



Book Review

Mosaic of autoimmunity: The novel factors of autoimmune diseases, 1st edition, C. Perricone, Y. Shoenfeld, editors (Academic Press, London) 2019. 728 pages. Price: Not mentioned.

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This book is a comprehensive treatise covering the totality of physiologic response including hormonal and neurologic, besides host immunity leading to the development of autoimmunity and autoimmune diseases (AIDs). It has 65 chapters arranged together in six theme-based sections with over 160 authors contributing to the content.

The section, ‘Cellular and Molecular Mechanisms’ has 16 chapters describing in detail the morphologic and functional characteristics of cells of the immune system, providing specific evidence of their participation in the pathophysiology of various AIDs. The classification criteria of rheumatic AIDs based on clinical features supported by the occurrence of specific autoantibodies have been well presented. Similarly, a full chapter has been devoted on the complement system and autoimmunity, highlighting the pathways of complement activation and regulation. The chapter on cytokines and chemokines describes their signalling role in coordinating an effective immune response in health and disease, with particular focus on rheumatoid arthritis and systemic lupus erythematosus (SLE). The description has been made easier with the inclusion of tables and figures.

The genetic and epigenetic aspects of autoimmunity provide the reader with the much-needed basic information, highlighting the fact that the clinical outcome of disease follows a complex interaction between host genetics, environment, hormonal influences and immunological factors. The advent of next-generation sequencing technology has opened up new vistas for genome-wide association studies in defining key molecular pathways of AID pathogenesis and towards biomarker discovery. Several AIDs have shown a strong association with specific human leucocyte antigen (HLA) alleles in various populations, often sharing the same HLA

haplotype. The book provides an in-depth analysis on the possible influence of several other genes that might influence disease susceptibility. These include cytokine genes, those associated with B- and T-cell-mediated or TH17 pathways, tyrosine kinase family of genes, STAT4 and many other non-HLA genes. Further accumulating evidence suggests the involvement of epigenetic mechanisms in immune regulation and pathogenesis of autoimmune disorders. There is discussion on how environment triggers promote epigenetic changes contributing to a disease like lupus, explore the interaction of epigenetic modifications and investigate the possible relationship between epigenetics and transcription factors. The reader will find the discussion stimulating and challenging towards developing personalized strategies for therapy of specific AIDs.

Cytokines and chemokines are the key signalling molecules that promote communication and coordination for generating an effective immune response. While their dysregulation is fundamental to autoimmunity, modulating their activity could be therapeutic for AIDs as described in Chapter 15. Autophagy has an important role in many biological processes, and an understanding of its involvement in the aetiopathogenesis of AIDs could be exploited for the development of new diagnostic and therapeutic strategies. An elegant description has been presented in Chapter 16 on the involvement of autophagy in innate and adaptive immunity and in diseases such as SLE, RA, MS, Sjogren’s syndrome and inflammatory bowel disease. This section of the book also has two separate chapters describing the laboratory set-up and the diagnostic and prognostic value of autoantibody determination. The aspect that imaging tools play a central role in the diagnosis and follow up of AIDs has been well covered including the diagnostic utility of MRI and ultrasonography.

Section III of the book devotes primarily to the discussion of classical factors such as hormones, human microbiota and infections on the pathogenesis and evolution of autoimmunity. The well-established sexual dimorphism observed on the prevalence rates

of a number of AIDs, such as RA and SLE, signifies differences in immune response in the two sexes. Apart from oestrogens and androgens, other hormones, neuropeptides and cytokines released by cells in the neuroendocrine system may be involved in the regulation of immune response. Chapter 19 describes the impact on autoimmune pathogenesis due to the exposure to sex hormones as oral contraceptives and of hormone replacement therapy during menopausal stages because of their known effect on the immune system. An important current debate is concerning the role of human microbiota on AIDs including possible therapeutic manipulations. Several clinical trials using microbiota as immune modulators are under way in immune-mediated diseases and these have been elegantly covered in this section.

