Introduction to Clinical Chemistry

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Objective.

- To introduce the students to the principles of clinical chemistry or chemical pathology.

Format of the lecture.

1. Concept of chemical pathology.
2. Aspects of Biochemistry
3. Laboratory investigations for biochemical disorders.
4. Steady state and compartmental analysis
5. Nature of clinical specimens for chemical pathology.
6. Normal range.

Clinical chemistry

- **Chemical pathology**:
- The study of the **changes** that occur in disease in:

1. **Chemical** constitution and
2. **Biochemical** mechanisms

➢ of the body.

Biochemical disorders and chemicals*

- Primary
- Secondary

- Apply:

1. **Physiology** and
2. **Biochemistry**

- to understand the **cause** and **nature** of disease*.

➢ Analysis of **body fluids** and **tissues** for chemicals to aid the **diagnosis** and **treatment** of diseases.

Biochemistry :

- The study of the **Structure**, **Composition**, and **Chemical reactions** of substances in **living** systems.
- Areas covered:

i. How living things obtain **energy** from food.

ii. **Chemical** basis of heredity.

iii. What fundamental **changes** occur in disease.

Incorporates:

- Molecular biology; immunochemistry; neurochemistry; and bioinorganic, bioorganic, and biophysical chemistry.
- Biochemistry also involves pharmacology, physiology, microbiology, and **clinical chemistry**.

Laboratory investigations for Biochemical disorders/diseases.

Factors to consider in clinical chemistry:

1. **State** of patient when requesting investigations.
2. **Reasons** for requesting investigations.

State of patient.

- Requested in:

1. **Resting** state
2. **Stressed** state

Resting state.

- In general, biochemical investigations of **function** first performed in the ***resting state*** as the patient presents ***clinically*.**
- This applies whether the **function** is of:

1. E**xcretory organ** such as the kidney or
2. S**ecretory organ** such as the pancreas, adrenal glands.

- **Gross changes** detected by such investigations.
- **Minor** abnormality may well be covered by **compensatory** mechanisms.

Stressed state.

- For investigation of ***minimal changes*.**
- Often necessary to test the **function** when ***stressed.***
- Sometimes helpful in determining the **physiological level** of an ***abnormality.***

Types of **stress** test:

a) ***Extreme*** load of a normal metabolite e.g ammonium chloride to test the ability of the kidneys to **acidify** urine.

b) Measure the **reserve ability** of a target organ to **respond** to a hormonal stimulus.

Reasons for requesting investigations.

- Either for:

I. **Selected** tests.

II. **Screening** tests.

Selected tests.

- Investigating a **patient** logical sequence as follows:

I. Decide ***what information*** is needed.

II. Choose the test(s) ***most likely*** to provide the information.

III. Use the analytical procedure that best combines ***speed*** and ***quality***.

IV. Correlate the result(s) with the existing information.

V. Decide whether ***further*** tests are needed.

- Laboratory investigations selected will give ***information*** of the following ***specific questions*** of individual patients:

I. Anything wrong?

II. What's wrong?

III. How badly wrong?

IV. What else is wrong?

‘Anything wrong?’:

- ***Biochemical investigation*** being used as the ***extension*** of a clinical examination to determine the ***presence*** or ***absence*** of an ***abnormality*.**
- Biochemical test ***more sensitive*** than clinical approach.

‘What’s wrong?’.

- A general clinical abnormality ***identified***, but the specific diagnosis ***unknown***.
- A ***discriminating*** biochemical test (or preferably and more usually a particular ***combination*** of tests) chosen.
- ***Different*** pattern of results in each of the several diseases of ***possible diagnosis***.

‘**How badly wrong?**’

- The specific diagnosis ***established***.
- Necessary to use a biochemical test to assess ***progression*** or ***regression*** (monitoring)
- **More sensitive** than clinical observation.

‘**What else is wrong?**’

A biochemical test used to detect:

1. ***Complication*** of the disease or
2. ***An expected*** or ***unexpected*** side-effect of treatment, before it becomes evident **clinically.**

Screening tests.

- Biochemical screening tests of **two** types:

I. ***Population*** screening

II. ***Admission*** screening

Population screening.

- Testing a whole ***apparent healthy*** population for a particular disease.
- Disease present at ***low*** frequency.
- Disease detected at a ***subclinical*** phase by a ***specific*** biochemical test.

Admission screening.

- Testing **all:**

1. Hospital in-patient admissions,
2. Out-patient referrals,
3. ‘Check-ups’ in a clinic.

- Large number (**10-20**) of biochemical variables on **plasma** at the same time.
- Done **irrespective** of patients’ presenting condition.

Steady-state.

