

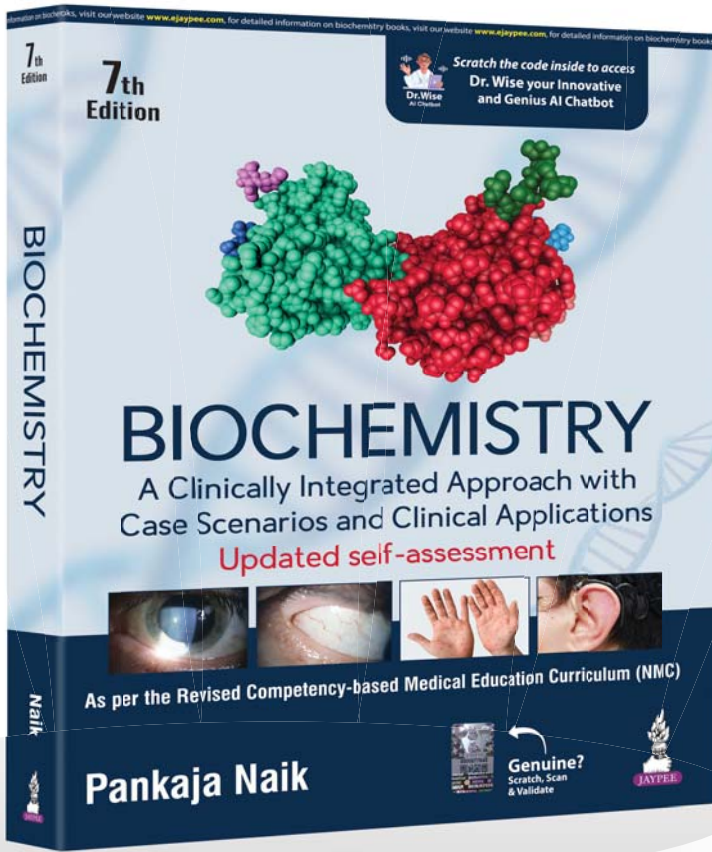


BIOCHEMISTRY

A Clinically Integrated Approach with Case Scenarios and Clinical Applications

Updated self-assessment

As per the Revised Competency-based Medical Education Curriculum (NMC)



7th Edition

Pankaja Naik



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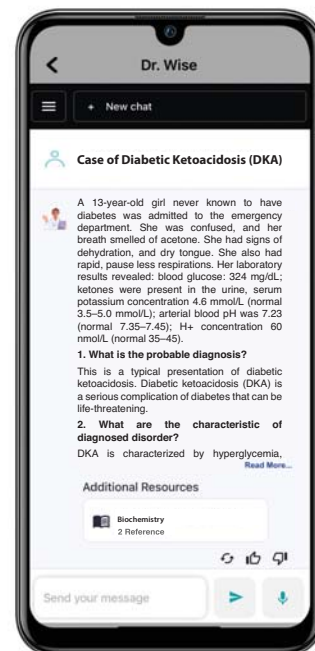
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Why to Buy this Book ?

- The four newly added chapters are: **Metabolism of Alcohol, Instrumentation and Techniques, Artificial Intelligence in Healthcare Industry, and AETCOM Module 7.1.**
- Each chapter begins with clearly defined **competencies and learning objectives** aligned with the **CBME framework**.
- Applied aspects of biochemistry are emphasized through: **Clinical case boxes, clinical approach discussions, image-based questions, rich clinical illustrations** related to key disorders, and **"insight" boxes** highlighting important and practical facts.
- This comprehensive approach eliminates the need for a separate book on clinical case studies.
- To reinforce learning, each chapter concludes with a variety of **assessment questions**, including: **Long-answer type questions, short notes, scenario-based case studies, reasoning questions, multiple choice questions (MCQs).**
- This **CBME-aligned textbook** has been recommended by several universities and medical colleges across India as part of the curriculum for the **Indian Medical Graduates (IMG).**



