THE EVOLUTION OF CHEMISTRY
FROM TASTE TESTING TO TEST TUBES TO AUTOMATION TO QC, QA, LIS
AND BEYOND

JOANNA C. BAKER-HORNICK, MSPH, MLS(ASCP) CM, SC (ASCP) CM
LABORATORY INFORMATION OFFICER
MONCRIEF ARMY COMMUNITY HOSPITAL, FT. JACKSON, SC

FREDERIC R. HORNICK, MS, MLS(ASCP) CM
QUALITY ASSURANCE TECHNOLOGIST
MONCRIEF ARMY COMMUNITY HOSPITAL, FT. JACKSON, SC

LET US TAKE A MOMENT AND THINK

Where did these thought processes originate?

WHAT IS THE BASIS OF THE THOUGHT PROCESS?
LOGIC?
HORSE SENSE?

Valid reasoning has been employed in all periods of human history. However, logic studies the principles of valid reasoning, inference and demonstration. It is probable that the idea of demonstrating a conclusion first arose in connection with geometry, which originally meant the same as "land measurement".

In particular, the ancient Egyptians had discovered empirical truths of geometry, such as the formula for the volume of a truncated pyramid.

WHAT'S THE DEFINITION OF LOGIC?

GREEK LOGIC

Plato's logic

None of the surviving works of the great fourth-century philosopher Plato (428–347) include any formal logic, but they include important contributions to the field of philosophical logic. Plato raises three questions:

What is it that can properly be called true or false?

What is the nature of the connection between the assumptions of a valid argument and its conclusion?

What is the nature of definition?

Aristotle's logic

The logic of Aristotle, and particularly his theory of the syllogism, has had an enormous influence in Western thought. His logical works, called the Organon, are the earliest formal study of logic that have come down to modern times. Though it is difficult to determine the dates, the probable order of writing of Aristotle's logical works is:

The Categories, a study of the ten kinds of primitive terms.

The Prior Analytics, a formal analysis of valid "syllogism".

The Posterior Analytics, a study of scientific demonstration.
Traditional logic or the Textbook Tradition:

Traditional Logic [1] generally means the textbook tradition that begins with Antoine Arnauld and Pierre Nicole’s Logic, or the Art of Thinking, better known as the Port-Royal Logic. Published in 1662, it was the most influential work on logic in England until the nineteenth century. The book presents a loosely Cartesian doctrine (that the proposition is a combining of ideas rather than terms, for example) within a framework that is broadly derived from Aristotelian and medieval term logic. Between 1664 and 1700 there were eight editions, and the book had considerable influence after that. The account of propositions that Locke gives in the Essay is essentially that of Port-Royal: “Verbal propositions, which are words, [are] the signs of our ideas, put together or separated in affirmative or negative sentences. So that proposition consists in the putting together or separating these signs, according as the things which they stand for agree or disagree.” (Locke, An Essay Concerning Human Understanding, IV, O, 6)

Rise of modern logic

The period between the fourteenth century and the beginning of the nineteenth century had been largely one of decline and neglect, and is generally regarded as barren by historians of logic. The revival of logic occurred in the mid-nineteenth century, at the beginning of a revolutionary period where the subject developed into a rigorous and formalistic discipline whose exemplar was the exact method of proof used in mathematics. The development of the modern so-called “symbolic” or “mathematical” logic during this period is the most significant in the 2,000-year history of logic, and is arguably one of the most important and remarkable events in human intellectual history.

Alchemy

predecessor of chemistry: an early, unscientific form of chemistry that sought to change base metals into gold and discover a life-prolonging elixir, a universal cure for disease, and a universal solvent alkahest

transforming or enchanting power: a power supposedly like alchemy, especially of enchantment or transformation

Alchemy is an early precursor, practice combining elements of chemistry, physics, astronomy, art, medicine, alchemy, metallurgy, mysticism, and religion.

There were three main goals many alchemists sought for:

1. The most renowned goal of alchemy is the transmutation of any metal into either silver or gold.

2. Also they tried to create a universal panacea, a remedy that would cure all diseases and prolong life indefinitely. The philosopher’s stone was the key in these goals. This mythical substance, which could just as well be powder or liquid as a stone, had the ability to do both.

3. The third goal was creating human life. Alchemy can be regarded as the precursor of the modern science of chemistry prior to the formulation of the scientific method.

