Clinical Biochemistry represents a part of laboratory medical sciences which basically deals with disease diagnosis, prognosis and screening as well as monitoring of treatments for diseases, playing an indispensable role in healthcare management. Although there are plenty of text books on the disciplines of Clinical Biochemistry, most of them have concerned on the analytical procedure and techniques used in biochemical testing. However, this book was prepared to provide an overall knowledge which should be acquired in clinical biochemistry in order to deliver a proper health care service, in terms of, sample collection and transport, categorization of biochemical tests, standard path of workflow in a clinical biochemistry laboratory, quality control and quality assurance of clinical biochemistry investigations, laboratory quality management, principals in interpretations of test results and basics in point of care testing, rather than analytical procedures or techniques in test performance. In this book a user friendly approach was employed using 100 questions with corresponding answers, rather than employing paragraphs with full of text to describe the facts and concepts.

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Anushka. S. Elvitigala

Essentials in Clinical Biochemistry for Health Care Delivery

Q & A approach

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Preface

Clinical Biochemistry represents a part of laboratory medical sciences which basically deals with disease diagnosis, prognosis and screening as well as monitoring of treatments for diseases, playing an indispensable role in healthcare management. Although there are plenty of text books on the disciplines of Clinical Biochemistry, most of them have concerned on the analytical procedure and techniques used in biochemical testing. However, this book was prepared to provide an overall knowledge which should be acquired in clinical biochemistry in order to deliver a proper health care service, in terms of, sample collection and transport, categorization of biochemical tests, standard path of workflow in a clinical biochemistry laboratory, quality control and quality assurance of clinical biochemistry investigations, laboratory quality management, principals in interpretations of test results and basics in point of care testing, rather than analytical procedures or techniques in test performance. The book was especially prepared as a reference for the undergraduates who engaged in the degree programs in health care related disciplines including, Medical Laboratory Science and Nursing; following a user friendly approach using 100 questions with corresponding answers, rather than employing paragraphs with full of text to describe the facts and concepts. However, as I believe anyone who severs as health care provider also benefits from the content of this book.

I would like to be highly grateful to the World Health Organization and its regional office for South East Asia, for preparation of hand book on laboratory quality management system and SOPs for Clinical Chemistry, respectively and made them freely available online, which were highly useful in preparation of this text book. Moreover I would like to thank all my colleagues in the faculty including the Dean and the head of the department for encouraging me to write this book. Finally I pay my gratitude to the publishing group of this book for selecting my book draft for prompt publication.

Anushka. S. Elvitigala

General Introduction

Health care is no longer considered as a simple process which just encompasses the examination of a patient or a client and prescribing him or her drugs to treat the suspected pathology. Health care services has rapidly branched out with the time and now become very complex with interdisciplinary approaches. With the rapid expansion of scientific medical knowledge, laboratory investigations on diseases gained tremendous importance in current practice in terms of diagnosis and monitoring of the treatments. Among the various laboratory medical sciences, **Clinical Biochemistry** which also coincides with the terms **Clinical Chemistry and Chemical Pathology** and deals with **diagnosis, prognosis, screening and monitoring of the treatments for a disease, employing chemical and biochemical methods based on non-morphological studies.**

The outcomes of the laboratory investigations pertaining to clinical biochemistry have been yielding useful information to clinicians, especially in determination of the treatments and patient management, promoting the evidence based practice. In this regard, field of molecular diagnostics and genetic screening play a prominent role. Thus, those investigations significantly contribute to mitigate the misery and mortality of patients throughout the world. Most of the investigations carried out to assess the biochemical status of the human body are based on simple, rapid and economical test procedures, which can be easily performed even in the peripheral areas of most of the developing countries. Majority of the biochemical tests have been especially recognized to be useful in management of lifestyle diseases such as diabetes mellitus and other cardiovascular complaints.

In early ages of Clinical Biochemistry, main concern was the methodology part rather than interpretation of the test outcomes. However, current trends focus on interpretative aspects and clinical co-relations, emphasizing the professional relationship between clinical chemists who basically performs the tests and practicing clinicians who directly involve in health care management.

Under the period of methodology development in clinical biochemistry, more effort was committed to develop different analytical techniques to measure various analytes in a large number of patient samples, to discover the possible ways of obtaining biological material and to establish normal ranges (reference values) for each test with respect to the healthy population. More importantly scientists have

paid careful attention in quality control of the developed tests. Later on the tests were performed using automated equipment, reducing their laborious nature. As a result of this whole endeavor, tests were developed to measure glucose in blood and urine, non-protein nitrogen to assess the renal function, amino-acid nitrogen to estimate the nutritional status, plasma and urinary proteins, lipids, enzymes, electrolytes (including calcium, magnesium and phosphorus), and parameters of acid base balance. Moreover, assessing hemoglobin and iron in diagnosis of hematological disorders as well as function of the drugs and poisons in the body were actively being developed.

With the successful progression of the field of clinical biochemistry, group of developed test were collectively assigned into **'test profiles'**; which represent the function of a specific organ or tissue in the body. Organ and tissue profiles were established mainly for liver, pancreas, bone, muscle, heart and kidney. Most of these profiles are based on the organ specific activity of enzymes. In addition to blood and urine, other body fluids such as cerebrospinal fluid and stools are also used as specimen samples in clinical biochemistry. Besides, endocrine function is measured using respective hormones which encompasses assessment of the gonadal function, feto-placental function (during pregnancy), and pregnancy.

Further development of the field was catalyzed through introduction of 'dynamic' functional tests, in which substance such as glucose is first administered to the body and then, its response is monitored in body fluids like blood plasma for a period of time. To date, with the advancement of technology, such as, radio-immuno assays, florescence based immune assays and enzyme linked immune assays, biochemical investigations related to endocrinology has drastically evolved. With the discovery of different bio-markers for prognosis (forecasting on susceptibility) and diagnosis of cancers along with therapeutic drug monitoring has changed paradigm of the field. However, the measurement of an increasing number of plasma proteins remains within the core of clinical biochemistry.

From early ages to-date, gathered and updated knowledge on clinical biochemistry is currently applied in most of the medical and surgical interventions. The focus was mainly on assessment of water and electrolyte metabolism and hydrogen atom homeostasis (hydrogen balance), leading to diagnosis and treatment of 'novel' clinical disorders. Diagnosis and monitoring was revolutionized by introduction of glycated hemoglobin (hemoglobin bound with sugar) as a measure of time-cause

glycemic control and treatment of diabetic coma. One of the critical methodological development in clinical biochemistry is **'point of care testing'**; in which introduction of a range of portable or small desktop analyzers and dry-reagent test strips has shown immense contribution on low-volume emergency testing in hospital wards as well as in self-testing by patients.

With the increasing number of patients, almost all the clinical biochemistry investigations are now being automated for high volume testing. Therefore issues regarding workflow management and computer system management should be properly maintained with substantial technological support.

Pediatric clinical biochemistry is one of the latest branches in clinical biochemistry, which recommends different reference values from those of adults, with respect to diagnostic/prognostic tests performed for infants and children. It also deals with diagnosis of inborn errors of metabolism.

In order to provide optimal health care for clients, accurate diagnosis and prognosis of a disease or monitoring of health condition is an essential factor. With respect to Clinical Biochemistry, there is a major role of clinicians and allied health care providers to achieve this goal. In one hand, the management of the process of sample analysis, assurance of quality of the process and provision of guidance on the selection of tests and assessment of the significance of the results (particularly with some of the less generally familiar tests) are critical province of a clinician. On the other hand, he or she needs to involve in management of patients according to the decisions made based on the test results.

