The Biochemistry Chronicles

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Commonly Used POCT in Biochemistry Tests

CAP Definition of POCT:

Tests designed to be used at or near the site where the patient is located, that do not require permanent dedicated space, and that are performed outside the physical facilities of the clinical laboratories.

Reason for Rapid Evolution of POCT

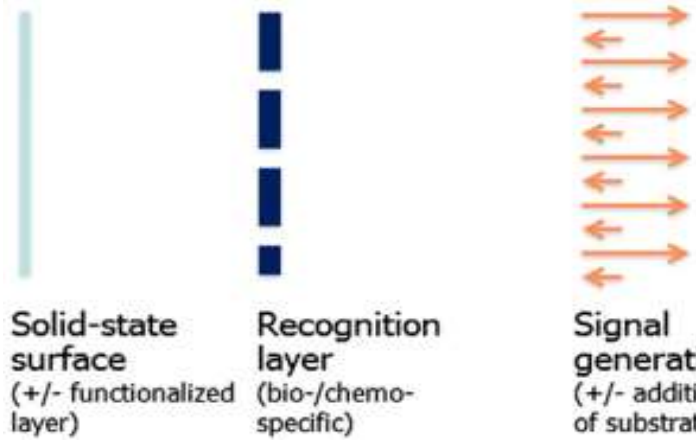
- Real-time measurements of a patient's status in a short period of time improving the **TAT**, allowing to address acute patient needs in quick diagnosis and management.
- POCT is recognized by **The Joint Commission (TJC) accreditation body** and the Clinical Laboratory Improvement Act (CLIA) of 1988.
- **Advances in medical technology**, such as prepackaged reagent systems, microprocessor-controlled reactions and calibrations, lab-on-a chip systems that use miniaturization, micromachining, microfluidics, nanotechnology and wireless communication have led to a modern generation of laboratory instruments that require less technical skill on the part of the operator.
- Point-of-care instrumentation tends to **consist of ergonomics** in terms of hand-held, durable units with easy analysis, simple QC, varied reporting methods, low throughput, and higher unit cost.

At present approximately **30% of global diagnostic market is occupied by POC testing** systems, which is predicted to grow further in coming decades.

Techniques employed in state of-the-art POCT devices

POCT devices often employ **biosensors** which are analytical device for the detection of analytes that combines a biological component with a physicochemical-detector component. This generally occurs through the use of miniaturized analysis systems, where biological components are immobilized on a solid-state surface, which, in turn, interacts with the analyte. These interactions may be detected by using either electrochemical or **optical methods**. Optical methods consist of **fluorescence** or **reflection spectroscopy.**

Detector Assembly **Transducer**



- **Optical readout**
- **Electrochemical readout**
- **Other readout modalities (thermometric, acoustic, magnetic etc.)**

General layout of biosensor used in many point-of-care testing (POCT) instruments. The recognition layer comprises attached recognition elements (antibodies, receptors, and aptamers) or immobilized enzymes. Amplified signal is finally processed by microelectronics and displayed.

Depending on the technique used, commonly practiced POCT of biochemical parameters can be categorized into various groups.

1) **Qualitative strip-based POCT methods**

These qualitative tests are mostly strip-based. Reports are read by simple visualization or by optical detection using a simple readout device. The detection principles range from chemical-indicator reactions to immunochromatography (performed as lateral flow assays). The strips are made of a porous matrix mixed with dried reagents onto a carrier element. The sample (e.g., urine, blood, stool) is deposited onto the matrix and starts the reaction while Penetrating and soaking the matrix layer. Very often used applications are urinary pregnancy testing, detection of blood in stool, urine dipstick analyses.

2) **Unit-use analyzers**

It is the simplest form of quantitative POCT device, with most of the analysis taking place on the respective test strips. A reader is used to read the result from the strips where the reaction has already taken place. The test strips are single-use articles. Classic example is glucometer for blood-sugar analysis, which is both historically and financially, the most commonly used POCT technique. Though not present in the scope of our discussion, strip-based POCT of international normalized ratio (INR) is another very commonly used parameter.

3) **Bench-top POCT analyzers**

These types of analyzers are more complex than unit-use analyzers and use different analytical principles.

3.1 Spectrophotometry/reflectometry: Spectrophotometric substrate and enzyme-activity

Measurement is usually applied for clinical-chemistry parameters. The analyzers use different test formats e.g. centrifugal disks, test strips or cassette analyzers.

3.2 Blood gas analyzers (BGAs): Potentiometry/amperometry or optical sensors for pH, pO_2 and pCO_2 are employed in BGAs. Ion-sensitive electrodes for the measurement of electrolytes and other substrates are also added. A remarkable development is additional configuration of BGAs with CO-oximetry unit.
The CO-oximetry unit is a miniaturized multi-wavelength spectro-photometer, which measures the typical absorption spectra of the various hemoglobin (Hb) species in order to distinguish O_2-Hb (oxy-Hb) from other Hb species and to determine the O_2-Hb saturation.

4) Continuous measurement with POCT systems

The most common example is continuous glucose monitoring (CGM). It is likely to replace the invasive, intravenous electrode by the minimally invasive location of a microdialysis catheter in subcutaneous tissue.

