Manual of Allergy and Immunology:

Diagnosis and Therapy

Edited by

Glenn J. Lawlor, Jr., M.D.

Thomas J. Fischer, M.D.

Manual of Allergy and Immunology:

Diagnosis and Therapy

Edited by

Glenn J. Lawlor, Jr., M.D.
Assistant Clinical Professor of Pediatrics, UCLA School of Medicine; Director, Allergy Clinic, UCLA Student Health Service, UCLA Center for the Health Sciences, Los Angeles

Thomas J. Fischer, M.D.
Assistant Professor of Pediatrics, University of Cincinnati College of Medicine; Director, Division of Allergy/Immunology, Children's Hospital Medical Center, Cincinnati

Little, Brown and Company
Boston

First Edition

Library of Congress Catalog Card No. 81-80890

ISBN 0-316-51665-1

Printed in the United States of America

HAL

Contributing Authors

Robert F. Ashman, M.D.	Professor, Department of Medicine, Chief, Division of Rheumatology, University of Iowa College of Medicine, Iowa City
Robert W. Ausdenmoore, M.D.	Clinical Professor of Pediatrics, University of Cincinnati College of Medicine; Attending Staff, Allergy/Immunology Division, Children's Hospital Medical Center, Cincinnati
I. Leonard Bernstein, M.D.	Clinical Professor of Medicine, Director, Allergy Research Laboratory and Allergy Training Program, University of Cincinnati College of Medicine; Director, Allergy Clinic and Attending Physician, Cincinnati General Hospital, Cincinnati
Gregory N. Entis, M.D.	Assistant Clinical Professor of Pediatrics, University of Cincinnati College of Medicine; Attending Physician, Bethesda Hospital and Children's Hospital Medical Center, Cincinnati
Michael K. Farrell, M.D.	Assistant Professor of Pediatrics, University of Cincinnati College of Medicine; Attending Physician, Division of Pediatric Gastroenterology, Children's Hospital Medical Center, Cincinnati
Stanley M. Fineman, M.D.	Assistant Clinical Professor, Department of Pediatrics, Emory University School of Medicine, Atlanta
Thomas J. Fischer, M.D.	Assistant Professor of Pediatrics, University of Cincinnati College of Medicine; Director, Division of Allergy/Immunology, Children's Hospital Medical Center, Cincinnati
Joseph E. Ghory, M.D.	Clinical Professor of Pediatrics, University of Cincinnati College of Medicine; Associate Director, Division of Allergy/Immunology, Children's Hospital Medical Center, Cincinnati
Henry Gong, Jr., M.D.	Assistant Professor of Medicine, UCLA School of Medicine; Attending Physician, Pulmonary Disease Division, UCLA Hospital and Clinics, UCLA Center for the Health Sciences, Los Angeles
Hemant H. Kesarwala, M.D.	Assistant Professor of Pediatrics, Attending Physician, Division of Allergy/Immunology, Rutgers Medical School, Piscataway, New Jersey
Glenn J. Lawlor, Jr., M.D.	Assistant Clinical Professor of Pediatrics, UCLA School of Medicine; Director, Allergy Clinic, UCLA Student Health Service, UCLA Center for the Health Sciences, Los Angeles