The content of this book basically covers the overall knowledge need to have in clinical biochemistry required to deliver a proper health care service, including, sample collection and transport, basic types of biochemical tests, standard path of workflow in a clinical biochemistry laboratory, quality control and quality assurance of clinical biochemistry investigations, laboratory quality management, key points in interpretations of test results and point of care testing, rather than analytical procedures or techniques in test performance.

Q & A section

Basics of Biochemical Testing

01. What is meant by the term "**Clinical Biochemistry**"?

Branch of medical laboratory science in which chemical and biochemical methods based on non-morphological studies are applied to investigate on a disease or collection of disease.

02. List two other terms which can be coincides with 'Clinical Biochemistry'

- *Clinical Chemistry*
- *Chemical Pathology*

03. Briefly describe the collective role of "Clinical Biochemistry" in health care management?

Clinical biochemistry (C.B.) only plays a part in the overall assessment of the patient. C.B. has very little or no role in disease diagnosis or patient management with some diseases; but with others many biochemical test are required, even with repetitions in aid of proper diagnosis of the disease and monitoring the treatment over a long period of time

04. What is meant by a '**sample'** or a '**specimen'** related to a laboratory investigation?

Sample *- one or more parts taken from a biological system and intended to provide information on the system – (according to the 'The International Organization for Standardization '(ISO) and Clinical and Laboratory Standards Institute (CLSI)*

*The term "**specimen**" is very commonly used to indicate a sample taken from the human. Hence, both terms can be used interchangeably.*

05. List several samples or specimens frequently used in Biochemical investigations.

- *Urine and blood, serum or plasma (**very frequent**)*
- ***Additionally** – Gastric aspiration, Cerebrospinal fluid (CSF), sputum etc…*

06. What is meant by the term '**serum**'?

*Blood plasma **without the clotting factors** is called serum. Generally whole blood is allowed to clot and then the resultant sample is centrifuged to obtain the supernatant which is known as the 'serum'*

07. State the approximate fraction of hospital laboratory investigations which is covered by biochemical tests.

Over 1/3 of the total hospital laboratory investigation are covered by biochemical tests

08. State which stages of health care management can results of biochemical investigations be used.

- ***Diagnosis of a disease** –*

Process of determining which disease or condition explains a person's symptoms based on the initial history and examination when the patient first presents

- ***Prognosis of a disease –***

Providing information on disease susceptibility –

***E.g.** Presence of cholesterol to predict the future development of cardio vascular disease.*

- ***Monitoring of a treatment***

***E.g.** After a drug treatment, evaluating the level of disease related marker in the body.*

- ***Screening for a disease -***

Detection of disease before it is clinically evident

E.g. Testing all infants at birth for a specific inherited disease

09. List the two main types of biochemical tests carried out in a clinical biochemistry lab which are categorized based on the performance frequency with examples.

Core biochemistry tests/ routine biochemistry tests

Commonly requested tests that are benefited on many patients, on a frequent basis

E.g. *Fasting blood glucose, Serum electrolytes, serum total proteins and albumin, serum creatinine, lipid profile, urine full report etc…*

Specialized tests.

Less commonly requested tests which are mostly carried out in specific labs with required facilities-

E.g. - *Molecular diagnostic tests, hormones and protein biomarkers in blood etc..*

10. What are **urgent biochemical tests**?

Biochemical tests; results of which likely influence the immediate treatment of the patient. These tests need to be performed as quickly as possible even out of hours (e.g. night time or weekends).

11. List most common abbreviations (cryptic language usages) with the original name which are used to denote biochemical tests in test request forms?

- *FBS – Fasting Blood sugar (Glucose)*

- *CK serum – Creatinine kinase in serum*
- *U &E – Urea and Electrolytes*
- *LFTs – Liver function tests.*
- *SGPT/SGOT - Serum glutamic pyruvic transaminase and serum glutamic-oxaloacetic transaminase (to asses liver function).*
- *TSH/FT_3/FT_4 - Plasma thyroid stimulating hormone/free triiodothyroninr/free trtraiodotyronine(thyroxin) – thyroid function tests*
- *GTT- glucose tolerance test*
- *PPG – Postprandial glucose level in blood.*

12. Approximately how many biochemical tests are available to date under the platform of clinical Biochemistry?

Over 400 tests

13. What are the three main methods of sample analysis in a clinical biochemistry lab? State them separately with the respective type of tests in terms of performance frequency

- *Manual analysis –. Carried out for less frequent tests. (but currently this method is rarely practicing in labs)*
- *Automated analysis – carried out for high volume tests*
- *'KIT' analysis – carried out for less frequent tests*

14. Briefly describe the each method mentioned in the answer of the question number 13.

- ***Manual Analysis*** *–*

  Involve a tedious procedures including measuring the exact volume or weight of chemicals, precipitation of proteins, incubation, transferring in to a detecting instrument and calculation of final numeric value.

- ***Automated Analysis*** *–analysis is carried out using automated analysers which are mostly connected with microprocessors and computerized system.*

- ***KIT analysis*** *– Analysis is carried out using readymade analysis KITs (pre-formulated chemical reagents with essential material) following the instructions provided with a user manual.*

Path of work flow in a clinical biochemistry lab

15. What is meant by the path of workflow in a clinical testing lab?

It is the route of the sample handling in a lab, from sample collection/ receiving to reporting of a result.

16.*Summarize the standard path of workflow in a clinical biochemistry lab.*

- ***Pre analytical (Pre examination) Phase***

In this initial phase, following activities are carried out according to the order denoted below.

Reception of the sample request form by the clinic or the ward

↓

Sample collection from the patient by the ward/clinic or one of the trained staff members of the lab with proper labeling of the sample

↓

Sample transport from the clinic /ward/ outside or sample reception from the clinic/ ward or outside.

↓

Matching the information on the request form and the sample label (usually through a unique identification number of barcode) and recoding the sample information

- ***Analytical (Examination) Phase***

  Processing the sample using appropriate analytical procedures/s and quality controlling those analytical procedures for reliable results.

- ***Post analytical (post examination) phase***

In this phase results are ready to release.

Collation and interpretation the test results

Note : Not all C.B. labs follow this step

Reporting the results

Sample collection, transport and reception

17. List the essential information need to be included in a test request form

- *Patient identification; Details of the patient, including name. age. gender etc.*
- *Tests requested*
- *Time and date of the sample collection*
- *Source of the sample, when appropriate;*
- *Clinical data, such as suspected pathology of the patient when indicated;*
- *Contact information of the health care provider requesting the test.*

18. What are the crucial factors to be considered in sample or specimen collection for the biochemical tests?

- ***Patient preparation –***
    - *Some test are associated with special timing issues, including fasting blood sugar test (fasting before obtaining the blood sample), drug levels and hormone tests*
- ***Patient identification-***
    - *Accurate identification of the patient from whom the sample need to be collected is very important. This can be easily accomplished by questioning the patient, by questioning an accompanying guardian, or by the use of an identifying wrist band or other device.*

- ***Type of sample required –***
    - *Specific information as to what sample is required for the test is essential to be known; Blood tests might require serum, plasma or whole blood. On the other hand others may require saliva or urine samples.*
- ***Type of container –***
    - *The container to which sample is collected is important since it will affect volume and any needed additives such as anticoagulants and preservatives. In the cases of collection of samples in containers with additives, sample and additives need to be mixed by gentle rotation or inversion of the container.*
- ***Sample labelling—***
    - *Label the sample with every essential information need is a must at the time of collection*
- ***Special handling-***
    - *Some of the samples need special handling, including immediate refrigeration, protection from light or rapid delivery to the laboratory with special precautions and safety precautions.*

19. State how clinicians or laboratory staff needs to be cautious when the sample is assigned to collect by the patient him or herself.

