

above' in the words of Ralph W. Emerson to the 'center of digital life below' as propounded by Steve Jobs, the author Richard Hamblyn provides a multifaceted narrative on nature's most versatile creation. Packed with colourful pictures, this book could easily be the most comprehensive and authoritative text on the subject. And, indeed it is.

Hamblyn, an English lecturer at the University of London, has attained undisputed mastery on the subject, having already published two books on clouds – *The Cloud Book* and *Invention of Clouds*. While the first book captures all things to do with the origin and development of clouds, the second is a cultural excavation on understanding the science of clouds. In this his third book, Hamblyn has brought clouds down to earth and unveiled their mysteriousness. Throughout human history attempts to understand clouds and their behaviour have been a subject of delight and fascination, offering limitless source of creative contemplation, from Socrates to Seneca and from Kalidas to Ruskin. Each attempt has helped in presenting a different story.

This book emerges as a magnificent collection of these stories – from their woolly journey through art, literature, music and photography, to their sinister manipulation for military use and anthropogenic modifications. American (failed) attempts at precipitating flash floods during the Vietnam War are part of the legend. Such secret military trials have invoked widespread concern from international community to declare clouds as 'a resource that belongs to no one'. Legal remedies for trespassing territories for appropriating clouds through artificial seeding would need to be curtailed as competition over access to rainwater escalates.

Since science is only beginning to understand the role of clouds in shaping future conditions on earth, a warm atmosphere may reorganize the day-to-day behaviour of clouds that could either amplify or mitigate climate change. The trouble, warns Hamblyn, is that clouds have a habit of behaving in complex and surprising ways. The fact that our warming climate is producing ever more lightning strikes is one of many surprises that clouds have in store. Each 1° rise in temperature increases lightning activity by around 12%. Will clouds turn out to be agents of global warming or will they end up saving the day by reflecting ever

more sunlight back into space remains unanswered?

It is evident that clouds are challenging human intelligence. Philosophers like Aristophanes, who always had their heads in clouds, had long professed that 'from clouds come our intelligence, our dialectic and our reason; also, our speculative genius and all our argumentative talents'. Wondering if clouds were objects or phenomenon or processes, Leonardo da Vinci had described them as formless triggers of visual invention; their fleeting magnificence and endless variability provides food for thought for scientists and daydreamers alike. The current predicament with clouds is taking us back in time to reimagine and re-understand clouds. There may be clues in arts and literature to make a fresh beginning.

Hamblyn's contention is that the law of unintended consequences needs to be kept in mind while embarking on geo-engineering projects that tamper with the atmosphere and clouds. Clouds are too sensitive not to be taken into account in such anthropogenic adventures, he cautions. In short, it is clear that there is no way of knowing what is really going to happen to our increasingly changing atmosphere, and just as in centuries past, when clouds were employed as ready metaphors of doubts and uncertainty, it looks as if they will continue to be so for centuries to come.

The crucial issue is that life without clouds would not be physically possible. Far from just being a source of water, these have a larger role in keeping the earth hospitable to living beings. The book provides insights into the history and science of clouds, and acts as a guide to pursue mankind to get a sensitive handling on the woolly product/process hovering between sky and the earth. Cogent and colourfully illustrated, this is the ultimate guide to the past, present and future of clouds.

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The personal reflections of a scientist, which has been part of so many earlier *Annual Reviews of Physiology*, is missing in this particular volume. I found that disappointing – there is something about being taken along a life's journey, sharing the pain, tribulations and ultimate triumph that has marked the lives of so many great scientists. Personal reflections allow scientists to share the uncertainties that they have faced and the measures they took to overcome them. These are lessons which are increasingly difficult to understand from published scientific papers, given the constraints of space and editorial oversight.

The special topic in this volume focuses on 'macrophages'. An understating of these cells has moved a long way from the 'scavenger' status that they were originally and solely endowed with. There are four articles devoted to macrophages. Peter Murray focuses on how macrophages are activated in space and time – a phenomenon called macrophage polarization. He provides a succinct timeline on a historical perspective of macrophage polarization and discusses various misconceptions that have existed. The article is comprehensive and covers issues of macrophage polarization in inflammation, its regulation and macrophage survival, among others. Hamidzadeh and colleagues focus on macrophages and recovery from acute and chronic inflammation. An important part of their article which will be of relevance to clinicians is the discussion of macrophage activation syndrome – a failure to regulate macrophage activation during inflammation. Macrophages can regulate tissue regeneration following injury and can also worsen tissue injury. Vannella and Wynn discuss how macrophages help in tissue repair across a range of organs and tissues, including the liver, heart, lungs, nervous system and intestine. The nature and role of glial cells have had an interesting history involving people like Rudolf Virchow and Ramon y Cajal. Microglia, which are the phagocytes of the brain and which play an important role in coordinating the immune response

## BOOK REVIEWS

of the brain are discussed by Wolf and co-workers.

