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Childhood Immunizations. An Immunological Perspective and Principles of Vaccinations. A Review

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Abstract

Although the history of Immunizations and vaccinations can be traced back to as early as the 5th Century Before Christ (BC), with work by Thucydides, in Athens, Greece, describing immunity to plague (-Bubonic plague is one of three types of plague caused by bacterium *Yersinia pestis.* The disease causes lymphatic swelling). The noun, immunity, the state of being immune from or insusceptible to a particular disease or the like. the condition that permits either natural or acquired resistance to disease, is derived from the Latin word "Immunitas" which referred to legal protection given to Roman Senators, during their terms of office.

The evolution of immunology in the Western hemisphere, can be traced back to the works of Edward Jenner and Louis Pasteur amongst others. Edward Jenner injected material from a cowpox postule into the arm of an 8 year old boy. When this boy was subsequently injected/inoculated with smallpox. the disease (small pox) did not develop. Jenner's breakthrough treatise on vaccination (Latin "vaccinus" or of from cows) was published in 1798. Small pox, was the first disease, demonstrating the important role of immunizations to the control of communicable diseases from a public health perspective, the others being good personal hygiene and good sanitation.

Immunizations may be passive or active. Immunizations is not synonymous with vaccinations, as immunity may be conferred through other routes other than injections of antigen e.g. Maternal transfer of protective immunity to the fetus/new born as well as passive transfer of Immunity through serum.

Pathogens/Microbes have evolved different mechanisms for evading the normal immune system and various strategies have been employed in vaccine development. Prior to licensure, all vaccines undergo rigorous immunogenicity and safety testing. Mild and self-limited adverse events (e.g. local pain and tenderness at the injection site) are true, causally associated reactions. Serious causally related adverse events also can occur but are rare

Many childhood diseases have been virtually eliminated through the process of immunizations, although this remains elusive for some diseases e.g. HIV, Malaria and more recently Corona Virus. The ultimate goal of immunization is control of infection transmission, elimination of disease, and eventually, eradication of the pathogen.

Keywords: *Immunizations; Childhood Diseases; National Immunization Programs (NIPs)*

Introduction

Vaccination is one of the great public health achievements of human history, the other being good sanitation and good hygiene. Vaccines used in national immunization programs (NIPs) are considered safe and effective when used correctly [1,2]. Vaccines are however,

not risk-free and adverse events will occasionally occur following vaccination. Public trust in vaccine safety is key to the success of vaccination programs [3]. Vaccination does not ensure immunity and the state of immunoprotection can be achieved by means other than infection or vaccination e.g. the transfer of antibodies from mother to fetus, or the injection of antiserum against a pathogen may provide immune protection. Thus, vaccination is an event, whereas immunization (the development of protection, is a potential outcome of that event.

History

Historians often credit Thucydides, in the fifth century BC in Athens, as having first mentioned immunity to an infection that he called plague (but that was probably not the bubonic plague we recognize today). The concept of protective immunity may have existed long before, as suggested by the ancient Chinese custom of making children resistant to smallpox by having them inhale powders made from the skin lesions of patients recovering from the disease.

Immunology, in its modern form, is an experimental science, in which explanations of immunologic phenomena are based on experimental observations and the conclusions drawn from them. The evolution of immunology as an experimental discipline has depended on our ability to manipulate the function of the immune system under controlled conditions. Historically, the first clear example of this manipulation, and one that remains among the most dramatic ever recorded, was Edward Jenner's successful vaccination against smallpox. Jenner, an English physician, noticed that milkmaids who had recovered from cowpox never contracted the more serious smallpox. On the basis of this observation, he injected the material from a cowpox pustule into the arm of an 8-year-old boy. When this boy was later intentionally inoculated with smallpox, the disease did not develop. Jenner's landmark treatise on vaccination (Latin vaccinus, of or from cows) was published in 1798. It led to the widespread acceptance of this method for inducing immunity to infectious diseases, and vaccination remains the most effective method for preventing infections. An eloquent testament to the importance of immunology was the announcement by the World Health Organization in 1980 that smallpox was the first disease that had been eradicated worldwide by a program of vaccination [1].

