

# ANATOMIC PATHOLOGY IN NORTH AMERICA: A BRIEF BUT RICH JOURNEY

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*Abstract.* Anatomic pathology was born on the new continent in the late 19<sup>th</sup> century, grew up with European tutors until the turn of the century, and rapidly developed to full maturity to become over the following six decades the global preeminent force that it is today. American work ethic and ingenuity, together with their innovative and pragmatic spirit were likely at the core of this progress in addition to the incremental economical and political growth in the 20th century. In this review the first part of that journey is depicted and the forefathers of American anatomic pathology remembered.

Reviewing the history of anatomic pathology in North America within the constraints of this format poses several challenges: the pathology practice and its scientific spectrum have significantly expanded in the last century, even more so in the last few decades; pathology as a discipline is remarkably understated and poorly understood not only to the general public but also by many non-pathology physicians; any attempt to abbreviate decades of clinical experience and research done by multiple individuals, groups and institutions is inherently subject to omission; finally, the author's professional and personal interest and affiliation are prone to a skewed presentation.

Scientific progress in any area spans centuries and in any given period of time throughout the world inroads were created by different scholars using different means, hypotheses, and experimental strategies. A comprehensive review of any discipline would require an encyclopedic approach unfeasible here therefore a decision was made to arbitrarily commence this review at the mid-19th century, acknowledging that essential moments from Antiquity, Ages of Renaissance and Enlightenment and giants such as Morgagni, Bichat, Laennec, Hunter, Horner, Rokitanski, Hodgkin, Cruveilhier, Waldayer will be virtually missing from this brief review despite their significant individual and collective transforming influence in the field.

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A short overview of the current pathology practice in North America will preface the historical considerations. Pathology is generally defined as the study of the nature and cause of disease which involves changes in structure and function. This general definition while all-encompassing is not entirely revelatory and somewhat vague, but explains why the evolution of modern medicine and pathology are parallel and closely inter-related. Important parts of the science, such as comparative, experimental or functional pathology will not be discussed or will be only briefly mentioned here. In the clinical practice of medicine today, two distinct branches of pathology are usually entirely separated in Europe and most of the world by clinical training, practice and departmental organization: anatomic pathology and clinical pathology. Anatomic pathology (AP) encompasses surgical pathology, autopsy, cytopathology, forensic pathology while under clinical pathology (CP, also referred to as laboratory medicine) are listed microbiology, chemistry, blood bank, cytogenetics, molecular diagnostics and immunopathology. Although various degrees of overlap exist between the two, only in North America are training programs usually combined (AP/CP) and the respective laboratories are administratively part of the same department albeit distinct divisions in most institutions. As a consequence, in the United States many general pathologists often have clinical duties in both fields of anatomic and clinical pathology and can obtain joint board certification (see below)

In parenthesis, pathology might be arguably the least understood and most misrepresented clinical discipline to the lay public in USA. Due in part to the current reflection in the media, depiction in popular television shows and movie industry, as well as the inherent limited, if any, direct contact with the patients, pathologists are viewed as the doctors doing the autopsies or responsible for forensic medicine whereas in reality both these branches of anatomic pathology currently represent a minute segment of clinical practice, the former in steep, constant decline in the last four decades (Wood, 2001). The vastly predominant clinical diagnostic responsibilities and the critical consultant function of the pathologist to the clinical physicians are largely unknown to the general public in USA (Gutman, 1998) and likely worldwide, another recent poll demonstrating a similar situation in Japan (Ikeda, 2000).

