

# Introduction to Clinical Chemistry

Sulaman Yaqub  
(ASCP)

## Syllabus

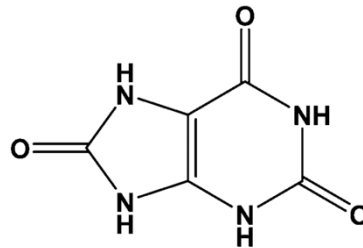
5. INTRODUCTION TO CLINICAL CHEMISTRY: Introduction and Importance of the clinical chemistry. Laboratory tests in diagnosis of diseases including Uric acid, Cholesterol, Billirubin and Creatinine.

## Introduction & Importance

- Laboratory tests are essential part of normal diagnosis practice
- Biochemical tests can be used for
  - Screening for diseases
    - Increased blood sugar level (BSL) in diabetes
  - Confirmation of a diagnosis
    - Gout patient have elevated uric acid levels
  - Monitoring progression of disease
    - S.creatinine levels indicate renal damage from risk to kidney failure
  - Monitoring outcome of treatment therapy
    - Difference of BSL from normal range after treatment
  - Research & Development of new drugs
- For clinical tests sample used are:
  - Blood sample & Urine sample are most common
  - Occasionally saliva and CSF
  - Very rarely tissue biopsy samples are also used



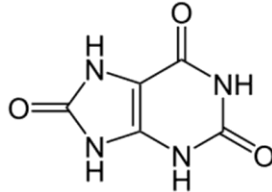
- **Abnormalities in levels of analytes in lab tests:**
- A variety of different conditions can lead to abnormalities of results of lab tests
  - Tissue injury results in the damage to cell membrane
    - Increased permeability of cell membrane
    - Leakage of intracellular material into bloodstream
    - E.g. Leakage of creatine kinase into blood after MI
  - Synthesis of proteins or hormones is increased or decreased
    - E.g. inflammatory states of glands secreting hormones
  - Kidney and liver failure leads to accumulation of a number of compounds
    - E.g. Creatinine, bilirubin respectively in blood



Diagnosis of diseases related to Uric acid

## URIC ACID

- Uric acid is chemically 2,6,8-trihydroxypurine and found in keto-enol isomers
- It is a metabolite of purine nucleotide
  - Purine is formed by fusing 5-member imidazole ring with 6 member pyrimidine ring
  - Produced as waste material and excreted through urine



- Purines, either produced in the body or taken exogenously, after metabolic breakdown produces uric acid
  - The biosynthesis occurs in liver, intestines and vascular endothelium mainly

- **Sources of Uric Acid:**

- Uric acid is the metabolic product of purines
  - Purines are provided in the body by two ways;
    - Endogenous Purines
    - Exogenous purines
- Endogenous Purines include;
  - Mononucleotides
    - AMP, GMP and inosine monophosphate (IMP)
  - Cellular breakdown products containing purines
- Exogenous Purines include;
  - Animal purines from food
    - Red meat, Organ meat (Liver, kidney, intestines, etc.)
    - Poultry and sea food

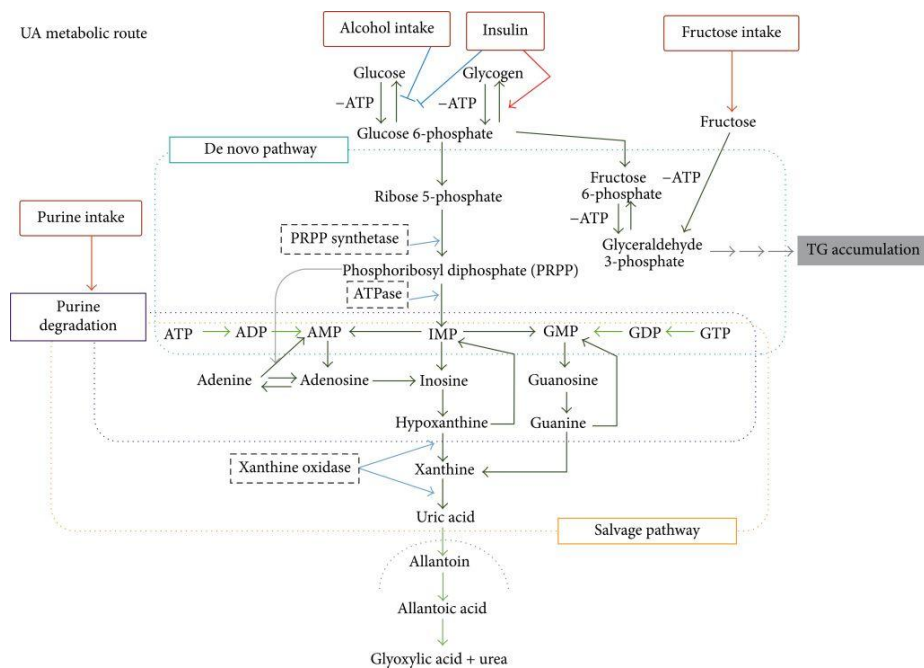
## – Plant Purines from food

- Purine derivatives (caffeine, theophylline, theobromine, xanthine and hypoxanthine) are abundantly found in plants and plant products
- Coffee beans, tea leaves, beans, peas etc. are good source of purine derivatives
- Mashrooms like asparagus is also a good source

