THE UNIVERSITY OF CHICAGO MEDICAL CENTER

MINI-MED SCHOOL

"All you need is curiosity"

THE UNIVERSITY OF CHICAGO MEDICAL CENTER

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Tuesday Evenings
March 7 to May 9
1995

7:30 to 9:30 p.m.

at the
Chicago
Cultural
Center

Schedule of Classes

Building the Bionic Human

The hip bone's connected to the thigh bone, but anatomists, when they're not singing that familiar ditty, also consider how the past is connected to the present and how form follows function over eons of evolution. The dinosaurs — always a popular subject — provide a useful model of vertebrate morphology, the gross body plan and structure of an animal. The Mini-Med students will study dinosaurs face-to-face to see how their anatomic features changed to adapt to shifts in the environment, allowing the movements needed to obtain food, escape predators, and find a mate. Humans have benefited from 300 million years of evolution since we shared an ancestor with the dinosaurs, yet the structure of our own skeleton still presents us with limitations, not only of size and speed, but also of durability. Today, however, bioengineers and orthopaedic surgeons are increasingly able to pick up where nature left off in the design of joints. An area of particular concern turns out to be where the hip bone's connected to the thigh bone. Mini-Med students will bone up on the design of the modern replacement hip that restores function to worn-out joints. They will learn how inorganic materials can be fused to living tissue, what happens where metal meets man, and why many space-age materials are unsuitable for use in the spaces between our bones.

Paul Sereno, Ph.D.

A well-known paleontologist and expert in dinosaur evolution and vertebrate structure, Paul Sereno is Associate Professor in Organismal Biology and Anatomy at the University of Chicago, where he teaches gross anatomy in the Pritzker School of Medicine.

Dr. Sereno has made several highly significant fossil discoveries, including the world's oldest and most primitive dinosaurs. He has studied dinosaur fossils in South America, Asia and Africa in his effort to understand how the dinosaur family tree developed and how the breakup of the continents affected dinosaur evolution. He led the 1991 expedition to Argentina that unearthed Eoraptor, the most primitive known dinosaur. Eoraptor was found only a mile from the site where three years earlier Dr. Sereno had found the first skull of the oldest known dinosaur, Herrerasaurus. In 1993, Dr. Sereno led an expedition across the Sahara Desert that uncovered two new species of dinosaurs.

Dr. Sereno has been profiled on the PBS series The *New Explorers*. In 1990 he received a five-year research award from the David and Lucile Packard Foundation.

A native of Naperville, Dr. Sereno is a graduate of Northern Illinois University, where he majored in art and biology and began assembling a portfolio of artwork for a career as an artist. He went on to study vertebrate paleontology and received his Ph.D. from Columbia University in 1987. He joined the University of Chicago faculty later that year.

Lawrence A. Pottenger, M.D., Ph.D.

Lawrence Pottenger is an orthopedic surgeon with a particular interest in arthritis and orthopedic problems in the elderly. He is Associate Professor of Surgery and Pathology at the University of Chicago.

Dr. Pottenger's laboratory research focuses on the composition of cartilage and the changes that occur in the progression of osteoarthritis — the common degenerative type of arthritis that results from wear and tear on the joints. In surgery, he performs many hip replacements and has pioneered techniques that avoid the use of cement, which is prone to loosening with continued use of the artificial joint. Dr. Pottenger also designs joints; he and a U. of C. colleague were recently issued a patent on a new artificial knee. Dr. Pottenger has also published on the surgeon's ethical obligation to treat HIV-infected patients. He is a Fellow of the American Academy of Orthopedic Surgeons and has long served the Illinois Chapter of the Arthritis Foundation.

Dr. Pottenger received his undergraduate degree, his Ph.D. in pathology and his medical degree (with honors) from the University of Chicago. He served his internship and residencies in general surgery and orthopedics at the Johns Hopkins Hospital. He joined the Chicago faculty in 1979.

