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Passive Immunization-The Production of Passive Immunity

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Abstract

Vaccination has had a huge impact on increasing human life expectancy. Immunity is the state of protection against infectious disease conferred either through an immune response generated by immunization or previous infection or by other non-immunological factors. Immunizations are often widely stated as less risky and an easier way to become immune to a particular disease than risking a milder form of the disease itself. Passive immunization by transfer of antibodies has the advantage of more rapidly establishing protection, but it is short-lived and may carry a risk of inducing *serum sickness*. The route and schedule of immunization, physical nature of the vaccine antigen, and immune status of the host all contribute to the relative effectiveness of any vaccination protocol, in ways which are still not fully understood. Passive immunization, in which antibodies against a particular infectious agent are given directly to the child or adult, is sometimes appropriate. These antibodies are taken from a donor and then processed so the final preparation contains high antibody concentrations. At that point, they are given in the vein or by shot to the patient. Passive immunization is often used in children and adults. It can be used with people who haven't been vaccinated against a disease to which they've been exposed. Most commonly for the prevention of measles, hepatitis-A, hepatitis-B, tetanus, varicella, rabies, and vaccinia. Although their use in the treatment of bacterial infection has largely been supplanted by antibiotics, antibodies remain a critical component of the treatment of diptheria, tetanus, and botulism.

Keywords: Immunization; Passive immunity; Immunoglobulin preparations

Introduction

Immunization [im″u-nĭ-za´shun] is the process of rendering a subject immune, or of becoming immune, called also inoculation and vaccination. Immunization: is the means of providing specific protection against most common and damaging pathogens. Immunization, or immunisation, is the process by which an individual's immune system becomes fortified against an agent (known as the immunogen). **Passive immunization** is neither spontaneous on the part of the patient, nor, active response by the patient, the stimulus having been applied externally. Treatment that provides immunity through the transfer of antibodies obtained from an immune individual (Hunt, 2004). Transient immunization produced by the introduction into the system of preformed antibody or specifically reactive lymphoid cells. The animal immunized is protected only as long as these antibodies or cells remain in the blood and are active—usually from 4 to 6 weeks. Passive immunity refers to the process of providing IgG antibodies to protect against infection; it gives immediate, but short-lived protection— several weeks to 3 or 4 months at most.

History

Antibodies were first used to treat disease in the late 19th century as the field of bacteriology was emerging.

The first success story involved diphtheria, a dangerous disease that obstructs the throat and airway of those who contract it.

In 1890, Shibasaburo Kitasato (1852-1931) and Emil von Behring (1854-1917) immunized guinea pigs against diphtheria with heat treated blood products from animals that had recovered from the disease. The preparations contained antibodies to the diphtheria toxin that protected the guinea pigs if they were exposed soon thereafter to lethal doses of diphtheria bacteria and its toxin.

By 1896, the introduction of diphtheria antitoxin was hailed as "the most important advance of the [19th] Century in the medical treatment of acute infective disease"
(http://www.merckmanuals.com/professional/infectious-diseases/immunization/passive-immunization).
Immunoglobulin therapy continued to be a first line therapy in the treatment of severe respiratory diseases until the 1930s, even after sulphonamides were introduced.

In 1890 antibody therapy was used to treat tetanus, when serum from immunized horses was injected into patients with severe tetanus in an attempt to neutralize the tetanus toxin, and prevent the dissemination of the disease.

1960s, human tetanus immune globulin (TIG) has been used in the United States in unimmunized, vaccine naive or incompletely immunized patients who have sustained wounds consistent with the development of tetanus. The

administration of horse antitoxin remains the only specific pharmacologic treatment available for botulism. Antitoxin also known as heterologous hyper immune serum is often also given prophylactically to individuals known to have ingested contaminated food.

IVIG treatment was also used successfully to treat several victims of toxic shock syndrome, during the 1970s tampon scare.

Antibody therapy is also used to treat viral infections.

In 1945, hepatitis A infections, epidemic in summer camps, were successfully prevented by immunoglobulin treatment. Similarly, hepatitis B immune globulin (HBIG) effectively prevents hepatitis B infection. Antibody prophylaxis of both hepatitis A and B has largely been supplanted by the introduction of vaccines; However, it is still indicated following exposure and prior to travel to areas of endemic infection.