- *Setting protocols to ensure that appropriate collection kits with instructions for collection, safety precautions and labeling are available for the patients.*

- *Instructions for the patients to be prepared using simple and easy-to-understand language and graphics.*

20. What are the essential information needs to be included in labeling of samples.

- *The patient's name*
- *A unique identification number—this might be a hospital /ward number or a number assigned by the laboratory*
- *The test that has been requested*
- *The time and date of collection*
- *The name of the person who collected the sample*

21. List three basic techniques used in collecting blood samples

- *Venepuncture – collection of blood from a vein.*
- *Arterial puncture – collection of blood from an artery*
- *Skin puncture – Collect capillary blood from the tip of the finger (or sole of the babies).*

22. List some common errors which can be occurred in sample collection for biochemical tests

- ***Technical difficulties in obtaining blood samples***
    - *This may lead to hemolysis with consequent resulting in release of potassium and other red cell constituents to blood which can show falsely high concentrations of such constituents in blood.*
- ***Prolonged stasis during venipuncture***

- *With the extended time, plasma water diffuses into the interstitial space and the serum or plasma sample obtained will be concentrated. As a result of this, components of plasma, such as calcium or thyroxin, will be falsely elevated.*

- ***Insufficient volume or amount of sample***
  - *This may affect the repetition of test for the reliability of the results and performance of multiple test using the same sample.*
- ***Errors in timing***
  - *Repeated collection of samples such as urine for 24 hours need to carried out with accurate time intervals along with correct volume at each time.*
- ***Incorrect sample container***
  - Correct container with the appropriate additive according to the requested test need to be carefully selected; otherwise the time taken to deliver the sample to the laboratory can affect the results.
    - **E.g.** Fluoride containing vessels need be selected for collecting samples for glucose, since fluoride can inhibit glycolysis.

Note -A sample collected into the wrong container**, should never be decanted into the correct tube again and use for the test**.

- **E.g.** blood that has been exposed, even briefly, to EDTA (an anticoagulant used in sample containers for lipids) will have a markedly reduced calcium concentration and falsely high potassium concentration (EDTA is a chelator of calcium and is present as its potassium salt).

- ***Inappropriate sampling site of the body***
  - *Blood samples should not be taken 'downstream' from an intravenous drip.*
    - ***E.g.*** *Collection blood for glucose needs to be taken from the opposite arm or below the line of intravenous infusion of glucose, otherwise the results will be biochemically incredible.*

23. What are the possible outcomes of the errors in sample collection?

- *Delays in reporting test results*
- *Unnecessary redraws/repletion of tests*
- *Decreased client satisfaction*
- *Increased costs*
- *Incorrect diagnosis or treatment*
- *Injury*
- *Death.*

24. What are **dangerous samples or specimens (also known as high risk samples)** with respect to Clinical biochemical testing?

Specimens or samples which are contaminated with infectious agents such as Hepatitis B and HIV that can cause life threatening conditions.

Note -*There are specific colors or labeling systems to denote these samples depending on the respective local health system of the respective country.*

25. List key points need be concerned, when the collected samples are transported to a local laboratory.

- *Sample need to be transported to the laboratory without any delay.*
- *If a delay is anticipated, whole blood may be kept at room temperature for about 2 hours.*
- *If there is a longer delay, the serum or plasma should be separated from the cells and stored in a refrigerator at 4°C.*
- *Certain molecules which are heat labile need to be kept under constant cold (chilled) conditions and delivered to the laboratory rapidly (within 10 min)*
    - *E.g. Some hormones and blood gases.*
- *For special tests, collector should contact the laboratory and follow the instructions on transport procedure provided by the lab.*

26. What are the main objectives of different regulations stipulated by national and international authorities, when clinical samples are transported between local, regional and reference laboratories, or between laboratories in other countries.

- *To deal with transportation accidents and spills,*
- *To reduce biohazards*
- *To keep samples intact for testing.*

27. What are the key steps need to be taken, prior to perform the biochemical test, once laboratory receives a sample?

- *Verification of the sample whether it is properly labeled, adequate in quantity, in good condition and appropriate for the test requested.*
- *Recording all the essential sample information into a register or log book.*
- *If sample is at suboptimal level, checking whether it complies with the procedures for handling suboptimum samples, including sample rejection criteria in the lab.*

28. What are the important information on samples need to be recorded in a register or a log book in the lab at the point of their reception.

- *Date and time of collection*
- *Sample received date and time to the laboratory*
- *Sample type*
- *Patient name and demographics, as required*
- *Laboratory assigned identification (e.g. number)*
- *Tests to be performed.*

29. What are the possible circumstances when samples are rejected for testing in a clinical biochemistry lab?

When lab receives

- *unlabeled sample*
- *broken or leaking tube/container*
- *insufficient patient information*
- *samples of which information on sample label and test request form do not match*
- *haemolysed sample (depending on test requested)*
- *samples from non-prepared patients, for tests that require patient preparation (e.g.- non fasting samples for test that require fasting)*
- *sample collected in wrong tube/container (e.g. using the wrong preservative)*
- *inadequate volume for the quantity of preservative*
- *insufficient quantity for the test requested*
- *samples with prolonged transport time or other poor handling during transport.*

30. What are next important steps to be taken by the lab after deciding to reject the sample received for testing?

- *Informing the authorized person as soon as possible that the sample is unsuitable for testing*
- *Requesting another sample to be collected following correct procedures as instructed by the lab*
- *Retaining the rejected sample pending a final decision regarding disposition.*

31. What is the main objective of establishing a sample tracking system in a C.B. lab?

To allow for tracking a sample throughout the laboratory from the time it is received until results are reported.

Sample processing

32. State the two strategies used to maintain such tracking system in a C.B. lab with respective procedures.

- ***Manual Tracking –***
  - *keeping records on the receipt of samples and date and time.*
  - *Labeling samples appropriately and keep with the test requisition until laboratory identification is assigned.*
  - *Tracking aliquots —they should be traceable to the original sample.*

- ***Computerized Tracking***

  Maintaining a database for tracking using following information

  - *Sample identification number*
  - *Patient information*
  - *Collection date and time*
  - *Type of sample (e.g. urine, blood etc)*
  - *Tests to be performed*
  - *Name of ordering Clinician or other health care provider*
  - *Location of patient (e.g. ward, clinic, outpatient)*
  - *Diagnostic test results*
  - *Time and date results are reported.*

33. What are the important factors to be considered if samples need to be stored and retained in the lab for future analysis or send for a reference lab?

- *Retention time*
- *Location of storage (considering the ease of access);*
- *Conditions for storage, such as atmospheric and temperature requirements;*
- *System for storage organization—*
  - *E.g. storing samples by day of receipt or accession number.*

34. What are the necessary measures need to be ensured when referring the samples to other laboratories.

- *Obtaining a laboratory handbook with detailed procedures from each laboratory.*
- *Ensuring the sample is labeled correctly, in the correct container accompanied by a requisition form that specifies the required test(s) and along with the sending laboratory's contact information.*
- *Carefully monitoring the samples that are referred*
- *Keeping a record of all tests and samples referred, date of referral and name of person referring the test*
- *Recording and reporting results received for each referred sample*
- *Monitoring the turnaround times and recording any problems encountered*

35. What are the crucial steps need to be followed by the C.B. lab to ensure proper disposal of the samples used in biochemical tests?

- *Application of national as well as international regulations for disposal of medical waste.*
- *Following standard procedures to disinfect samples prior to disposal*

36. What are the major sources of contamination of personnel who handles high risk (dangerous) samples already contaminated with infectious agents?

- *Hand-to-mouth contact*
- *Hand-to-eye contact*
- *Direct contact with superficial cuts, open wounds, and other skin conditions that permit absorption into subcutaneous skin layer*
- *Splashes or aerosol contact with skin and eyes.*

37. State the recommended precautions need to be taken to protect the personnel who handle high risk samples/ dangerous samples.