## – Beverages containing alcohol

- Ethanol is oxidized to acetaldehyde and acetate in the body which react with ATP to produce acetyl AMP
- Acetyl AMP is converted to IMP, that liberate inosine which is converted to uric acid through various biochemical reactions

- Purines are converted to hypoxanthine and then to xanthine which by the action of xanthine oxidase are converted to uric acid



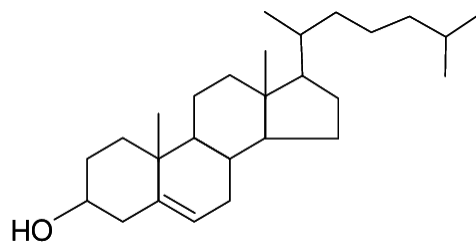
## Lab tests for Uric Acid

- Uric acid produced in the body is secreted in the blood from its site of synthesis
  - Most uric acid in the body is excreted through kidneys (10% of that present in the blood)
    - If fails to excrete it can accumulate in the tissues causing gout
      - Formation of uric acid crystals in synovial fluid of joints
  - Uric acid level can be measured in blood or urine
    - Fasting blood sample
    - 24 hours urine sample
  - Uric acid present in any sample can be determined by uricase method or phosphotungstate method
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- Normal Values for Uric acid level in blood are:
    - 1.5 to 5.5 mg/dL (for women)
    - 2.5 to 7.0 mg/dL (for men)
  - Normal Values for Uric acid level in 24 hour urine collected sample should be less than 600mg/day for normal diet
    - For high purine diet it should be less than 1g/day
  - **Importance of Uric acid test:**
  - Increase in its level can be used in diagnosis of:
    - Gout
    - Recurrent Kidney stones
    - Tumor lysis syndrome (increased necrosis due to chemotherapy or radiotherapy)

Diagnosis of diseases related to Cholesterol

## CHOLESTEROL

- From Greek word Chole meaning bile
  - First isolated from gall stones in 1784
- Cholesterol is the most abundant animal sterol
  - Found in all animal tissues
- Functions as component of membrane lipids, lipoproteins and precursor of steroid hormones, bile acids and vitamin D

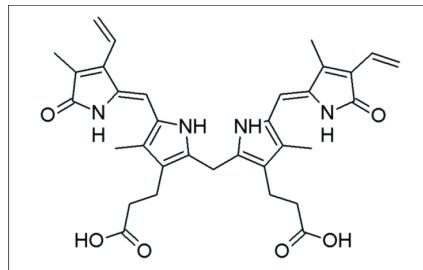


- **Sources:**
- Cholesterol is virtually present in all tissue
  - More than half is synthesized in the body
    - Remaining is provided by diet
- Synthesized in almost all tissues from acetyl-CoA but most active biosynthetic tissues are
  - Liver, intestine, adrenal cortex and reproductive tissues
- Liver plays a vital role in the metabolism of cholesterol
  - Synthesis
  - Esterification
  - Oxidation and
  - Excretion of cholesterol

- **Transportation of Cholesterol:**
- Transported to & from the tissues by cholesterol carriers called lipoproteins
  - LDL and VLDL in blood transport it to the tissues
  - Free cholesterol is removed from tissues by plasma HDL and transported to liver
    - Eliminated from the body as such or after conversion of bile acids
- **Lab test for cholesterol:**
  - A complete cholesterol test can be determined from lipid profile
    - Total cholesterol
    - LDL-cholesterol (bad cholesterol)
    - HDL-cholesterol (Good cholesterol)
    - Triglycerides



- Among these TAG test is not related with cholesterol
  - That should be less than 150 mg/dL
- Normal blood cholesterol level is 150 to 200 mg/dL
  - More than 65% of it is in esterified form
  - HDL (More than 60 mg/dL)
  - LDL (Less than 100 mg/dL)
- **LDL : HDL cholesterol ratio** provide an index of the risk of developing atherosclerosis
  - A high cholesterol level reveals a high risk of heart attack and other cardiovascular diseases
- Cholesterol up to 250 mg/dL is borderline while above 250 mg/dL is considered high
  
