2. Principles of Immunology and Immunization

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2.1 Definitions

Active immunity is protection that is produced by a person's own immune system. This type of immunity is usually permanent.

An **antibody** is a protein (an immune globulin molecule) produced by an organism in response to stimulation by an antigen. An antibody combines only with the specific antigen that induces its synthesis.

An **antigen** is any substance that is capable of inducing an immune response when introduced into an organism. This immune response may be expressed by the production of certain antibodies, by the production of antigen-specific cells, or by the absence of any response (tolerance). In infectious disease, the antigen may be a complete infectious agent, one of its constituents, or one of its products.

Inflammatory response is a non-specific defense mechanism elicited by tissue damage. It is generally characterized by four basic signs or symptoms: redness, pain, heat and swelling. It contributes to the elimination of micro-organisms, toxins and other foreign particles at the site of the injury, prevents their propagation to adjacent tissues and prepares the site for tissue repair.

The **immune system** is a complex system of interacting cells whose primary purpose is to identify foreign (non-self) substances.

Immunity is the ability of the human body to tolerate the presence of material indigenous to the body ("self") and to eliminate foreign ("not-self") material.

Immunization is the process by which immunity is conferred, either by injection of antigens (active immunization) or by injection of serum containing specific antibodies (passive immunization).

Immunogenicity is the capacity of an antigen to induce a specific immune response.

Immunologic memory is the capacity of immunological cells (B and T lymphocytes) that have already been exposed to an antigen to recognize it and mount a faster and more heightened response (for example, after injection of a booster dose). Immunologic memory lasts a very long time, even when the concentration of antibodies in the serum is below the detection limit. This phenomenon allows for continuation of primary immunization regardless of the time elapsed between doses.

Immunology can be defined as the branch of science concerned with the processes and consequences associated with the physiological recognition of self and not-self. The human body is equipped with a system (the immune system) that recognizes and tolerates its genetically determined constituent elements and rejects anything that is foreign to it.

Passive immunity is protection by products produced by an animal or human and transferred to another human, usually by injection. Passive immunity often provides effective protection, but this protection disappears with time, usually within a few weeks or months.

Primary immunization is the number of doses of a single immunizing product that must be administered for a subject to develop adequate immunity.

Seroconversion is the development of a specific antibody in the serum. The change of a serologic test from negative to positive indicates the presence of antibodies. Seroconversion may occur as a result of viral or bacterial infection or in response to vaccination. There is a varying lapse of time between the time of infection (or vaccination) and the time when the development of specific antibodies can be measured by serologic tests. The term "seroprotection" is sometimes used to indicate a high enough level of antibodies in the serum to protect a person against disease.

Vaccination is a method of preventing certain infections. It consists of introducing preparations called vaccines into an organism for the purpose of inducing active immunity.

A **vaccine** is an antigenic preparation which, when introduced into an organism, induces the production of antibodies capable of fighting off infection of that organism by a given micro-organism.

Vaccine effectiveness is the protection a vaccine gives to a population. Vaccine effectiveness is measured by means of field observations, which are conducted in accordance with epidemiological methods to evaluate protection against clinical disease and include comparing the incidence of the disease in vaccinated subjects and non-vaccinated subjects.

2.2 Natural Immunity

Natural immunity, which is, by definition, innate, consists of a series of biological and physicochemical mechanisms that act rapidly to protect an organism from penetration of a proliferation of infectious agents. This type of immunity is non-specific, in the sense that it does not distinguish among different infectious agents. It offers two lines of defense. The first is external and comprises the epithelial tissues that cover the body (skin and mucous membranes) and the secretions produced by these tissues (mucous, tears, gastric juice, etc.) The second is internal and is triggered by chemical mediators that prompt various cells and proteins to launch an indiscriminate attack on invading antigens that have breached the organism's external barriers. These mechanisms make use of phagocytes (neutrophils, monocytes and macrophages), cells that produce inflammatory mediators (basophils, mastcells and eosinophils) and natural "killer" cells. The components of immunity also include complement proteins and cytokines, such as interferon. Natural immunity is primarily called upon for the destruction of extracellular organisms, particularly bacteria. It is less effective against infection caused by intracellular organisms, such as viruses, mycobacteria, fungi, or parasites.

