(Review Article)

E-ISSN: 0975-8232; P-ISSN: 2320-5148



# PHARMACEUTICAL SCIENCES



Received on 29 November 2022; received in revised form, 12 February 2023; accepted 27 May 2023; published 01 August 2023

## AN OVERVIEW OF IMMUNITY AND IMMUNE SYSTEM-RELATED EFFECTS ON HUMAN HEALTH

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#### **Keywords:**

Immunity, Immune response, Autoimmune, Disorder or disease

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ABSTRACT: Immunity plays an important role in the protection of the human body and provides several beneficial effects on many infectious diseases and also immunity produces hyperactivity which also causes some problems for the human body, so we want to discuss a summarized knowledge about immunity and their important, advantages, disadvantages and effects on the human body. The present review focuses on various therapeutic effects through different disease conditions, such as autoimmune disorders, infectious diseases, and organ transplants. Thus the immune system and immunity are promising parts for the protection of the human body, which has wide importance in beneficial and another impact in therefore much research can be inspired in this area.

**INTRODUCTION:** A strong immune system requires balance and harmony in the body to fight harmful infections and illnesses. Having a strong immune system is one of the biggest advantages for humans. There are many steps individuals can take to help strengthen their immune systems to help fight infections and reduce the risk of contracting highly contagious diseases.

**Benefits of a Strong Immune System:** The following benefits for strong immune system are given below.

- ♦ Fights off pathogens
- ♦ Combats viruses and bacteria
- ♦ Battles foreign bodies
- It helps prevents infections and disease



**Example:** Immune system works when you get a small red bump on your skin following a mosquito bite. That itchy bump is a sign of your immune system keeping unwanted pathogens at bay <sup>1-2</sup>.

**Signs and Symptoms of a Weakened Immune System:** A weak immune system shows the following symptoms below.

**Stomach Complaints:** A weak immune system that produces many stomach-related complaints or disorders such as; diarrhea, constipation, and flatulence. Up to 70% of your immune system is located in your gut, so maintaining good gut health (lots of friendly gut bacteria) is essential for strong immunity <sup>3-4</sup>.

**Slow-healing Wounds:** Weak immune system also produces many other complications related to slow-healing wounds; your body relies on healthy immune cells for healing, sending nutrient-rich blood to the injury to regenerate. Your skin cannot heal or regenerate quickly when the immune system is low <sup>5-6</sup>.

**Frequent Infections:** Frequent infections is also represented to are peated infections such as ear, respiratory, coughs, colds and influenza and requiring more than two courses of antibiotics a year, are signs of a compromised immune system <sup>7-</sup>

**Fatigue:** Weak immune system also produces some other complications which directly related low immune; so are your energy levels as your body is trying to conserve energy to power your immune system to help protect against infections <sup>9</sup>.

**Definition of Immunity:** The words of "immunity refers to preventing or exhibiting by the host towards injury caused by microorganisms and their products. Production of immunity against infectious diseases is only one of the consequences of immune response" which is entirely as concerned with regulating the body against any foreign antigen.

Immunity can be classified as

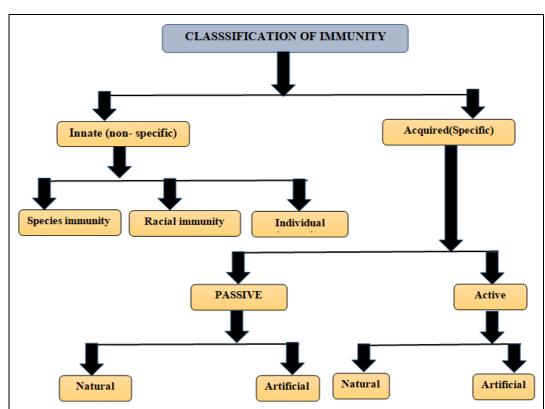
- 1. Innate immunity
- **2.** Acquired immunity.

#### Innate immunity is classified into following

- 1. Species
- 2. Racial
- 3. Individual

## Acquired immunity is again classified into following

- (i) Active
- (a) Natural
- (b) Artificial
- (ii) Passive
- (a) Natural
- **(b)** Artificial <sup>10-11</sup>.



Innate Immunity (Non-Specific Immunity): Innate immunity is the resistance to infectious which an individual possesses by his genetic and constitutional makeup. It is called the first line of defense.

