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 ca2+ and protein phosphorylation play role in pathogesis of AD.

Case 4

1. Early in the morning, 40 years old male patient came in emergency with complain of chest pain, perspiration and altered consciousness for 4 hours.
2. 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 food intake

Case 4

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

Case 4

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

Investigation

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

Question Case 4

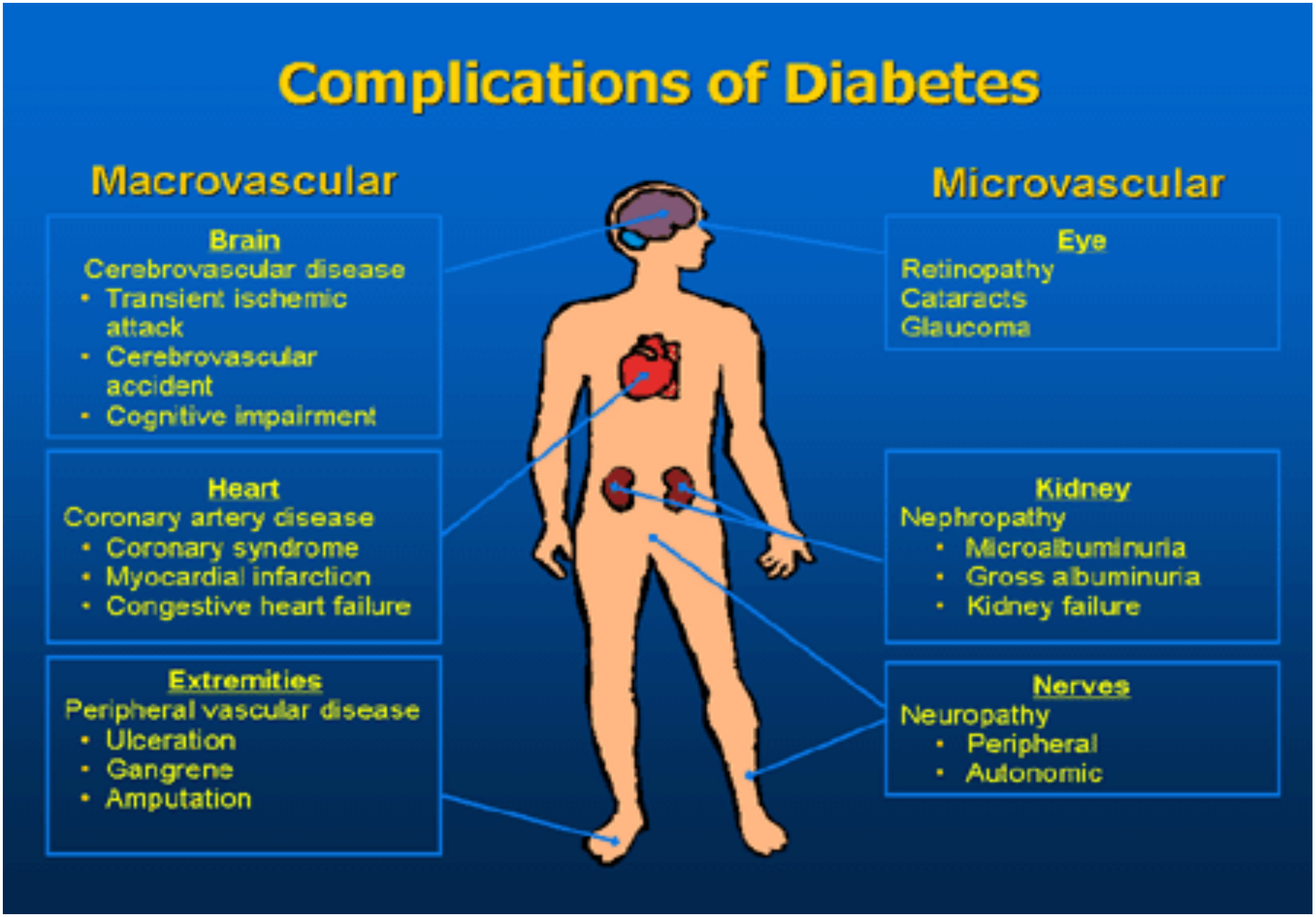
1. What are chronic complication of DM?
2. Why uncontroled diabetic mellitus increase chances of atherosclerosis?
3. What is cardiac function test?
4. Which test will you prefer to do for diagnosis of myocardial infarction, if patient come after 4 day of onset of chest pain?
5. How statin reduce cholesterol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

Question Case 4

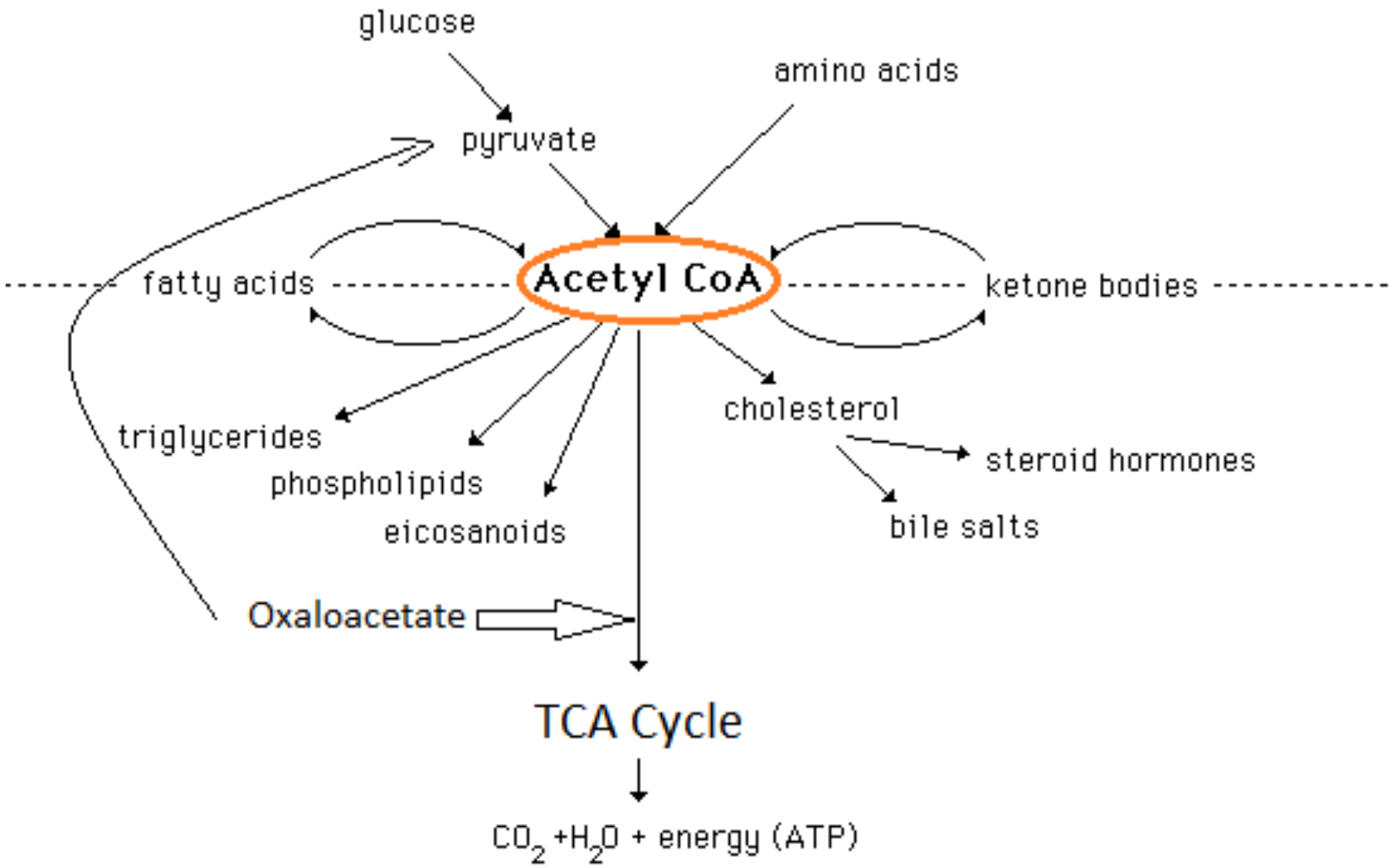
6. What is biochemical explanation of hypoglycemia?
7. Why physician asked to give injectable 50% Dextrose saline with Thiamine (Vitamin B1)?
8. What is role of fruits and fiber in chronic diabetes mellitus and atherosclerosis?
9. Why blood sample for blood sugar estimation is collected in fluoride containing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

What are chronic complication of DM?

What are chronic complication of DM?



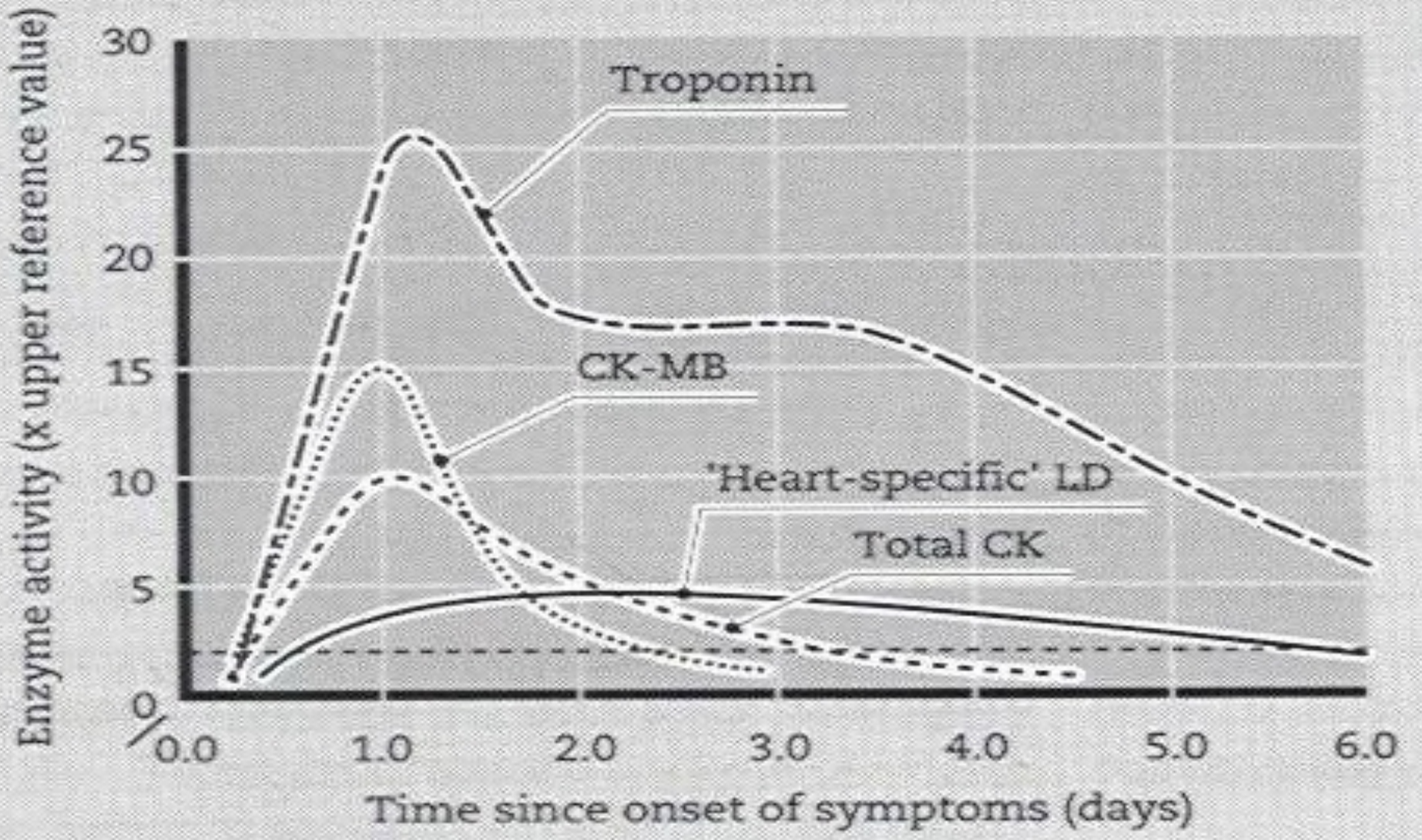
Why uncontroled diabetic mellitus increase chances of atherosclerosis?


glucose
amino acids
pyruvate
fatty acids
Acetyl CoA
ketone bodies
triglycerides
phospholipids
eicosanoids
cholesterol
steroid hormones
bile salts
Oxaloacetate
TCA Cycle
CO_2 +H_2O + energy (ATP)

6. What is cardiac function test?

6. Which test will you prefer to do for diagnosis of myocardial infarction, if patient come after 5 day of onset of chest pain?

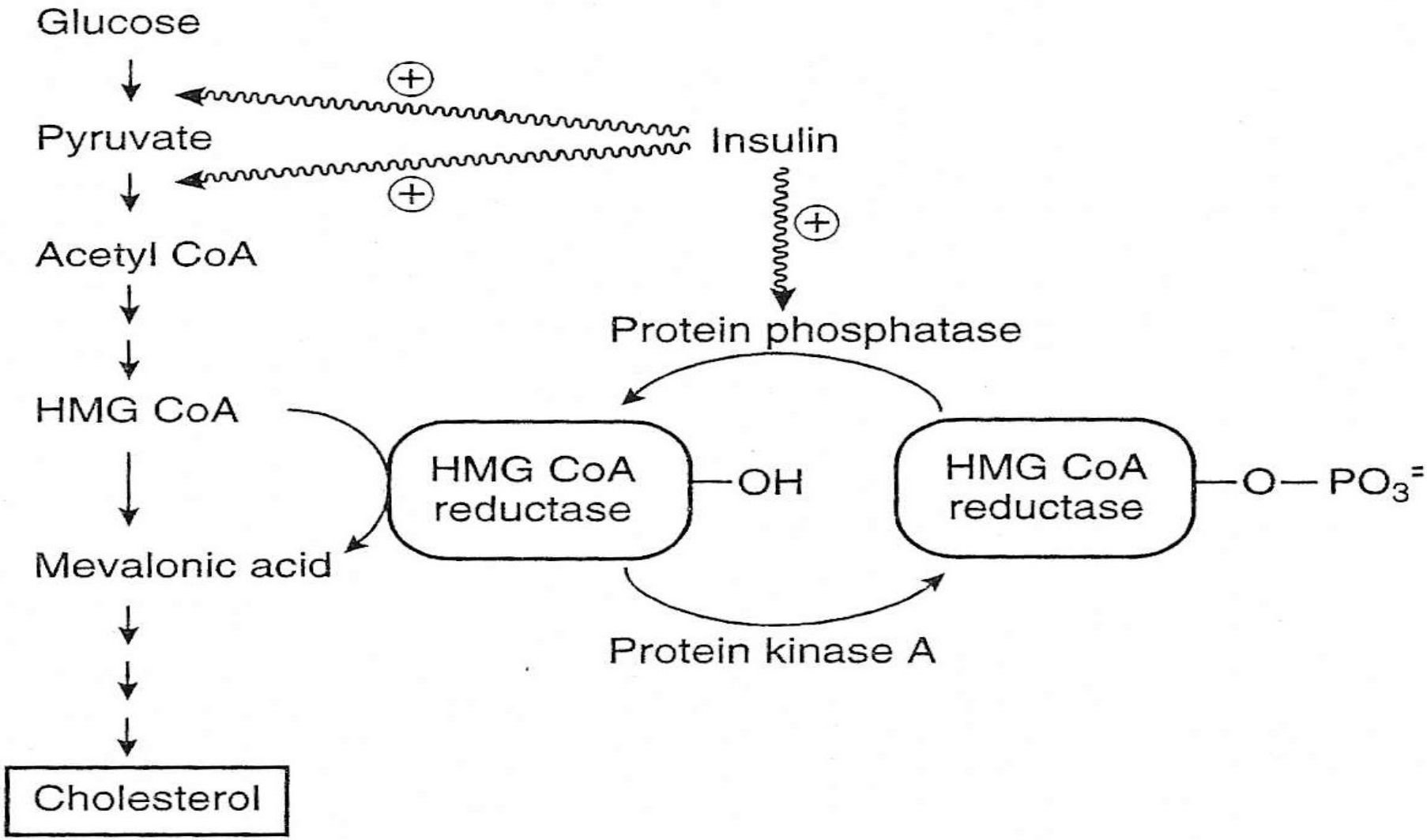
ENZYME ACTIVITY AFTER MYOCARDIAL INFARCTION



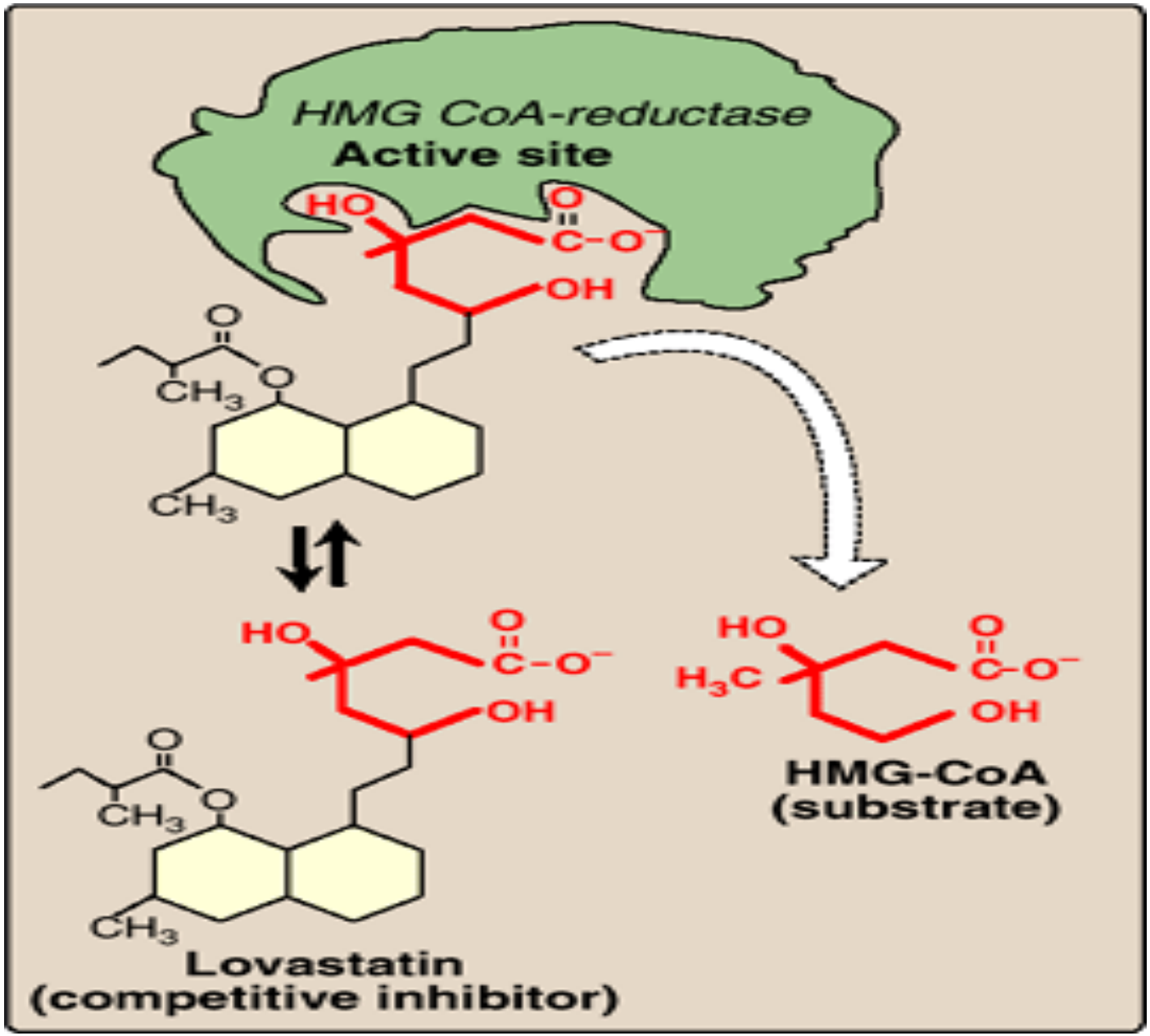
Type of LDH	Composition	Fraction of LDH in %	Location
LDH 1	HHHH	20-30 %	Myocardium
LDH 2	HHHM	30-40%	RBC
LDH 3	HHMM	20-25%	Lung
LDH 4	HMMM	10-15%	Kidney & Pancrease
LDH 5	MMMM	5-15%	Skeletal muscle & Liver

- How statin reduce cholesterol level?

