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THE GIFTS OF CHEMISTRY TO MODERN MEDICINE

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ABSTRACT

Human body is a Physico-chemical consortium. Human biochemistry or clinical chemistry reflects changes inside the body in health and disease. Chemistry offers a very useful tool in diagnosis of diseases and in their follow-up while under treatment. Advances in the field of medicine have been always on three lines: better chemicals, better instruments and better quantification.

The gifts of chemistry to modern medicine have been moulded in the crucible of today's chemical pathology. Its evolution from the pre-technological times to the technological age is exciting. It is a relatively new science. The advance of chemical pathology has followed the development of medicine, of biochemical knowledge, of advances in molecular biology, and of chemical analytical techniques. It is the study of the changes that occur in disease in the chemical constitution and biochemical mechanisms of the body.

The marriage between chemistry and physio-pathological activity in human health and disease is a natural phenomenon. The thought of explaining all biological activity on chemical basis - iatro chemistry (Greek: "iatros", physician) as initiated by Paracelsus (1493-1541) - Aureolus Theophrastus Bombastus von Hohenheim, Jean Bapiste Van Helmont (1577-1644), Franz De Le Boe (1614-1672) - Franciscus Sylvius and others is comparable to that of explaining all such activity on mechanical iatrophysical basis as postulated by Galileo Galilie (1564-1642), Sanctorius Santorio Santorio (1561-1636), William Harvey (1578-1657), Rene Descartes (1596-1650) and others. Iatrochemistry is the study of chemistry in relation to physiological and pathological processes, and treatment of disease by chemical substance as practiced by a school of medical thought in the 17th century. Iatrophysics is physics (its laws) as applied to medicine during the same period. Needless to say the gifts of physics to modern medicine in various aspects of diagnosis and treatment of diseases are enormous and spectacular in our time (Majumdar, 2004).

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The evolution of chemical pathology/clinical chemistry needs to be studied on the kaleidoscope of some major technological advances in more recent years in the context of historical observations from pre-technological era (Donaldson, 1999).

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As a fundamental science, it applies physiology and biochemistry to the elucidation of the nature and cause of disease. As an applied science, it seeks by analysis of body fluids and tissues to aid the doctor/clinician in diagnosis and treatment – here comes chemistry as the saviour.

By the middle of the 19th century physicians could analyse gastric juice for hydrochloric acid, urine for sugar (glucose) by Fehling's test evolved by the German chemist – Herman Von Fehling (1812-1885), for protein by boiling with acidification, and for bile by nitric acid. The classical "Lectures on Chemical Pathology" of 1847 by the British physician Henry Bence Jones (1814-1873) were based on quantitative analysis of urine. However, there were no important developments in the 19th century in general application of chemical knowledge to medicine by performance of biochemical analysis. But in the first two decades of the 20th century important advances in methodology were made, notable pioneers being Bernhard L. H. Bang (1848-1932), Danish veterinarian and physician, Otto Knut Olaf Folin (1867-1934) US biochemist and D. D. Van Slyke (1883-1971), US physician and chemist. By the early 1920's vene puncture had become routine practice, visual colorimeters were widely available, and analytical methods requiring only 1 ml of blood were generally adopted. This was the first revolution.

ANTIQUITY: A PEEP INTO THE PAST

The first proven reference to what could be termed the nidus of chemical pathology emanates from the ancient Indian Ayurvedic Medicine. Here there is mention of ants and other insects accumulating around the sites where certain people urinated in the fields; it was, we now realise, glucose in the urine of diabetics that attracted these creatures (Bolodeoku and Donaldson 1996). The second anecdote hails from the account of the Peloponnesian War (431-404 B.C.) by Thucydides (460-400 BC); he noted the very high death rate during the Plague of Athens, observing that those who had had the plague themselves and who had recovered from it (Thucydides, himself suffered this illness around 430-427 BC – and survived it) never had it again – or, if they did, had it only in mild form (Thucydides, 1954 translation). This was, surely, one of the first pertinent observations, nowadays so obviously referable to the basic understanding of 20^{th} century immunology. The third quote is from the voyage of Vasco da Gama (1469-1524 A.D.) with his 140 Portuguese sailors, commencing from Lisbon in July 1497; it was seven months later that many of the men fell ill with what, in retrospect, was clearly scurvy. The point of note in this instance is that at the end of that voyage there was presented an opportunity to purchase oranges from Moorish traders (Moorish rule in Spain: 711-1492 A.D.) who approached the boats; there was also the subsequent comment in the historical records, just 6 days later, stating that, "all our sick recovered their health for the air of this place is very good". It was, of course, the ascorbic acid (vitamin C) content of the oranges that was responsible for the rapid restoration of health (Carpenter, 1988).

