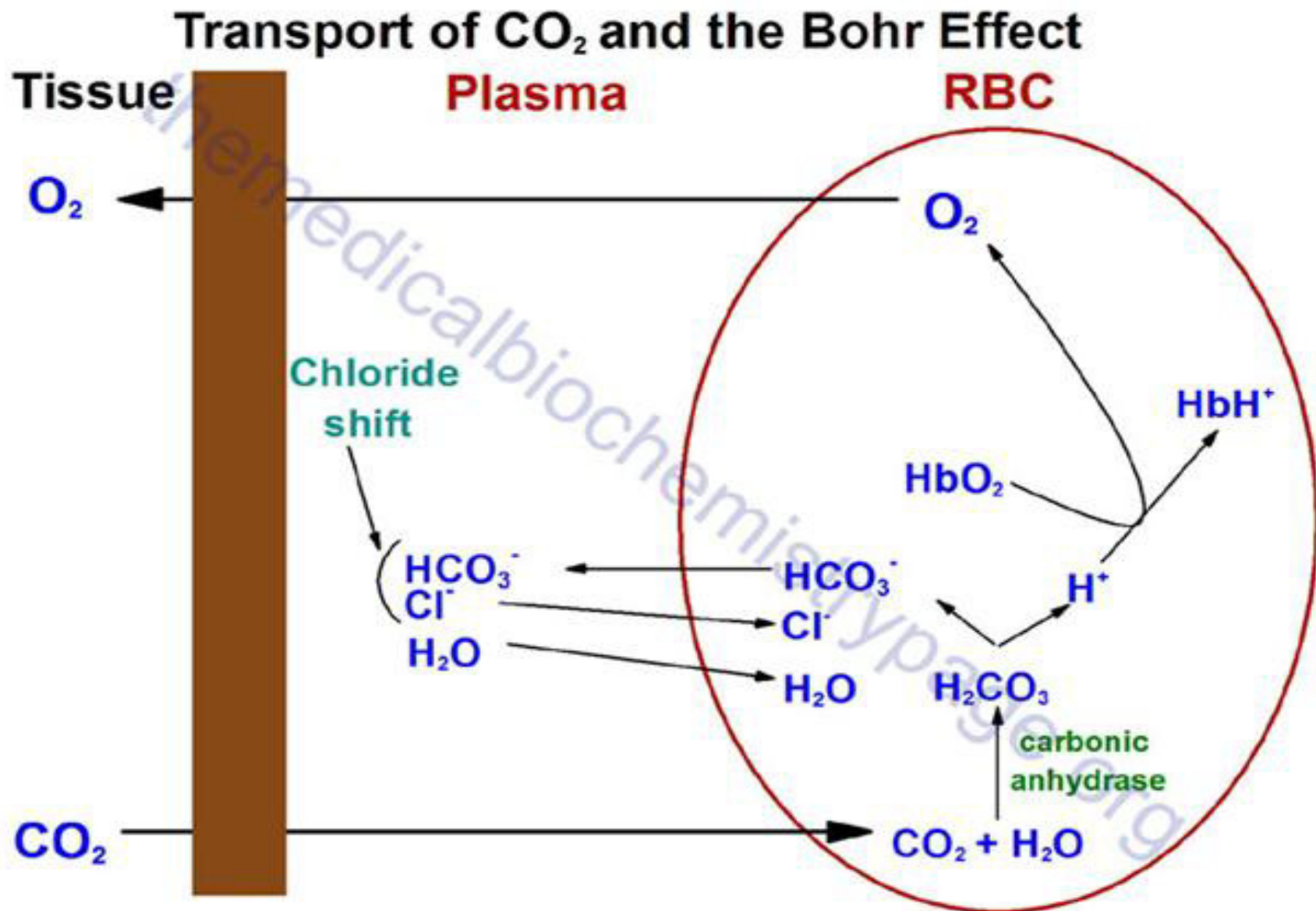
a

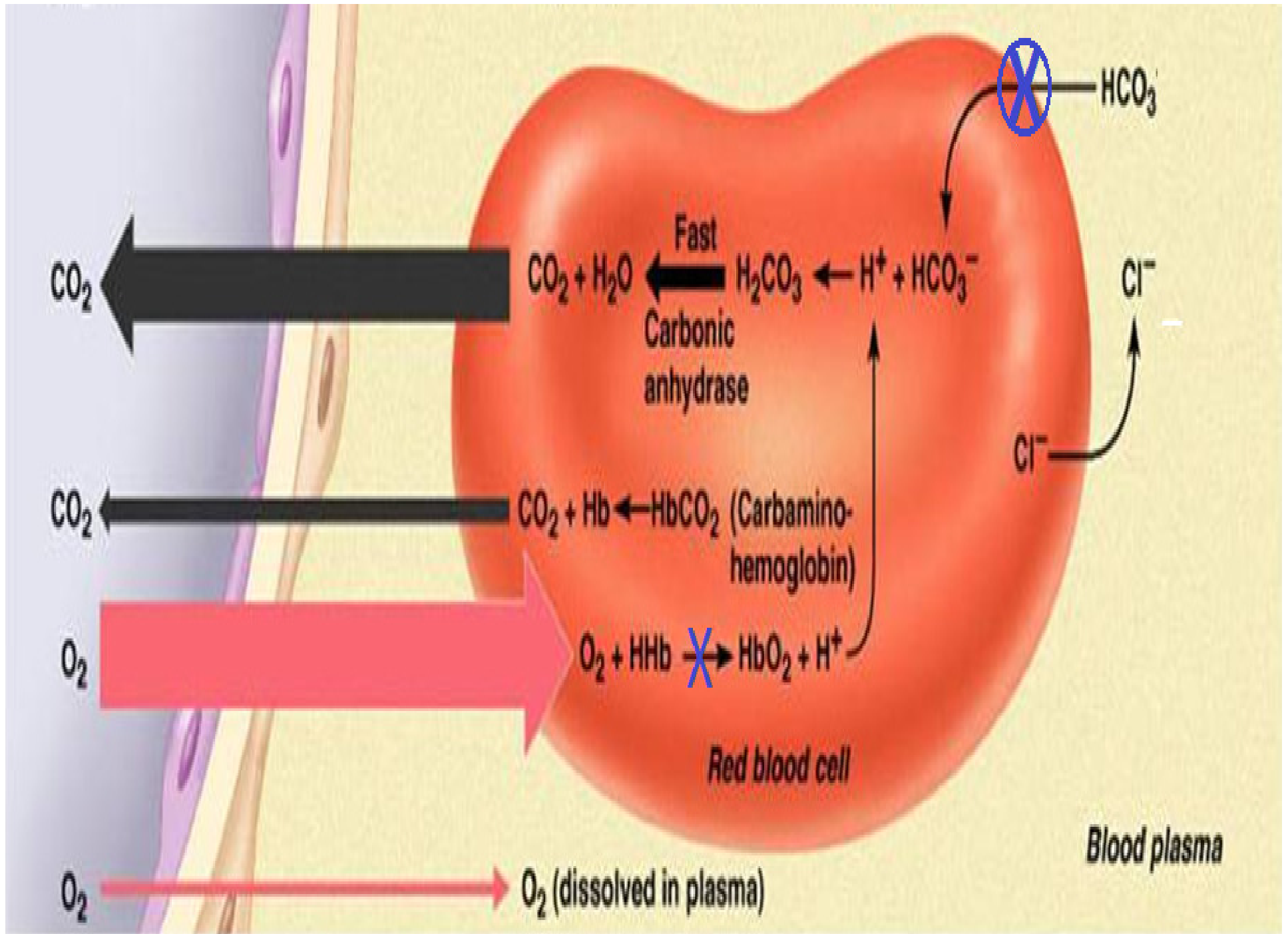


b



Effect of Acidosis on O₂- CO₂





Why after 24 hours serum acetone came down nearer to normal level?

Is it because of >>>>>>> ????

1. Normal saline ?
2. Insulin ?
3. Dextrose ?

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What is patho-physiology behind decrease urine output in this patient?

1. Dehydration