2.3 Acquired Immunity

Acquired immunity corresponds to the production (active immunity) or transmission (passive immunity) of a state of resistance to an antigen through the direct action of antibodies or cells specific to that antigen. This immunity improves with repeated exposure to a given antigen.

Active acquired immunity is the result of activation of the organism's immune system through contact with an antigen.

- **Natural active acquired immunity** results from an infection. The degree and duration of protection vary from one disease to another. This is why people must be vaccinated even when they have had certain infections in the past (e.g., typhoid fever, influenza).

- **Artificial active acquired immunity** results from the immunization caused by vaccination, without involving the potential consequences and complications of the disease. This immunity takes advantage of the characteristics of the immune system for preventive purposes.

Passive immunity results from the transfer of antibodies formed in another organism to a given individual. This protection is of limited duration.

- **Natural passive acquired immunity** is seen in babies during the first months of life as a result of antibodies transferred from the mother through the placenta or maternal milk. This immunity disappears during the first year of life.

- **Artificial passive acquired immunity** occurs when an organism receives antibodies produced by another human or animal organism. The protection supplied by specific and non-specific immune globulins is an example of this kind of immunity.

    - **Humoral immunity** results from the production of antibodies by the immune system's B lymphocytes. These antibodies may be found in many of the organism's biological fluids. Humoral immunity is primarily responsible for resistance to extracellular pathogens, such as bacteria. Antibodies are generally easy to measure in the laboratory and this measurement is used to determine the immune response to vaccines. However, antibodies represent only one part of the immune response.

    - **Cell-mediated immunity** primarily involves the lymphoid cells or the immune system's T lymphocytes. This immunity is primarily responsible for resistance to intracellular pathogens such as viruses, certain cancerous cells and transplants. It is much more difficult to measure in the laboratory. It may protect the individual even in the absence of detectable antibodies.

2.4 The Immune System

The immune system has four principal characteristics:

- Specificity refers to the immune system's capacity to recognize and eliminate certain pathogens or foreign molecules called antigens. Each antigen has a unique molecular structure that triggers the production of specific cells or antibodies to fight it.

- Diversity corresponds to the immune system's capacity to fight off millions of types of attackers by recognizing each by its antigenic markers.

- Recognition of self and not self refers to the immune system's capacity to distinguish between the organism's own molecules (self) and foreign molecules (not self).

- Memory indicates the immune system's capacity to remember antigens that it has encountered and to react promptly and effectively to subsequent exposures.

The organs of the immune system are known as lymphoid tissues. They are found almost everywhere in the human body. Bone marrow is where the lymphocytes, the smallest of the white blood cells, are produced. Lymphocytes that mature in the bone marrow become B lymphocytes, while those that migrate to the thymus differentiate into T lymphocytes. The lymph ducts and nodes are part of the circulatory system that transports the lymph, which consists primarily of lymphocytes. The spleen is a lymphatic organ in which immune system cells attack pathogens. The tonsils, adenoids, Peyer's patches and appendix are also lymphoid tissues. Lymphoid cells and foreign molecules enter the lymph nodes through blood vessels and lymph ducts.

Lymphocytes have antigen receptors on their plasma membranes that recognize specific antigens. In the case of B lymphocytes, these receptors are actually antibodies, while the T lymphocytes have specific receptors.