Cholesterol Regulation

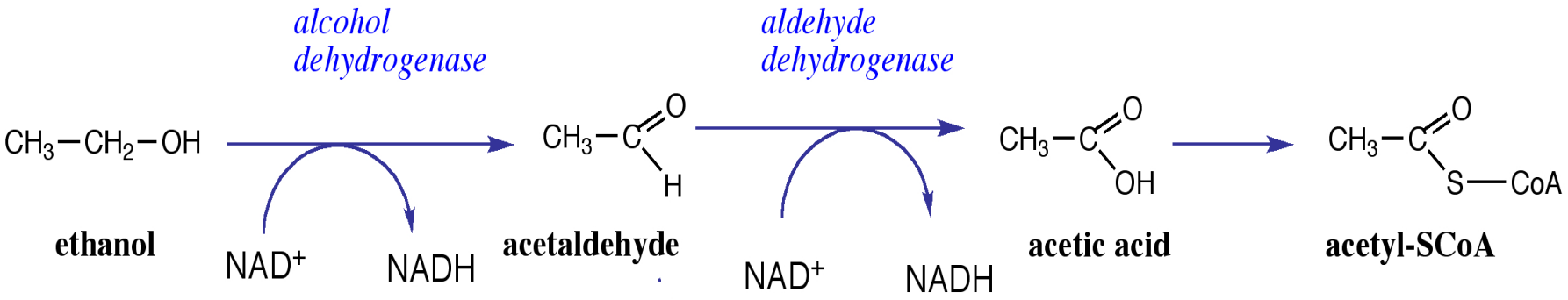


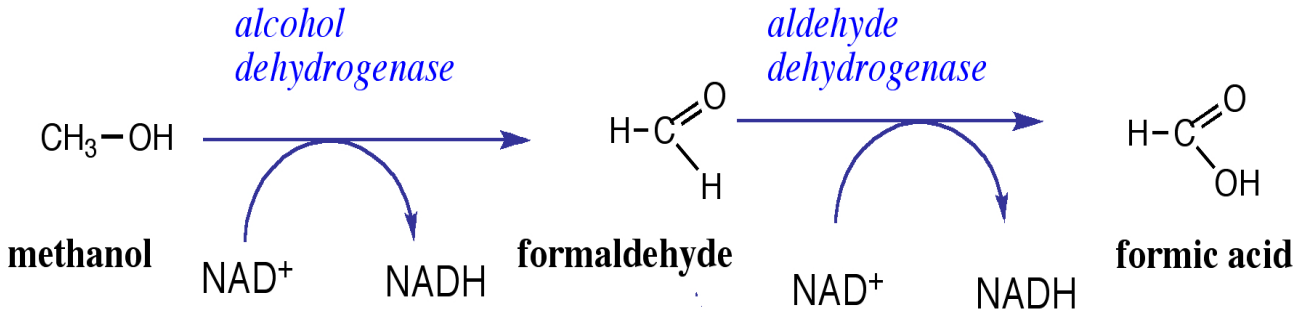
Competitive Inhibition

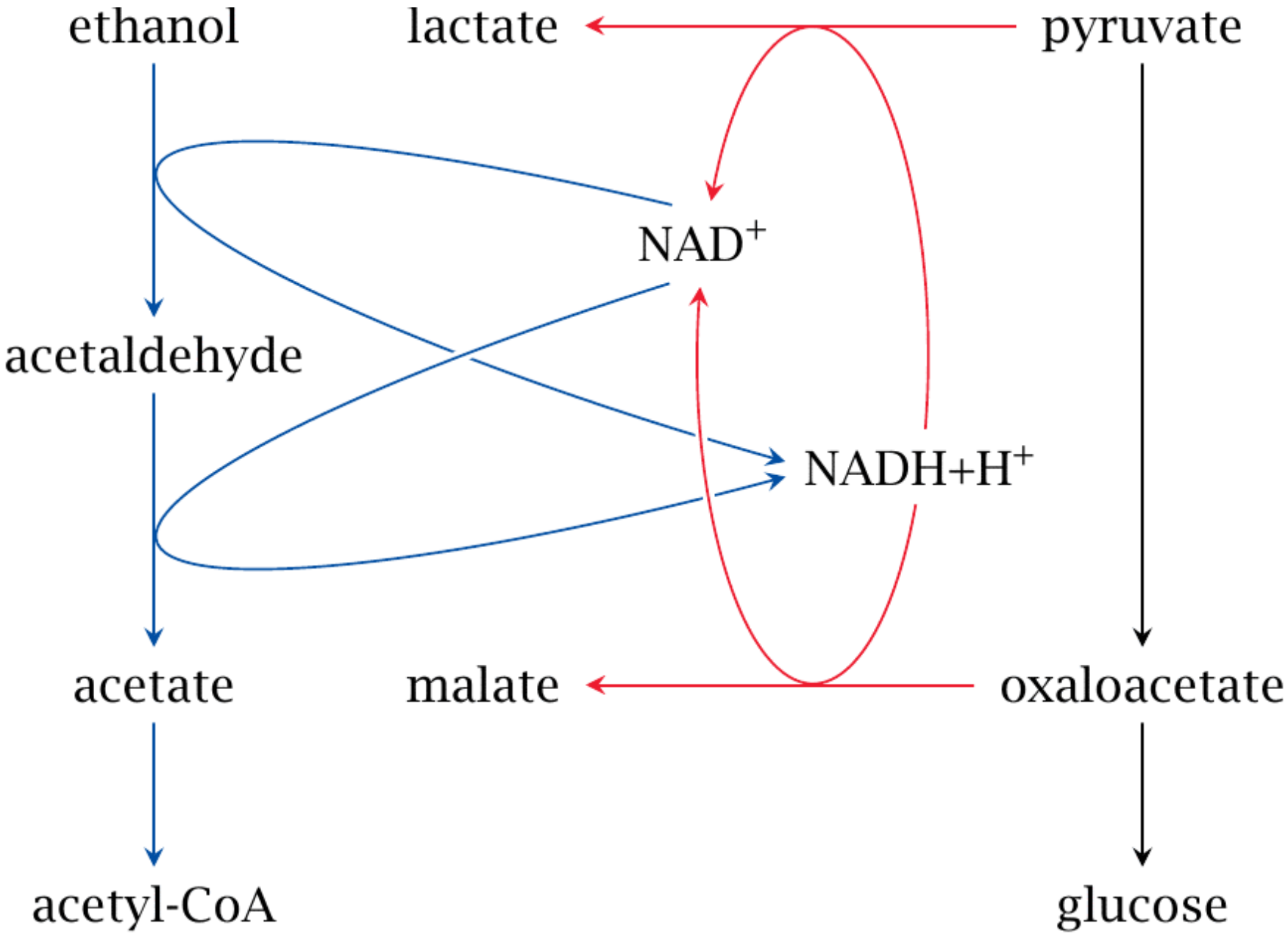


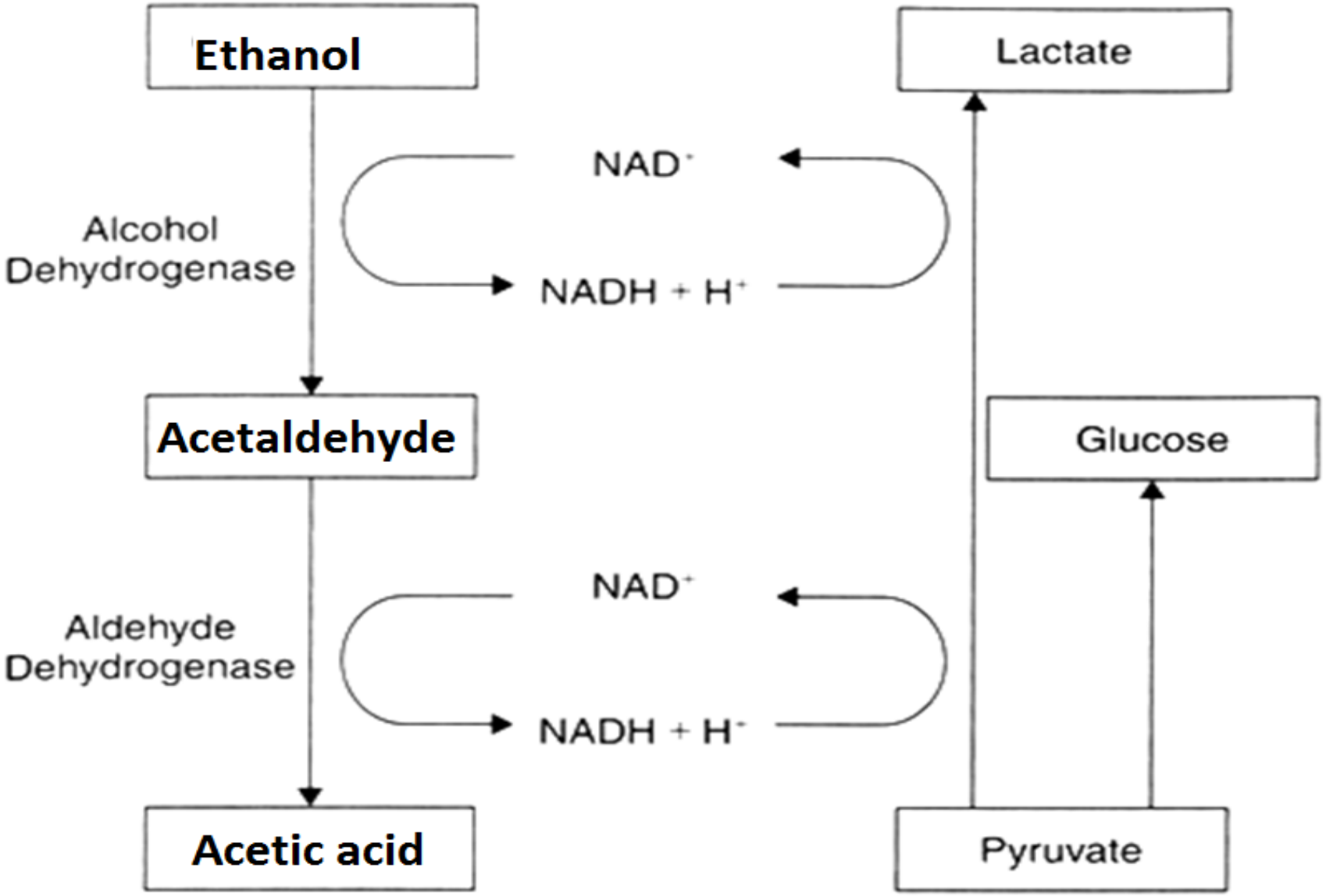
- What is biochemical explanation of hypoglycemia?

Alcohol Metabolism

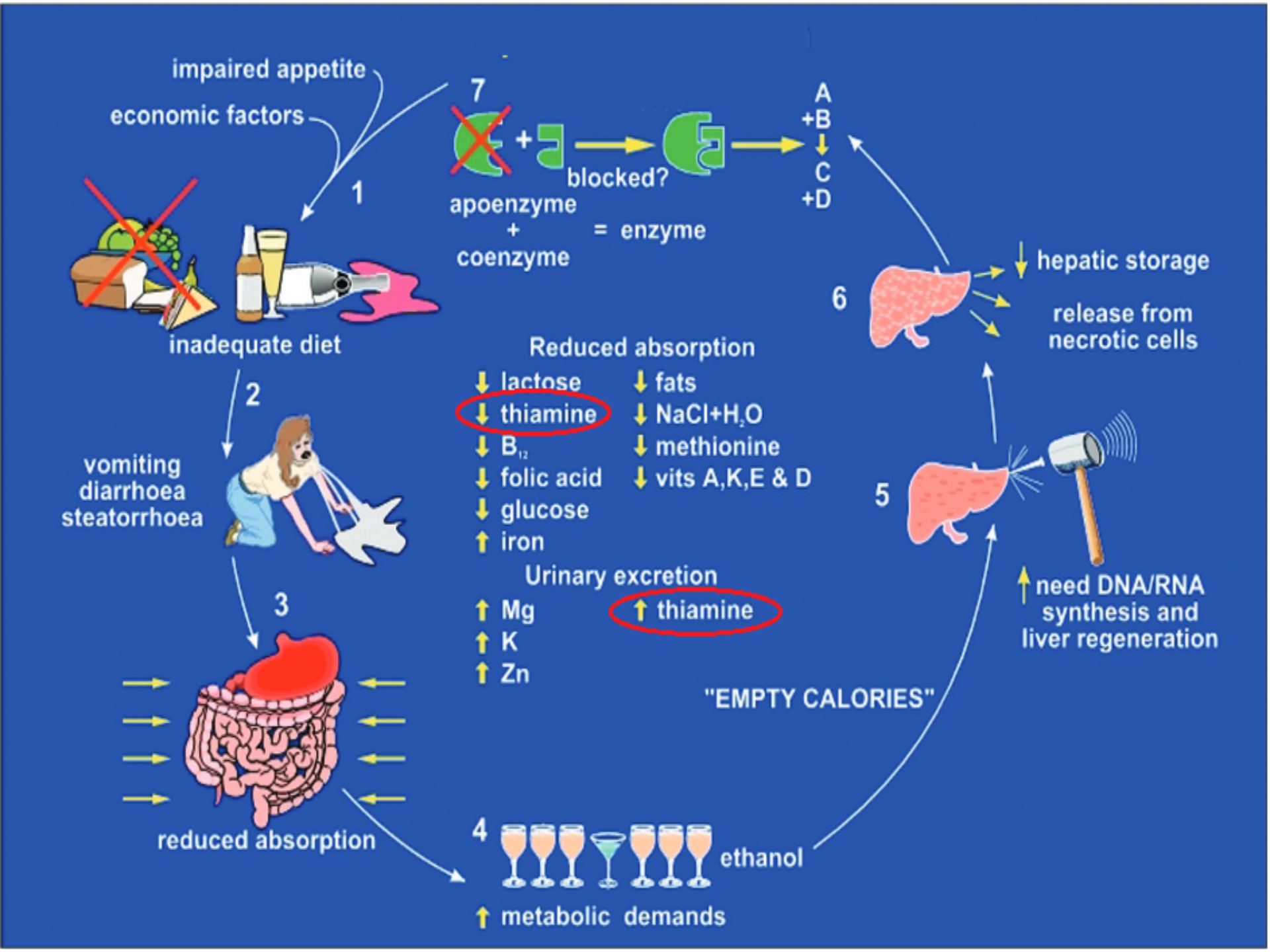





ethanol
lactate
pyruvate
NAD+
acetaldehyde
NADH+H+
acetate
malate
oxaloacetate
acetyl-CoA
glucose

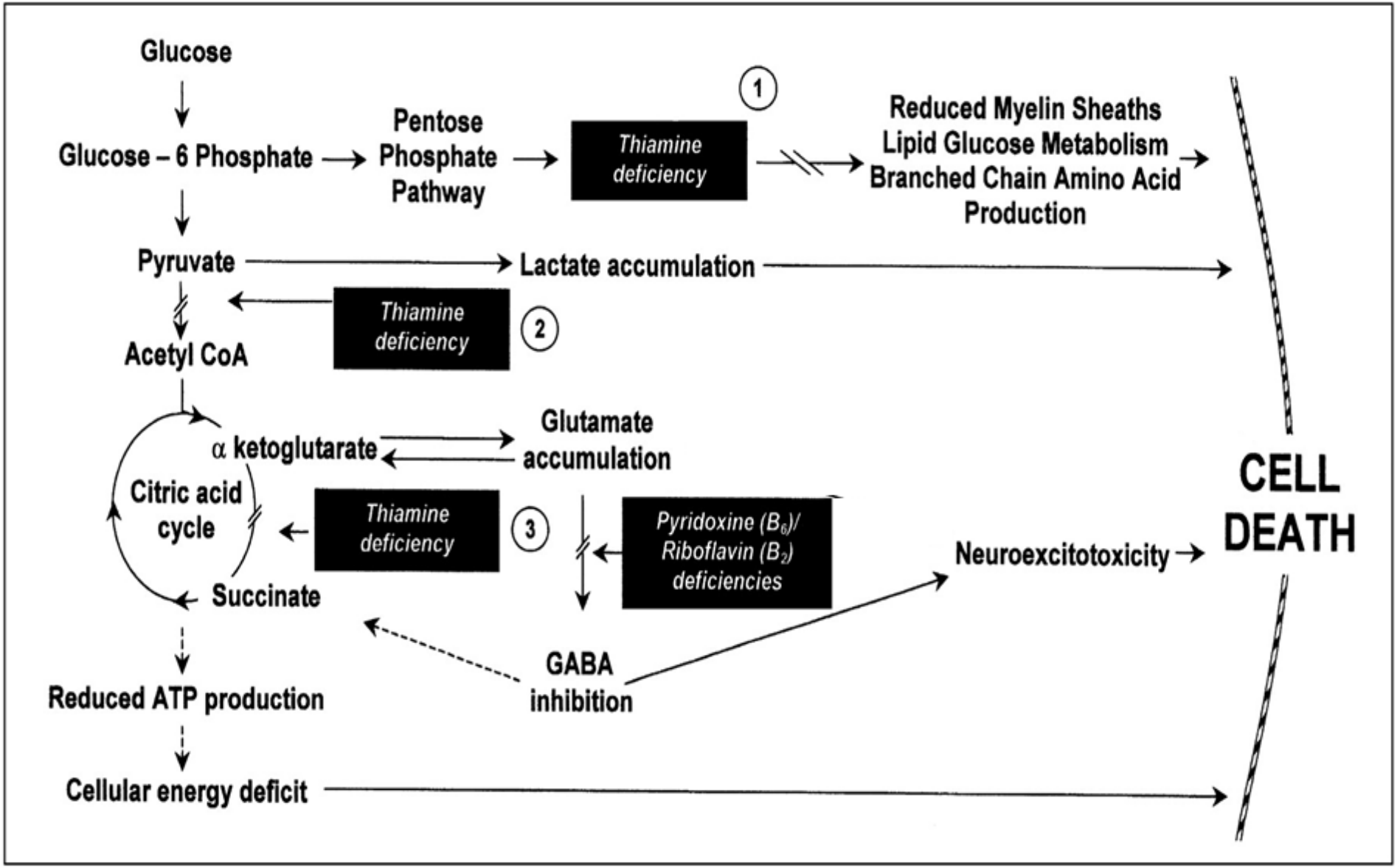

Ethanol
Lactate
NAD+
Alcohol
Dehydrogenase
NADH + H+
Acetaldehyde
Glucose
NAD+
Aldehyde
Dehydrogenase
NADH + H+
Acetic acid
Pyruvate

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


impaired appetite
economic factors
1
inadequate diet
2
vomiting
diarrhoea
steatorrhoea
3
reduced absorption
4
ethanol
metabolic demands
5
need DNA/RNA synthesis and liver regeneration
6
hepatic storage
release from necrotic cells
7
blocked?
apoenzyme + coenzyme = enzyme
A +B C +D
Reduced absorption
lactose
thiamine
B12
folic acid
glucose
iron
fats
NaCl+H2O
methionine
vits A,K,E & D
Urinary excretion
Mg
K
Zn
thiamine
"EMPTY CALORIES"

Thiamine Deficiency Due to Alcoholism

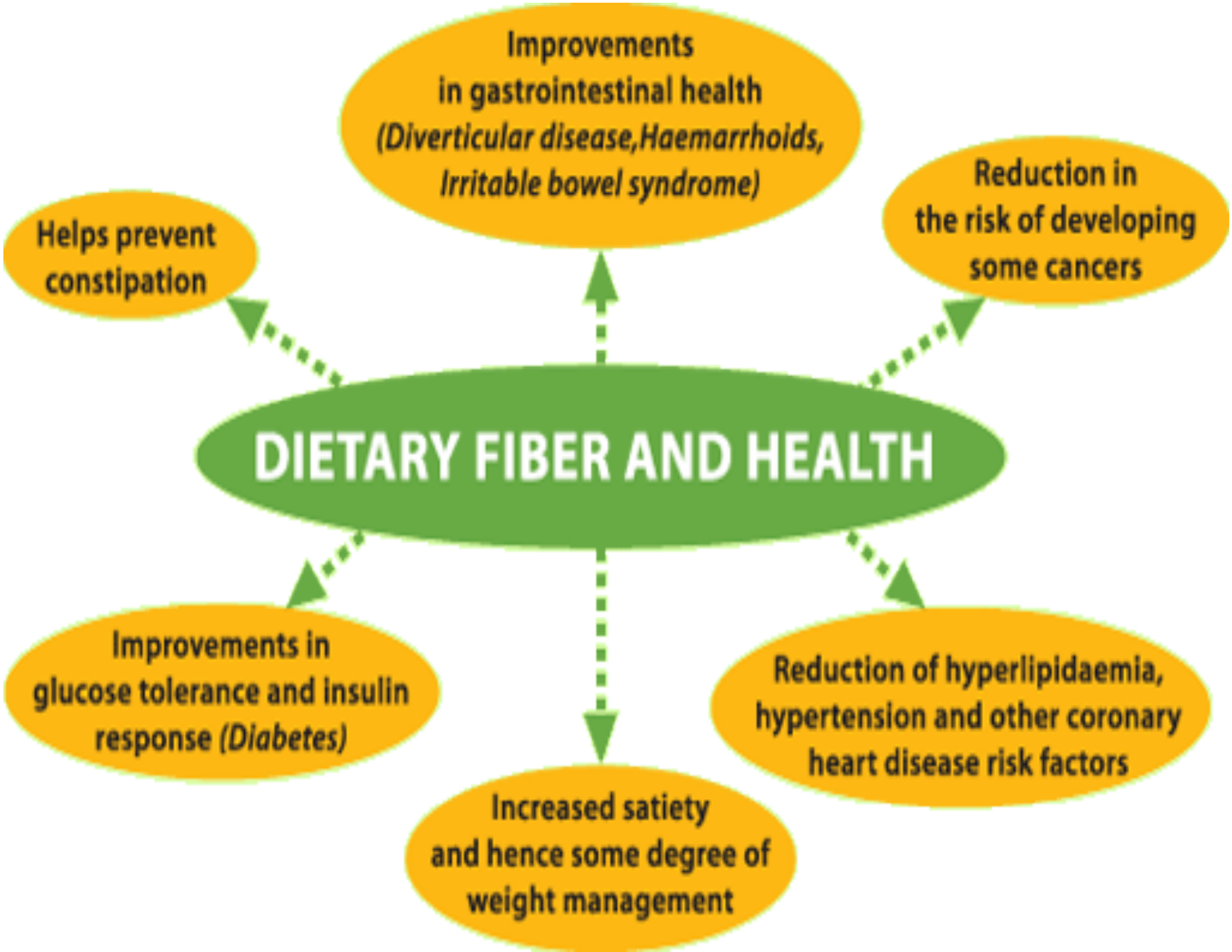
- Reduce GI Absorption
- Inadequate Diet
- Hepatic Damage
- Decrease Hepatic Storage
- Increase Diuresis
- Increase Metabolic demand



