PART I DEVELOPMENT AND STRUCTURE OF MUCOSAL TISSUE

Chapter 1 Overview of the Mucosal Immune System Structure

Immune inductive lymphoid tissue.
1-1 MALT is different from lamina propria or glandular stroma.
1-2 There are different types of gut-associated lymphoid tissue.
1-3 Organogenesis of murine PPs, isolated lymphoid follicles, and MALT is not synchronous.
1-4 There is lymphoid tissue in the nasopharynx and bronchi.
1-5 Mucosal B cells may be derived from tissues other than MALT.

B-cell activation in MALT.
1-6 FAE is an important site of antigen uptake in the gut.
1-7 Gut bacteria are important for the molecular interactions needed for germinal center formation.

B-cell differentiation in MALT germinal centers.
1-8 IgA expression and class switching are dependent on activation-induced cytidine deaminase (AID).
1-9 Different class-switching pathways operate in different mucosal sites.

How mucosal immune cells home.
1-10 Naive and activated immune cells occupy different microenvironments in GALT.
1-11 Homing molecules are important in homing of cells to extraintestinal sites.

Summary.
Further Reading.

Chapter 2 Phylogeny of the Mucosal Immune System

Phylogeny of receptor diversity.
2-1 T-cell receptors are similar in all jawed vertebrates.
2-2 Immunoglobulins have evolved in different ways in different lineages.
2-3 T and B cells are found in lower vertebrates.

The phylogeny of lymphoid tissue.
2-4 The lymphoid tissues in agnathans seem to have evolved from MALT.
2-5 Gnathostome lymphoid tissues differ between lineages.

The phylogeny of mucosal antibodies.
2-6 Immunoglobulin A is the secretory antibody in amniotes.
2-7 Amphibians have a unique antibody, immunoglobulin X.
2-8 Teleosts have a unique secretory antibody, IgT.

Summary.
Further Reading.

Chapter 3 Immunological and Functional Differences Between Individual Compartments of the Mucosal Immune System

Common and distinct features of the mucosal immune system in different tissues.
3-1 The ocular immune system contains inductive sites.
3-2 In the oral cavity, SigA dominates and sublingual tissue is a potential inductive site.
3-3 The upper and lower respiratory tract display discordant immunological features.
3-4 The upper and lower intestinal tract are the major source of Ig and the major site for the induction of immune responses.
3-5 Mammary glands are an important source of SigA.
3-6 IgG is the major Ig in urogenital tract secretions.

Antigen sampling in mucosal surfaces.
B-cell subsets in nasal and gut-associated tissues.
MALT organogenesis.
Influence of aging on mucosal immunity.

Summary.
Further Reading.

Chapter 4 Secreted Effectors of the Innate Mucosal Barrier

The intestinal epithelium: stem cells, self-renewal, and cell lineage allocation.
4-1 Wnt signaling regulates intestinal epithelial cell positioning and differentiation.
4-2 Notch signaling determines cell lineage specification in the intestine.

Secretory cells in mucosal epithelia.
4-3 Nonspecialized epithelial cells display remarkable plasticity.
4-4 Mucus-producing cells are abundant in the gastrointestinal epithelium.
4-5 Antimicrobial peptides are produced by specialized cells throughout the gastrointestinal tract.

Biophysical features of the secreted mucus barrier.
4-6 Mucin glycoproteins have common structural features.
4-7 Mucin release is a tightly regulated biological process.
4-8 Antimicrobial peptides play a key role in mucosal defense.

Role of mucosal cell products in mucosal microbe homeostasis.
4-9 Microbes influence the composition and structure of the secreted mucosal barrier.
4-10 The secreted mucosal barrier influences the composition of the gut microbiome.
4-11 Mucins and Paneth cell products contribute to protection against infectious pathogens.

Detailed Contents
Regulation of the secreted mucosal barrier by innate and adaptive immunity.  
Defects in mucosal barrier secretion and the pathogenesis of disease.

Summary.

Further Reading.

PART II  CELLULAR CONSTITUENTS OF MUCOSAL IMMUNE SYSTEMS AND THEIR FUNCTION IN MUCOSAL HOMEOSTASIS  

Chapter 5  Immune Function of Epithelial Cells  

Barrier function.

5-1 Stratified squamous and simple columnar epithelia form the major types of epithelial structures.
5-2 A polarized simple epithelium permits vectorial transport.
5-3 Epithelial cells form a paracellular barrier via intercellular junctions.
5-4 Various types of differentiated epithelial cells are derived from an epithelial stem cell.
5-5 Nonimmunologic and innate factors contribute to epithelial barrier function.
5-6 Adaptive immunologic factors contribute to epithelial barrier function.
5-7 Inappropriate barrier function leads to mucosal pathology.

Antigen uptake and presentation.

5-8 Three major mechanisms account for regulated antigen uptake across the epithelium.
5-9 The epithelium exerts important innate immune functions.
5-10 The epithelium can present antigen via classical and nonclassical antigen-processing and antigen-presentation pathways.
5-11 The epithelium can provide co-stimulatory and tertiary cytokine signals to lymphocytes.