When a pathogen breaches the non-specific natural defenses formed by the cutaneous and mucosal barriers and the phagocytic mechanisms, the immune system takes over. After partially digesting the microbial antigens, the macrophage becomes an antigen-presenting cell. Other cells, such as the dendritic cells, found primarily in the skin, are also very effective antigen-presenting cells. Antigen-presenting cells enable antigens to form a complex with the glycoproteins of the major histocompatibility complex (MHC) on the macrophage. These glycoproteins mark the macrophage as self. This complex will then be captured by a lymphocyte with the specific receptor able to bind to it. If the activated lymphocyte is a B lymphocyte, the effector lymphocytes become plasmocytes, which secrete specific antibodies to destroy the antigen. If the activated lymphocyte is a T lymphocyte, the effector lymphocytes will fall into two main categories: cytotoxic T lymphocytes (CD8+), which destroy infected and cancerous cells, and helper T cells (CD4+), which play a key role in stimulating humoral and cell-mediated immunity.

There are two types of helper T lymphocytes: Th1 and Th2 cells. Th1 cells are the regulatory cells in Th1 immunity. The main substance secreted by these cells is interferon, which, among other things, stimulates phagocytosis, promotes intracellular destruction of micro-organisms, facilitates presentation of the antigen to the T cells, and causes inflammatory reactions. Th1 immunity stimulates cell-mediated immunity, including the cytotoxic T cells, which are intensely phagocytic. Th1 immunity is usually associated with delayed hypersensitivity reactions. Th2 immunity stimulates the B cells, primarily through interleukins, and promotes the production of antibodies. This immunity is associated with allergic reactions, primarily because of the production of eosinophils, basophiles and IgE. Antigens that trigger humoral immune responses without the participation of T lymphocytes are called T-independent antigens; while those that cannot stimulate production of antibodies without helper T cells are called T-dependent antigens. The antibody response following stimulation by T-independent antigens is generally weaker.

Antibodies act primarily though neutralization agglutination or activation of the complement system. Antibodies have a neutralizing effect when they bind to the sites that the micro-organism must use to attach to the host cell. The avidity of the antibodies is proportional to the strength of the bond between the antigen and the antibody. Phagocytes then destroy the antigen-antibody complex. Agglutination occurs through antibodies that have more than one

antigen-binding site, allowing binding with adjacent antigens. Finally, antibodies may combine with the proteins of the complement system, prompting it to produce lesions in the membrane of the foreign cell and causing lysis of that cell. The principal antibodies are the IgG immune globulins found in the blood and tissues, IgM immune globulins, IgA immune globulins found in the mucous membranes, IgD immune globulins and IgE immune globulins.

In the majority of infections, Th1 immunity provides an initial defense, while Th2 immunity takes over when the inflammation generated by Th1 immunity resolves. The functioning of this system is complex, and the different components are closely interrelated and in constant balance. Several factors may lead to an inversion of the normal response process, such as a major stressor, immunosuppression, administration of glucocorticoids (cortisone or catecholamines), or a significant inoculation of antigens to induce the immune system to generate a Th2 response to an infection normally controlled by Th1 immunity.

After vaccination, some B lymphocytes rapidly differentiate into antibody-producing plasmocytes and others in to memory B cells, with the help of Th 2 cells. After reaching the final stage of this differentiation, the antibody-producing plasmocytes stop dividing and naturally disappear overtime. The maximum level of antibodies induced after vaccination directly reflects the number of plasmocytes generated by the vaccination. Similarly, the disappearance of antibodies reflects the disappearance of specific antibodies. The length of time for which the antibodies remain is directly related to the level reached after vaccination.

The memory cells are not reactivated unless they are again exposed to the antigen for which they are specific. In response to a vaccination (booster) or infectious exposure (disease), the memory cells proliferate very rapidly and differentiate, within three to five days, into plasmocytes producing high levels of antibodies or cytotoxic T lymphocytes capable of destroying the antigens or infected cells. In contrast to the plasmocytes, which do not divide any further and have a limited life span, the memory cells appear to persist for a long time, regardless of antigenic exposure.

2.5 Immunizing Products

Immunization gives the human body the means to defend itself against a biological attack before it occurs. In active immunization, the process consists of stimulating the immune system by means of a known and controlled immunizing product while avoiding the consequences associated with natural infection. In passive immunization, the process involves a transfer of antibodies, called immune globulins, from an immunized subject to a non-immunized one.