History of the modern day test strip

In many cultures urine was once regarded as a mystical fluid, and in some cultures it is still regarded as such to this day. Its uses have included wound healing, stimulation of the body’s defences, and examinations for diagnosing the presence of diseases.

It was only towards the end of the 18th century that doctors interested in chemistry turned their attention to the scientific basis of urinalysis and to its use in practical medicine.

1797 - Carl Friedrich Gänsslen (1772–1850) expressed a wish for an easy way of testing urine for disease at the patient’s bedside.

1797 - William Cumberland Cruikshank (1745–1800) described for the first time the property of coagulation on heating, exhibited by many urines.

1827 - English physician Richard Bright describes the clinical symptom of nephritis in “Reports of Medical Cases.”
The arrival of chemical urine diagnostics aimed at the detection of pathological urine constituents. 1850 - Parisian chemist Jules Maumené (1818 – 1898) develops the first “test strips” when he impregnated a strip of merino wool with “tin protochloride” (stannous chloride). On application of a drop of urine and heating over a candle the strip immediately turned black if the urine contained sugar.

1883 - English physiologist George Oliver (1841 – 1915) markets his “Urinary Test Papers”. approx. 1900 - Reagent papers become commercially obtainable from the chemical company of Helfenberg AG.

1904 - A test for the presence of blood by a wet chemical method using benzidine became known.

approx. 1920 - Viennese chemist Fritz Feigl (1891 – 1971) publishes his technique of “spot analysis”.

1930s - Urine diagnostics makes major progress as reliability improves and test performance becomes progressively easier.

1950s - Urine test strips in the sense used today were first made on industrial scale and offered commercially.

1964 - The company Boehringer Mannheim, today a top leader on the world market under the name of Roche, launched its first Combur test strips. Even though the test strips have changed their external appearance little since the 1960s, they now contain a number of revolutionary innovations. New impregnation techniques, more stable color indicators, and the steady improvement in color gradation have all contributed to the fact that the use of urine test strips has now become established in clinical and general practice as a reliable diagnostic instrument. The parameter menu offered has steadily grown longer in the intervening decades.

A very interesting quote from the article: “Predicting the future is tricky business. In 1967, a US Senate Subcommittee reportedly heard testimony forecasting that, by 1985, Americans would work 22 hours each week, 27 weeks a year, or that they would retire at age 38 (14). If only that had come to pass! On the other hand, some true visionaries got it just about right. "I have not been reading science fiction," wrote David Seligson in 1962, on the future of clinical chemistry in these pages (15). He continues:

“The time will come when blood is sent from a hospital to a large receiving center—that is, a laboratory which does large numbers of special analyses automatically and continually, day and night, weekends and holidays... special instruments can sort, analyze, punch out answers, and return reports. Even the latter, the report, will probably disappear in our new way of life because we shall have instruments which identify samples, analyze them, and electronically enter the result into a computer. The latter could be as much as 100 miles away.... Our laboratory instruments will feed the data into the computer and the computer will convert it to a final report and store the information.”

“A physician who wishes to know the electrolyte values for his patient will not call the laboratory, he will tell the computer what he wants and the computer will direct a typewriter which will give him the information at the rate of 1000 lines per minute. The same information can be requested 10 times in one hour without irritating the laboratory secretaries or anyone else. Furthermore, the laboratory will also have a computer outlet so that serial data on any patient can be observed for fluctuations. The clinical chemist will be able to get any information he needs in seconds without going to his own files or to the record room. There will be no useless files or the wasted effort of unnecessary searches. The computer will not lose data; the intern will not carry the precious report in his pocket where no one can find it. The computer will serve the laboratory in other ways too. It will provide automatic programs and will turn on and off the machines of the laboratory. It will digitalize data and provide direct readout of final answers. It will provide a new dimension for the clinical chemist.”
“As predicted by Seligson over 40 years ago (15), computers have had a powerful role in clinical chemistry, as in most other disciplines. As we look back on 50 years of articles, the advances in laboratory medicine in many ways parallel the spectacular achievements in the semiconductor and computer fields: ever faster/better/cheaper. In the last decade, computers and the Internet have played a dominant role in the dissemination of scientific information.”

**THE BASIS SETTING UP AND VALIDATING THE LIS IS THE APPLICATION OF LOGICAL CLINICAL PRINCIPLES**

Through knowledge of Principles behind all laboratory tests: Blood Bank, Microbiology, Chemistry, Special Chemistry, Urinalysis, hematology, coagulation, cytology, histology, genetics, molecular, special send out tests for reference labs.

