

# ASIP Centennial Editorial

## *The American Journal of Pathology Centennial Project*

### *Celebrating 100 Years of the American Society for Investigative Pathology*

The American Society for Investigative Pathology (ASIP) traces its origins to two predecessor societies, the American Society for Experimental Pathology (ASEP) and the American Association of Pathologists and Bacteriologists (AAPB). The ASEP was established in 1913 to provide pathological representation to the nascent Federation of American Societies for Experimental Biology (FASEB), and ASIP continues to convene annually at the FASEB meeting with some of its sister FASEB societies. The second branch of ASIP's genealogical tree, AAPB, was formed in 1900. The two societies merged in 1976 to become the American Association of Pathologists, which was subsequently re-incorporated in 1992 as ASIP.

To celebrate the founding of ASEP and 100 years of FASEB affiliation, ASIP is sponsoring *The American Journal of Pathology (AJP)* Centennial Project to highlight significant scientific discoveries published in *AJP* (the official journal of ASIP) and its predecessor journals, *The Journal of Medical Research* and the *Journal of the Boston Society of Medical Sciences*. During the next year, *AJP* will publish articles in a special *AJP* Centennial Project section of each issue, highlighting important articles, scientific topic areas, and advances in experimental pathology that have occurred during the past 100+ years. We hope that these articles will illustrate the breadth of ASIP's scientific impact, provide new insights on old issues, and generate enthusiasm for attending the Centennial Celebration at the ASIP Annual Meeting on Experimental Biology in 2013 in Boston, MA.

#### **Reflections on our History**

The formation of ASEP in 1913 represents an important milestone in ASIP's history and is undoubtedly worthy of a Centennial Celebration; however, the foundation for ASIP was laid before the turn of the 20<sup>th</sup> century. In an interesting editorial written in 2001 by Dr. James Madera,<sup>1</sup> in what was originally thought to be the centennial anniversary of *AJP*'s inaugural publication in 1901, under the title *The Journal of Medical Research*, he notes that *AJP* had actually evolved from the *Journal of the Boston Society of Medical*

*Sciences*, which was first published in 1896. At the risk of being imitative of Madera's 2001 *AJP* Centennial editorial, I'd like to provide my own reflections on the remarkable history of *AJP* (1925 to present) and its predecessors, the *Journal of the Boston Society of Medical Sciences* (1896 to 1900) and *The Journal of Medical Research* (1901 to 1924). (The complete archives of these journals can be accessed from the *AJP* website at <http://ajp.amjpathol.org>).

#### **The Early Years (1896 to 1924)**

Given that academic physicians in Boston founded the Boston Society of Medical Science and began publishing their scientific investigations in 1896 in a journal that would ultimately become *AJP*, it is perhaps only fitting that the site of Experimental Biology 2013 and ASIP's Centennial Celebration is Boston. Although the scientific prominence of its members is unquestionable, the provincial perspective of some of these early publications is at least mildly amusing to someone from the flyover portion of the United States. My personal favorite is an article entitled "Strength Tests and the Strong Men of Harvard,"<sup>2</sup> (p13) which includes the inspirational words "The great mass of young men who can never hope to make any of the University Athletic Teams . . . can have at least the satisfaction of trying to attain and pass the strength standard required of the members of these organizations." Thankfully, a subsequent article entitled "On the Relation of Age, Physique, and Preliminary Training to Class Rank in Pathology"<sup>3</sup> (p188) concluded that ". . . the scholarship of the students constituting the subjects of this investigation (Harvard Medical students) bears no conspicuous relations to their physical proportion," thus offering hope to us non-strong men and women that a productive career in pathology remains a possibility. [The average weight of the Harvard medical students studied in 1900 (all male) was just 145 pounds.]