EVOLUTION OF CHEMICAL PATHOLOGY

It was Thomas Willis who, in 1674, succeeded in tasting the sweetness of urine from a patient with diabetes – but this observation differed from the previous anecdotes in that it involved the use of a silver spoon as receptacle for the urine. The spoon could, therefore, be construed as the simplest possible piece of technology being applied in an early scientific test (Bolodeoku and Donaldson, 1996). Nevertheless, the story advances yet further when one brings Mathew Dobson of Liverpool into the discussion; it was he who, a century later, established that the presence of "sugar" was responsible for sweetness of the urine. However, he relied upon rather more sophisticated laboratory technology in his scientific confirmation than did Thomas Willis in his observations of 1674.

Over the years there has been increasing complexity and ingenuity in both thought and development of scientific aids and apparatus – in the continuous quest for establishing scientific truth. Urine was, in fact, one of the earliest biological fluids to be analysed– largely because it was so readily and freely available (Bolodeoku and Donaldson, 1996); blood testing came later (Bolodeoku, Olukoga and Donaldson, 1998). In the early years progress was very slow. Large volumes of blood were required for chemical tests in those early days; moreover, the duration of laboratory procedures was long and only one or two tests could be dealt with at any one time. New techniques developed in response to the challenges occurring. Smaller volumes of blood came to be needed as technology advanced, the spectrum of tests became wider and tests themselves became shorter in duration. Alongside all of this greater numbers of tests could now be accommodated and it became possible, therefore, to increase the frequency of testing on any one patient. From this increased frequency of sample testing emerged evidence of biochemical and biological variations – and then followed the exciting possibility of opening up a way of identifying the physiological responses to stimuli of various types. Later still, came the confirmation of circadian, menstrual, annual and other biological rhythms.

From then onwards unfolded a sequence of advances – at first involving early instrumentation and later concerning development of the early laboratory; there was invention of the hypodermic syringe, spectroanalysis, colorimetry, the photoelectric cell, the centrifuge, the Bunsen burner, emission spectroscopy, electrophoresis, blood gas analysis, chromatography, radioisotopes and detectors, mass spectrometry, automation and computerisation – together with, in very recent years, telephonic communication, photocopiers, fax machines, e-mail communication and access to the internet. All these inventions – and the very many others which could have been iterated, are fundamental to the modern day chemical pathology/biochemistry laboratory. From early times laboratory testing has involved the application of many types of analytical procedures – including gravimetric, volumetric, titrimetric, gasometric, manometric, chromatographic, colorimetric fluorimetric, trubidimetric, nephelometric, osmometric and radioimetric, to name but a few. Moreover, in the growing organisation that has occurred additional issues must now be heeded, e.g. quality control, health and safety, accreditation, etc.

FOUR FUNDAMENTAL HISTORICAL PILLARS OF CHEMICAL PATHOLOGY

In order to present a more graphic account of applied technological development a selection of four inventions, across the board, has been made; these are illustrative of progress over the centuries. The names of their inventors – or those responsible for publicising their use, will be briefly quoted (Olukoga, Bolodeoku and Donaldson, 1997).

The hypodermic syringe: The First Pillar

Although not actually a laboratory instrument, the syringe is of fundamental importance in providing a link between the patient and his/her quantitative blood results; it provides the means of extracting blood in a rapid and convenient manner. Names linked in the development include Francis Rynd (1803-1861) who introduced the hypodermic syringe in 1845, Alexander Wood (1817-1884) who was responsible for its modification in 1851 and Charles Gabriel Pravaz (1791-1853) who made further changes in the form of adding a plunger to the syringe; the latter adaptation made it eminently applicable for administering drugs by the intravenous route.

The Bunsen burner

The second technological illustration stems from Robert Wilheim Bunsen (1811-1899) of Göttingen, Germany, who was a scientific inventor and one of the great experimental inorganic chemists of the 19th century; he was responsible for a multitude of widely ranging major discoveries. Contrary to popular opinion he did not actually invent the Bunsen burner – but he introduced and first used it in 1855 – adapting it from a design by Michael Faraday (1791-1867), the British chemist and physicist; it does seem, however, that Peter Desdega also had involvement in its design. The Bunsen burner was for many years (and currently continues to have some application in microbiology laboratories) a basic piece of apparatus in many laboratory settings world-wide; it must be mentioned, however, that it was the forerunner of both the gas-stove burner and the gas furnace. Its ability to combine air and flammable gas in a controlled manner helps to create a very hot flame – up to a temperature of 1500º C. Although modern methodological procedures avoid the need for presence of a naked flame (thereby significantly limiting the danger of fire and explosion), in some less developed parts of the world Bunsen burners are still frequently used.

