“Change in all things is sweet” (Aristotle in Nicomachean Ethics, c. 350 BCE). Aristotle recognized that change in our world occurs naturally and can be both good and bad. Today, we recognize that adaptation is an essential physiological process by which our physiology changes in response to stressors of all sorts; some intrinsic and related to our natural life span, others environmental and related to the world in which we live, and still others that are self-inflicted and far too often destructive. Physiological adaptation can occur at different levels, from the molecular and subcellular level to whole cells, tissues, and organisms. It is now clear that many adaptive mechanisms evolved to enhance survival, but others provide no benefit or underlie disease conditions.

In this issue of Physiology, a clear example of physiological adaptation at the integrated whole organism level is evident by the response of some large mammals to climate change. Similarly, our adaptive responses to changing levels of oxygen, particularly hypoxia, are crucial for survival. In another review in this issue, the molecular mechanisms linking oxygen sensing and apoptotic cell death are discussed in the context of adaptive responses. As is evident by this review, the mechanisms underlying physiological adaptation are complex. In recent years, we have learned that physiological adaptation can involve epigenetic modifications that are heritable changes in gene activity without modifications of the DNA sequence itself. Another review within this issue explores epigenetic alterations involved in chronic lung diseases. As pointed out in this and other previous articles published in Physiology, adaptive responses can be triggered by our own lifestyles. For example, obesity is a major human problem that is linked to adaptive and maladaptive changes across a number of physiological systems. Similarly, as discussed in another review within this issue, alcohol abuse can lead to maladaptations triggering a variety of associated diseases. It is clear that physiological adaptations are important in both health and disease, so our interest in understanding underlying mechanisms is well justified. We are only scratching the surface, and, lucky for us as scientists, there is so much more to learn.

Global warming is a fact of life, and we all should be concerned about how we will adapt to this changing world. If large mammals are to survive the hotter, drier habitats in a climate-changed future, they will have to rely on their ability to alter their physiology. Genetic adaptation to climate change is unlikely because large mammals reproduce slowly and are long-lived. Human-made barriers also will prevent them from moving to more suitable environments, and their large body size limits microhabitats available for thermal refuge. In their review (2), Fuller et al. discuss how large arid-zone mammals, such as goats, oryx and kangaroos, alter their behavior and physiology to buffer hotter and drier environments. Traditionally, such studies investigating physiological adaptation have relied on measurements made from animals housed under artificial laboratory conditions. Although these investigations have yielded valuable insights, they do not accurately predict how animals function in their natural environment. Stress responses with human observers nearby also confound normal physiological and behavioral responses of the animals. In their studies, Fuller and colleagues use data obtained by biologging in free-living mammals. A detailed understanding of free-living mammalian physiology, such as thermoregulatory behavior, body temperature variability, and selective brain cooling, is required to accurately predict future ecological patterns and conserve biodiversity.

During evolution, global changes in oxygen availability became so important that physiological adaptation was required. The development of complex circulatory, respiratory, and neuroendocrine systems was necessary to maintain appropriate oxygen delivery to all tissues. These systems were accompanied by physiological mechanisms for sensing oxygen levels and providing adaptive responses to hypoxia (broadly defined as oxygen demand exceeding oxygen supply). Hypoxia usually results in a decrease in cellular function and, eventually, to cell death. Many of the physiological responses to hypoxia are orchestrated by the heterodimeric transcription factor hypoxia-inducible factor (HIF). In their review (6), Sendoel and Hengartner discuss the link between HIF and apoptosis, a programmed and highly controlled type of cell death. Mitochondria, the key organelles for energy production, constitute an important link between energy production and cell death signaling. An acute hypoxic event, such as stroke, can lead to cell death by both necrosis and apoptosis where the cell is not lethally damaged yet activates apoptosis. Similar apoptotic cascades are thought to occur during myocardial infarction. Understanding the molecular mechanisms underlying the induction of apoptotic cell death may lead to new therapies for diseases such as stroke, myocardial infarction, and cancer.

