

## Briefly about the Immune System: A Review Article

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### Abstract

The immune system is a system of organs that protects the body from attacks by foreign microorganisms (viruses, bacteria, fungi and parasites), their chemical substances (toxins), as well as its own altered (e.g. tumor) and spent cells. The immune system consists of organs located throughout the body and cells involved in immune responses, which can move throughout the body. The organs of the immune system are the bone marrow, thymus and lymph nodes.

**Keywords:** Immunity; Immune System; Immunodeficiency; Vaccination

### Introduction

The immune system provides effective defence against invading microorganisms and potentially harmful substances [1]. However, aberrations in the normal functioning of the immune system can often lead to disease. Immune disorders fall into three broad categories. The first category includes those diseases that result from an excessive or overactive immune response, such as allergies and asthma. The second are due to the generation of immune responses directed against self antigens and are known as autoimmune diseases. The third are characterized by an abnormal immune system resulting from an inherited genetic defect or mutation and are referred to as immunodeficiency diseases. All three groups of immune-mediated diseases can affect the mucosal immune system in some way.

The immune mechanisms responsible for mediating allergic responses and autoimmune reactions often share a common feature, which is a lack of proper immune regulation (immunodeficiencies are different, as they are caused by genetic defects). Without appropriate regulatory signals, immune cells have the potential to proliferate and exert excessive immunological effector functions. Excessive inflammation generally leads to tissue damage and disease. Moreover, the immune-mediated tissue damage is caused by the inappropriate induction of a specific adaptive immune response to an antigen that would normally be considered harmless. At the heart of immunoregulation, and therefore immunological disease, is a mechanism known as tolerance. Central tolerance occurs in the thymus and bone marrow, where T cells and B cells that are reactive to self antigens are deleted from the immune system. Peripheral tolerance occurs in secondary lymphoid tissues or the periphery and acts to maintain central tolerance and ensure that T cells and B cells do not respond to harmless antigens. When this mechanism of tolerance is disregulated, lymphocytes respond inappropriately to harmless antigens. In the case of allergies, lymphocytes respond to environmental antigens, while autoimmune reactions are associated with lymphocyte responses to self antigens.

Antibody-mediated immunity is most important in toxin-induced disorders, in microbial infections in which polysaccharide capsules determine virulence, and as a part of the host defense response to some viral infections [2]. However, in most microbial infections, it is cell-mediated immunity that imparts resistance and aids in recovery, though the cooperation of antibodies may be required. Furthermore, cell-mediated immunity is central in host defense against intracellular pathogens such as viruses and in combating tumor cells. The important role of cell-mediated immunity is underlined in clinical situations in which its suppression (eg, AIDS) results in overwhelming infections or tumors.

The cell-mediated immune system includes several cell types and their products. Macrophages present antigen to T lymphocytes via their cell surface-situated MHC proteins. T cell receptors recognize the antigen, and a specific T cell clone becomes activated and begins to proliferate.

### Immunodeficiency

The immune system can suffer from some diseases such as primary immunodeficiencies, secondary immunocompromised conditions including HIV infection, allergic diseases, autoimmune/autoinflammatory disorders, and cancer [3]. The immune system is responsible for graft rejection and/or survival. The reader can find the information on the development of diagnostic, therapeutic, and preventative strategies to combat this threat and an odd concept concerning atopic allergic conditions.

Diseases of the immune system are based on the reactivation of opportunistic microbes, a breakdown in the natural tolerance to self-antigens and allergens, and/or tumor transformation of the immune and other cells.

Immunodeficiency is a state in which the ability of the immune system to protect the body against pathogens and cancer is decreased or completely absent. The primary (hereditary/innate) immunodeficiencies are caused by gene mutations, whereas secondary immunocompromised conditions may occur due to the influence of harmful environmental and endogenous factors.

Developmental and functional defects in the immune system may severely impair the health of an individual [4]. Such defects may increase susceptibility to infections and reactivate latent infections (e.g. cytomegalovirus and Epstein-Barr virus infections and tuberculosis) that may be suppressed but not eradicated during normal immune responses. The incidence of certain cancers may also be increased. These consequences of defective immunity occur because the immune system normally defends individuals against infections and some cancers. Disorders that arise from defective immunity are called immunodeficiency diseases. Those diseases that result from genetic abnormalities in one or more components of the immune system are called primary immunodeficiencies. Other defects in the immune system may result from infections, nutritional abnormalities, or medical treatments that cause loss of or inadequate function of various components of the immune system. These defects are called secondary immunodeficiencies.

