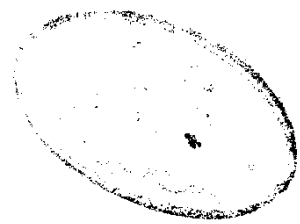
# EVALUATION OF AUTOANALYZERS IN CLINICAL CHEMISTRY IN EGYPT

Thesis

Submitted for Partial Fulfilment of the

M.D. Degree of Clinical and Chemical Pathology





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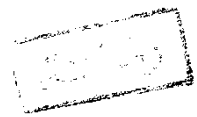

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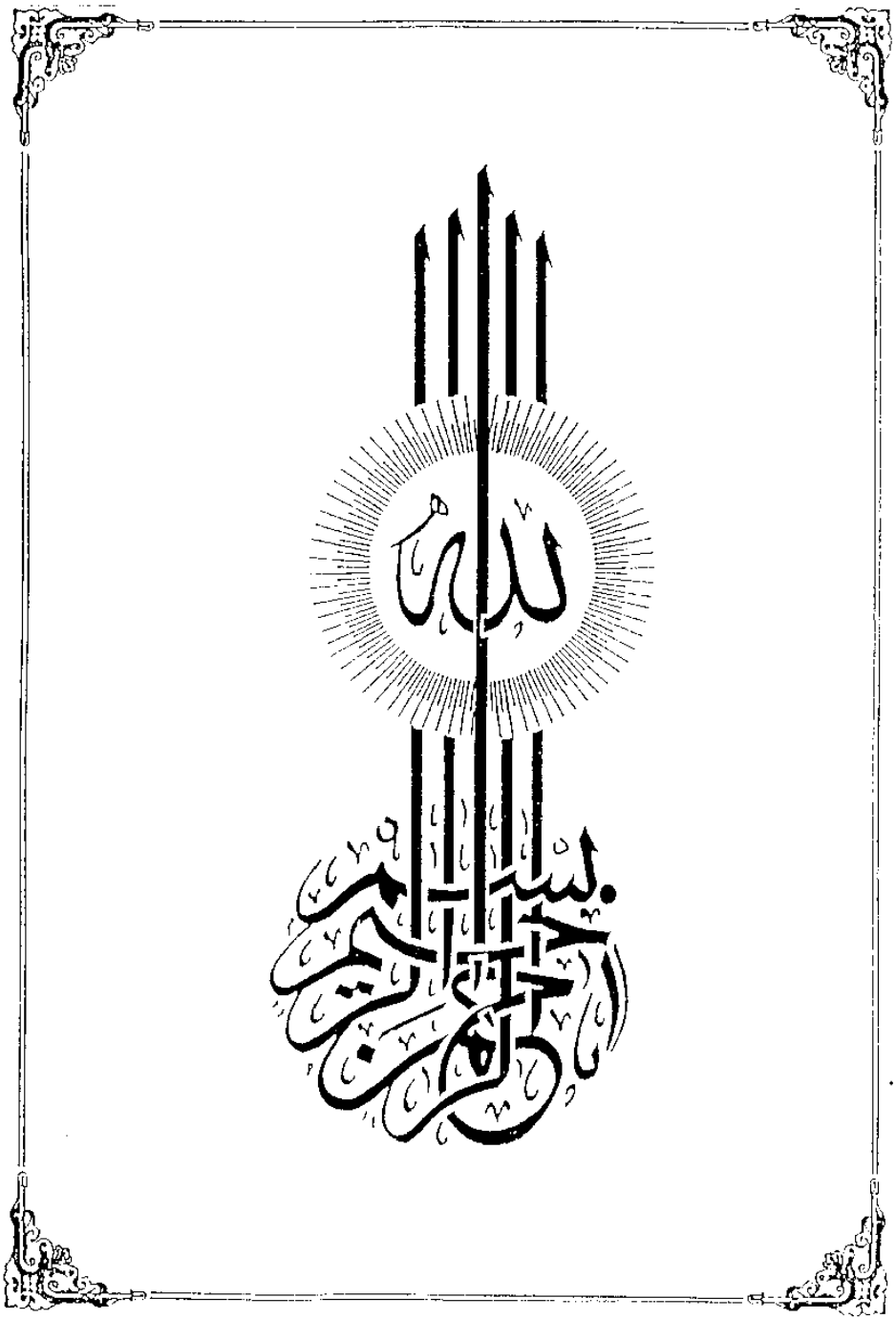
*1986*