Methodology

A literature search was done for all published peer review articles on PuBMed and Hinari search engines between January 2010 and December 2010. PubMed is a free search engine accessing primarily the MEDLINE database of references and abstracts on life sciences and biomedical topics. The United States National Library of Medicine at the National Institutes of Health maintain the database as part of the Entrez system of information retrieval.

Hinari Program set up by WHO together with major publishers, enables low- and middle-income countries to gain access to one of the world's largest collections of biomedical and health literature. Up to 16,000 journals, up to 63,000 e-books, up to 105 other information resources are now available to health institutions in more than 120 countries, areas and territories benefiting many thousands of health workers and researchers.

In addition, a review of standard textbooks of immunology was sought.

Results and Discussion

Definition of Vaccination

A vaccine is a substance that stimulates the production of antibodies and provides immunity against 1 or several diseases, prepared from the causative agent of a disease, its products, or a synthetic substitute, treated to act as an antigen without inducing the disease. A vaccine induces protection by utilizing pre-existing components of the immune response or by inducing the generation of antigen-specific memory cells.

Both the innate and adaptive immune subsystems are necessary to provide an effective immune response to an immunization. Further, effective immunizations must induce long-term stimulation of both the humoral and cell-mediated arms of the adaptive system by the production of effector cells and memory cells.

General requirements for a successful good vaccine

- Effective
- Appropriate adaptive immune response
- Stable
- Inexpensive
- Safe

Vaccine components

i) Antigen: Whole organism (live attenuated or killed), or subunit.

ii) Carrier: Provides helper T cell epitopes, the part of an antigen molecule to which an antibody attaches.

iii) Adjuvant: Non-specifically stimulates a specific immune response; depot + dendritic cell activator (= "PAMP," pathogen-associated molecular patterns, or PAMPs, are molecules associated with groups of pathogens, that are recognized by cells of the innate immune system called pattern recognition receptors (PRRs)) [4].

