Introduction to Clinical Biochemistry

Laboratory tests play an important role in helping physicians and other healthcare workers make diagnoses and other clinical judgments.

Major Uses of Biochemical Tests

Uses	Examples
Confirm diagnosis of specific diseases	Use of plasma cardiac troponin I levels in early diagnosis of myocardial infarction
Suggest rational treatment of disease	An elevated low-density lipoprotein cholesterol level is an indication for therapy with cholesterol-lowering drugs in persons at risk for cardiovascular diseases

Major Uses of Biochemical Tests

Uses	Examples
Are used as screening tests for the early diagnosis of certain diseases	Measurement of thyroid stimulating hormone levels in neonates helps in diagnosis of congenital hypothyroidism
Assist in monitoring the progress of certain diseases	Serum alanine transaminase activity is used to monitor the progress of viral hepatitis

Major Uses of Biochemical Tests

Uses	Examples
Help in assessment of the response of diseases to therapy	In patients with hypo- or hyperthyroidism, measurement of TSH levels helps in monitoring response of patients to treatment
Reveal the fundamental causes and mechanisms of disease	Demonstrate the nature of the genetic defect in cystic fibrosis

Accuracy

is the degree of agreement of an estimated value of an analyte with the "true“ value of the analyte in the sample.

Precision

denotes the reproducibility of an analysis and is the ability of the method used to consistently produce the same value when an analyte in a sample is repeatedly measured.

It is expressed as the variation seen when these repeated measurements of the analyte are done.

ASSESSMENT OF VALIDITY OF A LAB TEST

The clinical value of a lab test depends on its **specificity, sensitivity, and the prevalence** of the disease in the population tested

ASSESSMENT OF VALIDITY OF A LAB TEST

Sensitivity

is the percentage of positive results in patients with the disease.

Lab tests often have lower sensitivity in the early stages of many diseases, in contrast to their higher sensitivity in well-established disease.

ASSESSMENT OF VALIDITY OF A LAB TEST

In biochemical analysis, sensitivity refers to the ability of the method to detect small changes in the levels of the analyte. The lowest concentration of the analyte that can reliably be detected is called the limit of detection.

ASSESSMENT OF VALIDITY OF A LAB TEST

Specificity refers to the percentage of negative results among people who do not have the disease.

In biochemical analysis, specificity may also indicate if substances or factors other than the one being measured influence the assay in any way (positive or negative interference).

ASSESSMENT OF VALIDITY OF A LAB TEST

The **predictive value of a positive test (positive predictive value)** defines the percentage of positive results that are true positives.

The **predictive value of a negative test (negative predictive value)** defines the percentage of negative results that are true negatives.

VARIABLES THAT AFFECT VALUES OF ANALYSIS

Apart from age and sex, many **other factors (called pre-analytical variables)** may affect values of analytes and influence their normal ranges.

These include **race, environment, posture (supine vs. sitting), diurnal and other cyclic variations, pregnancy, fasting or postprandial state, foods eaten, drugs and level of exercise.**

VARIABLES THAT AFFECT VALUES OF ANALYSIS

Values of analytes may also be influenced by the **method of collection of the specimen.**

Inaccurate collection of urine over a 24-h period, hemolysis of a blood sample, addition of an inappropriate anticoagulant, and contaminated glassware or other apparatus are other examples of pre-analytical errors that may occur.

VARIABLES THAT AFFECT VALUES OF ANALYSIS

Errors may also be associated with the analysis of samples. **Random errors are those** errors that are not easily identified and are commonly associated with manual assays.

Automation of analysis can significantly lower random errors. On the other hand, **systematic errors are errors inherently associated with the method of analysis and result** in inaccurate results. These can often be identified and corrected if quality control procedures are adequately followed.

INTERPRETATION OF LAB TESTS

Normal values are generally considered to be those that fall within 2 standard deviations (± 2 SD) of the mean value for a healthy population.

This span of values constitutes a **reference range, which is constructed from results for an analyte obtained from a** particular population (adult males, females, neonates, infants, adolescents).