2. Hypotension
3. Decrease renal flow
4. Pre-Renal – Acute renal failure

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Give comment on patient ABG report.

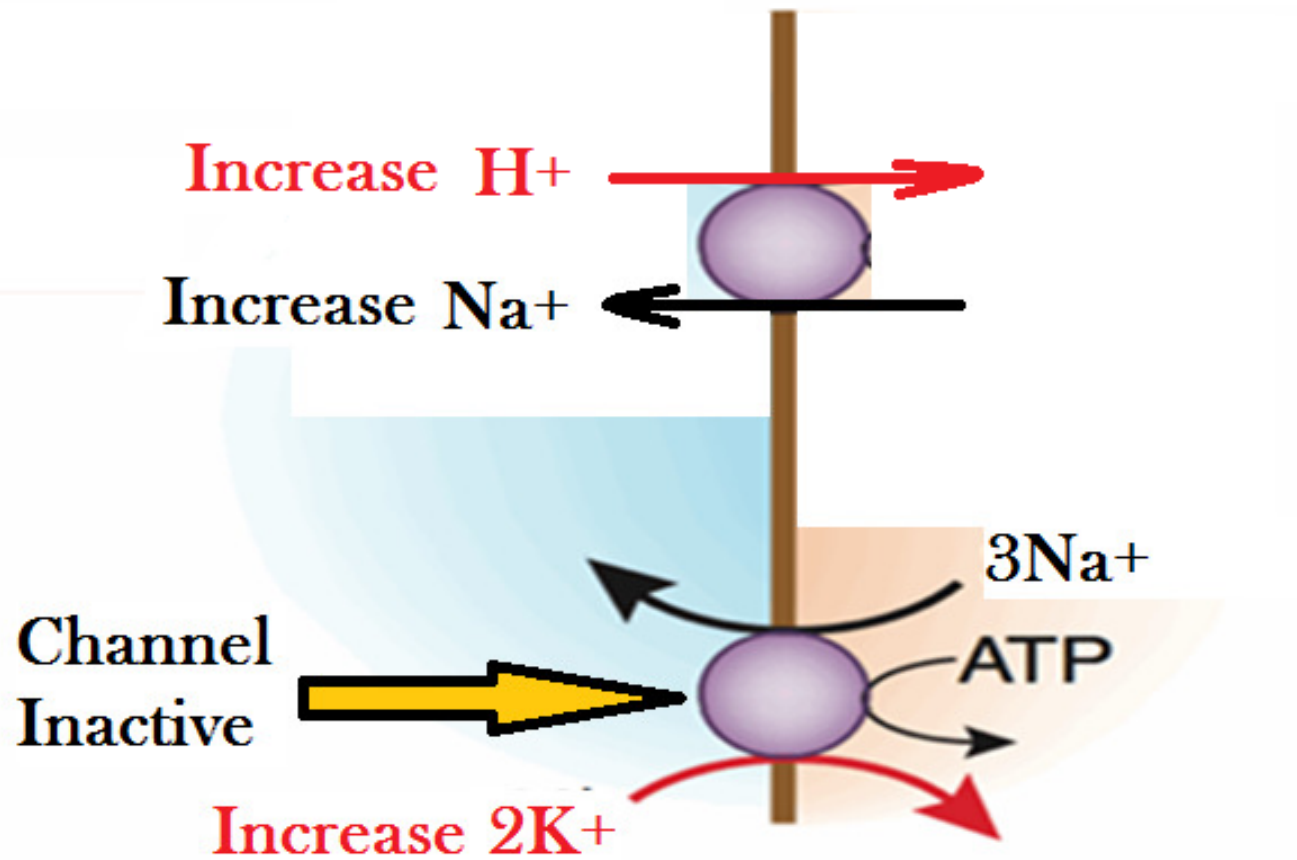
	Value	Ref. Value	Interpretation
pH	7.1	7.35 - 7.45	Low Acidosis
pO ₂	95	90 - 100 mmHg	Normal
pCO ₂	24	32 - 40 mmHg	Low Indicate Alkalosis. (Compensatory)
HCO ₃ ⁻	12	24 - 32 mmol/l	Low Indicate Acidosis