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# INTRODUCTION AND AIM OF THE WORK

## A) INTRODUCTION

For more than half a century, at an ever increasing pace, the industrialised world has been inventing and developing instruments and systems for the needs of its clinical laboratories. Automatic analysis has come to occupy an important place in the present-day practice in clinical chemistry. Because of the introduction of many of these systems, much human error was removed from analytical work and there was an improvement in the reliability of experimental results. As these became more precise, the significance of small differences between samples increased and more analytical work was demanded of the laboratory chemist. The increased workload together with the general shortage of skilled personnel, gave an impetus to research into automatic instruments which would perform part or all of an analytical process mechanically. The main aim was to relieve the chemist of a large proportion of his routine analytical burden. By relying on the machine for this, he could deploy his skills on non-routine work and more interesting and exacting tasks. As a bonus the machine could work much more quickly and for much longer hours than human workers. Also the time of processing a sample was reduced very considerably.

With physicians becoming increasingly dependent on laboratory data for diagnosis of diseases and monitoring of therapy, automation has become essential to process the increasing workload in hospital laboratories. The alternatives to automation are either a much larger laboratory staff or a much more judicious selection of appropriate laboratory tests by the physicians. Automation provides a means by which an increased workload can be processed rapidly and reproducibly, although it does not necessarily improve the accuracy of the results.

One of the main factors affecting the quality of laboratory results in developing countries, as Egypt, is the inappropriate selection and/or use of laboratory instruments.

This problem has been aggravated by the sudden introduction of large number of sophisticated instruments without any previous planning. This situation was based on the false contention that a new equipment leads necessarily to better results. The full implications of providing the right laboratory facilities for the developing countries have not been well appreciated. In many of these countries, several new equipments have been stored without being used because of the complexity and difficulties of installation and/or operation (Vazquez and Olazabal, 1982).

## B) AIM OF THE WORK

It would be impossible in this study to give a comprehensive survey of the automatic instruments available now. No single person can today acquire the overall expertise in the innumerable theoretical, practical, technologic and engineering facets of modern analytical instrumentation. An attempt will be made to discuss the general principles of the main types with the most important examples used nowadays in the clinical laboratories.

The aim of this work is:

1) To review the different classes of autoanalyzers and the different techniques employed in them.

2) To demonstrate the benefits gained from the administration of such high cost instruments.

3) To demonstrate how to evaluate a new autoanalyzer as regard to :accuracy, precision, carryover, linearity, sensitivity, drift and cost effectiveness.

4) To clarify the different basis by which we can select a suitable autoanalyzer for an appropriate purpose.

The material of this study are the autoanalyzers available in the Clinical Pathology Department, Faculty of Medicine, Ain-Shams University. These inlcude the Astra-8 with enzymes* and the Isamat* system. The parameters studied include: blood glucose, urea, creatinine, serum sodium and potassium, chloride, carbon dioxide, cholesterol, triglycerides, uric acid, total proteins, alanine and aspartate transaminases, alkaline phosphatase, creatine kinase, lactate dehydrogenase and gamma glutamyl transpeptidase.

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* See manufacturers' list.

# REVIEW OF LITERATURE

## A) TYPES AND CLASSIFICATION OF AUTOANALYZERS

"Automation" has been defined as a system of full mechanization with automatic control by feedback that detects and corrects any tendency to malfunction. Such desirable equipment is, as yet, hardly within the grasp of the clinical biochemist. Most systems available in clinical laboratories have no such feedback control, so that the term "automation" is a misnomer and should be replaced by "mechanization". However, the term "automated equipment " has been used to describe the present generation of instruments in which the feedback element is the human supervisor.

