Learning objectives:

By the end of this lecture, students will be able to:

1. Understand the role of Clinical Biochemistry in Laboratory Medicine and its various divisions.
2. Understand the use of Clinical Biochemistry testing in Clinical Medicine:
   - Diagnosis
   - Management
   - Prognosis
   - Screening
3. Know the needed information for a test request for Clinical Biochemistry.
4. Describe the types of specimens used in Clinical Biochemistry analysis.
5. Understand the factors affecting test results:
   - Pre-analytical
   - Analytical
   - Post-analytical
6. Understand the concept of reference range (value) of Clinical Biochemistry tests.
Main Reference Textbook
CLINICAL CHEMISTRY & METABOLIC MEDICINE

MARTIN A. Crook

SEVENTH EDITION

Whether you work in hospitals, laboratories, or in medical schools, you may find your clinical knowledge and skills are constantly changing. Clinical Chemistry and Metabolic Medicine is an authoritative text that provides a comprehensive understanding of clinical chemistry and the role it plays in the diagnosis and management of metabolic disorders.

KEY FEATURES:
- Comprehensive coverage of clinical chemistry and metabolic medicine
- Updated with new data and recent advances
- Includes an extensive list of references

ABOUT THE AUTHOR:
Martin A. Crook MB BS MSc PhD DSc FRCP
Consultant Physician in Clinical Chemistry, Papworth Hospital, Cambridge, UK

The book comes to your question
- Joan Zeena and Peter Hennin, who have written
- The book is an excellent introduction to the subject for medical students and practitioners in clinical chemistry.

Hodder Arnold

For more information, visit www.hodderarnold.com
Clinical Biochemistry

GEOFFREY BECKETT
SIMON WALKER
PETER RAE
PETER ASHBY

7th edition

Clinical Biochemistry

Lecture Notes: Clinical Biochemistry presents the fundamental science underlying common chemical investigations used in clinical practice. It takes a practical, relevant approach that enables medical students and junior doctors to:

- Understand the value and limitations of chemical investigations.
- Develop the skill to select appropriate investigations for diagnosis and management.
- Interpret investigations correctly.
- Develop a critical approach to diagnostic investigations.

Lecture Notes: Clinical Biochemistry takes a system-based approach. The underlying physiological rationale for any test is explained in the context of disruption by disease. This leads naturally to an integrated and practical understanding of chemical diagnostics.

Case studies at the end of each chapter provide a clinical setting to help develop test-selection skills.

Lecture Notes: Clinical Biochemistry provides the essential background to chemical investigations for medical students, junior doctors on foundation programmes, and nurses and practitioners involved in requesting and interpreting diagnostic services.

Of related interest

Metabolism at a Glance
J.G. Salway
2003
14051 07187
9781405107187

Medical Biochemistry at a Glance
J.G. Salway
Second edition published November 2005
14051 3227
978140513227

Blackwell Publishing

ISBN 1 4051 2096 X

www.blackwellstudent.com
Other suggested textbook
√ Chemical Pathology
√ Clinical Biochemistry
√ Clinical Chemistry
√ Metabolic Medicine
What is Clinical Biochemistry?

• A discipline of Laboratory Medicine that functions to provide diagnostic tests which are utilized by physicians to assess the health of an individual.

• Must be more than just a “service”.
• Dynamic interaction with all hospital departments (Emergency (ER), Intensive Care Unit (ICU), Cardiac Care Unit (CCU)) as well as physicians outside of the hospital to maximize health care through:
  - Consultation regarding tests to be requested.
  - Education: Medical students, Residents, Medical Technologists, Medical Staff.
What is Clinical Biochemistry?

- Development, Evaluation and Implementation of New Diagnostic Assays.
- Supporting Clinical and Basic Research.
- Interaction with all departments to maintain and/or improve the flow and accuracy of information (i.e. test results).
- Driving force is Patient Care......This must be done effectively and economically.
- As part of Laboratory Medicine Program must operate as a Non-profit business.
- Has a fixed yearly budget to cover staff, equipment and reagents.
Clinical Biochemistry Laboratory Organization

Core Lab Facility
- found at virtually all hospitals
  operates 24/7 to provide the essential most requested tests.
- Highly automated environment
  Instruments with Multi-analyte capabilities.

Special Biochemistry
- less frequently ordered tests
  labour intensive and often manual methods
  generally non-stat tests (result not required immediately).