Uncompensated Metabolic Acidosis

Acidosis (Increase H^+) increase K^+

Extracellular (Plasma)

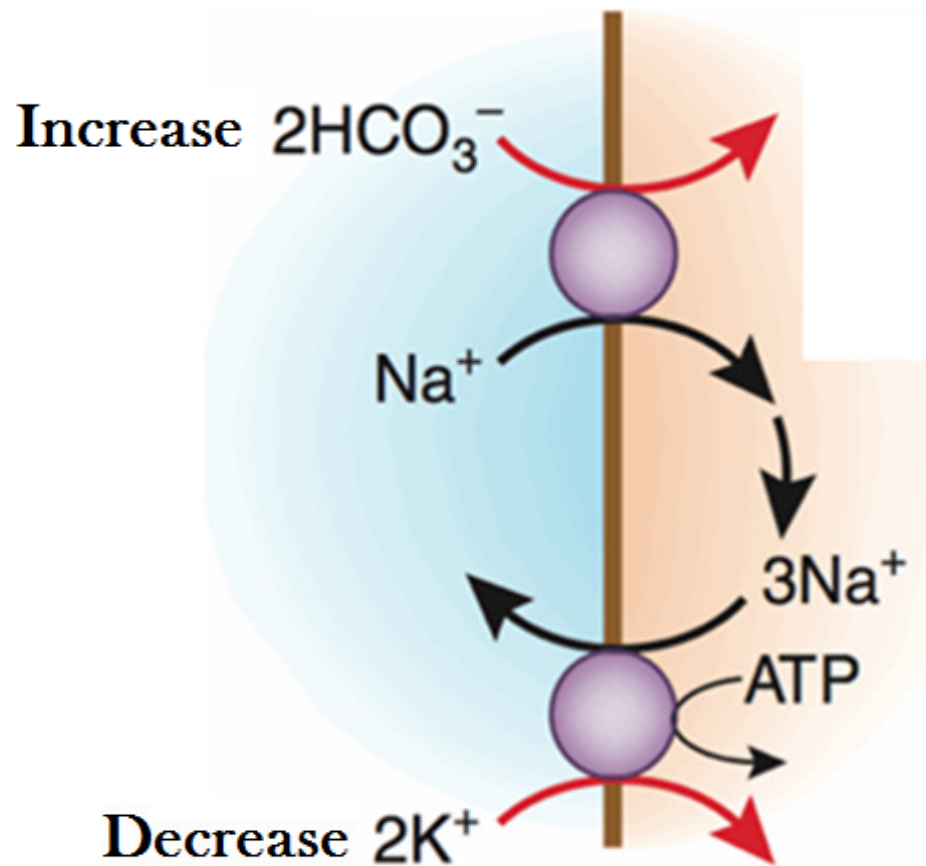
Intracellular



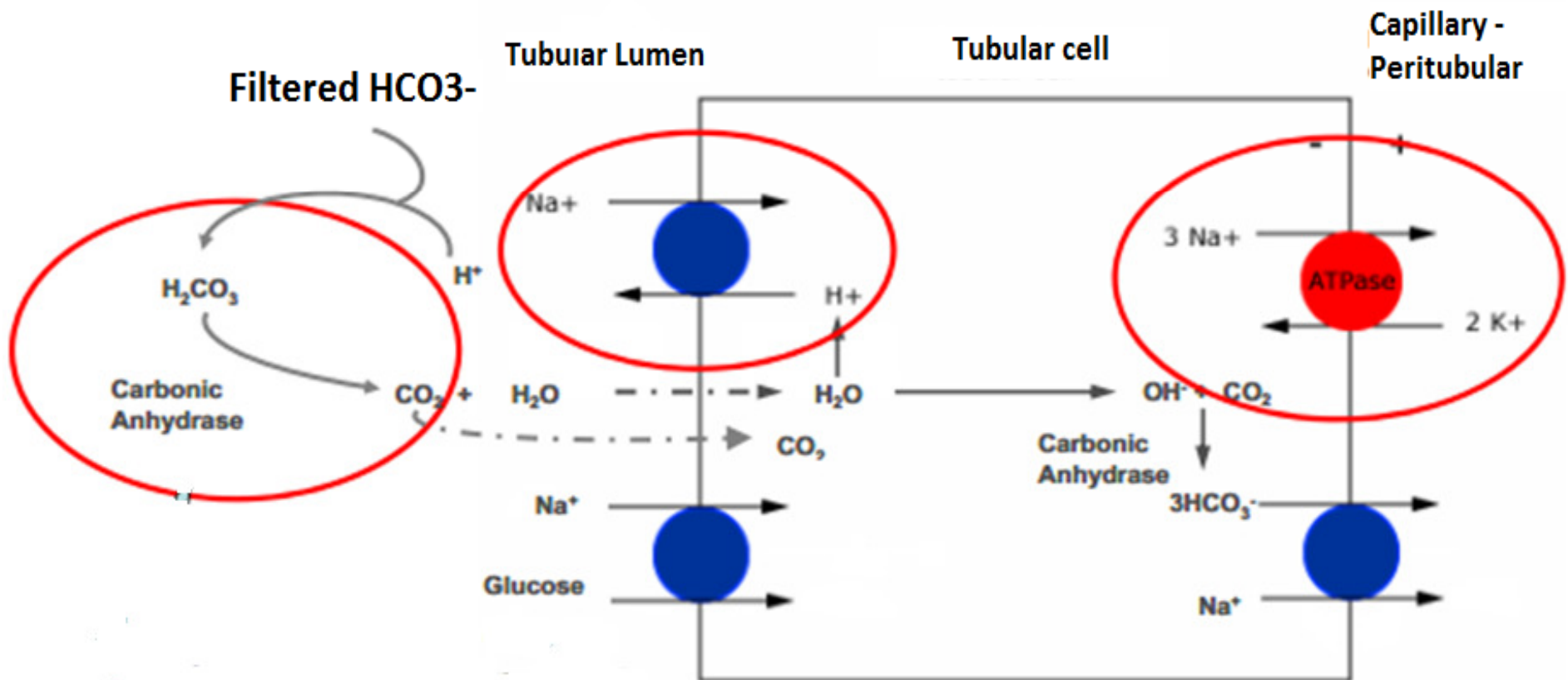
Bicarbonate correct plasma hyperkalemia

Extracellular (Plasma)

Intracellular



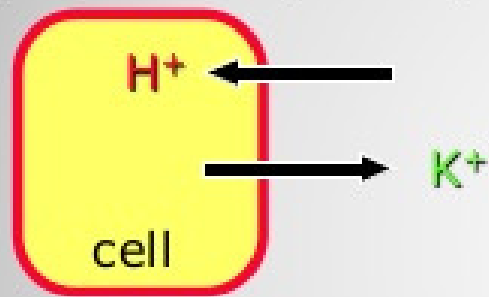
Renal Mechanism of H^+ excretion & HCO_3^- reabsorption



ELECTROLYTE SHIFTS

Acidosis

Compensatory Response

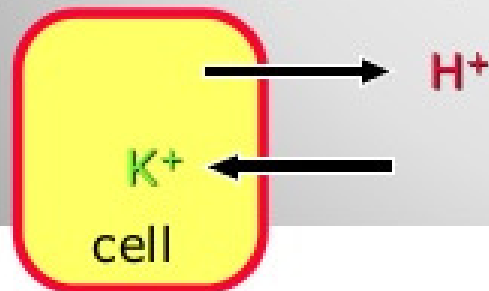


Result

- H⁺ buffered intracellularly
- Hyperkalemia