Clinical MCQs

Case Scenarios

Short Notes

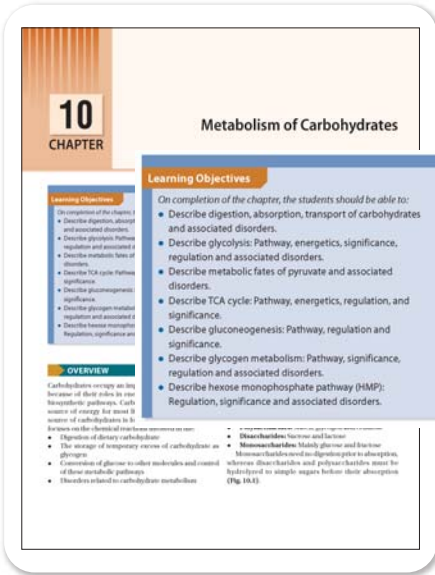
Long Notes

Images

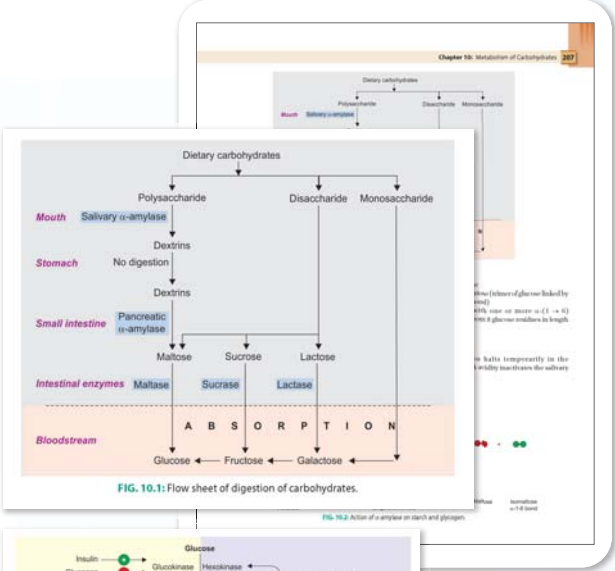
Flashcards

Comparison Tables

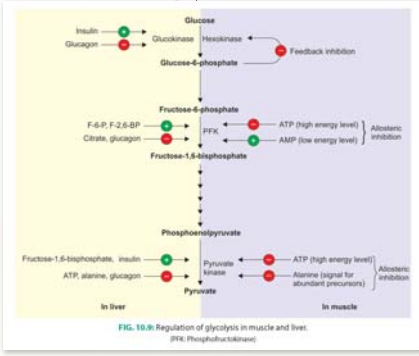
Each chapter begins with clearly defined **Competencies** and **Learning Objectives** aligned with the **CBME framework**.



Each chapter features **Figures and Flowcharts** to enhance the reader's understanding.



Specific Sections of the Book provide targeted **Insights, Tables, and Case Studies** that present information in a clear and easily understandable way for the reader.



INSIGHT 10.3

Isoenzyme Forms of Hexokinase

The human genome encodes **four different hexokinases, I to IV** all of which catalyze the same reaction. They differ with respect to their kinetic properties.

- Brain and kidney have chiefly the type I isoenzyme
- Skeletal muscle has type II
- Adipose tissue has both I and II
- Liver possesses all four isoenzyme of hexokinase but the principal form of hexokinase is type IV, commonly known as **glucokinase**.

The difference between muscle hexokinase and liver hexokinase, i.e., glucokinase is given in **Table 10.2**.

| Phase | Enzyme | Regulation |
|-----------|----------------|---|
| Phase I | Hexokinase I | Inhibited by its product, glucose-6-phosphate, at an allosteric receptor. |
| Phase II | Hexokinase II | Inhibited by its product, glucose-6-phosphate, at an allosteric receptor. |
| Phase III | Hexokinase III | Inhibited by its product, glucose-6-phosphate, at an allosteric receptor. |
| Phase IV | Glucokinase | Not inhibited by its product, glucose-6-phosphate. |

TABLE 10.1: Glucose transporters.

| Transporters | Occurrence | Function |
|--|---|--|
| Facilitative bidirectional transporters | | |
| GLUT-1 | Brain, kidney, colon, placenta and erythrocyte | Uptake of glucose |
| GLUT-2 | Liver, pancreatic β-cell, small intestine, kidney | Rapid uptake and release of glucose |
| GLUT-3 | Brain, kidney, placenta | Uptake of glucose |
| GLUT-4 | Heart and skeletal muscle, adipose tissue | Insulin stimulated uptake of glucose |
| GLUT-5 | Small intestine | Absorption of fructose |
| Sodium-dependent unidirectional transporter | | |
| SGLT-1 | Small intestine and kidney | Active uptake of glucose from lumen of intestine and reabsorption of glucose in proximal tubule of kidney against concentration gradient |