Michael H. Mellon, M.D.	Assistant Clinical Professor of Pediatrics, University of California, San Diego, School of Medicine; Staff Allergist, Kaiser Permanente Medical Center, San Diego
Roy Patterson, M.D.	Professor and Chairman, Department of Medicine, Northwestern University Medical School, Chicago
Raymond M. Ringenbach, M.D.	Clinical Instructor, Department of Dermatology, University of Cincinnati College of Medicine; Instructor, Cincinnati General Hospital, Cincinnati
Howard M. Rosenblatt, M.D.	Assistant Professor of Pediatrics, Texas Children's Hospital, Baylor Medical School, Houston
Andrew Saxon, M.D.	Assistant Professor of Medicine, UCLA School of Medicine; Chief, Division of Clinical Immunology/Allergy, Department of Medicine, UCLA Center for the Health Sciences, Los Angeles
Michael Schatz, M.D.	Assistant Clinical Professor of Medicine/Pediatrics, University of California, San Diego, School of Medicine; Staff Allergist, Kaiser Permanente Medical Center, San Diego
Mary J. Spencer, M.D.	Assistant Professor of Pediatrics, UCLA School of Medicine; Chief, Division of Ambulatory Services, Department of Pediatrics, UCLA Center for the Health Sciences, Los Angeles
Donald P. Tashkin, M.D.	Associate Professor of Medicine, UCLA School of Medicine; Attending Physician, Department of Medicine, UCLA Center for the Health Sciences, Los Angeles
John G. Winant, Jr., M.D.	Postdoctoral Fellow, Department of Pediatrics, Division of Allergy/Immunology, University of Cincinnati College of Medicine, Cincinnati
Allan Wirtzer, M.D.	Assistant Clinical Professor of Medicine/Dermatology, UCLA School of Medicine; Attending Physician, Dermatology Service, Wadsworth Veterans Administration Hospital Center, Los Angeles
Kwan Y. Wong, M.B., B.S.	Associate Professor of Pediatrics, University of Cincinnati College of Medicine; Assistant Director, Pediatric Hematology–Oncology, Children's Hospital Medical Center, Cincinnati
Paul M. Zeltzer, M.D.	Assistant Professor of Pediatrics, University of Texas Medical School at San Antonio; Staff Physician, Department of Pediatrics, Santa Rosa Children's Hospital, San Antonio

Preface

Manual of Allergy and Immunology is designed to serve the health care professional in the diagnosis and management of allergic diseases and other conditions associated with immunologic dysfunction. We have attempted to present this material in a clear, direct manner, anticipating questions that occur during decision making and providing specific information to allow an individualized approach to diagnosis and treatment.

Contributors to this book were chosen for their specific expertise and interest in their respective areas. Only currently accepted therapeutic regimens and dosages are presented; all material that we think is investigative is so identified.

Didactic material has been minimized; what is included has been carefully edited to allow a basic understanding of each subject. More definitive reference material is indicated for each chapter under Suggested Reading.

We feel the Manual contains all the basic information, collected in a single source, required in the practice of allergy and clinical immunology. The specialist will find it a convenient handbook while the generalist can use the Manual as a helpful guide in formulating a diagnostic and therapeutic approach to patients suspected of having an allergic or immunologic disorder or in choosing immunologic studies generally available (e.g., for patients with infectious diseases, hematologic disorders, or rheumatoid diseases). Students and house officers will find the Manual a useful introductory guide to the clinical practice of allergy and immunology.

We wish to thank all our contributors for unselfishly giving a considerable amount of time and effort to prepare their respective sections. We also want to thank Little, Brown and Company for providing us the opportunity of publishing the Manual; our editors, Lin Richter, who initially authorized the Manual; Diana O'Dell Potter, who provided initial support; Jim Krosschell, who supervised copyediting and production; and especially Kathleen O'Brien who patiently gave editorial assistance throughout the preparation. We also wish to thank Ms. Andrea Lippelman for her secretarial help in preparing the typed manuscript. We have enjoyed this undertaking and have found the writing and editing of this book a personal learning experience. We hope that others will find it equally informative.

G.J.L., Jr.
T.J.F.

Contents

1

Introduction to the Immune System

Hemant H. Kesarwala and
Thomas J. Fischer

The function of the immune system is to distinguish self from non-self and to eliminate the latter. Such a system is necessary for survival in all living creatures. In humans, a functioning immune system is required to prevent attack by internal forces (e.g., tumor cells, autoimmune phenomena) as well as external forces (microorganisms or toxic substances). Deficiency or dysfunction of the immune system in humans leads to a variety of clinical diseases of varying expression and severity, from such disorders as allergic rhinitis to severe rheumatoid arthritis, severe combined immunodeficiency, or malignancy. This chapter is a brief introduction to the complex immune system. Added explanations are found in subsequent chapters and the suggested reading lists at the end of each chapter.

