

IN CELEBRATION OF THE 100TH ANNIVERSARY OF *PHYSIOLOGICAL REVIEWS*

Sadis Matalon, Editor-in-Chief

University of Alabama at Birmingham, Birmingham, Alabama

Physiological Reviews is the flagship journal of the American Physiological Society, held in high esteem by the most distinguished scientists worldwide. As we celebrate our 100th anniversary, we should all rejoice in this great accomplishment.

When I became editor of *Physiological Reviews* in January 2018, I wrote an editorial titled “In the Shadow of Giants” (1). The giants of course are the highly distinguished scientists who served as Editors since the inception of *Physiological Reviews* in 1921 (TABLE 1), as well as the Associate Editors and Editorial Board Members. Many continue to volunteer time from their very busy schedules to ensure the success and longevity of our journal. Of course, special thanks also go to the authors who spend years creating insightful, thought-provoking, and definitive reviews on a large range of subjects appealing to biomedical scientists. Thanks to their efforts, *Physiological Reviews* has been consistently rated by Google Scholar, Scopus Citescore, and various other metrics as the number 1 journal in the field of physiology. Furthermore, with a 2020 impact factor of 37.312 and a Google Scholar h5-index of 82, Web of Science ranks it as the 43rd most impactful journal among 20,000 other biomedical journals (FIGURE 1).

Articles published in *Physiological Reviews* are highly authoritative documents that succinctly summarize an important topic and discuss unresolved questions, which serve as food for thought for early career and senior scientists alike. I believe that they are more than that. To me, each article published in *Physiological Reviews* meets the definition of a Greek tragedy as defined by the great philosopher Aristotle in *Poetics* (Περὶ ποιητικῆς), the earliest treatise of dramatic theory. He wrote, “Tragedy, then, is a process of imitating an action which has serious implications, is complete, and possesses magnitude; by means of language which has been made sensuously attractive. . .” Indeed, there are many similarities among the immortal works of Euripides, Sophocles, Aeschylus, and others and the articles published in *Physiological Reviews*. Each review deals with an in-depth, detailed, and complete treatise of the subject and contains hundreds of references. Every word is chosen carefully by the authors for the

“language to be attractive” and to make complicated subjects easier to understand. Of course, the conscientious and constructive comments of the Associate Editors, Editorial Board members, and guest reviewers help resolve ambiguities, point out omissions, and bring each review to a happy ending (publication). Here again we have another analogy with the Greek and Latin tragedies where the “Deus ex machina” (God out of the machine) seems to resolve very difficult situations. The final products, further enhanced by the talented graphical artists and production staff, provide critical and authoritative interpretation of significant areas of physiology and medicine, presented in a clear, pleasing, and compelling way. More than 36 articles throughout the years have been written by Nobel Prize winners on such topics as insulin, synaptic and neuromuscular transmission, active transport across the cell membranes, and most recently how birds orient themselves in space. It is no wonder that most of the authors invited to contribute an article in *Physiological Reviews* consider the invitation a badge of honor. It is true that each article takes a team of scientists at least 3 years to complete. The result is worth the effort: many of these articles have a major impact in their fields and are of considerable help to early career scientists getting started in a field.

I often wondered how and why the American Physiological Society (APS) decided to publish a review journal 100 years ago. After all, most scientists would prefer to write original papers on their most recent and exciting findings instead of extensive reviews. Well, it takes pioneers and forward thinkers to pave the road. In 1919, Donald Russell Hooker, the then Managing Editor of the *American Journal of Physiology*, and his mentor, William Henry Howell, who pioneered the use of heparin as an anticoagulant, made the bold proposal in the April 1919 APS council meeting that the society establish a review journal called either *Physiological Reviews* or *Quarterly Reviews of the Physiological Sciences* (2). The journal would “cover the subject of physiology, physiological chemistry, pharmacology, experimental pathology and such other subjects as may from time

Table 1. *Physiological Reviews* editors

Editor	Start Term	End Term
Donald Hooker*	1921	1946
No editor listed	1946	1947
Milton O. Lee*	1948	1965
R. G. Daggs†	1966	1972
H. E. Morgan	1973	1978
S. G. Shults	1979	1984
G. H. Giebisch	1985	1990
L. Reuss	1991	1993
W. F. Boron	1994	1999
S. L. Hamilton	2000	2008
D. Brown	2009	2017
S. Matalon	2018	Present