Alkalosis

Compensatory Response



Result

- Tendency to correct alkalosis
- Hypokalemia

What is biochemical reason for giving dextrose saline plus human insulin infusion if RBS is below 200 mg%?

What should be physician priority to correct earliest in DKA?

- Hyperglycemia?
- Acidosis due to acetone?
- Hyperkalemia due acidosis due to acetone?
- Hypotension due to dehydration due to acetone & glucose?

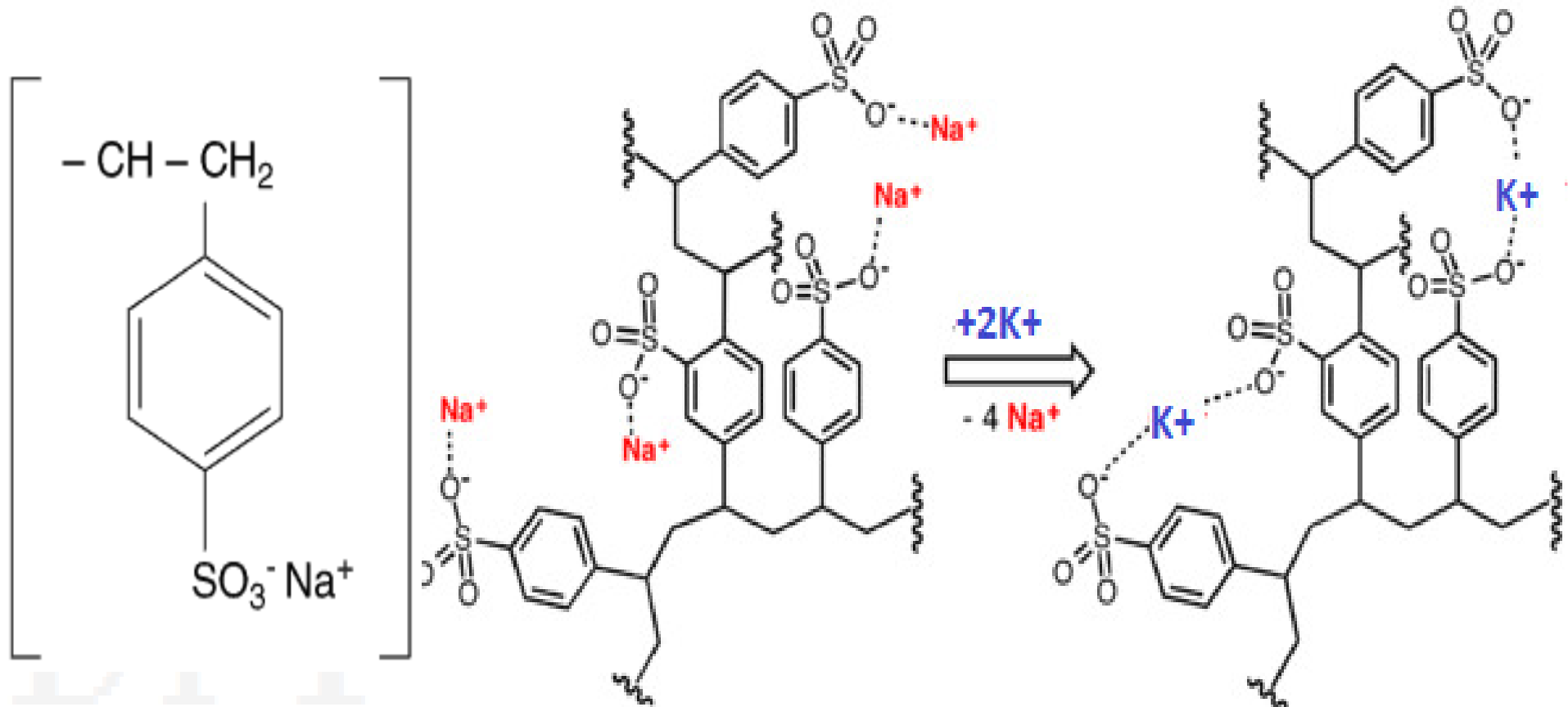
Which molecule come to normal level easily and faster with insulin ?