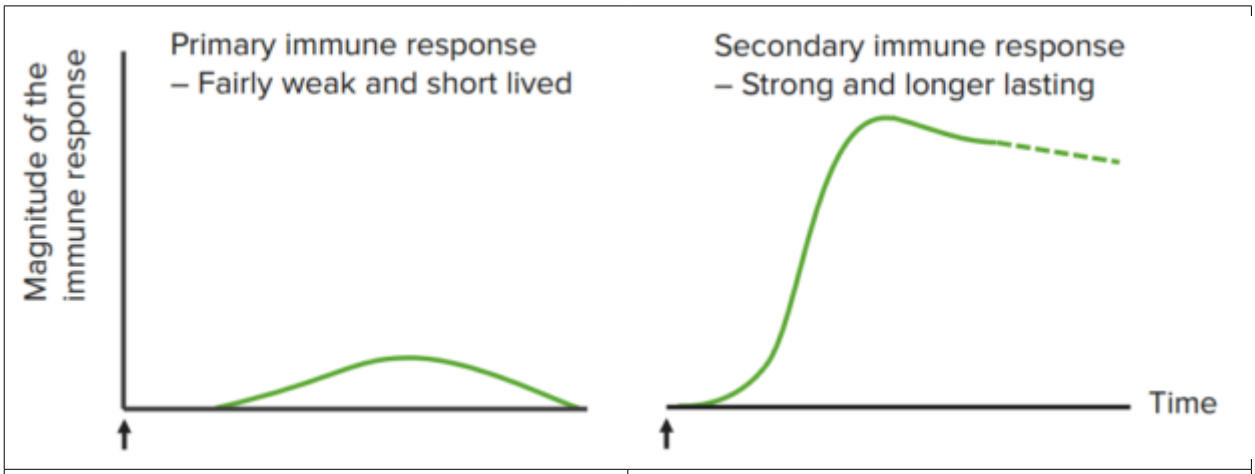
Active immunization

Active immunization involves administration of all or part of a microorganism or a modified product of a microorganism (e.g. a toxoid, a purified antigen, or an antigen produced by genetic engineering) to evoke an immunologic response and clinical protection that mimics that of natural infection but usually presents little or no risk to the recipient. Immunization can result in antitoxin, anti-adherence, anti-invasive, or neutralizing activity or other types of protective humoral or cellular responses in the recipient. Some vaccines provide nearly complete and lifelong protection against disease, some provide protection against the more severe manifestations and/or consequences of the infection if exposed, and some must be re-administered periodically to maintain protection. The immunologic response to vaccination is dependent on the type and dose of antigen, the effect of adjuvants, and host factors related to age, preexisting antibody, nutrition, concurrent disease, or genetics of the host. The effectiveness of a vaccine is assessed by evidence of protection against the natural disease. Induction of antibodies is an indirect measure of protection (e.g. antitoxin against *Clostridium tetani* or neutralizing antibody against measles virus), but for some infectious diseases, an immunologic response that correlates with protection is understood poorly, and serum antibody concentration does not always predict protection.

Vaccines are categorized as live (viral or bacterial, which almost always are attenuated) or inactivated. The term "inactivated vaccines," for simplicity, includes antigens that are toxoids or other purified proteins, purified polysaccharides, protein-polysaccharide or oligosaccharide conjugates, inactivated whole or partially purified viruses, recombinant proteins, and proteins assembled into virus-like participles. Recommendations for vaccines routinely advised for immunocompetent and immunocompromised individuals are updated annually in the harmonized schedule developed by the AAP, Centers for Disease Control and Prevention [3].

Categories of vaccines

- **An attenuated live vaccine:** Consists of an entire or partial organism (virus or bacteria) which is subjected to the process of attenuation. Attenuation reduces the viability of the organism as an infectious agent but still allows it to generate an effective immune response and often lasts in life long immunity. Attenuated live vaccines are believed to induce an immunologic response more similar to that resulting from natural infection than do killed vaccines.



First encounter with antigens from a pathogen. Seen in a nonpathogenic form. Memory T cells and B cells are generated.	Subsequent encounter with the actual pathogen. Because memory cells are already present as a result of vaccination, a secondary immune response occurs on the 1st encounter with the pathogen.

- **Inactivated (killed) vaccines:** Bacteria, viruses or rickettsia. Are composed of killed micro=organisms e.g. cholera and pertussis which results in an initial large antigen load followed by a plateau. Because the immune response is smaller/inferior that to that stimulate by live vaccines, these agents usually repeat administration.
- **Subunit vaccines:** Are composed of a constituent of the whole organism, e.g. bacterial capsular component e.g. Strep pneumococcus or a viral protein e.g. Hepatitis B surface antigen.
- **Toxoid vaccines:** Are rendered nontoxic but retain the ability to stimulate production of antibody.
- **Conjugate vaccines:** Pure polysaccharide vaccines are poorly immunogenic in children lees than two years. Covalent linkage of the polysaccharide to a carrier protein enhances the immune response. Conjugate vaccines comprise polysaccharides coupled to protein.

Novel approaches to vaccination

Recombinant vaccines: Recombinant vector vaccines are produced when one or more genes encoding for critical determinants of immunity from pathogenic microorganisms are inserted into a vector. e.g. HIV vaccine is still under development.

