

## Immunology and the medical student: a unique bond

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Of all the topics that are taught in modern medical schools, none has greater appeal for students than Immunology. Despite its conceptual complexity and arcane and unfamiliar vocabulary, medical students and physicians remain fascinated by the immune system and its amazing elegance. There are many reasons why the discipline of Immunology intrigues students of biology and disease.

The vital physiologic importance of the immune system is dramatically illustrated by many common clinical situations. A competent immune system is essential for protecting us against infections, and enables us to live in the hostile microbe-rich earth that we inhabit. The medical consequences of defective immunity were appreciated in the mid-1900s when congenital immunodeficiencies were recognized as a common cause of recurrent infection in children. In the last fifty years, we physicians have created the most common immune deficiencies by our treatments, such as radiation and chemotherapy for cancers, and immunosuppression for preventing the rejection of organ transplants. The appearance of AIDS in the 1980s has brought the terrible consequences of a failed immune system to the attention of not only physicians and students of the health sciences but also to the public. The devastation caused by this modern "plague" is unprecedented in the history of human civilization, and its impact will surely be felt for generations. Medical students see these problems every day and have become acutely aware of the importance of the immune system, and, therefore, of the discipline of Immunology.

Optimizing immune defenses by vaccination is by far the most successful medical intervention ever devised by physicians and scientists. The success of vaccination is best illustrated by the eradication of smallpox, and soon polio – the first diseases that have been eliminated from civilization. Vaccination promises to be the most effective, and perhaps the only practical, approach for many infectious diseases, such as malaria and AIDS, and enormous efforts are being devoted to the development and delivery of vaccines. The science behind vaccine development is firmly rooted in Immunology, and understanding Immunology will be the key to developing more effective vaccines and to understanding vaccine failures.

Whereas a defective immune system is the basis of increased susceptibility to infection, an overactive or uncontrolled immune system is the cause of allergic and autoimmune diseases. These diseases range from the nuisance of hay fever to the

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life-threatening problems of anaphylaxis, asthma, multiple sclerosis and type 1 diabetes. It is estimated that almost a quarter of the world's population suffers from such immune diseases, and the incidence of many of them seems to be increasing as we improve hygiene and control infections. As a result, every medical student will encounter patients with such disorders during clinical training, and will be expected to understand and explain the diseases. This understanding is also based on an understanding of the immune system.

As a science, Immunology is one of the most exciting modern biomedical disciplines. The "old" sciences of Medicine were Anatomy, Physiology, Biochemistry and Pathology – topics that dominated the early years of medical education through the mid-1900s. In the last fifty years or so, the four "new" sciences that have reached pre-eminence are Immunology, Stem Cell Biology, Genetics and Neuroscience. Of these, Immunology may be the most "mature", in terms of understanding. Until the 1960s, the functions of lymphocytes were not known, and some "experts" suggested that these cells lived and died having served no purpose! And today, we can describe in fairly precise molecular and cellular detail what happens after a microbe penetrates the skin - what cells capture the microbes (dendritic cells), where the microbes are taken (draining lymph nodes) and why (attracted by chemokines), how microbial antigens are displayed (e.g. peptide-HLA complexes), what cells recognize these antigens (T and B lymphocytes), how these cells are activated, and how effector cells and their products (such as antibodies) return to the infection site and get rid of the microbe. It is quite amazing that we can list essentially all the molecules involved in each stage of the reaction! This level of sophistication has not yet been reached in any other biomedical sciences.

Immunology intersects with virtually every other clinical specialty. Disorders of the immune system affect virtually every organ system. All branches of medicine have to deal with problems of the immune system – surgeons with transplants, gastroenterologists with inflammatory bowel disease, neurologists with multiple sclerosis, and so on. Therefore, knowledge of Immunology is relevant to all medical specialties.

Treatments based on understanding of the immune system hold tremendous promise for human diseases. The potential of vaccination was mentioned earlier. New therapies, such as antagonists of the pro-inflammatory cytokine tumor necrosis factor (TNF), are changing the course of diseases like rheumatoid arthritis and Crohn's disease that have been enormous clinical challenges. The TNF antagonists are among the best examples of rational drug design, an important goal for the future. It is estimated that half or more of the new drugs currently being explored by biotechnology and pharmaceutical companies target immune responses in some way. Appreciation of these "drugs of the future" will require an appreciation of Immunology.

The beautifully logical way in which the immune system functions normally, the devastating consequences of failed functions, and the enormous potential of therapies that target various aspects of immune responses all make the discipline of Immunology tremendously interesting for medical and allied health students. We the teachers of Immunology hope these are the students who will devote their careers to studying the immune system and its disorders, and developing new treatments that exploit the science of Immunology.