CASE STUDY 10.1: LACTOSE INTOLERANCE

Case Scenario

A 15-year-old African American boy came to India on an exchange visit for 2 months. After 2 weeks in India, he complained of abdominal discomfort, a feeling of being bloated, increased passage of urine, and more recently, the development of diarrhea. His only change in diet noted at the time was the introduction of milk. He was consuming about 1 to 1.5 liters per day. A diagnosis of lactose intolerance was made.

Questions

1. What is lactose intolerance?
2. What are the symptoms of lactose intolerance?
3. What are the causes of lactose intolerance?
4. How is lactose intolerance diagnosed?
5. How is lactose intolerance treated?

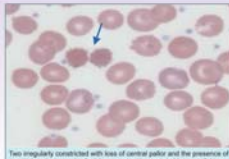
Discussion

1. Lactose intolerance is a clinical syndrome that manifests with characteristic signs and symptoms upon consuming food substances containing lactose, a disaccharide. Normally lactose is hydrolyzed into glucose and galactose by the lactase enzyme, which is found in the small intestinal brush border. Deficiency of lactase results in clinical symptoms.
2. Lactose intolerance presents with abdominal bloating and pain, loose stools, nausea, flatulence, and borborygmi (intestinal rumbling sounds caused by passing gas).

Answers to questions 3, 4 and 5: Refer given text under heading lactose intolerance.

IMAGE-BASED QUESTION 10.1

What is the most likely diagnosis for the 2-year-old black girl presenting with severe anemia, splenomegaly, jaundice, normal hemoglobin electrophoresis, normocytic anemia, normal platelet and white blood cell counts, and the presence of bizarre erythrocytes including spiculated cells on peripheral smear?



Two irregularly contracted cells with loss of central pallor and the presence of multiple spicules (red cells) (blue arrow) with pyruvate kinase deficiency.

- Sickle cell disease
 - Thalassemia
 - Pyruvate kinase deficiency
 - G-6-PD deficiency
- Discussion**
- a. Sickle cell disease:** Sickle cell disease is characterized by the presence of hemoglobin S (HbS), which causes red blood cells to take on a sickle shape. This condition commonly leads to anemia, pain crises, and organ damage. However, in the scenario provided, the hemoglobin electrophoresis was normal, making sickle cell disease less likely.
- b. Thalassemia:** Thalassemias are genetic disorders that result in reduced production of hemoglobin and abnormal red blood cell formation. They can lead to anemia, but the hemoglobin electrophoresis typically shows abnormal hemoglobin patterns. Since the hemoglobin electrophoresis was normal in this case, thalassemia is less likely.
- c. Pyruvate kinase deficiency:** Pyruvate kinase deficiency is a rare inherited disorder that affects the red blood cells' ability to generate energy. It leads to hemolytic anemia, jaundice, and splenomegaly. The presence of bizarre erythrocytes, including spiculated cells on peripheral smear, is suggestive of this condition. The normal hemoglobin electrophoresis is consistent with this diagnosis, as it doesn't involve abnormal hemoglobin types.
- d. G-6-PD deficiency:** Glucose-6-phosphate dehydrogenase (G-6-PD) deficiency is an enzyme deficiency that can cause hemolytic anemia, especially in response to oxidative stress. While it can result in jaundice and anemia, the scenario doesn't mention abnormal erythrocyte morphology or spiculated cells on peripheral smear. G-6-PD deficiency is less likely in this case.

Answer: The most likely diagnosis that aligns with the patient's symptoms, peripheral smear findings, and normal hemoglobin electrophoresis is:

- c. Pyruvate kinase deficiency.

Hexokinase Deficiency

- Genetic defects in hexokinase reduce the amount of hexokinase.
- Because hexokinase is the red blood cells' main source of energy, a deficiency of this enzyme leads to hemolytic anemia.
- Consequently, due to low levels of 2,3-BPG, less oxygen is available for the tissues. This defect will result in anemia.