In the early days of scientific journal publishing, titles of roles differed from what we see today. *Early volumes were overseen by Managing Editors. †Some years exhibited an overseeing Associate Editor in lieu of an Editor.

to time appeal to those interested in the biological sciences” and would be published once a year. Its complete charter is shown below:

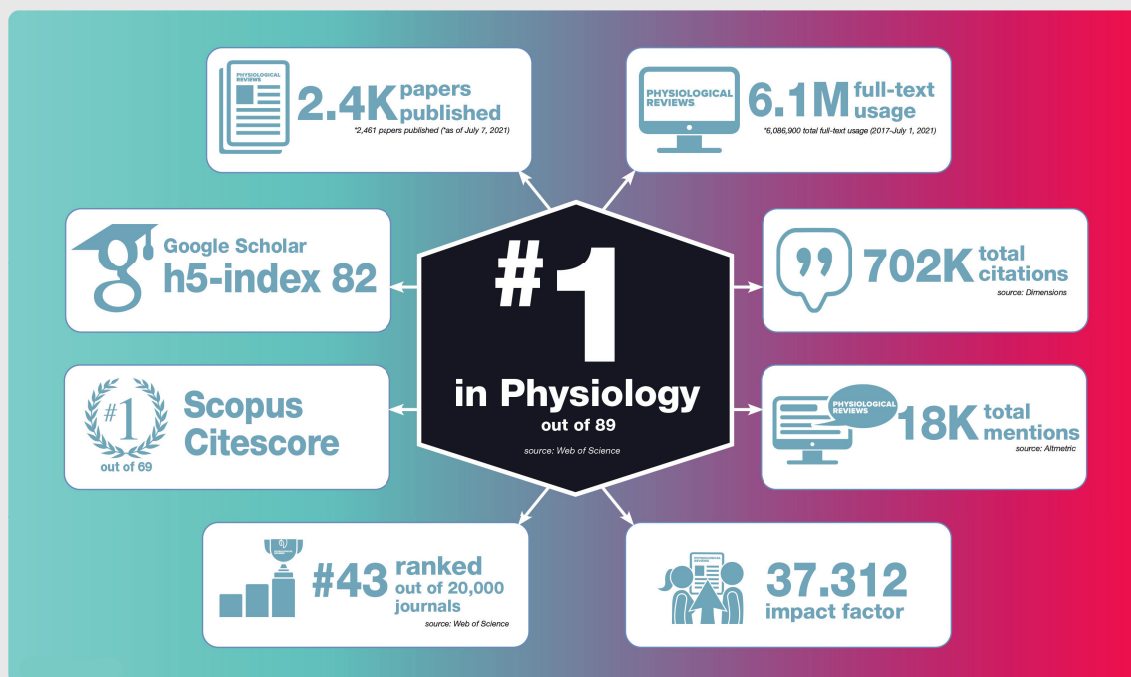
The main purpose of the PHYSIOLOGICAL REVIEWS is to furnish a means whereby those interested in the physiological sciences may keep in touch with contemporary research. The literature, as every worker knows, is so extensive and scattered that even the specialist may fail to maintain contact with the advance along different lines of his subject. The obvious method of meeting such a situation is to provide articles from time to time in which the more recent literature is compared and summarized. The abstract journals render valuable assistance by condensing and classifying the literature of individual papers, but their function does not extend to a comparative analysis of results and methods. Publications such as the *Ergebnisse der Physiologie*, the Harvey Lectures, etc., that attempt this latter task, have been so helpful as to encourage the belief that a further enlargement of such agencies would be welcomed by all workers. It is proposed, therefore, to establish a journal in which there will be published a series of short but comprehensive articles dealing with the recent literature in Physiology, using this term in a broad sense to include Bio-chemistry, Bio-

physics, Experimental Pharmacology and Experimental Pathology. (3)