2.5.1 Vaccines

A **vaccine** is a biological product manufactured from a whole bacterium or virus, its constituents (polysaccharides or proteins), or its products (toxins), from which the capacity to produce the disease is destroyed by various means, while the capacity to induce an immune response (immunogenicity) is preserved. Vaccines may be inactivated or live attenuated.

The **immunogenicity** of a vaccine depends on a number of factors, including the antigen's foreign source, morphology, chemical makeup, molecular mass, route of administration, and use of adjuvants. Generally speaking, proteins are the most potent immunogenic substances. In addition, the greater the molecular mass, the more immunogenic the antigen will be. For this reason, some vaccines made of polysaccharides with low molecular mass are conjugated to a

protein to make them more immunogenic at a younger age. The main proteins used for conjugation in current vaccine production are diphtheria anatoxin, tetanus anatoxin, the non-toxic variant of the diphtheria toxin (CRM197) and OMP protein from *Neisseria meningitidis* capsule.

Additional information on vaccine composition in Canada

Vaccines that are currently distributed in Canada contain many different components.

Antigens that induce active immunity
A vaccine may be monovalent (containing only one antigen), polyvalent (containing more than one antigen from one infectious agent), or combination (containing more than one antigen from more than one infectious agent).

Culture media
Vaccines are grown in various culture media. The ones used most frequently are bovine proteins, chick embryo cells, embryonated chicken eggs, human diploid cells and yeasts. The final product may contain trace proteins.

Suspending fluid
Depending on the vaccine, the suspending fluid may vary from saline or sterile water to a more complex protein liquid.

Preservatives or antibiotics
These prevent the growth of bacteria in the vaccine. The most common preservatives are formaldehyde, phenol, 2-phenoxyethanol and thimerosal. The most common antibiotics are neomycin and polymyxin B.

Stabilizers
The most common stabilizers are bovine albumin or bovine serum, human serum albumin, gelatin, glycine, lactose, sorbitol, sucrose, and saccharose. Polysorbates 20 or 80 (or Tween 20 or 80) are used as surfactants to make products homogeneous. Stabilizers are also found in some cake mixes and are used as emulsifiers in cosmetics and pharmaceutical products.

Adjuvants
Adjuvants are used to boost the immunizing power of the vaccine in order to obtain a better serological response and ensure more lasting immunity with few antigens and fewer doses. Adjuvants act by prolonging the presence of antigens at the site of inoculation. This allows them to be released over a variable period of time and promotes activations of the antigen-presenting cells (i.e., dendritic cells and macrophages) as well as production of cytokines. When a vaccine contains aluminum salts (generally aluminum phosphate or aluminum hydroxide), it must be administered intramuscularly, because injecting aluminum salts into the subcutaneous tissues may cause a significant inflammatory reaction, subcutaneous nodules and sometimes even sterile abscesses. Other adjuvants may also be used, such as the MF59 water-in-oil emulsion. The components in the last three categories, also called excipients, do not by themselves play an active role in establishing the desired immune response, but they facilitate the preparation and administration of a vaccine. They also serve as vehicles for the active ingredients.

2.5.2 Immune Globulins

Immune globulin consists of protein extracted from the serum fraction of blood. It contains antibodies that recognize and attack specific pathogens. Immune globulin contains mainly IgG with small amounts of IgM and IgA. It can be of human or animal origin. In Canada, human immune globulins are used most frequently. However, in some developing countries, animal immune globulins are used instead.

Questions are frequently asked about the risk of transmitting infectious agents through the administration of immune globulin and this issue merits attention. First, all blood donors are required to complete a questionnaire designed to detect risk factors for infections transmissible by blood. They are also given a physical examination during which the examiner looks for evidence of injections inside the elbow and takes their temperature. A donor can also cancel his or her donation in complete confidence, even if it has been accepted. People who are at risk of developing Creutzfeldt-Jakob disease are not allowed to donate blood.