Phosphoglucose Isomerase Enzyme Deficiency

- Phosphoglucose isomerase deficiency** is an autosomal recessive disorder characterized by congenital hemolytic anemia and progressive cardiovascular dysfunction beginning in early childhood.
- Many patients die from respiratory failure in childhood.
- The metabolic syndrome is variable, but usually includes lower motor neuron dysfunction with hypotonia (decreased muscle tone), muscle weakness

- Low concentrations of hexokinase in red blood cells cause hemolytic anemia and neurodegeneration.

Lactic Acidosis

- Lactic acidosis is the accumulation of lactic acid in the blood to levels that significantly affect the blood pH. The high concentration of lactate results in lowered blood pH (7.2).
- Under normal conditions, lactate is metabolized in the liver and the blood lactate level is in between 1 and 2 mM. With lactic acidosis, the blood lactate level may be 5 mM or more.
- Lactate accumulation in the body fluids can be due to increased formation or decreased utilization.
- A common cause of lactic acidosis is tissue hypoxia caused by shock, cardiopulmonary arrest, and hypoxia.

Each chapter includes **Image-Based Questions**, accompanied by detailed discussions.

264 Chapter 10: Metabolism of Carbohydrates

- which can lead to high levels of blood sugar if not treated.
- More than 90% of people with diabetes have type 2 diabetes.
- Over time, type 2 diabetes can cause serious damage to the body, especially nerves and blood vessels.
- Type 2 diabetes is often preventable. Factors that contribute to developing type 2 diabetes include being overweight, not getting enough exercise, and genetics.
- Early diagnosis is important to prevent the worst effects of type 2 diabetes.

- People with diabetes have a higher risk of health problems including heart attack, stroke, and kidney failure.
- Diabetes can cause permanent vision loss by damaging blood vessels in the eyes.
- Many people with diabetes develop problems with their feet (diabetic foot) from nerve damage and poor blood flow. This can cause foot ulcers and may lead to amputation.

Treatment

- People with type 1 diabetes need insulin injections for survival.
- One of the most important ways to treat diabetes is to keep a healthy lifestyle. To help prevent type 2 diabetes and its complications, people should:
 - Eat a healthy diet and avoid sugar and saturated fat
 - Get regular exercise
 - Stay physically active with at least 30 minutes of moderate exercise each day
 - Stop smoking
- Some people with type 2 diabetes will need to take medicine to help manage their blood sugar levels. These can be oral medicines or insulin injections or drops that cause additional release of insulin by the pancreas.
- Insulin** lowers blood glucose levels.
- Sulfonylureas** cause additional release of insulin by the pancreas.
- Glucagon-like peptide-1 receptor agonists (GLP-1 agonists)** cause additional release of insulin by the pancreas.
- Along with medicines to lower blood sugar, people with diabetes often need medicines to lower their blood pressure and statins to reduce the risk of complications.
- Additional medical care may be needed to treat the effects of diabetes.
- Foot care to treat ulcers
- Screening and treatment for kidney disease
- Eye exams to screen for retinopathy (which causes blindness)

CLINICAL APPROACH 10.7

Impaired Glucose Tolerance and Impaired Fasting Glycemia

- Impaired glucose tolerance (IGT) and impaired fasting glycemia (IFG) are intermediate conditions in the transition between normality and diabetes.
- The American Diabetes Association (ADA) recommends the diagnosis of IFG, whereas the World Health Organization (WHO) recommends a diagnosis of IGT.
- People with IGT or IFG are at high risk of progressing to type 2 diabetes.
- Persons with plasma glucose above the diagnostic limits for diabetes mellitus are at an increased risk of microvascular complications.
- IGT is also associated with increased cardiovascular risk, whereas IFG is just a risk factor for the future development of diabetes.

CLINICAL APPROACHS

Each chapter ends with diverse **Assessment Questions**, including **Long-Answer, Short Notes, Reasoning, and MCQs**.