#### **THE PIONEERS**

It is often stated that the birth of pathology took place in Renaissance when the first autopsy records by Benivieni were published in 1507 (Rosai, 1997). However, microscopy became widely used in analyzing tissue samples, and the cellular structure studied by biologists, botanists, zoologists and embryologists only in the 19th century. Johannes Muller (1801–1858), Theodore Schwann (1810–

1882), Jacob Henle (1809–1885) are remembered today as histologic eponyms, *but* were all instrumental in developing the cellular theory in the first half of 19<sup>th</sup> century through their observations and experiments. They marked the end of pathology as an exclusively postmortem science centered on autopsy and clinical pathological correlation and prepared the ground for the great impact of Rudolf Virchow's landmark concept that the cellular unit was the key for normal and disease processes crystallized in his 1855 work *Cellular Pathology. As Based upon Physiological and Pathological Histology*. Essentially a compilation of lectures given to medical students, the text is an undisputed milestone which essentially coalesced the Cell Theory concept proposed by Theodore Schwann two decades earlier and novel ideas of Robert Remak and John Goodsir (Malkin, 1993) Virchow was also a strong proponent of pathology as an independent discipline and was most interested in the understanding of disease through microscopic study, what he referred to as "scientific microscopy." He "proceeded to rebuild pathology on his true conception of the human body as an organized cell state, a social system of continuous development, in which each microscopic unit performed its part". (Long, 1965). His pervasive influence not only changed the diagnostic philosophy and reshaped the discipline but also influenced numerous physicians in Europe and subsequently some of the forefathers of American pathology, who trained with Virchow or his associates and pupils.

While in Europe significant conceptual, technical and clinical progress was made in the field, the situation was strikingly different in the United States for the most part of 19<sup>th</sup> century, when no full-time pathologists existed at the time (Fechner, 1997). Progress in modern medicine has been intertwined with, and many times a direct consequence of, the new discoveries and concepts emanated from pathology, and the sad status of medical education and clinical practice in the United States at the time was reflecting that. Malkin suggested four possible reasons for the medical delay of the second half of the 19<sup>th</sup> century: the early capitalist ethos of American society failing to identify any immediate potential financial gain from supporting medical and biologic research; the strong influence of church over society, individuals and education at the time (many colleges were established and owned by churches or had strong ecclesiastical affiliation) and its active fight against evolution at the time as postulated by Charles Darwin; absence of political support for any act that would increase taxes (continuing often even now ); and not in the least, the poor status and lack of regulation of medical training in the country (Malkin, 1993). Although pathology was gradually accepted as a discipline in the United States, the first chair devoted exclusively to pathology (pathological anatomy) being established at Harvard University in 1847, for most of the century the US pathologists were little more than museum curators, limited to gross pathology by necessity and victims of the prevalent speculative philosophies of disease of the time (Fechner, 1997). Experimental pathology was essentially nonexistent.

This dire situation was about to see a dramatic change through the work and diligence of several individuals, most of them directly influenced by the European pathologists of the time, most notably Virchow: Francis Delafield, William Welch, William Osler and James Ewing. Francis Delafield and T. Mitchell Prudden were arguably the pioneers of pathology in the United States. Delafield (1841–1915) graduated from Columbia College of Physicians and Surgeons (P & S) in 1877, had studied in Europe, and was well acquainted with Virchow's work. He was appointed Professor of Pathology and Practice of Medicine at the same institution in 1882 and he was the first New York laboratory clinician (i.e., pathologist) and probably the most prominent pathologist of his time in the country, publishing the *Handbook of Postmortem Examinations and Morbid Anatomy* in 1872. T. Mitchell Prudden followed him as director of the same laboratory. If Delafield and Prudden were the American pathology pioneers, two of their students, James Ewing and William H. Welch will arguably become the forefathers of American surgical pathology (Fechner, 1997). One of the first surgical pathology laboratories in the country was at Columbia in 1903-1905 and ran by a surgeon, William Clarke, another P& S graduate. It was in this laboratory where Arthur Purdy Stout started as an instructor in surgical pathology in 1914 and subsequently had an overwhelming role in surgical pathology development as an independent specialty within pathology, authoring numerous articles and training several generations of pathologists.