Regulation of immune responses.

5-12 Epithelial cells act as central organizers of immune responses.
5-13 Epithelial cells act as bystanders and participants in immune responses and inflammation.

Summary.

Further Reading.

Chapter 6  Intraepithelial Lymphocytes: Unusual T Cells at Epithelial Surfaces  

Uniqueness and heterogeneity of mucosal IELs.

6-1 Natural IELs are a unique cell type absent from the rest of the body.
6-2 Induced IELs are the mucosal counterpart of T cells found in the periphery.
6-3 Luminal factors control the numbers of IELs.

The TCR repertoire and specificity of IELs.

6-4 The TCR repertoire and antigen specificity of TCRy6 nIELs are different from T cells in the rest of the body.
6-5 TCRb IELs are highly unusual in that they are made up of a few dominant clones.

Development and differentiation of IELs.

6-6 There is controversy over thymic versus extrathymic development of IELs.  
6-7 Under euthymic normal conditions, all IEL subsets are progeny of bone marrow precursor cells that initially develop in the thymus.  
6-8 Natural IEL precursor cells migrate directly from the thymus to the epithelium.  
6-9 Cytokines and transcription factors are involved in the development and differentiation of TCRy6 nIELs.  
6-10 CD8ααTCRb nIELs with self-reactivity may be positively selected.  
6-11 nIELs are peripheral-antigen-driven progeny of conventional thymically selected CD4+ or CD8ααTCRb T lymphocytes.  

Migration to and local adaptation in the gut.  

6-11 Natural IELs are induced to home to the gut in the thymus.  
6-12 Natural IELs undergo local adaptation in the gut.  
6-13 Conventional thymically selected naive T cells are not found in the gut epithelium.  
6-14 Induced IELs undergo adaptation in the gut.

The beneficial functions of IELs.

6-15 The function of nIELs appears to be to maintain epithelial homeostasis.  
6-16 The functions of CD8ααTCRb nIELs remain largely unknown.  
6-17 TCRbCD8αβ iIELs appear to have a protective function.  
6-18 TCRαβ CD4 iIELs are involved in protective immunity.  

Potential aberrant function of IELs in inflammation.  

6-19 TCRαβ CD4 iIELs are involved in protective immunity.  
6-20 TCRy6 nIELs may be involved in pathology.  
6-21 CD8ααTCRb nIELs may also damage the epithelium.  
6-22 CD8αβTCRb iIELs may be involved in the pathogenesis of inflammatory bowel disease.  
6-23 Aberrant functions of CD4 TCRαβ iIELs driving gut inflammation.

Summary.

Further Reading.

Chapter 7  Lymphocyte Populations Within the Lamina Propria  

The origin and phenotype of mucosal T cells.  

7-1 Mucosal T cells traffic from MALT to mucosal lamina propria.  
7-2 Lamina propria T cells have the characteristics of activated lymphocytes.  
7-3 Cytokine production by mucosal T cells in healthy animals is Th1/Th17 dominated.  
7-4 IL-17 and IL-22 may play an important role in protecting mucosal surfaces.  
7-5 Different types of gut microbiota appear to induce different cytokine responses in mucosal T cells.  
7-6 The developmental pathways of Th17 cells are not well defined, especially at mucosal surfaces.  
7-7 It is unclear if Th1 and Th17 responses in the gut are due to local differentiation or selective migration.  
7-8 There appears to be considerable flexibility in the Th17 lineage.
Regulatory T cells and the control of effector T-cell responses. Human diseases due to single gene defects are informative in understanding gut inflammation and immune regulation. Regulation of mucosal immune responses is complex and depends on whether the effector T cell can be regulated.


Chapter 8 Mucosal B Cells and Their Function Cells and proteins involved in humoral immunity at mucosal surfaces. Mucosal B-cell responses. The instructions involved in inducing GALT B cells to migrate to effector sites. B-lineage activity in the lamina propria—current controversies.

Chapter 9 Secretory Immunoglobulins and Their Transport Features of secretory immunoglobulins. Epithelial transcytosis of secretory immunoglobulins.

Chapter 10 Role of Dendritic Cells in Integrating Immune Responses to Luminal Antigens Defining characteristics of dendritic cells. Intestinal dendritic cell populations. Unique functions of intestinal dendritic cells. Role of mucosal dendritic cells in IBD.
Invasive bacterial pathogens can exploit rapid M-cell transport to establish local and systemic infection.

Endocytosis of viruses by M cells results in mucosal and/or systemic disease.

M cells can be exploited for vaccine antigen delivery.

Summary. Further Reading.

Chapter 14 Lymphocyte Trafficking from Inductive Sites to Effector Sites

Basic concepts in immune-cell migration.

The adhesion molecules and chemotaxtants involved in immune-cell migration.

Immune-cell migration into tissues is a multi-step process.

Naive lymphocytes recirculate through MALT.