Normal or reference ranges vary with the method employed, the analytical instrument used, and conditions of collection and preservation of specimens.

INTERPRETATION OF LAB TESTS

Interpretation of lab results must always be related to the condition of the patient.

A low value may be the result of a deficit, or of dilution of the substance measured. Deviation from normal may be associated with a specific disease, or with some drug consumed by the subject.

INTERPRETATION OF LAB TESTS

The role of a clinician in assessing the probability of disease in the individuals tested cannot be overemphasized.

There needs to be a reasonable certainty about the presence or absence of a disease before a surrogate marker for the disease is checked for. This will ensure most optimal interpretation of test results. Whenever an unusual or unexpected result is obtained, one may wish to consult a clinical biochemist before initiating any treatment based on the result, to ensure that no pre-analytical error has occurred. If no such error is detected, the test should be repeated to rule out an analytical mistake.

The Reality of Laboratory Tests

Laboratory tests serve as surrogate markers for tissue pathology.

They do not provide definitive evidence of such pathology and hence should not be used as the sole means by which a diagnosis is made on a patient.

Information obtained from laboratory tests **needs to be combined** with a clinical history and data from other investigations to arrive at a diagnostic decision.

Automation of Laboratory Tests

Most modern clinical laboratories use a high degree of automation.

Automated analyzers improve efficiency and reduce random errors that are invariably associated with manual methods. The pre-analytical phase of laboratory testing may also be automated, thus reducing the lag time between collection of the sample and analysis.


BA 400
BioSystems


Erba
CK MB
Erba
ALAT/SGPT
R1
Erba
CK MB
R1

ORGAN FUNCTION TESTS

Tests that provide information on the functioning of particular organs are often grouped together as organ function tests and are sometimes ordered together by a clinician.

Liver Function Tests

Liver function tests are a group of tests that help in diagnosis, monitoring therapy, and assessing prognosis of liver disease.

Each test assesses a specific aspect of liver function.

Liver Function Tests

Test	Aspect of Liver Function Assessed
Serum bilirubin levels (total and conjugated)	Indicator of the ability of the liver to conjugate and excrete bilirubin (conjugation and excretory function)
Total serum protein and albumin	Measure of the biosynthetic function of the liver
Prothrombin time	Measure of the biosynthetic function of the liver
Serum enzymes: a. aspartate transaminase b. alanine transaminase c. alkaline phosphatase	 Serves as marker of injury to hepatocytes that contain AST in abundance Serves as marker of injury to hepatocytes that contain ALT in abundance Serves as marker of biliary obstruction
Blood ammonia	Indicator of the ability of the liver to detoxify ammonia

Renal Function Tests

A complete urine analysis provides valuable information on renal function. It includes assessment of the physical and chemical characteristics of urine.