- *Using gloves on hands when in contact with body fluids, such as serum, plasma, urine or whole blood*
- *Washing hands when gloves are removed or changed*
- *Performing procedures carefully to minimize aerosol formation*
- *Wearing protective clothing such as laboratory coats or aprons when working with specimens or samples*
- *Keeping hands away from your face*
- *Covering all superficial cuts before starting any work*
- *Disposal of specimens and other contaminated materials according to the recommended biohazard control procedures.*
- *Keeping the work area along with tools and other items which have been in any contaminated area, disinfected.*

38. List appropriate **emergency actions** need to be taken when surfaces are contaminated with **chemical spills**.

- *Regarding **minor spills** - If the person who spilled is familiar with the chemical, knows the associated hazards and knows how to clean up the spill safely.*
    - *Alert coworkers and then clean up the spill*
    - *follow procedures for disposal of materials used to clean up spill;*
    - *absorb free liquids with an appropriate absorbent, as follows*
        - *caustic liquids—use polypropylene pads or diatomaceous earth (powder of siliceous sedimentary rock*
        - *oxidizing acids—use diatomaceous earth*
        - *mineral acids—use baking soda or polypropylene pads*
        - *flammable liquids—use polypropylene pads*
    - *neutralize residues and decontaminate the area.*

- *Regarding **major spills** – Spills requires help from outside of the laboratory group*
    - *Alert coworkers,*

- *Move to a safe location and*
- *Call authorities to report the situation.*

39. List appropriate emergency actions need to be taken when surfaces are contaminated with **biological spills** such as body fluids like serum, urine etc...

- *Label and isolate the contaminated area.*
- *Alert coworkers.*
- *Make sure the appropriate protective wear are put on.*
- *Remove glass/lumps with forceps or scoop.*
- *Properly Disinfect the surface*
  - *Apply absorbent towel(s) to the spill; remove bulk and reapply if needed.*
  - *Apply disinfectant to towel surface and Allow adequate contact time (around 20 minutes).*
  - *Remove towel, mop up, and clean the surface with alcohol or soap and water.*
- *Properly dispose the materials.*
- *Notify the respective personnel (supervisor, safety officer, and other appropriate authorities).*

40. List the immediate steps need to be taken if a laboratory personnel become contaminated with Biological spills or splashes.

- *Clean exposed skin or body surface with soap and water, in the cases of contaminated eye and mouth with eyewash or saline, respectively.*
- *Apply first aid and treat as an emergency.*
- *Notify supervisor, safety officer, or security desk if it occurred after hours.*
- *Follow appropriate reporting procedures.*
- *Report to the relevant clinician for treatment or counseling.*

41. Briefly describe what is meant by the '**standard operating procedure**' (**SOP**) with respect to a biochemical test.

SOP is a clear, concise and comprehensive written instruction of a method or procedure which has been agreed upon and authorized as the operating policy of the laboratory.

42. What is the main purpose of maintaining SOPs in C.B. Labs?

Maintaining the same analytical quality of biochemical tests performing in the lab, over a long period of time; these procedures are a prerequisite of correct transfer of methods from one laboratory to another

43. List the standard content of a SOP with respect to a C.B. test

- *Introduction*
- *Principle of method*
- *Specimen types, collection and storage*
- *Reagents, standards and control - preparation and storage*
- *Equipment, glassware and other accessories*
- *Detailed procedure*
- *Calculations, calibration curve (If applicable)*
- *Analytical reliabilities – (Quality control and statistical assessment)–(If applicable)*
- *Hazardous reagents (if applicable)*
- *Reference range and clinical interpretation*
- *Limitations of method (e.g. interfering substances and troubleshooting)*
- *References – (published evidence that the procedures are scientifically valid).*
- *Date and signature of authorization*
- *Effective date with schedule for review*

44. Give an example for a SOP of a selected biochemical test.

Test name – Plasma Cholesterol – using cholesterol oxidase method

Introduction

The major constituents of plasma lipids are cholesterol and triglycerides. Cholesterol is an important compound of cell membrane and precursor for the synthesis of bile salts and steroid hormones. Cholesterol is synthesized in the liver and transported in the blood mainly in the form of LDL and HDL. In blood, cholesterol is present in free as well as esterified form. Over the decades serum cholesterol has been measured by methods employing Liebermann-Burchard reaction. The enzymatic method has become popular in recent years. The percentage of participants in the External Quality Assessment Scheme conducted from the author's laboratory, employing the enzymatic method, has increased significantly from 10 to 85 in the last decade.

Principle of the method

Cholesterol esters in serum are hydrolysed by cholesterol esterase. The free cholesterol is then oxidized by cholesterol oxidase to the corresponding ketone liberating hydrogen peroxide, which is then converted to water and oxygen by the enzyme peroxidase. Para aminophenazone (4 aminophenazone) takes up the oxygen and together with phenol forms a pink coloured quinoneimine dye, which can be measured at 515nm/ yellow green filter.

Specimen type, collection and storage

Serum or plasma can be used. A fasting blood sample is preferred for lipid profile test. However, if cholesterol alone has to be analysed, a random sample can also be used. The specimen is stable for a week at 2 - 8^{0}C and at least for 3 months at – 200 ^{0}C.

Reagents

All chemicals must be Analar grade

<u>General note:</u> Several companies provide compact kits for the measurement of cholesterol by the enzymatic method. These kits are most economical and readily available and therefore practically in most of the laboratories cholesterol is measured by using kits. Laboratories using kits are advised to

follow carefully the instructions given in the leaflet. Commercial companies generally provide a single reagent consisting of the following chemicals:

4 – aminophenazone *Cholesterol esterase*

Phenol *Cholesterol oxidase*

Peroxidase *Sodium azide*

The reagent is provided in the lyophilized form and proper instructions are given for reconstitution and use in the assay. The reagent is generally stable for one week when stored at 15 to 25^{0}C and one month at 2- 8^{0}C.

Equipment, glassware and other accessories

Relevant glassware or equipment need to be mentioned under this section, according to the availability in the lab, If commercial KITs are used it should be mentioned with the Catalog number and the manufacturer's details.

Procedure

The protocol of the procedure is described below.

Pipette the following into appropriately labeled 13 x 100 mm tubes

	Blank	*Standard*	*Test*	*QC*
Reagent solution (ml)	*2.0*	*2.0*	*2.0*	*2.0*
Standard (ml)		*0.02*		
Test sample/QC (ml)				
			0.02	*0.02*

Mix well. Incubate at 37^{0}C in a waterbath for 5 minutes or at room temperature (25- 35^{0}C) for 15 minutes. Remove from water bath and cool to room temperature. Set spectrophotometer / filter photometer to zero using blank at 510 nm / yellow green filter and measure the absorbance of standard, test and QC. This protocol is designed for spectrophotometers / filter photometers that require a minimum volume of reaction mixture in the cuvette of 1ml or less. Since economical use of the reagent is possible with this protocol, the cost per test can be kept to the minimum. However, if a laboratory employs

a photometer requiring a large volume of reaction mixture for measurement, viz. 5 ml, it is advised that the volumes of reagent, standard, and test sample/QC mentioned under #6 be increased proportionately.

Calculation and calibration graph

Linearity for calibration graph has been well documented by several kit companies. In the author's laboratory it is from 20 to 500 mg/dl.