Dr. Hooker was appointed the first Editor, and he held this position until 1946. The first volume, which appeared in 1921, contained 19 articles by the most prominent physiologists on such important topics as the regulation and conduction of the heartbeat, the regulation of pulmonary circulation, the physiology of undernutrition, and physiological adaptations to high altitude. *Physiological Reviews* proved an immediate and overwhelming success. By the end of the first year of operations, *Physiological Reviews* had 838 subscribers, and its readership grew astronomically during the following years. A list of editors throughout the years is shown in **TABLE 1**. I had the pleasure and honor of meeting some of them over the years, and I am truly awed by their scientific accomplishments, their willingness to mentor and offer advice to early career scientists, and their service to the American Physiological Society. I especially would like to thank my predecessor, Dr. Dennis Brown, who set such high standards for the journal and spared no effort to make the transition to my editorship as easy as possible. Also, my special thanks go to Dr. Barbara Cannon, a member and previous President of the Royal Swedish Academy of Science, who served as Deputy Editor and Chair of the European Board of Editors for *Physiological Reviews* for 12 years.

Amazingly enough, our current charter is not that different from the first charter from 1919. As stated on the website of *Physiological Reviews* at <https://journals.physiology.org/physrev/about>, we publish comprehensive, authoritative, nonbiased, and informative reviews in all areas of biomedical research. Our audience includes physiologists, neuroscientists, cell biologists, biophysicists, and clinicians with special interest in pathophysiology of disease. I am just going to list some articles that highlight the broad nature of our journal. We have published authoritative articles on the pathophysiology of migraine; the mechanisms of insulin action and resistance; new insights into the mechanisms of aging; the origins of metabolic diseases (4); mechanisms of insomnia (5); inflammation and thrombosis in COVID-19 (6); the complex nature of Alzheimer's disease (7); and many others. However, there are differences as well: the articles published in 1921 consisted of text only with no figures and one or two tables at most. Editors did not fret over the “impact factor” or other metrics; manuscripts arrived by post, which must have taken a significant amount of time, especially when the manuscripts crossed the Atlantic, and there was no such thing as electronic media. In contrast, articles published today contain at least 10 well-illustrated color figures, integrating key concepts at a glance; a graphical abstract, summarizing the contents of an article; a call-out-box for clinicians, pointing out clinical highlights; and a typeset layout that makes them easier

Seminal Works. Lasting Impact.



The American Physiological Society journal *Physiological Reviews* is turning 100! Celebrate this monumental step by checking out the most cited *Physiological Reviews* articles of all time.

View now at tinyurl.com/PRV100th.



**PHYSIOLOGICAL
REVIEWS**

FIGURE 1. 2021 *Physiological Reviews* statistics.

to read and more pleasing to the eye (8). In addition, articles appear in PubMed shortly after publication, and they are promoted widely in our electronic media. We also take pride that there is equal representation among the

sexes among our Associate Editors, Editorial Board Members, and authors. Our newly established Early Career Editorial Board enables the scientific leaders of tomorrow to become engaged with the workings of

Physiological Reviews and be mentored by the best scientists in the world on how to review papers. A lot of the topics published in *Physiological Reviews* in the last decade would be considered science fiction 100 years ago. As an example, see the excellent reviews on CRISPR (9), immunotherapy for cancer (10), genetic predisposition to asthma (11), and many other topics. Finally, the selection of review topics and the editorial process changed considerably. In the early days, authors were invited by the Editor in Chief; there is little information on the review process, although there is every reason to think that it was as stringent and that manuscripts were revised before publication. Today, review topics are suggested by the Editor and Associate Editors and merits of each topic as well as the qualifications of the authors are discussed in detail during the biannual meetings of the board of Associate Editors. Invited manuscripts undergo extensive editorial review by three expert referees, whose comments and recommendations are assessed by an Associate Editor and the Editor, who makes the final decision as to whether a manuscript should be accepted for publication, revised, or in some cases rejected.

Despite these differences, articles published then and now have one thing in common: they are definitive treatises of important subjects. I have asked a number of authors to write editorials comparing and contrasting the information contained in articles in the first volume with the state of the art today. Readers will be amazed with the wealth of information present in these early articles despite the lack of sophisticated instruments to perform precise measurements. It is no wonder that many articles published in *Physiological Reviews* have received thousands of citations and shaped the fields. A list of our most-cited papers (some of them with thousands of citations) can be found at <https://journals.physiology.org/physrev/100th-anniversary-collection>.