William H. Welch (1850–1934) was undoubtedly one of the most influential personalities in American pathology. He received his medical degree at Columbia in 1875 and then he worked with Delafield and Prudden at Bellevue Hospital. As most American prominent pathologists of the time, he pursued further studies in Europe with Ernst Wagner, Waldayer, von Recklinghausen and Cohnheim, the latter a former Virchow student and a preeminent German pathologist who strongly recommended him for the appointment at Johns Hopkins medical institutions that would change his career and, subsequently, American medical practice. He was appointed first Professor of Pathology and Dean at the not yet built Johns Hopkins Hospital and University in 1884, the year when he returned to Europe to study bacteriology with Robert Koch, recognizing the great importance of the newly emerging field. Together with William Stewart Halstead, first Professor of Surgery, William Osler, first Professor of Medicine and Physician in Chief and Howard Kelley, first Professor of Gynecology (depicted in John Singer Sargent's famous portrait "The Four Doctors"), Welch played a major role in shaping the future of this institution and its medical school. Through the standards they established at Johns Hopkins and by the many generations of physicians they trained these individuals changed American medicine in general and pathology in particular. In Welch's laboratory, Osler combined investigations in pathologic anatomy, bacteriology and experimental pathology, with an emphasis on the latter. Welch

had done important work in pathology and physiology: for instance, while working together with Cohnheim (arguably the parent of pathophysiology) in Germany, he proposed the mechanical theory of pulmonary edema (Belknap, 1951). Although his pathology knowledge was beyond doubt, his personal traits, astuteness in identifying talent in others, ability to stimulate and encourage the curiosity for research of his students, the vision to promote collaborative work, his modesty—all were at the core of his tremendous influence (Malkin, 1993). His decision and success in bringing William Osler to the Johns Hopkins was undoubtedly one of his major accomplishments for the new institution.

William Osler (1849–1919) graduated from McGill medical school in 1872 and pursued further studies in Europe (England and then Germany) where he became acquainted with Virchow and Traube's work. Upon his return at McGill University, he insisted that all students become acquainted with the use of the microscope thus making this institution the first in the world with a practical curriculum in histology and pathology. The state of the art microscopes were acquired with funds from his own salary, received while volunteering in the smallpox ward, where he commenced doing the first of over 800 autopsies he performed here. 150 dissected specimens by his hand, many being still preserved today in the pathological museum at McGill (Malkin, 1993) gave this institution a future major role in the birth of what is today one of the largest pathology organizations in North America and worldwide (USCAP). Osler was an expert microscopist early in his career due to his life-long interest in blood, platelet disorders and malaria, and one of the 4 courses he was teaching, Clinical Microscopy was "specially designed to meet the requirement of the practitioner". Being both a clinical physician but also a competent pathologist he continued uniting the two fields in the next decade at University of Pennsylvania (1878–1888), prior to his recruitment to Johns Hopkins in 1889 (Long, 1962). Many of the administrative changes instituted by him at Hopkins in both the training structure and staff hierarchy are still at the core of today's American medical practice. Most importantly, by combining clinical practice with autopsy and microscopy throughout his career, by emphasizing the role of laboratory methods in diagnosis, by his passionate, often lyrical writings he epitomized the American reference to pathologists in the broad medical community as the "doctor's doctor". He was not technically a pathologist but an exquisite clinical diagnostician with a strong interest in understanding the mechanisms of disease and furthering the diagnostic arsenal. It is interesting that Osler's prominence in pathology and medicine was not the fruit of any groundbreaking scientific discovery but of his prescient incorporation of pathology within clinical medicine, as crystallized in his lectures, addresses and the ever classic *Principles and Practice of Medicine*.

The branching of surgical pathology from the general pathology has a fascinating history. At the end of 19<sup>th</sup> century the existing full time pathologists

were exclusively autopsy pathologists with virtually no involvement in the operative theater or even interest in tissues removed. The academic pathologists' focus lay almost exclusively in laboratory medicine, especially microbiology. It is not then entirely surprising that the first surgical pathologists were the physicians most interested in the nature of a tumor to be removed, namely the surgeons, usually at the time of surgery (Fechner, 1997). In fact, surgeons that chose to function as their own pathologists (i.e., surgical pathologists) were the pioneers of this new brand of pathology. Surgeons like Joseph Colt ("Bloody") Bloodgood at Johns Hopkins and William C. ("Wild Bill") Clarke at Columbia University were the first surgical pathologists of the time (Rosai, 1997), and therefore the first surgical pathology laboratories were affiliated with Surgery and not Pathology departments at the turn of the century. This was true not only for surgical pathology as a specialty. When the interest in pathology of clinical physicians started rising in the 19<sup>th</sup> century, before the rapid growth witnessed in the following century that established pathology as an independent discipline, the clinician and pathologist were originally one person. Even today, in a time of an extremely complex, continuously expanding multifaceted diagnostic process, there are still few medical specialties (most notably Dermatology and Hematology) in which the practicing physician's responsibilities around the world (including within the USA) encompass a biopsy or aspirate morphologic interpretation after obtaining the sample. That physician today is not much different from his centennial predecessor, reaching a diagnosis with, and deciding the therapy based upon, clinical findings and morphologic evaluation of removed tissue samples.

