there are many more applications that are not included in the book, I feel that the authors have covered some of the most important applications.

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Jane Goodall, the famed naturalist who is known for her work on chimpanzees, was recently awarded the prestigious Templeton Prize for 2021. Her work has brought into focus our role in maintaining the immense variety of life on this interconnected planet. As a medical physiologist, I have been dismayed at how comparative physiology has all but disappeared in courses that teach human physiology. This anthropocentric view of physiology is certainly detrimental to our broader understanding of life. Comparative physiology allows us to understand bodily function in an evolutionary context. It also brings to bear the scale of adaptation of physiological function. Thus, my interest was immediately drawn to the first article of this review on 'The remarkable cardiovascular system of giraffes'. The long neck of the giraffe presents a functional problem since blood pressures need to be maintained at the cranial end of the neck to allow for perfusion of the brain. At the same time, major haemodynamic shifts occur when giraffes stoop to drink water and then raise their heads soon after. Aalkjaer and Wang present an extremely lucid account of the noteworthy experiments that have been conducted to elucidate a better understanding of the cardiovascular physiology of the giraffe and the remarkable structural and functional adaptations in this animal.

The relationship between the kidney and cardiovascular function has been recognized for over 150 years, although the mechanisms involved were not initially known. The physiologists, Robert Tigerstedt and Per Bergman injected kidney extracts into rabbits and demonstrated a dramatic rise in blood pressure. In 1934, Harry Goldblatt established the first animal model of hypertension by constricting the renal artery in one or both kidneys. Subsequent research identified the role of renin and of the renal sympathetic nerves. Studying the renal sympathetic nerves in humans is particularly challenging, but has been extensively evaluated by Murray Esler and his colleagues in Australia by means of a radiotracer technique with labelled norepinephrine and regional blood vessel sampling using central venous catheterization. These studies have highlighted, among many others, the role of the renal sympathetic nerves in hypertension and heart failure. It is always exciting when research can be translated to improve human function and treat disease. In recent years, methods have evolved to denervate renal nerves. Sharp and Lefer, in their article on 'Renal denervation to treat heart failure' discuss the historical evolution of renal denervation and the current physiological understanding of its therapeutic role in heart failure with and without reduced ejection fractions. This is a topic of current and evolving interest, which should appeal to physiologists and clinicians.

Compared to other functional tissues, brown adipose tissue (BAT) has had a relatively recent history. It was identified as a thermogenic organ only in the early 1960s. Since then, the basis of its thermogenic effect and the role of uncoupling protein has been elucidated. The existence of BAT in adults was demonstrated in the 1980s and subsequent research has demonstrated that BAT can exist in dormant or competent states, that 'browning' of white adipose tissue can occur, and that BAT has effects on metabolic rate, insulin sensitivity and fat metabolism. Till date, however, BAT activity has not been conclusively linked to weight loss. Henningsen and Scheele in their interesting conceptual article 'Brown adipose tissue: a metabolic regulator in hypothalamic cross talk?' discuss the multiple interactions between the hypothalamus and BAT. This cross talk may provide an understanding of how the body weight set point is reset and could lead to the development of pharmacological targets against metabolic disorders and obesity. In another article 'Cellular heterogeneity in adipose tissue', Silvia Corvera describes how adipose cells even when structurally similar can have remarkably different functional characteristics, as for instance in their adipogenic capacity. This article raises more questions than it answers at this stage of our understanding – to what extent is the heterogeneity in adipocytes regulatable, and by what? What are the implications of this heterogeneity in health and disease?

Atrial fibrillation (AF) is a cardiac arrythmia, the occurrence of which increases with age. More than 20% of strokes are attributable to atrial fibrillation which also increases cardiovascular morbidity and mortality by over twofold. While AF is associated with a range of comorbidities and risk factors such as advanced age, heart failure, hypertension, valvular heart disease, cardiac surgery, obesity, alcohol consumption and even exercise, these act through relatively constrained pathways including the autonomic nervous system, the renin–angiotensin–aldosterone system, inflammation, and volume-pressure changes in the heart. The article 'Dynamics of atrial fibrillation. Mechanisms and comorbidities' reviews the understanding of the cellular physiological mechanisms of AF in these various comorbidities to better delineate the dynamic nature of AF risk factors and subsequent AF risk. This is clearly an important area of research given the scale of this clinical problem.

Tamm-Horsfall protein, the most abundant urinary protein in physiological conditions, was rediscovered in the 1980s, as uromodulin. Produced by the epithelial cells of the thick ascending limb of the Loop of Henle and the Distal Convoluted Tubule the last few decades have revealed a wide range of functions including protection against urinary tract infections and kidney stones, renal sodium, calcium and magnesium transport, and immunomodulation. The article 'Uromodulin: roles in health and disease' is a very well written paper of a story in evolution. For, while the putative functions of uromodulin have been extensively described, the clinical use of uromodulin (in urine and serum) as a biomarker of renal function and in the prognosis of disease, especially chronic kidney disease, continues to be explored and refined.

Ever since Hans Selye proposed three stages of a general adaptation syndrome to stress and Cannon's earlier work on the role of the 'symapthicoadrenal' system, physiologists have sought to understand the biology of stress and its implications in disease. Regarding this aspect, a welcome shift is an article entitled 'Sestrins in physiological

stress responses' which focuses on Sestrins that help the body to adapt to physiological stresses, resist stress and restore homeostasis. Sestrins are activated in response to a host of stressors including oxidative stress, immune stress, hypoxia, and a variety of nutritional stresses, among others. They work across organs including the liver, heart and skeletal muscle and evoke a wide range of responses. In the liver, for instance, they preserve hepatic insulin sensitivity, maintain hepatic endoplasmic reticulum homeostasis, and suppress hepatic stellate cell activation and inflammation, reducing fibrosis. It is interesting that caloric restriction and exercise training induce Sestrins and contribute to 'hormesis' – the adaptive responses of cells to intermittent stress that are ultimately beneficial for health. This underscores, despite all other advances, the age-old wisdom of paramount importance of healthy lifestyles and behaviour.

As with previous editions, the compilation of articles is divided into organ-based sections. There is no special section in this Annual Review, where multiple articles address a single theme and as has been the case for several years now and no prefatory chapter that focuses on the life and work of a distinguished scientist. Other articles in this issue relate to cardiac regeneration, biology of calcium in terms of voltage-gated calcium channels and mitochondrial calcium uptake, temperature sensation, olfactory circuits and the physiology of lung repair, and pulmonary hypertension, among others.

William Osler, the noted Canadian physician and 'Father of Modern Medicine' in his Yale University lectures on the History of Medicine alluded to the progression of truth, which was integral to its practical application. In the present Annual Review, I was happy to see several articles which traced earlier work while unfolding the minutiae of our current understanding. This historical preface, I believe, is essential for a student of the subject, if we are to appreciate the enormous efforts that have contributed to our contemporary insights. A historical understanding also helps curb the unrestrained hubris that so often characterizes current perceptions of knowledge.

In a rapidly changing field, the task of the editors to choose articles is an unenviable one. In this Annual Review, I believe that the editors have performed very creditably with a mix of articles across organ systems which appeal to the basic scientist, the clinical researcher and the clinician.

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