Automation

Aim :-

Introduction to automation and its application and use in clinical biochemistry laboratory.

Definition :-

Automation is the process whereby an analytical instrument performs many tests with minimal involvement of an analyst. It is the controlled operation of electronic device with minimal human interventions.

Basic Concepts :-

- Automated analyzers generally incorporate mechanized versions of basic manual laboratory techniques and procedures.

- Modern instrumentations is packaged in a wide variety of configurations.

1) Continuous - flow
2) Modular
3) Centrifugal analyzers
4) Random access analyzer

- The most common configuration is the random access analyzer.

- In random access analysis, analyses are performed

sequentially on a collection of specimens, with each specimen analyzed for a different selection of tests.

- In Random access analyzer different vials of reagents are stored on board the analyzer this approach permits measurement of a variable number and variety of analytes in each specimen.

- Continuous flow analyzers historically were the first automated analyzers used in clinical laboratories. Initially, these analyzers were used in a single channel analysis configuration and carried out a sequential analysis of each specimen.
- Subsequently, multiple channel analysis versions were developed in which analysis of each specimen was performed on every channel in parallel.

- Modular analyzers were developed by manufactures to provide

Centrifugal analyzers use discrete pipetting to load aliquots of specimens and reagents sequentially into the discrete chambers in a rotor, and the specimens subsequently were analyzed in parallel (parallel analysis) by spinning the rotor to exert centrifugal force to mix the specimens and reagent and to drive the mixtures into cuvettes located on the periphery of the rotor.

Automation of the Analytical processes:-

The following individual steps required to complete an analysis often are referred to collectively as unit operations.

- Specimen identification
- Specimen Preparation
- Specimen delivery
- Specimen loading and aspiration
- Specimen processing
- Sample introduction and internal transport
- Reagent handling and Storage
- Reagent delivery
- Chemical reaction Phase
- Measurement approaches
- Signal processing, data handling and process control.

Specimen Identification :-

Identifying link between patient and specimen is noted at the patient's bedside and maintenance of this connection throught (1) Transport of the specimen to the laboratory (2) specimen analysis (3) Preparation of a report is essential.

In practice, automatic identification includes only those technologies that electronically detect a unique characteristic or unique data string associated with a physical object

- For example, Identifiers such as.
  - Serial numbes
  - Part number
  - color
  - manufacturer
  - Patient name
  - medical record number
  - Labeling
  - Bar coding

* Specimen preparation :-

- The clotting of blood in specimen collection tubes, their subsequent Centrifugation and the tounsfer of serum to secondary tubes requires a finite time to complete.

- When whole blood is used in an assay systems, Specimen preparation time is essentially eliminated.

Specimen Delivery :-

- Following Automated methods are used to deliver specimen to the laboratory.
  - couriers service (historic method)
  - pneumatic tube systems
  - Electric truck vehicles
  - mobile robots

1) Pneumatic Tube systems → bullet shaped containers are used to hold specimens

Advantage ① Rapid and reliable transport when installed as point-to-point services

Disadvantage: ① Misrouting of carriers when switching mechanisms are introduces (multiple locations)

② Sudden accelerations and decelerations leads to hemolysis of samples. So proper packing material needs to be used. Therefore close attention to the design of pneumatic tube system is necessary to prevent hemolysis.

2) Electric Track Vehicles → Trucks are made by use of the space in ceiling plenum above the laboratory.

Advantage :- ① larger capacity than pneumatic tube

② Do not have problems with damaging specimen by acceleration and deceleration

③ Use of gimbal maintain the carrier in upright position, enabling the carrier to move both vertically and horizontally on an installed electric truck.

④ The containers can hold dry ice or refrigerated gel packs with specimen if desired.

⑤ Quick transport between floors and laboratory locations that are some distance away and joined by ceiling plenum.

Disadvantage :- ① cost of moving track
② Requirement of loading & Unloading station
③ If station is not located directly in central laboratory, additional staff may be necessary to unload cart and transportation of specimen to final location.

2) Mobile Robots / Automated guided vehicles

Advantage :- ① Useful for transport of specimen within the laboratory and outside the laboratory.

② Easily adapted to carry various sizes and shapes of specimen containers and reprogrammable with changes in lab. geometry.

③ Cost effective

Disadvantage :- ① Need to batch specimens for greater efficiency.

② Need of lab personnel to place onto or remove the specimen from the mobile robot at each stopping place.

→ Some mobile robot have been integrated with robotic systems that automate loading and unloading, other initiate audible or visual signal of their arrival at specified station.

Specimen loading and Aspiration

The loading zone of an analyzer is the area in which specimens are held in the instrument before they are analyzed.