- The body considered as a set of **open steady-state** systems.
- Composition varies **regularly** and **irregularly.**
- With factors - **meals**, **exercise**, and **circadian rhythms.**
- A **steady state** - a situation in which **all** state variables in the body are **constant** in spite of ongoing processes that strive to **change** them.

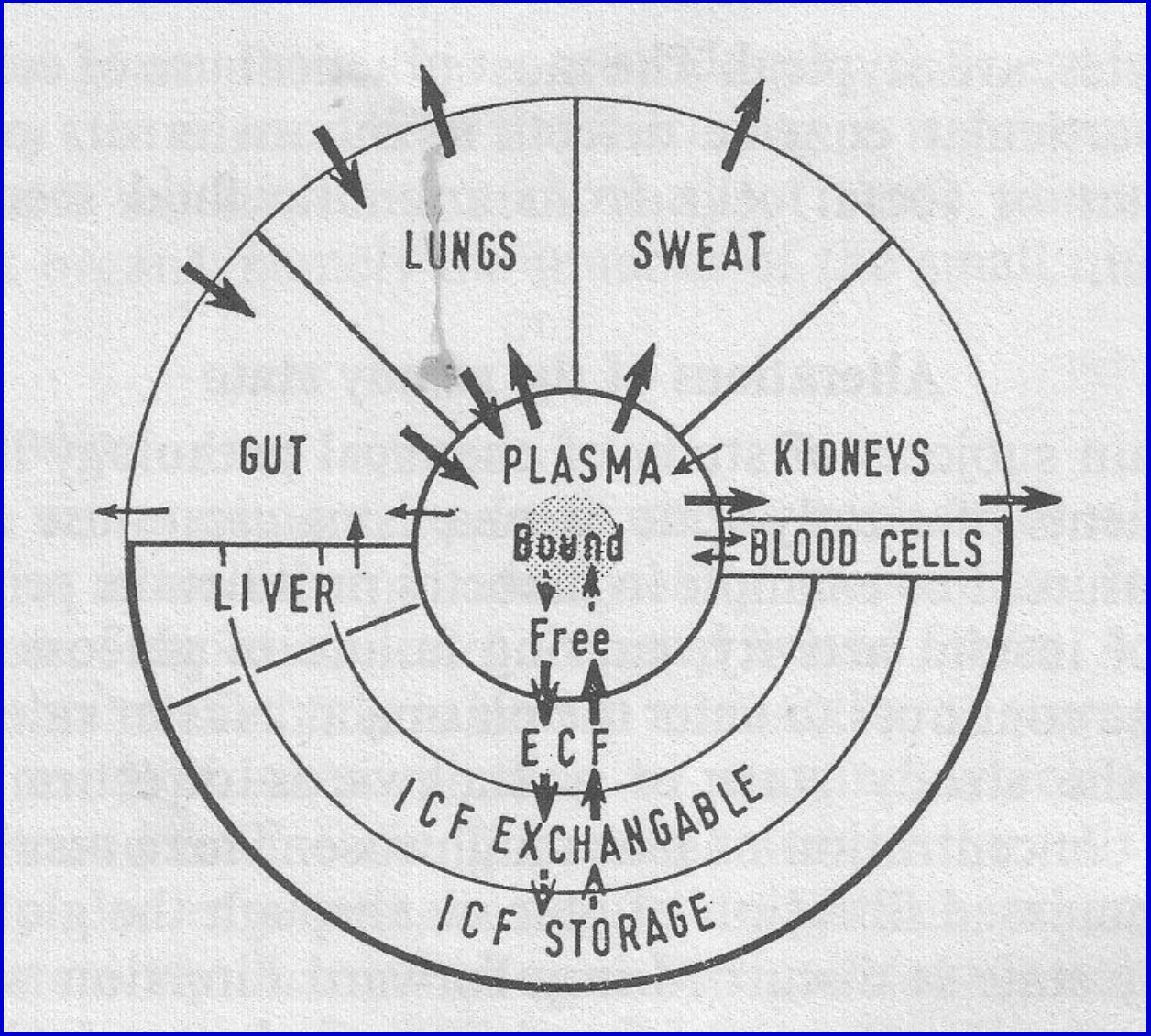
- Entire system to be at ***steady state***, i.e. for **all** state variables of a system to be **constant**, there must be a ***flow through*** in the system.
- **The body compartments:**

1. **Plasma (main)**.
2. **interstitial fluid (*(extracellular)***
3. **Intracellular fluids**,
4. **Transcellular** fluids such as **lymph** or **intestinal contents**.

- Each compartment - ***different*** and slightly ***variable*** composition, and movement between the compartments is **not** necessarily free.
- The **GIT** -main site of ***intake*** and ***excretion***, both of itself and because of the ***bile*** derived from the ***liver cells***.
- The **lungs** -sites of ***intake*** and of ***excretion***.

