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BOOK REVIEW*

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REFORMA DEL SECTOR DE LA SALUD EN LAS AMÉRICAS

El número más reciente de la *Revista Panamericana de Salud Pública/ Pan American Journal of Public Health* versa por entero sobre el tema de la reforma del sector de la salud en los países del Caribe y de América del Norte, América del Sur y Centroamérica. Este número doble, que corresponde a los meses de julio y agosto de 2000 y que tiene 150 páginas, presenta un análisis actualizado de las reformas sanitarias que han efectuado los países de la Región con el propósito de brindar servicios de salud más efectivos y de lograr un acceso más equitativo a estos servícios.

En un artículo se describen las tendencias y los resultados de las reformas iniciadas en los años noventa: en otros se examinan el futuro de las iniciativas de reforma, así como las relaciones entre los sistemas de salud y de seguridad social de los países, las dificultades que plantea la situación de las personas que carecen de acceso a atención de salud, y las actividades esenciales que competen al sector de la salud pública. El número también presenta estudios de casos basados en las experiencias que han tenido seis países en aspectos particulares del proceso de reforma. Los artículos y estudios de casos están en español, inglés y portugués.

La *Revista Panamericana de Salud Pública/Pan American Journal of Public Health* es la principal publicación cientificotécnica de la Organización Panamericana de la Salud (OPS), entidad dedicada a mejorar la salud pública y las condiciones de vida en todos los países del continente americano y que és, al mismo tiempo, la Oficina Regional de la OMS para las Américas.

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BOOK REVIEW*

ANNUAL REVIEW OF IMMUNOLOGY, vol. 18, 2000; edited by William E. PAUL, C. GARRISON FATHMAN & L.H. GLIMCHER. Palo Alto, Annual Reviews Inc., 2000. 1096p. ilust.
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The volume 18 of the Annual Review of Immunology offers a broad updated information on selected topics in Basic Immunology for students and researchers.

The area of **Immunology of Infectious Diseases** has been the target for several publications in previous volumes of this scientific series. In 2000, this important area is covered in 5 chapters. CD_8^+ T lymphocytes are important mediators of adaptative immunity against certain viral, protozoan, and bacterial pathogens. Each of these pathogens has developed a unique interaction with the host to cause infection, and the nature of the pathogen–host interaction may determine which effector mechanisms are required for immunity. In a excellent review, **J.T. HARTY** *et al*. summarize current understanding of the effector functions used by CD_8^+ T cells in resistance to microbes. Access to the complex area of cellular dynamics of virus-specific T cell responses has been greatly enhanced by the recent development of tetramers (tretrameric complex of MHC Class-I glycoprotein + peptide) that allow the direct staining of antigen–specific CD_8^+ T cells. **P.C. DOHERTY & J.P. CHRISTENSEN** discuss the insights and questions that have been raised by this recent technological breakthrough in the area of quantitative and functional analysis of CMI to viruses. A proper host defense against viral pathogens is essential and is aimed at several levels such as: mechanical protection afforded by skin and epithelia, rapid deployment of cells and molecules of the innate immune system, and finally, in many cases, through acquired immunity. In an informative and didactic chapter, **D. TORTORELLA** *et al*. focus on the diverse array of pathways and molecular targets that are used by viruses to elude immune detection and destruction. This review includes four hundred and eighteen literature citations. Current available vaccines are capable of inducing long–lived antibody responses, which are the principal agents of the immune protection against most viruses and bacteria. By the other hand, vaccination against intracellular organisms that require cell mediated immunity, such as HIV and the agents of malaria, tuberculosis and leishmaniosis are either not available or not effective. **S. GURUNATHAN** *et al.* review the mechanisms by which a new form of vaccination, the DNA vaccines, elicit immune responses. A list of potential applications in a variety of preclinical model is also provided. It is becoming clear that viral reservoirs established early in the HIV-1 infection not only prevent sterilizing immunity but also represent a major obstacle to curing the infection with the potent antiretroviral drugs currently in use. There are several potential cellular and anatomical reservoirs for HIV-1 that may contribute to long-term persistence of HIV-1, such as central nervous system and male urogenital tract. In a very exciting chapter, **T. PIERSON** *et al.* discuss a new stable reservoir in which HIV-1 can potentially persists for life even in patients on effective antiretroviral therapy. This reservoir consists of a small pool of latently infected resting TCD4+ cells that carry an integrated copy of the HIV-1 genome and can produce infectious virus when the cells are activated by the appropriate antigen.

