The Evolution of Clinical Chemistry as Reflected in Textbooks Published in the United States

On the occasion of the 50th anniversary of the American Association for Clinical Chemistry, Dr. Thomas Annesley, Book Reviews Editor of Clinical Chemistry, felt that a review of clinical chemistry textbooks covering the past three decades would enable the younger generation of clinical chemists to appreciate the profound changes that have taken place in the clinical chemistry laboratory. He also felt that having worked in clinical chemistry laboratories for 40 years, which is tantamount to “being present at the creation”, qualified me for this assignment. While preparing this review, I recognized an interdependence among the practice of clinical chemistry and the contents of textbooks and Clinical Chemistry. As to what comes first, in my slightly biased opinion the Journal has set, and is setting, the pace for textbooks and laboratory practice. I focus on the book of N.W. Tietz, because comparison of the four editions depicts the dramatic changes that occurred in the clinical chemistry laboratory from 1970 to 1993, and on the 1964 book of R.J. Henry, because it was the most comprehensive and informative book of clinical chemistry of its time. Although there are several other important clinical chemistry textbooks, as depicted in Table 1, they were not reviewed because the changes between the first and last edition do not depict the metamorphosis of the clinical chemistry laboratory from the mid-1960s to the mid-1990s.

R.J. Henry published the first comprehensive textbook of clinical chemistry in 1964; it dealt almost exclusively with the analytical aspects of the new, evolving medical laboratory discipline. Its 29 chapters covered principles of spectrophotometry, flame photometry, gasometric techniques, electrophoresis, accuracy, precision, control charts, significant figures (still abused by most authors and journals), and normal values. Analytical methods were described for various proteins and amino acid metabolites found in urine in various inborn errors of metabolism, non-protein nitrogenous products (including blood non-protein nitrogen), inorganic ions, blood pH and gases, electrolytes, enzymes, carbohydrates and metabolites, vitamins, hemoglobins and derivatives, porphyrins and precursors, kidney function tests, and lipids. Included in the liver function tests were the cephalin-cholesterol flocculation test, thymol and zinc sulfate turbidity, the icterus index, and the determination of fecal bilirubin. Thyroxine, measured as protein-bound iodine, was the sole hormone for which a method was described.

Some of the most valuable aspects of this book were the “notes”, which followed almost every procedure. These notes, based on studies done by the author and his associates in Bio-Science Laboratories, provided invaluable information on linearity (Beer’s law), sample stability, standards, interferences, reagent and sample blanks, and accuracy and precision. Also very valuable was the discussion on alternative methods, including their evolution through the years, and the justification for selecting the method(s) presented.

The detailed chapter on quality control reflected Dr. Henry’s interest in monitoring and documenting the reliability of laboratory results. Soon after the publications of Archibald (Anal Chem 1950;22:639) and of Levey and Jennings (Am J Clin Pathol 1950;20:1059), Dr. Henry submitted a paper to several journals on the running of standards and the use of the control chart in clinical chemistry; this was at a time when very few clinical chemists had an appreciation of the importance of quality control. The paper was rejected by several journals; fortunately (for clinical chemistry) it was eventually published (J Clin Pathol 1952;5:305–11).

The second, and last, edition of this book (longer than the first edition by 500 pages) appeared in 1974. It maintained the general approach of the first edition, that is, it dealt only with the analytical aspects of the tests. Among the new topics were electrometric techniques (ion selective electrodes), chromatography (column, gas, and thin layer), immunochemical and in vitro radioisotopic techniques, automation and on-line computers for continuous flow analyzers, and lipoproteins. Deleted in the new edition (which was intended as a supplement to the first) were gasometric techniques (including the time-honored Van Slyke apparatus), plasma and blood volumes, and thyroxine. Automated procedures, exclusively adapted to the Technicon AutoAnalyzer, were added for many analytes. Atomic absorption spectrophotometry was introduced for measurement of trace metals; procedures for immunoglobulins, lipoproteins, 10 new enzymes, vitamin B₁₂, and folate were added; and the chapter on amino acids and metabolites was substantially expanded.

The first edition (1970) of the Tietz book was similar to Henry’s book concerning analytical methods. It was, although less detailed, a broader book because it included chapters on endocrinology (steroid and protein hormones), pancreatic function tests, toxicology, and analysis of amniotic fluid. Furthermore, included in every test was a discussion of the clinical significance and interpretation.

The second edition (1976) reflected the changes in the field. A new chapter on automation covered 13 automated analytical systems, of which only the DuPont ACA is still in use. Other additions were principles and measurement of radioactivity, laboratory computers, immunoglobulins, immunochemical principles and techniques and immuno-
assays for a variety of plasma proteins, hemoglobin electrophoresis, lipoproteins, isoenzymes of lactate dehydrogenase (LDH), vitamins, and an expanded section on thyroid function tests. Gravimetric and volumetric analyses and microtechniques were dropped, presumably as no longer useful. I will note here that the last two editions of Tietz’s *Fundamentals of Clinical Chemistry* are not reviewed because they are abbreviated versions of the *Tietz Textbook of Clinical Chemistry*.