Of Microbes and Men

The study of the human body begins with the cell, the basic unit of life. The 10 trillion cells in the body share fundamental features not only with one another, but with even the simplest single-cell organisms — bacteria, amoebe and yeast. These microbes have guided the study of basic cellular processes like growth and division and how energy is used to power life. Mini-Med students will hear about the machinery cells use to eat, digest, move and reproduce. They will also learn how some microorganisms have evolved the ability to produce antibiotics to kill bacteria without harming themselves. Humans have now expropriated some of these antibiotics for our own defense, but our scientific triumph over our tiny tormentors is incomplete. Microbiologists are still finding previously unknown microbes underlying diseases, as in the case of Legionnaires disease 20 years ago. Headlines remind us that it is the resurgence of old, familiar foes — TB, cholera, strep — now grown resistant to our most potent weapons, that pose the greatest threat to public health. What can be done to stop these resilient ancient enemies? Are we destined for a reprise of the plagues of the past?

Theodore L. Steck, M.D.

A physician with a strong interest in understanding how life works at the most basic level, Ted Steck is Professor of Biochemistry and Molecular Biology and of Molecular Genetics and Cell Biology at the University of Chicago. He is a member of the Committee on Cell Physiology and also holds a faculty appointment in the College, where he chairs the Environmental Studies Program.

Dr. Steck's focus on the basic processes of life has taken him from the human red blood cell to a prototype for our cells, a simple amoeba. He notes that our cells utilize the basic plan of operation worked out by such simple cells two billion years ago.

Dr. Steck received a Schweppe Foundation Scholarship and an American Cancer Society Research Award. He is a past Robert A. Welch Foundation Lecturer and is an elected member of the American Society Of Biological Chemistry and Molecular Biology.

Dr. Steck is a *summa cum laude* graduate of Lawrence College and received his M.D. from Harvard Medical School. After an internship at Beth Israel Hospital, he was a research fellow at Harvard and the National Cancer Institute before joining the Chicago faculty in 1970.

Robert S. Daum, M.D.

Robert Daum is a pediatrician and a specialist in the infectious diseases of childhood. He is Professor of Pediatrics and Chief of Pediatric Infectious Diseases at the University of Chicago.

Dr. Daum is an expert in vaccine development and in the use of antibiotics. He has served on many advisory and review committees for the National Institutes of Health and the Department of Health and Human Services. He is a member of the City of Chicago Communicable Disease Technical Advisory Group.

Dr. Daum received his bachelor's, master's and medical degrees from McGill University in Montreal, Quebec, Canada. He served his internship and residency at Montreal Children's Hospital, where he was named chief pediatric resident. After a fellowship in infectious diseases, also at Montreal Children's Hospital, he went to Tulane University to head the section of pediatric infectious diseases. He joined the Chicago faculty in 1988.

Session 3: Dr. H.B. Herscowitz

IMMUNOLOGY

Who am I? I am myself.

Introduction
- Threats to individuality - host response
- *Immunity* and *Immunology* - definitions
- Function of the immune system

Historical Perspective - a brief history

Types of Immunity
- Innate immunity - inborn, unchanging
  - *External* - 1st line of defense
    - Physiological barriers
  - *Internal* - 2nd line of host defense
    - Phagocytosis - eating cells
    - Inflammation

- Acquired (adaptive) immunity - develops through experience
  - Types of acquired immunity - 3rd line of host defense
    - *Active* - natural and artificial
    - *Passive* - natural and artificial
  - Specific effector functions
    - *Humoral immunity* - B cells and antibody
    - *Cell-mediated immunity* - T cells and cytokines

The immune system
- Antigens, antibodies and cytokines
- Anatomy - organs and cells
- Differentiation, self-discrimination and clonal selection
- Antigen recognition molecules
  - Major Histocompatibility Complex (MHC) - antigen processing and presentation
- Cellualr interactions - how the system works

Model of Immunologic Responses
- The "Yellow Brick Road" - cast of characters
  - The environment
  - Target cells
  - Inflammatory cells
  - Mediator cells
  - B-cell system
  - T-cell system

Outcomes of immunity
- *Protective* - immunity vs. microbes and cancer
- *Destructive* - allergy, autoimmunity, graft rejection

Dr. H.B. Herscowitz

GLOSSARY OF IMMUNOLOGICAL TERMS

Acquired immunity - immune reaction displaying features of specificity, diversity, memory, and self/nonself recognition.