Therefore a single standard (viz. 200 mg/dl) can be used and cholesterol in patients' samples can be calculated using the formula.

$$\frac{\text{Absorbance of test}}{\text{Absorbance of standard}} \times \frac{\text{Conc. of Std ..... mg/dl}}{(200)}$$

Anaytical reliabilities

Include one internal QC (quality control) in every batch of samples analysed every day irrespective of the number of samples in a batch. Since cholesterol is analysed in a single batch in a day in an intermediate laboratory, it will not be possible to analyse several QC samples and calculate within-day precision. However, even if a single QC sample is analysed in a day, this value can be pooled with the preceding 10 or 20 values obtained in the previous days and between-day precision can be calculated and expressed as %CV. Ensure that this is well within the acceptable limit, i.e. 8%. Once a week it will be good to analyse another QC serum from either a low QC or a high QC pool. "Assayed" QC sera with stated values (ranges) are available from several commercial sources, viz. Boehringer Mannheim, BioRad & Randox. If a laboratory uses QC sera from a commercial source, it is important that the company certifies that their QC materials are traceable to international reference materials.

Hazardous materials

This procedure uses phenol, which is caustic. Do not swallow, and avoid contact with skin and mucous membranes.

Reference range and clinical interpretation

Serum Cholesterol - 150-250 mg/dl Serum cholesterol is increased in hypothyroidism, diabetes mellitus, nephrotic syndrome and in various hyperlipidaemias especially those causing xanthomatosis. Elevated serum cholesterol is a serious risk factor for the development of coronary artery disease. Decreased serum cholesterol is seen in severe hepato-clellular disease, hyperthyroidism and anaemia.

Limitations

Haemolysis and lipaemia cause elevated cholesterol levels. Serum bilirubin >5mg/dl and ascorbic acid > 10 mg/dl also cause elevated cholesterol levels. Do not report results from specimens with suspected interference. Inform the requesting physician of the problem.

Reference

(1) Allain CC, Poon LS, Chan CSG et al. (1974) Clin Chem 20 : 470

45. *What attributes should a standard SOP ensure with respect to a biochemical test?*

- ***Consistency*** *-*
    - *Tests need to be performed exactly the same way so that the same result can be expected from all staff.*
    - *Consistency enables clinicians who depend on the laboratory results to observe changes in a particular patient's results over time.*
    - *If the same SOPs are used by different labs, comparisons of their results can be made easily.*
    - *All the members of the laboratory staff are expected to follow the SOPs exactly as a mandate.*
- ***Accuracy-***

- *Laboratory staff can produce more accurate results based on written procedures rather than relying on memory alone because they will not forget steps in the process.*

- ***Quality –***
  - *Consistent (reliable) and accurate results are primary goals of the laboratory, and can be attributed to the quality in the laboratory.*

46. What are the features of a good SOP.

- *Detailed, clear and concise which enable lab staff to follow the SOPs*
- *Easily understood by new personnel or students in training (usage of simple language whenever possible)*
- *Reviewed and approved by the laboratory management to ensure that the procedures being used for testing in the laboratory are up to date and appropriate*
- *Up dated on a regular basis.*

47. What is a **'Job aid'** or **'Work Instructions'** with respect to a biochemical test**?**

It is a shortened version of a SOP which is designed for use directly at the testing site to serve as a reminder of the test steps that need to be completed. It should be placed in a visible location for easy access.

48. Compare the content of a SOP with that of a job aid.

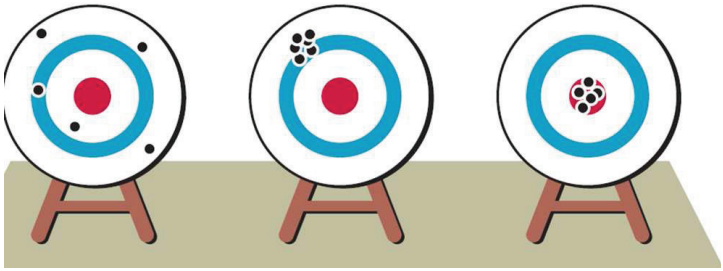
- *Job aid is only a supplement to a SOP; it cannot replace a SOP*
- *The job aid and the SOP must include the same instructions*
- *A Job aid does not include all the details that are provided in the SOP.*

49. According to the nature of the results produced by a biochemical test, state the three main categories of biochemical analysis on clinical samples with a brief description.

- ***Quantitative tests***
    - *Measure the quantity of a substance in a sample, yielding a numeric result which is usually presented with a relevant unit of measurment.*
        - ***E.g.*** *Blood glucose level - 5 mmol/L*
- ***Semi-quantitative tests***
    - *Similar to qualitative examinations, but testing does not measure the precise quantity of a substance or the analyte (an estimate of how much of a measured substance is present using relative arbitrary values).*
        - ***E.g.*** *Proteins in urine*
            - *Definite nongranular cloud without flocculation - 1+*
            - *Heavy and granular cloud without flocculation - 2+*
            - *Dense cloud with marked flocculation - 3+*
            - *Thick curdy flocculation & coagulation - 4+*
- ***Qualitative tests –***
    - *Measure only the presence or absence of a substance.*
    - *qualitative terms such as "positive", "negative", "reactive", "nonreactive", "normal" or "abnormal".*
        - ***E.g.*** *Bilirubin in urine*
            - *No color change in the precipitate : Negative*
            - *Appearance of a green or blue color : Positive*

50. Define the terms '**accuracy and precision'** with respect to the results of a biochemical test.

- ***Accuracy*** *is the closeness of a measurement to its true value.*
- ***Precision*** *is the degree of closeness in the measurements to each other;*
    - *The less variation in a set of measurements represents high precision; thus, measurements are reproducible.*



Imprecise ***Precise but not accurate*** ***Accurate***

51. What is meant by '**quality control' (QC)** of biochemical tasting?

Use of control materials to monitor the accuracy and precision of all the processes associated with the examination (analytic) phase of testing.

52. Based on what parameter does the variation of the QC process depend?

QC process varies depends on the type of the result which is generated by the biochemical test concerned, designated as quantitative, semi-quantitative or qualitative.

53. List two main types of variations which can be observed relevant to a laboratory test results.

- *Biological variation – intend to measure using a test.*
- *Analytical variation – non intentional*

54. List main causes of analytical variations in biochemical test results.

-
- *Failures in test systems*
- *Changes in environmental conditions*
- *Defects in operator performance*

55. What is the main goal of QC of biochemical testing?

To detect, evaluate and correct errors due to test system failure, environmental conditions, or operator performance, before patient results are reported

56. What are the two basic types of errors can be occurred in a biochemical testing process?

- *Random errors –*
    - *There will be a variation in QC results that show no pattern.*
    - *This type of error generally does not reflect a failure in some part of the testing system, and is therefore not like to reoccur.*

- *Systemic errors –*
    - *This type of errors is not acceptable, as it indicates some failure in the system and should be corrected.*

57. What is a QC material? Briefly explain the main purpose of using QC material for QC process.

- *Substances that contain an established amount of the analyte being tested which shows same consistency with the analyte in patients' test sample is called QC material. (E.g. glucose in a serum sample)*
- *These control material are tested at the same time and in the same way as patient samples.*
- *The purpose of the control is to validate the reliability of the test system and evaluate the operator's performance and environmental conditions that might impact results.*

58. Describe what a **calibrator or standard is;** differentiating its usage from a QC material.

- *Calibrators are solutions with a specified defined concentration that are used to set or calibrate an instrument, kit, or system before testing is begun.*
- *It should not be used as a control since they are used to set the instrument.*
- *They usually do not have the same consistency as patients' samples.*
- *Calibrators are often provided by the manufacturer of an instrument.*

59. List the criteria to be used when selecting an appropriate QC material?

- *The substance being measured (analyte) in the test must be present in the control in a measurable form*
- *The amount of the analyte present in the controls should be close to the medical decision points of the test*
    - *Controls should check normal values/ normal range of values as well as low values and high values with respect to the normal value or normal range of values.*
- *Controls should have the same matrix as patient samples. (based on serum, urine or plasma etc.)*

60. What are the commercially available different forms of the QC material

-
- *Free dried (lyophilized) form*
- *Frozen form*
- *Chemically preserved form*

61. State what precautions need to be taken when some of the above materials (in question No. 56) are used in the biochemical testing?