Organs of the Immune System

Several tissues and organs play roles in host defense and are functionally classified as the immune system.

I. **Primary lymphoid organs** are the thymus and the bursa of Fabricius in birds and the thymus and bone marrow (and/or fetal liver) in mammals.

   A. The **bone marrow** is the source of pluripotent stem cells, which differentiate into lymphocyte, granulocyte, erythrocyte, and megakaryocyte populations. In mammals, the bone marrow also supports differentiation of lymphocytes. Deficiency or dysfunction of the pluripotent stem cell or the various cell lines developing from it can result in immune deficiency disorders of varying expression and severity.

   B. The **thymus,** derived from the third and fourth embryonic pharyngeal pouches and located in the mediastinum, exercises control over the entire immune system. Its reticular structure allows a significant number of lymphocytes to migrate through it to become fully immunocompetent thymus-derived cells (T cells). A large number of cells also die within the thymus and are apparently phagocytosed, a mechanism to eliminate lymphocyte clones reactive against self-antigens. The thymus also regulates immune function by secretion of multiple soluble hormones. Absence of the thymus or its abnormal development results in T-lymphocyte deficiencies (e.g., DiGeorge syndrome).

II. **Secondary lymphoid organs** in mammals (lymph nodes, spleen, and gut-associated lymphoid tissue) are connected by blood and lymphatic vessels. Through these vessels, lymphocytes circulate and recirculate, responding to antigen and spreading the specific experience of this antigen exposure to all parts of the lymphoid system.

   A. **Lymph nodes** are the peripheral organs of the immune system that attempt to localize and prevent the spread of infection. Lymph nodes have a framework of reticular cells and fibers that are arranged into a cortex and medulla. Bursal equivalent lymphocytes (B cells), the precursors of plasma cells, are found in the cortex (the follicles and germinal centers) as well as the medulla. T-lymphocyte areas are primarily found in the medullary and paracortical areas of the lymph node (**Fig. 1-1**).

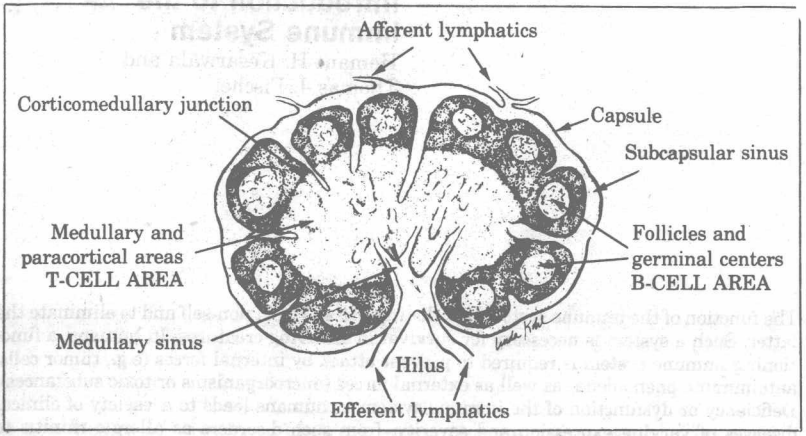

Fig. 1-1. Lymph node structure indicating primary T-cell and B-cell areas. (From M.S. Thaler, R.D. Klausner, and H.J. Cohen. In Foundations of the Immune Response. *Medical Immunology*. Philadelphia: Lippincott, 1977.)

B. The **spleen,** functionally and structurally divided into T-cell and B-cell areas like those of the lymph nodes, filters and processes antigens from the blood.

C. Gut-associated lymphoid tissue (tonsils, Peyer's patches of the small intestine, and the appendix) shows a similar separation into T cell–dependent and B cell–dependent areas. Many lymphocytes are also seen within the lamina propria of the small intestinal villi and between the epithelial cells of the intestinal mucosal surface. Gut-associated lymphoid tissue may play a role in the differentiation of stem cells into B-lymphocytes.