Much information can be obtained on the field of **Lymphocyte Development, Activation and Differentiation.** The coordinated activation of T cells in response to foreign antigen ensures antigen-specific T cell clonal expansion and differentiation. The T cell signaling pathways identified biochemically in experiments with agonistic anti-TCR/CD_3 antibodies, the morphologic changes that occur during T cell activation, and the interactions between TCR signal transduction pathways and T cell cytoskeleton are reviewed by **O. ACUTO & D. CANTRELL.** The genes encoding immunoglobulin and T cell receptor proteins are unique in being split into multiple gene segments in the germline that are then made contiguous by recombination in somatic tissues. The assembly process, known as V(D)J recombination proceeds through a series of protein:DNA complexes mediated in part by the RAG1 and RAG2 proteins, which are responsible for sequence-specific DNA recognition and DNA cleavage. The properties and activities of the RAG proteins, particularly the protein:DNA complexes in which they participate, were reviewed by **S.D. FUGMANN** *et al.* The developmental regulation of T helper responses during infection is critically important to the form and effectiveness of acquired immunity. The initial recognition of polarized T cells subsets defined by cytokine production was followed by a search to define the intracellular processes set in motion during Th_1/Th_2 development, particularly by the strongly polarizing cytokines IL-12 and IL-4. In a updated chapter, **K.M. MURPHY** *et al.* focus on the progress primarily in signaling and transcriptional regulation in Th_1/Th_2 development, including IL-18, the Th_2-selective T_1/ST_2 product, and heterogeneity in dendritic cells capable of directing cytokine-independent Th development. Literature cited includes three hundred and nine references. The thymus is essential for the initial establishment of the peripheral T cell pool in animals and humans. Recent advances have provided new opportunities to understand the role that the human thymus plays in immune reconstitution, in aging, in bone marrow transplantation, and in HIV-1 infection. In a very didactic manner, **B. F. HAYNES** *et al*. review recent data on human postnatal thymus function which support the notion that the human thymus is functional well into the sixth decade and plays a role throughout life to optimize human immune system function. NF-KB (nuclear factor – KB) is found in essentially all cell types and is involved in activation of a large number of genes in response to infections, inflammation, and other stressful situations requiring rapid reprogramming of gene expression. **M. KARIN & Y. BEM-NERIAH** discuss a unifying hypothesis regarding the signaling mechanisms involved in NF-KB regulation. Finally, the important field of functional genomics of the immune system is reviewed by **L.M. STAUDT & P.O. BROWN.**

It has recently come to light that lymphocytes bearing antigen receptors may actively attempt to express new ones, which can lead to expression of multiple receptors, inactivation of previously expressed receptors, or replacement of old receptors with new ones – a process called receptor editing. In a very up-to-date overview, **D. NEMAZEE** discusses features of both T cell receptor and immunoglobulin loci that promote secondary receptor gene rearrangement. The evidence for receptor editing in B and T cells is also discussed.

The area of **MHC** is covered in 3 chapters. In addition to the well-characterized MHC Class-II molecules that present peptides to CD_4^+ T cells, two other class-II-like proteins are produced from the class II re-

*This book is available at the Library of the Instituto de Medicina Tropical de São Paulo

gion of the MHC, HLA-DM (DM) and HLA-DO (DO). **C. ALFONSO & L. KARLSSON** present an overview of the current knowledge of these non-classical class-II molecules, including their function and their influence on antigen presentation. In a very interesting review, the role of the MHC class I – related neonatal Fc receptor (FcRn) in either the passive delivery of immunoglobulin Gs from mother to young and the regulation of serum IgG levels are discussed by **V. GHETIE & E. S. WARD**. Dendritic cells are not only critical for the induction of primary immune responses, but may also be important for the induction of immunological tolerance, as well as for the regulation of the type of T cell-mediated immune response. **J. BANCHEREAU** *et al.* summarize recent progress in our understanding of DC development and immunoregulatory functions.

A complementarily exists between the two branches of immunity: innate immunity detects relatively few structures that are highly consumed and transmits this information to adaptive immunity by promoting the activation of those lymphocyte clones that express receptors capable of binding antigens associated with the infectious process. In an excellent review, **D.T. FEARON & M.C. CARROLL** discuss as the membrane protein complex CD_{19}/CD_{21} couples the innate immune recognition of microbial antigens by the complement system to the activation of B cells.