The clinical diagnosis of a probable immunodeficiency disease is based on a variety of criteria, such as history of recurrent infections, the pattern of infections, length of time to clear the infections, types of infecting organism(s), particularly when involving opportunistic or unusual organisms, and responses to antibiotic therapy [5]. The clinical history should include a complete family history to determine if there are patterns of inheritance such as autosomal codominant, X-linked, or autosomal recessive disease patterns. Questions should include infant deaths due to infections, familial patterns of autoimmune disease, recurrent pneumonia, or spontaneous angioedema among family members. The physical exam should explore findings associated with immune disorders such as failure to thrive and growth retardation, eczema, easy bruising or bleeding, abnormal hair and dentition, skeletal abnormalities, congenital heart disease, history of neonatal tetany, or albinism. One should consider possible causes of secondary immune deficiency, such as HIV infection, as well as the possibility of nonimmune causes of recurrent infections (e.g. cystic fibrosis, occult malignancy, congenital heart disease, and sickle cell anemia). Laboratory results should be interpreted in the context of the patient's age. Finally, if no obvious diagnosis can be made after the initial evaluation is complete, a followup plan for evaluation and further referral should be implemented.

### Allergy

The most prevalent immune-mediated illness is allergy, which is caused by an immunological reaction to an antigen in the environment [1]. An allergen is any substance that triggers an allergic reaction.

Most people do not have an immune response to allergens, but persons who are allergic to them have an allergic immune response that can lead to disease. Allergens can be breathed, eaten, or come into contact with the skin and are found everywhere. Grass pollen, house

dust mites, and animal fur are all common allergies. Allergies can develop on a seasonal basis or be a year-round problem, depending on the nature of the allergen. Pollen from grasses and trees, for example, is only released for a short time in the spring, and as a result, people experience seasonal allergies. House dust mites, on the other hand, live beside us all of the time and thus provide a continual concern for allergy sufferers. Although the majority of allergies are airborne particles like grass pollen, others include food allergens, insect venom or poisons, contact allergens such as heavy metals, and some pharmaceuticals or treatments. Most people do not develop an allergy to a specific substance at birth, but rather develop one over time as a result of repeated exposure with that material. An initial sensitization event is required for the establishment of an allergic immune response (first contact). Subsequent encounters with the same allergen trigger an allergic immunological response. Repeated exposure to an allergen can often result in a more chronic, long-term condition, such as asthma in adults.

### Autoimmune diseases

Autoimmune disorders are a group of diseases characterised by an abnormal immune response directed at self-components, culminating in an overreaction against one's own cells, leading in immunopathology and tissue destruction [1]. A illness must meet one or more criteria to be categorised as an autoimmune disease. There must be proof that autoreactive antibodies directed against a self antigen exist, that these antibodies can cause immunopathology, that autoantigen-reactive T cells exist, and that these autoreactive cells can transfer an autoimmune phenotype in an experimental paradigm. The line between a true autoimmune disease and an immune-mediated disease that does not have an autoimmune component is frequently blurred. Psoriasis, for example, is sometimes regarded an autoimmune skin condition, despite the fact that no autoimmune antigen has been identified. Similarly, chronic obstructive pulmonary disease (COPD) is linked to a persistent activation of the immune system, however the role of an autoimmune antigen is controversial. These aren't your normal autoimmune diseases; instead, they're diseases triggered by an overabundance of immune responses.

The lack of immune regulation provided by immunological tolerance to self molecules is important to the development of autoimmune disease. T cells that are reactive to self antigens are lost in the thymus during negative selection in normal circumstances, a process known as clonal deletion theory.

This is the foundation of central tolerance, which is bolstered by peripheral tolerance, which is mediated by Treg cells and involves T cell anergy induction (known as the clonal anergy theory). In the bone marrow, B cells are subjected to negative selection, which results in the deletion of self-reactive B cells. Indeed, rather than being directly mediated by the T cell system, the bulk of autoimmune disorders are likely to be mediated by self-reactive antibodies. The topic of how autoimmune illnesses develop in the first place remains unanswered, especially given the tolerance mechanisms in existence.

### Vulnerability

The world has become increasingly vulnerable to the emergence, and, more importantly, the widespread and even worldwide transmission of both new and ancient infectious illnesses. This newfound vulnerability isn't all that mysterious [6]. The globalisation of disease is driven by the tremendous growth in global mobility of people, goods, and ideas. People are travelling more than ever before, and they are travelling faster and to more places than ever before. When the symptoms of sickness strike, a person carrying a life-threatening virus can easily board a jet plane and be on another continent. Insects can be transported by the jet plane and its cargo, carrying infectious pathogens into new ecological environments. Few environments on the planet are really isolated or undisturbed, as tourists and other travellers travel to formerly inaccessible locations in quest of new vistas, business, or enjoyment.