Cells of the Immune System

I. Lymphocytes are responsible for the initial **specific** recognition of an antigen. They are principally divided into B-lymphocytes (bursal) and T-lymphocytes (thymic) on the basis of several functional tests, the most obvious being the production of antibody as a measure of B-lymphocyte function and cell-mediated cytotoxicity for T-lymphocyte function. B cells and T cells also have distinguishable surface structures. The B cell is coated with surface membrane–bound immunoglobulin (SmIg) and also has receptors for complement and the Fc portion of immunoglobulins. T cells are quantitated by the ability to cause adherence of sheep red blood cells to their surface (E rosettes). Structurally, T and B cells cannot be distinguished from each other under the light microscope. About 15% of peripheral blood lymphocytes are not labeled with either marker (null cells). These cells may represent precursors of B cells and T cells. Further separation of T-lymphocyte subpopulations is accomplished by immunofluorescence using monoclonal antibodies reactive with individual cell-surface antigens.

T cells mediate a number of functions, notably the "cell-mediated immune responses," such as graft rejection and delayed (tuberculin-type) hypersensitivity. In addition, the discovery of different subsets of T-lymphocytes, such as T-helper cells, T-suppressor cells, and T-killer cells, has provided new insight into the complex function of T-lymphocytes. B cells are the direct precursors of mature antibody-secreting cells (plasma cells). Although ongoing investigations indicate an array of complex interactions between B and T cells and tend to obscure distinctions between these two systems, the division into B and T cells with different developmental and

functional characteristics allows for an operational understanding of the immune system.

II. **Phagocytic cells** (polymorphonuclear leukocytes, eosinophils, and monocyte-macrophages) reach maturity in the bone marrow, circulate in the blood for a short time, and enter the tissue spaces by diapedesis through capillary walls in response to chemotactic factors released by inflammation.

A. **Macrophages** play a central role in the immune response. Derived from the blood monocytes, they circulate for a few days in the blood and then leave the vascular compartment to become active tissue macrophages. Macrophages have the following important functions: chemotaxis (cell movement), phagocytosis (antigen engulfment), antigen-processing, and presentation of the antigen in an immunogenic form to the lymphocytes. However, macrophages have no antigen specificity, as do lymphocytes.

B. **Polymorphonuclear leukocytes** originate from the bone marrow. These cells circulate in the blood and tissue, and their primary function is phagocytosis and destruction of foreign antigens.

C. **Eosinophils** are often found in inflammatory sites or at sites of immune reactivity, but they phagocytose and kill less efficiently than do polymorphonuclear leukocytes. Although they show certain functional characteristics similar to those of neutrophils, their role has still not been completely determined. However, they appear to have a modulatory or regulatory function in various types of inflammation.

III. **Basophils** and **mast cells** release the mediators of immediate hypersensitivity, e.g., histamine, SRS-A, ECF-A (see **Chap. 2**), which have significant effects on the vasculature and on the inflammatory response. Basophils are present in the circulation, while mast cells are present only in tissue, but in much larger numbers.

Development of the Immune System

I. **Phylogenetic development.** In unicellular animals, nonspecific mechanisms of host defense consist of phagocytic processes and hydrolytic enzymes, while primitive prevertebrate organisms acquire external and internal surface barriers as well as specialized phagocytes. In primitive vertebrates with notochords, immunocytes with primitive recognition and memory capacity are added, which help to amplify and direct the phagocytic process. With progressive evolution, the immune system in higher animals and humans has evolved with increasing complexity in terms of its specific antibody and cell-mediated immune response capacity. Despite the complexity of the human immune system, host defense is still highly dependent on surface barriers and phagocytic mechanisms. Absence of phagocytic function (e.g., severe neutropenia) or loss of surface barriers (e.g., extensive surface burns) can present a tremendous risk of fulminant, life-threatening invasion by microorganisms that normally are not pathogenic.