ASSESSMENT QUESTIONS

Long Answer Questions

- Regulation of ATP produced per glucose?
- Significance of ATP produced per glucose?
- Describe diabetes mellitus under the following headings:
 - Types
 - Cause
 - Clinical features
 - Metabolic changes
 - WHO criteria for diagnosis of diabetes mellitus
 - Laboratory investigations for the diagnosis
- Describe the homeostasis of blood glucose level under the following headings:
 - Normal blood glucose level
 - Regulation of blood glucose level
 - Significance of blood glucose level
 - Clinical features of diabetes mellitus
 - Metabolic changes
 - WHO criteria for diagnosis of diabetes mellitus
 - Laboratory investigations for the diagnosis

Short Answer Questions

- Write different types of glycogen storage diseases with their defective enzyme and clinical manifestations.
- What is galactosemia? Give different types and causes.
- What is galactosemia? Write its causes, and clinical manifestations.

Reasoning Questions

- Why aerobic glycolysis releases more energy than anaerobic glycolysis? Why does anaerobic glycolysis occur in RBC?
- Why is anaerobic glycolysis the most favorable pathway for tumor cells?
- Why does glycolysis under anaerobic conditions proceed to lactate and not just stop at pyruvate formation?
- Why the citric acid cycle is called the amphibolic pathway?
- Why Glucose is stored as glycogen instead of fat?
- Why does the liver contribute in maintaining blood glucose but the muscles not?
- Why does the liver store glycogen and not glucose?
- Why acetyl-CoA could not be used as a substrate for gluconeogenesis?

- Why hyperglycemia is the risk factor for cataract formation, peripheral neuropathy, retinopathy and nephropathy?
- Why does lactate disappear from the blood of a diabetic patient at a normal rate?

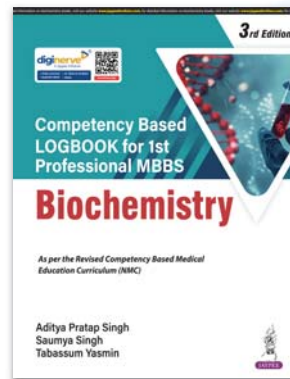
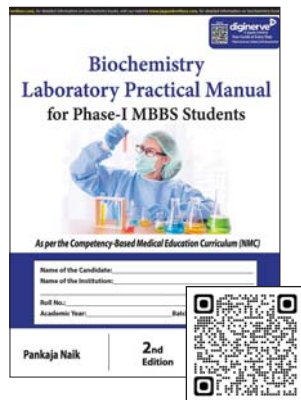
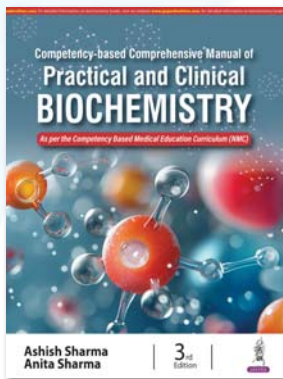
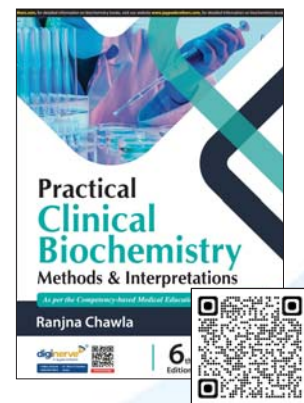
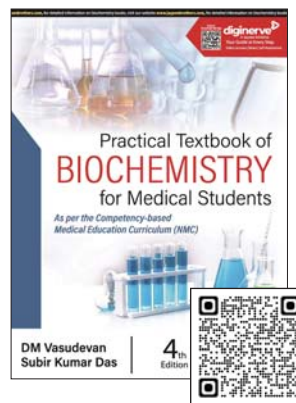
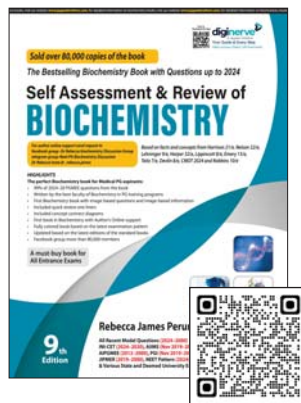
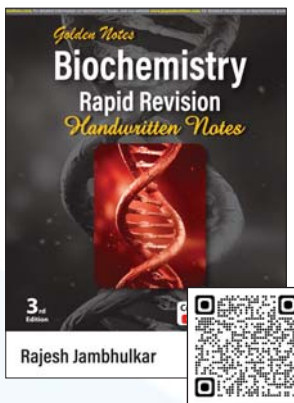
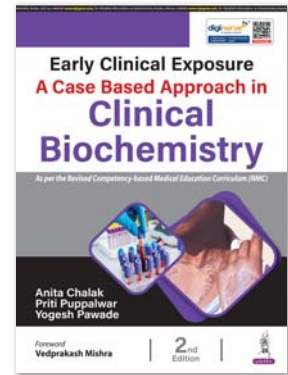
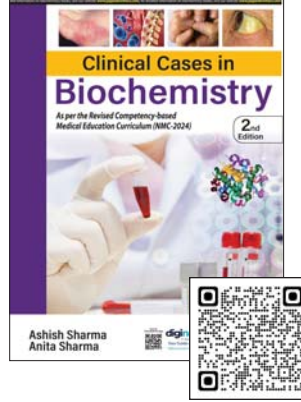
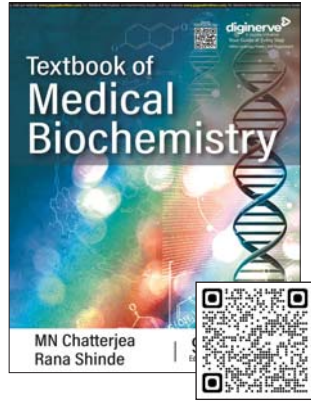
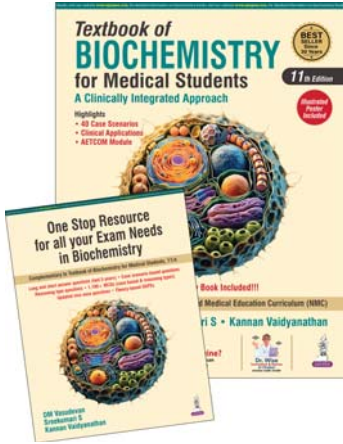
Short Answer Questions