James Ewing (1866–1943) was another giant of American anatomic pathology and the only pathologist to date selected for the Time magazine cover for his scientific accomplishments (Anon., Time Magazine, 1931). After graduating Columbia University College of Physicians and Surgeons (P & S) in 1891, he was exposed to pathology during an internship at Roosevelt Hospital in New York, allegedly the first American hospital with an established pathology laboratory, and worked with Delafield there, and through him, met Prudden. The latter offered him a position at Columbia in histology and deeply influenced his formation and career (Koss, 1997). In 1894 the inevitable European training visit followed, for him in Vienna where he became familiar with the Austrian school of pathology established by Carl Rokitansky. On his return, he was appointed assistant in clinical pathology at Columbia and at the age of 33 he was offered in 1899 the professorship at Cornell University, established the year before. His first book appeared in 1901, *Clinical Pathology of the Blood*, enriched by his experience as his contract surgeon in the Spanish American War (1898) during which he examined the blood smears from more than 800 patients (Ewing, 1898), using the dual aniline dye staining developed by the previous decade by Paul Ehrlich the decade before. His fame and influence stem without doubt from his interest in cancer pathology and treatment, and his

brilliant career at Memorial Hospital in New York. The first hospital for cancer in America was opened in 1887 but was renamed in 1898 as General Memorial Hospital for treatment of Cancer and Allied Diseases signaling a shift from the original mission to a more general practice due to financial and public opinion pressure. It was Ewing's influence 15 years later that returned the hospital to its original mission under the new name of Memorial Hospital for Cancer and Allied Diseases in 1913, when he became president of the medical board, director of research and hospital pathologist. Dubbed in the media "Cancer Man" and the "Chief" by revering colleagues, James Ewing influence on his peers, students and successors such as Frank W. Stewart (1894-1991) who followed him as the director of the laboratory, strengthen the rapidly developing field and established a strong school of surgical pathology.

Contemporary with Ewing, Dr Roswell Park, a nationally renowned surgeon was instrumental in the foundation of the first cancer-dedicated, government-supported research laboratory (which will expand to become what is today Roswell Park Cancer Institute) in Buffalo, NY in 1898 and proposed a "comprehensive", multidisciplinary approach to cancer therapy, education and research (Park, 1899) that is currently standard practice in most cancer centers in USA and worldwide. Of note, the perception of cancer was for the most part of the 19<sup>th</sup> century akin to leprosy due to the dismal prognosis, lack of therapy options and the misconception associated with its origin (many believed it was a venereal and contagious disease) (Butler, 1955). It is even more remarkable that the first attempts to organize the treatment and research of malignant tumors took place in USA where the medical field was just starting to develop independently from the powerful European influence. Despite the stigma that general public and even physicians associated with the patients and, not uncommonly, with the few brave physicians who attempted to treat such a hopeless disease, it was the conviction, drive, enthusiasm and political ability of pioneers and visionaries like Ewing and Park that brought the study of cancer into focus. Ewing's Bausch and Lomb monocular microscope is kept visible this day in the Department of Pathology at Memorial Sloan-Kettering Cancer Center—a memento for a generation of pathologists of the power of this instrument (almost primitive by today's standards) when used by an inquisitive mind.