II. **Ontogenetic development**

A. Cellular precursors of **T cells** are derived in early fetal life from the fetal yolk sac. By 4 to 5 weeks of gestation, they arise from the liver and thereafter from the bone marrow. T-lymphocyte precursors undergo differentiation and maturation under the influence of the thymus, which is formed from the third and fourth pharyngeal pouches at 6 to 8 weeks of gestation. Functional cellular responses, heavily dependent on T-cell immunocompetence, are not fully developed in the fetus, neonate, and young infant as compared with the adult.

B. **Precursor B cells,** derived from the same sources as T-cell precursors, can synthesize small quantities of IgM antibody. After antigenic stimulation, B cells differentiate into plasma cells, which are responsible for antibody formation. The antigenically stimulated human fetus is able to synthesize IgM antibody by 10½

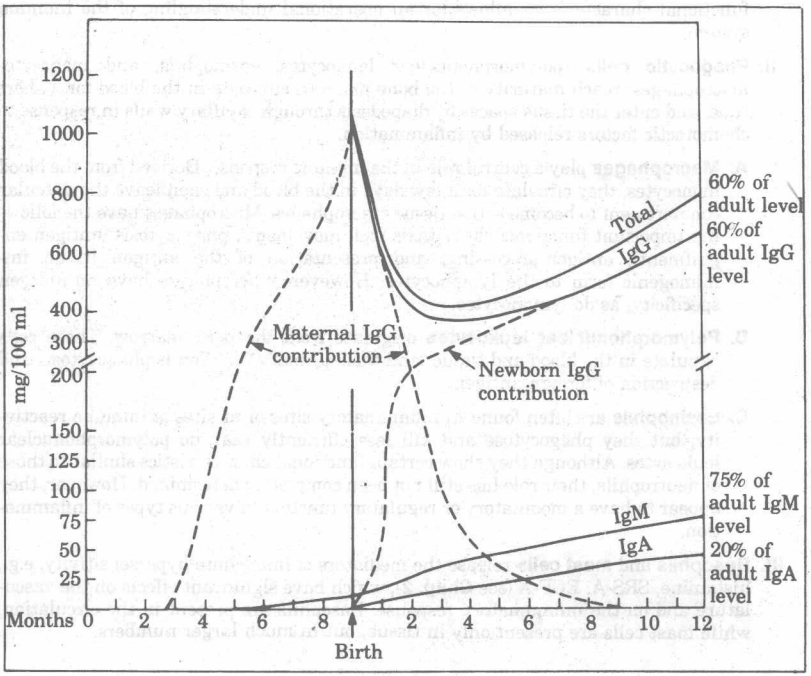

Fig. 1-2. Immunoglobulin (IgG, IgM, IgA) serum levels in the fetus and infant in the first year of life. The IgG in the fetus and newborn infant is solely of maternal origin. The maternal IgG disappears by the age of 9 months, at which time endogenous synthesis of IgG by the infant is well established. The IgM and IgA at birth are entirely neonatal in origin (no placental transfer). (From E.R. Stiehm. Immunoglobulins and Antibodies. In E.R. Stiehm and V.A. Fulginiti [Eds.], *Immunologic Disorders In Infants and Children*. Philadelphia: Saunders, 1973.)

weeks of gestation, IgG antibody by 12 weeks, and IgA antibody by 30 weeks. The normal human infant, usually born without antigenic stimulation unless infected in utero, has little circulating IgA and IgM antibody. IgG antibody is almost completely derived from the mother by active and selective transport across the placenta. Adult serum levels of IgG, IgM, and IgA immunoglobulins are attained separately (**Fig. 1-2**) (see **Appendix VII**).

C. **Phagocytic cells** are seen in the human fetus at 2 months of gestation as a few myelocytes and histiocytes, present in the early yolk-sac stage of hematopoiesis. Monocytes first appear in the spleen and lymph nodes at 4 to 5 months of gestation, with gradual maturation of macrophage function with advancing fetal age. Isolated newborn polymorphonuclear leukocytes have normal phagocytic activity when tested in vitro in the presence of adult serum. However, cells from a premature infant phagocytose less effectively than do those from a term infant. Chemotaxis (cell movement) of leukocytes and monocytes appears to be deficient in the newborn.