Thiamine dependent enzymes:-

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

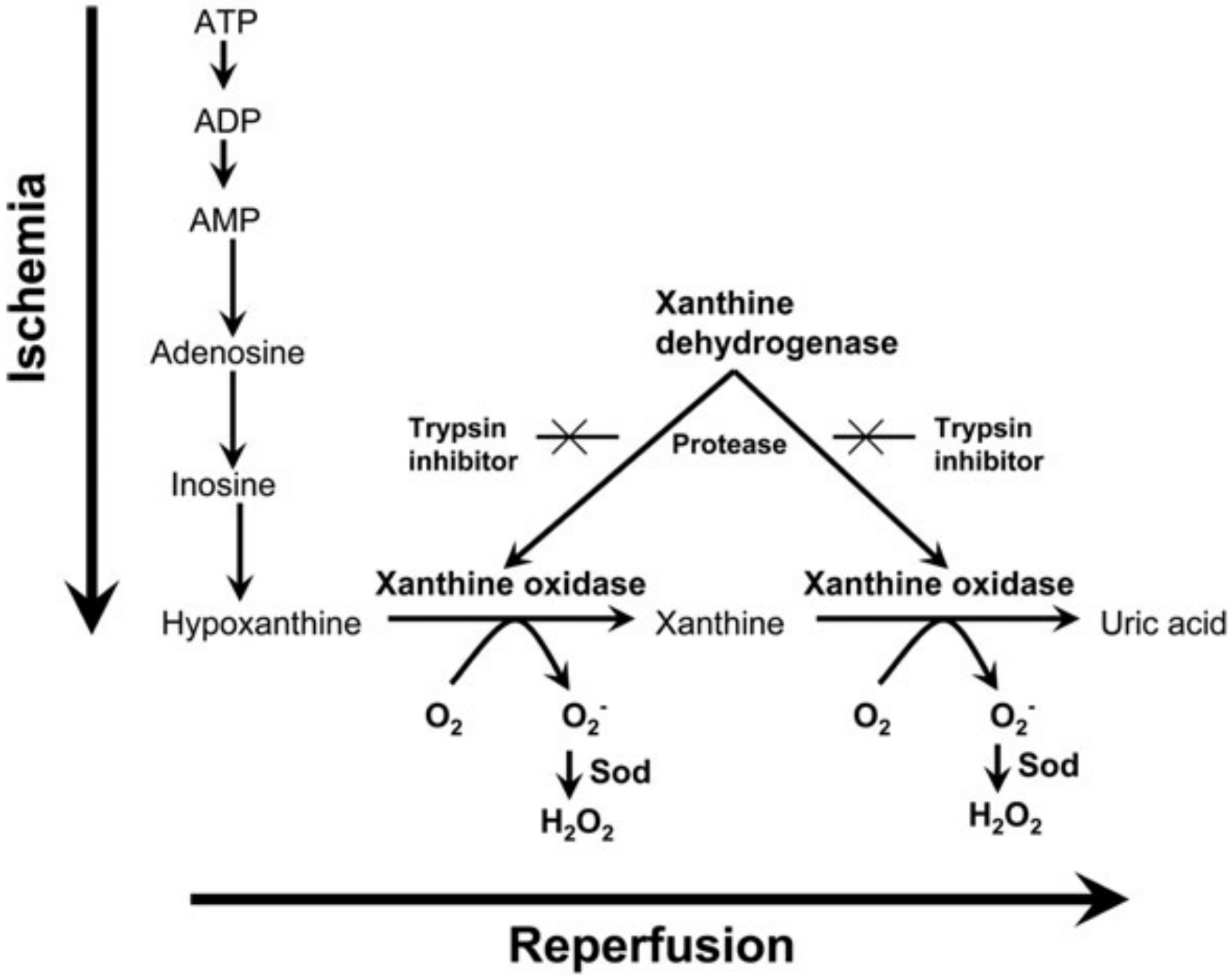
- What is role of fruits and fiber in chronic diabetes mellitus and atherosclerosis?


Improvements
in gastrointestinal health
(Diverticular disease,Haemarrhoids,
Irritable bowel syndrome)
Helps prevent
constipation
Reduction in
the risk of developing
some cancers
DIETARY FIBER AND HEALTH
Improvements in
glucose tolerance and insulin
response (Diabetes)
Reduction of hyperlipidaemia,
hypertension and other coronary
heart disease risk factors
Increased satiety
and hence some degree of
weight management

- Why blood sample for blood sugar estimation is collected in fluoride containing vial?

- Inhibit Enolase
- Glycolysis
- Inhibit utilization of Glucose by cells
- Get actuall blood sugar even after few hours.

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


Ischemia
ATP
ADP
AMP
Adenosine
Inosine
Hypoxanthine
Xanthine dehydrogenase
Trypsin inhibitor
Protease
Trypsin inhibitor
Xanthine oxidase
Xanthine
Xanthine oxidase
Uric acid
O2
O2-
Sod
H2O2
O2
O2-
Sod
H2O2
Reperfusion

- How will you calculate patient's LDL cholecterol?

Friedewald formula

Total Cholesterol =

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

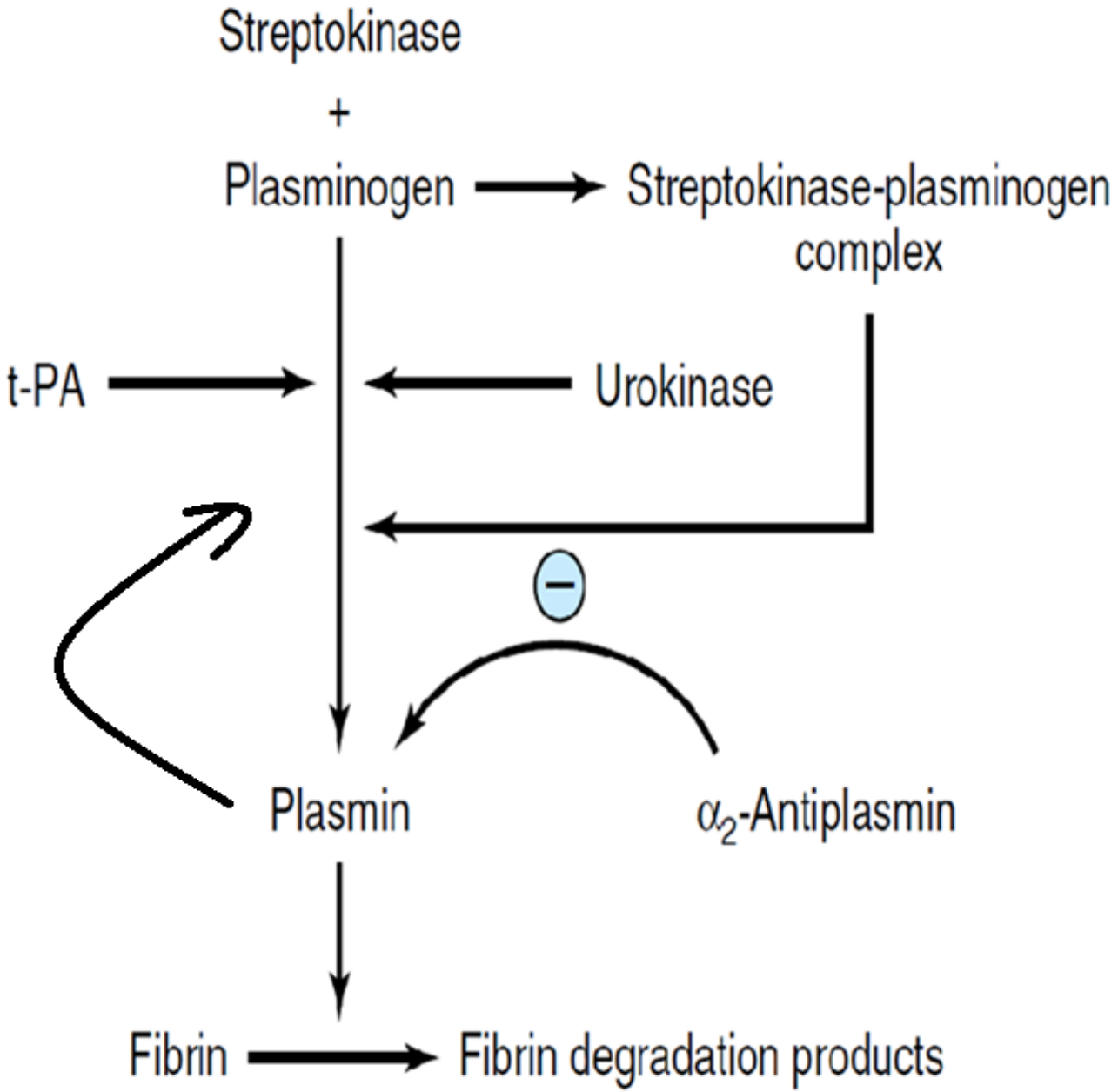
VLDL-cholesterol =

S. Triglyceride / 5

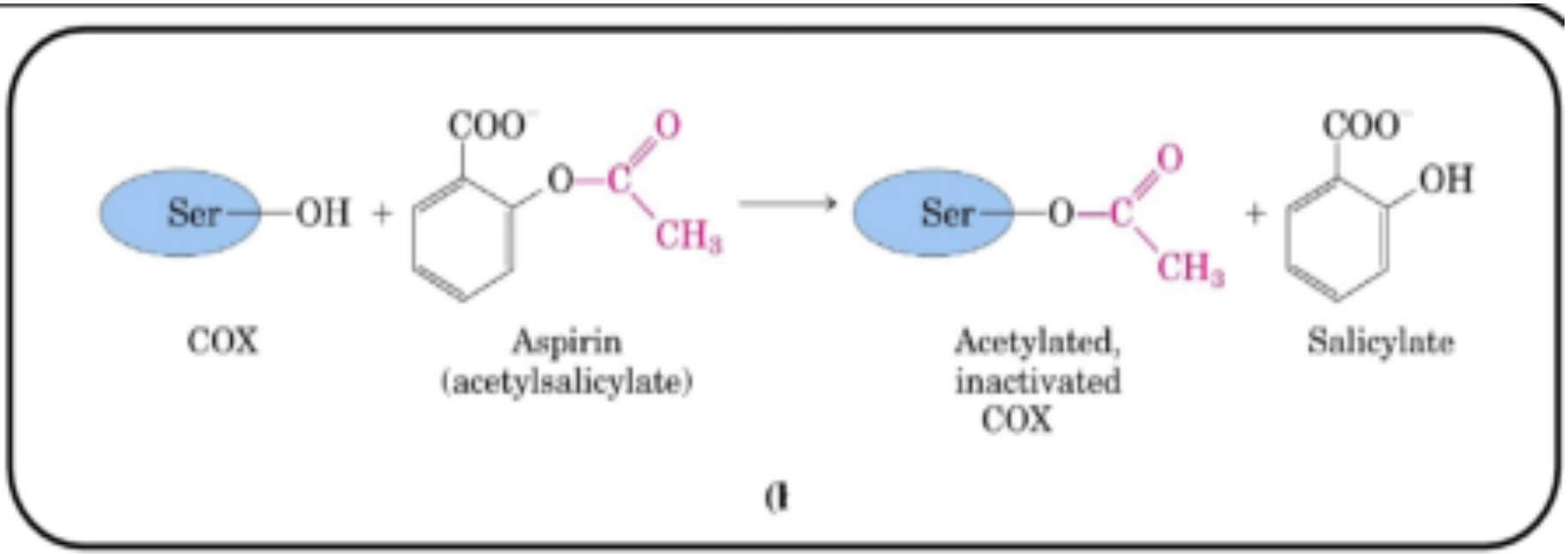
LDL-cholesterol =

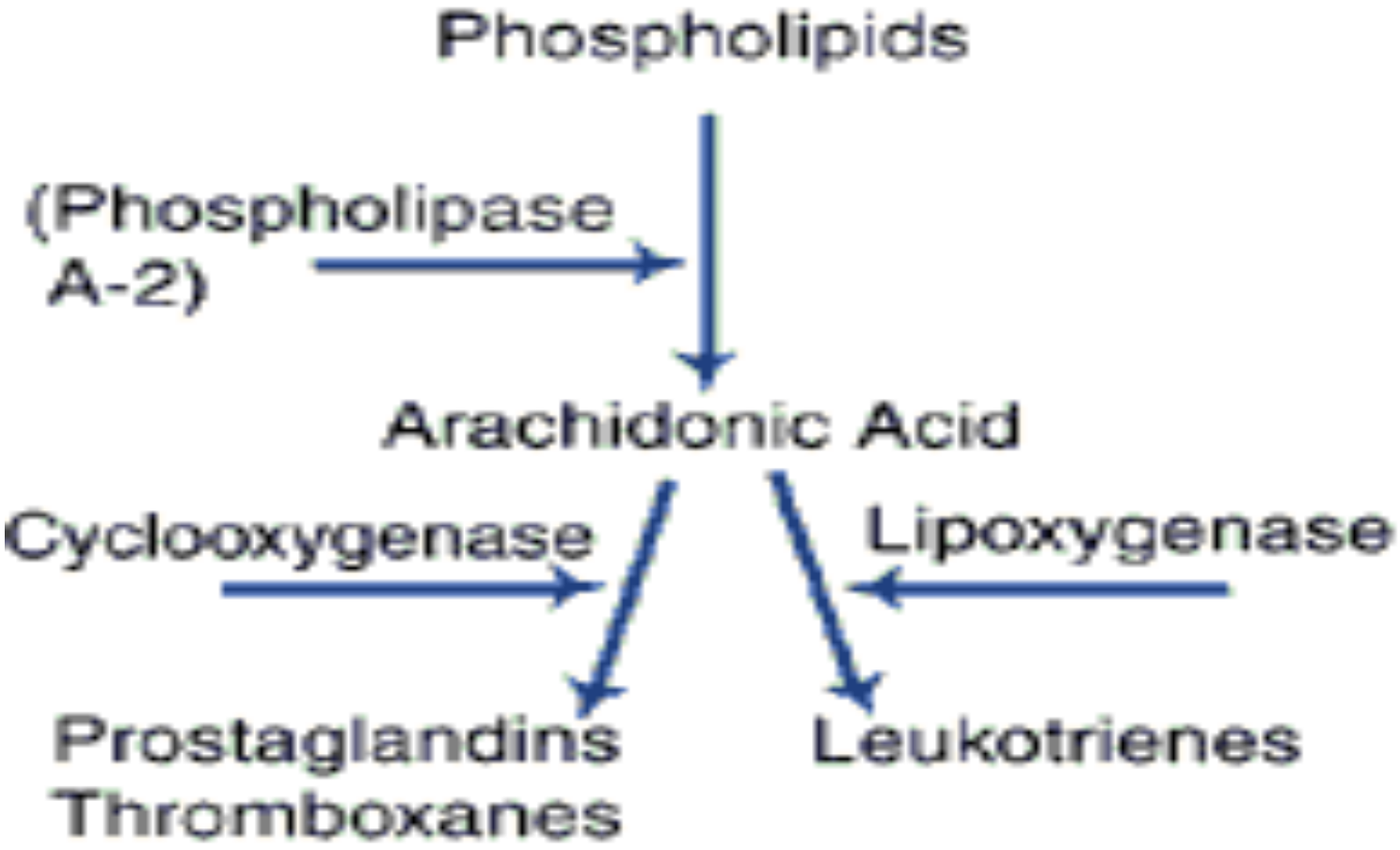
Total cholesterol – (TG/5) – HDL

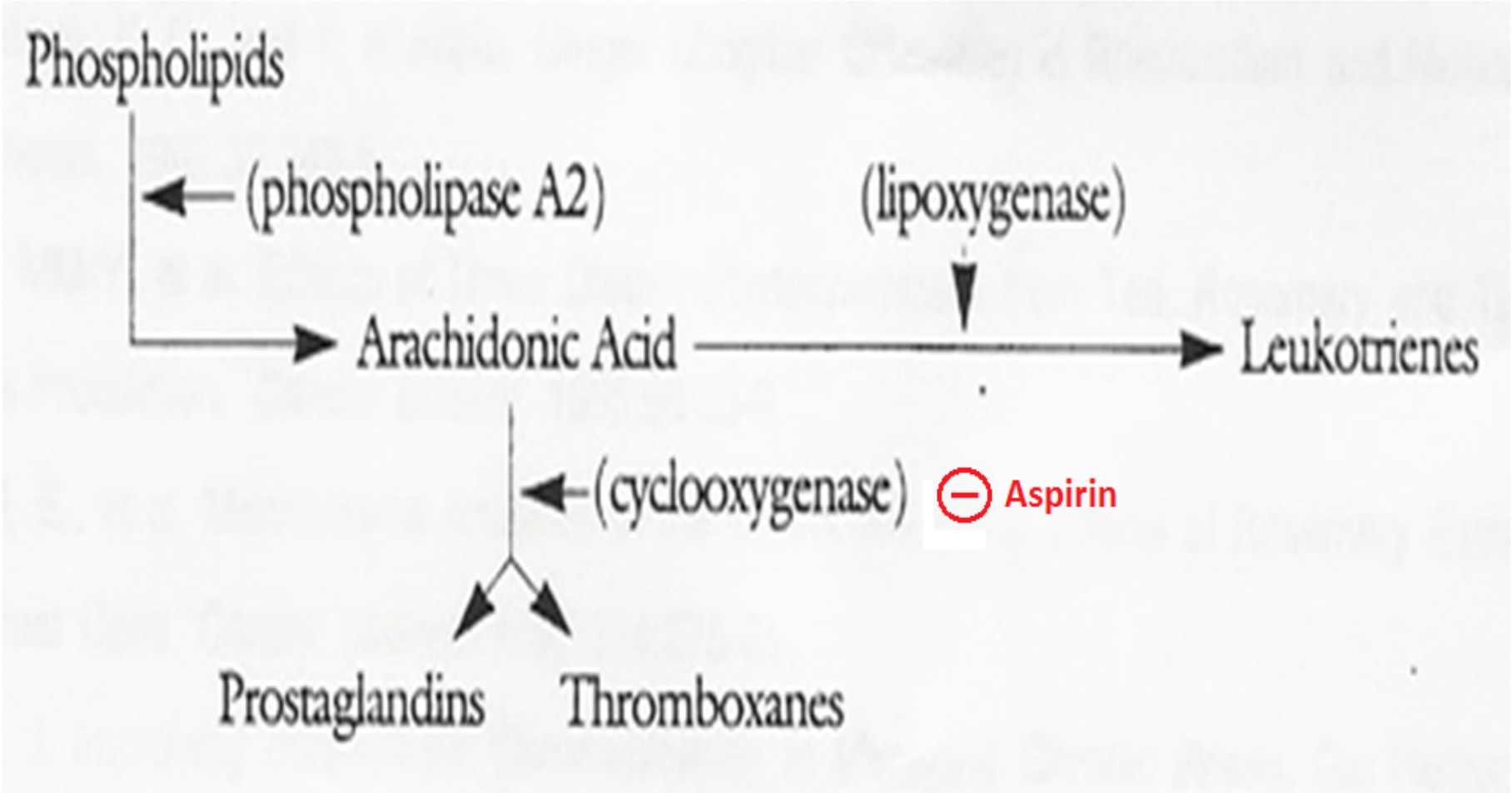
- What is role of fibrinolytic drugs (streptokinase) in myocardial infarction?


Streptokinase
+
Plasminogen
Streptokinase-plasminogen complex
t-PA
Urokinase
Plasmin
α_2-Antiplasmin
Fibrin
Fibrin degradation products

- Give biochemical explaination of antiplatelet drug- Aspirin.




Phospholipids
(Phospholipase
A-2)
Arachidonic Acid
Cyclooxygenase
Lipoxygenase
Prostaglandins
Thromboxanes
Leukotrienes


Phospholipids
(phospholipase A2)
(lipoxygenase)
Arachidonic Acid
Leukotrienes
(cyclooxygenase)
Aspirin
Prostaglandins
Thromboxanes

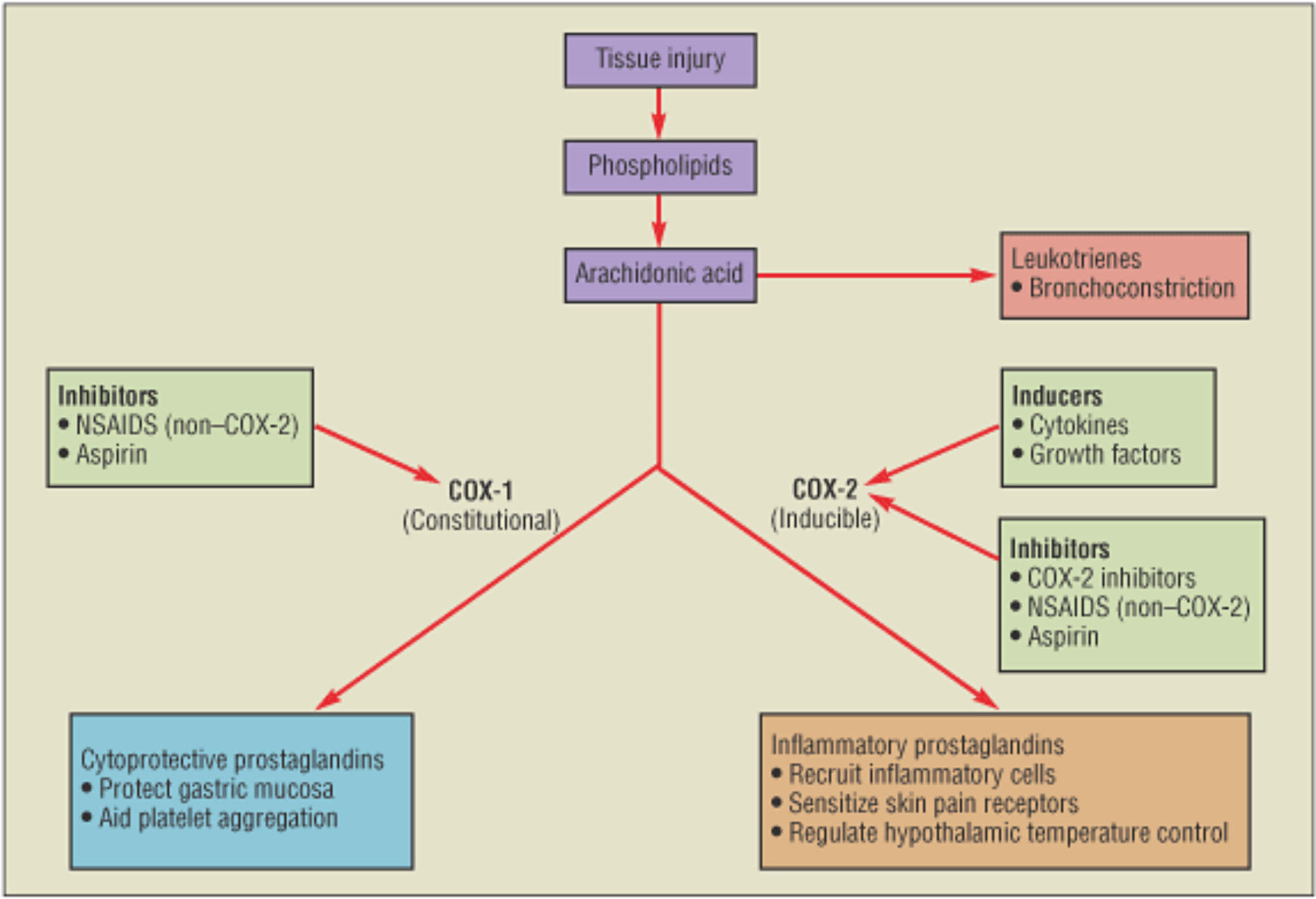


FIGURE 1. Algorithm of the biochemical pathway shows that the formation of prostaglandins occurs via both cyclooxygenase enzymes (COX-1 and COX-2).