Lymphocytes move around inside lymph nodes and leave to return to the blood.

Lymphocyte migration into mucosal tissues—generation of tissue-tropic lymphocyte subsets.

Specific integrin–adhesion-molecule interactions and chemokines direct cell migration into mucosal tissues.

Different homing molecules control lymphocyte migration to gut and skin.

Dendritic cells are critical in the generation of tissue-tropic effector lymphocyte subsets.

Vitamin A is required for the generation of gut-tropic effector T lymphocytes.

Lymphocyte migration to sites of mucosal inflammation—therapeutic opportunities.

Summary.

Further Reading.

Chapter 15 Mucosal Tolerance

General features of mucosal tolerance.

Mucosal tolerance involves many mechanisms including anergy, deletion, and the induction of active regulatory pathways.

Mucosal tolerance is likely induced in organized lymphoid structures associated with mucosal tissues and is disseminated widely throughout the mucosa-associated lymphoid tissues.

A wide variety of immune effector functions are subject to the effects of mucosal tolerance, which can be enhanced by mucosal adjuvants.

Mucosal tolerance in experimental autoimmune and inflammatory disease.

Mucosal tolerance can be elicited to autoantigens in experimental model systems.

The mechanisms of mucosal tolerance that are induced in response to autoantigens are similar to those induced against model antigens.


Mucosal (oral) tolerance is a property of normal human mucosal tissues.

Mucosal tolerance may be amenable to therapeutic manipulation in human immune-mediated disease.

Mucosal tolerance can be used in the treatment of human allergic disorders.

Summary. Further Reading.

PART III MICROBIAL COMMENSALISM

Chapter 16 Recognition of Microbe-Associated Molecular Patterns by Pattern Recognition Receptors

Principles of pattern recognition and signaling.

TLRs comprise a family of conserved receptors that recognize specific PAMPs.

NOD1 and NOD2 are NLR family members that recognize peptidoglycan motifs.

TLR and NOD signaling pathways converge on downstream NFκB and MAPK.

Function of pattern recognition molecules in healthy mucosa.

Negative regulation prevents prolonged and detrimental TLR/NOD signaling.

TLR function is involved in the maintenance of mucosal barrier integrity.

NOD2 modulates antimicrobial peptide secretion and bacterial clearance via autophagy.

Genetic alterations in pattern recognition.

NOD2 is a major susceptibility gene for Crohn’s disease.

TLR polymorphisms may modulate IBD severity.

Summary. Further Reading.

Chapter 17 The Commensal Microbiota and Its Relationship to Homeostasis and Disease

Principles and definitions of the commensal microbiota.

The microbial communities at mucosal surfaces.

The upper respiratory microbiome of the nares is distinctive with similar phyla between individuals.

The oral microbiome is characterized by the formation of biofilms.

The gut microbiome is the most complex of the commensal ecosystems of the host.

Host–microbe interactions.

The host perceives and responds to the microbiota.

Life without microbiota results in profound changes in the host.

T-cell responses appear to be modulated by the microbiota.

Segmented filamentous bacteria specifically drive Th17 responses.

The intestinal microbiota influences autoimmunity.

The microbiota appears to be involved in inflammatory bowel disease, particularly Crohn’s disease.

Defective immune system handling of intestinal microbes leads to intestinal inflammation.

Influence of microbiota on host metabolism.

Alterations in the community structure of colonic microbes are linked to obesity and the metabolic syndrome.
PART IV GENITOURINARY TRACT

Chapter 18 The Immune System of the Genitourinary Tract

Anatomy of the human male and female reproductive tract. 263
Hormonal regulation of female reproductive function. 264

18-1 Cytokines, chemokines, and antimicrobial products contribute to protection of the female reproductive tract. 264
18-2 Cellular immunity is also important in the reproductive tract. 266

Endocrine control of immune protection in the reproductive tract. 267
18-3 Sex hormones directly and indirectly regulate immune-cell function in the reproductive tract. 267
18-4 Immune protection is integrated in the female reproductive tract during the menstrual cycle. 268
18-5 Immune mechanisms contribute to protection of the male reproductive tract. 268
18-6 Innate immunity is an important component of the male reproductive tract immune system. 269
18-7 Adaptive immunity in the male reproductive tract is mediated predominantly by CD8+ T cells. 270

Infection and immune protection against sexually transmitted diseases in the male and female reproductive tract. 271
18-8 Chlamydia trachomatis is the most common sexually transmitted disease worldwide. 271

Summary. 273
Further Reading. 273

Chapter 19 Mucosal Immune Responses to Microbes in the Genital Tract

Global prevalence of sexually transmitted pathogens. 275
Diseases caused by sexually transmitted pathogens. 276