It may be - circular tray
- Rack or series of racks built into a cassette
- A serpentine chain of containers into which individual tubes are inserted.

Analyzers may Aspirate Sample

Directly from primary collection tube.
↓
Such tube contain separator material that forms a barrier between serum or plasma and cells.

From cups
↓
The sample is transferred from primary tube into cups.
↓
Characteristics of sample cup
↓

(1) Unique for particular analyzer
(2) designed to minimize dead volume, so excess serum must be present in a cup to permit aspiration of full volume.
(3) cup must be made from inert material so they do not interact with analytes being measured.
(4) Should be disposable to minimize cost, contamination
(5) Their shape should minimize evaporation by minimizing the surface area of sample exposed.

to air, even without cap.

(6) Specimen should not undergo degradation.

(7) Photodegradation is reduced by use of semiopaque cups and placement of smoke or orange colored plastic covers over the cups.

(8) Thermolability is minimized when specimen and calibrators are held in refrigerated loading zone.

When specimens are not identified automatically, they must be presented to sampling device in the correct sequence, as specified by loading list.

For most analyzers, specimens for a subsequent run may be prepared on a separate tray while one run is already in progress. This permits human and operation actions to proceed in parallel for optimal efficiency.

Ability to insert new specimens ahead of specimens already in place in loading zone allows the timely analysis of specimen with high medical priority.

Infectious disease transmission → through splatter of serum / blood during acquisition of samples from rapidly moving specimen probes.

↓

① Prevention by use of level sensors which restrict the penetration of probe into sample

② Provision of software for smoother motion control use splatter.

(3) Use of Close Container Sampling System in which probe passes through hollow needle that penetrates the primary container's rubber stopper.

↓

After probe is withdrawn, needle also withdrawn and stopper reseals & No sample escape this also reduces carryover.

Sample pretreatment

Automation of analytical procedures requires the capability to remove proteins and other interferents from some specimens to ensure the specificity of an analytical method.

Dialysis, column chromatography and filtration have been used for these purpose.

Sample Introduction and Internal Transport

The method used to introduce the sample into the analyzer and its subsequent transport within the analyzer is the major difference between continuous flow and discrete systems.

In continuous flow system, the sample is aspirated through the sample probe into a stream of flowing liquid, whereby it is transported to analytical section in the instrument.

- In discrete system, the sample is aspirated into the sample probe and then is delivered, often with the reagent through the same orifice into a reaction cup or other container.

- Carry over is potential problem with both types of systems. It may be sample to sample carryover or Reagent to reagent carryover.

- Carryover is defined as the transfer of a quantity of analyte or reagent from one specimen reaction into a subsequent one.

- In discrete systems with disposable reaction vessels and measuring cuvets, carryover is caused by the pipetting system.

- In instruments with reusable cuvets / flowcells carryover may also arise from incomplete cleaning of cuvettes or flowcell between assay.

- Most of discrete systems use sample to sample carry over by using disposable pipette tips or by incorporating wash solutions for sample probe that flush the internal and External surface of probe with copious amounts of diluent.

- Appropriate choice of sample probe material, geometry and surface condition also influence carryovers.

Sample to sample carryover can be detected by preparation of two sample pools
(1) having high analyte concentration
(2) having low analyte concentration.

By running sequences of tests such as HHHLLLHHLL HHLL.

Reagent to Reagent Carryover can occur in system that use a common reagent probe for pipetting all the reagents.

Detection of reagent to reagent carryover is difficult.

Reagent handling and Storage :-

Many automated system use liquid reagents stored in plastic or glass containers.

For those analyzer in which working inventory is maintained in the system, the volumes of reagents stored depend on the number of tests to be performed without operator intervention. In larger systems, sections of the reagent storage compartments are maintained at 4 to 10 °C.

For many analyzers in which specimens are not processed continuously, reagents are stored in lab refrigerators and are used when required.

Some systems use reagents or antibodies that have been immobilized in a reaction coil or chamber to allow their repetitive use in a chemical reaction.

Other systems use enzymes immobilized on membranes coupled to sensing electrodes. The reaction products are measured by the sensing device.

Only a buffer is required as a diluent and a wash solution, thus the membrane has an extended life, which lowers the cost of each test.

Reagent Delivery :

liquid reagents are acquired and delivered to mixing and reaction chambers by pumps or by positive displacement syringe devices.

In these analyzer in which more than one reagent is acquired and dispended by the same syringe, washing or flushing of probe is essential to prevent reagent carry over.

Chemical Reaction Phase.

- Sample and reagents react in Chemical reaction phase.

- Factors that are important in this phase include

(1) Vessel in which the reaction occurs
(2) Cuvet in which the reaction is monitored
(3) Timing of reaction
(4) Mixing and transport of reactants
(5) Thermal Conditioning of fluids
(6) For some immunoassay systems, separation of bound and unbound fractions.