The difference between automation and mechanization is nevertheless important and should shape the thinking of inventors of analytical machines of the future. With mechanized systems, once the process has been initiated, human intervention is necessary at intervals dictated by the machine. The operator has thus become a cog in a machine-dominated analytical sequence. A fully automated system once initiated requires no further operator intervention until the stage of deciding upon the result output (Riley and Cook, 1978).

As the field of automation has developed, a large number of automated devices has been offered commercially with widely varying degrees of success. Mitchell in 1970 tried to classify the present types employing three main pairs of independent contrasting properties. This provides basic classes, into one of which almost every available device will fall. These three pairs are described by the adjectives: complete versus partial, serial versus parallel and discrete versus continuous flow. Any device should be classified according to these criteria as a necessary preliminary to understand it or to judge its applicability in any given situation.

"Complete automation" would be represented by a device attached to the patient in such a way as to obtain its own specimen, provide an analytical result and

produce some automatic action on the patient based on the result. Although such devices have been built (Kadish and Hall, 1965), the first and the last steps are usually omitted as requirements for complete automation. Serum or some other fluid is provided as the starting material and the result is obtained as numerical concentration values or precursors of them. If any procedural steps are omitted, other than those mentioned, the term "partial automation or semi-automation" is applied. Automated photometry of solutions, in which the preceding steps have been performed manually, fits this classification.

In "serial automation", the instrument works on each sample in sequence and no two specimens occupy precisely the same stage in the procedure. The continuous flow analyzers are good examples of the serial type of automation. In "parallel automation", the device analyzes several specimens passing through the same procedure simultaneously as in the centrifugal analyzers.

In 1957, Skeggs introduced his ingenious system of "continuous flow analysis" from which the Technicon AutoAnalyzers* were developed. In this system, all specimens are sent through a greatly elongated container or pipeline where they are mixed with reagents and are segmented with air bubbles. The air bubbles are of cardinal importance in maintaining the integrity of the samples. The pipeline leads to a series of modules in which the samples are dialyzed, mixed with reagents and incubated. The line leads finally to a flow cell of a colorimeter or other detector and the output from these detectors is displayed as a series of peaks on a millivolt recorder as shown in figure 1.

* See manufacturers' list.

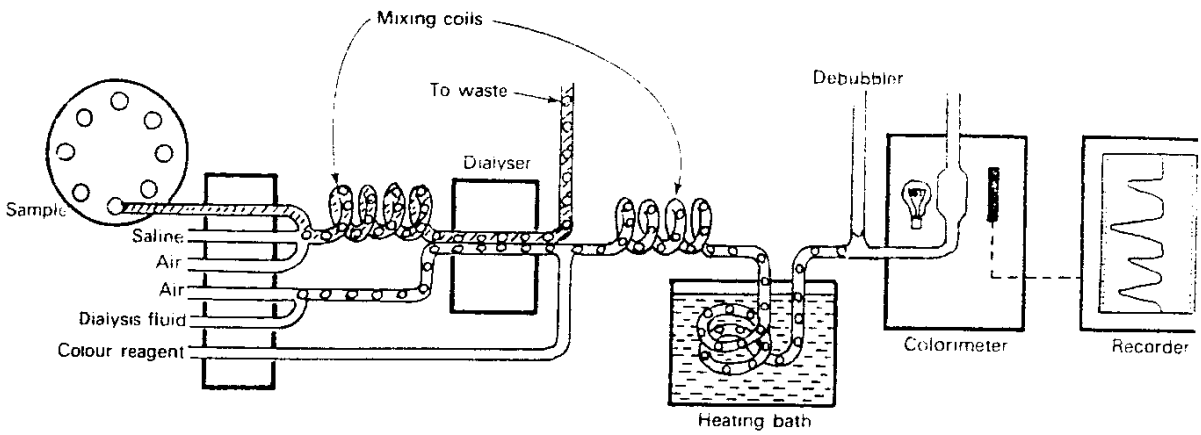


Fig. 1: Components of typical continuous-flow autoanalyzer. (Riley and Cook, 1978).