What is significant of high HbA1c ?

HbA = Adult hemogolbin

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

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 %
- Serm Albumin : 2.0 gm%
- Serum Ammonia : Very High
- Serum Total Billirubin : 20 mg%
- APTT – Test : 60 second
- APTT – Control : 30 second
- APTT – INR : 2
- Haemogloin : 6 gm%

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

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 explaination about following symptoms in chronic alcoholic
   - Alter conciousness
   - Haemetemesis
2. Biochemical explaination 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 explaination about following symptoms in chronic alcoholic
   - Alter conciousness
   - Haemetemesis
2. Biochemical explaination about following signs in chronic alcoholic
   - Edeme
   - Ascites
   - Hypotension
3. What is hepato-renal syndrome?

Case 5 - Question

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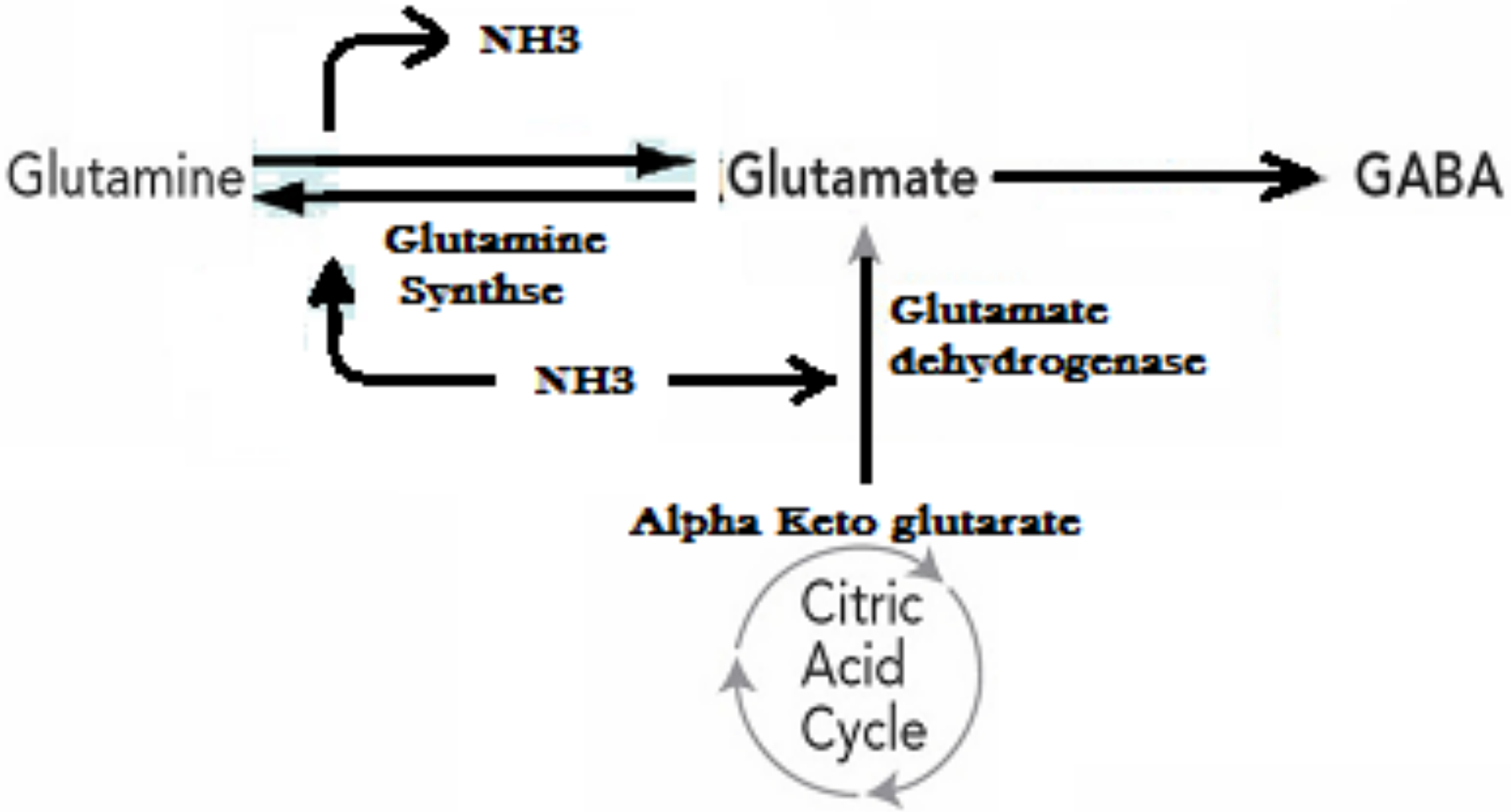
   - Dextrose plus thiamine
   - Vitamin K
   - 10% Albumin
   - Oral Neomycin (Anti-microbial, Antibiotic)
   - Liq Lactulose (Laxative)
   - Oral Phenylbutarate

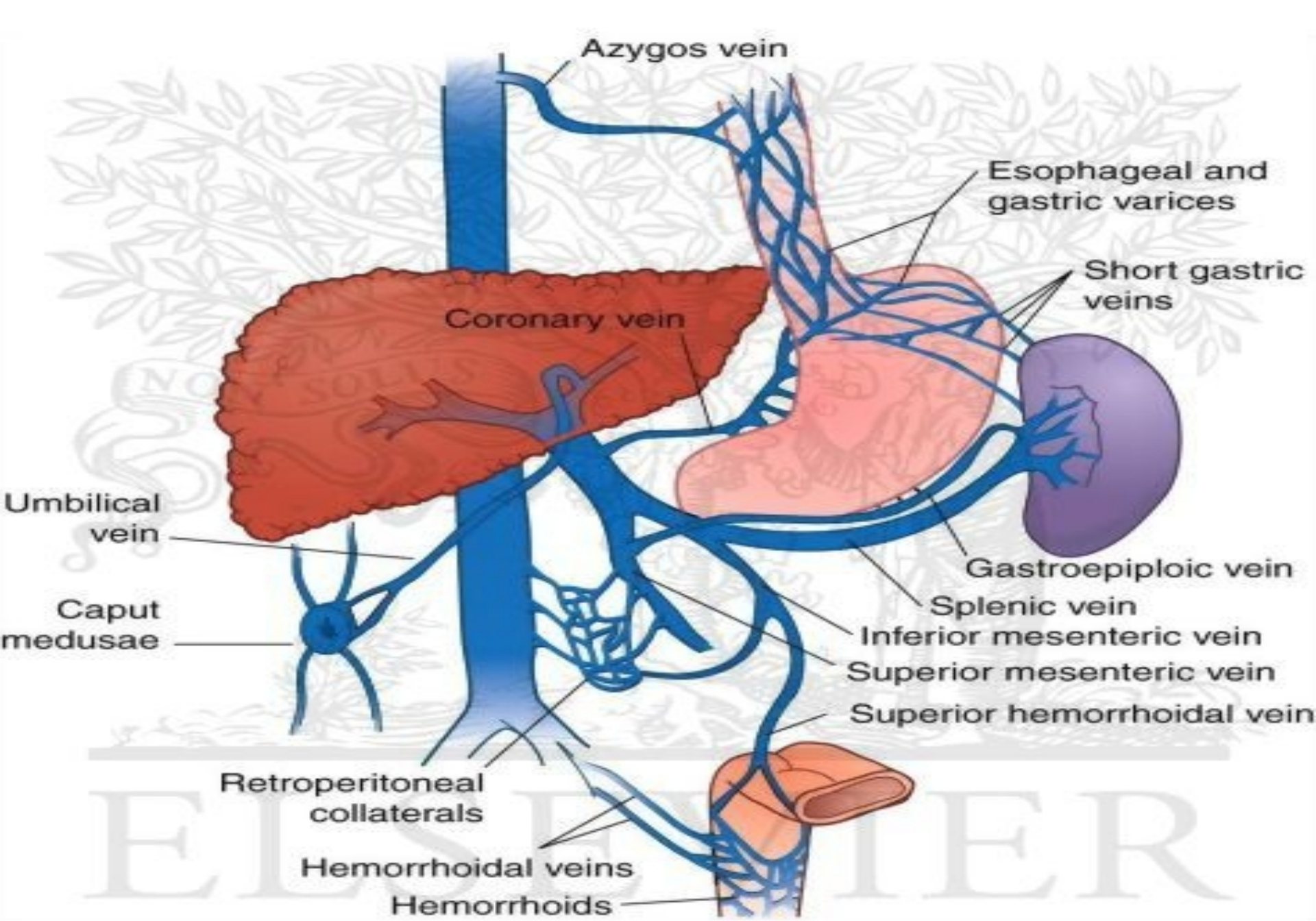
Biochemical explaination
Alter consciousness in chronic alcoholic

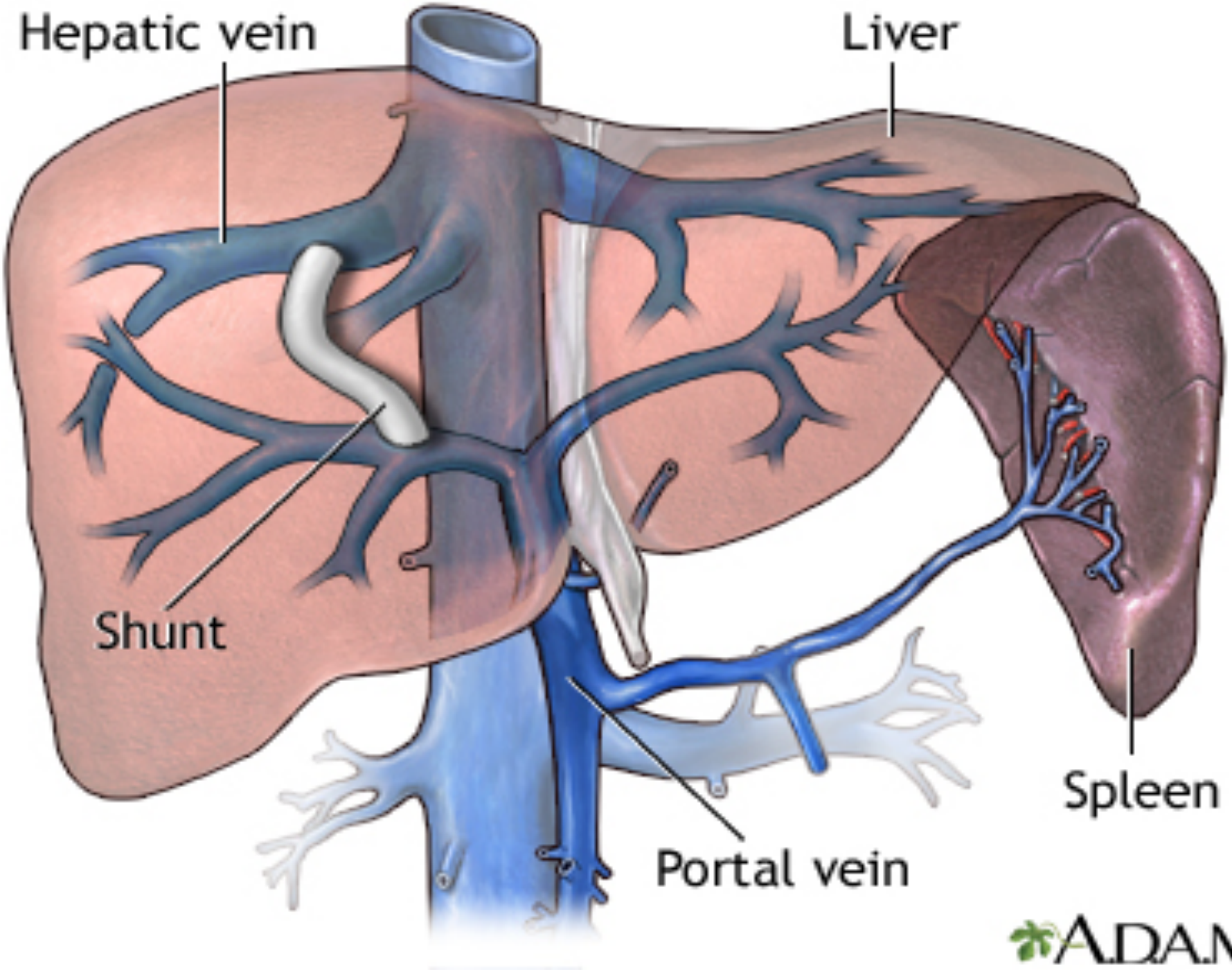
- Hypoglycemia
- Ureamic encephlopathy
- Hepatic encephlopathy


NH3
Glutamine
Glutamate
GABA
Glutamine
Synthse
NH3
Glutamate
dehydrogenase
Alpha Keto glutarate
Citric
Acid
Cycle

Biochemical explaination of Haemetemesis in chronic alcoholic

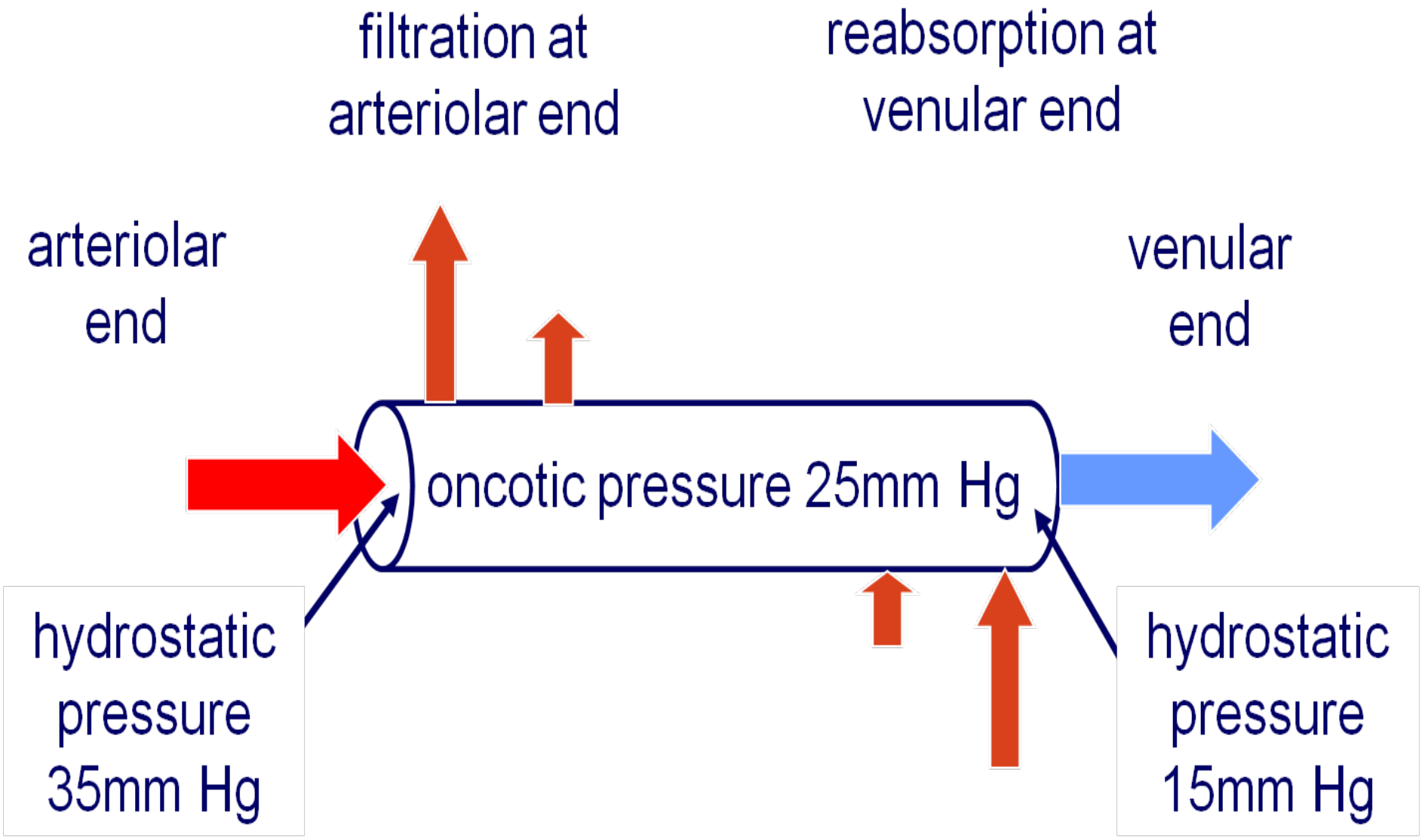
- Liver damage
- Less Plasma protein
- Less Albumin
- Less Fibrinogen store
- Less synthesis & store of cloting factor
- Less store of Vitamin K
- Portal Hypertension




Hepatic vein
Liver
Shunt
Spleen
Portal vein
A.D.A.M.

1. Biochemical explaination of Edema Ascites Hypotension in Chronic alcoholic

filtration pressure = hydrostatic pressure - oncotic pressure



Hepato- Renal Syndrome

Hepato- Renal Syndrome

- Decrease Albumin & Total protein
- Colloidal pressure decrese
- Edema
- Intravascular volume decrease
- Glomerulus filtration & Renal perfusion
- Urine output decrease
- Blood volume increase
- Hydrostatic increase
- Increase edema

Biochemical reason for giving following in patient of chronic alcoholic

- Dextrose plus thiamine
- Vitamin K
- 10% Albumin

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

Neomycin

KILL

Intestinal Flora (Lactobacilli)

Intestinal flora produce Enzymes

- Urease
  - (Urea - - - - - Ammonia)
- Protease & Peptidese
  - (RBC – Haemoglobin – Globin – Protein – Amino acid – Ammonia)

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

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.