- Glucose
- Potassium
- Acetone
- H⁺

Would you like to give insulin for

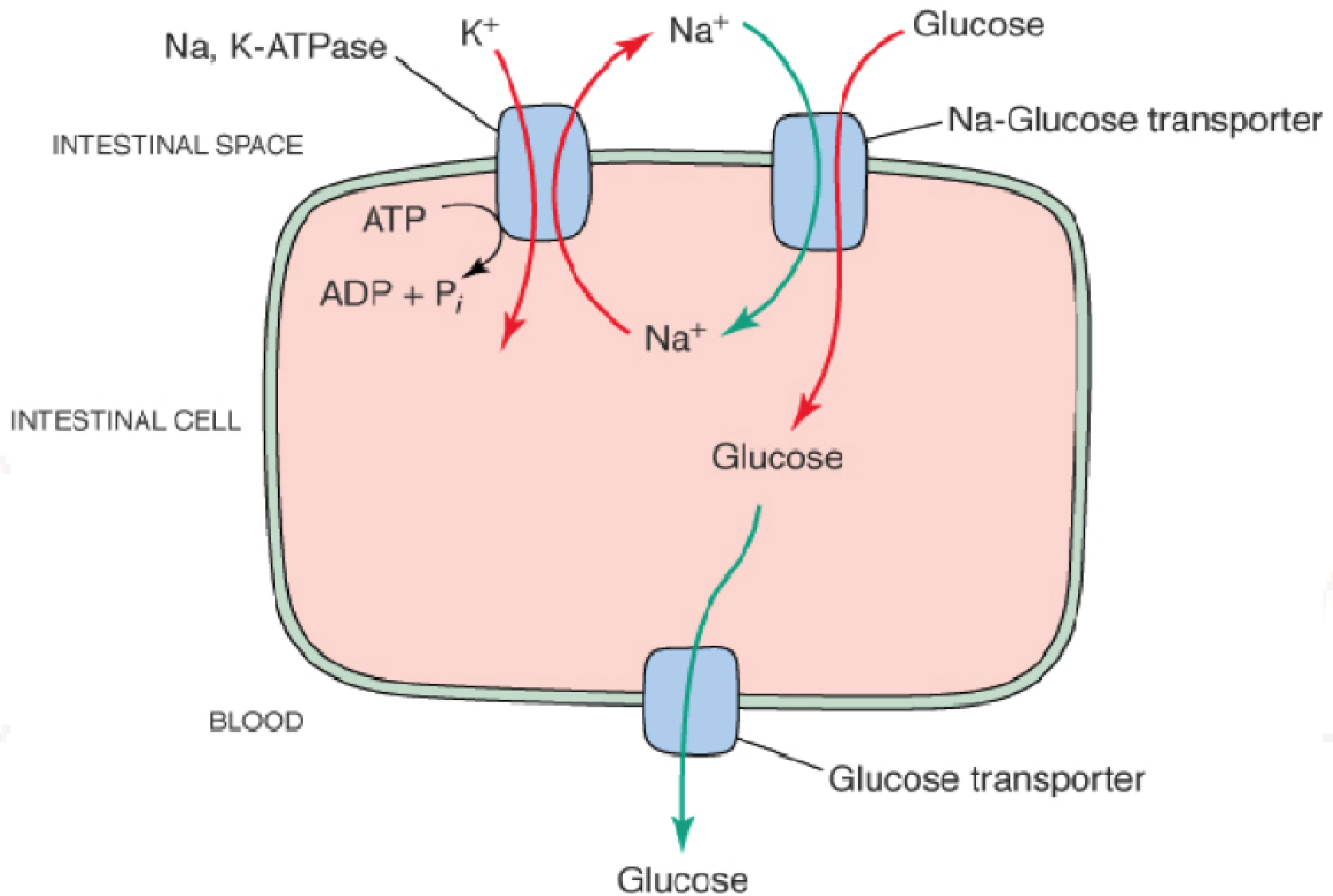
- Shorter period?
- Longer period?

How bicarbonate, insulin and K⁺ binding resin reduce serum potassium level?