Every blood donation is then analyzed for hepatitis B, hepatitis C, HIV-1, HTLV-l and 2 (lymphotropic virus), West Nile virus and syphilis. The diseases and the tests used to detect them may vary over time, as more effective tests become available. Any blood that tests positive for one of these diseases is rejected. Secondly, the processes used to extract immune globulin from the blood include the use of heat and alcohol, which are capable of inactivating HIV, HB and HCV.

To date, the administration of the intramuscular immune globulin marketed in North America has never been associated with the transmission of an infectious agent, including HIV and hepatitis C. Furthermore, no human case of Creutzfeldt-Jakob disease has been causally linked to blood transfusions.

Two preparations are used to prevent and treat infectious diseases: non-specific (standard) immune globulin of human origin and immune globulin containing high titers of specific antibodies to a particular micro-organism or its toxin. The specific immune globulin may be of human or animal origin. Maximum plasma levels are reached between 48 and 72 hours after administration of these products.

2.6 Immunology of Vaccination

Like a natural infection, vaccination can induce either a humoral or a cell-mediated immune response. The response will vary according to two parameters: the type of vaccine administered (live or inactivated) and factors associated with the host.

Humoral Immune Response Induced by Different Types of Vaccines

Live vaccines

After the administration of a dose of live vaccine, an infection occurs, although no clinical signs are usually apparent. This infection induces immunity, which can be measured by a serum antibody determination. The humoral immune response and the protection conferred by the live vaccine appear to be similar in nature and intensity to those resulting from natural infection.

Inactivated whole-cell or inactivated purified protein vaccines

Two types of response correspond to the inactivated vaccine, depending on whether it is the organism's first contact with the protein antigen or subsequent contacts with the same antigen. The characteristics of the first response are the following:

- a relatively long latent period before the appearance of antibodies
- low intensity (usually insufficient to confer adequate protection)
- short duration
- primarily IgM

In comparison, the secondary, or anamnestic, response following another exposure is faster, stronger, and longer lasting; it primarily consists of IgG.

The quantity injected, number of doses, and intervals between doses are important factors in the success of an inactivated vaccine. For example, second antigenic stimulation too soon after the first may be ineffective because of elimination of the antigen by the high concentration of serum antibodies still present; it is therefore important to comply with the minimum interval between doses.

Polysaccharide vaccines
Polysaccharide vaccines directly stimulate B lymphocytes but not T lymphocytes (primarily stimulated by proteins), resulting in a production of antibodies, but not memory cells. This is a T-independent lymphocyte response.

Conjugate vaccines
Conjugation, which is the combining of polysaccharide with proteins, induces a T-dependent immune response very early in life. The antibodies produced are more effective than those induced by the unconjugated polysaccharide vaccine, and their affinity for the bacterial antigens improves with time. The immune response induced by a conjugate vaccine is therefore similar to the response induced by an inactivated whole-cell vaccine or an inactivated purified protein vaccine.

Host Factors

Age

During the first 2 or 3 months of life, the immune system is relatively immature. It is nevertheless capable of generating a relatively complete immune response, both humoral and cell-mediated. There is one exception: B lymphocytes in the infant are unable to respond to T-independent antigens such as polysaccharides until the age of about 2 years. Recent studies show that an infant's immune system can deliver a significant response: a calculation based on the number of lymphocytes available at that age show that an infant could receive up to 10,000 vaccines simultaneously without deleterious effects on the immune system, which has the capacity to regenerate up to two million CD4+T lymphocytes a day.

Maternal antibodies, passively transmitted to the child in utero or through breastfeeding, may have an inhibitory effect on the immune response.

The quality and intensity of the humoral response in the infant is closely linked to the continuing presence of specific maternal antibodies and their protective efficacy, which is highly variable from one infection to another. Immunization schedules take these factors into account.

The ability to generate a good immune response declines with age, since the pool of undifferentiated plasmocytes decreases over time. Nevertheless, elderly people respond relatively well to immunization.