Active immunity - immunity resulting from exposure; natural or artificial.

Activated lymphocyte - lymphocytes stimulated by antigen or mitogen.

Activated macrophage - cell whose metabolic state is enhanced as a result of exposure to a variety of stimuli, including phagocytosis or cytokines, which enables them to kill microbes and tumor cells more effectively.

Adjuvant - substance which nonspecifically enhances an immune response.

Allergen - substance that induces an allergic reaction manifest as a Type I hypersensitivity reaction.

Allergy - immune response induced by environmental agents that usually has deleterious effects on the host resulting in tissue injury.

Allograft - graft between members of the same species.

α/β T cells - T cells in which α and β chains of the T cell receptor are rearranged and expressed on the cell surface. Most T cells are this type.

Alternative complement pathway - activation of the complement system by direct stimulation of C3 by molecules on bacterial surfaces.

Anamnestic response - an enhanced immune response seen in a previously immunized individual following a subsequent exposure. Often referred to as a *secondary, booster* or *recall* response.

Anaphylaxis - immediate hypersensitivity (Type I) reaction, triggered by IgE-mediated degranulation, releasing pharmalogically-active mediators that produce vasodilation and smooth muscle contraction.

Antibody (Ab) - protein (immunoglobulin) found in the serum or other body fluids that reacts specifically with the antigenic determinant that induced its formation.

Antibody-dependent cellular cytotoxicity (ADCC) - a form of cytotoxicity in which Fc receptor-bearing cells kill antibody-coated target cells.

Antigen (Ag) (immunogen) - a substance that elicits a specific immune response when introduced into an immunocompetent individual.

Antigen presentation - process by which cells expressing peptides derived from antigens in association with Class I or II MHC molecules interact with specific receptors on lymphocytes.

Antigen-presenting cells (APC) - accessory cells which present fragments of antigen in association with MHC molecules to specific receptors on lymphocytes; includes macrophages, dendritic cells, B-cells, and others.

Antigen processing - the conversion of an antigen into peptides that can be recognized by specific receptors on lymphocytes.

Classical complement pathway - mechanism of complement activation by antigen-antibody complexes through a sequential enzymatic cascade involving C1-C9 and ultimately leading to cell lysis.

Clonal selection - central theory in immunology in which antigen binds to a specific receptor on individual cells from a large pool of pre-programmed lymphocytes to select it to undergo differentiation and proliferation into a clone of cells with the same antigenic specificity as the original cell.

Complement (C') system - group of serum proteins activated in sequence by Ag-Ab complexes or some surfaces; have several defense functions including cytolysis, opsonization, chemotaxis, inflammation, etc.

Constant (C) region gene segments - gene segments that encode the constant regions of immunoglobulins and T-cell receptors.

Constant region (C-region) - invariant region of heavy and light immunoglobulin chains and the corresponding chains of the T-cell receptor.

Contact dermatitis - a Type IV delayed hypersensitivity reaction in which sensitivity to simple chemical compounds is manifested by skin reactivity, e.g., poison ivy.

Cytokines (**lymphokine, monokine**) - secreted low molecular weight proteins that regulate the intensity and duration of an immune response by stimulating or inhibiting the growth and proliferation of immune cells or secretion of their products.

Cytotoxic T-lymphocyte (CTL) - subset of T-cells capable of mediating lysis of target cells following recognition of processed antigen presented by an MHC molecule on the target cell.

Degranulation - release of intracellular granules containing vasoactive amines from basophils and mast cells in Type I hypersensitivity.