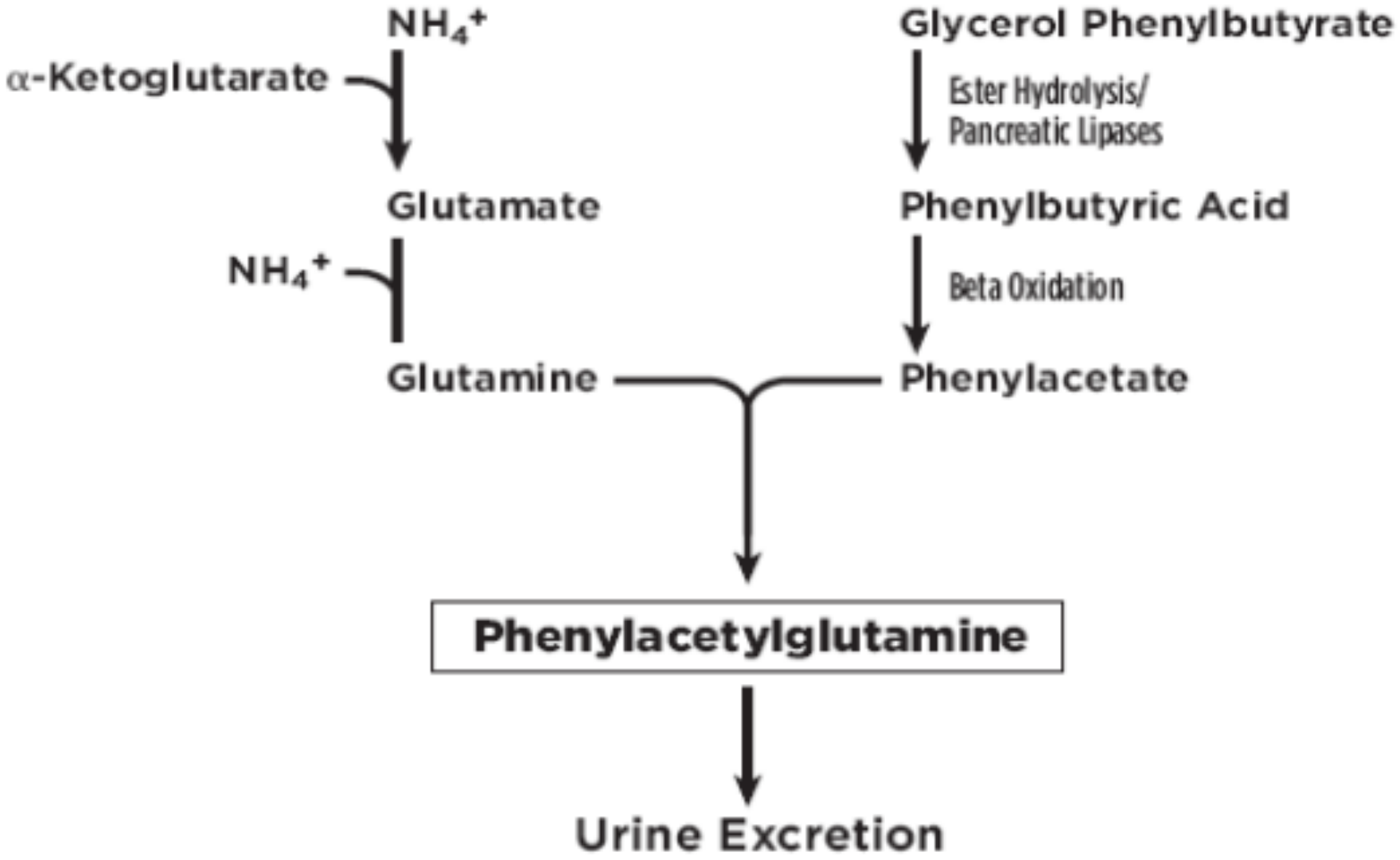
Rx ONLY

16 fl oz (473 mL)

pai 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

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 (tachypnia) 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
pO2	95 mmHg	90 - 100 mmHg
pCO2	24 mmHg	32 - 40 mmHg
HCO3- (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

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)

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

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

- **Reason of Unconsciousness in DKA**
  - Dehydration
  - Shock
  - Hyponatriemia
- **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

Alteration in cardiac rhythme

Decrease cardiac contractility

Hypotension

Alteration in Oxygen binding capacity

Impair consciouness level

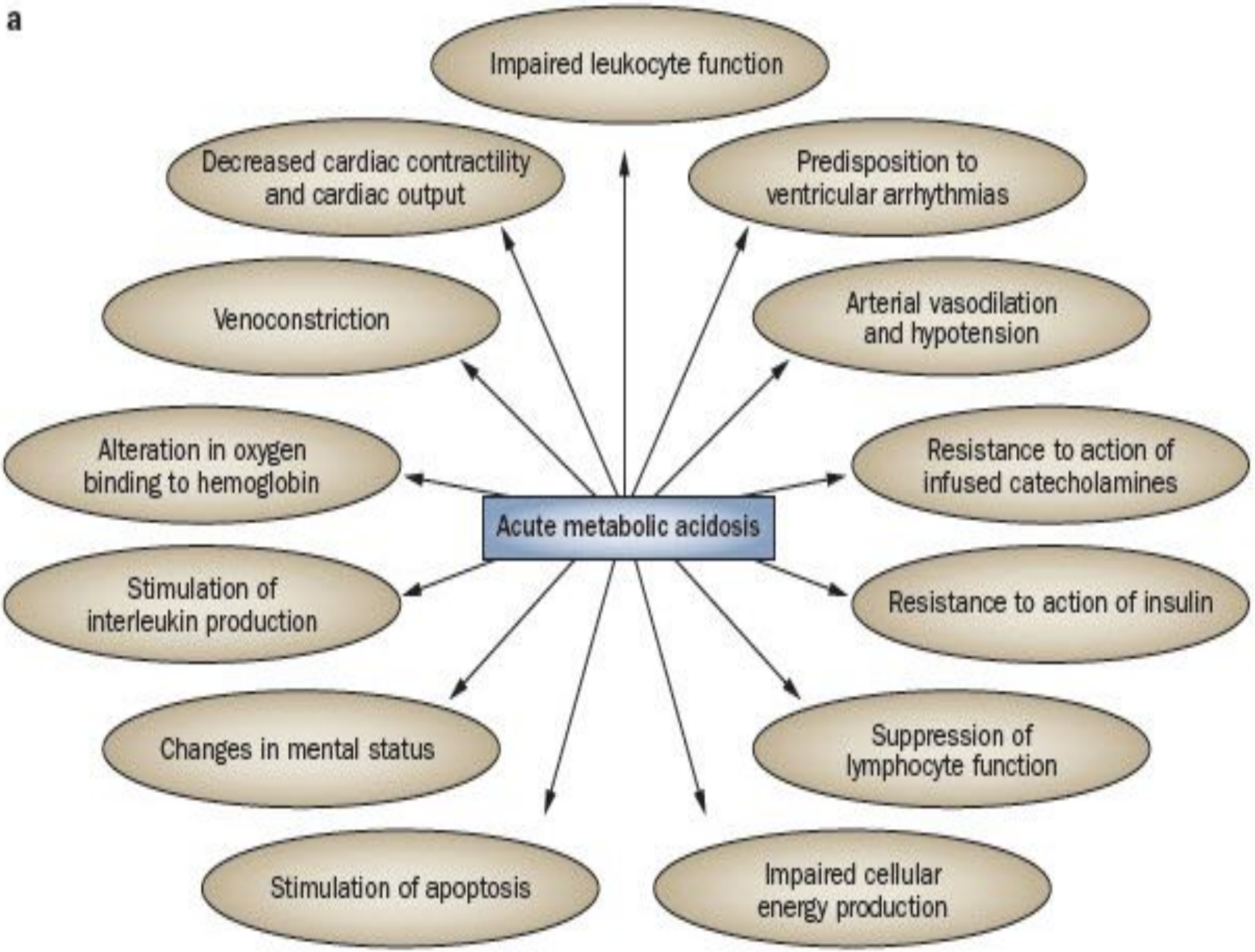
Suppressed lymphocyte function

Impaired cellular energy production

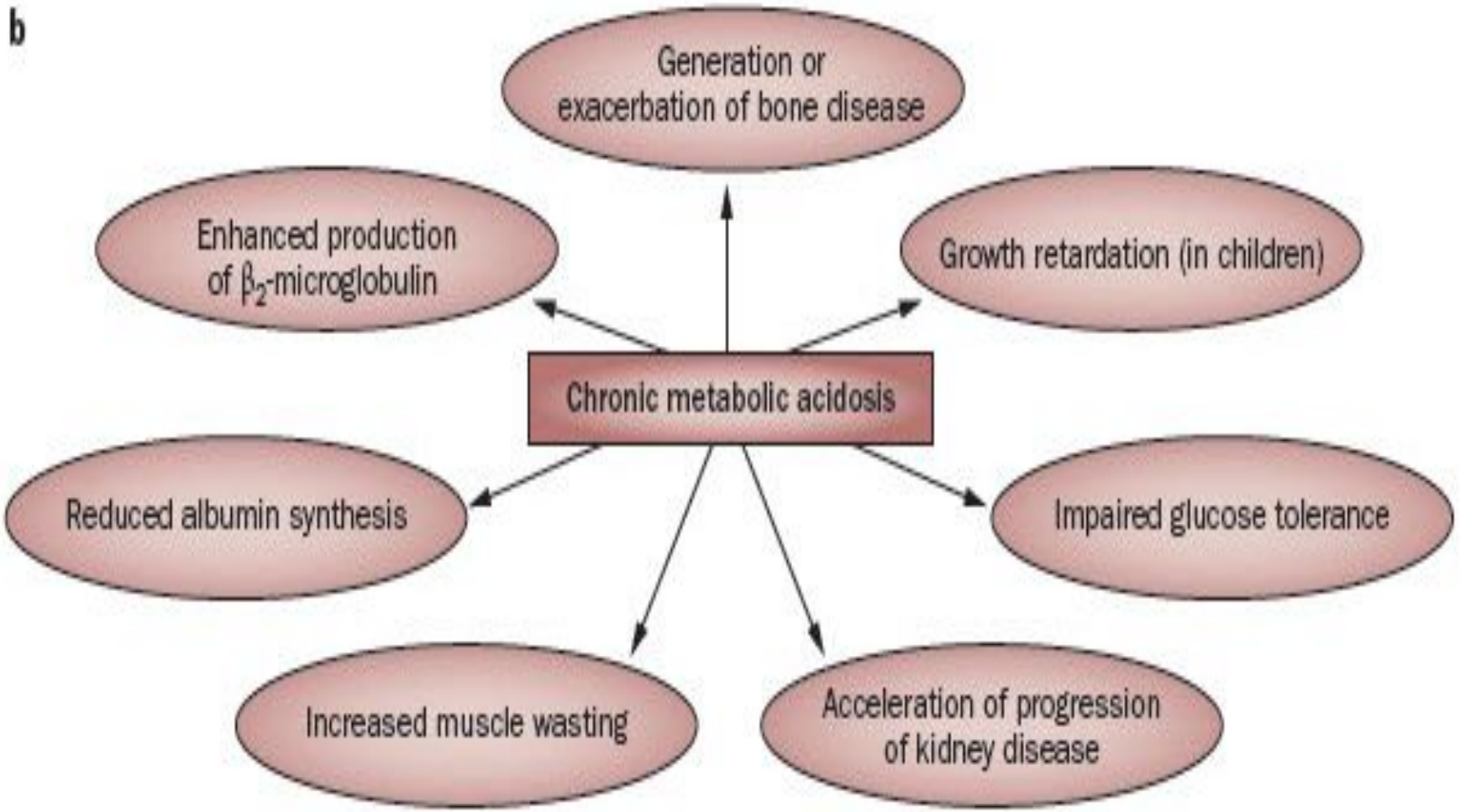
Increase insulin resistance

Arterial vasodilation

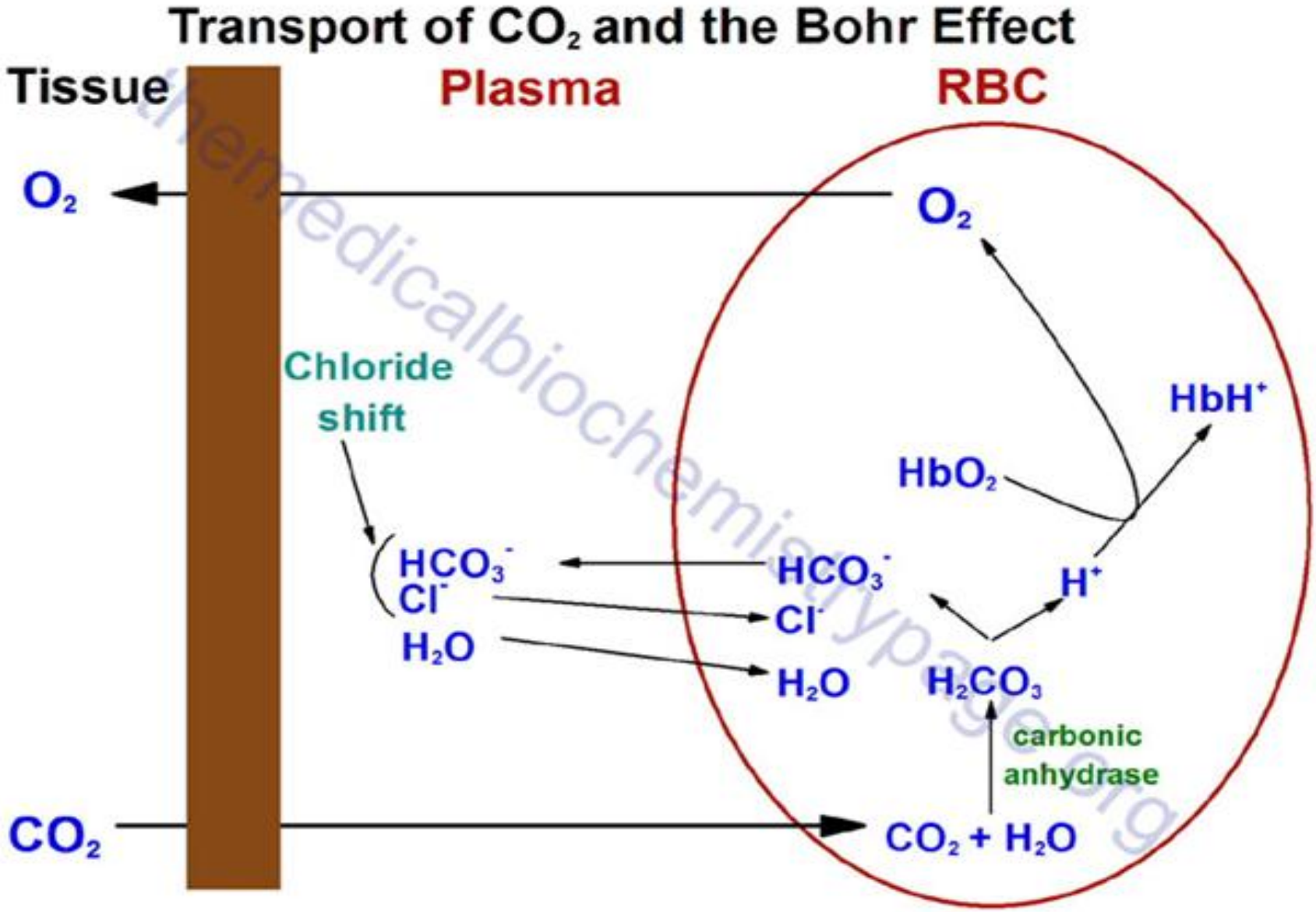
a

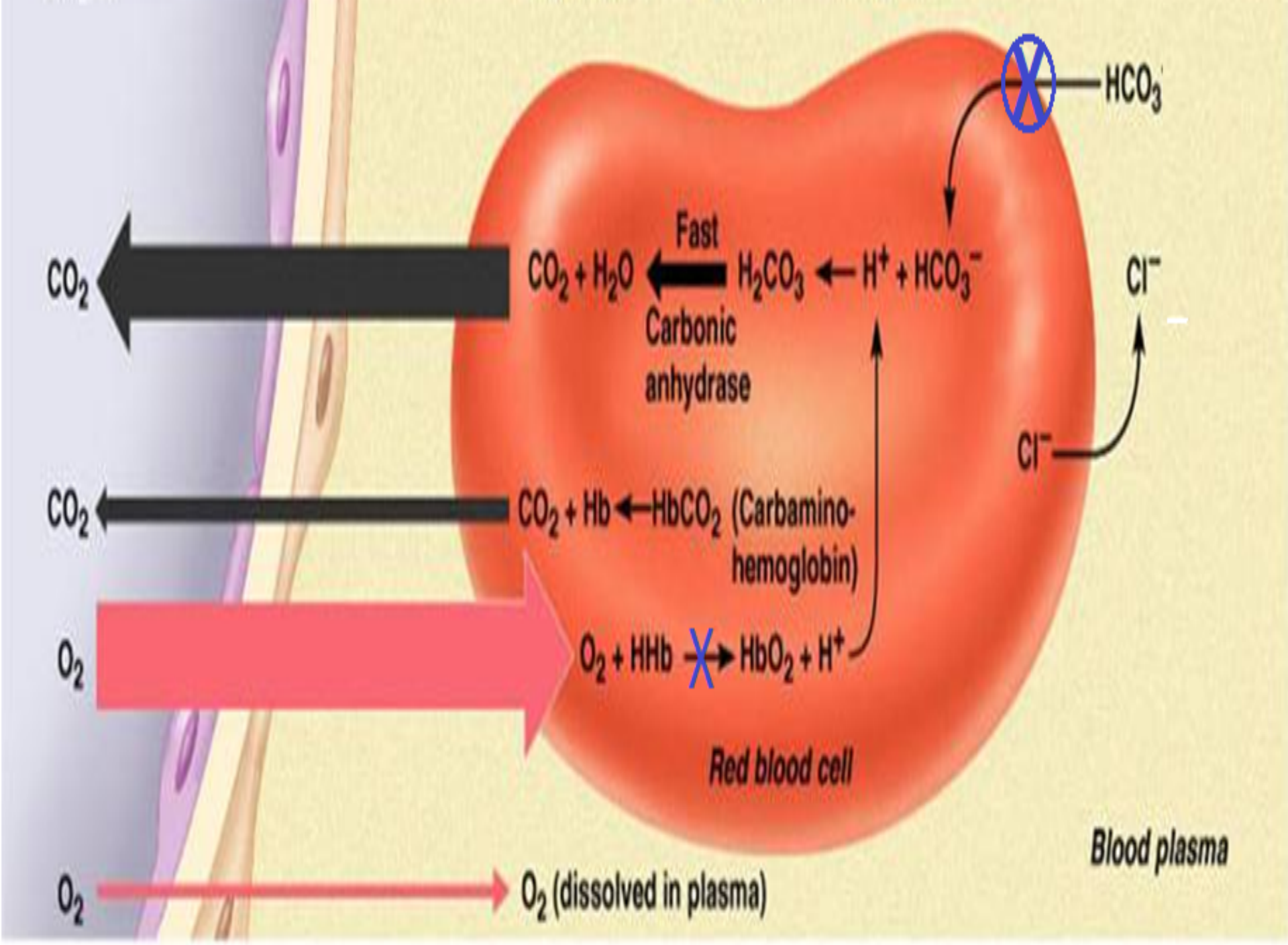

Impaired leukocyte function
Decreased cardiac contractility and cardiac output
Predisposition to ventricular arrhythmias
Venoconstriction
Arterial vasodilation and hypotension
Alteration in oxygen binding to hemoglobin
Resistance to action of infused catecholamines
Acute metabolic acidosis
Stimulation of interleukin production
Resistance to action of insulin
Changes in mental status
Suppression of lymphocyte function
Stimulation of apoptosis
Impaired cellular energy production

b


Generation or exacerbation of bone disease
Enhanced production of β_2-microglobulin
Growth retardation (in children)
Chronic metabolic acidosis
Reduced albumin synthesis
Impaired glucose tolerance
Increased muscle wasting
Acceleration of progression of kidney disease

Effect of Acidosis on O2- CO2 diffusion




HCO_3^-
Fast
$CO_2 + H_2O$
H_2CO_3
$H^+ + HCO_3^-$
Carbonic anhydrase
Cl^-
CO_2
$CO_2 + Hb$
$HbCO_2$ (Carbamino-hemoglobin)
O_2
$O_2 + HHb$
$HbO_2 + H^+$
Red blood cell
Blood plasma
O_2 (dissolved in plasma)

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

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

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

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

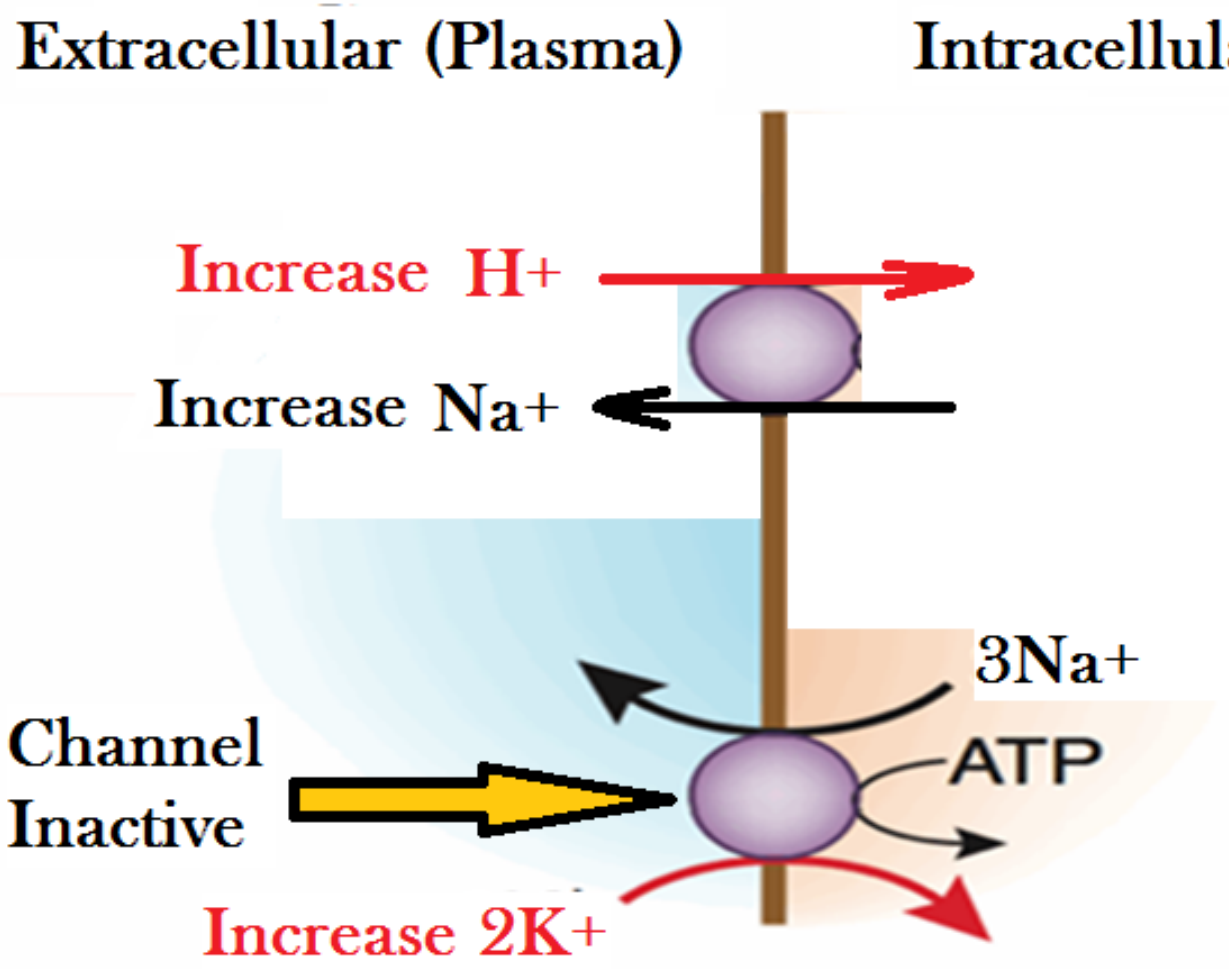
1. Dehydration
2. Hypotension
3. Decrease renal flow
4. Pre-Renal – Acute renal failure

Give comment on patient ABG report.