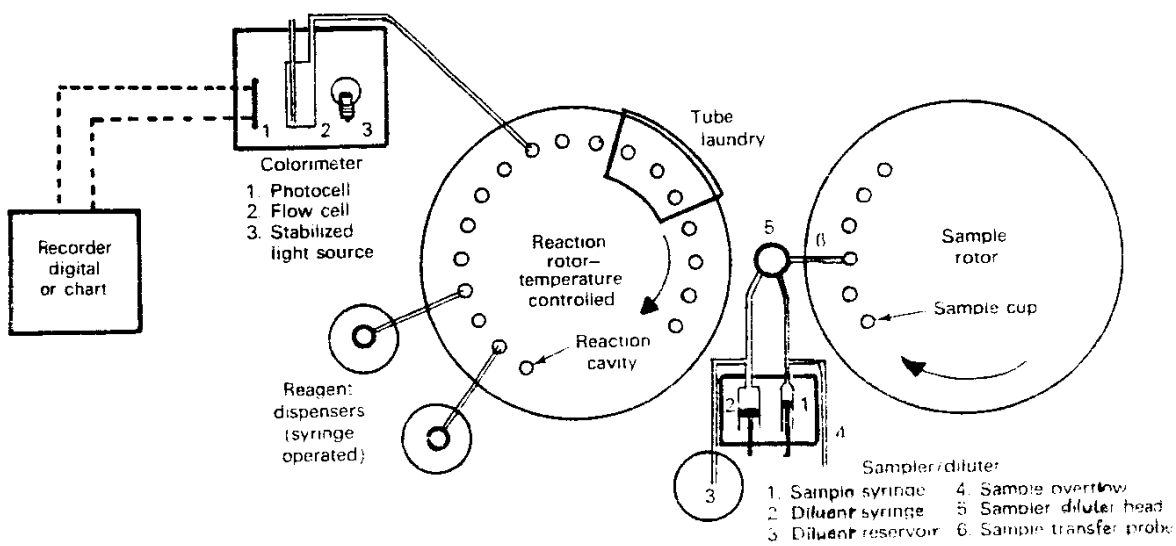


Fig. 2: Diagrammatic representation of a discrete autoanalyzer. (Riley and Cook, 1978).

In "discrete analyzers", each specimen with its accompanying reagents occupies a separate container. Although specimen may change containers, it never shares a common container with other specimens. Figure 2 shows a general diagram of a discrete analyzer.

Centrifugal analyzer is a comparative newcomer to the field, being invented by Anderson in the late 1960s. They are subtypes of discrete analyzers. The basic feature of the machine is a rotor which has a number of radially arranged connected cavities. Each channel contains two or more wells into which the sample and reagents are pipetted. The wells are so arranged that samples and reagents remain in their separate compartments until the rotor is mounted in the machine and rotated rapidly. Samples and reagents are then transferred centrifugally and almost instantaneously into outer chambers, where, after rapid mixing, the change in absorbance of the solution is measured. This is achieved by means of a light source and photomultiplier mounted in such a way that the light beam passes vertically through the cuvet chambers when they rotate as shown in figure 3.

In general, each automated device falls rather clearly into one of the above classes. However, the "flow through photometer", a continuous flow device, is employed as the last stage of many discrete analyzers and is used in a discrete fashion.

Instruments can also be classified on a fourth basis depending upon how many different determinations can be performed simultaneously on one specimen. Each determination requires one so-called "channel". Single channel devices are most common, but multichannel instruments having from 2 to 40 or more channels are invented.