In Boston John Barnard Swett Jackson was appointed the first Professor of Pathology at Harvard and in the country, but a true local Pathology school was established with the arrival of William T Councilman in 1892 from Johns Hopkins. Councilman graduated from University of Maryland in 1878, trained in Europe under Cohnheim and von Recklinghausen and had been practicing for several years in Baltimore as an accomplished pathologist before Welch was preferred over him at the newly established Hopkins institutions. He remained Welch's close collaborator for 8 years and, strongly supported and recommended by him, accepted the appointment of

professor at Harvard in 1892. Councilman made significant contributions in the field of infectious diseases (Scully, 1997) but his influence in establishing a school of pathology, similar to Prudden and Delafield in New York, was through the training of two of his pupils, Frank Burr Mallory and James Homer Wright, who furthered the development of surgical pathology and hematopathology, respectively, through technical developments, conceptual progress (tumors differentiation, description and classification), and most importantly in their time future training of a hundred pathologists in Boston, many to become leaders on their own.

In 1905 Rochester was a small town in Minnesota, population 7,233. In the same year William J. Mayo and Charles H. Mayo performed 4000 operations at their clinic (Woolner, 1997). The Mayo brothers were not only exceptional surgeons but also pioneers in building the first integrated medical practice in the world. It is no surprise that pathology has a rich history at the Clinic and surgical pathology today would be very different without Mayo's contributions. Louis B Wilson was the first pathologist who arrived in 1905 at Mayo Clinic after 8 years at University of Minnesota. The Clinic's high volume, increasing number of autopsies and surgical efficiency demanded prompt histologic diagnosis in the small 5x5 m laboratory adjacent to Mayo's operating theater. At William Mayo request, he developed a method for frozen sections that arguably marked the official birth of this essential pathology intraoperative consultation tool, his methylene blue staining method still being used in Mayo's surgical pathology department today (Gal, 2005). A scientist with encyclopedic interests, he was also a pioneer in color photography of surgical specimens and an expert in thyroid pathology. Following his tenure, Drs. William C. MacCarty and later Albert C. Broders became the next leaders of pathology at Mayo Clinic in subsequent years and benefitted of the immense clinical volume (for example, Dr MacCarty detailed records indicated that he reviewed 70,453 cases during a ten years tenure, a 3–5 times a higher volume than a current American pathologist would review today) (Woolner, 1997), experience they used to establish and develop new techniques, expand and refine the use of intraoperative consultation, and generate an impressive body of research including essential conceptual progress in definition of *in situ* carcinoma and early cancer diagnosis, novel tumor classification and grading proposals, some still ubiquitously employed in pathology reports throughout the world today.

Any history of surgical pathology in America would be incomplete without a reference to the Armed Forces Institute of Pathology (AFIP) which currently hosts the National Museum of Health and Medicine. First curator of the museum was Major Walter Reed, who played a central role in identifying the insect vectors (common fly and mosquito respectively) involved in the transmission of typhoid fever and yellow fever, the first major American scientific medical discovery (1900–1901). Started as a military museum, the Army Medical Museum was at the origin of National Library of Medicine, Walter Reed Army Institute of Research and the Army Institute of



Pathology. AFIP rapidly expanded its scope (Ishak, 1997) throughout the 20<sup>th</sup> century functioning as a referral consultation center for thousands of difficult cases, from both military and civilian patients. Through the American Registry of Pathology the Institute edited the *Atlas of Tumor Pathology* (now at its 4<sup>th</sup> edition) and played an important role in several editions of *WHO International Histological Classification of Tumors*, both series widely used by American and foreign pathologists as reference textbooks since 1940s in USA and throughout the world. The AFIP has educated numerous pathologists and other physicians through the fellowship programs and courses and has been the site for extensive clinicopathologic research of tumors.

As pointed earlier, this brief citation of the early prominent figures in pathology is by necessity fraught with numerous and important omissions. The postwar period witnessed the blooming of surgical pathology in the US but was outside the scope of this review. Dr Lauren V. Ackerman (1905–1993), born around the same time as the discipline on this side of the Atlantic fully deserves mentioning since the name is the eponym for the American surgical pathologist. As a teacher he trained dozens of current and past pathology leaders and as writer helped thousands of pathologists, American and foreign alike, over the last 50 years with his textbook of *Surgical Pathology* (currently at its 9<sup>th</sup> edition), a major reference for every diagnostician's desk. During his career and doubtless due to his brilliance and efforts, surgical pathology became an integral part of pathology (formerly widely structured within surgery departments, a Johns Hopkins model) and the American surgical pathology discipline progressed to its preeminent position worldwide.