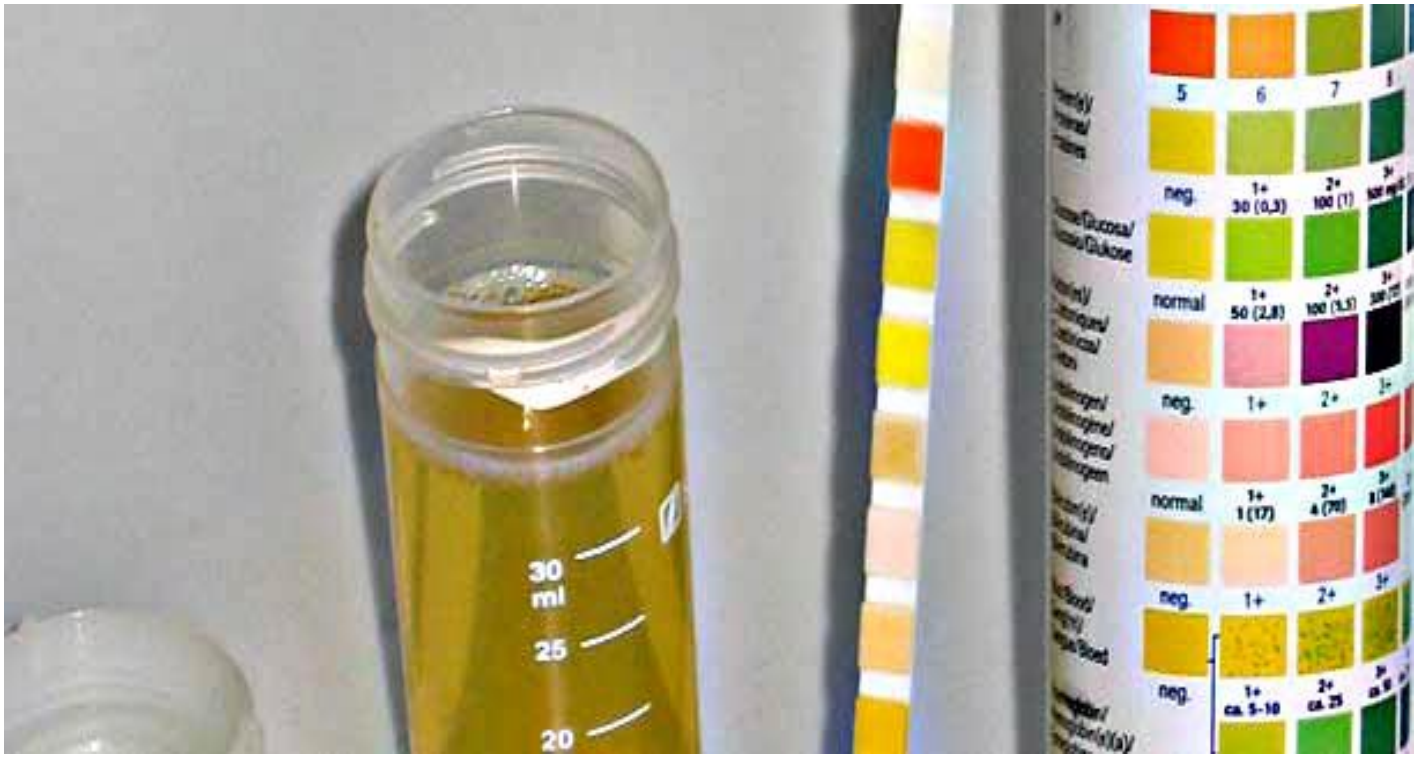
The physical characteristics to be assessed include **urine volume, color, appearance (clear or turbid), specific gravity, and pH.**

Renal Function Tests

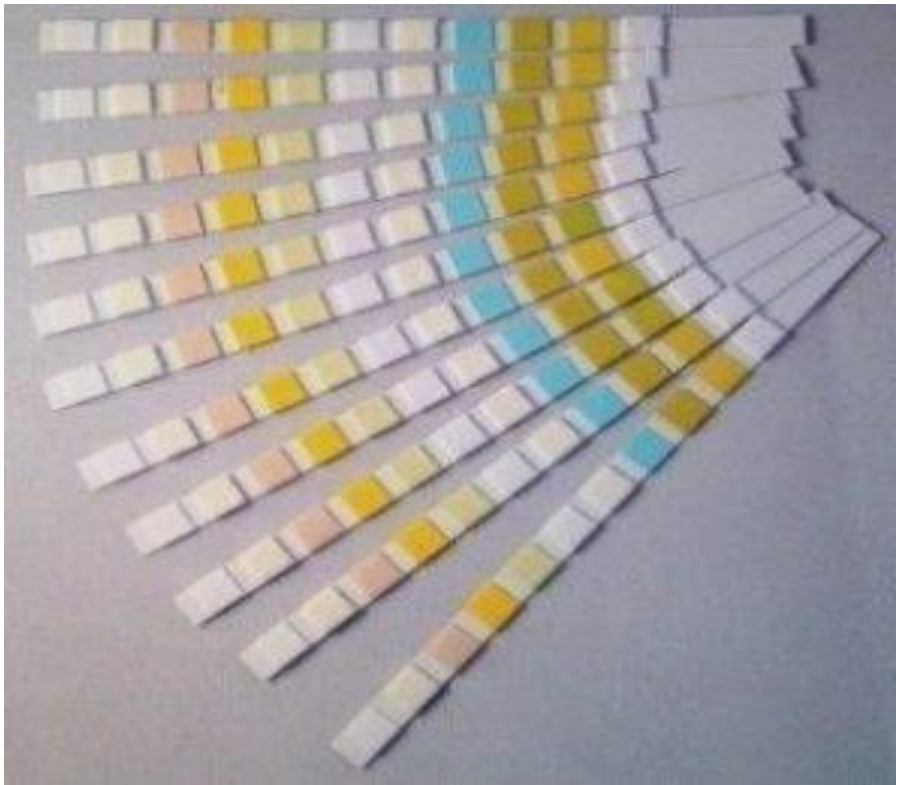
Protein, glucose, blood, ketone bodies, bile salts, and bile pigments are abnormal constituents of urine,

