

## BOOK REVIEW

**Annual Review of Physiology, 2022.** Mark T. Nelson and Kenneth Walsh (eds). Annual Reviews, 4139 El Camino Way, P.O. Box 10139, Palo Alto, California 94304-0139, USA. Vol. 84. viii + 654 pages. Price: US\$ 118.00.

Although not clustered under specific sub topics or systems, this volume of the *Annual Review of Physiology* has several focus areas.

About 17.9 million people died from cardiovascular diseases in 2019, accounting for 32% of deaths globally. Therefore, it is not surprising, that cardiac physiology continues to be a major focus of the *Annual Reviews* and is addressed in articles that relate to cardiac transverse tubules in normal physiology and in heart failure, the role of cardiomyocyte microtubules, adrenergic regulation of calcium channels in the heart (which has a small but welcome section on the history of our understanding of sympathetic nervous regulation of the heart), and the role of mineralocorticoid receptors in cardiovascular and cardio-renal disease. I found the article on the cardiac transverse tubules particularly engaging. Integral to the process of excitation–contraction coupling in the heart, the authors provide a clear and detailed account of the current state of knowledge and the issue of remodelling of T-tubules in heart failure. An important issue for future research is how therapies for heart failure can reverse or mitigate T-tubule remodelling and restore cardiac contractility. Optimizing therapies for heart failure is important, given the scale of the problem. In India, for instance, it is estimated that the incidence of heart failure could be anywhere between about half a million to close to two million per year.

The issue of energy metabolism and obesity is also the subject of several articles that assess the role of  $\beta$ -adrenergic receptors and adipose metabolism,  $\beta$ -arrestins as regulators of glucose and energy homeostasis, the implications of adipose tissue fibrosis in obesity and the role of mitochondrial  $H^+$  leak in thermogenesis. Obesity and its metabolic consequences are a health and economic issue. Thus, some estimates suggest that obesity-related diseases will cost India about US\$ 13 billion by 2025. This staggering figure seems likely to rise as we witness a continued increases in overweight and obesity in rural and urban areas. For those embedded in metabolic physiology, the article by Sheila Collins on the evolution of the role of  $\beta$ -adrenergic receptors in adipose tissue metabolism is a delightful read. Peppered with throwbacks to classical work

while addressing our present understanding, the article was a welcome mix of history and science for me.

Renal physiology is discussed in terms of newer understandings of renal cell types and structure–function relationships. These innate bacteriostatic mechanisms defend the urinary tract and mechanisms that underlie calcium nephrolithiasis. The kidney fulfils a range of excretory and non-excretory functions that include water, electrolyte and acid–base balance, elimination of waste products, regulation of blood pressure and secretion of hormones. Despite the large redundancy in kidney functions, such that we require only 30% capacity to fulfil a renal function, it is estimated that between 5 and 7 million people globally require renal replacement therapy due to end-stage kidney failure. I found the article ‘How many cell types are there in the kidney and what do they do?’ especially intriguing. This seemingly innocuous title masks the newer approaches to cell type definitions driven by transcriptomics, metabolomics and proteomics, which are a far cry from the earlier characterizations based on microscopic morphological appearance. Based on this characterization the article highlights the wider variations in cell types and the demarcation of function. It is an essential read for all students of physiology.

The article by Prashar *et al.* on how *Helicobacter pylori* evades host response is of special importance to researchers and clinicians in India, where infection with the pathogen can be in excess of 80% in some areas and where peptic ulcer disease, a sequela of the infection, affects over 20 million Indians. The article is a comprehensive update on how the pathogen not only survives, but flourishes in one of the harshest environments of the body – a churning, acidic stomach. It is written in a style that will appeal to the general reader without compromising on the details and nuances of research in the field. Another article pertaining largely to gastrointestinal physiology relates to the interesting phenomenon of paligenesis, where mature cells use evolutionarily conserved programmes to re-enter cell cycles and replenish damaged tissues. This process adds to our understanding of cellular replacement from stem cells. Paligenesis is a double-edged process – promoting repair on the one hand, while also possibly increasing the risk of cancer on the other. Several interesting questions arise: What causes the shift in repair from stem cells to mature cells? Can this process be regulated and reversed? What is its role in normal

physiology and in disease? I can see physiologists being engrossed in this article.

A common problem faced in hospitals is sepsis-induced immunosuppression. This is likely to increase with the demographic shift to an ageing population, the concomitant increased prevalence of co-morbidities and the use of immunomodulatory drugs. Thus, the article by Torres and colleagues on this topic is timely on several counts. First, it provides a comprehensive update on the mechanisms involved in sepsis-induced immunosuppression, which has been the subject of a considerable amount of work of late. Second, there is a review of current therapies that might negatively impact immune function, including the use of vasopressors and glucocorticoids. Third, biomarkers are listed which can be used to identify sepsis-induced immunosuppression and finally, potentially new therapies are discussed that may be used in this condition. The article is noteworthy because it provides not only an overview of the basic physiology of sepsis-induced suppression, but proceeds right through to the translational work aimed at finding new and more effective therapies.

One aspect that I like about the *Annual Review of Physiology* is that it often addresses issues which are relatively new and topical, and in a sense, stories in progress. In this volume, Park *et al.* discuss vaping and lung inflammation and injury. The rapid growth of ENDS (electronic nicotine delivery systems; the use of which is estimated to be 10% to more than 25% in middle school and high school students respectively, in the USA) has resulted in acute clustered outbreaks of severe respiratory distress with fatalities and has also emerged as a wider public health problem. The range of devices and the diverse array of e-liquids used to produce flavours that appeal to all people, has presented unique challenges to researchers. Current research shows that the effects of vaping are not only restricted to the airways and lung parenchyma, but also result in systemic effects in the brain, heart, liver and kidneys. While these data show unequivocally the harmful effects of vaping, the pathophysiology of EVALI (electronic cigarette or vaping use-associated lung injury) remains largely unknown because of the wide array of chemical additives used. This could be a major research area in the future, given the increasing use of ENDS and the absence of comprehensive regulatory systems regarding their use. A particular issue that needs to be addressed is the effect of ENDS on foetal outcomes when used by pregnant women.

Other articles in this volume address the pathophysiology of chronic obstructive pulmonary disease, small vessel disease in the brain, functions of membrane channels and alcohol-associated tissue injury, among others.

Overall, this volume of the *Annual Review of Physiology* provides comprehensive updates on cellular and molecular mechanisms in the areas that have been highlighted above. This allows us to understand the pathogenesis of disease better, identify new markers of early disease and disease progression, which help in prognostic evaluations, define

new targets for therapeutic intervention, and explore refinements to current therapeutic interventions to ensure greater specificity and fewer side effects. There is a significant focus on translational work in this volume. However, the gap between early translational work and actual clinical practice remains considerable. It remains to be seen to what extent the promise of early physiological work finds itself in clinical therapies. Physiologists reading the articles will sometimes need to contend with a different language and methods, that of epidemiology and clinical research, as basic researchers

attempt to ground their work in areas of clinical need.

This volume has an interesting mix of articles which address a wide readership. In my opinion, an editorial outlining the reasons for the choice of articles and the specific intent of this volume would have helped readers, especially students.

MARIO VAZ

*International Medical School,  
M.S. Ramaiah Campus,  
Bengaluru 560 054, India  
e-mail: mariovaz361@gmail.com*

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