

Annual Review of Nutrition, 2022. Patrick J. Stover and Rudi Balling (eds). Annual Reviews, 1875 S. Grant Street, Suite 700, San Mateo, California 94402, USA. vol. 42. x + 480 pages. Price: US\$ 118.

The current volume of the *Annual Review of Nutrition* continues the tradition of the series by providing a deep dive into a diverse array of topics, such as personalized nutrition, the impact of the gut microbiome on health and the nexus between nutrition and environmental sustainability that collectively shape our understanding of the vital role of nutrition in human health and well-being. There is also an article on 'A female career in research' by Katherine Flegal. Flegal narrated a thought-provoking and insightful exploration of the challenges women encounter in pursuing scientific research, including the Matthew and Matilda effects and the unconscious bias based on gender. This article not only addresses the gender disparities that have long been evident in various disciplines but also serves as a valuable source for researchers, policy-makers and institutions to create a more equitable ambience for women pursuing scientific research.

The article by Guccio *et al.* provides a comprehensive overview of how a 42-amino acid long peptide, glucose-dependent insulinotropic polypeptide (GIP) became an incretin hormone capable of potentiating glucose-dependent insulin secretion from pancreatic β -cells and physiological importance of GIP axis. It highlights the therapeutic potential of the GIP receptor and glucagon-like peptide receptor agonists in people with T2D. Further, it also touches upon the role of incretins in adipose tissue, bone, CNS and the nutritional and hormonal stimuli that can induce or inhibit its secretion.

Obesity has tripled since 1975, and according to the WHO¹, over a billion people worldwide are obese. In addition to other life style changes, such a steep rise is attributed to excess energy intake relative to energy expenditure, and in this context, one of the most significant changes in food consumption in modern society was the increased intake of fructose. Jung *et al.* have comprehensively examined the historical trends in fructose consumption, delved into biochemical and molecular pathways involved in fructose metabolism in various organs and its interaction with gut microbiota. This review also describes the critical role of fructose in the development of metabolic diseases such as non-

alcoholic fatty liver, type 2 diabetes, CVD, cancer and kidney disease. Finally, it sheds light on the lingering questions surrounding the treatments of these ailments. Obesity significantly impairs both the response to influenza infection and the effectiveness of vaccination. These effects arise from a complex interplay of mechanisms encompassing dysregulated innate and adaptive immunity. Thus, it is imperative to understand how obesity diminishes the capacity to mount an effective response against viral infections. In this context, Shaik *et al.* delve into a body of research encompassing both human and animal studies related to influenza infection and vaccination, revealing the detrimental impact of obesity on immune function. This review also identifies the gaps in knowledge, particularly concerning diet and nutrition. It suggests investigations into several key areas, such as how heterogeneity of obesity contributes to immune dysregulation, the role of dietary fat on inflammation and infection, and assessing the impact of gut and lung microbiome profile of the host on susceptibility to disease.

Non-alcoholic fatty liver disease (NAFLD), associated with obesity, encompasses a range of relatively benign hepatic steatosis to more severe non-alcoholic steatohepatitis (NASH). Recent research has illuminated the pathophysiology of NAFLD/NASH, shedding light on the role of genetic, epigenetic and dietary factors, as well as metabolic dysfunctions in various tissues, all contributing to excess hepatic fat accumulation and liver injury. Single-cell RNA sequencing studies have also provided insights into the molecular intricacies of liver cell heterogeneity, intrahepatic communication, and reprogramming of the liver immune and stromal vascular microenvironment. Rui and Lin present the latest advancements in these areas, highlighting emerging concepts of NASH pathogenesis and exploring potential novel therapeutic avenues.