- *The freeze-dried or lyophilized materials must be reconstituted as instructed in the vendor's protocol and stored under recommended conditions.*

- *The volumes need to be carefully measured by pipetting to ensure the correct concentration of the analyte in the final, ready to use QC material.*
- *Need to take safety measures (wearing hand gloves, lab coats and safety glasses etc.) when handling with the materials, since mostly they are based on body fluids.*
- *Frozen materials need to be thawed and arranged as aliquots to be used at a time and freeze again for storage. Thus, small amount can be thawed and used at a time as required. (frequent freeze thaw cycles with respect to the same lot of QC material can degrade the analyte)*

62. Briefly summarize the basic steps in assaying the QC material against any quantitative biochemical test run to ensure whether it is **in control** (values are reading properly with respect to the expected ones) or **out of control** (vise-versa) .

Running each control 20 times over 30 days

↓

Recode each value generated by the each test trial

↓

Calculate the mean and the standard deviation (SD) of the values generated

(Mean ± SD)

↓

Determine the variation of values based on SD

↓

Establish a normal range of variation for the selected test in the lab

63. What are the expected steps to be followed by the lab with recommended pre-cautions, when the QC sample that is used in a test run **is out of the acceptable range (out of control)**.

- *The testing process should be stopped and the operator must immediately try to identify and rectify the problems.*
- *Once possible sources of error have been identified and corrections have been made, the control material should be re-evaluated against the test.*
- *If the test out comes lies in correct range, then patient samples, along with another QC sample, should be repeated.*
    - ***Note** - Do not simply repeat the testing without looking for sources of error and taking corrective measures.*
- *Patient results should not be reported until the problem is resolved and the controls indicate proper performance.*

64. What are the possible reasons for analytical errors leading to out of control test results?

- *Degradation or expiration of reagents or kits*
- *Degradation or expiration of control materials*
- *Errors due to operator.*
- *Failure to comply with manufacturer's instructions*
- *Following an outdated analytical procedure*
- *Failure of one or more equipment.*
- *Error in calibration of instruments.*

65. What are the controls can be used in semi-quantitative and qualitative tests? Briefly explain the nature of those controls used in frequent biochemical tests.

- *Positive control – Generally indicate the presence of the analyte in QC material*

- *Negative control - Generally indicate the absence of the analyte in QC material*

Note –
*Commonly these controls are known as **bult-in controls or internal controls**. These control tets are frequently performed automatically with each test with respect to test KITs . The manufacturer's product instructions may also refer to these controls in the user manuals.*

66. What are the significant outcomes of releasing inaccurate results with respect to biochemical tests?

- *Unnecessary treatments on the patients*
- *Treatment complications on patients*
- *Failure to provide the proper treatment*
- *Delay in correct diagnosis*
- *Additional and unnecessary diagnostic testing.*

67. What are meant by the terms **'analytical sensitivity'** and **'analytical specificity'** of a biochemical test?

- ***Analytical Sensitivity –***
  - *How little of the analyte can be detected by the concerned biochemical test /method*
  - ***Note-** If two methods A and B are suggested for detecting the same analyte, but A can detect a very small amount compared to B as its least amount of detection, the sensitivity of method A is higher than that of B.*
- ***Analytical Specificity***
  - *How good the method can discriminate the analyte of interest with other potentially interfering substances*
  - *In other words it an estimate of the systematic error caused by other materials that may be present in the specimen being analyzed*
  - ***Note –**If two methods, A and B are used to detect a same analyte x in serum, but A can also detect other analytes (usually called*

interfering substances) in addition to the analyte X, but B can only detect X, specificity of method B is higher than to that of A, with respect to the analyte X.

Interpretation of Results and reporting

68.*Define the terms* ***'test specificity'*** *and* ***'test sensitivity'***

Test specificity –
The probability that a test (relevant to a semiquantitative a or qualitative test) will be negative when an analyte is absent from a sample

Test Sensitivity-
The probability that a test will detect an analyte , when it is present in a sample.

Note – *An Ideal test should show 100% test specificity and sensitivity.*

69. What are **false positive and false negative results,** with respect to semi-biochemical testing?

- ***False positive results–***
  - *An* ***abnormal result*** *with respect to a test sample of a person, subsequently who is found not to have the tested pathological condition.*
- ***False negative results-***
  - *A* ***'normal result'*** *with respect to a test sample of a patient who is actually found to have the tested pathological condition.*

70. What is meant by a **reference interval** with respect to results of a biochemical test?

*Values/ range of values of generated as outcomes of biochemical tests performed on **healthy volunteers** representing 95% of selected population*

***Note -** This reflects that, by definition, 5% of any population will have a result outside the reference interval. However, the result lies out the reference intervals more likely to indicate the tested pathology.*

***E.g.** Reference interval for fasting blood glucose level - 72-112 mg/dL*

71. What are '**critical (alarm) values'** with respect to the results of a biochemical test?

Results that require prompt and rapid clinical attention to avoid significant morbidity or mortality of the respective patient

***E.g.** Fasting blood glucose level - <50 mg/dL or >350 mg/dL*

72. List the potential biological factors which can influence the **interpretation of results** related to biochemical tests with a brief description on the potential influence with respect to the each factor.

- *Sex of the patient -*
  - *Reference intervals can be varied between males and females for some test results*
    - *E.g. Serum creaitinine kinase level*
- *Age of the patient*
  - *There may be different reference intervals for neonates, children, adults and the elderly patients.*
- *Diet*
  - *The sample may not be suitable for testing if taken when the patient is fasting or right after a meal.*
- *Timing*
  - *Results of some tests can vary depending on the sampling time in the day; as day time and night time*

        - *E.g.- Serum cortisol level –*
            - *280–720 nmol/L (morning)*
            - *60–340 nmol/L (evening)*
- *Stress and anxiety of the patient*
    - *These factors can affect the level of analyte (such as hormones) in the blood.*

- *Posture of the patient*
    - *Redistribution of body fluids may affect the result.*
- *Effect of exercise*
    - *Severe exercise may lead to release enzymes from tissues and intron can change the level of some analytes.*
- *Medical history*
    - *Infections or injuries can influence the results of biochemical tests, independent to the actual pathology.*
- *Pregnancy*
    - *Reference intervals of some analytes relevant to some test results are different in pregnancy period.*
- *Menstrual cycle*
    - *Measurements will vary throughout the menstrual cycle.*
- *Drug history*
    - *Some drugs can act in the body and change the concentration of some analytes in body fluids.*

73. List the content of a biochemical test report according to the required by **ISO – 15189 standards**.

- *Identification of test*
- *identification of the laboratory*
- *Unique identification and location of the patient, where possible,*
- *Destination of the report;*
- *Name and address of test requestor*
- *Date and the time of collection, and time of receipt in laboratory;*
- *Date and time of issuance of the report;*
- *Primary sample type*

- *Results reported in SI units or units traceable to SI units, where applicable*
- *Biological reference intervals, where applicable*
- *Interpretation of results, where appropriate*
- *Applicable comments relating to quality or adequacy of sample, methodology limitations or other issues that affect interpretation*
- *Identification and signature of the person authorizing issuance of the report*
- *if relevant, notation of original and corrected results.*

74. In addition to the above mentioned biological factors, what other factors may drive clinicians to decide on the next treatment or management plan with respect to the relevant patient.