- **Importance of Cholesterol test:**
- Cholesterol level indicate the risk of cholelithiasis (gall stone) and cardiovascular diseases
  - Atherosclerosis
  - High blood pressure
  - Coronary artery disease
    - Angina pectoris (chest pain)
    - Heart attack
  - Stroke
  - Peripheral arterial disease
  - Non-alcoholic Fatty liver disease
  - Chronic kidney disease etc.
- HMG-CoA reductase inhibitor drugs are effective to lower blood cholesterol levels (e.g. statins)

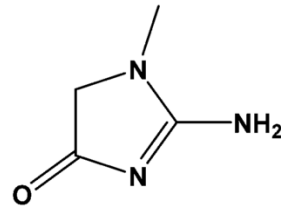


Diagnosis of diseases related to Bilirubin

## BILIRUBIN

- Bilirubin is the degradation product of heme
  - Heme is the prosthetic group of
    - Hemoglobin
    - Myoglobin
    - Cytochromes
    - peroxidases
- Bilirubin is secreted in the blood and transported to liver by albumin where it is excreted
  - Glucuronic acid-conjugates of bilirubin is excreted as bile pigments
- Intestinal bacteria act on bilirubin and produce urobilin and stercobilin
  - Stercobilin is oxidized to brownish pigment (impart feces color)
  - Part of Urobilin is absorbed from intestine and excreted through urine (oxidation impart yellow urine color)

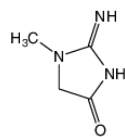
- Lab test is performed on blood sample to determine serum level of bilirubin
- Normal value is 1mg/dL
  - Value between 1 to 2.5mg/dL is subclinical jaundice
  - Serum level beyond 2.5 to 3mg/dL have clinical significance
- **Importance of Bilirubin test:**
  - Elevated level of serum bilirubin indicates jaundice and the intensity of liver damage
    - Hepatitis
    - Liver cancer
    - Gall stone
    - Hemolytic anemia
  - Bilirubin test is also advised in Liver cirrhosis and chronic drinking habits



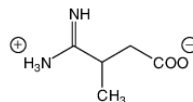
Diagnosis of diseases related to creatinine

## CREATININE

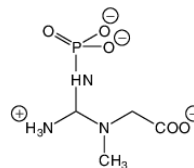
- Creatinine is a heterocyclic organic compound of nitrogen
  - Non-toxic waste product of muscle proteins (endogenous creatinine)
- Exogenous creatinine is provided to the body in diet by
  - Dietary proteins (meat, particularly beef)
  - Amino acid supplements
- **Synthesis of creatinine:**
- Creatinine is formed by spontaneous, non-enzymatic dehydration of creatine in muscle cells
  - Result in cyclization of creatine by change in pH and temperature
- Creatine is a nitrogenous organic acid generated in kidney and liver from glycine, arginine and methionine
  - Transported to muscles (specially skeletal and cardiac)
- In muscles creatine kinase phosphorylates some of creatine to creatine phosphate
  - Creatine phosphate is used as a readily available source of energy in muscles
  - Particularly during early phase of intense muscular contractions
- Primary source of creatinine in human is derived from skeletal muscles
  - Due to constant rate of conversion almost all of the body creatine is found in muscle tissue



Creatinine



Creatine



Phosphocreatine

- Creatinine is excreted in urine and is a marker of renal function
  - **Creatinine clearance** is tested through GFR
- The volume of plasma from which a compound is completely cleared by the kidney in unit time
  - 77 to 160 mL/min/BSA for healthy adult
- Creatinine level can be analyzed from blood or 24-hour urine samples
- Serum creatinine elevated levels indicate its poor excretion
  - Normal value for serum creatinine is:
    - 0.8 to 1.3 mg/dL (for men)
    - 0.6 to 1.1 mg/dL (for women)
  
- Normal urine creatinine is 1-3 g/day
  - 24 hour urine creatinine concentration can be used to estimate muscle mass
- **Importance of Creatinine test:**
- Elevated serum creatinine levels indicate:
  - Dehydration
  - High muscle activity
  - Renal damage
    - Glomerulonephritis
    - Urinary tract obstruction (prostate dysfunction in men)
    - Kidney infection (UTI)
    - Diabetes induced nephropathy
    - Chronic obstructive renal artery stenosis
    - Reduced blood flow to the kidneys (Shock or CHF)

## **Important questions from Past Papers**

- Q: What are the endogenous and exogenous sources of uric acid? [8 Marks – A/2021, S/2021]