A substantial body of evidence indicates ceramides as lipotoxic contributors and potent biomarkers in nutrition-related chronic diseases. Addressing the bottleneck of harmonizing sphingolipid measurement methods and establishing reference populations is imperative. Furthermore, it is essential to develop effective strategies for lowering ceramide levels to reduce hyperceramidaemia-related cardiometabolic disease risk. Nicholson *et al.* provide an in-depth exploration of our current knowledge regarding the biochemical pathways governing cera-

mide synthesis, production and action, and their functional roles. They also delve into how dietary factors impact ceramide levels and explore the potential utility of circulating ceramides as clinical biomarkers of metabolic disease. Furthermore, they discuss the intricate molecular mechanisms that connect ceramides to altered metabolism and cell survival and the development of nutritional or pharmacological approaches aimed at reducing ceramides in therapeutic ways.

Litichevskiy and Thaiss provide an in-depth investigation of the oscillating gut microbiome by exploring the fascinating connection between host circadian biology and gut microbiota. The authors have thoroughly reviewed the characteristics of the dynamic gut microbiome, uncovering its origins through factors such as feeding-fasting cycles, nutritional content, microbial circadian clocks, and other contributing elements. The profound effects of the gut microbiota on the circadian rhythms of the host and how it affects span changes in host gene expression, fluctuations in serum metabolites and sex hormones, shifts in host immune function, and alterations in host lipid absorption are discussed.

The chapter by Wells *et al.* sheds light on the crucial role of the intestinal barrier in safeguarding infants against infections and allergies. Through a meticulous analysis of microbiota, mucus, immune responses and their interplay, the authors unveil the intricate defence mechanisms at play. The review underscores the significance of early life nutrition, including breastfeeding, in nurturing intestinal health and immunity and mitigation of infection risks. Further, the crucial role of nutritional components such as milk components along with probiotics, prebiotics and micronutrients in maintaining the integrity of the intestinal barrier in infancy is emphasized.

Fang *et al.* describe the origin, evolution and future of dietary methionine restriction, wherein they explain the effects of dietary methionine restriction (MR) and its metabolic effects on energy balance, insulin sensitivity, lipid metabolism and inflammatory markers in liver and adipose tissue. While dietary MR can be used as therapeutic diets for reduction of body weights without food restriction, the major obstacle in developing MR as therapeutic diets is poor palatability and compensating effects of MR by cysteine. An alternative approach to dietary MR that reduces methionine and cysteine content by targeted oxidative deletion of sulphur amino acids is also touched upon. There is a chapter that reviews studies on

sex dimorphism in nutrition research and uncovers disparities in nutrient intake, nutrient metabolism, nutrient restriction and dietary interactions with the gut microbiome based on gender. Within each of these domains, the influence of sex chromosomes, sex hormones, and sex-specific loci is emphasized. In the end, a comprehensive understanding of the relative contributions of hormonal and genetic factors to sex differences sets the stage for crafting tailored, efficient and personalized medical and dietary recommendations, aiming to optimize health outcomes for humans of both genders.

Ferroptosis is a form of cell death regulated by many nutritional and metabolic modulators such as antioxidant and iron-homeostasis. The review by Mishima *et al.* highlights the physiological role and implications of ferroptosis in diseases like cancer, ischemia-reperfusion injury, neurodegenerative disease and COVID-19. Importantly, this article delves into the topic of how targeting ferroptosis by pharmacological approach or metabolic reprogramming has great potential for the treatment of ferroptosis-associated diseases.

Iron – heme and non-heme are essential for maintaining good health, but they can become harmful when present in excessive amounts. Therefore, the body tightly regulates levels of iron and heme to ensure they are sufficient for biological functions but are nontoxic. Iron's ability to transition between Fe^{2+} and Fe^{3+} contributes to its biological function but can also make it toxic in excess. In their review, Dutt *et al.* explore the molecular and physiologic aspects of iron and heme metabolism. They focus on various aspects, including dietary absorption, cellular import, utilization, export, recycling and elimination, with an emphasis on recent findings. They also discuss the current challenges and needs in the field of iron and heme biology.