In 1953, human vaccinia immunoglobulin (VIG) was used to prevent the spread of smallpox during an outbreak in Madras, India, and continues to be used to treat complications arising from smallpox vaccination.

During a 1995 Ebola virus outbreak in the Democratic Republic of Congo, whole blood from recovering patients, and containing antiEbola antibodies, was used to treat eight patients, as there was no effective means of prevention, though a treatment was discovered recently in the 2013 Ebola epidemic in Africa. Only one of the eight infected patients died, compared to a typical 80% Ebola mortality, which suggested that antibody treatment may contribute to survival. Immune globulin or immunoglobulin has been used to both prevent and treat reactivation of the herpes simplex virus (HSV), varicella zoster virus, Epstein Barr virus (EBV), and cytomegalovirus (CMV)

Types of Passive Immunity

Passive immunity is usually classified as natural or acquired.

Naturally acquired passive immunity

Maternal passive immunity is a type of naturally acquired passive immunity, and refers to antibody mediated immunity .The transfer of maternal tetanus antibody (mainly IgG) across the placenta provides natural passive immunity for the newborn baby for several weeks/months until such antibody is degraded and lost. Passive immunization occurs physiologically, when antibodies are transferred from mother to fetus during pregnancy, to protect the fetus before and shortly after birth.

In humans, maternal antibodies (MatAb) are passed through the placenta to the fetus by an FcRn receptor on placental cells. This occurs predominately during the third trimester of pregnancy, and thus is often reduced in babies born prematurely (http://www.who.int/maternal_child_adolescent/topics/newborn/nutrition/breastfeeding/en). Immunoglobulin G (IgG) is the only antibody isotype that can pass through the human placenta, and is the most common antibody of the five types of antibodies found in the body. IgG antibodies protects against bacterial and viral infections in foetuses (http://www.merckmanuals.com/professional/infectious-diseases/immunization/passive-immunization).

Immunization is often required shortly following birth to prevent diseases in newborns such as tuberculosis, hepatitis B, polio, and pertussis, however, maternal IgG can inhibit the induction of protective vaccine responses throughout the first year of life. This effect is usually overcome by secondary responses to booster immunization.

Passive immunity is also provided through colostrum and breast milk, which contain IgA antibodies that are transferred to the gut of the infant, providing local protection against disease causing bacteria and viruses until the newborn can synthesize its own antibodies. Maternal antibodies protect against some diseases more than others such as measles, rubella, and tetanus compared to the protection provided against polio, and pertussis. Maternal Passive immunity offers immediate protection, though protection mediated by maternal IgG typically only lasting four to six months after birth. Protection mediated by IgA is dependent on the length of type that an infant is breastfed, which is one of the reasons the World Health Organization recommends breastfeeding for at least the first two years of life.

A vial of diphtheria antitoxin, dated 1895 only a few other species besides humans transfer maternal antibodies before birth, including primates and lagomorphs (which includes guinea pigs and rabbits). In some of these species IgM can be transferred across the placenta as well as IgG. All other mammalian species predominantly or solely transfer maternal antibodies after birth through milk. In these species, the neonatal gut is able to absorb IgG for hours to days after birth. However, after a period of time the neonate can no longer absorb maternal IgG through their gut, an event that is referred to as "gut closure". If a neonatal animal does not receive adequate amounts of colostrum prior to gut closure, is does not have a sufficient amount of maternal IgG in its blood to fight off common diseases. This condition is referred to as failure of passive transfer. It can be diagnosed by measuring the amount of IgG in a new-born's blood, and is treated with intravenous administration of immunoglobulins. If not treated, it can be fatal.