Sodium Polystyrene Sulfonate Cation Resin

Insulin stimulate S.GLUT receptor

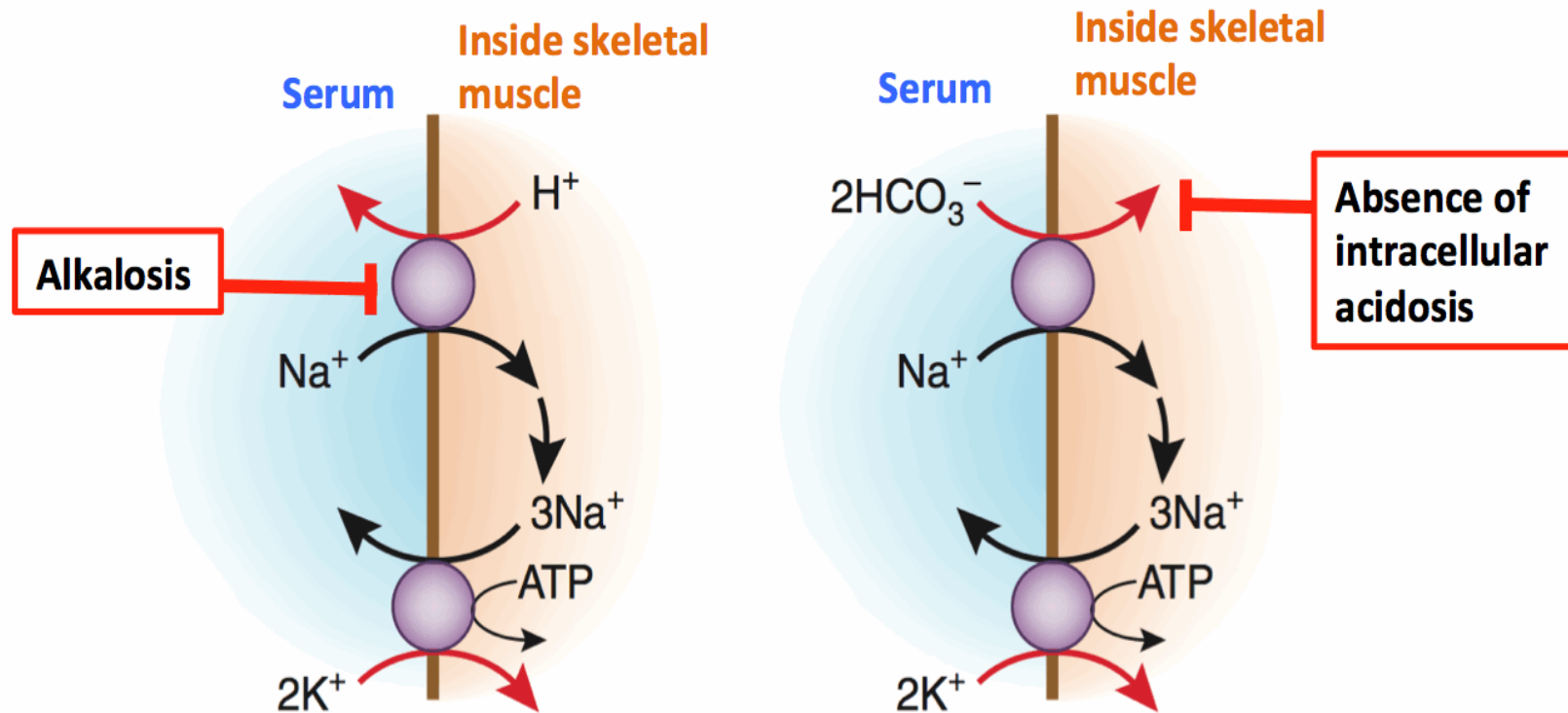


Potassium correction with HCO₃⁻

Bicarbonate-induced potassium shift is less effective in alkalosis

H⁺/K⁺ exchange

HCO₃⁻/K⁺ cotransport



Modified from Aronson PS and Giebisch G, J Am Soc Nephrol 2011 22:1981

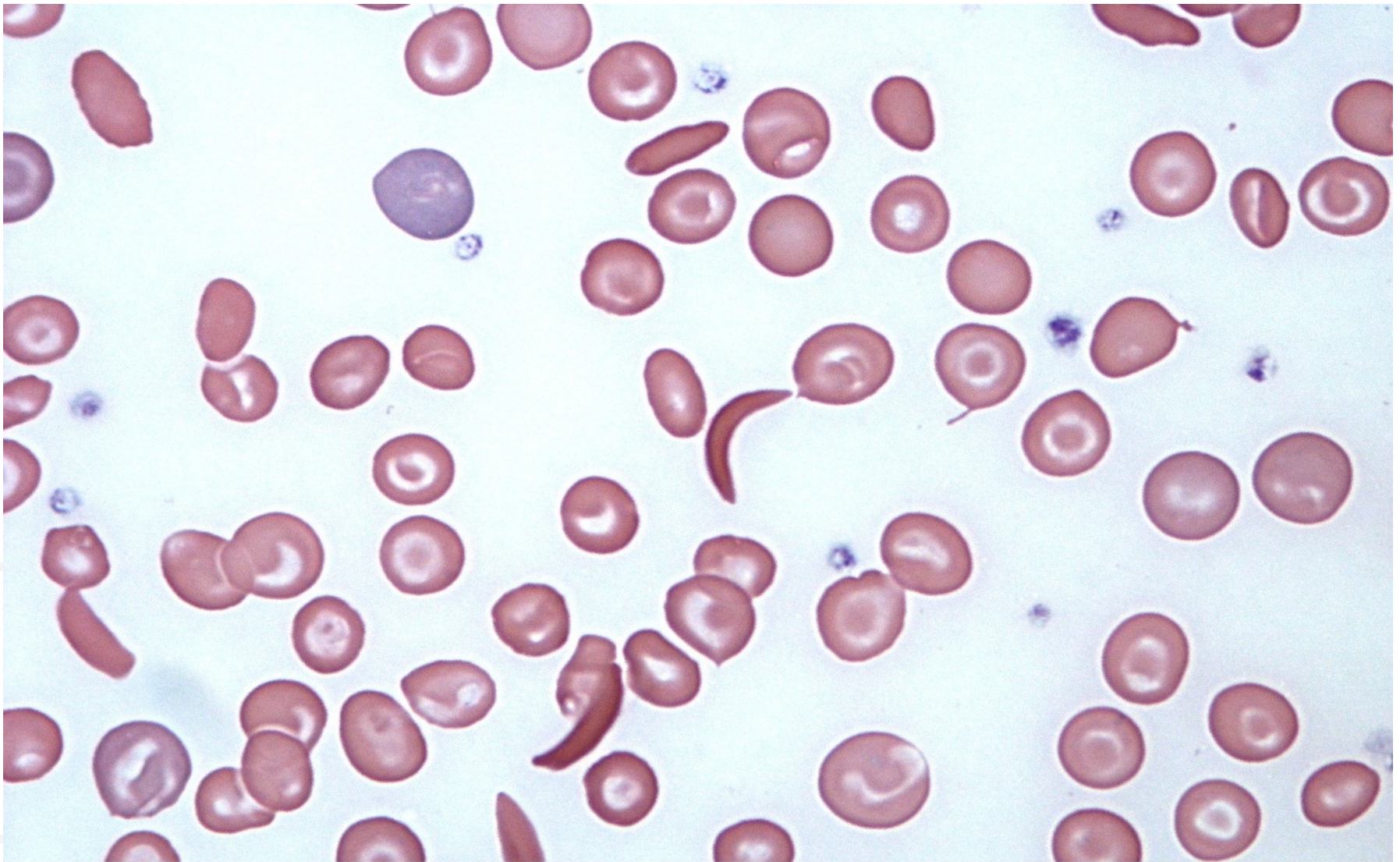
Case 7

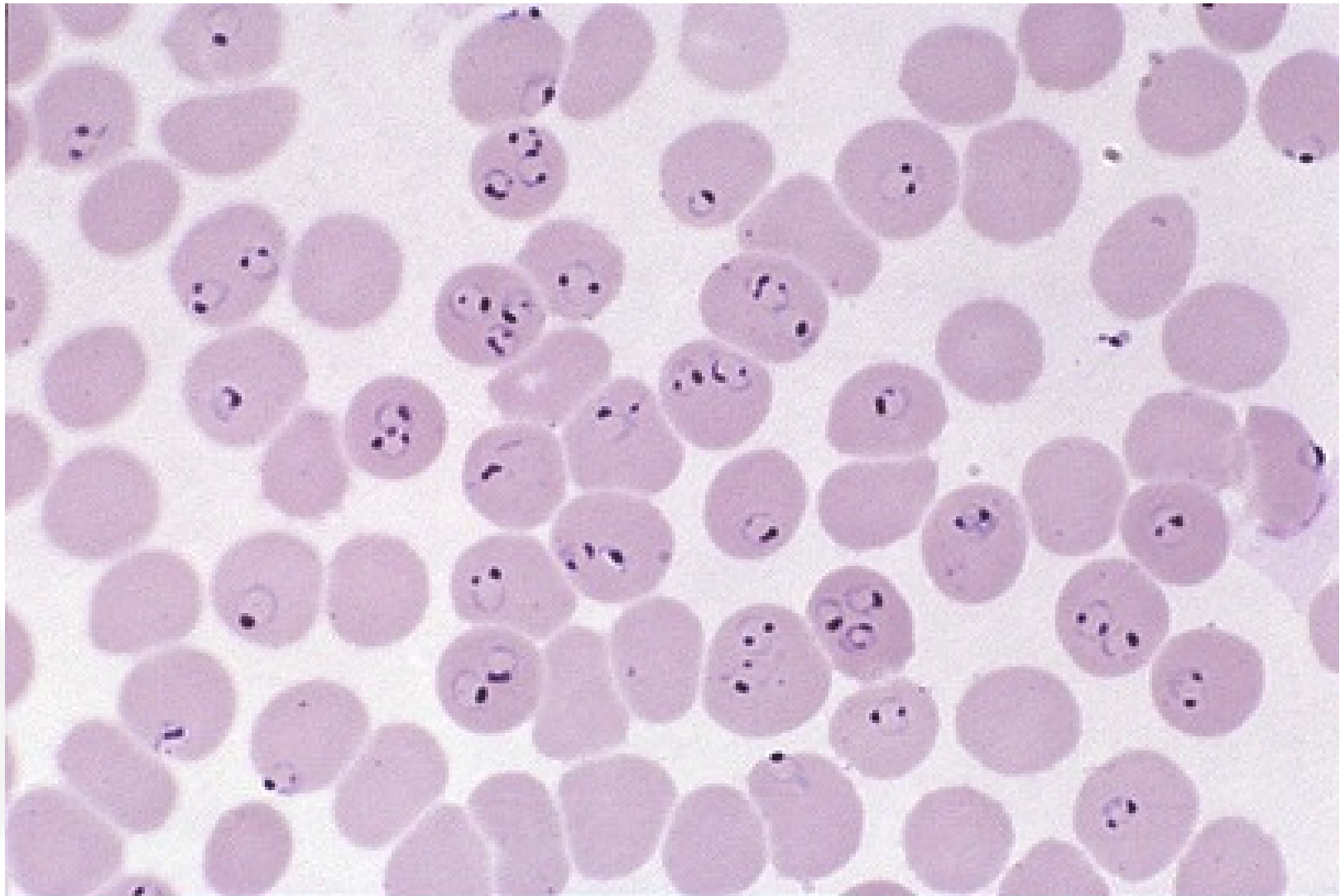
- 14 years male child come in emergency with complain of
 - Acute abdominal pain since 12 hours
 - Acute hip joint pain since 2 days
 - High grade fever with Rigor since 3 days
- Pediatrician examined patient. He asked for ICU admission and for following investigation

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Laboratory Investigation

Parameter	Value	Reference range
Haemoglobin	6.5 gm%	12 – 16 gm%
WBC	12000	4000-11000/cu.mm
Peripheral Smear examination	Sickle shape RBC & Schizonts of Plasmodium Vivex Seen	
S.Total Billirubin	3.4 mg%	0.2 – 1.2 mg%
S.Direct Billirubin	0.8 mg%	0.1 – 0.2 mg%
S.Indirect Billirubin	2.6 mg%	0.2 – 1.0 mg%
S. ALT	40 IU/L	0 – 45 IU/L
S. Alkaline Phosphatase	950 IU/L	80 – 240 IU/L
S.LDH	2000 IU/L	150 – 350 IU/L



