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The pedagogical value of autopsy

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“WHERE WE HAVE BEEN”

Knowledge of human anatomy was acquired through dissections of the human body that may have begun as long as 4000 years ago, in Babylonian times. Later documentation was in Egyptian times (3000 BC-1600 BC), as exemplified with the Ebers and other papyri. Around 300 BC, the Greek physician, Herophilus (335-280 BC), wrote a treatise on human anatomy and Erasistratus (304-250 BC), his student and colleague at the medical school of Alexandria, produced the first description, albeit brief, of liver cirrhosis observing that the liver of a man who died with anasarca (“hydrops”) was “as hard as a rock”, contrasting it with the soft consistency of the liver of another man who died from the bite of a poisonous snake. This description is evidence of Erasistratus’s ability, based on observation, to correlate the diseased organ with the consequence of its involvement and may be the first example of a clinicopathological correlation.

The original writings of Herophilus and Erasistratus were lost and the first written record about autopsy dates from the 12th century work, the *Gesta Regum Anglorum* (“Deeds of the kings of the English”), by the English monk William of Malmesbury (1095-1143). William recounts the story of Sigurd I Magnusson, also known as the Crusader, King of Norway. In 1111, when Sigurd was returning from Jerusalem, many of his soldiers died in Constantinople. The hypothesis that death had occurred due to wine intake led to the

opening of one of the bodies in an attempt to find the possible cause of death by studying the viscera.

A century later, in 1286, Salimbene di Adam of Parma, a Franciscan friar, examined the heart of a patient who died from the plague, comparing it to the heart of a chicken thought to have been affected by the same disease. It is worth noting that Pope Innocent III, in 1209, had already recommended that all unexplained deaths should be evaluated by an experienced physician; this ruling reversed the church’s position against violation of the corpse.

However, it was only at the height of the Italian Renaissance that Antonio Benivieni (1443-1502), a physician to the most important families of Florence, began to regularly rely on autopsies to explain the various causes of death and disease. Considered by many to be the creator of pathology as a science, he studied more than 100 clinical cases, 16 of which had autopsies. His *De abditis nonnullis ac mirandis morborum et sanationum causis* (“On some hidden and strange causes of disease and cure”) was published in Florence five years after his death and documents his commitment to ascertaining, via *post mortem* examination, the reasons for death in patients whose diagnosis during life had not been clear.

The thirst for knowledge emblematic of the Italian Renaissance gave impetus to the study of human anatomy and led to the reconsideration of the validity of the concepts of Galen (129-217), the famous

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Roman physician of Greek origin. Andreas Vesalius (1514-1564), in his great 1543 work, *De humani corporis fabrica libri septem* ("The structure of the human body in seven books"), corrected Galen's writings which were, up to that time, universally accepted dogma, in both Europe and the middle east, while also creating the first of the three pillars (anatomy, physiology, pathology) upon which modern medicine rests.

Almost two centuries after Benivieni, in 1679, the Swiss physician, Théophile Bonet (1620-1689), published *Sepulchretum sive anatomia practica ex cadaveribus morbo denatis* ("Repository of anatomical studies practiced on corpses affected by disease"). This work, based on more than 3000 autopsies, includes references to some of the most illustrious names in the history of medicine, including Gabriele Falloppio (1523-1562), William Harvey (1578-1657), Thomas Bartholin (1616-1680), and Marcello Malpighi (1628-1694).

In the 17th century, the Italian, Marcello Malpighi (1628-1694), regarded as the founder of microscopic anatomy, reported the first description of the capillary circulation, which had been postulated by Michael Servetus (?1509-1553) in 1553 and William Harvey (1578-1657) in 1628. Harvey's work was the beginning of scientific physiology, the second component of the foundation of modern medicine. Malpighi described the vesicular structure of the human lung, establishing the basis of respiration; moreover, he hypothesized that capillaries were the connection between arteries and veins that allowed blood to flow back to the heart. Subsequently, Giovanni Maria Lancisi (1654-1720) proposed the first classification of heart disease and linked syphilis to aortic aneurysm, while Herman Boerhaave (1668-1738), a Dutch physician, emphasized the importance of clinical history, reporting, in 1724, the case of an admiral who, having vomited after a copious meal, developed excruciating chest pain and subcutaneous emphysema resulting from esophageal perforation, currently known as Boerhaave syndrome.