Genetic factors

Some people respond better than others to immunization. This is partly because of genetic factors such as the ABO blood systems and the HLA histocompatibility antigens.

Immunodeficiency

Whether acquired or hereditary, immunodeficiency generally decreases the immune response, in the case of both humoral and cell-mediated immunity.

Malnutrition

This factor primarily results in a decline in cell-mediated immunity.

2.7 Impact of Acquired Immunity on the Individual and the Community

Immunity, whether acquired naturally or artificially through vaccination, plays an important role in the epidemiology of communicable diseases through an individual effect and a collective effect.

Individual Effect

Immunity protects the individual against reinfection, and this protection is specific. However, this protection is not necessarily permanent. People who have been vaccinated do not always develop a protective immunity.

Collective Effect

Transmission of a contagious disease is directly related to the proportion of susceptible subjects in the community. Transmission declines as the number of immune people rises. When this number is high enough, the infectious agent stops circulating among the population. This has a protective effect on the entire population, including non-immunized people. This effect is known as community or herd immunity. This is the basis for mass immunization programs.

In a population where only some individuals are protected, there is a critical threshold below which an epidemic may occur and another threshold beyond which the disease will disappear for lack of sufficient susceptible subjects who might pass it on.

These thresholds vary with the disease in question, its attack rate, and in the case of vaccine-preventable diseases, the immunization coverage rate in the population.

Immunization programs may have varying objectives, depending on such factors as the effectiveness of the available vaccines, the capacity to reach the target populations, and the epidemiology of the disease. The first objective may be eradication, or complete elimination of the disease world wide. The WHO declared smallpox officially eradicated in 1980. A second objective may be elimination of the disease, or the absence of sustained (endemic) transmission of the disease. Elimination has occurred if the epidemic potential is low enough that, on average, one case induces less than one other case. The third objective may be to control the rate of mortality or morbidity attributable to the disease.

2.8 General Recommendations for Effective Application of Immunization Concepts

Age at Which Immunizing Products Are Administered

Factors influencing the recommended ages for administration of vaccine include:

- potential antagonistic interference between immune system response and passive transfer of maternal antibodies
- the capacity of an individual of a given age to develop an immune response (immune system maturity)
- the age-related risk of developing a disease or its complications

Vaccination before the minimum recommended age may result in a suboptimal immune response and should not be counted as part of the primary immunization. The dose should therefore be readministered at the age initially recommended, provided the time between the dose given too early and revaccination complies with the minimum interval between two doses of the same vaccine.

Vaccination Intervals

Intervals between doses of the same vaccine

Many vaccines require at least two doses to give effective protection, as well as periodic booster doses to maintain this level of protection.

Unless otherwise indicated, doses given at less than the recommended interval may result in suboptimal antibody response and should not be counted as part of a primary series. These doses should therefore be readministered by calculating the minimum or recommended interval initially established from the time of the dose that was administered too early. For example, if the third dose of DaPTP+Hib was administered at the age of 6 months and the fourth dose at 11 months, the minimum interval was not observed, since 5 months had passed since the third dose rather than the minimum of 6 months. The fourth dose is considered invalid and must be readministered 6 to 12 months (minimum and recommended intervals) later, or at the age of at least 17 months. This dose will be considered the valid fourth dose of the primary immunization. Immunization should then continue in accordance with the recommended schedule.

When the minimum interval between two doses of a vaccine is 1 month, this interval is generally considered equivalent to 4 weeks (28 days).

As a general rule, interruption of a primary series of vaccinations does not require starting the series over again. Instead, the series should be continued where it was left off, regardless of the interval elapsed since the last dose, even if it is a matter of years.

Intervals between different vaccines

Most of the commonly used antigens can be given simultaneously.

Inactivated vaccines can be administered at the same time or at any time before or after a live vaccine or an inactivated vaccine.