Spectroscopy

The third topic in this section is that of spectroscopy. Among the many scientific inventions credited to Robert Wilhelm Bunsen (1811-1899) of Göttingen in Germany, was that of spectrum analysis and chemical spectroscopy – he was a pioneer of these tools; it was his work with Gustav Kirchhoff (1824-1887), in or around 1859, that led to the observation that each element emits light of characteristic wavelength. Each chemical element possesses, therefore, its own unique spectrum. Indeed, Kirchhoff attributed the dark Fraunhofer lines found in the solar spectrum in 1859 to absorption, by the elements in the cooler atmosphere of the surface of the sun, of the continuous spectrum emitted from the hotter interior. Applications of spectrum analysis extend both far and wide to include, in astronomy, those of the solar and stellar systems; it is in this way that the identification of certain elements in distant stars can be confirmed. The work of both Bunsen and Kirchhoff established the immense value and importance of spectroscopy in chemical analysis. More down to earth, however, but also linked with this technique, were Bunsen's and Kirchhoff's discovery of caesium and rubidium in 1861. Emanating from this very basic investigative technique has evolved many sophisticated analytical procedures including spectrophotometry in all of its many current forms – ranging from infra-red, visible, and ultraviolet spectrophotometry to photochemistry magnetic resonance spectroscopy (MRS), which is a powerful technique for analysing both the quantity and structure of chemical compounds in complex mixtures in solution, is currently being developed – although it has not, as yet, achieved wide application in chemical pathology/clinical chemistry.

Electrophoresis

The fourth illustration chosen is that the electrophoresis; the moving boundary apparatus was devised by Arne Wilhelm Tiselius (1902-1971) in 1937. Application to clinical practice permitted great advancement in the knowledge of protein chemistry; subsequent advances opened the way of electrophoresis of proteins on starch gel, filter paper, cellulose acetate, agar gel and acrylamide gel etc. It is the presence of positive and negative charges, on the amino acids within the protein molecule as a whole, that determines the rate of migration of proteins (within serum or other biological materials) when exposed to a potential gradient along the strip – when a voltage is applied across the electrodes. The combination of applying an electrical gradient, together with various subsequent immunological techniques, has made possible enormous advances in the knowledge of proteins. Protein electrophoresis now comprises a very fundamental part of daily laboratory life; in cases where there is clinical suspicion of moncional and polyclonal gammopathies (e.g. including myelomatosis) and of globulin deficiency states these procedures are nowadays so vitally fundamental.

THE EPILOGUE

The application of newer inventions in physics and chemistry to modern medicine in various fields of diagnosis, prevention and treatment of diseases has a chequered history in the 20th century (Majumdar, 2000). Over the years it has become clear that technological advances in science, generally, have been determinant of progress in the laboratory-based science of clinical chemistry. A chemical pathology laboratory comprises, overall, physics (i.e. laboratory machinery, pressures, voltages, etc), chemistry (i.e. the chemical solutions flowing through the tubes of the machinery, at the correct concentrations, etc) and biology (i.e. the personnel in charge of the technology and computerisation); it is interaction between these three that collectively constitutes the working laboratory. It is, furthermore, the chemical pathologist who provides diagnostic interpretation of the results being produced – in the context of his awareness that the variability of values being produced falls within acceptable statistical limits (as judged by quality control schemes integrated into the total working system).

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सारांश

आधुनिक आयुर्विज्ञान में रसायन शास्त्र का योगदान

शिशिर के. मजुमदार

मानव शरीर भौतिक अंशों एवं रसायनों का संगम है। मानव जैव रसायन शास्त्र या नैदानिक रसायन शास्त्र शरीर की स्वस्थता एवं व्याधिग्रस्त अवस्था में होने वाले परिवर्तनों को दर्शाता है। रसायन शास्त्र उपयोगी साधन बनकर व्याधियों के निदान एवं चिकित्सा के समय में अनुगमन करने में सहायक सिद्ध होता है। बेहतर रसायन, बेहतर यन्त्र एवं बहेतर मापदण्ड के आधार पर अयुर्विज्ञान के क्षेत्र में निरन्तर उपलब्धियाँ जोडे गये है।

आधुनिक आयुर्विज्ञान को जो उपलब्धियाँ रसायन शास्त्र के रूप में प्राप्त है उनका मूल रसायनिक रोग निदान में पाये जाते हैं। पूर्व तकनीकी युग से तकनीकी युग तक का इसका विकास क्रम अत्यन्त रोचक है। यह एक आधुनिक एवं नया क्षेत्र है। व्याधिरसायन शास्त्र ने आयुर्विज्ञान के विकास यथा, जैवरसायनिक ज्ञान, परमाणु विज्ञान तथा रसायनिक विश्लेषणात्मक पद्धतियों का अनुगमन किया है। इसकी विषय वस्तु का सम्बन्ध व्याधिग्रस्थ शरीर में होने वाले रसायनिक एवं जैव रसायनिक क्रियाओं से है।