**EVERY CHANGE MADE IN THE LIS MUST BE VALIDATED AND DOCUMENTED!**

- Validation of any changes in the LIS includes but is not limited to:
  - Units of measure (e.g. mg/dL, g/dL, etc.)
  - Boolean Equations
  - Algorithms
  - Panels - tests within panels
  - Status/priority (e.g. Routine, STAT, ASAP)
  - Testing Laboratory
  - Reference Ranges
  - Interpretations

**LIS LABORATORY INFORMATION SYSTEMS**

- The LIS controls the most important product of the Medical Laboratory: INFORMATION

- INFORMATION must be accurate and timely to be utilized in the patient’s diagnosis and/or treatment.

**Prouet’s An Inquiry Into the Nature and Treatment of Diabetes, Calculus, and Other Afections of The Urinary Organs (1825)** included a list of Tests, Apparatus, &c. required in making Experiments on the Urine.

- “These with one or two small test tubes, and small stoppered phials, containing solutions of pure ammonia, potash, and nitric acid, can be readily packed into a small portable case, or pocket book, and will be sufficient, by the aid of a common taper or candle, to perform all the experiments on the urine, and urinary productions, that are commonly necessary in a practical point of view.”

- Barely 1 year later, Richard Bright’s studies of renal disease would add a spoon to this portable laboratory, for revealing the presence of albumin in heated urine. Citing the lack of progress in animal

Although forms of Laboratory testing had been occurring since the early 1800s the impetus for clinical testing accuracy was not formally questioned by an organized group until 1945

- Physicians would draw blood and divide the sample and sending it to two different labs and would obtain divergent results.
A group of Medical Directors in Philadelphia petitioned the Philadelphia Medical Society to establish a special Clinical Pathology Section of that Society.

The University of Pennsylvania had adequate ampuling facilities and served as the central agency which prepared and distributed serum specimens to members.

The petition was granted, and 10 to 15 directors of laboratories in the Philadelphia area met regularly each month to review various phases of our specialty.

The Committee on Laboratories of the Pennsylvania Medical Society requested checks upon the accuracy of the more common chemical measurements made in hospital laboratories throughout the state.

At one of the early meetings, in 1945, it was decided to distribute unevaluated serum specimens among the members and to report the results of analyses at the following scheduled meeting.

This was undertaken by distributing, in the spring of 1946, carefully prepared solutions to the directors of hospital laboratories in Pennsylvania with the request that the results be returned anonymously.

The University of Pennsylvania had adequate ampuling facilities and served as the central agency which prepared and distributed serum specimens to members.

The results revealed surprising inadequacies.

The Committee on Laboratories of the Pennsylvania Medical Society requested checks upon the accuracy of the more common chemical measurements made in hospital laboratories throughout the state.

The findings of this original survey were published in 1947 by Belk and Sunderman.

For Example:

Two hemoglobin solutions were included in this survey.

Of 92 participating laboratories, only 14 reported hemoglobin concentrations within the accepted range for the sample containing 9.8 ± 0.3 g/dl.

The reported range of values was 5 to 15.5 g/dl.

Only 12 laboratories reported hemoglobin concentrations that were within the accepted range for the sample containing 15.1 ± 0.5 g/dl.

The reported range of values was 12.5 to 18 g/dl.

The College of American Pathologists (CAP) was founded in 1946 at the same time that the Pennsylvania survey was being undertaken.

One of the first projects initiated by the Founding Board of Governors of the College were national proficiency surveys similar to the ones undertaken in Pennsylvania.

Results for the first two CAP surveys in 1947 and 1948 were sent to CAP but were never released.

The results were exceptionally disquieting in light of their unfavorable findings.

As a result of these surveys, workers in clinical laboratories became determined to improve their laboratory performance and sought ways and means for corrective modifications.

It became unthinkable that faulty laboratory practices should continue. What had not been apparent, except to those possessing long and intimate laboratory experience, was that the validity of laboratory data can seldom be determined by mere inspection, and that unsatisfactory laboratory work is prone to escape detection.
Fostered by the Communicable Disease Center (CDC; later changed to the Centers for Disease Control), the Clinical Laboratory Improvement Act of 1967 was passed.

In the Senate subcommittee hearings before passage of the 1967 Act, the statements of the Director of the CDC presented that "erroneous results are obtained in more than 25 percent of all tests analyzed."

The results of the Belk and Sunderman 7) reported 22 years previously, were cited.