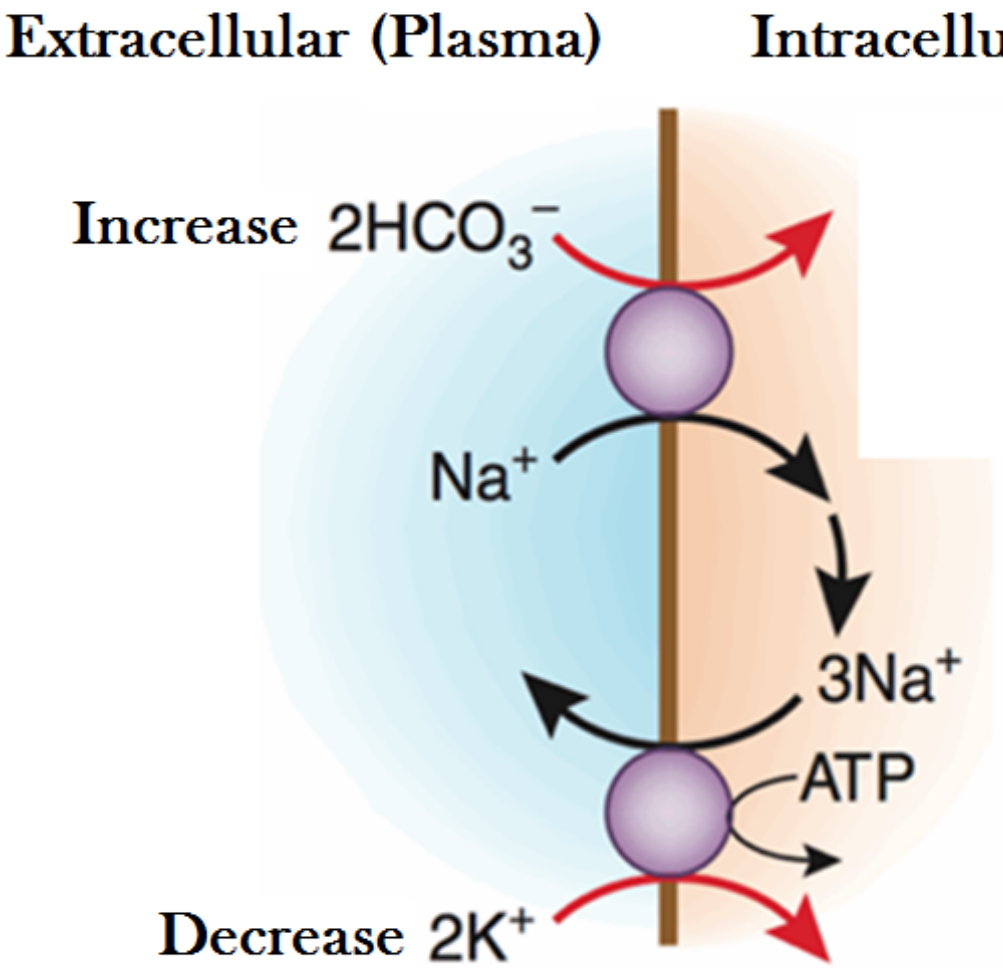
	Value	Ref. Value	Interpretation
pH	7.1	7.35 - 7.45	Low Acidosis
pO2	95	90 - 100 mmHg	Normal
pCO2	24	32 - 40 mmHg	Low Indicate Alkalosis. (Compensatory)
HCO3-	12	24 - 32 mmol/l	Low Indicate Acidosis

Uncompensated Metabolic Acidosis

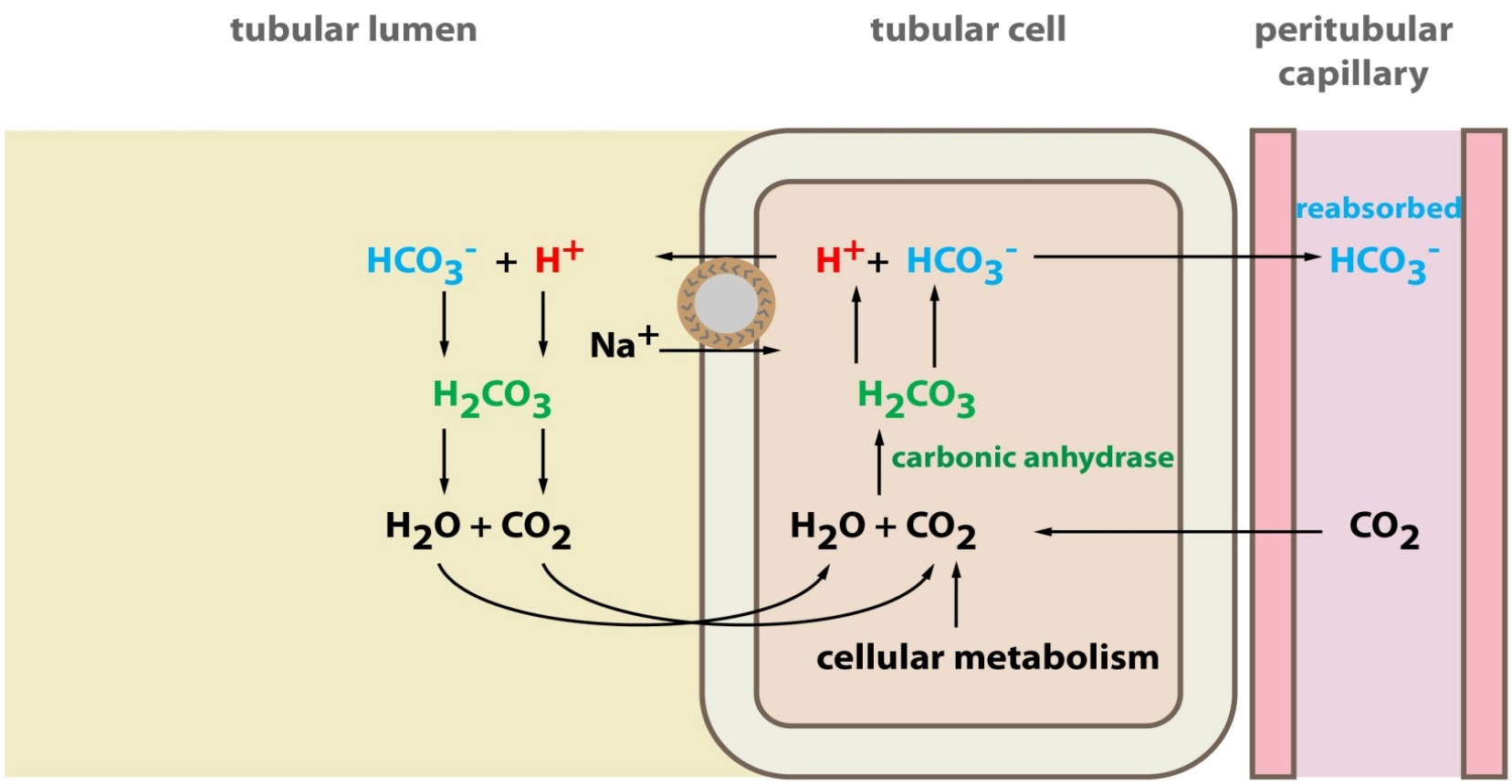
Acidosis (Increase H+) increase K+



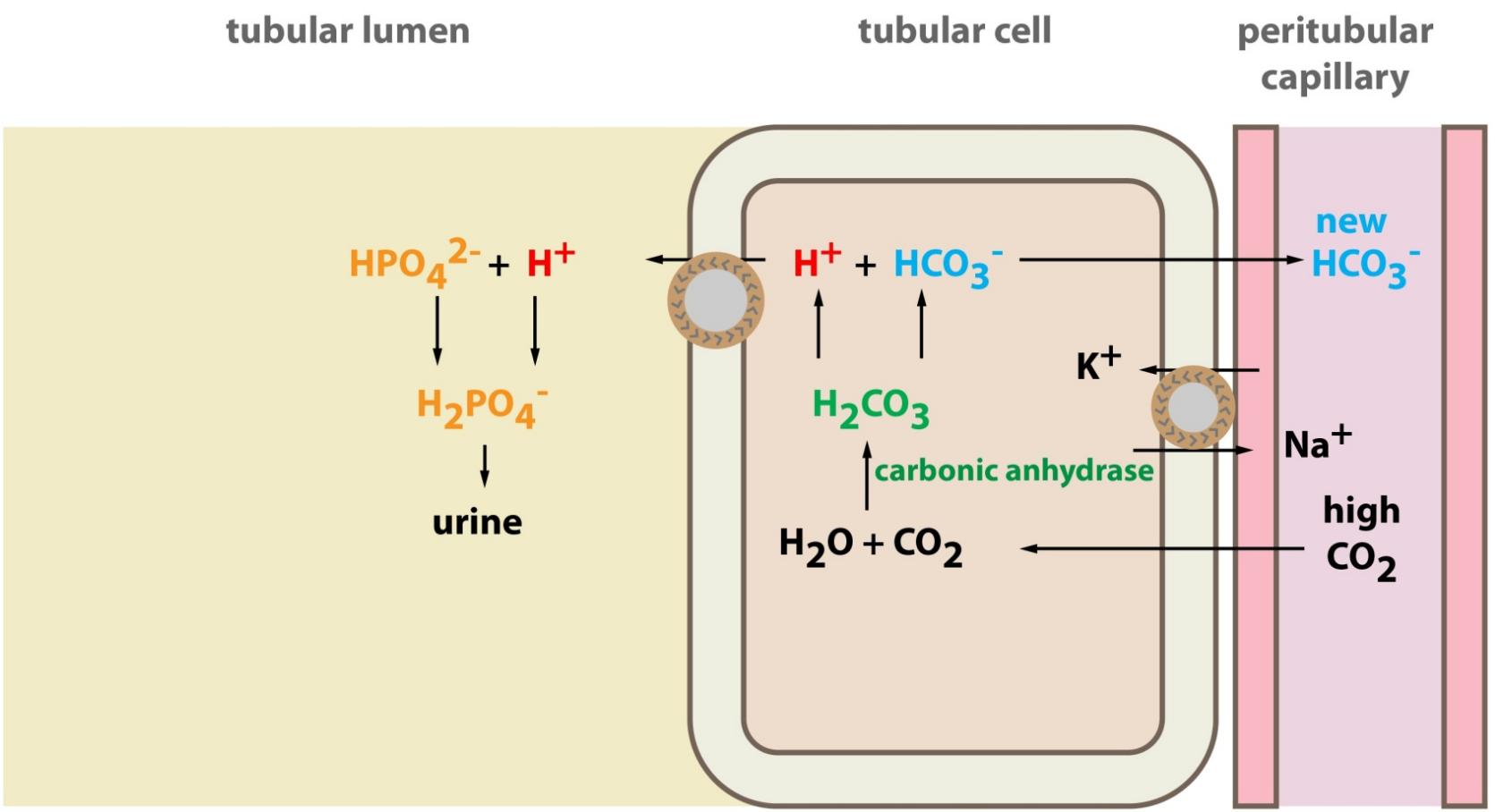
Bicarbonate correct plasma hyperkalemia



Renal Mechanism of HCO3- reabsorption



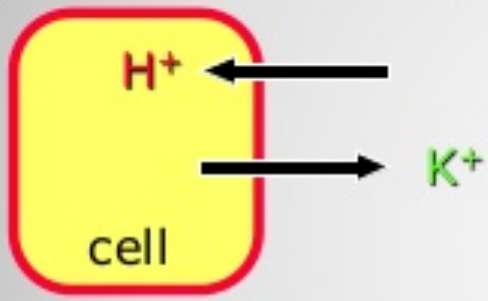
Renal Mechanism of H+ excretion



ELECTROLYTE SHIFTS

Acidosis

Compensatory Response

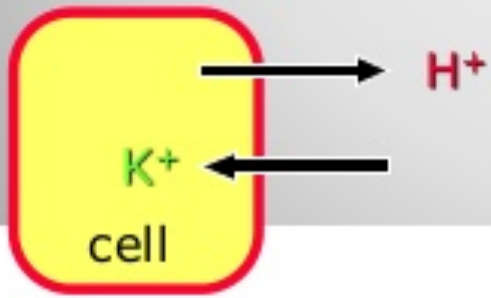


Result

- 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?

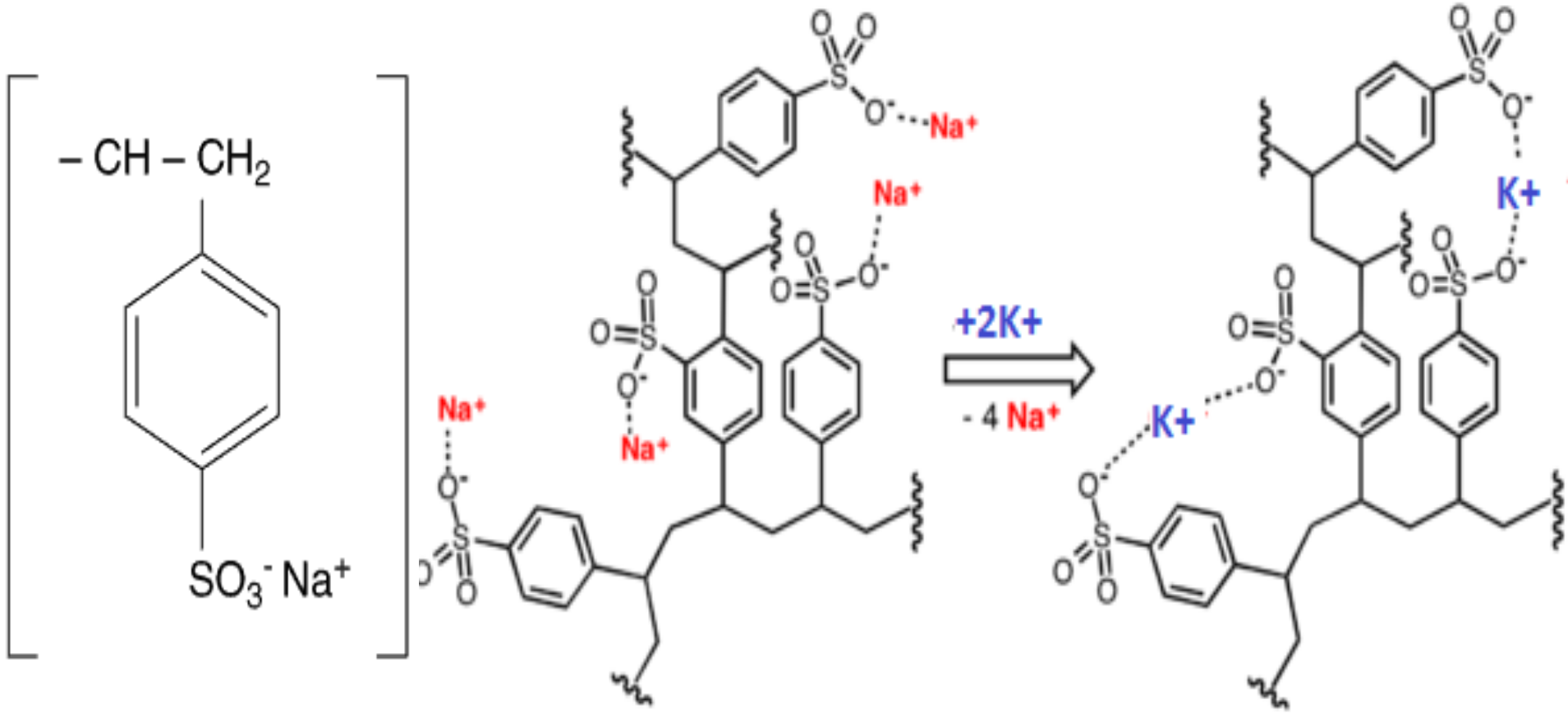
Which molecule come to normal level easily and faster with insulin ?

- Glucose
- Potassium
- Acetone
- H+

Would you like to give insulin for

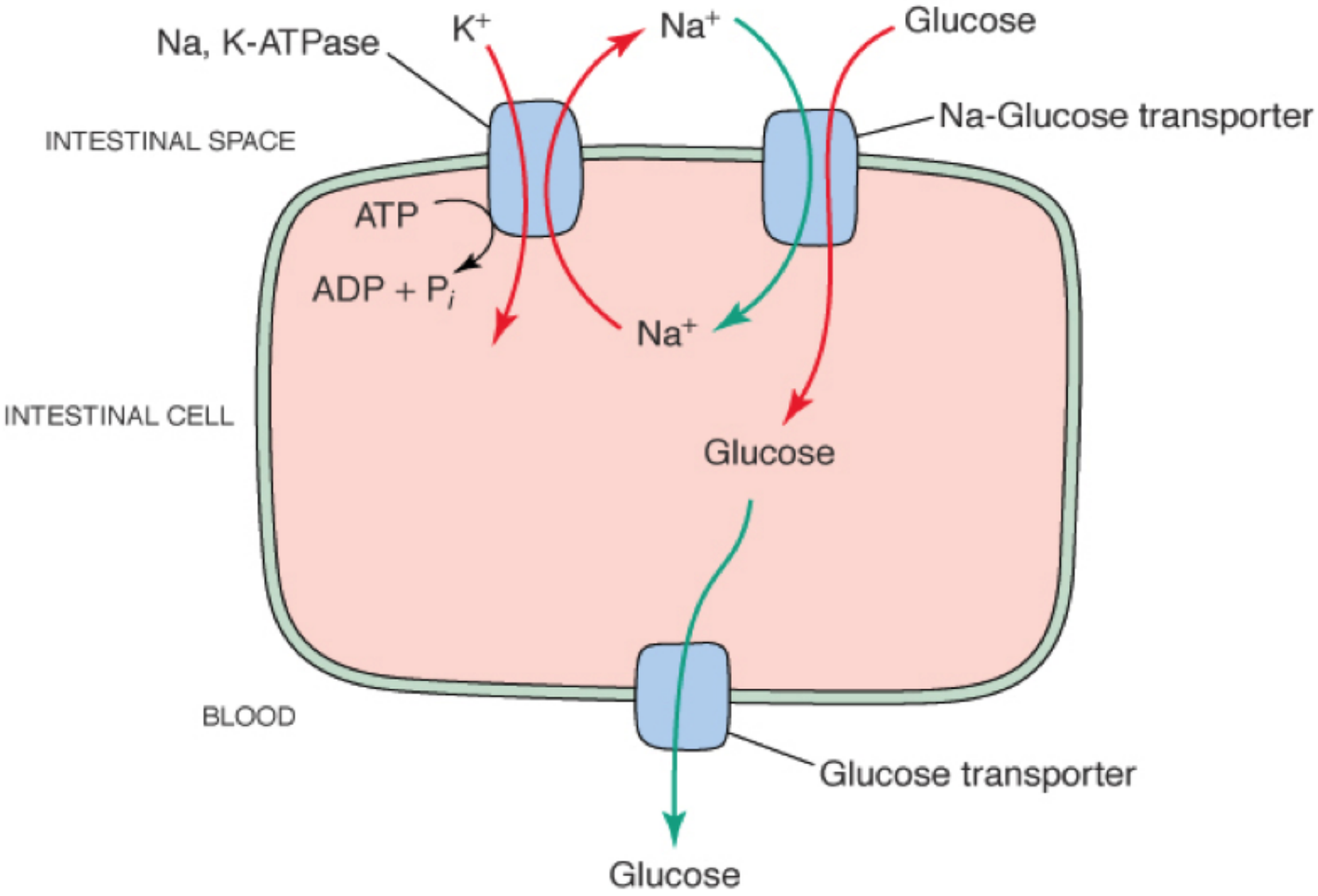
- Shorter period?
- Longer period?