Point of Care Testing (POCT)
- Instruments located outside of clinical biochemistry laboratory such as CCU, ER, ICU or satellite centre (clinic).
• **What is Clinical Biochemistry?**

“It is a branch of Laboratory Medicine in which chemical and biochemical methods are applied to the study of disease”.
# The clinical biochemistry repertoire

## Core biochemical tests

<table>
<thead>
<tr>
<th>Test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sodium, potassium, chloride and bicarbonate</td>
</tr>
<tr>
<td>Urea and creatinine</td>
</tr>
<tr>
<td>Calcium and phosphate</td>
</tr>
<tr>
<td>Total protein and albumin</td>
</tr>
<tr>
<td>Bilirubin and alkaline phosphatase</td>
</tr>
<tr>
<td>Alanine aminotransterase (ALT) and aspartate aminotransferase (AST)</td>
</tr>
<tr>
<td>γ-glutamyl transpeptidase (γGT)</td>
</tr>
<tr>
<td>Creatine kinase (CK)</td>
</tr>
<tr>
<td>H+, PCO₂ and PO₂ (blood gases)</td>
</tr>
<tr>
<td>Glucose</td>
</tr>
<tr>
<td>Amylase</td>
</tr>
</tbody>
</table>

## Specialized tests

<table>
<thead>
<tr>
<th>Test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hormones</td>
</tr>
<tr>
<td>Specific proteins</td>
</tr>
<tr>
<td>Trace elements</td>
</tr>
<tr>
<td>Vitamins</td>
</tr>
<tr>
<td>Drugs</td>
</tr>
<tr>
<td>Lipids and lipoproteins</td>
</tr>
<tr>
<td>DNA analyses , Amino acids analysis.</td>
</tr>
</tbody>
</table>

## Emergency tests

<table>
<thead>
<tr>
<th>Test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urea and electrolytes</td>
</tr>
<tr>
<td>Blood gases</td>
</tr>
<tr>
<td>Amylase</td>
</tr>
<tr>
<td>Glucose</td>
</tr>
<tr>
<td>Salicylate</td>
</tr>
<tr>
<td>Paracetamol</td>
</tr>
<tr>
<td>Calcium</td>
</tr>
</tbody>
</table>
Steps in the Investigation of a Patient

Patient History

Clinical examination

Laboratory testings

Diagnostic imaging

Diagnosis

Therapy

Evaluation
The place of clinical biochemistry in medicine

- History
  - Clinical examination
    - Diagnostic services
      - Imaging
      - Physiology tests: ECG, EEG, lung function
    - Laboratory services
      - Haematology
      - Histopathology
      - Immunology
      - Microbiology
    - Clinical biochemistry
      - Emergency services
      - Core biochemistry
      - Specialized tests
      - Others
Laboratory Medicine Services

- Clinical Biochemistry: 40%
- Immunology: 12%
- Microbiology: 8%
- Histopathology: 5%
- Others (e.g. Blood Bank; Cytogenetics): 10%
- Haematology: 15%
Steps in obtaining a clinical biochemistry test

- Test is requested by physician and ordered on the computer. Barcode is generated.
- Specimen is collected.
- Specimen and order are transported to the lab.
- The specimen is accessioned in the lab.
- The specimen is processed.
- The specimen is analyzed.
- The results are reviewed and verified by an Chemical pathologist.
- The results are released to the patient's record.
Circuit diagram of the clinical biochemistry process
Why are laboratory tests ordered?

- Diagnosis.
- Monitor progression of disease.
- Screening population for diseases.
- To identify complications of treatment.
- For predicting survivability, employability.
- To check the accuracy of an unexpected data.
- To conduct research.
- To prevent malpractice.
- For educating residents.
- To assess nutritional status and health of a healthy individual.
- Responding to total uncertainty.
So many questions are asked?

1. How often should I investigate the patient?
2. When is a laboratory investigation considered "Urgent"?
3. How to interpret the results.
4. Is the abnormality of test of diagnostic value?
5. Has there been a clinically significant change in the laboratory tests?
• How Clinical Biochemical Tests are used?

✓ Diagnosis
✓ Management
✓ Prognosis
✓ Screening
Diagnosis

- It is based on:
  - History
  - Examination
  - Investigations

√ Occasionally, clinical biochemical tests are diagnostic (e.g. OGTT).

√ Often clinical biochemical tests confirm a diagnosis or indicate a particular metabolic disease is present (e.g. Endocrine disorders).