19-1 Chlamydia is a disease caused by the bacteria Chlamydia trachomatis. 276
19-2 Gonorrhea is an STD that is caused by a bacterium, Neisseria gonorrhoeae. 276
19-3 Syphilis is caused by infection with the bacterium Treponema pallidum. 276
19-4 Trichomoniasis is initiated within either the female cervico-vaginal epithelium or the male urethral epithelium. 279
19-5 Genital herpes infection initially targets the stratified squamous epithelium. 280
19-6 Trichomoniasis is initiated within either the female cervico-vaginal epithelium or the male urethral epithelium. 279
19-7 Hepatitis B virus (HBV) is a hepatotropic virus that is transmitted through sexual contact. 278
19-8 Chlamydia exhibits distinct infectious (elementary body) and replicative forms (reticulate body). 278
19-9 Hepatitis B virus (HBV) is a hepatotropic virus that is transmitted through sexual contact. 278
19-10 Gonorrhea infects the apical surface of simple columnar epithelium and once invaded inhibits the function of the adaptive immune system. 279
19-11 Treponema pallidum, the cause of syphilis, invades humans at mucosal epithelia where it causes infections and gains access to the blood and lymph systems. 279
19-12 HIV-1 gains access to the immune system by crossing the epithelial cell barrier. 279
19-13 HIV-1 gains access to the immune system by crossing the epithelial cell barrier. 279
19-14 Genital herpes infection initially targets the stratified squamous epithelium. 280
19-15 HPV infection requires access to the basement membrane for infection of basal keratinocytes of stratified epithelium. 280
19-16 HBV is a mucosal pathogen in approximately one-third of infections in adults. 281

The innate immune system of the genital mucosa and its relation to infections. 281
19-17 Mucus is a first line of epithelial defense. 282
19-18 Female and male genitourinary secretions contain antimicrobial factors. 282
19-19 The female and male genitourinary systems possess an endogenous (commensal) microbiota that provides colonization resistance against pathogenic infections. 283
19-20 Innate immune cells provide defense against invading pathogens within the female and male genitourinary tract. 283

Innate recognition of sexually transmitted pathogens. 284
19-21 Chlamydia trachomatis is recognized by multiple PRRs. 284
19-22 Host cells utilize immunoglobulin-related molecules such as CEACAM3 to initiate internalization and elimination of Neisseria gonorrhoeae. 284
19-23 Treponema pallidum lacks lipopolysaccharide but contains internal lipoproteins which can stimulate Toll-like receptors. 285
19-24 Innate immune recognition of HIV-1 occurs after cellular infection. 285
19-25 Toll-related receptor and retinoic acid-inducible gene-related pattern recognition is involved in detecting genital herpes infection. 286
19-26 HPV infection is sensed by innate and adaptive immune cells through Toll-like receptors. 286
19-27 HBV impairs innate immune responses as a means of immune evasion. 287

Adaptive immune responses against sexually transmitted pathogens. 287
19-28 Chlamydia infection triggers the activation of local DCs to migrate to the draining lymph nodes and initiate T-cell activation. 288
19-29 CD4 cells mediate immunity against gonorrhea. 288
19-30 Protective immunity to syphilis is undefined but likely exists. 288
19-31 CD4 cells mediate immunity against syphilis. 288
19-32 Adaptive immunity is the mainstay of resistance to genital herpes infection. 288
19-33 CD4 cells mediate immunity against genital herpes infection. 288
19-34 Cellular and humoral immunity is essential for immunity to HIV-1. 289
19-35 Adaptive immunity is critical to limiting and resolving HBV infection. 289

Challenges ahead. 290
Summary. 290
Further Reading. 291
PART V  NOSE, AIRWAYS, ORAL CAVITY, AND EYES  

Chapter 20  The Nasopharyngeal and Oral Immune System  

The nasopharyngeal–oral mucosal immune system.  
20-1  There are shared features of antigen uptake in the MALT of the gut and upper airway.  
20-2  NALT is a major IgA inductive site for the nasal and oral mucosa.  
20-3  The nasal passage contains a new type of mucosal tissue.  
20-4  The salivary glands have features of both secretory and systemic immunity.  

Induction of acquired immune responses via the oral and nasal mucosal immune system.  
20-5  Enterotoxin-based nasal adjuvants are the most effective method for the induction of antigen-specific immunity.  
20-6  Safe mucosal adjuvants have been developed as delivery systems for nasal vaccines.  
20-7  Nasal adjuvants activate the innate immune system.  
20-8  The mouth is a delivery site for the induction and modification of antigen-specific immune responses.  
20-9  The nasal immune system escapes mucosal aging.  
20-10  T-cell independent mucosal IgA responses are induced in the nasal and oral cavities.  

Summary.  
Further Reading.  

Chapter 21  Bronchus-Associated Lymphoid Tissue and Immune-Mediated Respiratory Diseases  

General anatomy and physiology of the central and lower airways.  
21-1  BALT is a potential inductive site.  
21-2  The airway mucosa contains effector sites that are similar to those in other mucosal tissues.  

Response of the lung to environmental challenges.  
21-3  Two major chronic inflammatory diseases of the lung are asthma and chronic obstructive pulmonary disease (COPD).  
21-4  The inflammation in COPD is characterized as either chronic bronchitis or emphysema.  
21-5  Allergy is a central mechanism in the pathogenesis of asthma.  