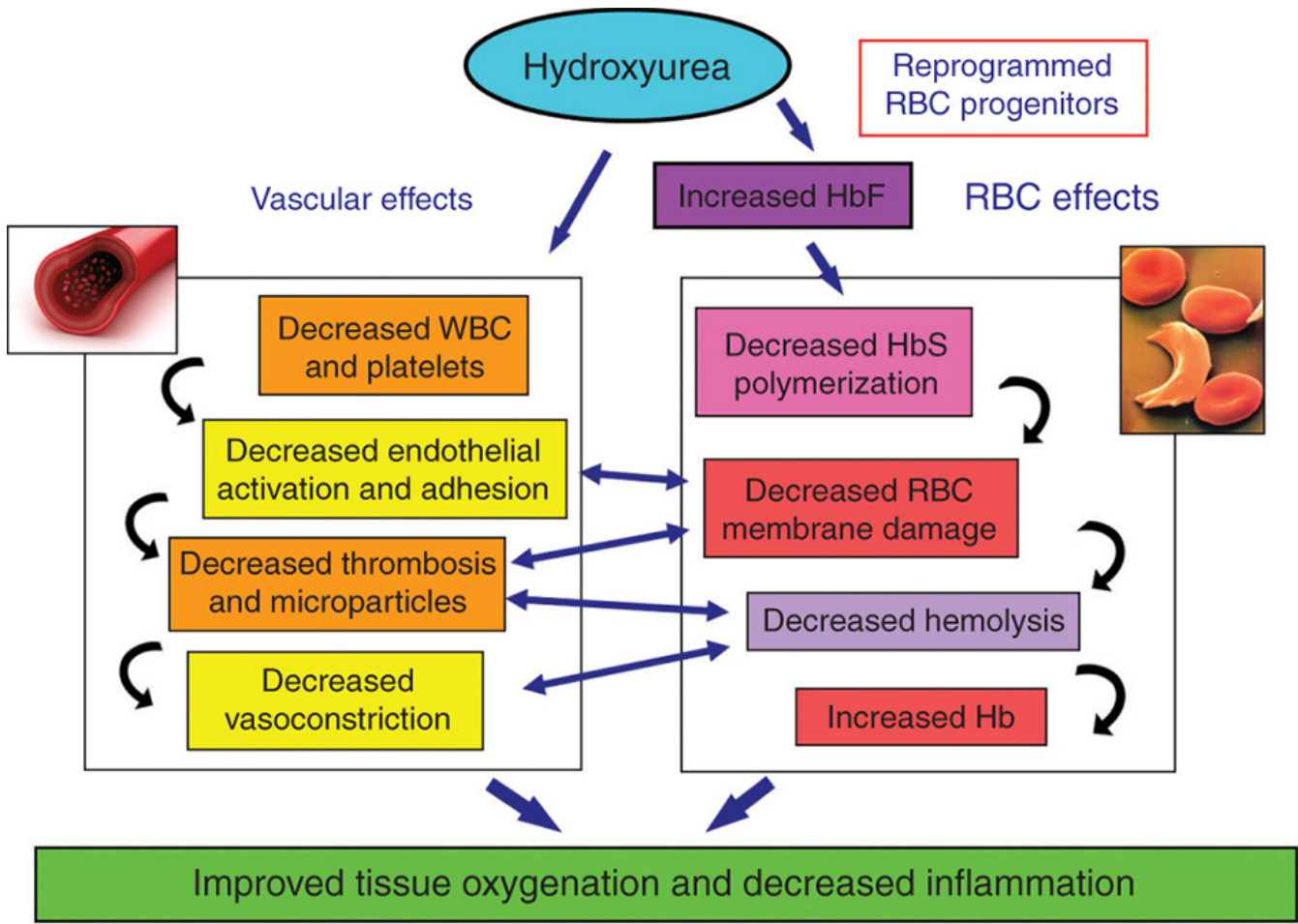


Wellcome Images

Diagnosis

Plasmodium Vivex with Sickle cell crisis

- Following Treatment is given
- Oxygen inhalation
- Inj ArtesunateIV 12 hourly
- Inj ParacetamolIV
- Inj Normal SalineIV
- Inj Whole Blood IV trasfusion
- Tab Hydroxyurea 500 mg twice day orally



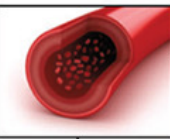
Hydroxyurea

Reprogrammed RBC progenitors

Vascular effects

Increased HbF

RBC effects



- Decreased WBC and platelets
- Decreased endothelial activation and adhesion
- Decreased thrombosis and microparticles
- Decreased vasoconstriction



- Decreased HbS polymerization
- Decreased RBC membrane damage
- Decreased hemolysis
- Increased Hb

Improved tissue oxygenation and decreased inflammation

- A mother came to a pediatric clinic with her 6 month old male child, who was on breast feeding. He was taking breast feeding every 2 hourly. Pediatrician advised mother to give start artificial diet simultaneously.
- He advised to give some liquid food and start giving semi solid and crushed food material.
- After initial liquid food material, pediatrician advise to give
 - Artificial Milk with Nutritional Powder having DHA
 - Crushed Rice + Dal + Ghee
 - Jaggary + Ghee
 - Crushed Apple + Banana

Dr Piyush Tailor

- What are the important carbohydrate nutrient & protein nutrient in milk?
- What is DHA ?

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- 3 years old boy came in civil hospital with
- How to calculate daily requirement?
- Why does he require high protein diet?
- What are
- What is role of essential fatty acid in growing child?

Dr. Piyush Tailor