- The kidneys - site of ***excretion*** and to a certain extent of ***synthesis***.
- The sweat glands -only a site of ***excretion***
- The ***plasma*** compartment exchanges its components with the ***blood cells*** and through the ***interstitial fluid*** with ***body cells***.

A generalized picture of the exchanges between the exterior, the plasma, the extracellular fluid (ECF), and the intracellular fluid (ICF) that maintain the composition of the body compartments



Compartmental analysis

- **Basis** for chemical pathology

1. Plasma concentration.

➢ Measurement of only the ***plasma*** concentration of a body component in a disease **not** enough:

a) A limited view of the ***disturbed*** rates of ***flow*** of the component between the body compartments,

b) Limited view of any ***changes*** in the ***size*** of the compartmental pool.

Plasma concentration of a component in a sample analysed is:

- the ***Ratio***, at a given point in time, between its ***total*** content in the plasma compartment, and the ***total volume*** of the plasma compartment assuming ***even*** distribution.

2. **Measurement of the actual *secretion*** or ***production*** rate, usually of a hormone, difficult.
3. **An alternative approach** - measure ***intake*** and ***output*** (urinary and/or faecal) of the ***component*** under study by a balance technique.

4. Measurement of ***urinary excretion*** of a substance: indicator of the ***excretion rate*** or ***production rate*** of that substance or of its ***precursor***.

Mechanism of change in compartment*.

- **Plasma concentration** of a constituent remains **unchanged** as long as inward and outward flow are equal.
- **Plasma conc rises** when the rate of entry of the component **exceeds** the rate of disposal, provided that there is **no** diminution of **plasma water.**

- **Rise** goes on until if possible a **new steady state** set up in which inward and outward flow are again equal.
- **Reverse** arguments apply to a **fall** in a concentration in plasma.

Types of tests in clinical chemistry.

1. **General or routine** chemistry tests- commonly ordered **blood chemistries** (e.g., **liver** and **kidney** function tests).
2. **Special chemistry** - elaborate techniques such as **electrophoresis** manual testing methods.
3. **Clinical endocrinology**- the study of **hormones** , and diagnosis of endocrine disorders.

4. **Toxicology**- the study of drugs of abuse.
5. **Therapeutic drug monitoring** - measurement of therapeutic medications **blood levels** to optimize dosage.
6. **Urinalysis**- chemical analysis of urine for a range of diseases,
7. **Analysis** of **other fluids (**e.g Cerebral Spinal Fluid, effusions such as peritoneal, synovial, pleural, and pericardial).
8. **Stool examination**– GIT and other biochemical disorders.

Types of clinical specimens for clinical chemistry.

1. **Blood** (Plasma)
2. **Fluid** in body cavities (Peritonium,Pleura,Pericardium,Cerebral Spinal fluid)
- Synovial fluid
3. **Saliva**
4. **Urine**
5. **Stool**
6. Various types of **solid tissue**, including specific cell types

Normal range and interpretation of clinical chemistry results.

- **Reference range**
- **Defn**: A set of values established as **normal minimums** and **maximums** for a given chemical in a body fluid.
- For any analysed body constituent , **convenient** but artificial concept.

- e.g:-Normal range for plasma sodium is 136-148 mmol/l means **strict** boundary between **normal** and **abnormal**.
- All **normal** subjects (‘**normal**’- healthy **general population**) -plasma sodium values within that range,
- **Abnormal** to have a plasma sodium <136 or >148
- NR applied to all chemicals in all body fluids.

Factors affecting Normal range :

1. Methodology.

- Virtually for all substances analysed, **no** method either ***absolutely precise*** and ***reproducible***, or absolutely ***accurate*** and ***specific***.
- In ***Interpretation*** of possible clinical significance of ***changes*** in results: consideration of ***variability*** due to the **method** important.

2. ***Physiological*** **(non-pathological) variations**:

a) Time of day
b) Menstrual cycle,
c) Recumbency (lying down),
d) General diet,
e) Specific meals.
f) The existence of seasonal variations - uncertain.

3. ***Racial.***

Due to:

- Partly nutritional,
- Partly environmental (including endemic diseases),
- Possibly Genetic.

4. **Age**
5. **Sex**

Age & sex

- Main causes of **variation** in the normal range in a **healthy** population.

Age.

- Plasma concentrations usually tend to ***rise*** with age, probably due to **diminution** of renal clearance.

➢ **Except** for **albumin** and **iron.**

Sex.

- In general, plasma conc in men are **higher** than in women.
- Difference is **hormone-mediated**, tends to disappear after **menopause**.

➢ **Except** for **chloride**, **phosphate**, & **protein-bound iodine**,

FIN