Characteristics of allergens.  
21-6  Allergens have intrinsic properties as defined by their ability to be directly recognized by specific receptors.  

Role of innate immune cell types in the induction of asthma.  
21-7  DCs and alveolar macrophages are the major APCs in asthma.  
21-8  Mast cells, basophils, and eosinophils are the main innate immune cells that are recruited to the airways during asthma.  

Late phases of asthma.  
21-9  The late-phase response of asthma is characterized by the infiltration of the airways with inflammatory cells.  

21-10  T_{reg} cells are also recruited or induced locally during asthma and provide restraint on the inflammatory response.  

Genetic basis of asthma.  
21-11  Asthma is a complex genetic disease.  
21-12  The marked increase in the prevalence of asthma supports the importance of environmental factors.  

The complexity of asthma.  
21-13  Consistent with its genetic heterogeneity, asthma involves other pathways beyond the T_{reg}2 paradigm.  
21-14  Innate pathways and their associated cytokines can initiate asthma.  

Mediators involved in the development of asthma.  
21-15  TSLP is a novel IL-17-like cytokine that promotes T_{reg}2-related immune responses.  
21-16  IL-25 is an IL-17 cytokine family member that amplifies T_{reg}2 responses.  
21-17  IL-33 is an IL-1 family member that enhances the activity of mast cells, basophils, and eosinophils.  
21-18  IL-17 derived from T_{reg}17 cells and innate immune cells enhances neutrophilic responses in asthma.  
21-19  IL-22 derived from T_{reg}2 cells promotes epithelial cell responses associated with the asthma phenotype.  

Innate effector cells in the development of asthma.  
21-20  Lung epithelial cells may have a central role in the induction and maintenance of asthma.  
21-21  Natural helper cells/nuocytes are lymphoid tissue inducer (Lt)-like cells that initiate T_{reg}2-related inflammation.  
21-22  Alternatively activated macrophages promote T_{reg}2 inflammation in asthma.  
21-23  NKT cells have a central role in the initiation of the asthma phenotype in mouse models.  
21-24  NKT cells may be central mediators of human asthma.  

Summary.  
Further Reading.  

Chapter 22  The Ocular Surface as a Mucosal Immune Site  

Organization of the eye-associated lymphoid tissue.  
22-1  The EALT contains organized and diffuse populations of lymphocytes.  
22-2  The lacrimal gland and the lacrimal gland-associated lymphoid tissue are anatomically located within the upper eyelid.  
22-3  Conjunctiva-associated lymphoid tissue (CALT) covers the external surface of the eye with three anatomic regions (palpebral, bulbar, and fornix).  
22-4  Tear-duct-associated lymphoid tissue (TALT) is present in rodents and humans and is subject to a pathway of organogenesis that is distinct from GALT.  

Induction and expression of immunity at the ocular surface—the good and the bad.  
22-5  Regulatory mechanisms exist in the EALT that restrict an inflammatory response.  
22-6  Immunization through the ocular mucosal immune system can, however, induce an immune response.  

Diseases associated with dysfunction of the ocular mucosal immune system.  
22-7  Loss of tear fluid results in dry eye syndrome.  

Summary.  
Further Reading.
Chapter 22 Sjögren’s syndrome is an autoimmune disease of the lacrimal and salivary glands.

Chapter 23 Ocular cicatricial pemphigoid is an autoimmune disease that is directed against components of the basement membrane.

Chapter 24 Allergy is a common clinical manifestation in the eye due to its exposed surfaces.

Chapter 25 Herpetic stromal keratitis is a pathologic response against the cornea after herpes virus infection has been cleared.

Chapter 26 The interior of the eye is an immune privileged site due to its exposed surfaces.

Chapter 27 Sjögren’s syndrome is an autoimmune disease of the lacrimal and salivary glands.

Chapter 28 Ocular cicatricial pemphigoid is an autoimmune disease that is directed against components of the basement membrane.

Chapter 29 Allergy is a common clinical manifestation in the eye due to its exposed surfaces.

Chapter 30 Herpetic stromal keratitis is a pathologic response against the cornea after herpes virus infection has been cleared.

Chapter 31 The interior of the eye is an immune privileged site due to its exposed surfaces.

Chapter 32 Sjögren’s syndrome is an autoimmune disease of the lacrimal and salivary glands.

Chapter 33 Ocular cicatricial pemphigoid is an autoimmune disease that is directed against components of the basement membrane.

Chapter 34 Allergy is a common clinical manifestation in the eye due to its exposed surfaces.

Chapter 35 Herpetic stromal keratitis is a pathologic response against the cornea after herpes virus infection has been cleared.

Chapter 36 The interior of the eye is an immune privileged site due to its exposed surfaces.

Chapter 37 Sjögren’s syndrome is an autoimmune disease of the lacrimal and salivary glands.

Chapter 38 Ocular cicatricial pemphigoid is an autoimmune disease that is directed against components of the basement membrane.