D. **Complement components** are synthesized by the fetus early in gestation, either at the same time of, or just before, the beginning of immunoglobulin synthesis. There is almost no placental transfer of complement components from mother to fetus. The levels of individual complement components C1q, C2, C4, C3, and C5

and the total hemolytic complement in the newborn are low. Such deficiency and dysfunction may be responsible for the relative opsonic deficiency in newborns.

Immune System Components

The immune system consists of specific and nonspecific components that have distinct but overlapping functions. Antibody (humoral) and cell-mediated immune systems provide specificity and a memory of previously encountered antigens. Phagocytic cells and complement proteins are respectively **nonspecific** cellular mechanisms and **nonspecific** humoral factors. Despite their lack of specificity, these components are essential because they are largely responsible for the natural immunity to a vast array of environmental microorganisms.

I. **Antibody immunity.** Lymphocytes passing through the bursa-equivalent organ in humans acquire the characteristics of B cells that undergo transformation into plasma cells. The plasma cell has an increased endoplasmic reticulum, indicating active protein synthesis.

A. **Immunoglobulin structure.** All immunoglobulin molecules have a certain structural similarity, with four polypeptide chains divided into two light and two heavy chains linked by disulfide bonds (**Fig. 1-3**). Disulfide linkages are also present on each chain. There are five classes of immunoglobulins, termed **IgA, IgG, IgM, IgD,** and **IgE,** based on the structure of their heavy chain (alpha [α], gamma [γ], mu [μ], delta [δ], and epsilon [ϵ] respectively) (see **Table 1-1**). There are only two classes of light chain: kappa (κ) and lambda (λ). Each immunoglobulin molecule has only one class of light chain and only one class of heavy chain, although each class of immunoglobulin can have either kappa or lambda light chains. Accordingly, the structural formula for each immunoglobulin molecule can be written $\alpha_2 \kappa_2$, $\alpha_2 \lambda_2$, etc. Monomers consist of a single immunoglobulin molecule, e.g., IgG antibody, while polymers have multiple basic units, e.g., IgM antibody which consists of five basic units of 10 light chains and 10 heavy chains. In addition to the polypeptide chains, other structures can be incorporated into the immunoglobulin molecule, e.g., J chains and the secretory piece of IgA.

B. **Structural-functional correlates.** Study of the immunoglobulin subunits can help to localize and specify the function of biologically active sites.

1. Agents used in cleaving the immunoglobulin molecule include enzymes such as papain and pepsin, dilute acids, or wetting agents such as urea (see **Fig. 1-3**). The enzymes papain and papsin break the immunoglobulin molecule into different fragments. Papain breaks the molecule into two Fab fragments and one Fc fragment. Pepsin breaks the molecule into a single $F(ab')_2$ fragment and multiple Fc fragments.

   a. The **Fab end** of an immunoglobulin molecule is called the amino-terminal end, which, with the presence of both light and heavy chains, is the antibody-combining site. The amino-terminal end possesses marked variability in the amino acid sequence. This variability enables the immunoglobulin molecule to combine with a variety of antigens.

   b. The **Fc end** is the carboxy-terminal end, which contains only heavy-chain components. This Fc, or constant, region (fixed amino acid sequence) is responsible for conferring biologic activity on the immunoglobulin molecule, such as placental transfer, complement fixation, binding to skin and cells (macrophages, platelets, granulocytes, mast cells), and determining its rate of synthesis and catabolism. The Fc fragment is not involved in specific antigen recognition.