- **1.** It is not affected by prior contact with microorganisms or immunization.
- **2.** It may be non-specific when it initiates a degree of resistance to infections in general or specific

when resistance to a particular pathogen is concerned  $^{12}$ .

Innate immunity may be classified as:

- a) Species immunity,
- b) Racial immunity or
- c) Individual immunity.

Species Immunity: Species immunity generally refers to all species members' total or relative resistance to pathogens. For instance, all humans are insusceptible to plant pathogens and too many animal pathogens such as rinderpest or distemper. It's something a person takes from the as a birthright because he belongs to the human species. The mechanism of species immunity is not clearly understood. Still, it's may be due to physiological and biochemical differences between the tissues of the different host species, which determine whether or not a pathogen can multiply in them. Pasteur's experiments gained an early insight into the basis of species immunity in astute frog's, which are naturally resistant to the disease but become susceptible when their body temperature is raised from  $25^{\circ}$ C to  $35^{\circ}$ C <sup>13</sup>.

Racial Immunity: Racial immunity is a species produced by different races that may show differences in susceptibility to infection. This is known as racial immunity. The classic example of this in the high resistance of Algerian sheep to anthrax, such racial differences are known to be genetic in origin, and by selection and in breeding, it is possible to develop at will races that possess high degree of resistance or susceptibility to pathogen. It is difficult to demonstrate marked differences in immunity in human races, as controlled breeding is not possible in the human species. It has been reported that the Negroes in the USA are more susceptible than the Whites to tuberculosis. But such comparisons are initiated by external influences such as differences in socioeconomic levels. An interesting instance of genetic resistance to Plasmodium falciparum malaria is seen in some parts of Africa and the Mediterranean coast. A hereditary abnormality of cull silk ling, prevalent in the area, confers immunity to infection by the malarial parasite, which may be developed from the survival advantage conferred by a malarial environment 14.

**Individual Immunity:** The difference in innate immunity exhibited by different individuals in a race is known as individual immunity. The genetic basis of individual immunity is evident from studies on the incidence of infectious diseases in twins. It is well documented that homozygous twins are susceptible to leprosy and tuberous <sup>15</sup>.

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**Factors Affecting Innate Immunity:** Influence the level of innate immunity in an individual depends upon the factors given below.

**Age:** Age is the most important factor that directly impacts the development of strong or susceptible immunity, so we know that age is important in producing immunity. The two extremes of life early higher susceptibility to infectious disease than adults. The fetus in the uterus is normally protected from maternal infection by the placental barrier. Newborn humans & animals are more susceptible to experimental infections than older ones. Coxsackie viruses cause fatal infections in suckling mice but not in the adult. Old persons are highly susceptible to infection due to gradually waning their immune responses <sup>17</sup>.

**Hormonal Influences:** Hormonal influence is also a major portion that directly affects the production of antibodies or triggers immunity or decreased immunity. Endocrine disorders such as Diabetes mellitus, Hypothyroidism, and Adrenal dysfunction are associated with enhanced susceptibility to infections. This high incidence may be related to the increased level of carbohydrates in tissues. Corticosteroids exert an important influence on the response to infection. They depress the host resistance by their anti-inflammatory and antiphagocytic effects and by suppressing antibody formation and hypersensitivity. They also have a beneficial effect in neutralizing the harmful effects of bacterial products such as endotoxins. The elevated steroid level during pregnancy may have a relation to the increased susceptibility of pregnant women to many infections; the reported effect of stress in increasing susceptibility to infections may, in some, be due to the release of steroids <sup>18</sup>.

**Nutrition:** Nutrition is the main part that plays an important role in developing immunity in the human body. The interrelation between malnutrition and immunity is complex, but humoral

and cell-mediated immune procedures are generally reduced in malnutrition. Cell-mediated immune responses such as the Monteux test become negative in severe protein deficiency, as in kwashiorkor. Because of prevalence. its malnutrition may be the commonest form of immunodeficiency. Paradoxically, there is some evidence that certain infections may not become clinically apparent in the severely ill-nourished. Malarial infection in the famine-stricken may not induce fever, but clinical malaria develops once their nutrition is improved. It has also been reported that some viruses may not multiply in the tissues of severely malnutrition individuals <sup>19</sup>.