Physiological Reviews articles have influenced our thinking, and reading the journal has started the careers of many investigators. Each one of us has our favorite articles. I remember reading, as a first-year graduate student, the influential review on Pulmonary Edema by Dr. Norman Staub (12). During the last 20 years, my colleagues and I have discussed in detail, argued about the fine points, and benefitted tremendously from the outstanding reviews on lung fluid balance (13), nitric oxide and peroxynitrite in health and disease (14), sources of nitric oxide and reactive species by the vasculature (15), comparing and contrasting normoxia in vitro and in vivo (16), mechanisms of oxygen and carbon dioxide sensing (17), and the importance of heme oxygenases in health and diseases (18), to name just a few. Actually, this last article led me to collaborate with Dr. Agarwal, one of the authors, to show that induction of heme oxygenase 1 decreased lung injury following inhalation of oxidant

gases (19, 20). Thus, like many of us, *Physiological Reviews* has had a significant impact on my science and on my career. Its broad reach makes it the world's most authoritative source of information on many areas of scientific endeavor, and this is what makes the job of the editor in chief both challenging and exciting.

CONCLUDING REMARKS

Physiological Reviews is in great shape thanks to the hard work of the Deputy and Associate Editors, the Editorial Board, our Senior Editorial assistant (Ms. Amy McEver), the Journal Supervisor (Mr. Sean Boyer), the Publications Director, Editorial and Production (Dr. Audra Cox), the Associate Publisher, Art (Eric Pesanelli), the Chief Publishing Officer of the APS (Ms. Colette Bean), and the many dedicated staff in the APS Publications Division (<https://journals.physiology.org/staff>). Some people look to the future and see challenges. We see opportunities to increase its impact and improve its quality. The best years are ahead of us.

CORRESPONDENCE

S. Matalon (smatalon@uabmc.edu).

ACKNOWLEDGMENTS

The author thanks Emma O'Hagan, Associate Professor of Library Sciences and Anesthesiology at the University of Alabama at Birmingham, for help with various historical references and Dr. Audra Cox from the American Physiological Society for help with editing this editorial.

DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the authors.

AUTHOR CONTRIBUTIONS

S.M. prepared figures, drafted manuscript, edited and revised manuscript, and approved final version of manuscript.

REFERENCES

1. Matalon S. In the shadow of giants: challenges and opportunities for the new editor of *Physiological Reviews*. *Physiol Rev* 98: 555–557, 2018. doi:[10.1152/physrev.00060.2017](https://doi.org/10.1152/physrev.00060.2017).