#### SOCIETIES, PUBLICATIONS, TRAINING AND ACCREDITATION

As American pathology entered its adolescence at the turn of the century, most pathologists were trained by the German school and publish their findings usually in German medical journals (Long, 1962). American Medical Association (AMA) was founded in 1847, but its first journal was not published until 1883 while a section of Pathology and Bacteriology was organized in 1900. The Association of American Physicians (AAP) was envisioned in 1885–1886 to advance medical research and was established mostly by pathologists including Delafield, Osler and William Pepper and later Councilman, Fitz, Welch, Wright and F.B. Mallory. The first exclusively pathologists association was the American Association of Pathologists and Bacteriologists, which derived from AAP and was officially born in New York with Councilman as president. *Journal of Medical Research* followed shortly in 1901 in which AAP members published their work until 1925, when it was replaced by American Journal of Pathology as the official AAP publication, still in existence today and the highest ranked publication in the field. The second pathology journal was founded a year later, affiliated with the AMA, *Archives of Pathology and Laboratory*

*Medicine* also currently a very popular publication with practicing anatomic and clinical pathologists. In 1921 the American Society of Clinical Pathologists was created with a focus on the necessity of improving the status and recognition of clinical pathologists as consultants, improving the laboratory standards, education and patient care. *Journal of Laboratory and Clinical Medicine* was ASCP official publication until 1931, today still printing under the name of *American Journal of Clinical Pathology* (Long, 1962). In the following decades, the exponential accumulation of knowledge, research and expanding subspecialty development witnessed a dramatic increase in number and quality of pathology publications. From the 3 journals mentioned above in America in the first half of 20<sup>th</sup> century, significantly lagging behind the European scientific production (for instance, Virchow's Archives had been founded in 1847, over 50 years before the American publications) the growth and contribution of American pathology has been unprecedented and today a significant majority of the over 60 English-language pathology journals in circulation is published in the United States (Journal Citation Reports, 2007).

From the infancy of the discipline when the treating clinician functioned as a pathologist having a sketchy, facultative pathology education originally exclusively in autopsy interpretation, the training and credentialing of the pathologist evolved to its complex and rigorous state today. From the 2–3 pioneering teaching centers on the East Coast a century ago, there are today to over 130 residency programs and 28 subspecialty fellowships throughout the country, graduating thousands of pathologists every year (ICPI, 2008), programs accredited and regulated by the Accreditation Council of Graduate Medical Education (ACGME, 2008). The American Board of Pathology was established in 1936 with the main objective of defining the qualifying standards for the physician-pathologist (Long, 1962) and today certifies diplomats in the two main pathologic areas (anatomic and clinical) as well as 10 subspecialties.

#### TECHNOLOGIC PROGRESS IN PATHOLOGY

The microscope invention is credited to Jensen in 1590, but it was not until mid 19<sup>th</sup> century that the achromatic lenses were introduced and in the following decades immersion lens first developed in the Zeiss factory. Saffron-derived stain was first used for a microscopic slide on 1719 by van Leeuwenhoek (Fechner, 1997), but alum hematoxylin was not discovered until 1865 by Böhmer, while the eosin was introduced in 1875. Hematoxylin eosin is still the vastly predominant stain used in surgical pathology laboratories throughout the world today, although various combinations and many special stains still employed with original formulas from the 19<sup>th</sup> century or slightly modified versions, coined after their inventors during that vibrant period (Ziehl, Gram, van Gieson, Weigert).

Paraffin was used for embedding tissue in 1869 by E. Klebs and in the same decade microtomes were built by Zeiss. Most of the developments above were

made on the old continent. Frozen section was first documented for diagnostic purposes in 1896 at Hopkins but did not become the routine diagnostic procedure known today until 1905 at Mayo Clinic (see above).

