

## Evolution of Pathology – a time travel

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This is my pleasure to write a few words for Medical Science - an opportunity to introduce the readers with our journal & society activities. We are pleased to announce that Dr. Prasanna. L.C, Associate professor, Dept of Anatomy, Kasturba Medical College, Manipal University will be serving as Editorial board member. We heartily welcome and congratulate him for being a part of our journal. We also congratulate Sankalan Sarkar and Dr. Manish Kiran Shrestha for best paper award & highest viewed article award given to them by CMRA. Now, serving almost one & half decade as a pathologist, I am writing a few lines on how Pathology unfolded over time.

Pathology literally means study of disease. History of pathology started with other medical specialties, all of which emerged together due to human inquisitiveness to the causation of different diseases and ailments. Over a span of almost 5000 years the concepts of disease and medicine kept on changing. In the earliest days of history of mankind, identifying ailments and symptoms as a “disease” was a challenging task. Ailments have been related to gods and

goddesses or even stars and aliens. Progress in medicine over thousands of years has been accelerated by several remarkable persons who mostly driven by their own effort and curiosity contributed in their own ways. Several different theories have been put forward in the past so many years, most of which were far from the modern medicinal concept and eventually failed the test of time.

Documentation of disease and anatomical observations began in Egypt with Edwin Smith Papyrus in 17th century BC. Despite flaws in his humoral theory of nature of disease, descriptions on inflammations and infections like tuberculosis have been documented in his era. The foundational text of Chinese medicine is the Huangdi Neijing written between 500 and 300 BC. In India, Sushruta (600 BC) and Charaka (300 BC) in their own text books mentioned about detailed clinical examination, diagnosis and even treatments of many conditions. Sushruta is known to write 184 chapters including 1120 conditions and 300 surgical procedures.

### Humoral Theory

However It was Hippocrates (460 – 370 BC) who created lasting impact on modern Greek and Roman medicine and is considered the “*father of Western Medicine*”. He used terms like acute, chronic, endemic, epidemic exacerbation, relapse, and resolution. Herophilos (335-280 BC) and Erasistratos (304-250 BC) are among the first to pursue anatomy as a science and to correlate anatomy with disease and symptoms. They have performed dissections of animals, dead humans and even living criminals as part of punishment.

With time Greek culture was transferred to Rome which emerged as a more important centre of civilization. Celsus (30 BC – 38 AD) wrote 8 volumes of his text book and gave the classic definition of inflammation which is studied by each medical student till date. Galen (129-200 AD) was a prominent Greek physician and surgeon in Roman Empire. He influenced development of physiology, pathology, pharmacology as well as neurology and according to many he is one of the greatest medical figures of all time. He had traveled extensively and studied diseases of various nature. He followed Hippocratic humoral theory but kept his mind open. He described cancer as “crab like” growth and also



added the fifth sign in the definition of inflammation (i.e., “loss of function”). Till 14th and 15th centuries, efforts continued to follow and prove Galen’s theories - dissections and their documentation became more and more common.

#### **New insight**

A new era started with William Harvey (1578-1628) who changed the concepts of disease causation and it was with him that the Galen’s theory started diminishing. He had made important observations on blood circulation, function of heart and also pathologic heart. Among different writers on autopsy documentations, Theophile Bonet (1620-1689) needs a special mention as he collected an enormous 3000 autopsy reports with reference and comments. Theories of Hippocrates and Galen which already started losing its importance were scientifically challenged by Giovanni Morgagni (1682-1771). Since the time of Morgagni, concept of modern pathology emerged and progressed steadily over time. He correlated symptoms with pathological findings in the autopsy studies. Since his time it was generally accepted that diseases and symptoms are “organ based”.

John Hunter (1728-1793) wrote several papers on diverse topics and first use of primitive microscope was documented by him. It can be said that with him, the older humoral and other theories became obsolete and experimental pathology started. He for the first time commented that inflammation is primarily a defense mechanism and secondarily a reparative process. Hunter museum in London is an evidence of all his achievements. Bichat (1771-1802), though without the use of microscope, identified different types of tissues in human body and correlated clinical findings with the “type” of tissue. Thomas Hodgkin (1798-1866), a general physician in UK, published two volumes of “Lectures on Pathologic Anatomy”. He recorded cases of tuberculosis and also the disease that later was named after him. Carl von Rokitsky (1804-1878) an eminent Viennese pathologist had performed an astonishing 20000 autopsies and in addition supervised 60000 in his lifetime. He considered that diseases resulted from chemical anomalies in blood. By the late 1800s, an exhaustive literature was produced on gross anatomical findings characteristic to a particular disease.

#### **Origin of microscopic pathology**

Rudolf Virchow (1821-1902) student of Muller and Rokitsky challenged Rokitsky’s idea and emphasized the study of cellular manifestations in different disease condition.

The original invention of microscope is not easy to identify. First compound microscope was perhaps developed in Netherlands in late 1500s. Giovanni Faber coined the term microscope to Galileo Galilei’s compound microscope in 1625. Significant contribution in use of microscope came from Antonie van Leeuwenhoek who discovered RBC,

spermatozoa and micro-organism by 1676 and popularized its use.

Virchow is recognized as “father of modern (microscopic) pathology” as he was one of the first to use the microscope in tissue analysis. The scientific concept of disease causation and manifestations which began from humoral theory transformed through “organ based” disease to the “cellular level” changes – and the new era of modern or microscopic pathology started. In the second half of nineteenth century pathology started being considered as a separate specialty. Since 1850s with the use of microscope diagnostic histopathology gained its importance. First microtome suitable for sectioning tissue was constructed in 1848. Paraffin embedding was introduced in 1869. H&E staining technique was first described in 1875-78. Formalin was first used as a fixative in 1893. By the end of nineteenth century, improved histo-techniques, established tissue processing methods, several cellular and biological stains as well as newly improved microscopes have been come into use. Among several eminent figures in last decade of 19<sup>th</sup> century, Friedrich von Recklinghausen (1833-1910) known for identifying multiple neurofibromatosis and his works on bone tumor and Edwin Klebs (1843-1913) known for discovering *Corynebacterium*, both were disciples of Virchow and deserve special mention.

#### **Twentieth century**

With the beginning of 20<sup>th</sup> century, the pace of research, discoveries and publications as well as technical advancement grew enormously in all fields of medicine including pathology. In the early half Aschoff developed the concept of reticulo-endothelial system and Anitschkov described histopathology of heart in rheumatic fever. In 1953 Watson and Creek described double helical structure of DNA. With time, many terms, diseases and new entities were defined and classified, re-defined and re-classified. Emergence of immunohistochemistry in 1980s was a revolution and with it the use of electron microscopy became somewhat obsolete. Cytology became more popular after mid 80s. New techniques like FISH, DNA studies, molecular and chromosomal studies came into vogue and each of them has its own importance in diagnosis and prognosis of the ever increasing types and subtypes of neoplasms.

We look forward in the future with the optimism that all the newer techniques and inventions will be accessible to people from all socio-economic classes across the globe and more newer type-specific therapy will be invented and available which will improve prognosis in all neoplastic diseases.

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