√ Molecular genetic analysis is diagnostic (biochemical phenotype).
Case Study #1

Consider the following three OGTT cases ( [Glu] in mmol/L ):

<table>
<thead>
<tr>
<th>Time (min)</th>
<th>0</th>
<th>30</th>
<th>60</th>
<th>90</th>
<th>120</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient #1</td>
<td>6.2</td>
<td>7.0</td>
<td>10.7</td>
<td>12.7</td>
<td>14.0</td>
</tr>
<tr>
<td>Patient #2</td>
<td>5.4</td>
<td>7.7</td>
<td>10.8</td>
<td>12.7</td>
<td>9.9</td>
</tr>
<tr>
<td>Patient #3</td>
<td>4.8</td>
<td>11.6</td>
<td>7.2</td>
<td>5.5</td>
<td>3.8</td>
</tr>
</tbody>
</table>

- **Diabetic** (intermediate & 120min samples > 11.1 mmol/L)
- **Impaired GT** (intermediate & sample > 11.1 mmol/L, 120min Sample 7.8-11.1 mmol/L)
- A lag storage curve (normal except for intermediate sample > 11.1 mmol/L)
Management

√ Assessment of disease severity (e.g. Tissue damage in patients with hepatitis).

√ Following the response to therapy in acute disorders (e.g. DKA, Hyperkalaemia, Acute RF).

√ Assessing treatment in chronic disorders (e.g. DM, CRF, Hypothyroidism).

√ Assessing drug therapy:
  - compliance
  - achieving therapeutic range
  - investigating overdosage
  - sensitivity/toxicity.

√ Urgent testing (e.g. Hypoglycaemia, MI).
Case Study # 2

The following biochemical data were those of a jaundiced, unwell 14 year old boy.

<table>
<thead>
<tr>
<th>Test</th>
<th>Results</th>
<th>RR</th>
</tr>
</thead>
<tbody>
<tr>
<td>ALT (U/L)</td>
<td>4000</td>
<td>&lt;35</td>
</tr>
<tr>
<td>ALP (U/L)</td>
<td>150</td>
<td>30-120</td>
</tr>
<tr>
<td>Total protein (g/L)</td>
<td>78</td>
<td>62-82</td>
</tr>
<tr>
<td>Albumin (g/L)</td>
<td>44</td>
<td>30-50</td>
</tr>
<tr>
<td>Bilirubin (umol/L)</td>
<td>98</td>
<td>&lt;20</td>
</tr>
<tr>
<td>Urine Bilirubin</td>
<td>+ve</td>
<td></td>
</tr>
</tbody>
</table>

Typical biochemical features of acute infectious hepatitis (jaundice with ↑↑ ALT and normal ALP)
Two patients with uncontrolled DM were attending a Diabetic Clinic for the last 18-months to monitor their DM. The following are their HbA$_{1c}$ values during the management observation period.

<table>
<thead>
<tr>
<th>Time (months)</th>
<th>0</th>
<th>3</th>
<th>6</th>
<th>10</th>
<th>13</th>
<th>15</th>
<th>18</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Patient #1</strong></td>
<td>14.6</td>
<td>12.1</td>
<td>11.7</td>
<td>12.3</td>
<td>14.2</td>
<td>11.6</td>
<td>12.2</td>
</tr>
<tr>
<td><strong>Patient #2</strong></td>
<td>12.7</td>
<td>10.5</td>
<td>9.8</td>
<td>9.5</td>
<td>9.4</td>
<td>9.2</td>
<td>8.5</td>
</tr>
</tbody>
</table>

**Case Study # 3**

- **Improved control of DM**
- **Poorly-Controlled DM**
A 70-year old man was diagnosed with prostatic carcinoma. He was started on treatment. This resulted in a considerable improvement of the symptoms. The following serial changes in plasma and ALP levels were obtained:

<table>
<thead>
<tr>
<th>Time (Weeks)</th>
<th>0</th>
<th>4</th>
<th>7</th>
<th>20</th>
<th>37</th>
<th>55</th>
<th>63</th>
<th>66</th>
</tr>
</thead>
<tbody>
<tr>
<td>PSA (ug/L)</td>
<td>73</td>
<td>37</td>
<td>9</td>
<td>1.7</td>
<td>0.5</td>
<td>1.6</td>
<td>5.1</td>
<td>6.1</td>
</tr>
<tr>
<td>ALP (U/L)</td>
<td>470</td>
<td>421</td>
<td>357</td>
<td>194</td>
<td>206</td>
<td>195</td>
<td>195</td>
<td>200</td>
</tr>
</tbody>
</table>

- **Before therapy**
- **During therapy**
- **Recurrence of prostatic carcinoma**
It is undertaken to detect the presence of disease which is not apparent and for which there is no specific indication on clinical grounds.