Much of the modern history of diagnostic pathology is written in North America where new technologies such as electron microscopy, immunohistochemistry and molecular techniques were either introduced or significantly developed, enriching the diagnostic armamentarium throughout the second half of 20<sup>th</sup> century. Other recent developments associated with the explosive growth of the internet are telepathology and the increased access to pathology-related information for pathologists, other physicians and patients. Clinical practice in pathology is also undergoing rapid changes with various degrees of sub-specialization, widespread in large academic or referral centers but also in private practice. In cancer centers, pathologists are today essential members of ‘Tumor Boards’, where, in Oslerian tradition, a patient’s disease is reviewed from its clinical to histological and molecular aspects to decide the optimal management. The major difference is that the discussion includes today the surgeon, the medical oncologist, radiation oncologist, pathologist all bringing their individual expertise to the table.

As in other field, while many discoveries were made by accident, they were always associated with industrious, extraordinarily talented and dedicated individuals. Throughout history, the actual discovery, its medical implications and historical credit given to certain individuals are often disconnected and not necessarily consequent. One such example is that of Rober Remak, a biologist contemporary with (and rival of) Virchow who reached before him the conclusion *omnis cellula e cellula*, although the dictum was coined by and is today attributed to the latter (Malkin, 1993). Another illustrative example is that of Papanicolaou, who while studying reproductive biology recognized malignant cells in the vaginal smears while working at Cornell University and presented the results in 1928 in an obscure meeting (Papanicolaou, 1928). He has not pursued the life-saving clinical value of this observation until 13 years later, at the gynecologists’ insistence (Koss, 2000). In fact, it is well established that Aurel Babeş, a Romanian pathologist has the chronological priority to this important step with extraordinary consequences in the prevention of cervical cancer: in 1927 he had presented in Romanian a new diagnostic method for cervical cancer in smears obtained by means of a bacteriologic loop and in 1928 they published their findings in a French paper of wide circulation (Babeş, 1928) before Papanicolaou’s communication. None of the two followed on their original important discovery and most likely the paternity attributed to Dr Papanicolaou was due to the subsequent work undergone at clinical suggestion and the widespread use of the eponym staining combination used today in most cytopathology laboratories (Koss, 2003).

### PRESENT AND FUTURE OF PATHOLOGY

The history of American pathology spans one and a half century beginning with the museum curators and exclusively macroscopic diagnosticians of the 19<sup>th</sup> century to the current pathologists integrating in their report complex information such as immunophenotype, genotype, prognostic markers and molecular profiling, advances that will hopefully lead to personalized medicine for most if not all future patients.

The question that persisted (and progressively gained intensity) in the last decades for all anatomic pathologists is the following: will the 130 years-old hematoxylin-eosin stained slide, still at the core of pathologic diagnosis, become obsolete and be supplanted by various molecular techniques? What will be the role of histology in the next 30 years, if any? Will the pathologists of the near future analyze only gels and microarrays? Any prediction is obviously hazardous but it is probably safe to state that our genetic and molecular understanding of disease, albeit growing exponentially, it is still matched against the gold standard of diagnosis, microscopic examination. Molecular tests are widely available and for some diagnoses even required in current classifications (e.g., chronic myelogenous leukemia), but their interpretation without clinical-pathologic correlation is often confusing and even dangerous. Surgical pathologists today are incorporating more of that information in their diagnostic process. The power of microscopic examination by itself, backed by more than a century of accumulated empirical and clinical experience, in trained hands, is still unmatched (Rosai, 2007). Regardless of the future, we live an exciting time where the sophistication and complexity of diagnostic process is increasing daily. Promoting and asserting the pathologists' essential role in the diagnosis and management of virtually all tumors and many other diseases, and increasingly integrating novel genetic and molecular testing in the pathology reports while functioning as critical gatekeepers of the appropriate testing and analysis was deemed crucial for the future of the discipline (Fletcher, 2008).

A humble effort to acknowledge the giants whose efforts brought us here is very important. Virchow's *dictum* 'there is no life but through direct succession' holds true not only in the cellular theory but also in the history of any science, maybe none other more so than pathology.

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