2. Various **genetic markers** have been demonstrated on the constant region of light and heavy chains. Genetic variations in light chains produce amino acid changes at certain positions, creating genetic allotypes. On kappa chains these

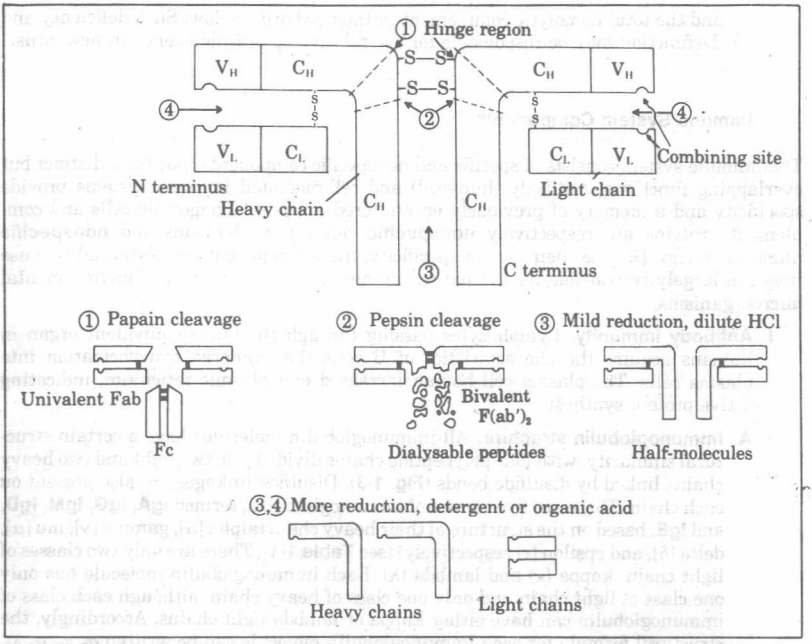

Fig. 1-3. Basic immunoglobulin structure with immunoglobulin subunits produced by enzyme, acid, or wetting agents. Interchain disulfide bonds are shown (large S-S), but intrachain bonds have been omitted for clarity. The number of H-H disulfide bonds varies with each class and subgroup of immunoglobulin. Numbers 1 through 4 show points of attack of various agents, with the cleavage products noted in smaller diagrams in the bottom half of the figure (V_H and V_L indicate variable regions of heavy and light chains respectively; C_H and C_L indicate constant regions of heavy and light chains). Polymeric forms of IgM and IgA are not shown but are joined at the Fc region near the carboxy terminus. (From R. Hong. Immunoglobulin Structure and Function. In E. Middleton, C.E. Reed, and E. F. Ellis [Eds.], *Allergy Principles and Practice*. St. Louis: The C.V. Mosby Co., 1978.)

are called Km (Inv) markers; a nonalleic marker on lambda chains is either present or absent (Oz+, Oz−). Genetic variations on heavy chains also produce allotypes called Gm, Am, and Mm markers, which are inherited by mendelian genetic ratios.

C. Immunoglobulin classes. Immunoglobulins are divided into five major classes. The characteristic features of each are summarized in **Table 1-1**.

1. **IgG** is the immunoglobulin primarily involved in the secondary or recall immune response. IgG antibodies are composed of two light chains and two heavy chains. This molecule is further divided into four different subclasses termed **IgG_1, IgG_2, IgG_3,** and **IgG_4,** based on structural differences in the gamma heavy chain. These subclasses also have functional variations in terms of complement fixation, alternative complement pathway activation, macrophage adherence, and ease of placental transfer. The ability of IgG to diffuse into body tissue facilitates combination and efficient elimination of antigens.
2. **IgM** immunoglobulin is the major part of the early humoral response, especially in response to nonprotein bacterial antigens. The IgM molecule consists