Chapter 39 Allergy is a common clinical manifestation in the eye due to its exposed surfaces.

Chapter 40 Herpetic stromal keratitis is a pathologic response against the cornea after herpes virus infection has been cleared.

Chapter 41 The interior of the eye is an immune privileged site due to its exposed surfaces.

Chapter 42 Sjögren’s syndrome is an autoimmune disease of the lacrimal and salivary glands.

Chapter 43 Ocular cicatricial pemphigoid is an autoimmune disease that is directed against components of the basement membrane.

Chapter 44 Allergy is a common clinical manifestation in the eye due to its exposed surfaces.

Chapter 45 Herpetic stromal keratitis is a pathologic response against the cornea after herpes virus infection has been cleared.

Chapter 46 The interior of the eye is an immune privileged site due to its exposed surfaces.

Chapter 47 Sjögren’s syndrome is an autoimmune disease of the lacrimal and salivary glands.

Chapter 48 Ocular cicatricial pemphigoid is an autoimmune disease that is directed against components of the basement membrane.

Chapter 49 Allergy is a common clinical manifestation in the eye due to its exposed surfaces.

Chapter 50 Herpetic stromal keratitis is a pathologic response against the cornea after herpes virus infection has been cleared.

Chapter 51 The interior of the eye is an immune privileged site due to its exposed surfaces.

Chapter 52 Sjögren’s syndrome is an autoimmune disease of the lacrimal and salivary glands.

Chapter 53 Ocular cicatricial pemphigoid is an autoimmune disease that is directed against components of the basement membrane.

Chapter 54 Allergy is a common clinical manifestation in the eye due to its exposed surfaces.

Chapter 55 Herpetic stromal keratitis is a pathologic response against the cornea after herpes virus infection has been cleared.

Chapter 56 The interior of the eye is an immune privileged site due to its exposed surfaces.

Chapter 57 Sjögren’s syndrome is an autoimmune disease of the lacrimal and salivary glands.

Chapter 58 Ocular cicatricial pemphigoid is an autoimmune disease that is directed against components of the basement membrane.

Chapter 59 Allergy is a common clinical manifestation in the eye due to its exposed surfaces.

Chapter 60 Herpetic stromal keratitis is a pathologic response against the cornea after herpes virus infection has been cleared.

Chapter 61 The interior of the eye is an immune privileged site due to its exposed surfaces.

Chapter 62 Sjögren’s syndrome is an autoimmune disease of the lacrimal and salivary glands.

Chapter 63 Ocular cicatricial pemphigoid is an autoimmune disease that is directed against components of the basement membrane.

Chapter 64 Allergy is a common clinical manifestation in the eye due to its exposed surfaces.

Chapter 65 Herpetic stromal keratitis is a pathologic response against the cornea after herpes virus infection has been cleared.

Chapter 66 The interior of the eye is an immune privileged site due to its exposed surfaces.

Chapter 67 Sjögren’s syndrome is an autoimmune disease of the lacrimal and salivary glands.

Chapter 68 Ocular cicatricial pemphigoid is an autoimmune disease that is directed against components of the basement membrane.

Chapter 69 Allergy is a common clinical manifestation in the eye due to its exposed surfaces.

Chapter 70 Herpetic stromal keratitis is a pathologic response against the cornea after herpes virus infection has been cleared.

Chapter 71 The interior of the eye is an immune privileged site due to its exposed surfaces.

Chapter 72 Sjögren’s syndrome is an autoimmune disease of the lacrimal and salivary glands.

Chapter 73 Ocular cicatricial pemphigoid is an autoimmune disease that is directed against components of the basement membrane.

Chapter 74 Allergy is a common clinical manifestation in the eye due to its exposed surfaces.

Chapter 75 Herpetic stromal keratitis is a pathologic response against the cornea after herpes virus infection has been cleared.

Chapter 76 The interior of the eye is an immune privileged site due to its exposed surfaces.

Chapter 77 Sjögren’s syndrome is an autoimmune disease of the lacrimal and salivary glands.

Chapter 78 Ocular cicatricial pemphigoid is an autoimmune disease that is directed against components of the basement membrane.

Chapter 79 Allergy is a common clinical manifestation in the eye due to its exposed surfaces.

Chapter 80 Herpetic stromal keratitis is a pathologic response against the cornea after herpes virus infection has been cleared.

Chapter 81 The interior of the eye is an immune privileged site due to its exposed surfaces.

Chapter 82 Sjögren’s syndrome is an autoimmune disease of the lacrimal and salivary glands.

Chapter 83 Ocular cicatricial pemphigoid is an autoimmune disease that is directed against components of the basement membrane.

Chapter 84 Allergy is a common clinical manifestation in the eye due to its exposed surfaces.

Chapter 85 Herpetic stromal keratitis is a pathologic response against the cornea after herpes virus infection has been cleared.

Chapter 86 The interior of the eye is an immune privileged site due to its exposed surfaces.