Such a devastating disease would clearly have profound implications for international relations and the global economy. With death tolls rising, vaccines and drugs in short supply, and the potential for the virus to spread further, governments would feel obliged to take drastic measures that could inhibit travel, limit worldwide trade, and alienate their neighbors. It is even doubtful that any of the world's

wealthy nations would be able to meet the needs of their own citizenry, much less those of other countries. Domestic vaccine purchasing and distribution schemes currently primarily assume that only the very young, the elderly, and the immunocompromised are at serious risk of dying from the flu. Every year the United States plans for 185 million vaccine doses, trusting that the flu will kill only the usual risk groups. If that guess were wrong, if all Americans were at risk, the nation would need at least 300 million doses. That is what the entire world typically produces each year. There would thus be a global scramble for vaccine.

### Genes

A genetic component can be found in nearly every human disease [7]. Some disorders, such as cystic fibrosis and Huntington's disease, are caused primarily by a single gene mutation. These illnesses are all relatively uncommon, with roughly 1% of people in communities suffering from them. Other diseases, such as heart disease, diabetes, common malignancies, and psychiatric illness, are far more prevalent and are caused by the combination of several genetic changes in a person. Non-genetic variables like as food, sedentary lifestyle, and exposure to harmful substances such as tobacco smoke also have a significant impact.

Over the last three decades, significant progress has been made in identifying the genes that cause single-gene illnesses. The development of hundreds of genetic 'markers' has been a significant component of this accomplishment. The locations of these short DNA sequences in the human genome are known and vary from person to person. Importantly, they're simple to test in the laboratory. As a result, they form a succession of distinguishable signposts on the genetic map.

Using information on the transfer of intact chromosome sections, researchers may scan the genome for specific markers co-inherited with a disease from parent to offspring among family members (genetic linkage). More than 2,000 disease-causing genes have been uncovered as a result of this research.

Common diseases pose a larger challenge to geneticists due to their complicated causes. Instead of isolating a single genetic mutation in an affected individual, many or more alterations, as well as non-genetic predisposing variables, may be required. As a result, progress in finding the genetic components to prevalent diseases has been modest, but the huge public health burden of these diseases has sparked a lot of research. Large collections of affected individuals and families, rapid computational tools and gear, and the finding of millions of novel markers throughout the genome are all contributing to the project's early success.

The declaration that the vast majority of the human genome has been sequenced [8] heralded the start of the new millennium. Numerous conceptual and technological developments preceded this significant step forward in the study of the human genome. Among them are the clarification of the DNA double-helix structure, the discovery of restriction enzymes and the polymerase chain reaction (PCR), the invention and automation of DNA sequencing, and the Human Genome Project's compilation of genetic and physical mapping (HGP). The implications of this abundance of knowledge for medical treatment are enormous, yet integrating genetics into daily practise remains difficult. To date, genetics has had the greatest influence in improving our understanding of illness aetiology and pathophysiology. We may expect genetics to play a larger role in disease diagnosis, prevention, and therapy in the near future.

Traditionally, genetics has been studied through the lens of relatively uncommon single-gene illnesses.

These uncommon illnesses account for up to 10% of paediatric hospitalizations and childhood mortality when taken collectively. However, with the exception of mild trauma, it is becoming increasingly clear that practically every medical disease has a hereditary component. Many prevalent ailments, such as hypertension, heart disease, asthma, diabetes mellitus, and mental problems, are heavily influenced by a patient's genetic background, as evidenced by a patient's family history. These polygenic or multifactorial disorders involve the contributions of many different genes, as well as environmental factors, that can modify disease risk. Cancer has a genetic basis since it results from acquired somatic mutations in genes controlling growth and differentiation. In addition, the development of many cancers is

associated with a hereditary predisposition. The prevalence of genetic diseases, combined with their severity and chronic nature, imposes a great financial, social, and emotional burden on society.

### Vaccination

The biological basis of successful vaccination is our own complex immune system and its response to pathogens [9]. Vaccination can induce an immune response that mimics natural infection or tries to do even better than our response to a pathogen. Vaccination induces an immune response in the individual vaccinated. A population of hosts has a collective level of immunity that results from the level of immunity in the individuals that compose it. The collective immunological status of a population of hosts, as opposed to an individual host, with respect to a given pathogen is called herd immunity. Maintenance of individual immunity can depend on repeated boosting by natural infection. The level of transmission may be diminished by high levels of immunization or natural immunity in a population to the point that natural boosting of immunity does not occur. Thus for some infections, a complex interplay between individual and population level immunity is maintained through the dependent happenings.

The immune response is also the source of many safety considerations of vaccination. Before a vaccine can be shown efficacious against infection or disease in a large-scale field study, it must be shown to elicit an immune response and to be safe in smaller studies.