that appear in different disease conditions .

Most of these parameters can now be estimated semiquantitatively using "dipstick" strips.



Dipsticks are plastic strips on which specific chemicals are impregnated. When the portion of the strip that contains the chemicals is dipped into a sample of urine, they react with specific constituents of urine to produce a color change that is proportional to the concentration of that substance in the sample of urine.



Major Renal Function Tests

1. Urine analysis

a. Physical characteristics - assessment of volume, color, odor, appearance, specific gravity, and pH.

b. Chemical characteristics - checking for the presence of protein, reducing sugar, ketone bodies, blood, bile salts, and bile pigments.

c. Microscopy - checking for the presence of WBCs, RBCs, and casts.

2. Serum markers of renal function

a. Serum creatinine

b. Serum urea (or blood urea nitrogen [BUN])

3. Estimation of glomerular filtration rate (GFR)

a. Creatinine clearance

b. Inulin clearance

4. Tests of renal tubular function

a. Water deprivation test

b. Urine acidification test

Some Abnormal Constituents of Urine

Constituent	Clinical Significance	Examples of Conditions in which Present
Protein	Glomerular proteinuria refers to the presence of albumin in urine due to a breach in the integrity of the glomerular basement membrane.	Nephrotic syndrome, acute glomerulonephritis, diabetic nephopathy, etc
	Overflow proteinuria is due to the presence of abnormally high levels of low molecular weight proteins in the plasma that are filtered by the glomerulus and thus appear in the urine.	Multiple myeloma (light chains of immunoglobulins appear in urine, resulting in Bence-Jones proteinuria)
	Tubular proteinuria refers to the presence of low molecular weight proteins (like 2-microglobulin) in urine, due to impaired reabsorption of these proteins by the proximal tubule.	Fanconi's syndrome, nephrotoxicity due to aminoglycoside antibiotics, heavy metals, etc
	Postrenal proteinuria refers to the presence of proteins in urine derived from the urinary tract.	Urinary tract infection (UTI) resulting in inflammatory exudates in urine

Some Abnormal Constituents of Urine

Glucose	Hyperglycemic glucosuria: Presence of glucose in urine is usually seen when plasma glucose rises above the renal Threshold of ~10 mmol/L. Renal glucosuria: Presence of glucose in urine due to impaired reabsorption of glucose in the proximal tubule	Uncontrolled diabetes mellitus Fanconi's syndrome and inherited defects in the sodium glucose transporter 2
Ketone bodies	Detectable levels in urine (ketonuria) are seen in conditions characterized by increased ketogenesis.	Diabetic ketoacidosis and starvation ketoacidosis.
Blood	Hematuria refers to the presence of red blood cells in urine, due to bleeding into the urinary tract. Hemoglobinuria refers to the presence of hemoglobin in urine, which occurs due to intravascular hemolysis.	Renal stones or urinary tract infections Incompatible blood transfusions, malaria etc
Bile salts and bile pigments	Presence of these in urine is associated with obstruction of the biliary tract	Gall stone or carcinoma of the head of pancreas obstructing the common bile duct