Chapter 87 Sjögren’s syndrome is an autoimmune disease of the lacrimal and salivary glands.

Chapter 88 Ocular cicatricial pemphigoid is an autoimmune disease that is directed against components of the basement membrane.

Chapter 89 Allergy is a common clinical manifestation in the eye due to its exposed surfaces.

Chapter 90 Herpetic stromal keratitis is a pathologic response against the cornea after herpes virus infection has been cleared.

Chapter 91 The interior of the eye is an immune privileged site due to its exposed surfaces.
Cervico-vaginal dendritic cells (DCs) capture, disseminate, and trans infect mononuclear cells.  
Cell-associated HIV-1 is transmitted across inner foreskin mucosa.  
HIV-1 entry into gut mucosa is mediated by epithelial cells and DCs.  
Few HIV-1 virions are transmitted in acute HIV-1 infection.

T-cell depletion in early HIV-1 infection.

HIV-1 causes rapid, profound, and prolonged CD4+ T-cell depletion in the intestinal mucosa.

HIV-1 alters intestinal epithelial permeability, promoting microbial translocation.

Mucosal infections associated with HIV-1 infection.

HIV-1-induced immunosuppression leads to opportunistic infection of gut mucosa by viral, parasitic, bacterial, and fungal pathogens.

Mucosal vaccine formulations and delivery systems.

The ability to divide, present native antigens, and stimulate innate immunity are key features of live attenuated vaccines.

There are effective inactivated whole-cell bacterial oral vaccines.

Plant-based ‘edible’ vaccines may represent a strategy for mucosal vaccination.

Targeted mucosal vaccines can use lectins and microparticles.

Limitations of mucosal vaccines due to unique conditions in the tropics and the age of the vaccinees.

Mucosal adjuvants and their function.

The ADP-ribosylating toxins and their derivatives are mucosal adjuvants.

Autoimmune disease can be treated by mucosal vaccination.

Biofilms and inflammatory periodontitis.

Resolvins can help prevent periodontitis.

Resolvins can treat periodontitis.

The celiac lesion.

Villous blunting and crypt cell hyperplasia are characteristic histological features.

Intraepithelial lymphocytes are prominent.

Endogenous generation of pro-resolution agonists is important in periodontal disease.

The resolution phase of acute inflammation is as important as the onset phase.

Endogenous resolving molecules as therapeutic agents in periodontal disease.

Resolvins can help prevent periodontitis.

Resolvins can treat periodontitis.

Biofilms and inflammatory periodontitis.

Summary.

Chapter 26 Infection-Driven Periodontal Disease

Etiology of periodontal disease.

Biofilms are important for the development of periodontitis.

Pathogen-associated molecular patterns are important in periodontal disease.

T cell and B cell immune responses are involved in periodontitis.

Cytokines are involved in bone resorption in periodontitis.

Inflammation drives the pathogenesis of periodontitis.

The arachidonic acid pathway is important in periodontal disease.

Regulation of inflammation is a major determinant of bacterial colonization and disease.

Endogenous generation of pro-resolution agonists is important in periodontal disease.

The resolution phase of acute inflammation is as important as the onset phase.

Endogenous resolving molecules as therapeutic agents in periodontal disease.

Resolvins can help prevent periodontitis.

Resolvins can treat periodontitis.

Biofilms and inflammatory periodontitis.

Summary.

Chapter 27 Principles of Mucosal Vaccine Strategies

Principles of mucosal vaccination.

The problem with mucosal vaccines is tolerance.

There are unique compartmentalization and cell-migration pathways in mucosal immune responses.

There is preferential dissemination of mucosal immune responses after different routes of vaccination.

Mucosal vaccine formulations and delivery systems.

The ability to divide, present native antigens, and stimulate innate immunity are key features of live attenuated vaccines.

There are effective inactivated whole-cell bacterial oral vaccines.

Plant-based ‘edible’ vaccines may represent a strategy for mucosal vaccination.

Targeted mucosal vaccines can use lectins and microparticles.

Limitations of mucosal vaccines due to unique conditions in the tropics and the age of the vaccinees.

Mucosal adjuvants and their function.

The ADP-ribosylating toxins and their derivatives are mucosal adjuvants.

Autoimmune disease can be treated by mucosal vaccination.

Biofilms and inflammatory periodontitis.

Resolvins can help prevent periodontitis.

Resolvins can treat periodontitis.

The celiac lesion.

Villous blunting and crypt cell hyperplasia are characteristic histological features.

Intraepithelial lymphocytes are prominent.

Endogenous generation of pro-resolution agonists is important in periodontal disease.

The resolution phase of acute inflammation is as important as the onset phase.

Endogenous resolving molecules as therapeutic agents in periodontal disease.

Resolvins can help prevent periodontitis.

Resolvins can treat periodontitis.

Biofilms and inflammatory periodontitis.

Summary.
Chapter 29 IgA Nephropathy

Clinical presentation of IgA nephropathy.

29-1 IgA nephropathy is characterized by sporadic and familial forms.