Delayed type hypersensitivity (DTH) - a cell-mediated immune reaction (Type IV) resulting in a cellular infiltrate and edema that appears 36-72 hrs after a subsequent exposure to the inciting agent. Due to presence of previously-sensitized T-cells that respond to the agent by producing and releasing cytokines which recruit and activate macrophages.

Dendritic cell (DC) - mononuclear cells that present antigens in lymphoid tissue but are distinct from the monocyte/macrophage lineage.

Diapedesis - the outward passage of cells through intact vessel walls.

Diversity (D) segment - portion of an immunoglobulin heavy-chain gene or T-cell receptor gene, situated between the V and J gene segments, that encodes part of the hypervariable region.

Domain - homologous structural unit into which the immunoglobulin heavy and light chains, T-cell receptor and MHC molecules, among others are organized. Each unit is about 110 amino acids and contains an intrachain disulfide loop of about 60 amino acids that is folded into a three-dimensional structure known as the immunoglobulin fold.

Heavy chain (H) - the larger polypeptide of an immunoglobulin (Ab) molecule, composed of one variable region and 3-4 constant region domains. Defines the isotype of the immunoglobulin molecule.

Helper T cells (T_H) - functional subset of T-cells that recognizes peptide fragments of antigen in association with Class II MHC molecules. Release growth and differentiation factors (cytokines) which enhance both cell-mediated and humoral immune responses.

Hematopoiesis - generation or development of blood cells.

Heterologous (xenogeneic) - originating from a different species.

Hinge region - region of the immunoglobulin heavy chains between the Fc and Fab regions which gives flexibility to the molecule allowing the two antigen-binding sites to function independently.

Histamine - vasoactive amine released from basophils and mast cells following cross-linking of bound IgE in Type I hypersensitivity.

Homologous - originating from the same source or species.

Human leukocyte antigen (HLA) - molecules encoded by the human major histocompatibility complex; includes HLA-A, B, C, DP, DQ and DR.

Humoral immunity - immunity that can be transferred by antibodies present in the plasma, lymph, and tissue fluids.

Hypersensitivity - immune response resulting in tissue injury. Types I, II, and III are mediated by antibody, Type IV is mediated by cells.

Hypervariable regions - amino acid sequences within the variable regions of heavy and light immunoglobulin chains and α/β polypeptides of the T cell receptor that form the antigen-binding site.

Immediate type hypersensitivity - tissue reaction occurring within minutes after interaction of allergen with antibody (IgE).

Immune complex - complex of antibody bound to antigen. Circulating immune complexes can elicit Type III hypersensitivity (immune complex disease).

Immunization - the process of rendering a state of immunity. Active immunity occur following inoculation of a specific antigen, while passive immunity results from administration of pre-formed antibodies or cells.

Immunogen - substance capable of eliciting an immune response. All immunogens are antigens but, not all antigens are immunogens.

Immunoglobulin (Ig) - serum protein which can have antibody activity.

Inflammation - tissue response to injury characterized by pain, heat, redness, and swelling. The response consists of altered patterns of blood flow, an influx of phagocytic and other immune cells, removal of the foreign antigen, and healing of the damaged tissue.

Innate immunity - natural, nonspecific host defenses that exist prior to exposure to a specific antigen.

Lymph - intercellular tissue fluid circulating through lymphatic vessels.

Lymphadenopathy - enlargement of the lymph nodes.

Lymph nodes (LN) - small secondary lymphoid organs containing populations of lymphocytes, macrophages, and dendritic cells which serve as sites of filtration of antigens and activation of lymphocytes.

Lymphocyte - small mononuclear cell containing a nucleus with densely packed chromatin and a small rim of cytoplasm with poorly-developed organelles found in blood, tissues and in specialized lymphoid organs.

Lymphoid follicle - tightly packed aggregates of lymphocytes found in the cortex of the lymph node or in the white pulp of the spleen after antigenic stimulation that develop into germinal centers.