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

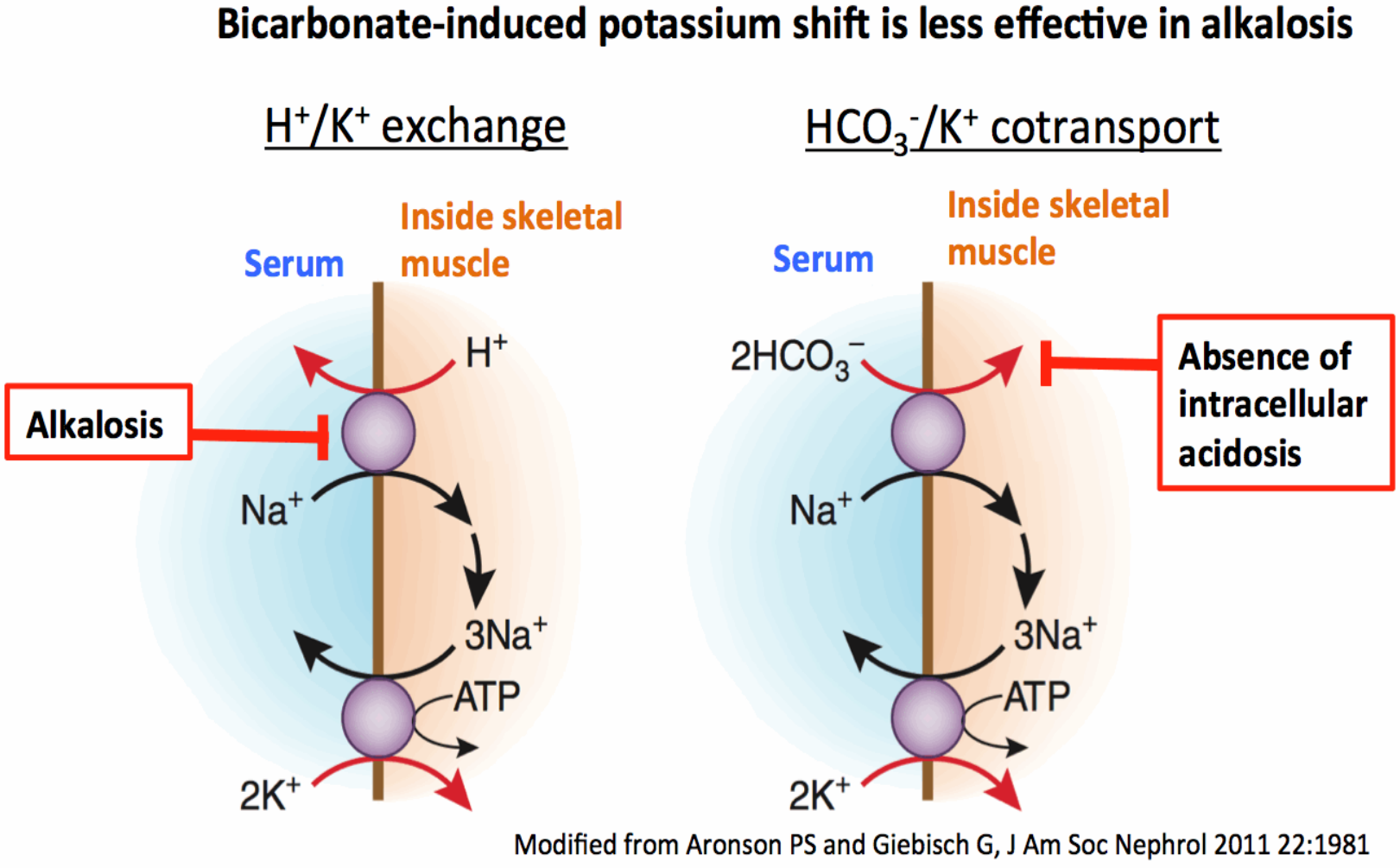


Sodium Polystyrene Sulfonate Cation Resin

Insulin stimulate S.GLUT receptor



Potassium correction with HCO3-



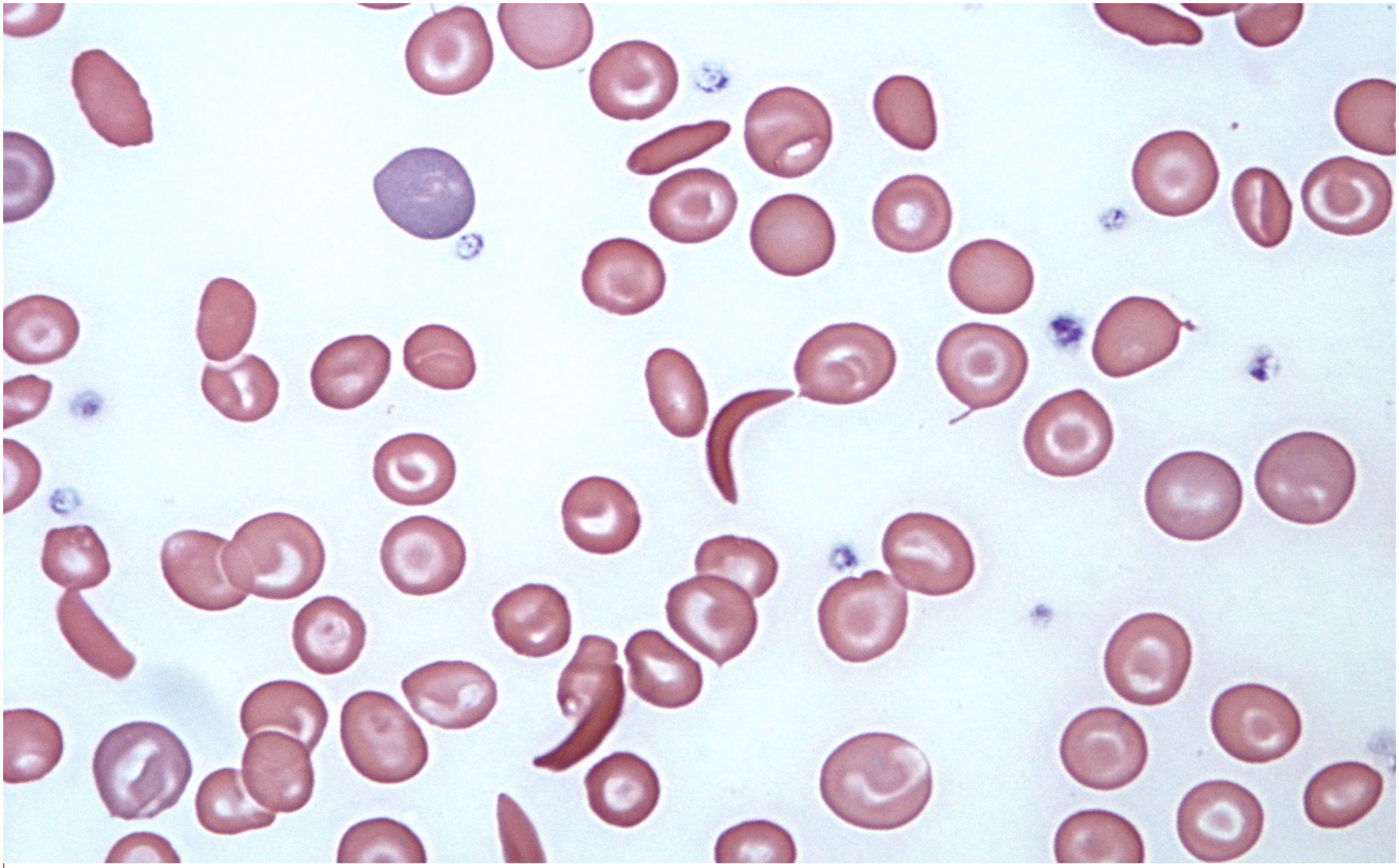
Modified from Aronson PS and Giebisch G, J Am Soc Nephrol 2011 22:1981

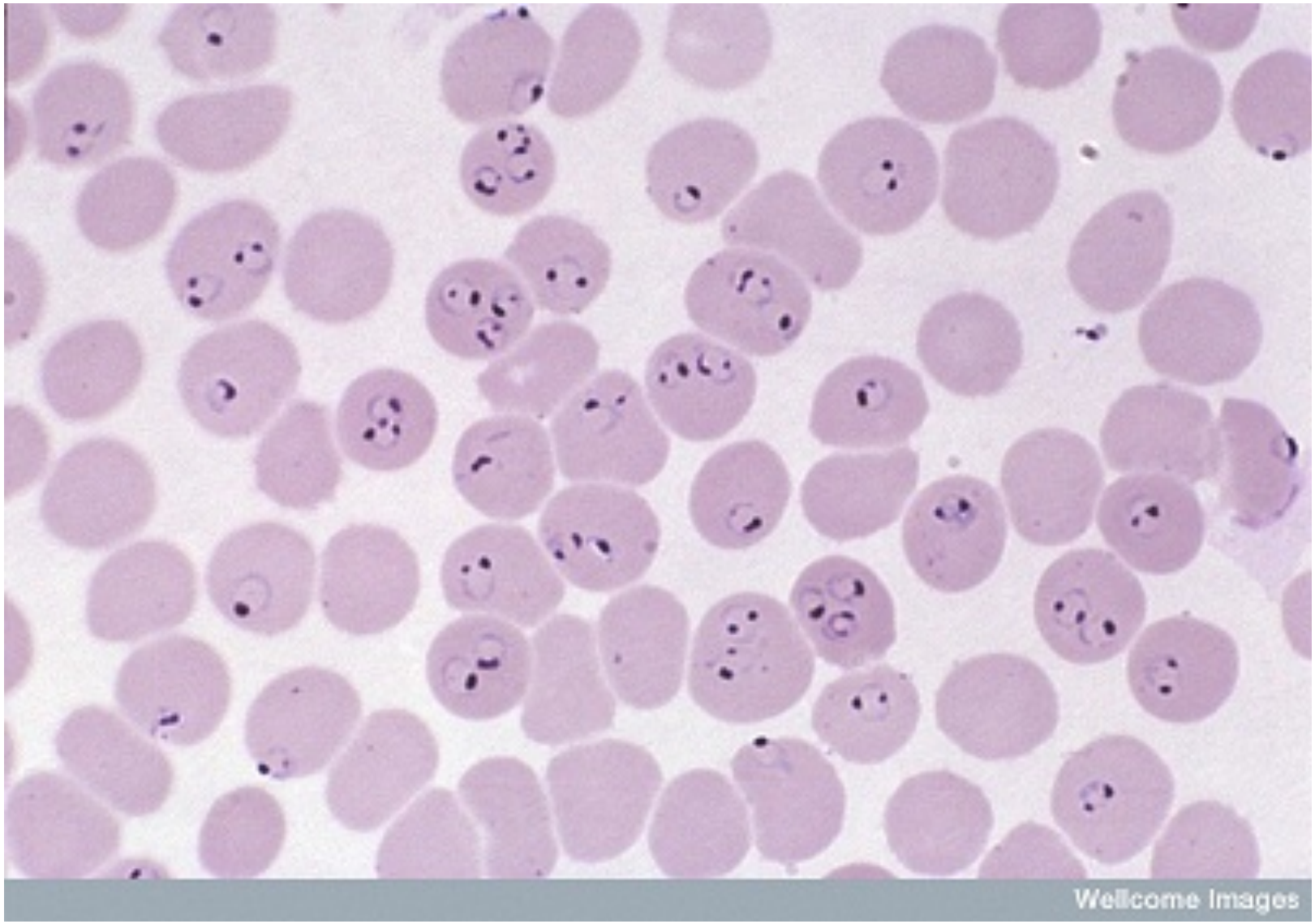
Case 7

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

Laboratory Investigation

Parameter	Value	Reference range
Haemoglobin	6.5 gm%	12 – 16 gm%
WBC	10000	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

Investigation

- Doctor is advised for following investigation for confirm diagnosis of sickle cell disease.
  - haemoglobin electrophoresis
- Patient diagnosed as “ Sickle Cell Disease”

Diagnosis
Plasmodium Vivex with Sickle cell crisis

- Following Treatment is given
- Oxygen inhalation
- Inj Artesunate ……IV 12 hourly for 3 days
- Inj Paracetamol ……IV slowly if fever
- Inj Normal Saline ….IV slowly 10ml/kg
- Inj Whole Blood ……IV transfusion one unit
- Tab Hydroxyurea 500 mg twice day orally

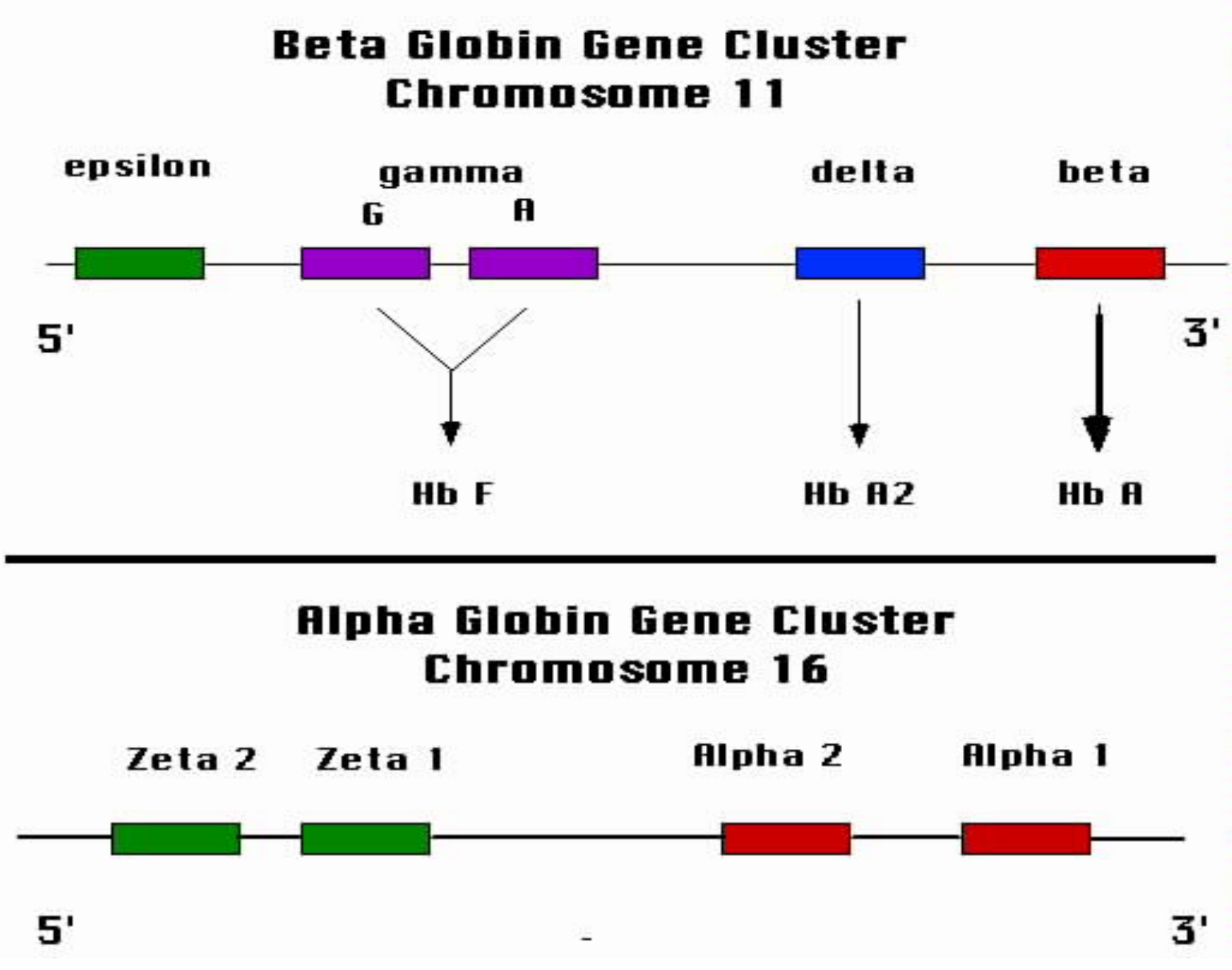
Question

- What is pathogenesis of Sickle cell disease?
- What is difference between sickle cell disease & trait?
- What significant of increase LDH & alkaline phosphatase in this case?
- What significant of increase total billirubin & indirect billirubin this case?
- What can be reason for sickle cell crisis?
- What is difference in pathogenesis of plasmodium vivex & plasmodium falciparum in this case?

- What is role of electrophoresis & HPLC in diagnosis of disease?
- What is screen test of sickle cell disease?
- What is mechanism action of hydroxyurea ?
- What is role of oxygenation ?
- What can advantage of hydration to this patient?

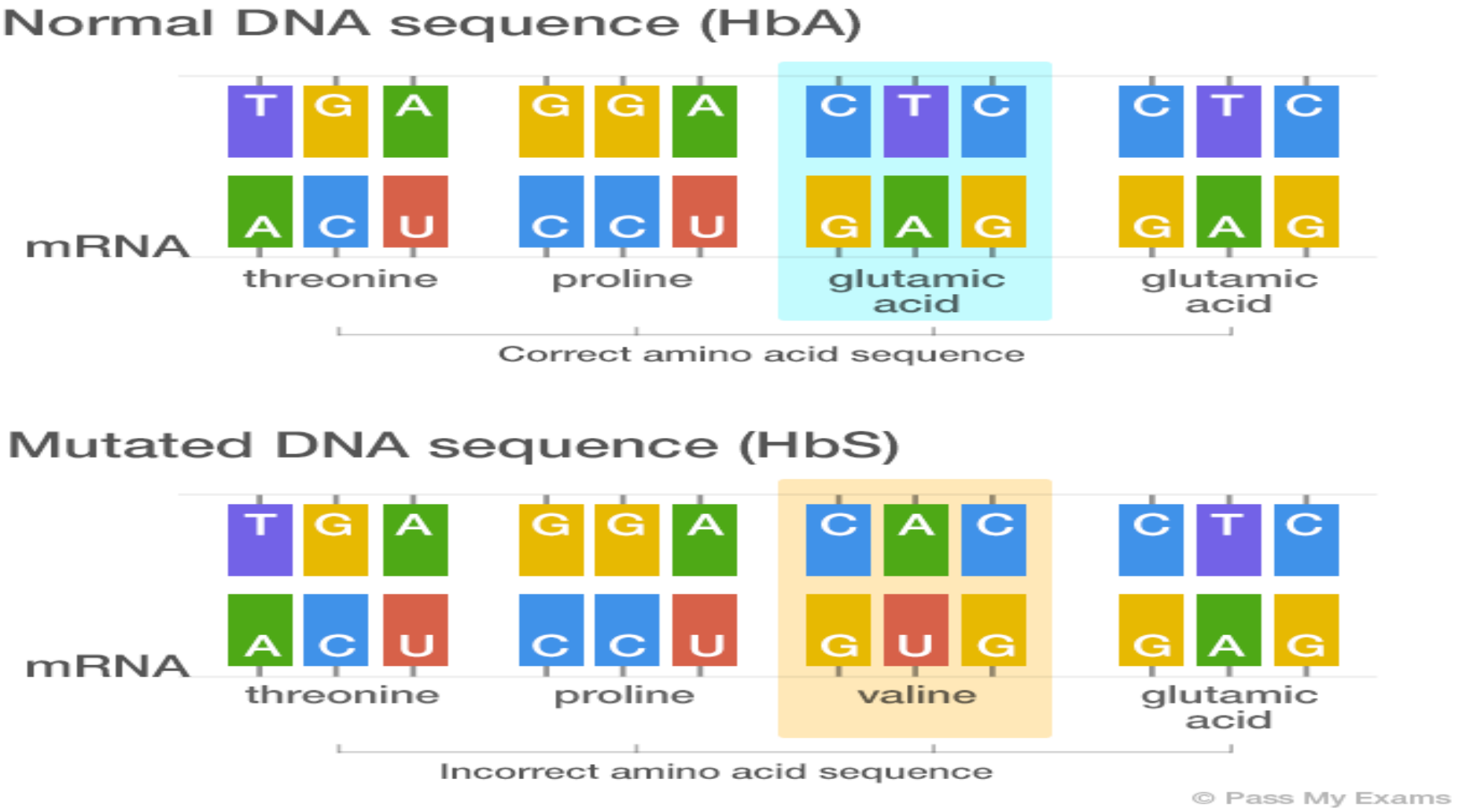
What is pathogenesis of Sickle cell disease?

- Alpha chain genes = 2 Alletes = 16 no. chromosome
- Beta chain genes = 1 Alletes = 11 no. chromosome
- **Haemoglobinopathy = Chain Varient**

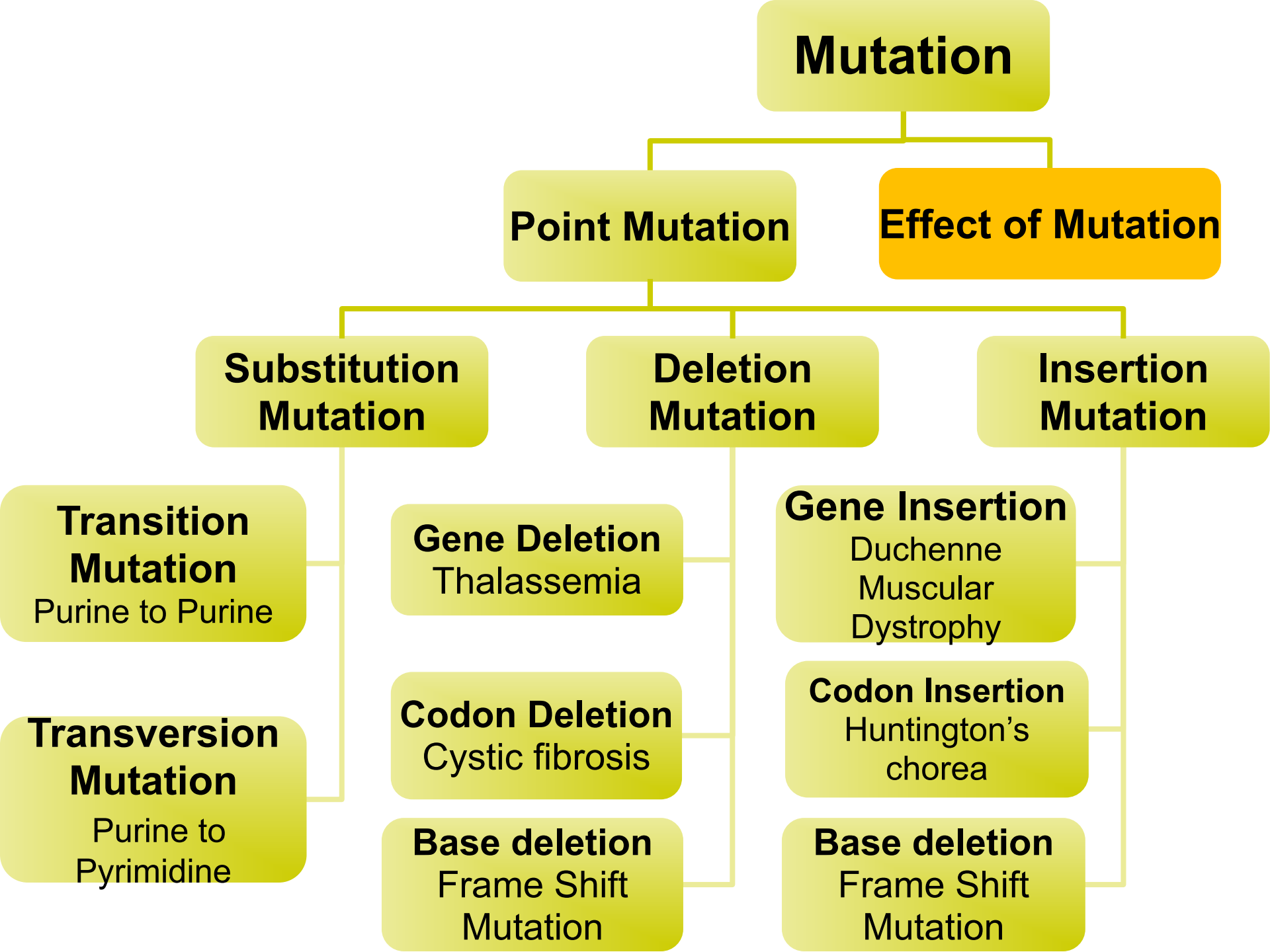

Beta Globin Gene Cluster
Chromosome 11
epsilon
gamma
G
A
delta
beta
5'
3'
Hb F
Hb A2
Hb A
Alpha Globin Gene Cluster
Chromosome 16
Zeta 2
Zeta 1
Alpha 2
Alpha 1
5'
3'

Sickle Cell Disease

- 6th Position Glutamic acid of Beta Chain is replace by Valine
- Glutamic acid = Hydrophilic & Negative Charge
- Valine = Hydrophobic & Neutral Charge
- HbS can bind and transport O2.
- The sickling occur under deoxygenated state.
- The sickled cells form small plugs in capillaries and occlude the major vessels,lead to infarction in organs.