Giovanni Battista Morgagni (1682-1771) provided the third element, pathologic anatomy, in setting the firm basis for modern medicine. He condemned speculation without an observational basis by emphasizing the importance of pathological correlation substantiated by autopsy findings. Born in the city of Forlì, Italy, he graduated from the University of Padua,

where he was, in 1715, appointed to the Chair of Anatomy, previously occupied by Vesalius, Fallopio, and Girolamo Fabrizio ("Fabricius") Acquapendente (1537-1619). His immortal work, published in 1761, ten years before his death, was *De sedibus et causis morborum per anatomen indagatis* ("On the causes of diseases investigated by anatomical means"), in which he corrected several inaccuracies in *Sepulchretum* while acknowledging Bonet's contributions. Further, he questioned Galen's humoral theory, replacing it with the concept of demonstrating the origin of diseases in the organs.

In this five-volume work, Morgagni describes more than 600 autopsies and correlates the signs and symptoms of patients with pathological findings. Morgagni's *De sedibus* is a milestone of modern medicine.

Today, when autopsies have been inappropriately relegated to a secondary role in medical practice, Morgagni's comment is even more valid: "*Physicians who have done or seen many autopsies have learned at least to mistrust their diagnosis; the others who don't confront themselves with the often discouraging findings of autopsies, live in the clouds of a vain illusion*".

François Marie Xavier Bichat (1771-1802) was born in the year Morgagni died. A surgeon at *L'Hôtel Dieu* of Paris, he was a brilliant investigator whose meticulous dissections, without the aid of the microscope, led to the concept of tissues as described in his work *Traité des membranes*. This expanded Morgagni's perspective by concentrating on tissues as the site of disease, rather than organs. Sadly, this great physician died at the age of 31 from tuberculosis.

The importance of autopsies was dramatically emphasized by the work of Karl von Rokitansky (1804-1878), founder of the "New Viennese School". Drawing on the contributions of Morgagni and Bichat, he systematized the examination of the body and was one of those responsible for the recognition of pathology as a medical specialty. Although he used the microscope, Rokitansky primarily relied on macroscopic evaluation, personally performing more than 30,000 autopsies. In this period the English pathologist, Thomas Hodgkin (1798-1866), whose seminal work is the disease (Hodgkin lymphoma) named after him, worked with Joseph Jackson Lister (1786-1869), the father of Joseph Lister (1827-1912),

a remarkable British surgeon who pioneered principles of antiseptics. Together Hodgkin and the older Lister developed the achromatic lens, greatly enhancing the resolution, and usefulness, of the microscope.

The next important step in understanding the pathogenesis of disease came from the German, Rudolph Virchow (1821-1902). Virchow worked at a time when microscopy was more widely used and he significantly contributed to its implementation. In 1876 he published a book on autopsy techniques, emphasizing that all the organs needed to be thoroughly examined and that a full autopsy should not take less than three hours to perform. From this time on, the practice of performing autopsies spread throughout Europe, pathology was separated from anatomy and itself became a recognized discipline. Virchow's ground-breaking work *Die Cellularpathologie* contains his famous aphorism "*Omnis cellula e cellula*" and establishes the concept that the origin of disease is to be found in the cell. For this reason he is called "the father of cellular pathology".

In 1910, Richard Clarke Cabot (1868–1939) created the challenging clinicopathological conference format, which, from 1924, would become the famous Case Records of the Massachusetts General Hospital, still published in the *The New England Journal of Medicine*. In 1912, Cabot's seminal paper, *Diagnostic pitfalls identified during the study of three thousand autopsies*, showed how the autopsy often identified significant diagnostic errors. After that the autopsy rate of a hospital became one of the principal standards to evaluate and accredit hospitals.

"WHERE WE ARE"

After World War II, hospitals often gained renown because of the pathologists on their staff, whose autopsy studies led to major discoveries. However, in recent decades, increased clinical reliance on newer, more sophisticated diagnostic tools, in clinical and research laboratories, as well as imaging, has contributed to worldwide decline in the utilization of the autopsy. As example, at the Hospital Universitário of the University of São Paulo (HU-USP), the autopsy rate declined from 57% in 1990 to 8% in 2007. The rate continues to decline despite ongoing documentation of significant discrepancy between clinical and pathological diagnoses at major medical

centers throughout the world. In 1971, the Joint Commission on Accreditation of Health Organizations (JCAHO) no longer required that a minimum number of autopsies should be performed for accreditation of hospitals in the United States.