Chronic respiratory diseases are a major cause of disease and death worldwide. Many of these diseases appear to be driven by environmental exposure to pollutants triggering physiological adaptation. The prevalence of these respiratory diseases is higher in some families but with no clear genetic basis. The study of inheritable changes to gene function without alteration of the gene sequence is known as epigenetics. In his review (3), Haggood discusses the importance of epigenetic alterations underlying physiological adaptation in chronic lung diseases such as idiopathic pulmonary fibrosis, chronic obstructive pulmonary disease, bronchopulmonary dysplasia, and pulmonary hypertension. A better understanding of the impact of epigenetic alterations on lung physiology has become an integral part of our understanding of the complex processes of tissue remodeling in multiple lung diseases and is likely to provide many breakthroughs that will improve quality and quantity of life for millions.
Physiological adaptation is an intrinsic process throughout our life from conception to death. In the beginning of our lives, successful embryo implantation involves three distinct processes: embryo apposition, attachment, and penetration through the luminal epithelium of the endometrium to establish a vascular link to the mother. After penetration, stromal cells underlying the epithelium differentiate and surround the embryo to form the embryo implantation barrier, which blocks the passage of harmful substances to the embryo. In their review (4), Liu and colleagues discuss new insights about the contribution of ion/water channels to embryo implantation barrier construction during early pregnancy. Although ion/water channels can be expected to act as classical channels in establishing and shaping membrane potential, various other functions, such as triggering cellular signaling pathways via ligand-activated effects, have been observed during embryo implantation. A better understanding of the links between embryo implantation and ion/water channels should provide new insights into the physiological basis of natural and assisted human reproduction.

We are all tempted by the abundance of food in our lives, and for some the normal homeostatic processes that are important in balancing energy supply and demand are abrogated, leading to obesity and physiological adaptation. Excess weight gain is the most significant, preventable cause of elevated blood pressure in patients with primary (essential) hypertension. However, the mechanisms by which obesity increases arterial pressure remain unclear. In their review (1), da Silva and colleagues discuss the importance of the brain melanocortin pathway in linking obesity with increased sympathetic nerve activity and elevated blood pressure. In humans, reduced function of melanocortin 4 receptors (MC4R) causes morbid obesity; yet these individuals do not exhibit increased sympathetic nerve activity and have a lower incidence of hypertension compared with obese controls. Thus, the brain melanocortin system, in particular the MC4R, appears to be a major regulator of appetite and body weight homeostasis that also controls sympathetic nerve activity and blood pressure. Although MC4R activation promotes weight loss and could be a good anti-obesity therapy, its negative effects on sympathetic nerve activity and blood pressure preclude its use. A better understanding of the mechanisms by which MC4R exerts its actions on energy balance and cardiovascular function may offer new approaches to treatment of obesity and cardiovascular disease.

Alcohol abuse is the most common and costly form of drug abuse and the third leading lifestyle-related cause of death in the United States. It plays a major factor in many diseases, including cardiovascular and liver disease, stroke, and infections. Alcohol permeates all tissues in the body and can cause tissue injury and predispose to a secondary challenge such as an infectious disease. In addition, because alcohol abuse is frequently a chronic condition, the cumulative burden to the host in maintaining homeostasis produces marked derangements in multiple physiological processes. In their review (5), Molina et al. discuss the principal mechanisms of nonneuronal tissue and organ injury and their contribution to alcohol-associated comorbid conditions. Although some of these conditions, such as in the liver, are well recognized, other organs (e.g., the lungs and skeletal muscle) are less frequently recognized as targets for alcohol-induced tissue injury. Research on the biomedical consequences of alcohol abuse is critical to better inform the general public, biomedical researchers, and health care providers about prevention and intervention measures that can decrease the impact of chronic alcohol abuse.

References