There is one review that retraces the historical journey that led to the recognition of selenium (Se) as an essential nutrient. It delves into Se-responsive diseases in both animals and humans, providing insights within the contemporary context of our understanding of the molecular mechanisms underlying these conditions. It also provides a comprehensive examination of various aspects, including dietary sources, nutritional utilization, metabolic functions, and dietary requirements of Se across diverse species. In addition, a comparison between the roles and regulation of selenogenomes and selenoproteomes in rodents, food animals, and humans is provided. Further, it

identifies research areas that are important for advancing both fundamental scientific knowledge and practical applications of dietary Se in the realms of food, nutrition, and health across species.

Forde and Decker review the critical relationship between food processing, eating behaviour, and promoting of healthy and sustainable diets. While food processing is crucial for preserving and providing accessible, nutritious, and sustainable food options worldwide, it also presents health challenges due to the formation of harmful substances like acrylamide and the potential for excessive levels of salt, sugar, and fat in processed foods. They discuss how different levels of food processing, including ultra-processing and formulation, can influence energy intake, dietary choices and chronic diseases. Despite these concerns, food processing and formulation offer an opportunity to leverage technological advancements and ingredient innovations to create foods that reduce the risk of over-eating, ultimately contributing to a safer and more sustainable food supply.

National dietary surveillance studies play a pivotal role in generating crucial dietary intake data for diverse purposes, including the development and assessment of national food and nutrition policies. However, there is a need for regular innovations to enhance data collection methods, improve data quality, and ensure relevance. Moshfegh *et al.* evaluate the strengths and limitations associated with current and emerging methods in national dietary data collection. They emphasize the utilization of technology and emerging technological applications to bolster the effectiveness of data operations. In pursuit of this, they outline some goals for national dietary surveillance that should guide the future dietary surveillance programs. It is imperative to harness the potential of new technologies to enhance efficiency and objectivity in data collection processes while continuing to collect accurate dietary information that is standardized, validated, and publicly transparent. This is very relevant for many national nutritional surveys in India for efficient and accurate dietary data collection, considering the large sample size and diversity in dietary patterns/intakes.

A chapter by Crider *et al.* reviews the basic metabolic aspects of folate (FA) and its role in the prevention of birth defects, particularly neural tube defects (NTDs). It provides an overview of 30 years of the journey of folic acid supplementation, including mandatory FA fortification and the

impact of these programs on NTD and blood folate concentrations. Mandatory FA fortification in many countries alleviated the NTD rates and increased the serum FA without adverse outcomes. This chapter also discusses the epidemiological risk factors such as diabetes, obesity, B12 deficiency, and other factors in inducing NTD, emphasizing the need for population-based studies on RBC folate concentration. Further, it suggests addressing the concerns about the safety and effectiveness of the FA program, such as effects of interaction between high folate and low B12 status on anaemia, metabolism, and cognition and potential effects of antenatal maternal FA exposure and risk of developing cardiometabolic diseases. In this context, it may be mentioned here that, based on RBC folate levels, a high national prevalence of FA deficiency in Indian children (23–26%) and adolescents (36%) was reported².

Kumanyika reviewed the prevalence of obesity worldwide with emphasis on disparities in obesity prevalence by racial/ethnic and other socially marginalized populations. It describes evidence of progress in equity-focused obesity efforts such as supplemental nutrition programs for women, infants and children, retail food access and the supplemental nutrition assistance program, school meals, etc. Kumanyika suggests that health equity in obesity is an achievable goal subject to the ability to solve the epidemic overall, with targeted efforts directed to populations of colour and low-resource communities while hinting at the challenges for achieving this goal. Some recommendations are made for accelerating the progress in equity-focused efforts to reduce obesity.

In summary, the current volume is a remarkable compilation that encapsulates the current trends, breakthroughs, and research directions within the realm of nutritional science. Its well-structured and thoughtfully curated content makes it an indispensable resource for anyone seeking a comprehensive understanding of the dynamic field of nutrition.

1. <https://www.who.int/news-room/fact-sheets/detail/obesity-and-overweight>
2. Shalini, T. *et al.*, *Nutrients*, 2023, **15**(13), 3026; doi:10.3390/nu15133026.

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