- Write different types of glycogen storage diseases with their defective enzyme and clinical manifestations.
- What is galactosemia? Write its causes, and clinical manifestations.
- How carbohydrates are digested and absorbed in the body?
- What is glucose tolerance test? Write its clinical importance.
- What is Rapoport-Luebering cycle? Give its significance.
- What is Cori cycle? Write its pathway and significance.
- What is lactose intolerance? Write its cause and clinical manifestations.
- Write formation of 2,3 BPG and its significance.
- What is glycated hemoglobin? Give its reference value in blood and its clinical importance.
- What is the role of liver in regulation of blood sugar?
- What is the importance of uronic acid pathway in the body?
- Give significance of sorbitol or Polyol pathway.
- List the laboratory investigations for diagnosis of diabetes mellitus.
- What is resistant starch? Give its clinical importance.
- List differences between hexokinase and glucokinase.
- WHO criteria for diagnosis of diabetes mellitus.
- What is the biochemical basis of development of cataract in diabetes mellitus?
- What are the consequences of diabetic ketosis?
- Write anaplerotic pathways of citric acid cycle.
- A 12-year-old male had complained of abdominal discomfort, a feeling of being bloated, increased passage of urine and development of diarrhea after taking milk.
 - Name the probable disorder.
 - What is the biochemical basis of the symptoms?
 - What will you suggest the patient to relieve the symptoms?

Multiple Choice Questions

- 2,3-bisphosphoglycerate is:
 - A high energy substrate
 - Involved in substrate level phosphorylation
 - An intermediate in pentose phosphate pathway
 - An allosteric effector that decreases the O_2 affinity of Hb
- Muscle glycogen is not available for maintenance of blood glucose concentration because:
 - Muscle lacks glucose-6-phosphatase activity
 - There is insufficient glycogen in muscle
 - Muscle lacks glucose transporter GLUT-4
 - Muscle lacks glucagon receptors
- The primary metabolic fate of lactate released from muscle during intense exercise is:
 - Excretion of lactate in urine
 - Transported to liver for replenishment of blood glucose by gluconeogenesis
 - Conversion to pyruvate
 - Gradual reuptake in muscle during the recovery phase following exercise
- Which of the following cannot take place in the human body?
 - Transformation of lactate into glucose
 - Transformation of glycerol into glucose
 - Transformation of propionyl-CoA into glucose
 - Transformation of acetate into glucose

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