Two articles in the section on cardiovascular physiology address the domain of developmental biology. Bikram Sharma and colleagues focus on 'Coronary artery development: progenitor cells and differentiation pathways', while Wu and co-workers address the 'Developmental mechanisms of aortic valve malformation and disease'. Both these issues have considerable health implications. Coronary artery disease is the major cause of mortality worldwide, while a calcific aortic valve may affect as much as 25% of the aged population and some studies indicate that 2% of newborns have some developmental abnormality of the aortic valve. A developmental biology approach to these problems is important, and has the potential to identify new therapeutic targets in the long term. Potente and Carmeliet address the issue of angiogenesis, or new vessel formation and endothelial metabolism. Conventional approaches to the role of endothelial cells in angiogenesis have focused on how these cells coordinate and migrate and proliferate in response to growth factors to form new vessels. In order to achieve these ends, however, endothelial cells need to also address their own changing metabolic demands. This is the focus of the article entitled 'The link between angiogenesis and endothelial metabolism'.

The increasing prevalence of obesity worldwide and its consequences in terms of disease morbidity and mortality continue to challenge the medical profession. In morbid obesity, one of the therapeutic options is bariatric surgery such as gastric bypass and partial gastrectomy, among others. In the United States as many as 200,000 such procedures are performed annually, and these surgeries are becoming increasingly commonplace in India as well. Bariatric surgery is associated with greater and more durable weight loss and better glucose control. While the weight loss would intuitively account for a considerable amount of the health benefits achieved, Evers *et al.* focus on the weight loss-independent mechanisms of benefit in their article entitled 'The physiology and molecular underpinnings of the effects of bariatric surgery on obesity and diabetes'. Areas that they cover include increases in gastric emptying, fluctuations in gut peptides and hormones, micronutrient absorption

and changes in pancreatic morphology and in the gut microbiome. Of relevance to obesity and food intake is another article by Sternson and Eiselt entitled 'Three pillars for the neural control of appetite'. The authors indentify the three pillars as: (1) the agouti-related protein expressing neurons in the hypothalamic arcuate nucleus which elicit food intake when activated; (2) various circuits of the lateral hypothalamus (the classical 'feeding centre' identified by lesioning and stimulation studies; and (3) calcitonin gene-related peptide neurons in the parabrachial nucleus that strongly suppress eating when activated.

Chronic obstructive pulmonary disease (COPD) is a global problem linked to smoking throughout the world and to both indoor and outdoor air pollution in developing countries. In India, non-smoking women who cook food with firewood or agricultural residue in poorly ventilated huts are a particularly susceptible group and exposure of children to these pollutants is a special concern. Peter Barnes in his comprehensive article entitled 'Senescence in COPD and its comorbidities', discusses the pathophysiology of COPD in terms of accelerated lung ageing. He also reviews potential therapeutic targets and outlines the role of pharmacological and lifestyle interventions. 'Mitochondrial dysfunction in lung pathogenesis' is discussed by Pianadosi and Suliman. Mitochondria are now known to have a host of new roles beyond being the 'powerhouse' of the cell. They are critical monitors of oxidation-reduction processes and this has implications in inflammasome activation, cell proliferation and prevention of fibrosis. Mitochondria also have important roles in cell signalling and apoptosis. The authors discuss the role of mitochondria in a host of lung pathologies, including acute injury and chronic inflammation in the lungs, fibro-proliferative diseases and lung cancer. They also highlight the promise and limitations of mitochondrial quality control as a therapeutic target in lung diseases.

In 1954, Andrew Huxley who later won the Nobel Prize for Physiology and Medicine (1963) together with Alan Hodgkin, described in *Nature* (Huxley, A. F. and Niedergerke, R., 1954, **173**(4412), 971-973), the structural changes in muscle during contraction using interference microscopy. A year earlier and in the same year, i.e. 1954,

his namesake (unrelated) Hugh Huxley together with Jean Hanson also elaborated upon the nature of muscle contraction in two separate articles in *Nature*. The work of the two Huxley's, Hanson and Niedergerke (who worked with Andrew Huxley) all contributed towards the sliding filament theory of muscle contraction. Huxley and Hanson observed that myofibrils retain elasticity even after the removal of the thick and thin filaments, and proposed the existence of an additional elastic filament. Lidstredt and Nishikawa explore this 'missing' filament in their article entitled 'Huxley's missing filament: form and function of titin in vertebrate striated muscle'. The article is comprehensive – it builds on a vast body of earlier work that has spanned many decades (historical and evolutionary), before focusing on the current understanding of titin, which at 4.2 MDa is the largest known protein. The role of titin in the development of tension in skeletal and cardiac muscles is discussed in detail as also the 'winding filament hypothesis', which attempts to explain the nature of titin-filament interactions during changes in sarcomere length.

In order to cater to the varied interests of physiologists, this volume, as in earlier editions, is divided into sections: cardiovascular physiology, cell physiology, ecological, evolutionary and comparative physiology, endocrinology and metabolism, gastrointestinal physiology, neurophysiology, renal and electrolyte physiology and respiratory physiology. However, the downside of this is that at a time of increasing specialization, there may well be nothing for many. The task of the editors in this context, is unenviable – the need to balance, basic science with its applications, work of current value with that of potential value for the future, and the interests of a diverse group who all see themselves as physiologists. Despite these limitations, the *Annual Review of Physiology* will continue to be an important resource for reference in libraries and for people engaged in the field. It has certainly been so for me.

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