Vaccines are most commonly administered using a needle and syringe; however, their use is associated with numerous drawbacks such as needlestick injuries to health care workers and the costs and logistical challenges associated with the safe disposal of sharps in the medical waste stream [10]. The seriousness of these issues, the need to simplify global immunization programs, and the development of needle-free vaccine delivery have become a global priority. One needle-free vaccine approach being developed is the use of a vaccine patch which delivers the vaccine through the skin. Referred to as transcutaneous immunization (TCI), the topical application of a vaccine formulation on the skin targets the skin as an immunologically active site.

Government authorities usually rely on expert advisory committees to make recommendations for the use of vaccines, such as the Advisory Committee on Immunization Practices (ACIP) in the United States [11]. European countries make recommendations at the national level rather than across the European Union. WHO provides guidance for use of vaccines in developing countries. These advisory committee recommendations provide guidance on vaccine use in different ages and risk groups as well as information on what is known about the safety of the vaccine. Recommendations include guidance on groups or individuals who should not receive the vaccine due to safety concerns. For example, guidance is given for individuals with underlying conditions that might predispose to serious adverse events in order to prevent possible vaccine-associated injuries. Generally live vaccines are not given to persons with serious immune deficiency disorders, but some live vaccines are safe in those with less serious immunological conditions. Vaccine recommendations may include guidance for use in populations not studied in clinical trials, such as pregnant women. There is wide variability in vaccine recommendations globally as there are many differences in the burden of disease, and considerations of risks and benefits from vaccines.

### COVID-19

The way the global vaccine research and development system is currently constructed and operated is not optimized to develop, manufacture, and equitably distribute vaccines [12]. Given these conflicting realities, a new approach to health innovation is required.

Specifically, we argue that any COVID-19 vaccines must be re-conceptualized as global public goods rather than publicly subsidized, privately controlled commodities. By “public good” we mean that COVID-19 vaccines-while material in form-are, at bottom, information-based products. That is, once knowledge about a given vaccine’s safety and effectiveness against SARS-CoV-2 is in hand, only resources (for example, manufacturing facilities) and law (for example, patent law) can limit its consumption; the underlying knowledge about how to make and use them, absent these limitations, is both non-rivalrous and non-exclusive. Because of the demand for such vaccines, and

their central importance to securing adequate public health within and across countries, no one nation, or private manufacturer, alone can guarantee their provision; rather, their development and production will, of necessity, be a global endeavour, thus the term “global” public goods. We argue that this conceptualization of COVID-19 vaccines as global public goods must be carried through the entire process of producing, testing, manufacturing, and distributing any resulting COVID-19 vaccines. To make it concrete, we outline how this global public goods approach might be achieved in the Canadian setting, while also recognizing that the approach must be adopted elsewhere as well if global needs are to be met.

Like many other knowledge-based goods in the health domain, vaccines are not usually treated as public goods, on the strength of the argument that without the promise of exclusivity, private companies would not undertake the lengthy, costly process of developing them for human use. Patent rights and other legal protections from potential competitors are used to motivate, coordinate, and sustain vaccine R&D, from discovery and preclinical stages of research (often performed by publicly funded institutions) through to clinical trials involving human participants, manufacturing, and regulatory approval (usually run by the private sector). Most vaccines and drug therapies that reach the market follow this pattern.

There are several limitations associated with this publicly subsidized, privately appropriated approach. Principal among them are that health conditions or diseases which afflict the world’s poor or carry less predictable financial returns typically command very little interest. Prior to COVID-19, coronaviruses were an example of this lack of interest: only six interventions reached the clinical trial phase of development, all of which relied heavily on public funding.

### Conclusion

The immune system has developed a complex network of checks and balances that can be called innate and adaptive immunity. Everyone is born with innate immunity. The components of the immune system involved in innate immunity respond similarly to all foreign substances, and antigen recognition does not differ from person to person. As its name suggests, adaptive immunity is adaptive. At birth, a person’s immune system has not yet come into contact with the outside world or begun to develop its “memory files”. The immune system learns to respond to every new antigen it encounters. Adaptive immunity is, therefore, specific to antigens that a person comes in contact with throughout life. The main feature of specific immunity is the ability to learn, adapt and remember. The immune system carries a record or memory of every antigen a person encounters, whether it is through the lungs (breathing), the intestines (diet) or through the skin. This is possible because lymphocytes are long-lived. When a lymphocyte encounters an antigen a second time, it develops a rapid, effective, and specific response to that particular antigen. This specific immune response is the reason why people can get chickenpox or measles only once and what makes vaccination effective in preventing the disease.

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