The field of **Regulation of the Immune Response** is examined in five chapters. In a very interesting issue "Population Biology of Lymphocytes: The Flight for Survival", **A. A. FREITAS & B. ROCHA** suggest that the primary goal of the cells of the immune system is to ensure their own growth and survival. As pointed out by the authors, the individual cells of the immune system follow a hierarchical organization in which the survival and the rate of replication of the different cell types are restrained and their number controlled within the limited constraints imposed by the host. In this way, in response to competition, T and B lymphocytes, and naive and memory/activated T and B cells, use different survival signals within different ecological niches during cell differentiation. The authors also analyze how niche differentiation allows the co-existence of different cell types and guarantees both repertoire diversity and efficient immune responses. Over the last three decades considerable evidence has accumulated that CD_8^+ T cells control the emergence of autoreactive CD_4^+ T cells as well as CD_4^+ T cells reactive to conventional antigens, including alloantigens. **H. JIANG & L. CHESS** first summarize the evidence that this immune suppression mediate by CD_8+ T cells is dependent, in part, on specific interactions between MHC class-I restricted regulatory CD_8^+ T cells and antigen-activated CD_4^+ T cells. Moreover, the authors review the evidence that regulatory CD_8^+ T cells in a TCR specific manner is restricted by the MHC class Ib molecule, Qa-1, which unlike conventional MHC molecules, is preferentially and transiently expressed on activated and non resting CD_4^+ T cells. The components of immunocomplexes include antigens, antibodies and, sometimes, complement. Such complexes interact with the B-cell receptor and Fc and complement receptors and play immunoregulatory functions. In some situations, the presence of antibody can act to inhibit or to enhance antibody responses. **B. HEYMAN** focuses on the regulation of antibody responses via antibodies, complement and Fc receptors. The vascular bed of an individual tissue can express molecules specific for that particular tissue. This is true for lymphoid and for nonlymphoid tissues. **E. RUOSLAHTI & D. RAJOTTE** discuss specific features of the vasculature of normal nonlymphoid tissues and tumors. $\gamma\,\delta$ cells have been reviewed before in other volumes of Annual Review of Immunology series. In this volume, **A.C. HAYDAY** focuses on experimental systems and findings that illustrate the immunoprotective and regulatory functions of $\gamma\delta$ cells in vivo.

Allergic diseases constitute one of the major problems of modern day medicine, and epidemiologic studies of families and large numbers of twins indicate a genetic component to atopic diseases. In a very interesting article, **S.J. ONO** reviews multiple groups attempts to identify disease-susceptibility/protection genes via either a candidate gene approach or by genoma-wide scans. To date, human tumor immunotherapy has met with only limited success. Several approaches have used bone marrow–derived dendritic cells (DC), phenotypically distinct and extremely potent antigen-presenting cells, to present tumor-associated antigens and thereby generate tumor-specific immunity. The ability of DC to prime T cells capable of recognizing and killing tumor cells in an antigen-specific fashion has also been demonstrated in various animal models. Human trials using DC loaded with antigens are underway at several institutions, and promising results from clinical studies in patients with lymphoma, melanoma, and prostate cancer are discussed by **L. FONG** and **E. G. ENGLEMAN**.

Three chapters deal with Tolerance and Autoimmunity in a very didactic manner. As pointed out by **A.L. MELLOR & D.H. MUNN** in their very exciting review, mammalian reproduction poses an immunological paradox because fetal alloantigens encoded by genes inherited from the father should provoke responses by maternal T cells leading to fetal loss. Why and how the maternal T cells repertoire tolerates the fetus throughout gestation? This important question is discussed by the authors that focus on the regulation of maternal T cells responsiveness during gestation. Celiac disease (CD), or gluten sensitive enteropathy, is a condition in which ingested wheat gluten or related proteins from rye and barley are not tolerated. HLA and non-HLA genes together with gluten and possibly additional environmental factors involved in disease development are reviewed by **L.M. SOLLID**. In the late 1960-1980s, it was proposed that T cells could act as regulatory cells that could suppress the immune response by producing soluble factors that were responsible for their biologic activity (suppressor T cells). The discovery of Th_1/Th_2 prompted most workers to abandon the concept that suppressor T cells were a specialized population: suppression was merely considered the result of the activity of counter-regulatory cytokines. **E.M. SHEVAC** resurrects the concept that suppressor T cells is a member of a separate lineage of cells that mediates its down-regulatory functions by a variety of effector mechanisms with emphasis on their role in the prevention of organ-specific autoimmunity.

The members of the chemokine superfamily are molecules that not only control hemopoietic cell migration, but also are involved in a number of other physiological and pathological processes. These include inflammation, cell recruitment, wound healing, lymphoid trafficking, Th_1/Th_2 development, angiogenesis and metastasis. **D. ROSSI & A. ZLOTNIK** highlight some of those areas of chemokine biology with new developments or therapeutic potential. **F. SALLUSTO** *et al.* review the role of chemokine receptors in primary, effector and memory immune responses. Finally, **H. YASUKAWA** *et al.* focus on the mechanisms of negative regulation of cytokine signaling pathways by the CIS family of proteins.

Steroides mediate their biological effects by binding an intracellular receptor (GR) that, in turn, translocates to the nucleous and regulates gene transcription in virtually cell types. **J.D. ASHWELL** *et al.* focus on one particular type of steroid – the glucocorticoids – and review accumulating evidence that has suggested an unexpected role for glucocorticoids in regulation of thymocyte development and selection.

Finally, the prefatory chapter "Discovering the Role of the Major Histocompatibility Complex in the Immune Response" by H. McDEVITT is obligatory to all readers.

The tradition of the series Annual Review of Immunology is to present the state of the art in different fields of Immunology. Like other volumes, this book is mostly target to posgraduates and reseachers who wish to bring themselves up to date on Basic Immunology.

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