Lymphokine activated killer cells (LAK) - killer and natural killer cells which, when activated by IL-2, kill tumor cells more effectively.

Lysosomes - cytoplasmic granules that contain hydrolytic enzymes which play a role in processing of antigens by antigen-presenting cells and digestion of phagocytosed materials.

Macrophage (MΦ) - large, phagocytic, myeloid cell derived from monocytes that function as antigen-presenting cells and as cytotoxic cells in ADCC.

Major histocompatibility complex (MHC) - complex of genes encoding cell-surface molecules that are responsible for rapid graft rejection and are involved in antigen presentation to T-cells.

MHC restriction - the requirement that T-cells recognize antigen only when antigenic peptides are displayed in association with self-MHC.

Mast cell - tissue cell which resembles circulating basophils and which have Fc receptors that bind IgE. Upon antigen cross-linking of the surface IgE, it degranulates, releasing histamines and other mediators.

Memory - characteristic of a specific immune response in which a 2nd exposure to the antigen results in a faster and more potent response.

Memory cells - clonally-expanded progeny of T- and B-cells formed following a primary immune response. Are responsible for the speed and heightened levels of the secondary (anamnestic) immune response.

Mitogen - non-specifically induces DNA synthesis and cell division.

Mixed lymphocyte (leucocyte) culture (MLC) - an <u>in vitro</u> test for cellular immunity in which lymphocytes or leucocytes from genetically dissimilar individuals are mixed and mutually stimulate DNA synthesis.

Monoclonal - derived from a single cell.

Monoclonal antibody (moAb) - homogeneous antibody produced by myeloma or hybridoma cells.

Monocyte - mononuclear, phagocytic cell which circulates briefly in the bloodstream before migrating to the tissues to become a macrophage.

Phylogeny - the developmental history of a group of individuals.

Pinocytosis - type of endocytosis in which extracellular fluid and soluble materials contained within that fluid are ingested.

Plasma cell - terminally differentiated antibody-producing cell derived from an antigen-stimulated B-cell.

Platelet (thrombocyte) - small anuclear cytoplasmic structure derived from megakaryocytes, containing vasoactive substances and clotting factors important in coagulation, inflammation, and allergic reactions.

Polyvalent - refers to an antiserum that reacts with a number of different antigenic determinants on an antigen.

Primary immune response - the initial cellular and humoral immune response to antigen, comprised largely of IgM immunoglobulins and sensitized T-cells.

Primary lymphoid organs - organs in which lymphocytes undergo antigen-independent maturation to become immunocompetent cells. In humans, B- and T-cells mature in the bone marrow and thymus, respectively.

Prophylaxis - preventive treatment often with a vaccine.

Reticuloendothelial system (RES) - collective term for the system of phagocytic cells found in connective tissue throughout most of the body.

Secondary response - more rapid, heightened and longer-lasting response occurring after second exposure to an antigen in which IgG predominates.

Secretory IgA (sIgA) - dimeric form of IgA containing a secretory component that is found in mucous secretions.

Secretory component (Transport piece) - a portion of the surface poly-Ig receptor on epithelial cells lining mucosal surfaces that binds to dimeric IgA and transports it across mucous membranes.

Sensitized lymphocytes - lymphocytes that, when exposed to antigen, respond and clonally expand, generating an immune response.

Serum - fluid portion of blood which is free of cells and clotting factors.

Serum sickness - Type III inflammatory hypersensitivity reaction consisting of fever, rash, joint pain and glomerulonephritis resulting from deposition of circulating, soluble antigen-antibody complexes.

Severe combined immunodeficiency (SCID) - congenital disorder of lymphocyte development resulting in deficiencies of both B- and T-cells.

sIg - surface immunoglobulin.

Specificity - capacity for discrimination between antigenic determinants by antibody, T-cell receptor or MHC.

Stem cell - progenitor cell from which differentiated cells derive.