Different live vaccines should be administered simultaneously or at least 4 weeks (28 days) apart. A decrease in the effectiveness of the varicella vaccine has been shown when the interval between the MMR and varicella vaccines was too short.

Since the MMR vaccine affects hypersensitivity to tuberculin (anergy or transient hypoallergy), the tuberculin skin test (TST) should be done before, at the same time as, or at least 4 weeks after administration of the MMR vaccine. It is possible that other injectable live vaccines, such as the varicella and yellow fever vaccines, may similarly falsify the TST results. If an injectable live vaccine must be administered and a TST is required, the test should be done before, at the same time as, or at least 4 weeks after the vaccination. Live vaccines administered orally probably do not have any effect on the response to TST.

Interval between immune globulin (IG), other blood products, and vaccines

Inactivated vaccines may be administered on the same day as immune globulin and other blood products or at any time before or after without affecting the immune response.

Vaccines containing live measles or varicella viruses should be given at least 2 weeks before immune globulin or at least 3 months after the administration of immune globulin, since passive immunization may interfere with the immune response to these vaccines. If these intervals are not observed, the vaccines must be readministered.

Administration of immune globulin does not interfere with the immune response to other live vaccines.

2.9 Contraindications and Precautions to Vaccines

General Contraindications to Vaccines

A contraindication is a condition that significantly increases the chance that a serious adverse event will occur if the vaccine is given.

- anaphylactic reaction to a constituent of vaccine or to a previous dose, either of the same vaccine or of another vaccine with the same constituent.
- significant immunosuppression (live vaccines only)
- immunodeficiency such as ammaglobulinemia, hypogammaglobulinemia, or dysgammaglobulinemia
- leukemia, lymphoma, or other generalized neoplastic disorders capable of altering immune mechanisms
- treatment with immunosuppressive agents (corticosteroids, antimetabolites, or other immunosuppressive agents)
- HIV and AIDS infections (some live vaccines are contraindicated for people infected with AIDS
- pregnancy

General Precautions to Vaccines

A precaution is a condition that may increase the chance of an adverse reaction following immunization or that may compromise the ability of the vaccine to produce immunity.

- persons who have chronic underlying illness or who are immunocompromised, in whom there may be a reduced response to the vaccines.

- persons with a history of Guillain-Barre syndrome (GBS) with onset within 8 weeks of a previous immunization.

Factors That Are Not Contraindications to Immunization

- significant local reactions to a previous dose of vaccine, for example, swelling of the entire limb, following administration of a previous dose of DTaP-IPV Hib
- minor illness without fever, such as a cold or mild diarrhea in an otherwise healthy person
- antibiotic treatment
- prematurity
- pregnancy of the subject's mother or any other woman in contact with the subject
- recent exposure to infectious disease
- breastfeeding: the only vaccinal virus that has been isolated in maternal milk is the rubella virus; however, it has not been shown that its presence in the milk presents a risk to the infant's health
- personal or family history of non-specific allergy
- history of allergy to chicken or chicken feathers
- family history of sudden infant death syndrome
- family history of convulsions associated with vaccination
- family history of adverse reactions to vaccination not associated with immunosuppression
- administration of an inactivated vaccine to immunocompromised people
- multiple sclerosis or any other auto immune disease
- evolving neurological conditions: there is no need to defer pertussis vaccination for children with such conditions
- hypotonic-hyporesponsive episodes: children experiencing such reactions to a previous dose of vaccine have not had problems with the administration of subsequent doses
- afebrile convulsions and encephalopathy temporally associated with administration of a vaccine including pertussis: it has not been shown that the a cellular vaccine was responsible
- febrile convulsions: these may be more likely in a susceptible child who develops high fever; parents should be advised of how to relieve post-vaccination fever
- persistent, inconsolable crying lasting 3 hours or more, within 48 hours of vaccination; it is believed that these reactions are caused by pain at the injection site
- thrombocytopenia

References:

1. Adapted from Nova Scotia Immunization Manual, by the Government of Nova Scotia, 2008. Adapted with permission.