2. Appel TA. One hundred years of journal publication. **Am J Physiol Lung Cell Mol Physiol** 274: L455–L464, 1998. doi:[10.1152/ajplung.1998.274.4.L455](https://doi.org/10.1152/ajplung.1998.274.4.L455).
3. Maheu E, Zaim M, Appelboom T, Jeka S, Trc T, Berenbaum F, Maasalu K, Berenbaum F. Comparative efficacy and safety of two different molecular weight (MW) hyaluronans F60027 and Hylan G-F20 in symptomatic osteoarthritis of the knee (KOA). Results of a non inferiority, prospective, randomized, controlled trial. **Clin Exp Rheumatol** 29: 527–535, 2011.
4. Hoffman DJ, Powell TL, Barrett ES, Hardy DB. Developmental origins of metabolic disease. **Physiol Rev** 101: 739–795, 2021. doi:[10.1152/physrev.00002.2020](https://doi.org/10.1152/physrev.00002.2020).
5. Van Someren EJ. Brain mechanisms of insomnia: new perspectives on causes and consequences. **Physiol Rev** 101: 995–1046, 2021. doi:[10.1152/physrev.00046.2019](https://doi.org/10.1152/physrev.00046.2019).
6. Sriram K, Insel PA. Inflammation and thrombosis in COVID-19 pathophysiology: proteinase-activated and purinergic receptors as drivers and candidate therapeutic targets. **Physiol Rev** 101: 545–567, 2021. doi:[10.1152/physrev.00035.2020](https://doi.org/10.1152/physrev.00035.2020).
7. Ferrari C, Sorbi S. The complexity of Alzheimer's disease: an evolving puzzle. **Physiol Rev** 101: 1047–1081, 2021. doi:[10.1152/physrev.00015.2020](https://doi.org/10.1152/physrev.00015.2020).
8. Matalon S, Remme CA, Samson WK. *Physiological Reviews*: the past, the present, and the future. **Physiol Rev** 101: 733–738, 2021. doi:[10.1152/physrev.00001.2021](https://doi.org/10.1152/physrev.00001.2021).
9. Breunig CT, Koflerle A, Neuner AM, Wiesbeck MF, Baumann V, Stricker SH. CRISPR Tools for physiology and cell state changes: potential of transcriptional engineering and epigenome editing. **Physiol Rev** 101: 177–211, 2021. doi:[10.1152/physrev.00034.2019](https://doi.org/10.1152/physrev.00034.2019).
10. Riera-Domingo C, Audigé A, Granja S, Cheng WC, Ho PC, Baltazar F, Stockmann C, Mazzone M. Immunity, hypoxia, and metabolism—the menage a trois of cancer: implications for immunotherapy. **Physiol Rev** 100: 1–102, 2020. doi:[10.1152/physrev.00018.2019](https://doi.org/10.1152/physrev.00018.2019).
11. Ray A, Camiolo M, Fitzpatrick A, Gauthier M, Wenzel SE. Are we meeting the promise of endotypes and precision medicine in asthma? **Physiol Rev** 100: 983–1017, 2020. doi:[10.1152/physrev.00023.2019](https://doi.org/10.1152/physrev.00023.2019).
12. Staub NC. Pulmonary edema. **Physiol Rev** 54: 678–811, 1974. doi:[10.1152/physrev.1974.54.3.678](https://doi.org/10.1152/physrev.1974.54.3.678).
13. Matthay MA, Folkesson HG, Clerici C. Lung epithelial fluid transport and the resolution of pulmonary edema. **Physiol Rev** 82: 569–600, 2002. doi:[10.1152/physrev.00003.2002](https://doi.org/10.1152/physrev.00003.2002).
14. Pacher P, Beckman JS, Liaudet L. Nitric oxide and peroxynitrite in health and disease. **Physiol Rev** 87: 315–424, 2007. doi:[10.1152/physrev.00029.2006](https://doi.org/10.1152/physrev.00029.2006).
15. Tejero J, Shiva S, Gladwin MT. Sources of vascular nitric oxide and reactive oxygen species and their regulation. **Physiol Rev** 99: 311–379, 2019. doi:[10.1152/physrev.00036.2017](https://doi.org/10.1152/physrev.00036.2017).
16. Keeley TP, Mann GE. Defining physiological normoxia for improved translation of cell physiology to animal models and humans. **Physiol Rev** 99: 161–234, 2019. doi:[10.1152/physrev.00041.2017](https://doi.org/10.1152/physrev.00041.2017).
17. Cummins EP, Strowitzki MJ, Taylor CT. Mechanisms and consequences of oxygen and carbon dioxide sensing in mammals. **Physiol Rev** 100: 463–488, 2020. doi:[10.1152/physrev.00003.2019](https://doi.org/10.1152/physrev.00003.2019).
18. Ayer A, Zarjou A, Agarwal A, Stocker R. Heme oxygenases in cardiovascular health and disease. **Physiol Rev** 96: 1449–1508, 2016. doi:[10.1152/physrev.00003.2016](https://doi.org/10.1152/physrev.00003.2016).
19. Aggarwal S, Lam A, Bolisetty S, Carlisle MA, Traylor A, Agarwal A, Matalon S. Heme attenuation ameliorates irritant gas inhalation-induced acute lung injury. **Antioxid Redox Signal** 24: 99–112, 2016. doi:[10.1089/ars.2015.6347](https://doi.org/10.1089/ars.2015.6347).
20. Ahmad I, Molyvdas A, Jian MY, Zhou T, Traylor AM, Cui H, Liu G, Song W, Agarwal A, Jilling T, Aggarwal S, Matalon S. AICAR decreases acute lung injury by phosphorylating AMPK and upregulating heme oxygenase-1. **Eur Respir J** 2003694, 2021. doi:[10.1183/13993003.03694-2020](https://doi.org/10.1183/13993003.03694-2020).