29-2 Definitive diagnosis of IgA nephropathy requires a renal biopsy.

29-3 IgA nephropathy is characterized by mesangial deposits of IgA.

The immunopathogenesis of IgA nephropathy.

29-4 IgA, the target of IgA immune complexes, is the major immunoglobulin isotype produced in the body.

29-5 Human IgA1 has a unique hinge region containing sites that are amenable to O-linked glycosylation.

29-6 Circulating IgA1 in IgA nephropathy contains aberrant O-linked glycans.

29-7 Anti-glycan antibodies develop against aberrantly glycosylated IgA1 in IgA nephropathy and form immune complexes.

29-8 Gal-deficient IgA1-containing immune complexes in IgA nephropathy are inflammatory.

29-9 Urinary immunoglobulins are potential biomarkers of IgA nephropathy.

Summary.

Further Reading.

Chapter 30 Mucosal Manifestations of Immunodeficiencies

Antibody deficiencies.

30-1 Congenital agammaglobulinemia, or X-linked agammaglobulinemia, is the prototypic disorder of genetically determined antibody deficiency.

30-2 Common variable immunodeficiency (CVID) is the most common form of clinically significant primary immunodeficiency.

30-3 IgA deficiency is the most common primary immunodeficiency.

Combined immunodeficiencies.

30-4 Severe combined immunodeficiencies (SCIDs) are a heterogeneous group of genetically determined disorders.

30-5 CD40 ligand (CD40L) deficiency is a disorder with broad immunologic consequences due to the wide range of cell types that express its receptor, CD40.

30-6 CD40 deficiency is a disorder that reproduces the clinical phenotype of CD40L deficiency.

30-7 Major histocompatibility complex class II (MHC-II) deficiency leads to extensive deficiencies in humoral and cellular adaptive immune function.

30-8 Deficiency of a nuclear protein, SP110, of unknown function leads to hepatic veno-occlusive disease with immunodeficiency.

Immunodeficiencies affecting regulatory factors and populations of lymphocytes that produce these factors.

30-9 Genetically mediated Foxp3 deficiency leads to the immune dysregulation, polyendocrinopathy, enteropathy, X-linked (IPEX) syndrome.

30-10 Wiskott-Aldrich syndrome (WAS), due to deficiency in Wiskott-Aldrich protein (WASP), affects multiple lineages of hematopoietic cells and consequently diverse aspects of immune function.

Summary.

Further Reading.

Chapter 31 Inflammatory Bowel Disease

Genetic basis of IBD.

31-1 Epidemiological observations support the idea of a genetic basis of IBD.

31-2 IBD susceptibility genes were identified before the era of genome-wide association studies.

31-3 Genome-wide association studies reveal large numbers of genes associated with IBD.

31-4 Environmental factors are clearly involved in IBD pathogenesis.

31-5 Bacteria and potentially viruses are major drivers of pathogenic inflammation in the gut.

Association of IBD with innate immunity abnormalities.

31-6 Genes involved in innate immunity, endoplasmic reticulum stress, and autophagy are important in IBD.

31-7 Autophagy-related proteins are linked to IBD.

31-8 Impairment of intestinal epithelial cell function may also be a key factor for the development and/or perpetuation of colitis.

31-9 Excessive innate immune response toward the microbiota causes chronic inflammation in the gut.

31-10 There is a link between innate immunity dysfunction and Crohn’s disease and Crohn’s-like disease.

31-11 NOD2/CARD15 is involved in the control of defensins in the gut.

Adaptive immunity in the pathogenesis of IBD.

31-12 Genes associated with T-cell activation and differentiation are also involved in IBD.

31-13 Ongoing inflammation in IBD is driven by T cells.

Summary.

Further Reading.

Chapter 32 Food Sensitive and Eosinophilic Enteropathies

Basic principles of the immune response to foods.

32-1 Healthy individuals are tolerant to the great diversity of antigens present in food.

32-2 Aberrant immune responses to foods can be IgE and non-IgE mediated.

32-3 Food sensitive enteropathies are diagnosed by laboratory and clinical parameters.
Induction of food-specific IgE can lead to mast-cell degranulation and both local and systemic allergic symptoms.

Eight types of food account for most allergic responses.

Allergies initially manifest at peripheral sites such as the skin, but progress to the airways.

Sensitization to food antigens may occur outside the gastrointestinal tract.

Food allergy has a genetic component.

It remains unclear at which time it is best to begin introducing food antigens into the infant diet.

The eosinophilic gastrointestinal diseases (EGIDs).

There is considerable confusion regarding the definitions of mucosal eosinophilia.

Eosinophilic esophagitis (EoE) is the commonest form of EGIS.

The environmental allergens contributing to EoE can be both dietary and airborne.

Eosinophils play a critical role in the pathogenesis of EoE.

Eosinophilic gastroenteritis is uncommon.

Allergic reactions to foods sometimes manifest only in the colon.

Prevalence of food sensitive enteropathies.

Treatment for food sensitive enteropathies.

Summary.

Further Reading.