For screening to be effective certain criteria should be met:

1. The disease has a significant effect on the length or quality of life.
2. There is a period during the natural history of the disease in which irreversible damage does not occur and during which the condition may be detected.
3. Treatment is available, acceptable and effective during the asymptomatic period.
4. An effective screening test should be available.
5. The prevalence of the disease and benefits of therapy should justify the cost of screening.
6. A population at risk can be defined.
Screening

- Population (e.g. cholesterol)
- Selective (e.g. PKU, CHT)
- Individual (e.g. Down's syndrome)

 Biochemical Profiling
 Functionally-related tests (LFT, Bone, Thyroid)
How often to investigate?

Many biochemical tests are repeated at intervals. How often depends on how quickly significant changes are liable to occur, and there is little point in requesting tests if a numerical change will **NOT** have an influence on treatment.
In order to carry out clinical biochemical analysis, it is important that the Laboratory is provided with:

1. The correct specimen for the requested test.

2. The correct and complete clinical information including patients:
   - Age
   - Sex
   - Nationality
   - ID
   - Provisional indication of the suspected pathology
   - Time/date of the request
   - Status of the request
   - Diet
   - Drugs
<table>
<thead>
<tr>
<th>Information</th>
<th>Reason</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient’s name</td>
<td>Identification and (age, sex) interpretation of results</td>
</tr>
<tr>
<td>unit number</td>
<td></td>
</tr>
<tr>
<td>date of birth</td>
<td></td>
</tr>
<tr>
<td>sex</td>
<td></td>
</tr>
<tr>
<td>Return address (e.g. ward, clinic surgery:</td>
<td>Delivery of report</td>
</tr>
<tr>
<td>telephone/page number if urgent)</td>
<td></td>
</tr>
<tr>
<td>Name of clinician (and telephone/page number)</td>
<td>Liaison</td>
</tr>
<tr>
<td>Clinical details (including drug treatment)</td>
<td>Audit</td>
</tr>
<tr>
<td>Test requested</td>
<td>Billing</td>
</tr>
<tr>
<td>Sample(s) required</td>
<td>Justification of request</td>
</tr>
<tr>
<td>Date (and time, if appropriate)</td>
<td>Audit</td>
</tr>
<tr>
<td></td>
<td>Interpretation</td>
</tr>
<tr>
<td></td>
<td>Selection of appropriate tests</td>
</tr>
<tr>
<td></td>
<td>Choice of analytical method (to avoid drug interference)</td>
</tr>
<tr>
<td></td>
<td>Interpretation (with timed/sequential requests)</td>
</tr>
<tr>
<td></td>
<td>Audit</td>
</tr>
</tbody>
</table>
Table # 3 Specimens used for biochemical analyses

<table>
<thead>
<tr>
<th>Specimens</th>
</tr>
</thead>
<tbody>
<tr>
<td>Venous blood, serum or plasma</td>
</tr>
<tr>
<td>Arterial blood</td>
</tr>
<tr>
<td>Capillary blood</td>
</tr>
<tr>
<td>Urine</td>
</tr>
<tr>
<td>Faeces</td>
</tr>
<tr>
<td>Cerebrospinal fluid (CSF)</td>
</tr>
<tr>
<td>Sputum and saliva</td>
</tr>
<tr>
<td>Tissue and cells</td>
</tr>
<tr>
<td>Aspirates: e.g. pleural fluid, ascites, joint (synovial) fluid, intestinal (duodenal), pancreatic pseudocysts.</td>
</tr>
<tr>
<td>Calculi (stones)</td>
</tr>
</tbody>
</table>

• Choice of specimen type depends on
  - Analyte to be measured
  - Ease of collection
Collection Tubes

The most widely used tubes for blood collection are evacuated tubes (Vacutainers):

- Negative pressure facilitates collection
- Easy to use
- Sterile
- Universally used colour-coded rubber stoppers to denote tube type.
- Tubes can contain various anticoagulants for the collection of whole blood or plasma.
- Tubes can have additives for specific tests (glucose, metals).
Collection Tubes (Vacutainers)

Separator Gel

Serum Separator Tube (SST)

Serum
Separator Gel
Clot
Collection Tubes

- Red-top tubes contain no anticoagulants or preservatives
- Red-top tubes are used for collecting serum:
  - 10-15 minutes is required to allow blood to clot before centrifuging
  - Used for blood bank specimens, some chemistries