The prioritization of diagnostic tests, particularly the refined imaging methods at the expense of observation, medical history, and physical examination of the patient, have increased beyond what would be reasonable. Most contemporary physicians, who have great self-confidence, judge themselves immune to errors and fail to utilize the autopsy as a quality control mechanism for their practice. Nevertheless, it seems that these professionals ignore the high incidence of discrepancies between clinical and autopsy diagnoses, which have hardly changed since the early 20th century, especially in elderly patients and those in critical condition, if cared for outside the centers of excellence. It should be remembered that modern diagnostic methods are fairly accurate, but not foolproof, as stated by Alfredo José Mansur MD PHD, professor of the Heart Institute of Hospital das Clínicas of the University of São Paulo and, for many years, the editor of the Clinicopathological Session of the *Arquivos Brasileiros de Cardiologia*:

The "images" are actually reconstructions obtained from sensors. The arising lines and contours are not the "object" itself, the "thing in itself", but a reconstruction of the joining points gathered by the sensors. Although the imaging methods have substantially advanced and greatly aid us, it is undeniable that there is certain "virtuality" in the image. The physical and pathological references of the diseases can be considered a relevant mechanism to prevent that the "virtuality" degenerates into "abstraction" or "drafting false images" or even "improper images". (Personal communication, Dr. Alfredo J. Mansur)

The statement of Professor Mansur is even more relevant when considered in terms of medical education, when it is essential that the learner sees specifically what he is supposed to learn. In terms of clinical practice, Professor Mansur recalls that:

Preventing the "virtuality" may represent the care to prevent treating "pictures" instead of patients. The lessons gathered from the autopsy help the clinician to interpret the images, which do not always speak for themselves. (Personal communication, Dr. Alfredo J. Mansur)

The key attributes of the autopsy, consistent with the classic goals of a student, are the obstinate pursuit

of diagnostic certainty ("truth") and the cultivation of the analytic approach. Without these the high quality of medical practice does not exist. The *post mortem* discovery of important medical conditions, unsuspected during life, expands our knowledge and, as a consistent clinicopathological correlation, carries over to our assessment of future patients. According to Vera Demarchi Aiello MD PHD, pathologist-in-chief of the Surgical Pathology Section of the Laboratory of Pathology at the Heart Institute of Hospital das Clínicas – University of São Paulo and co-editor of the Clinicopathological Session of the *Arquivos Brasileiros de Cardiologia*:

Some specialties of Pathology like Cardiovascular Pathology find in autopsy important information (especially at the macroscopic level) that positively and significantly contribute to the development of cardiac surgeons and cardiologists, especially with regard to understanding morphological lesions that are potentially treatable, surgically or medically, and which still evade recognition with modern diagnostic techniques. (Personal communication, Dr. Vera D. Aiello)

The reluctance of families to allow a *post mortem* examination may be based on: (i) religious beliefs; (ii) the lack of awareness of the autopsy's purpose; (iii) the fear of external mutilation of the corpse; and (iv) the delay in burying their loved one. All of these reasons, and possibly more, likely contribute to the decline in the number of autopsies. Quite often, the request for the authorization of the procedure is not provided by the attending physician, but by an accessory physician (medical residents in the case of teaching hospitals) who is unknown to the family. Therefore, there is no emotional bond with that physician and the request will usually be denied. In addition, in order that the family understands the need to perform the autopsy, the requesting physician needs to be particularly convinced of its usefulness. Currently, in the vast majority of Brazilian medical schools, the experience of future professionals with autopsies and/or anatomoclinical sessions during graduation is scarce or null; thus, unaware of the value of such practices, the newly qualified doctors have great difficulty convincing the deceased's family of the importance of a *post mortem* examination.

Other factors, such as the expense and the time consuming procedure, have been identified

as impediments. Some argue for the hiring of a specific medical pathologist who should receive fair remuneration commensurate with the importance of the procedure. Moreover, in an exciting editorial, "Who will perform my autopsy?", published in *Autopsy and Case Reports* in 2014, Dr. Stephen A. Geller, a professor at the David Geffen School of Medicine and Weill Cornell Medical College, draws attention to the lack of experienced autopsy professionals.

The burden of routine tests, heavy teaching duties, and onerous administrative tasks that pathologists have to deal with in academia, certainly discourage the most experienced pathologists to engage in the practice of autopsies. In itself, the *post mortem* examination is a time-consuming procedure both in terms of the actual performance of the autopsy and the subsequent, often laborious analysis of histological preparations.