The next Tietz effort appeared in 1986 and was titled *Textbook of Clinical Chemistry* (first edition). There were substantive changes in the content of the book. Clinical aspects of testing, diagnostic utility, interpretation of results, and functional evaluation of organs and tissues were emphasized. The size of the book increased 50% over the previous book; chapters in endocrinology, renal, liver, gastric, pancreatic, and intestinal function were updated, emphasizing detection of abnormalities and diagnosis of disease. Detailed methods and step-by-step procedures were, in many cases, replaced by principles of measurements and references to complete reagent kits available from commercial sources. Added to the chapter on instrumentation were HPLC, mass spectrometry, and guidelines for selection of instrumentation.

Responding (I assume) to laboratory concerns over increased governmental and nongovernmental regulators, new chapters were added on establishment and use of reference values, analytical goals and clinical relevance of laboratory procedures, evaluation of methods, quality assurance, specimen collection and processing, and sources of biological variation; the chapter on statistics was lengthened extensively. The first 500 pages of the book dealt not with the measurement of analytes, but with what is called today “good laboratory practices”.

More tests for individual proteins appeared. Creatine kinase (CK)-2 (CK-MB), LDH-1, and the ratio LDH-1/LDH-2 appeared in the enzyme chapter for the diagnosis of acute myocardial infarction. Other new chapters included nutrition, vitamins and trace elements, calcium and phosphate metabolism, biochemical aspects of hematology, therapeutic drug monitoring, and biochemical aspects of pregnancy. Endocrinology was expanded, covering new assays for a variety of hormones for which analytical methods became available. Glycohemoglobin was added as a monitor of diabetic control.

The second edition of the book (1993) was a pleasant surprise to older clinical chemists (the average age of US clinical chemists is increasing constantly). A larger font coupled with darker print on a white background made this edition more readable than all the previous ones.

Dropped from the automation chapter were old laboratory workhorses such as the Technicon SMA and the Beckman ASTRA. Added were examples of automated instruments for “off-site” (point-of-care) laboratories and of immunoassay analyzers. The statistical procedures chapter was renamed “chemometrics” (Isn’t a camel always a camel?), and quality assurance became “quality management”. Nucleic acid biochemistry and diagnostic applications, tumor markers, and mineral and bone metabolism were some of the most important additions. In endocrinology the time-honored procedures for 17-ketosteroids and 17-ketogenic steroids were deleted. Nonisotopic assays for hormones are starting to replace the radioimmunoassays. The transition from “procedural” to clinical (interpretation of results, pathophysiology, and diagnosis) continued in this edition. The number of procedures described in detail is small, reflecting changes in the laboratory; if something is not automated and requires the use of hands, it is simply not done (at least in most laboratories). The scope of the last two editions has changed from a book of clinical chemistry to that of clinical laboratory science.

The third edition of *Tietz Textbook* is just now being published. Some of the new chapters—transplantation, cytokines, and cardiac function—listed in the Table of Contents confirm the continuous transition from clinical chemistry to clinical laboratory science.

In the 1950s clinical (actually analytical) chemists were busy developing analytical methods for blood and other body fluid constituents. Adapting most manual routine procedures to the single or dual channel AutoAnalyzer (which in 1984 found its well-deserved place in the Smithsonian) was the hallmark of the 1960s. In the 1970s we were preoccupied with the “numbers”, that is, the number of results produced per year by the clinical chemistry laboratory; with the help of the SMA12/60 and the SMAC it was not too difficult for most laboratories to hit one million. Tightening the belt became necessary in the 1980s, when the US government invented DRGs (Diagnosis Related Groups). “Managing the laboratory” became the buzzword (later it was expanded to “data management”, “quality assurance management”, “total quality management”, and other related terms), and a large number of us rushed to register for management...
courses. I believe that the transformation, the change from the analytical chemist/laboratory manager to a real clinical laboratory scientist, that is taking place in the 1990s is anything but transient because becoming an indispensable member of the healthcare team, whether in a hospital, commercial laboratory, point-of-care location, or the diagnostic manufacturing industry, will be essential for the survival of the species. While maintaining our analytical skills and absorbing and applying new diagnostic modalities, we must move closer to the clinician and patient.

In the early 1960s satellites were circling our planet, President Kennedy had committed the US to put a man on the moon by the end of the decade, and graduate students in the Department of Biochemistry of the University of Tennessee were making predictions on the future of analysis (mostly manual at that time) of body fluids. Over a pitcher of cold beer on a hot and humid summer day, one of us dared to prophesy that someday there would be instruments in which you could put serum or even whole blood at one end and get the results at the other; “printed, too”, concluded the optimist of the group. In the same vein, today’s optimist could predict that in the not-too-distant future a complete gene analysis would be performed on 1 nL of blood in 10 min or less.

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