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 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.
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 cholesterol?
12. What is role of fibrinolytic drugs (streptokinase) in myocardial infarction?
What are chronic complication of DM?
What are chronic complications of DM?

**Complications of Diabetes**

**Macrovacular**
- **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 uncontroled diabetic mellitus increase chances of atherosclerosis?
• 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?
• How statin reduce cholesterol level?
Cholesterol Regulation

Glucose → Pyruvate → Acetyl CoA → HMG CoA → Mevalonic acid → Cholesterol

Insulin +

Protein phosphatase

HMG CoA reductase

Protein kinase A

HMG CoA reductase
Competitive Inhibition

HMG CoA-reductase
Active site

[Chemical structures and reactions]

Lovastatin (competitive inhibitor)

HMG-CoA (substrate)
• What is biochemical explanation of hypoglycemia?
Alcohol Metabolism

Ethanol metabolism:

\[ \text{ethanol} \xrightarrow{\text{alcohol dehydrogenase}} \text{acetaldehyde} \xrightarrow{\text{aldehyde dehydrogenase}} \text{acetic acid} \xrightarrow{\text{NAD}^+ \text{ dehydrogenase}} \text{acetyl-SCoA} \]

Methanol metabolism:

\[ \text{methanol} \xrightarrow{\text{alcohol dehydrogenase}} \text{formaldehyde} \xrightarrow{\text{aldehyde dehydrogenase}} \text{formic acid} \]
Ethanol → Acetaldehyde → Acetic acid

Alcohol Dehydrogenase

NAD⁺ → NADH + H⁺

Lactate → Glucose → Pyruvate

Aldehyde Dehydrogenase

NAD⁺ → NADH + H⁺
• Why physician asked to give injectable 50% Dextrose saline with Thiamine (Vitamin B1)?
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?
Dietary fiber and health:

- Improvements in gastrointestinal health (Diverticular disease, Haemorrhoids, Irritable bowel syndrome)
- Helps prevent constipation
- Reduction in the risk of developing some cancers
- Improvements in glucose tolerance and insulin response (Diabetes)
- Increased satiety and hence some degree of weight management
- Reduction of hyperlipidaemia, hypertension and other coronary heart disease risk factors
• 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?
• How will you calculate patient’s LDL cholesterol?
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

→ Plasmin

→ Fibrin → Fibrin degradation products

t-PA

Urokinase

α₂-Antiplasmin
• Give biochemical explanation of antiplatelet drug - Aspirin.
Phospholipids

(Phospholipase A-2) \rightarrow \text{Arachidonic Acid}

\text{Cyclooxygenase} \rightarrow \text{Prostaglandins, Thromboxananes}

\text{Lipoxygenase} \rightarrow \text{Leukotrienes}
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
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
- Haemoglobin : 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 explanation about following symptoms in chronic alcoholic
   - Alter conciousness
   - Haematemesis

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 conciousness
   – Haemetemesis

2. Biochemical explanation about following signs in chronic alcoholic
   – Edeme
   – Ascites
   – Hypotension

3. What is hepato-renal syndrome?
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
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
1. Biochemical explanation of Edema, Ascites, Hypotension in Chronic alcoholic
filtration pressure = hydrostatic pressure - oncotic pressure
Hepato- Renal Syndrome
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
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 Hyperammononemia

\[ \alpha\text{-Ketoglutarate} \rightarrow \text{Glutamate} \rightarrow \text{Glutamine} \rightarrow \text{Phenylacetylglutamine} \rightarrow \text{Urine Excretion} \]

\[ \text{Glycerol Phenylbutyrate} \rightarrow \text{Phenylbutyric Acid} \rightarrow \text{Phenylacetate} \]

\[ \text{Ester Hydrolysis/ Pancreatic Lipases} \]