Interestingly, the *Journal* was originally distributed free of charge (perhaps an early attempt at open access), but by June 1897, the editor reported, "The amount of material offered is so great that the funds of the society will not permit the continuance of the present plan."<sup>4</sup> (p1) Several of these

early articles described highly useful and practical advances in microtome design,<sup>5</sup> high-volume slide staining,<sup>6</sup> and an anti-vibration bench for improving photomicrography.<sup>7</sup> The *Journal* editor, Dr. Harold C. Ernst, expressed “his readiness to receive conditional orders from those who wish to possess reproductions of the Minot-Blake Microtome.”<sup>5</sup> (p77) Although it is difficult to imagine *AJP* publishing advances in equipment design and manufacturing at present, or the *AJP* editor in chief accepting equipment orders, such articles had a significant impact on advancing experimental pathology in the early part of the 20<sup>th</sup> century.

The *Journal of the Boston Society of Medical Sciences* became a more nationally inclusive publication in 1901 when it was renamed *The Journal of Medical Research* and was published in conjunction with the newly organized AAPB. In contrast to some of today’s dense societal mission, vision, and purpose statements, Dr. William T. Councilman’s opening remarks from the First Annual Meeting of the AAPB refreshingly commented, “It seems to me that it would be out of place for me to occupy your time in any general statement of the purposes of the association, and the means for their accomplishment. We are here to learn something from one another, to show each other the results of our work and the methods we have used.”<sup>8</sup> (p2) Given its close association with the field of microbiology, it is not surprising that numerous advances in virology, bacteriology, and infectious disease research were published during the *Journal’s* 25-year existence. Some of the most highly cited publications during this period included articles on the transmission of herpesvirus,<sup>9</sup> a definitive description of the cause of Rocky Mountain spotted fever,<sup>10</sup> and the classification of streptococci.<sup>11</sup> These publications and others by Ernest W. Goodpasture, Leo Loeb, Ernest E. Tyzzer, Lewis H. Weed, Simeon B. Wolbach, and other prominent authors began to explore topics as diverse as experimental carcinogenesis, cerebrospinal fluid flow dynamics, and myocardial infarction and regeneration.

### ***The Emergence of AJP (1925 to 1950)***

*The Journal of Medical Research* was renamed *The American Journal of Pathology* in 1925. Its Board of Editors included Frank B. Mallory (Editor-in-Chief), James W. Jobling, Howard T. Karsher, Paul A. Lewis, H. Gideon Wells, George H. Whipple, and Hans Zinsser. (We can unambiguously look forward to the Centennial Celebration of *AJP’s* founding in 2025.) Many of the major advances in experimental pathology during the first 25 years of *AJP’s* existence were the result of the development and publication of improved histochemical staining techniques. Multiple reports by George Gomori, Frank B. Mallory, Paul Masson, and others described novel staining methods that quickly became widely used and cited and provided fundamental tools to describe and characterize normal and diseased organs and tissues. These reports often contained colorful descriptions that are rarely found in today’s scientific literature. Gomori wrote definitively in an article describing various histochemical methods for the demonstration of iron that “the alleged

superiority of the Tirmann-Schmelzer modification of Turnbull’s blue method is based partly on erroneous theoretical conceptions and partly on the misinterpretation of artifacts.”<sup>12</sup> (p662) Similarly, comments such as “the obvious contradiction between his two statements seems to have escaped his attention” and “it can be easily shown that the assertion of Mallory does not hold”<sup>12</sup> (p659) suggest that scientific debate was not discouraged by *AJP* editors.

During this period, acknowledgment of financial support for the published investigations became more frequent. Such acknowledgments sometimes cited direct institutional support [eg, “aided by a grant from the research fund of the Graduate School, University of Minnesota”<sup>13</sup> (p263)] or indirect private support via funding of the institution itself [eg, “Aided by an appropriation from a grant made by the Rockefeller Foundation to Washington University for research in science”<sup>14</sup> (p329)]. It was not until the 1950s that acknowledgment of US government support for research became common. Interestingly, as a result of World War II, *AJP* published a series of well-cited studies on the effects of thermal injury<sup>15–17</sup> and a 174-page report on the “Pathology of Atomic Bomb Casualties,”<sup>18</sup> tragic reminders of the pathological consequences of human military conflict.