Artificially acquired passive immunity

In contrast, acquired passive immunity refers to the process of obtaining serum from immune individuals, pooling this, concentrating the immunoglobulin fraction and then injecting it to protect a susceptible person. Artificial passive immunization is normally administered by injection and is used if there has been a recent outbreak of a particular disease or as an emergency treatment for toxicity, as in for tetanus. In this high levels of antibodies specific to a pathogen or toxin (obtained from humans, horses, or other animals) are transferred to nonimmune persons through blood products that contain antibodies, such as in immunoglobulin therapy or antiserum therapy

Artificially acquired passive immunity is a short term immunization achieved by the transfer of antibodies, which can be administered in several forms; as human or animal blood plasma or serum, as pooled human immunoglobulin for intravenous (IVIG) or intramuscular (IG) use, as hightiter human IVIG or IG from immunized donors or from donors recovering from the disease, and as monoclonal antibodies (MAb). Passive transfer is used to prevent disease or used prophylactically in the case of immunodeficiency diseases, such as hypogammaglobulinemia. It is also used in the treatment of several types of acute infection, and to treat poisoning. Immunity derived from passive immunization lasts for a few weeks to three to four months.

There is also a potential risk for hypersensitivity reactions, and serum sickness, especially from gamma globulin of nonhuman origin.

Passive immunity provides immediate protection, but the body does not develop memory, therefore the patient is at risk of being infected by the same pathogen later unless they acquire active immunity or vaccination (Coico *et al*., 2003).

Passive immunization is provided in the following circumstances:

- When people cannot synthesize antibody.
- When people have been exposed to a disease that they are not immune to or that is likely to cause complications.
- When people have a disease and the effects of the toxin must be ameliorated.

Methods of Passive Immunization

Injection of *antibody* to a pathogen can provide very *rapid*, although *short-lived*, resistance to infection, and is referred to as **passive immunization**. Passive immunization is generally used when there is no time to wait for the development of active immunity (see below), or when no effective active vaccine exists (Janeway *et al*., 2001).

i) **Human antibodies**. Normal human IgG, prepared from pools of many individual donors, contains significant levels of antibody to *measles* and *hepatitis* viruses. High levels of protective antibody for *tetanus* can be obtained from immunized donors, and anti-*Zoster* antibodies from the serum of patients collected during recovery from an infection. In each case, these antibodies can be administered to recipients who are at high risk for acquiring the disease.

ii) **Heterologous antibodies**. Horse antibodies to *diphtheria toxin* or to the toxins of *snake and spider* venoms have been very effective in neutralizing the effect of these dangerous molecules. The use of heterologous serum of course, introduces a substantial risk of inducing *serum sickness* or an *allergic reaction* (Stiehm, 1982).

The most important elements of the immune system that are improved by immunization are the T cells, B cells, and the antibodies B cells produce. Memory B cells and memory T cells are responsible for a swift response to a second encounter with a foreign molecule.

Passive immunization is direct introduction of these elements into the body, instead of production of these elements by the body itself.

Passive immunization is where presynthesized elements of the immune system are transferred to a person so that the body does not need to produce these elements itself. Currently, antibodies can be used for passive immunization. This method of immunization begins to work very quickly, but it is short lasting, because the antibodies are naturally broken down, and if there are no B cells to produce more antibodies, they will disappear.

The four most commonly used immunoglobulin preparations for immunization are as Follows-

1. Human Hepatitis B Immunoglobulin
2. Human Rabies Immunoglobulin
3. Human Tetanus Immunoglobulin
4. Human Varicella-Zoster Immunoglobulin.

Passive immunization in treatment of infectious disease

Passive immunization may be use used to treat many infectious diseases like-

a) BACTERIAL INFECTIONS
   - Respiratory Infections
   - Diphtheria
   - Pertussis
   - Tetanus
   - Other Clostridial Infections
   - Staphylococcal Infections
   - Invasive Streptococcal Infection
   - Shock, Intensive Care, and Trauma

- *Pseudomonas* Infection

b) VIRAL DISEASES

- Hepatitis A
- Hepatitis B
- Hepatitis C
- Human Immunodeficiency Virus Infection
- Respiratory Syncytial Virus Infection
- Herpesvirus Infections
- Parvovirus B19 Infection
- Enterovirus Infections
- Ebola
- Rabies
- Measles, Rubella, and Mumps
- TickBorne Encephalitis

Passive transfer of cell-mediated immunity

The one exception to passive humoral immunity is the passive transfer of cell mediated immunity, also called adoptive immunization which involves the transfer of mature circulating lymphocytes. It is rarely used in humans, and requires histocompatible (matched) donors, which are often difficult to find, and carries severe risks of graftversushost disease. This technique has been used in humans to treat certain diseases including some types of cancer and immunodeficiency. However, this specialized form of passive immunity is most often used in a laboratory setting in the field of immunology, to transfer immunity between "congenic", and deliberately inbred mouse strains which are histocompatible (Osborn *et al*., 1952).