\[ \text{Beta Oxidation} \]
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.
<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
<th>Reference range</th>
</tr>
</thead>
<tbody>
<tr>
<td>RBS</td>
<td>500 mg/dl</td>
<td>140 mg/dl</td>
</tr>
<tr>
<td>Serum Acetone</td>
<td>10 mg/dl</td>
<td>&lt;1 mg/dl</td>
</tr>
<tr>
<td>Serum Creatinine</td>
<td>2.5 mg/dl</td>
<td>0.4 - 1.4 mg/dl</td>
</tr>
<tr>
<td>Blood Urea</td>
<td>150 mg/dl</td>
<td>15 - 45 mg/dl</td>
</tr>
<tr>
<td>Serum Na+</td>
<td>120 mmol/l</td>
<td>135 - 145 mmol/l</td>
</tr>
<tr>
<td>Serum K+</td>
<td>6.0 mmol/l</td>
<td>3.5 - 5.0 mmol/l</td>
</tr>
<tr>
<td>pH</td>
<td>7.1</td>
<td>7.35 - 7.45</td>
</tr>
<tr>
<td>pO2</td>
<td>95 mmHg</td>
<td>90 - 100 mmHg</td>
</tr>
<tr>
<td>pCO2</td>
<td>24 mmHg</td>
<td>32 - 40 mmHg</td>
</tr>
<tr>
<td>HCO3- (Bicarbonate)</td>
<td>12 mmol/l</td>
<td>24 - 32 mmol/l</td>
</tr>
</tbody>
</table>
Diagnosed = “Diabetic ketoacidosis with acute renal failure”
Advised to following treatment.

- **Inj normal saline** fast I.V. (4-5 litre in 1\textsuperscript{st} 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

- 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
Acute metabolic acidosis

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

- Generation or exacerbation of bone disease
- Growth retardation (in children)
- Reduced albumin synthesis
- Impaired glucose tolerance
- Increased muscle wasting
- Acceleration of progression of kidney disease
- Enhanced production of $\beta_2$-microglobulin
Effect of Acidosis on O2- CO2 diffusion
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.

<table>
<thead>
<tr>
<th></th>
<th>Value</th>
<th>Ref. Value</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>pH</td>
<td>7.1</td>
<td>7.35 - 7.45</td>
<td>Low Acidosis</td>
</tr>
<tr>
<td>pO2</td>
<td>95</td>
<td>90 - 100 mmHg</td>
<td>Normal</td>
</tr>
<tr>
<td>pCO2</td>
<td>24</td>
<td>32 - 40 mmHg</td>
<td>Low Indicate Alkalosis. (Compensatory)</td>
</tr>
<tr>
<td>HCO3-</td>
<td>12</td>
<td>24 - 32 mmol/l</td>
<td>Low Indicate Acidosis</td>
</tr>
</tbody>
</table>

Uncompensated Metabolic Acidosis
Acidosis (Increase H+) increase K+

Extracellular (Plasma)  Intracellular

Increase H+

Increase Na+

Channel Inactive

Increase 2K+

3Na+ ATP
Bicarbonate correct plasma hyperkalemia

Extracellular (Plasma)       Intracellular

Increase $2\text{HCO}_3^-$

Decrease $2\text{K}^+$

$\text{Na}^+$

$3\text{Na}^+$

ATP
Renal Mechanism of
H+ excretion &
HCO3- reabsorption
ELECTROLYTE SHIFTS

**Acidosis**
Compensatory Response

<table>
<thead>
<tr>
<th>Compensatory Response</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\text{H}^+$ buffered intracellularly</td>
<td></td>
</tr>
<tr>
<td>Hyperkalemia</td>
<td></td>
</tr>
</tbody>
</table>

**Alkalosis**
Compensatory Response

<table>
<thead>
<tr>
<th>Compensatory Response</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tendency to correct alkalosis</td>
<td></td>
</tr>
<tr>
<td>Hypokalemia</td>
<td></td>
</tr>
</tbody>
</table>
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**

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
## Laboratory Investigation

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

- Following Treatment is given
- Oxygen inhalation
- Inj Artesunate ..................IV 12 hourly
- Inj Paracetamol ...............IV
- Inj Normal Saline ..............IV
- Inj Whole Blood ........ IV trasfusio
- Tab Hydroxyurea 500 mg twice day orally
Hydroxyurea

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

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

Improved tissue oxygenation and decreased inflammation

Reprogrammed RBC progenitors
• 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?