In 1975, an amendment to expand of CLIA ’67 referred the same data without acknowledging the age of the data.

JAMES O. WESTGARD. PH.D., FACB

Dr. Westgard's early interest was in the development of method evaluation protocols and he served as the first chairman of the Evaluation Protocols Area Committee in CLSI (then known as NCCLS).

He published extensively in this area during the 1970s and 1980s, including a monograph on Method Evaluation published by ASCLS.

His interest in quality control began in 1976-77 when he was on sabbatical leave at Uppsala University in Sweden where he worked with Professor Carl Henrik deVerdier and Drs Torgny Groth and Torsten Aronsson.

This work led to the multi-rule control procedure, internationally known as “Westgard Rules.”

Those of us involved in clinical laboratory medicine must comply with the Clinical Improvement Act (CLIA) of 1988. There are two lessons I’ve learned from the study of history. First, history repeats itself and second, those who do not learn from history are doomed to repeat it. In many ways the CLIA legislation closely parallels the course previously transversed by GLP. The food and drug industry, because of mistakes, required federal regulations to ensure safe consumer products. Our industry, because of such incidents as Pap smear mills producing erroneous results, needed strict federal intervention to ensure quality and accurate patient specimen results.

CLIA began in the late 1960’s when problems arose in the cytology laboratories that read PAP smears. The personnel in these laboratories were overworked and had a very high error rate.

Many women suffered or died because the cytologists had missed the early stages of cancer on the PAP smears. In 1967, the Clinical Laboratory Improvement Amendment was passed and the first laboratory regulations were born. In 1988, a second amendment was passed but did not go into effect until 1992 when the new regulations were approved.
Although no one seems to know who Murphy was but Murphy’s Laws are applicable to work in clinical laboratories.

Murphy’s Laws read
  + (1) Nothing is as easy as it looks.
  + (2) Everything takes longer than you think.
  + (3) If anything can go wrong, it will.

THE BEYOND............

Molecular Testing will become “ROUTINE”
Genetic Testing at birth will become “ROUTINE”
Anatomical Pathology and Radiology will combine.
Human visual reading of tissue slides will be obsolete.
Computerized reading of probes within the cells will replace the Pathologist at the Microscope!

EDUCATION IS THE KEY—WHERE CAN I LEARN MORE?

There are Courses and CEs available on the internet.
Free CEs are offered by various companies (e.g. Quest, CAP with surveys, Siemens, etc.)

AACC offers 16 hour Certificate Programs on line in 8 disciplines at a reasonable cost.

AACC CERTIFICATE PROGRAMS

Basic Principles and Architecture of Laboratory Information Systems Certificate Program
Sponsored by AACC and the Laboratory Information Systems (LIS) Division.
This certificate program is aimed at the basic levels of laboratory personnel in mind. It is a certificate program to prepare you for taking these essential LIS decisions.

Clinical Laboratory Leadership and Management Certificate Program
Sponsored by AACC and the Management Sciences and Patient Safety (MSP) Division.
This certificate program is to prepare the next generation clinical laboratory leaders for the leadership role they will be assuming.

Fundamentals of Molecular Pathology Certificate Program
Sponsored by AACC and the Molecular Pathology Division.
This certificate program presents the essentials of molecular pathology.

Laboratory Support for Diabetes Testing Certificate Program
Sponsored by AACC and the National Academy of Clinical Biochemistry.
This certificate program provides a comprehensive review of current theory and practices in the laboratory’s support for diabetes testing.

Statistical Methods for Clinical Laboratorians Certificate Program
Sponsored by AACC and the Management Sciences and Patient Safety Division.
This certificate program teaches you how to accurately collect, report, and interpret laboratory statistics which are at the foundation of every scientific study.

Molecular Testing in Clinical Laboratories Certificate Program
Sponsored by AACC.
This certificate program is to introduce the laboratory professionals to the basics of Mass Spectrometry and the potential of using tandem mass spectrometry for clinical testing.

Point-of-Care Specialist Certificate Program
Sponsored by AACC and the Critical and Point of Care Testing Division.
This certificate program will prepare point-of-care specialists for this critical role and to promote standardized best practices in near patient testing.

QUESTIONS?

Contact information:
joanna.baker@amedd.army.mil (work)
frhjch123@aol.com (home)
frederic.hornick@amedd.army.mil (work)
aknosc2@aol.com (home)
Mail: Moncrief Army Community Hospital
Department of Pathology
4500 Stuart Street, box 484
Fort Jackson, South Carolina 29207