- **Point Mutation**
- Transversion type of Point Mutation
- Replacement type of Point Mutation


Mutation
Point Mutation
Effect of Mutation
Substitution Mutation
Deletion Mutation
Insertion Mutation
Transition Mutation
Purine to Purine
Transversion Mutation
Purine to Pyrimidine
Gene Deletion
Thalassemia
Codon Deletion
Cystic fibrosis
Base deletion
Frame Shift Mutation
Gene Insertion
Duchenne Muscular Dystrophy
Codon Insertion
Huntington's chorea
Base deletion
Frame Shift Mutation

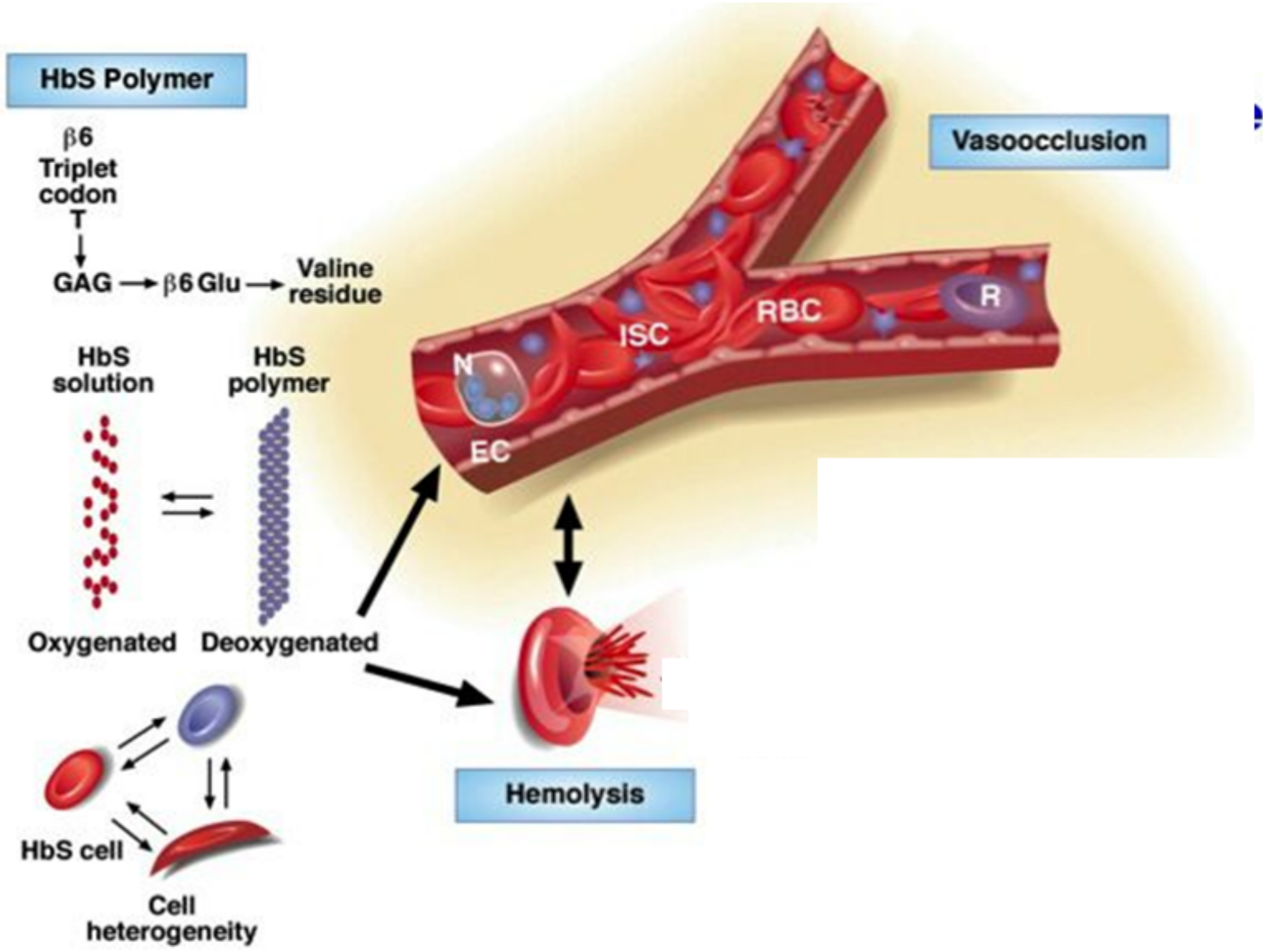
What is difference between sickle cell disease & trait?

- **Sickle cell trait - In heterozygous (AS)**
  - **50% of Hb in the RBC is abnormal.**
  - **50% of Hb in the RBC is normal.**
- Does not produce clinical symptoms.
- Hypoxia causes manifestration.
  - At higher altitudes
  - Chronic lung disorder

Sickle Cell Disease - Pathogenesis

- Hypoxia induce formation of deoxy –HbS
- Make polymerization of Hb
- Sickle Shape of RBC
- Turbulence & Occlusion of blood flow
- Small Capillary & End Arteries Affected
- Ischemia & Later Infarction to Distal Tissue
- Splenic Infarct & Avascular Necrosis of Femur Head
- Abdomina Pain & Joint Pain

Sickle Cell Disease Pathogenesis



What significant of increase LDH & alkaline phosphatase in this case?

- LDH
  - No Specific
  - Liver , RBC, Gall bladder , Bone
  - Monitor haemolysis
  - Daily LDH Measurement
    - Prognosis
    - Effectiveness of treatment
- Alkaline Phosphatase
  - Bone infaction
  - > 1500 U/L

What can be reason for sickle cell crisis?

- Plasmodium Vivex
- P.vivex utilized Oxygen for it's multilication
- Hypoxia
- Sickling & Decrease life span of RBC
- Crisis & Severe hemolysis

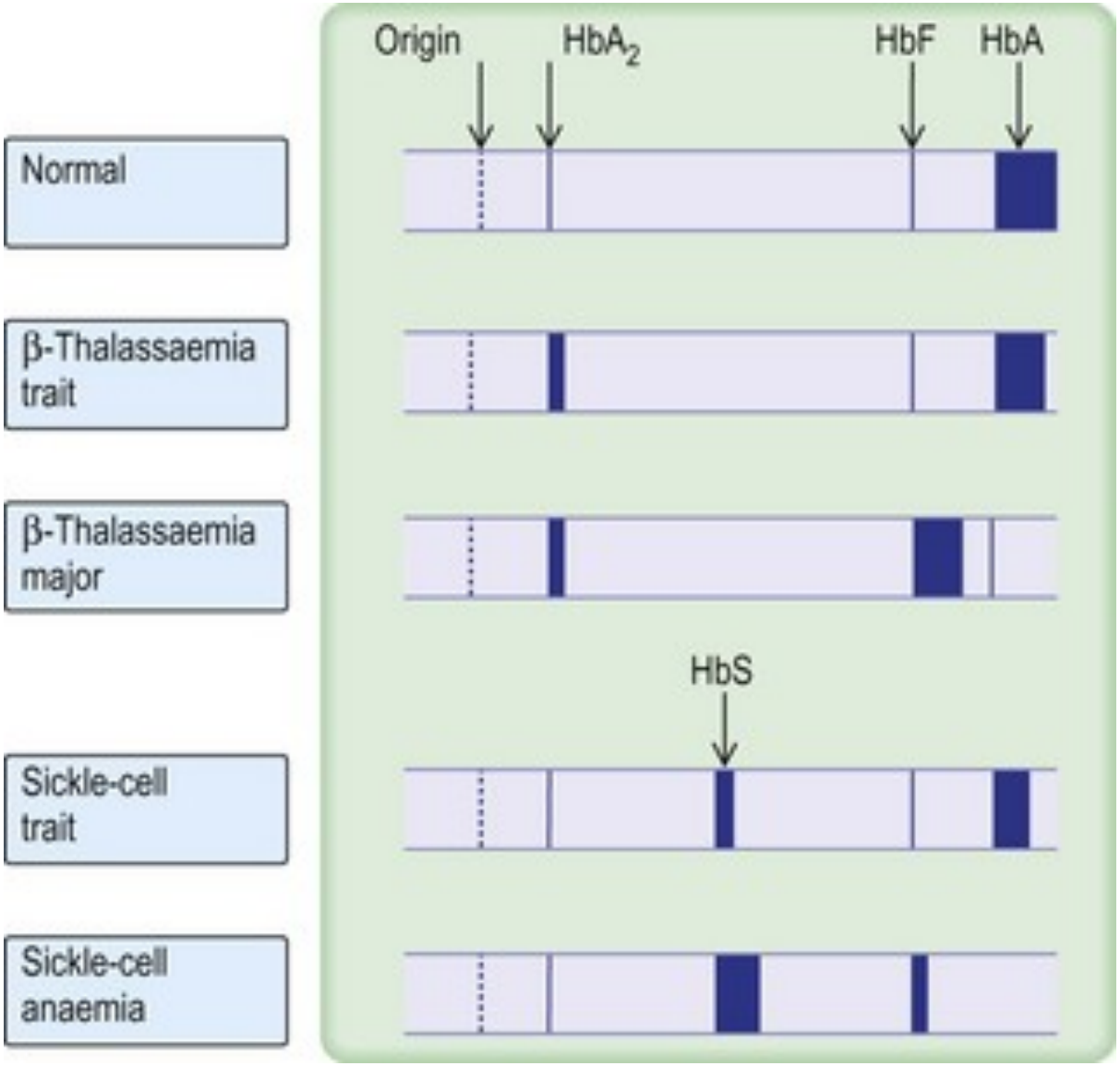
- ?????Plasmodium Falciparum???

What is role of electrophoresis & HPLC in diagnosis of disease?

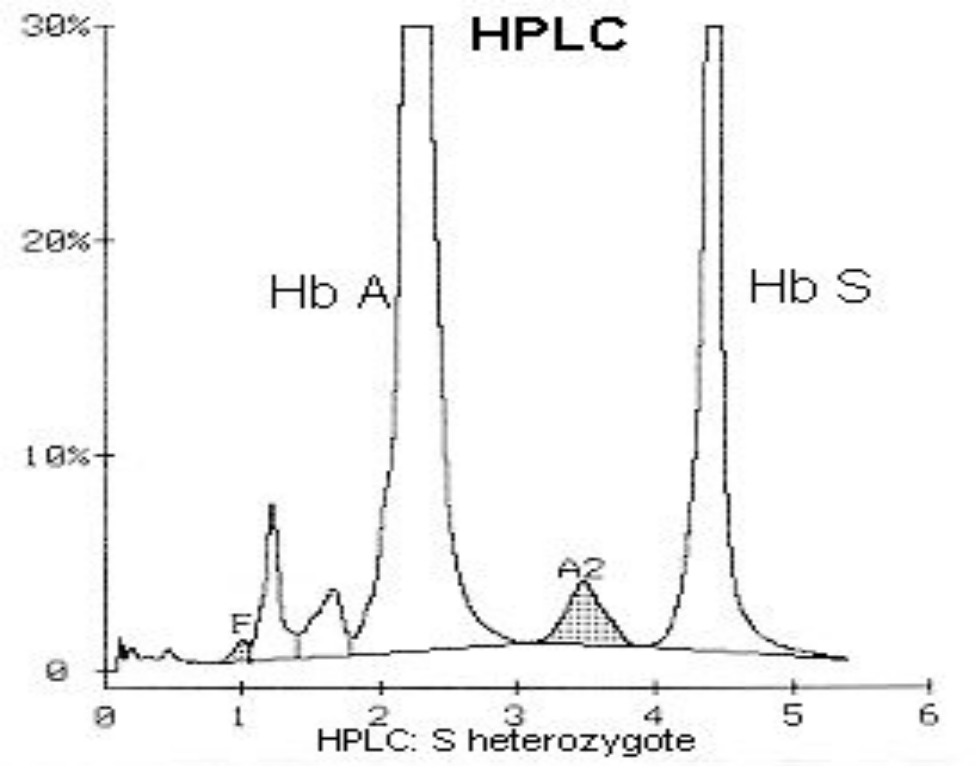
Electrophoresis:

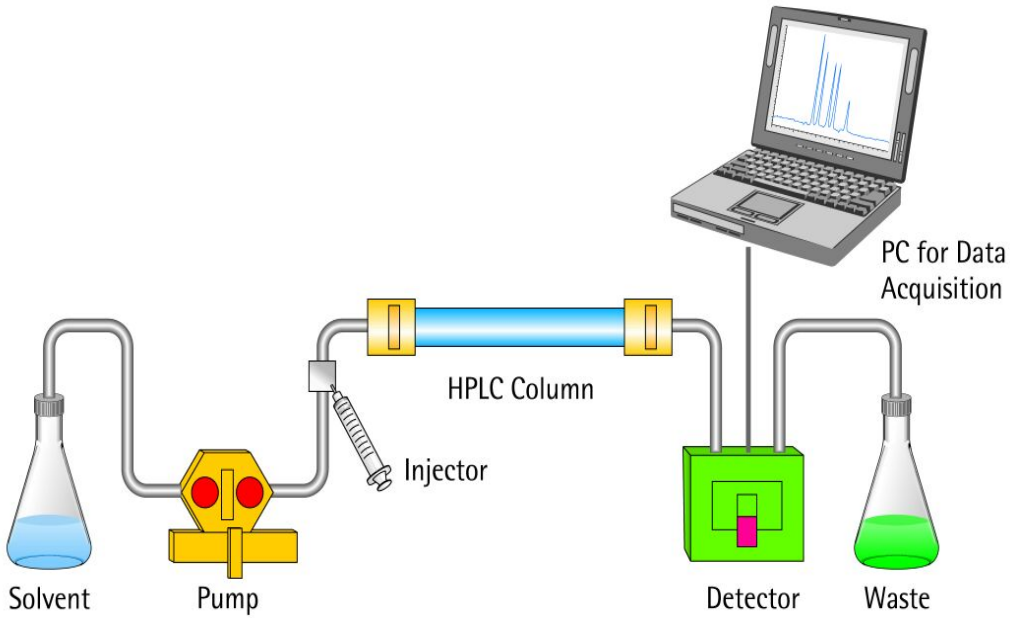
- Lack of Carboxyl group of Glutamic acid in HbS
- Lack of Negative charge Glutamic acid.
- HbS - less negatively charged
- Decreases electrophoretic mobility
- HbS move slower than HbA

Electrophoresis

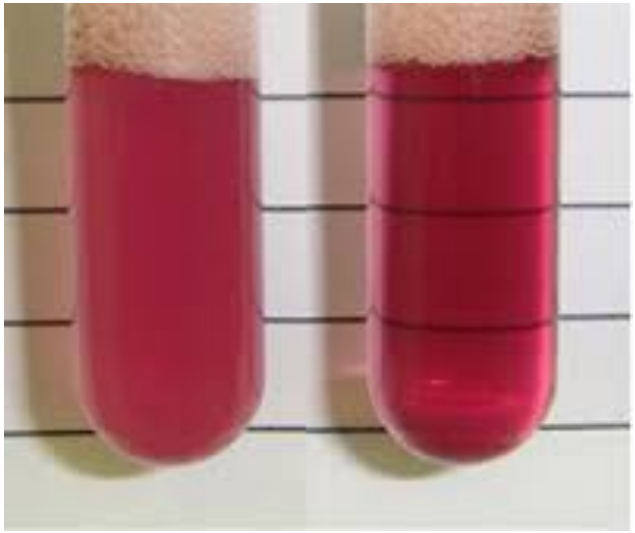


High Performance Liquid Chromatography (HPLC)

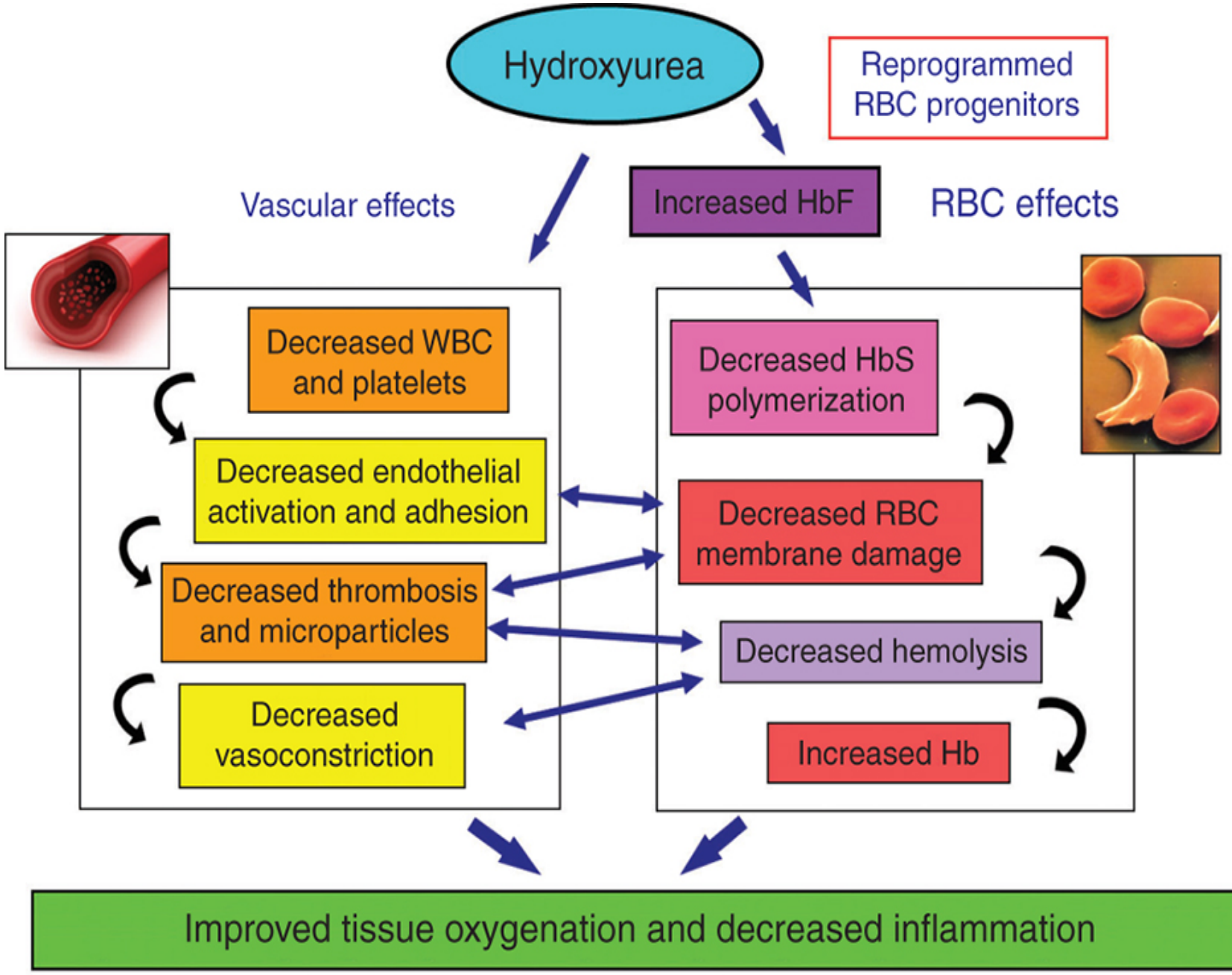




Dithionite test – Sickling Test



- Inexpensive & Rapid
- Use for Screening
- Less Sensitive
- The reagent consists
  - Saponin - Make RBC Haemolysis
  - Na-dithionite - Make Hb deoxygenates
  - Principle :
  - Reagent make Hb deoxygenated and causes polymerazition of HbS and Turbidity of Sample


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

Role of Oxygen + Hydration + Hydroxyurea

- **Hydroxyurea**
  - Induce gene for gamma globin chain
  - 5 to 10 % fetal Hb synthesis (HbF)
  - Interfere with polymerization of deoxy HbS
  - Prevent crisis and improve oxygenation
- **Oxygenation**
  - Decrease concentration of deoxygenated Hb
  - Decrease in polymerization & Decrease lysis of RBC
- **Hydration**
  - Increase in body fluid
  - Increase in circulation – Arterial dilatation
  - Increase in oxygenation & Decrease polymerization
  - Decrease in lysis of RBC

- 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 Rise + Dal + Ghee
  - Jeggary + Ghee
  - Crushed Apple + Banana

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

- 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?