A lack of communication with the clinicians, whether through private consultation or anatomoclinical meetings, also discourages the pathologist, who does not feel valued to the extent that he does not reap the fruits of his complex labor. On the other hand, the delay in completing the autopsy report discourages clinicians in seeking the pathologist or even requesting an autopsy examination at a forthcoming opportunity.

The overconfidence of modern physicians, supported by guidelines and provided with refined diagnostic means, makes them feel immune to error, and consequently unconcerned with autopsies. There may be fear of litigation because of diagnostic errors and/or wrong therapeutic choices, although, in general, the autopsy proves supportive of a physician whereas the absence of autopsy can be interpreted as an effort to conceal errors. Both overconfidence and the fear of detection of errors further contribute to the drastic reduction in the number of autopsies being performed. In strong contrast, by accepting and/or understanding the value of the autopsy, physicians can demonstrate that they are open to criticism as well as to understanding the multidisciplinary of the profession.

Despite all of these obstacles, the autopsy has undeniable value, functioning as an important resource of medical education when students interact with professionals from various medical specialties, promoting discussion between the young and the seniors. The autopsy synthesizes problem-based learning, which is currently adopted

by some medical schools, either through attendance at the *post mortem* examinations or by taking part in anatomoclinical sessions. In addition, the autopsy (i) provides an opportunity to teach human anatomy, pathology, pathophysiology, clinical reasoning, and medical ethics; (ii) cultivates systematic doubt and the critical spirit; (iii) relativizes the value of laboratory tests and diagnostic imaging methods; (iv) exposes medical fallibility even by the most skilled physicians; (v) functions as quality control for the medical service provided; and (vi) reinforces the importance of teamwork.

“WHAT IS OUR BATTLE FOR”

The HU-USP is a general hospital of secondary complexity, which is currently in charge of 25% of all the undergraduate courses of the Faculty of Medicine, and 40% of medical internships (fifth and sixth years of the medical course). The autopsies of patients who died of natural causes are performed in the hospital's pathology service. Between July 2007 and May 2015, 533 autopsies (5.6 autopsies per month) were performed. A study conducted at HU-USP between 1989 and 1990, when the autopsy rate was 57%, showed a diagnostic discrepancy rate of 30% (n=130 autopsies). Between 2004 and 2009 (when the autopsy rate was 13%) another similar study with 162 cases showed a discrepancy rate (Classes I and II of Goldman) of 50%, which were mainly represented by malignancies (lymphoma, lung and pancreatic cancers), pneumonia, pulmonary thromboembolism, intestinal ischemia/infarction, tuberculosis, acute pancreatitis, and myocardial infarction. The autopsy rate in HU-USP follows the global trend at around 5%. The autopsied cases are not randomly selected, but represent cases that generated many diagnostic doubts and unexpected therapeutic responses, or when the patient died without an established diagnosis, or when death was unexpected.

Since 2007, clinicopathological meetings have taken place at HU-USP every week, joining teachers of the Pathology Service, the Department of Radiology, the Division of Pediatrics, the Internal Medical and Surgery Clinic, as well as medical residents, students, and trainees. At these meetings, the clinical data (history, physical examination, and laboratory exams) are discussed before the presentation of the gross

and microscopic findings of the autopsy. Either the pathologist or the clinician is responsible for the final correlation and conclusion. Between July 18, 2007 and May 27, 2015, there were 279 meetings held. From September 26, 2012, these meetings took on an interactive nature, when they were transmitted by teleconference to the Hospital das Clínicas of the Faculty of Medicine of the University of São Paulo, the Federal University of Minas Gerais, and the Federal University of Sergipe. Based on these meetings, the idea to publish the most educational and interesting cases was born. For this purpose, in 2011, the online magazine *Autopsy and Case Reports* was created. To date (June 2015), 18 issues have been published. Recently accepted to be indexed in the PubMed Central database, it is one of the few magazines around the world that is focused on pathological correlation based on autopsies.

Our experience with the anatomoclinical meetings has been the best of our careers, not only for personal learning but also for providing the medical residents and graduating students the opportunity to discuss the autopsied cases in a systematic and thorough way. Moreover, the transmission of the meetings via teleconference provides enriched interaction between doctors and professors from three universities. In forums held with the medical residents of the Internal Medicine Department, this activity has emerged as one of the most appreciated, which reinforces its importance and encourages us to improve it even more.

Notwithstanding the aforementioned arguments, those who still doubt the educational value of autopsies are invited to read the *Autopsy and Case Reports* articles and/or to participate in the anatomoclinical meetings transmitted monthly by teleconference from the HU-USP.

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