- *Compatibility of the biochemical test results with the history and clinical examination of the patient.*
- *Means of explaining the test results or make repetition of the test, if there is a discrepancy between the test results and the clinical evidence or history of the patient.*
- *Effects of test results on the present plan of treatment or management procedure of the patient.*

75. Tabulate the common analytes;, concentration of which in body fluids is measured by the biochemical tests, with the corresponding SI unit as well as the conventional units used to report the results

Analyte	***SI Unit***	***Conversion factor (from SI unit to conventional unit)***	***Conventional Unit.***
Albumin	*g/L*	*X 0.1*	*g/dl*
Bilirubin	*µmol/L*	*X 0.058*	*mg/dl*
Calcium	*mmol/L*	*X 4*	*mg/dl*
Cholesterol	*mmol/L*	*X 38.6*	*mg/dl*

Cortisol	*nmol/L*	*X 0.036*	*µg/dl*
Creatinine	*mmol/L*	*X 11.3*	*mg/dl*
Glucose	*mmol/L*	*X 18*	*mg/dl*
Iron	*µmol/L*	*X 5.6*	*µg/dl*
Lactate	*mmol/L*	*X 9*	*mg/dl*
Magnesium	*mmol/L*	*X 2.4*	*mg/dl*
PCO_2	*kPa*	*X 7.5*	*mmHg*
PO_2	*kPa*	*X 7.5*	*mmHg*
Potassium	*mmol/L*	*X 1*	*mEq/L*
Protein (Total)	*g/L*	*X 0.1*	*g/dl*
Sodium	*mmol/L*	*X 1*	*mEq/L*
Thyroxine	*nmol/L*	*X 0.078*	*µg/dl*
Triglyceride	*mmol/L*	*X 88.5*	*mg/dl*
T_3	*nmol/L*	*X 65.1*	*ng/dl*
Urate	*mmol/L*	*X 16.8*	*mg/dl*
Urea	*mmol/L*	*X 6*	*mg/dl*

Note-

- *T_3- Tri iodothyronine*
- *mEq – Milliequivalents*

Information Management

76. What is meant by a **laboratory Information management system** (LIMS or LIS)?

A system that incorporates all the processes needed for effective management of the data, including both incoming and outgoing patient information. System can be partly paper-based with some computer support, or it may be entirely computer based.

77. What the main intended are out comes of a good LIMS?

A good LIMS should be able to

- *ensure that all data, (the final product of the laboratory) is well managed;*
- *ensure the accessibility, accuracy, timeliness and security of data;*
- *ensure confidentiality and privacy of patient information.*

78. What are the two possible ways of establishing a LIMS in a C.B. lab?

- *Developing an in-house computer network*
  - *Herein locally developed systems are used based on commercially available database software like Microsoft Access*
- *Purchasing fully developed laboratory systems*
  - *This encompasses computers, software and training.*

79. List some characteristic features of an efficient LIMS.

- *Flexibility*
- *Adaptability,*
- *Ease of evolution and support, and*
- *Relatively higher system speed*

80. List the advantages of using a LIMS in a C.B. lab.

- *Mitigate potential errors*
  - *Organized computer system can check for potential errors in the whole system in a lab including work flow.*
- *Facilitate the quality control management*
  - *LIMS can keep quality control records, perform analysis on quality control data and generate automated statistics.*
- *Provide user friendly approach in data searching.*
  - *Using computer based system, multiple parameters can be used for data retrieval with respect to any biochemical test performed, including name of the patient, patient number, test results and name of the analysis etc.*

- *Provide access to the recent history of lab data for a patients*
    - *This aid in collation of data of a patient, to compare* most *recent results against previous data of that patient which in turn lead to monitor the treatment of a disease.*
- *Facilitate in generation of legible, detailed and rapid lab reports in a standard format*
- *Provide facilities to track a lab report*
    - *This will eventually uncover,*
        - *when the analysis was finished,*
        - *who perform the tests,*
        - *when the data was reviewed and*
        - *when the report was issued.*
- *Facilitate the tracking and analysis of the trends*
    - *Computer based databases provide strong search capacities and, possibilities to retrieve and use large amounts of data effectively to track and analyze different trends related to health conditions.*
- *Improve the maintenance of confidentiality of lab data*
    - *Computer usage is more effective in maintaining confidentiality of laboratory data by using passwords and codes to access the data.*
- *Open a avenues to computer systems outside the laboratory*
    - *Integrated systems can be set-up to receive data from a patient registration point, forward instructions or requests via online platforms on biochemical tests by the clinicians and issue reports to the clinicians.*

81. List the disadvantages of using a LIMS in a C.B. lab.

- *Expenses and time consumption for training lab personals on LIMS.*
- *Time to adapt to a new system from conventional system*
- *High cost for the establishment and maintenance of the system*
- *Physical restrictions, basically on infrastructure including space and electrical requirements.*
- *Need for a back-up system of the data and its security.*

Quality Management System

82. What is meant by a **quality management system** in a C.B. laboratory according to the International Organization for Standardization (ISO) and Clinical and Laboratory Standards Institute (CLSI)?

It is a system of coordinated activities to direct and control a lab with regard to quality with respect to all aspects of the laboratory operations, including the organizational structure, processes and procedure, to ensure the accuracy, reliability and timeliness of reported test results

83. What are **quality system essentials** with respect to quality management system of a testing laboratory?

The necessary infrastructure or foundational building blocks in a testing lab that need to be in place and functioning effectively in order to support the work operations in the lab, so that they proceed smoothly.

84. List the twelve (12) quality system essentials prepared by CLSI according to the ISO standards, with respect to all of the coordinated activities in a testing laboratory.

- *Organization*
  - *strong supporting organizational structure for implementation and monitor a quality system*
- *Personnel*
  - *The quality management system addresses many elements of personnel management, supervision along with encouragement and motivation of the lab staff*
- *Equipment*
  - *Components in equipment management including choosing the right equipment, installing it correctly, ensuring that new equipment works properly, and having a system for maintenance is essential in a lab.*

- *Purchasing and inventory*
    - *Management of purchasing and inventory is essential to ensure that all reagents and supplies are of good quality, and that they are used and stored in a manner that preserves integrity and reliability and available as required.*
- *Process control*
    - *Under this quality of the test performance is ensured in which quality control for testing, appropriate management of the sample, including collection and handling, and method verification and validation are inclusive.*
- *Information management*
    - *Laboratory data needs to be carefully managed to ensure accuracy and confidentiality, as well as accessibility to the laboratory staff and to the health care providers using suitable systems.*
- *Documents and records*
    - *Information generated in the lab need to be kept as records and documents which must be carefully maintained to be accurate and accessible.*
- *Occurrence management*
    - *An "occurrence" is an error or an event that should not have happened. There should be a system which can detect these problems or occurrences, to handle them properly, and to learn from mistakes and take action to minimize reoccurrence.*
- *Assessment*
    - *Assessment is a process in which laboratory performance is examined and compared to standards, benchmarks or the performance of other laboratories.*
    - *It can be both internal (performed within the laboratory using its own staff) and external (carry out by a group or agency outside the laboratory)*
- *Process improvement*
    - *Continuous and systematic improvement of the processes in the lab is required for its quality.*

- *Plan, Do, Check and Act (PDCA) cycle to move from "problem faced" to "problem solved"*

- *Customer/ patient service*
  - *Since laboratory is a service organization; it is essential that clients/ patients of the laboratory receive what they need, as recommended by the clinicians.*
- *Facilities and safety*
  - *This encompasses*
    - ***Security*** *– to avoid the entrance of unwanted risks and hazards to the laboratory space*
    - ***Containment*** *– to avoid the emission of hazards from the lab space to the community*
    - ***Safety*** *– To prevent harm to staff workers, visitors and the community.*
    - ***Ergonomics*** *– to provide facility and equipment adaptation to allow safe and healthy working conditions at the laboratory site.*