Table 1-1. Characteristic Features of the Five Classes of Immunoglobulins

Immunoglobulin	Heavy Chains	Light Chains	Molecular Weight (daltons)	Serum Concentration (mg/dl)	Localization in Secretions	Presence of Other Structures	Serum Half-Life (days)	Placental Transfer	Classic Complement Activation	Alternate Complement Activation	Biologic Activity (Function)
IgG	Gamma (γ_1) (γ_2) (γ_3) (γ_4)	Kappa or lambda	150,000	1200	–	–	23	+	+[a]	–	Neutralization, opsonization, bacteriolysis, agglutination, hemolysis
IgM	Mu (μ)	Kappa or lambda	900,000	150	±	J chain	5	–	+	–	Neutralization, hemolysis, agglutination, bacteriolysis, opsonization, first detectable antibody
IgA	Alpha (α_1) (α_2)	Kappa or lambda	160,000 (secretory IgA 370,000)	300	+	J chain and secretory component for secretory IgA	6	–	–	+	Neutralization, present in body secretions
IgD	Delta (δ)	Kappa or lambda	180,000	3	–	–	3	–	–	+	?
IgE	Epsilon (ϵ)	Kappa or lambda	200,000	0.03	±	–	2	–	–	+	Mast-cell binding and increased vascular permeability on antigen exposure

+ = present; – = absent; ± = possibly present.

[a]Except IgG_4.

Table 1-2. Differences between Humoral and Cell-mediated Immunity

Humoral-mediated Immunity	Cell-mediated Immunity
Antibody-mediated	Cell-mediated
Responsible cell: B-lymphocyte	Responsible cell: T-lymphocyte cells or cell products required for transfer of immunity
Transfer of immunity with serum	Responsible for host defense against viruses, fungi, intracellular organisms, tumor antigens, allograft rejection
Primary defense against bacterial infection	

of five IgG-like subunits that are linked by disulfide bonds and J chains. This immunoglobulin is incapable of placental transfer, but its polymeric structure makes for efficient agglutination or lysis of antigens.

3. **IgA** is the primary immunoglobulin of all mucosal surfaces and exocrine secretions. It exists either as a monomer, dimer, or even a trimer of the basic four-chain structure. IgA can be found in the serum or in exocrine secretions. Secretory IgA is equipped with a polypeptide (a secretory piece) that permits secretion of the IgA molecule across mucous membranes, providing initial protection against pathogens at the mucosal level. Selective IgA deficiency is the most common primary immunodeficiency in humans.

4. **IgD** immunoglobulin is present in very small quantities in the serum. Its functional role is not well characterized. Its structure is similar to that of other immunoglobulins, i.e., either kappa or lambda light chains linked to its own distinct delta heavy chains.

5. **IgE** immunoglobulin, also known as reaginic antibody, is normally present in a very small concentration, although elevated levels are seen in atopic disease and a number of other disorders (see **Table 2-3**). IgE antibody is made up of the basic four-chain structure of IgG, with either two kappa or two lambda light chains and two epsilon heavy chains. Mast cells and basophils have receptors for the Fc region of IgE, and the bridging of two IgE molecules by antigen results in the release of inflammatory mediators.

II. **Cell-mediated immunity** consists of a set of immune phenomena distinct from antibody-mediated immunity. The differences between the two systems are outlined in **Table 1-2**. Cell-mediated immunity is mediated by T-lymphocytes and monocytes-macrophages and requires intact cells that carry out their immune functions either by direct cell-to-cell contact or by production of soluble factors for specific immunologic functions, e.g., recruitment of phagocytic cells into sites of inflammation. The actions of these soluble factors, or **lymphokines**, are summarized in **Table 1-3**.

A. Although T cells were previously thought to be of a single cell type, a degree of functional heterogeneity exists among these T cells, which are now classified as helper, suppressor, or killer cells. These functions can be antigen-specific or antigen-nonspecific. T cells are recognized to play an increasing role in immunoregulation.

B. The **macrophage** is also important in promoting cell-mediated immunity. The macrophage processes antigen, activates T cells, and responds to lymphokines by entering the area of an inflammatory response. The mononuclear cell infiltrate induced by lymphokines comprises 95% macrophages and 5% lymphocytes.

C. In summary, cell-mediated immunity is responsible for the following immune phenomena:

1. Delayed hypersensitivity reactions (e.g., tuberculin test)