One can classify instruments that are designed to measure rate of reaction differently from those designed to measure the equilibrium position or end point of the

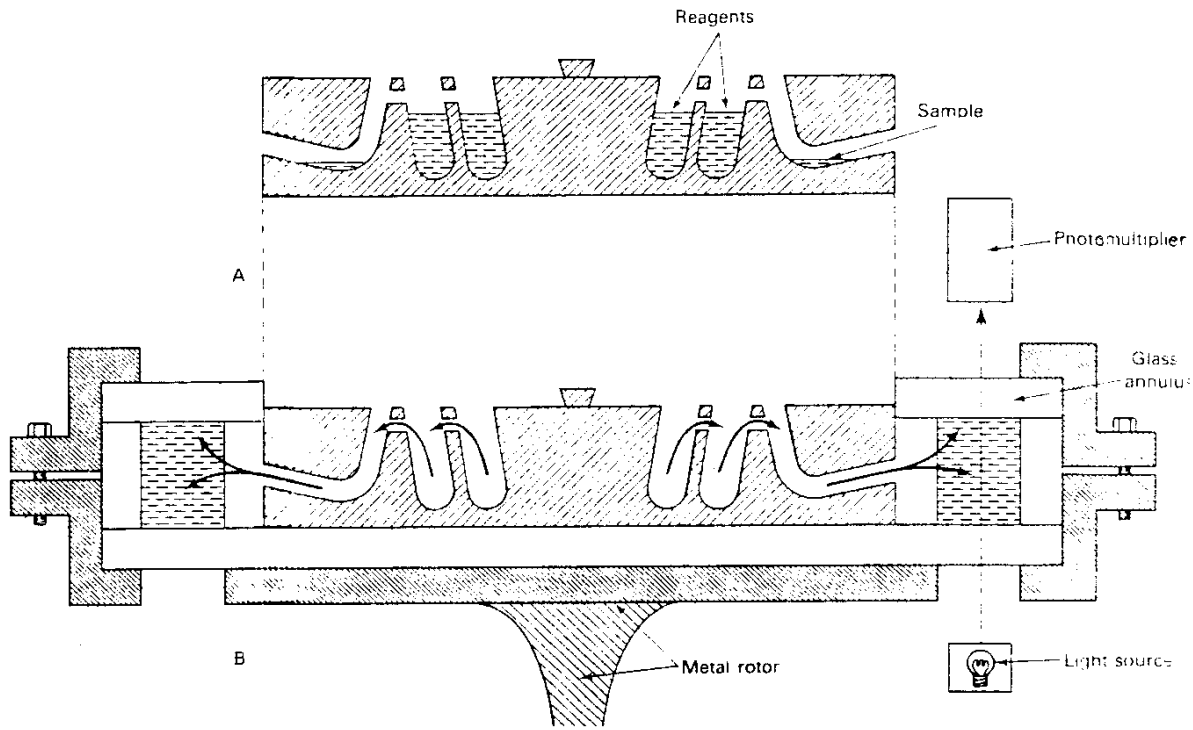


Fig. 3: Centrifugal analyzer (Riley and Cook, 1978).
(A) Transfer disc with unmixed sample.
(B) Transfer disc and cuvet after centrifugation.

reaction. Some instruments are highly specialized for measuring reaction rate, while others can measure either equilibrium or rate reactions. The main difference exists in the data processing rather than the sample handling portion of the instrument.

Automated analyzers capable of performing more than one analysis per sample at the same time are called "simultaneous analyzers". "Batch analyzers" can only perform a single test at a time on all samples presented to it. To do another test in batch analyzers, changing of reagents and/or an instrument component is required.

Multichannel instruments are called "selective" if the required tests for each individual sample can be specified and if no sample and no reagents are consumed by tests that were not requested. Instruments that are "non-selective" perform all available tests for all samples regardless of the exact tests requested. Selective analyzers have also been called "random-access analyzers" for their ability to process different test combinations for each individual sample.