- In continuous flow systems each specimen passes through the same continuous stream and is subjected to the same analytical reactions as every other specimen and at the same rate. In such system, the reaction occurs in the flow-through component.

- In discrete system, each specimen in a batch has its own physical and chemical space, separate from every other specimen.

- Discrete analyzers use individual reaction vessels transported through the system after sample and reagent have been dispensed, or they use a stationary reaction chamber.

In a discrete system various techniques include
1) forceful dispensing
2) Magnetic stirring
3) vigorous lateral displacement
4) physical stirring
5) ~~Vigorous lateral displacement~~
mixing can contribute to reaction-to-reaction carryover.

Measurement Approches :-

Automated chemistry analyzers traditionally have relied on photometers and spectrophometers to measure the absorbance of the reaction produced in chemical reaction phase.

Alternative approches now being incorporated into analyzers include reflectance photometers, fluorometers and luminometers.

Immunoassay systems have used reaction schemes that produce fluorescence, chemiluminescence, and electrochemiluminescene to ~~enchance~~ enhance sensitivity.

Ion-selective electrodes and other electrochemical techniques also are used widely.

Signal Processing, Data handling and process Control :-

- The interfacing and integration of computers in to automated analyzers and analytical systems had a major impact on the acquisition and processing of analytical data.

- Analog signals from detectors are converted to digital signals. Computer software then processes the digital signals into useful and meaningful output.

- Data processing has allowed automation of complex calibration relationships.

- Computer workstations provide a central point of communication with the user regarding

  - Instrument status
  - Order entry
  - Result display
  - Quality control functions
  - Instrument troubleshooting
  - Cross verification of result

Types of Auto Analyzers :-

1) Continuous flow analyzers :-

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Types of Auto Analyzers :-

Continuous flow analyzers :-

In these system, sample and reagents are passed sequentially through the same analytical pathway

They are separated by means of air bubbles.

The relative proportion of sample and reagents were determined by their individual flow rates. Mixing occurs when tubes joined to form common pathway.

Basic components include :-
- Probe
- Samples
- The proportioning pump
- The dialyzer
- Heating bath
- Colorimeter
- Printer

Commonly used models are

- Technicon Glucose / urea analyzer (Single channel)
- SMA : 6
- SMA : 12

It performs 6 / 12 tests simultaneously, which may not be required by physician.

⇒ Discrete Analyzers :-

- Mainly of 2 types → 1) Batch analyzers
  2) Stat analyzers (Random access)

1) Batch Analyzer :-

- They are convenient to analyze specimen in batches like sugar, urea, creatinine etc.
- They are further differentiated into semiauto and fully auto analyzers.
- In case of semiautomated analyzer, the initial part of the procedure i.e. pipetting of reagent and sample, mixing and incubation are carried out manually. Rest of the procedure is carried out by the analyzer.
- Examples of semiauto analyzers are :-
  Erbachem -5
  Hitachi -4020
  Semiauto Pacer
  SEAC
- In case of fully auto analyzer, all the functions are carried out by the analyzer.

Examples are :-
Erbachem -10
Clinicon - Corona
Autopacer

(2) Stat (Random Access) Analyzer :-

- In these analyzers, many reagents can be pipetted one after another, so that various biochemical determinations can be performed on one specimen. According to the number of tests ordered for that patient. Hence these are patient (Specimen) oriented auto analyzer.

- Examples are :-
  - Hitachi 704 and 705
  - BT 2245
  - Abbott Spectrum
  - Erba Stallion-200
  - Centrifuged fast analyzers
  - Dry chemistry analyzer

* Benefits of automation in laboratory :-

Automated instruments enables laboratories to process a large number of specimens without help of more man power, so it decrease the need of more staff.

It reduces the variability of results and errors of analysis through the elimination of tasks that are repetitive and monotonus for most individuals.

The improved reproducibility gained by automation has lead to significant improvement in the quality of laboratory tests.

Chances of manual errors are reduced by automation and thus results obtained are more accurate and reliable.

Turn around time of the samples are easily maintained by such analyzers.

So, the automated instrument not only save the labour and time but allow reliable quality control reduce subjective error and work economically by using smaller quantities of samples and reagents.

In addition to the automated devices discribed above, a variety of other instruments and processes have been automated and used in the clinical laboratory.

They include :

- Urine Analyzers
- Cell counters
- Nucleic acid Analyzers
- Microfilter plate system
- Automated pipetting Stations
- Point of care testing analyzers.

Application of fully automated procedures in efficient performance and control of operations in all the stages of / sample ~~automatical~~ process

Tofey