<u>Biochemical parameters available in POCT systems</u>

1. ***Glucose*** testing is the most commonly used POCT item in the field of clinical chemistry comprising more than 50% of the total global POCT market. Variety of blood samples can be tested in POC glucometers, e.g. whole blood in ICU setting to finger-pricked capillary blood for self-monitoring of blood glucose (SMBG) of diabetic patient at home.
   Continuous glucose monitoring (CGM) systems, a newly introduced POC system for blood glucose may help to alleviate the risks associated with glucose fluctuations in the ICU. The implantable CGM system is reported to provide accurate glucose readings through the intended 90-day sensor life with a favorable safety profile in participants with type 1 or type 2 diabetes.

2. Point-of-care testing for ***HbA_{1c}*** is increasingly performed in outpatient conditions to monitor glucose control in diabetes mellitus. Many studies have shown advantages of the POC HbA_{1c} test in terms of patient satisfaction and cost-effectiveness.
3. Point-of-care testing for ***cardiac markers*** in the ED is remarkable. Diagnosis of acute myocardial infarction is dependent on the change of ***cardiac troponin (cTn)*** concentrations, with at least one measurement above the 99th-percentile upper reference limit and laid down clinical criterion. The use of point-of-care ***cTnI*** measurement allows early rapid diagnosis or exclusion of myocardial infarction.

4. To monitor the risk of acute heart failure in the ED or community outpatient settings, ***N-terminal pro–B type natriuretic peptide (NT-proBNP)*** levels can also be done in POCT systems. These parameters are an important objective tool in diagnosis, prognosis, and management of heart failure.
5. POCT technology for ***creatinine*** is feasible and particularly useful for screening patients at risk for post contrast acute kidney injury, exposed to iodinated contrast for radiological investigations.

6. Abdominal pain, cramps, spasm and obstetrical complications are leading causes for women between 15 to 60 years of age to attend ED. Qualitative urine ***human chorionic gonadotropin (hCG)*** POCT is widely used in the ED to assess patient pregnancy status. Due to extensive commercialization and non-

invasive, easy-to-perform nature of this strip-based hCG POCT, it is frequently used domestically to detect pregnancy before proceeding to further radiological investigations and medical attention. However, an evaluation of sensitivity for the hook effect caused by hCG β-core fragments showed that susceptibility to inhibition of POCT equipment available in market varied greatly; only very few devices exhibited minimal to no susceptibility to hCG β-core fragments. Laboratory physicians and clinicians should be aware of the limitations of using urine hCG POC devices to rule out early pregnancy.

7. ***C-reactive protein (CRP)*** provides diagnostic value for ruling in or ruling out serious bacterial infection in febrile children. Semi-quantitative strip test can distinguish between normal and increased level of CRP. Immunochromatography is used in semi-quantitative strip tests, whereas different methods like immunoturbidimetric assay or solid-phase sandwich immunoassay were used in quantitative CRP analyzers.

8. Patients presenting to the ED with acute psychiatric symptoms such as agitation, ataxia, delirium, altered mental status, or psychosis are potential candidates for ***drug screening.*** Parameters that can be detected by POCT toxicology screen are amphetamines, benzodiazepines, cannabinoids, cocaine, and opioids.

9. Point-of-care testing blood gas analyzers for ***acid-base balance, electrolytes*** and basic metabolic panels including ***β-hydroxybutyrate*** and ***lactate*** measurements has found almost a permanent place in ED and ICU setups. Arterial blood gas (ABG) analysis remains the gold standard to assess acid-base, ventilation, and oxygenation status in critically ill patients. There is fair evidence that POCT of arterial blood gas results in the ICU and ED leads to improved clinical outcomes when POCT reduces therapeutic turnaround time compared with central laboratory testing. Venous blood gas analysis has been shown to correlate with ABG analysis and has been proposed as safer, less invasive alternative to ABG analysis. Appreciable agreement has been found between ***sodium, potassium***, and ***ionized calcium*** results obtained from blood gas and central laboratory analyzers to enable prompt clinical decision-making.

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POCT testing vs laboratory testing:

The main advantage of **point-of-care testing** is the shorter time it takes to obtain a result. POC testing can also be performed by people who have not had formal laboratory training. This includes nurses, doctors, paramedics and testing by patients themselves. These tests often require relatively easy sample collection such as body fluids (e.g. saliva or urine) or finger-prick blood. The tests that are available on POCT platform range from blood glucose to cardiac, coagulation and sepsis markers to pregnancy tests & urine toxicology.

However, POC testing can have disadvantages. For example, based on the available technology used in the device, studies have shown that errors may be more frequent with POC testing than with laboratory testing. This can arise because the POC testing environment is generally less controlled than laboratory conditions and the results can be at higher risk of external interference than laboratory processes, which can lead to inaccuracy. **POC** approaches can also be more costly than laboratory-based testing.

Method validation of devices ensures that their performance meets pre-specified analytical criteria and is a requirement assessed by accreditation bodies. But verifying these criteria by end users is essential to uncover potential bias or variability in performance. Comparability and accuracy between your laboratory instrument and your point of care instrument can be verified before putting it into operation. Common discrepancies that may come up in an institute where both lab instruments and POCT instruments are used could arise due to different units, measuring ranges, sensitivity, interferences, matrix used, lack of stringent quality control measures.

The SOP for POCT device must specify about instrument verification, maintenance procedures and quality checks and must clearly indicate the responsible person for testing. The patients pay more for POCT testing, and they have plenty of queries about the POCT report. Many a times, the onus of explaining the POCT report or discrepancy from lab reports, lands on the Lab doctor!

Life Isn't about Waiting for the Storm to Pass.

It's about Learning How to Dance in the Rain.

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