Advantages and Disadvantages of Passive Immunity

Advantages

- An individual's immune response of passive immunity is "faster than a vaccine" and can in still immunity in an individual that does not "respond to immunization", often within hours or a few days.
- Passive immunity is that maternal antibodies that are passed to the newborn during nursing boosts the newborn's immune system having lasting effects on the baby's health such as decreased risk of obesity.
- Quick acting, producing an immune response within hours or days, faster than a vaccine.
- Passive immunization can override a deficient immune system, which is especially helpful in someone who does not respond to immunization.

Disadvantages

- Producing antibodies in a laboratory is expensive and difficult to do.
- In order to produce antibodies for infectious diseases, there is a need for possibly thousands of human donors to donate blood or immune animals' blood would be obtained for the antibodies.
- Patients who are immunized with the antibodies from animals may develop serum sickness due to the proteins from the immune animal and develop serious allergic reactions.
- Antibody treatments can be time consuming and are given through an intravenous injection or IV, while a vaccine shot or jab is less time consuming and has less risk of complication than an antibody treatment.
- Passive immunity is effective, but ephemeral (lasting a short amount of time).

Conclusion

Antibodies were one of the first tools used against specific infectious diseases. As antibiotics came to be widely used, and as vaccines were developed, the use of passive immunization became less common. Even today, however, antibodies play a role against infectious disease when physicians use antibodies to achieve passive immunity and to treat certain diseases in patients. Scientists are investigating new applications for passive immunization and antibody treatment as well as new and more efficient methods of creating antibodies

Today, patients may be treated with antibodies when they are ill with diphtheria or cytomegalovirus. Antibody treatment may be used as a preventive measure after exposure to a pathogen to try to stop illness from developing (such as with respiratory syncytial virus [RSV], measles, tetanus, hepatitis A, hepatitis B, rabies, or chickenpox). Antibody treatment may not be used for routine cases of these diseases, but it may be beneficial to high-risk

Individuals, such as people with immune system deficiencies.

The use of human MAb or humanized MAb to key epitopes of infectious pathogens may further define thehumoral responses with significant therapeutic potential. Since many infections are now caused by bacteria resistantto antibiotics (e.g., *S. aureus*, *Enterococcus* species, and *S. pneumoniae*). The development of immune therapy forsuch resistant microorganisms may potentially provide a new lifesaving strategy.

The use of MAbs may lead to more effective post exposure prophylaxis including their use in tranasally in viral disease. A major question is whether such prophylaxis can be effective at an acceptable cost and treatment frequency. Treatment of established viral

infections with antibody is rarely successful, but there are important exceptions (parvovirus, vaccinia virus, and enterovirus). As MAb recognizing key epitopes are developed, theymay have enhanced therapeutic potential.

To date, only one MAb treatment is commercially available for the prevention of an infectious disease. This is a MAb preparation for the prevention of severe disease caused by RSV in high-risk infants. Physicians are also increasingly using MAbs to combat non-infectious diseases, such as certain types of cancer multiple sclerosis, rheumatoid arthritis, Crohn's disease, and cardiovascular disease. Scientists are researching other new technologies for producing antibodies in the laboratory, such as recombinant systems using yeast cells or viruses and systems combining human cells and mouse cells, or human DNA and mouse DNA.

Bio-terror threats In the event of the deliberate release of an infectious biological agent, biosecurity experts have suggested that passive immunization could play a role in emergency response. The advantage of using antibodies rather than vaccines to respond to a bio-terror event is that antibodies provide immediate protection, whereas a protective response generated by a vaccine is not immediate and in some cases may depend on a booster dose given at a later date.

Candidates for this potential application of passive immunization include botulinum toxin, tularaemia, anthrax, and plague. For most of these targets, only animal studies have been conducted, and so the use of passive immunization in potential bioterror events is still in experimental stages.

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