### ***New Tools, New Insights (1951 to 2012)***

During the next quarter century, *AJP* reported several definitive ultrastructural studies made possible by advancements in electron microscopic instrumentation and techniques. Diabetic glomerulosclerosis, Alzheimer’s disease-affected brain, and atherosclerotic lesions all became subject to ultrastructural analysis that provided key insights into disease pathogenesis.<sup>19–21</sup> Many of these publications deserve careful rereading and reanalysis, given more recent investigations into the molecular and genetic factors affecting disease susceptibility and pathophysiological responsiveness. This time period also heralded the onset of authorship creep. Before the 1950s, most articles had one or, at most, two authors. Three-author articles became more common in the 1950s and 1960s, and articles containing five or more authors became common by the 1990s. A quick survey of recent *AJP* issues reveals an average of more than eight authors per article. If this trend continues, the list of authors for *AJP* articles will need to scroll across our computer screens much like movie credits do today.

Just as new histochemical stains and advances in electron microscopic techniques positively affected earlier generations of experimental pathologists, the development of highly specific monoclonal antibodies and improved immunohistochemical and *in situ* hybridization techniques dominated the most highly cited *AJP* articles in the 1970s and 1980s. These new reagents contributed to significant advances in diagnostic surgical pathology, tumor classification, and basic cell biology.<sup>22–24</sup> Many of the most highly cited *AJP* articles in the 1970s and 1980s focused on myocardial ischemia, atherosclerosis, and angiogenesis, further enhancing *AJP’s* long-standing reputation for publishing fundamental advances in cardiovascular disease research.<sup>25–27</sup> Although human autopsy reports have not been the top priority in *AJP’s* publication strategy, the emer-

gence of the AIDS epidemic in the early 1980s challenged the entire experimental pathology community. *AJP* published one of the first and most highly cited reviews of AIDS autopsy pathological findings,<sup>28</sup> in addition to a variety of primary articles on AIDS pathogenesis throughout the 1980s and 1990s.

Studies on the molecular and cellular regulation of mammalian cell death exploded in the 1990s, and ASIP members and *AJP* authors played major roles in leading this field. *AJP* articles published by Drs. Guido Majno, John C. Reed, Andrew H. Wyllie, and others became extremely well cited, and investigations of cell death mechanisms in a variety of pathological conditions, including neurodegenerative disease, atherosclerosis, and cancer, remain a hallmark of *AJP*.<sup>29–31</sup> *AJP* has continued to evolve in the new century, and we have experienced the emergence of TMAs, gene expression analysis, proteomics, metabolomics, and whole-genome sequencing as still more powerful new tools in experimental pathology research. Now more than ever, we are challenged by information overload and we are beginning to see the incorporation of powerful informatics and systems biology approaches into experimental and clinical pathology. How well we integrate these exciting new tools into our investigations of disease pathogenesis will determine our future success as a scientific discipline.

### *Toward the Celebration*

ASIP has much to celebrate beyond its mere century-long existence. Eight Nobel laureates and innumerable other prestigious national and international award winners have been, or are, ASIP members. Its membership is diverse and increasingly committed to growing the experimental pathology community. Its journal, *AJP*, is the most frequently cited publication in the discipline of pathology, and major advances in experimental pathology continue to grace its pages. During the next year, the *AJP* Centennial Project will present you with a series of interesting and provocative perspectives, commentaries, and review articles highlighting its century-long history of remarkable achievements and challenges. All of these articles will be marked with a special ASIP Centennial logo (see this article's title page). Articles on the evolution of our understanding of macrophage form and function, the controversy surrounding the concept of vascular mimicry, and the impact of genomics on 21<sup>st</sup>-century experimental pathology are just a few of the topics that will be covered in the Centennial Project. I am optimistic that you will enjoy reading these upcoming articles and hope that you will join us in Boston in April 2013 to celebrate the 100<sup>th</sup> anniversary of the founding of ASEP.

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