DNA vaccines: Utilize nucleic acid that encodes for critical antigens thereby decreasing the risks associated with of:

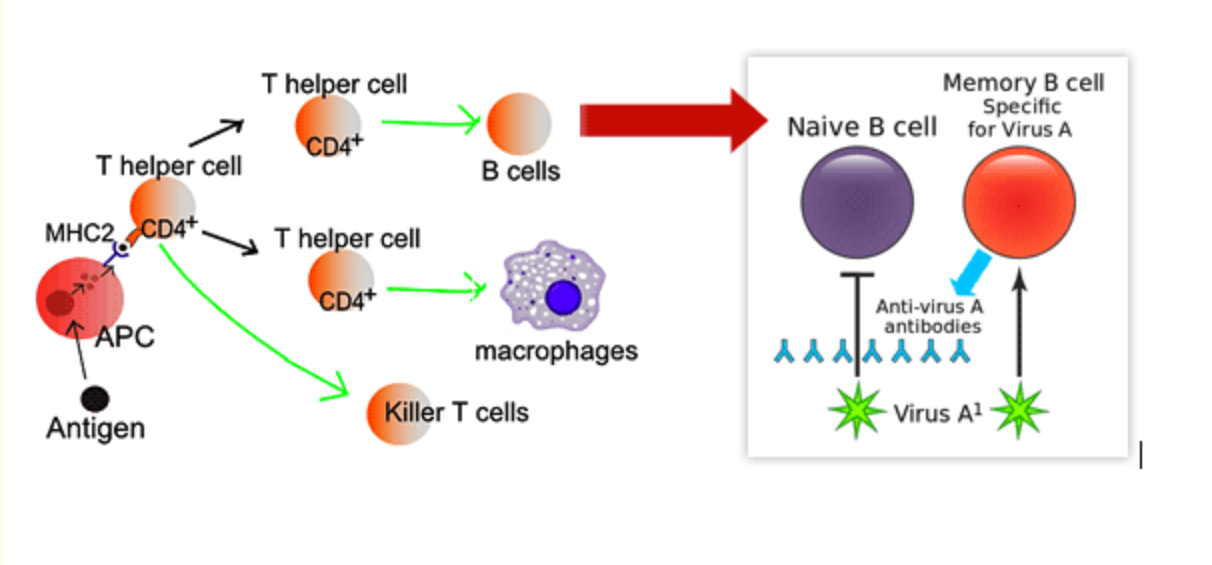
Childhood vaccines/vaccine preventable diseases

Vaccines to prevent other diseases have become available since the introduction of EPI and are recommended by the WHO for global use. They cover diseases such as hepatitis B disease, diarrhoeal disease caused by rotaviruses, and pneumonia and other respiratory tract infections caused by *Haemophilus influenzae* type B and pneumococcal bacteria. Others, such as the vaccine against yellow fever, are recommended in countries where the disease burden is significant.

The main vaccine-preventable diseases targeted by the Expanded Program on Immunizations (EPI) and the associated vaccines

Tubercle bacillus	Bacillus Calmette-Guérin (BCG) vaccine
Poliovirus	Oral polio vaccine (OPV) vaccine, Inactivated polio vaccine (IPV) vaccine
Corynebacterium diphtheriae (Diphtheria)*	Diphtheria toxoid** vaccine
Clostridium tetani (Tetanus)*	Tetanus toxoid (TT) vaccine
Pertussis*	Whole-cell pertussis (wP) vaccine, Acellular (cell-free) pertussis (aP) vaccine
Measles virus	Measles vaccine
Hepatitis B virus	Hepatitis B vaccine
Rotavirus	Rotavirus vaccine
Haemophilus influenzae type B (Hib)	Hib conjugate vaccine
Streptococcus pneumoniae (Pneumococcal infection)	Pneumococcal vaccines
Yellow fever virus	Yellow fever vaccine

Mechanisms of immunologic response by which immunizations/vaccinations stimulate immunity/vaccine strategies



Conclusion

Immunizations saves lives. It protects you, your family and your community. Immunizations helps protect future generations by eradicating diseases. Many infectious diseases are rare or eradicated now as a result of immunization programs, but new infectious diseases are appearing around the world. E.g. Severe Adult Respiratory Syndrome (SARS), Zika, Ebola and Corona virus-19.

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