85. What are the ISO standards which are specific to the quality management requirements in laboratories?

- *ISO 15189:2012 -For medical testing labs*
- *ISO/IEC 17025:2005 -For testing and calibration labs*

86. What is the basic difference between a document and a report in a C.B. lab?

Documents provide written information about policies, processes and procedures, whereas records are the collected information produced by the laboratory in the process of performing and reporting a laboratory test

Documents vs Records

87. What are the common characteristics of a document?

- *Documents communicate information to all persons who need it, including laboratory staff users and laboratory management personnel;*
- *Documents need to be updated or maintained;*
- *Documents need to be changed when a policy, process or procedure changes;*
- *By documents formats can be established for recording and reporting information by the use of standardized forms—(once the forms are used to record information, they become records.*

88. What are the common characteristics of a record?

- *Records can be easily retrieved or accessed*
- *Records contain permanent information which does not require updating.*

89. List some common documents which can be found in a C.B. lab.

- *SOPs*
- *Quality manual –*
    - *Document which specify the quality management system of a C.B. lab*
- *Reference material*
    - *Useful in finding scientific and clinical information about diseases, laboratory methods, and procedures as well as in interpretation of test results*

90. List some records which are used in C.B. Lab.

-
- *Sample logbook, registers;*
- *Laboratory workbooks or worksheets*

- *Instrument manuals—maintenance records*
- *Quality control data;*
- *External quality assessment records;*
- *Patient test reports*
- *Personnel records*
- *Results of internal and external audits*
- *Continuous improvement project reports*
- *Incident reports;*
- *User surveys and customer feedback*
- *Critical communications such as letters from higher authorities*

91. What factors need to be considered when documents and records are stored in a C.B. lab for future use?

- *Permanence-*
  - *Either a paper based system or computer based system is used, durability of the data should be considered, by proper maintenance of bound documents or computer system is essential*
- *Accessibility-*
  - *Information can be easily retrieved whenever needed.*
- *Security*
  - *Maintaining patient confidentiality and protecting against environment hazards (if it is a paper based system) is an essential.*
- *Traceability*
  - *Ability to trace a specimen/sample throughout the entire process in the laboratory by searching the recoded history, including the facts like the tests performed, operator of the performed tests and test results etc.*

Point of Care testing

92. What is meant by '**Point of Care Testing** (POCT)'.

*POCT which is also known as '**Near Patient Testing** (N.P.T)' is referred to any analytical test including biochemical tests performed outside the laboratory and may be performed either within a hospital as a subsidiary to the main laboratory or for primary healthcare outside the hospital setting.*

93. What are the main categories of biochemical tests can be performed under 'point of care testing'

- *Test performed at medical or nursing settings*
- *Test performed at home or non-clinical settings*
- *Alcohol tests frequently used in assessing the fitness to drive a vehicle.*

94. In general, who are the operators or uses of POCT?

Non-laboratory staff including, nurses, clinicians and patients

95. What are the main advantages of POCTs for patents as well as clinicians?

- *POCTs can provide rapid test results, which in turn enable clinicians to take quick clinical decisions*
- *POCTs provide good solution in diagnostics, prognostic or screening testing which should be performed in remote areas, far away from testing labs, by reducing the test turnaround time.*
- *Most of the POCTs are simple, ready to use tests or tests with few steps procedures, which can be easily performed.*
- *Almost all the test are accompanied with either bench top or hand held devices with automated calibrations, which are more convent to handle*
- *Test requires only a small volume of sample for a large test menu*

96. List some common POCTs used in routine practice.

- *Dipstick technology for urine analysis – (e.g. glucose, bilirubin, ketones, specific gravity of urine etc.)*
    - *Simply immersing the commercially available test-strips in urine and follow the instructions in user manual*
- *Glucometers with test strips to determine the glucose level in blood.*

- *Bench top biochemical analyzers to determine the concentration of different analytes in blood including*

- *Electrolytes such as sodium, potassium, chloride etc.*
    - *Creatinine*
    - *Glucose*
    - *Hemoglobin*
    - *pCO_2*
    - *pO_2*
    - *pH*

97. What are the general drawbacks associated with POCTs.

- *High cost –*
    - *Many of the POCT s are expensive even though it replaces the conventional tests performed in the labs, with rapidness and convenience*
    - *Most of the cost is aroused due to initial cost of the instrument and supplies like test strips*
- *Operator or user need to take the responsibility of the test results*
    - *Generally POCTs are performed by non-laboratory personnel including clinicians and nurses or patients by them self who should assume a number of responsibilities that would normally be those of the laboratory staff.*
    - *Assay need to be performed appropriately according to the manufacturer's instructions and results need to be accurate, precise and meaningful.*

- *Precision and accuracy of POCTs are known to be lesser than lab-based methods, and fall short of the sensitivity and specificity associated with laboratory analyzers.*

98. What are the two main types of analytical problems associated with POCTs?

- *Problems related to assay technology – Little or no effect on test results*
    - ***Note** – However, compared to lab based tests , accuracy of the results generated by POCTs are said to be relatively law, since the lab test are properly managed by a good quality system.*

- *Operator errors - render major impact on test results*

99. List commonly encountered analytical problems with respect to operator errors of POCT.

- *Improper or lack of calibration of the instruments*
- *Improper cleaning of the instruments*
- *Lack of using quality control materials*
- *Use of expired test strips for preforming tests*
- *Storage of reagents or test strips under inappropriate conditions.*

100. List the possible means of overcoming the operator errors relevant to POCTs

- *Carefully following the manufacturer's instruction relevant to the respective POCT.*
- *Taking short training on usage of the POCT instruments*
- *Proper and regular maintenance of the instruments*
- *Performing simple quality control checks*
- *Performing simple quality controls cross checks with the main biochemistry laboratory.*

Further Readings

1. Laboratory quality management system: handbook. 2011, World Health Organization,

2. Kanagasabapathy, A S, Kumari, S, 2000, Guidelines on standard operating procedures for Clinical Chemistry, World Health Organization Regional Office for South-East Asia

3. Gaw, A, Murphy, M.J, Srivastava, R, Cowan R.A and St J O'Reilly, D, 2013, Clinical Biochemistry, an illustrated colour text, 5th Ed, Churchill Livingstone, Churchill Livingstone (Elsevier). London.

4. Bradshaw, A E, McNamara C, 2017, Laboratory organization, management and safety In Bain B J, Bates, I, Laffan, M.A. (Eds) Dacie and Lewis practical hematology 12 th Ed (Elsevier) London (p 511-532).

5. Lewandrowski, K. 2009, Point-of-Care Testing: An Overview and a Look to the Future (Circa 2009, United States), Clinics in Laboratory Medicine, 29, 421-432.

Glossary of technical terms

Analyte – *component or the Substance in a sample which is of interest in detection of an analytical procedure or a test.*

Biohazard *- biological substance that poses a threat to the health of living organisms, primarily humans and environment.*

Clinicians *- Healthcare professional qualified in the clinical practice of medicine*

Evidence based practice *- the integration of the best research evidence, clinical expertise and patient needs that will result in the best patient outcomes.*

Ergonomics - *The science of improving the design of products to optimize them for human use*

Genetic Screening - *The application of a test on people for the systematic early detection or exclusion of a hereditary disease, a genetic predisposition to a disease, or*

to determine whether a person carries a predisposition which may produce a hereditary disease in their offspring (Health Council of the Netherlands: 1994)

Molecular Diagnostics - *Family of techniques used to analyze biological markers in an organism (specifically in their genome) and to analyze how their cells express their genes as proteins*

Sputum *- Mucous material from the lungs that is produced by coughing.*