Editorial:

Changing face of clinical chemistry laboratory under the influence of industry and technology

Early clinical laboratories date back to the period between 1790 to 1840, when the French physician and chemist Antoine Francois Fourcroy (1755-1809)[1] proposed setting up of a chemical laboratory near the ward in hospitals, so that, "excretions, urine and various discharges of the sick" could be subjected to chemical analysis so as to investigate the nature of disease. Alexander Marcet (1770-1822)[2] developed chemical tests for examination of calculi while William Prout (1785-1850)[3] developed a simple test for diagnosing diabetes and diseases of the urinary tracts. During this phase, chemical tests for diagnosing disease were performed occasionally on the bedside of the patients using few reagents and glassware without a separate laboratory room.[4]

The second phase of development started around 1840 with establishment of independent clinical laboratories in various university hospitals in Germany. This phase saw the development of a "chemical apparatus" when Johann Joseph Scherer, a physician who later studied organic chemistry, could get a small room for chemical examinations in 1841 at *Würzburg Juliusspital*. For the first time he used the term "clinical chemical laboratory". In 1856, Rudolf Virchow set up a "chemical department" within the Institute for Pathology. This phase saw the use of some equipment such as spectroscopes, colorimeters, spectrophotometers, etc. A change in directorship was also seen with the clinicians taking up the lead role in laboratories.[4]

Colorimeter remained the main instrument for nearly half a century till it got transformed in the early 1960s into autoanalyzer. Initially, autoanalyzer was a continuous flow instrument that reacted with specimen and reagents to produce a measurable color density recorded on a moving chart.[5] As time passed, further modifications took place and now autoanalyzers are capable of performing more chemistry tests with random selection of tests at a lower cost with an ever-expanding test menu. This led to another significant development of prepackaged, ready-to-use assay reagents, first introduced in the 1950s by the Sigma Chemical Company.[6] Further advances in the measurement techniques saw the evolution of radioimmunoassay by Yalow and Berson in 1959[7] followed by immunoasssays with other labels like enzymes and chemiluminescence.[8] The introduction of immunoassays paved the way for measurement of molecules present in nano and picomolar quantities in biological fluids. Thus technological advances had a huge impact on the laboratories as in other walks of life.[9]

Simultaneously the importance of investigations in patient care has increased. Both diagnosis and follow up of treatment started depending heavily on biochemical investigations. This has increased the number of samples received by the laboratory and decreased the expected turnaround time (TAT). Developments in laboratory automation led to identification of the importance of pre-analytical phase spanning the period between requesting an investigation to actual analysis of sample. Currently 46%-68% of laboratory errors are traceable to the pre analytical phase which involves the doctor,

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the hospital and the laboratory.[10] To cope up with this situation, the concept of total laboratory automation (TLA) arrived i.e automation of the pre-analytical, analytical and post-analytical phases. This helped in not only catering to the ever-increasing sample load but also in improving patient care by eliminating possible sources of human error. As a result of these developments, clinical chemistry has grown sufficient enough to have a separate identity combining components of medicine and chemistry. It has become necessary for the team leaders who manage the clinical chemistry laboratories to have insight into both medicine and technology apart from concepts of laboratory error and its management.

The industry added one more component to the clinical laboratory in the second half of last century, that of quality. The concept of statistical quality control (SQC) introduced by Shewhart in 1930s for industrial QC[11] was later adopted in clinical chemistry laboratories. Levey and Jennings introduced this concept of SQC to medical laboratories in 1950s, considered to be the first generation QC for manual methods.[12] In 1976-77, Westgard[13] put forth multi-rule control charts to improve detection of errors. The 3rd generation QC system saw the designing of QC procedures to fit the performance characteristics of different analytical systems.[14] The identification of medical decision limits have led to development of controls having values for different parameters relevant to the patient care. Clinical Laboratory Improvement Amendments (CLIA) recommended in 1992 minimum standard for analyzing at least two levels of QC per run, or 2 levels every 24 hours.[14] The early 1990s saw the new dimension of total quality management being added to laboratory medicine, incorporating both pre-analytical and analytical sources of errors. The six sigma percolated from industry and ushered in the 5th generation QC and introduced tolerance limits defined as defects per million.[14]

Automation of laboratory testing does not remove the need for human expertise. It eases concerns about error reduction, TAT and safety. Thus, the laboratory physician's contribution to "patient care with confidence" or evidence based medicine started increasing. The responsibility of having result that matches with other laboratories also gained importance with the growth of interactions between various health care centers as part of patient care. Introduction of external quality assurance programs ensured this. The concept of traceability introduced by the meteorological community[15] refers to the influence of calibration procedure and its specificity on the result. Use of this concept in the laboratory helped to ensure the correct laboratory-based clinical and public health decisions. These developments necessitated the laboratory physician to become familiar with the developments in medicine, technology and quality control procedures.

The beginning of this century has seen yet another concept from industry get into the laboratory, i.e., laboratory accreditation. This is defined by the joint technical committee of the International Organization for Standardization (ISO) and the International Electrotechnical Commission (IEC) as formal recognition that the testing laboratory is competent to carry out specific tests or specific types of tests. The primary requirements are a management system and manual in the laboratory. International Federation of Clinical Chemistry (IFCC) recognizes the requirements for quality and competence in ISO 15189:2007 for medical laboratories as the basis for getting accreditation.[16] There are different accreditation bodies in different countries. National Accreditation Board for Testing and Calibration Laboratories (NABL) looks after this in India.

Thus the clinical chemistry laboratory, started with a couple of chemistry experiments three centuries ago, has now grown into a full-fledged independent discipline of modern medicine playing a crucial and decisive role in patient care. The laboratory physician leading the clinical chemistry laboratory

is now required to be a specialist with equal knowledge and expertise in medicine, technology and quality management, evolution from a profession without a face to one with a multifaceted expert. However, majority of these developments did not percolate into undergraduate medical training in India. As a result, many clinicians are not familiar with the correct and current concepts of role of clinical laboratory in patient care and the importance of preanalytical errors. Hence, incorporation of basic concepts about functioning of clinical chemistry laboratory into undergraduate medical curriculum will remove the conceptual barriers in the minds of clinicians that exist now and help to transmit the benefits of all the advances that have happened in the laboratory to the patients. This needs immediate attention by the authorities regulating medical education.

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