Infections by bacteria and viruses could lead to breakdown of the innate and adaptive immune responses and accelerate autoimmunity in genetically susceptible individuals. In this context, autoimmune rheumatic diseases present excellent model systems to study interactions between viral pathogens and microbiome. The task to discriminate the bad from the good microbiome is arduous, because while the composition could be pathogenic in one disease, it appears to be beneficial or prophylactic in another signifying complexity of the pathologic processes. The generally intact intestinal barrier ensures mucosal homeostasis due to tolerance to commensal bacteria, largely because of the protective action of soluble IgA and dominance of anti-inflammatory cells such as the T and B regulatory cells in the mucosa. This has been well described in Chapters 20 and 21.

Section IV of the book has 21 chapters that discuss the geoepidemiology of environmental influences most comprehensively, highlighting the fact that although heredity and immunity are important, it may not be sufficient to explain the wide clinical variability observed in AIDs. The concept of 'exposome' takes into consideration the effect of environmental factors encompassing all putative non-hereditary factors, both exogenous and endogenous. In this context, infections have been cumulatively grouped as a component of the 'infectome' that trigger the initiation of autoimmune and chronic inflammatory diseases. The best example is that of Epstein-Barr virus that has been associated not only with SLE but also a whole lot of other AIDs, including RA, Sjogren's syndrome, autoimmune hepatitis and others.

Among the environmental factors, a full chapter discusses the role of photobiology and ultraviolet radiation in triggering and exacerbating systemic AIDs and how phototherapy could ameliorate the symptoms. The role of vitamin D supplementation in the prevention/treatment of various AIDs and for improvement of glucose metabolism, muscle and adipose tissue function has been discussed. Chapter 26 focuses on the involvement of vitamin D in pregnancy and autoimmunity and to assess if its supplementation should be introduced in clinical practice.

An interesting discussion revolves around the role of smell on autoimmunity since olfactory dysfunction has been noted in a range of autoimmune conditions, frequently associated with disease activity and progression. Breastfeeding and autoimmunity is another area of importance because of the profound effect of human milk in shaping the immune repertoire. Other factors that are known to influence the immune system and thus the development of AIDs include vaccines, adjuvants, silicone-based implants and psychological stress. The role of all of these has been discussed individually giving examples wherever necessary.

Nutritional aspects of autoimmunity are another area of intense investigation since dietary habits have long been known to have profound effect on human health including the complex array of mosaic of autoimmunity. Curcumin leads to elevated expression of antioxidative stress and anti-inflammatory genes and increased Treg cell expression with concomitant shift towards regulatory B cells leading to a rise in protective antibodies. Similarly, the impact of gluten, a major constituent of modern human food, and its impact on initiation, maintenance and progression of AIDs has been well covered in Chapter 32.

The book also covers the impact of physical activity (Chapter 36) and obesity (Chapter 35) on autoimmunity. In general, patients with AIDs remain physically inactive and counselling them for a lifestyle change by including exercises in their daily curriculum is potentially beneficial. Smoking is another area of concern since it could act as a potentiator of disease exacerbation, particularly in genetically susceptible people. The book also has interesting discussions on the possible influence of cannabinoids and of plastics in autoimmune and rheumatic diseases. The active compound in plastics is bisphenol A which acts as

an environmental oestrogen and thus promote the autoimmune process.

Section V of the book describes the classical AIDs one by one, focussing on their aetiopathogenesis, clinical features, immunopathology, laboratory parameters, genetic and epigenetic features and management strategies. Spread over 12 chapters, the section deals with diseases such as RA, psoriatic arthritis, SLE, Sjogren's syndrome, neurologic disorders and others. The last section of the book is devoted exclusively to the novel treatment strategies, including the use of small molecules targeting intracellular signalling kinases or kinase inhibitors, biologics and biosimilars and the use of intravenous immunoglobulins in rheumatic diseases.

In summary, this is an extraordinary book that highlights both the basic aspects of autoimmunity

and current research on classical AIDs. The title, 'mosaic of autoimmunity' is justified because the focus is on discussing complex interaction of genetic, hormonal, immunological and environmental factors in the pathogenesis of AIDs. The book is equally useful to both the basic scientists and researchers and the clinicians. It fulfils the unmet need and its easy presentation style with appropriate figures and tables is profoundly appealing.

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