Protective Mechanisms of Innate Immunity: Innate immunity comprises four types of defensive barriers anatomy, physiological endocytic and phagocytic, and inflammatory. Tissue damage and infection induce leakage of vascular fluid containing serum proteins with antibacterial activity and the influx of phagocyte cells into the affected area. The following barriers are working as protection for immunity which are given below <sup>20</sup>.

- a) Anatomic barriers
- **b)** Physiological barriers
- c) Endocytic and phagocytic barriers

Anatomic Barriers: Physical and anatomic barriers that tend to prevent the entry of pathogens and an organism's first line of defense against infection, the skin and the surface of mucous membranes, are included in its particular category because they provide effective barriers to the entry of most microorganisms. The skin consists of these two distinct layers: a relatively thin outer layer of the epidermis and a thicker layer of the dermis. The epidermis contains several layers of tightly packed epidermal cells. The outer epidermal layer consists of dead cells filled with a waterproofing protein called keratin, Old epidermal cells are removed from the surface and are replaced by new cells next to the dermis; as a result, the epidermis is completely renewed every 15-30 days. The epidermis does not contain blood vessels, and the epidermis causes it instead of bathed in nutrients that differ from the underlying dermis. The dermis, composed of connective tissue, contains blood vessels, hair follicles, subcutaneous glands, and sweat glands. The subcutaneous glands

associated with the hair follicles and produce an oily sebum secretion. Sebum consists of lecithin and fatty acids maintaining the skin's pH between 3 the growth inhibiting microorganisms. Some bacteria that metabolize sebum live as common skin salts and are responsible for severe acne. One acne drug isotretions (Acutance) is a vitamin A derivative inhibiting sebum formation. The skin prevents the penetration of most pathogens and inhibits most bacterial growth to its low pH. Its break to the skin, even small ones, resulting from wounds or abrasion, is the obvious route of infection. The skin is also inhibition from biting insects (e.g., Mosquitoes, mites, ticks, fleas, and sandflies). If these harbor pathogenic organisms, they can introduce the pathogen into the body as they feed. The protozoan that causes malaria, e.g., is carried by mosquitoes who deposit it in humans when they take a blood meal. Similarly, the bite of flies spreads bubonic plague, and Lyme disease is spread by the bite of ticks <sup>21-22</sup>.

**Physiological Barriers:** The physiological barriers contributing innate immunity to temperature, pH, O, tension, and soluble factors. Some species are susceptible to certain diseases simply because their body temperature inhibits pathogens' growth. Chickens e.g., display innate immunity to anthrax because their high body temperature inhibits the growth of this pathogen; gastric acidity also provides an innate physiologic barrier to infection because very few ingested microorganisms can survive at the low pH of the stomach. One reason new bears are susceptible to some diseases that do not affect adults is that their stomach contents are less acidic than that of adults. A variety of soluble factors also contribute to nonspecific immunity. Among these soluble Proteins are lysozyme, interferon, and complement.

Lysozyme, a hydrolytic enzyme found in mucous secretions, can cleave the peptidoglycan layer of the bacterial cell wall. Interferons comprise a group of proteins produced by virus-infected cells. Among the many functions of interferons is the ability to bind to nearby cells and induce a generalized antiviral state. Complement is a serum protein group that circulates in an inactive proenzyme state. These proteins can be activated by various specific and non-specific immunological

mechanisms that convert the inactive proenzymes into active enzymes <sup>23</sup>.

Endocytic and Phagocytic Barriers: Another modification of the innate defense mechanism is included in the extracellular macromolecules via endocytosis and particulate material via phagocytosis. These two internalization processes bring different types of extracellular material into the cell and differ in several other ways. In endocytosis. macromolecules within the extracellular tissue fluids are internalized by cells via the invagination (inward folding) and pinching off of the small regions of the plasma membrane (pH). The resultant endocytic vessels are small, approximately 0.1 mm in diameter. Endocytosis occurs through one of two processes: pinocytosis or mediated endocytosis. Pinocytosis, non-specific invagination, internalizes membrane macromolecules in proportion to their extracellular concentrations <sup>24</sup>.

Macromolecules are selectively internalized in receptor-mediated endocytosis after binding to specific membrane receptors. The endocytic vesicles formed by either force fuse with coli or other fare delivered to endosomes, which are the intracellular acidic compartment that produces filtering to function The Audi interior endosomes facilitates dissociation macromolecular ligands from their receptors. The cattle are then recycled back to the cell surface. Three macromolecules include some components within endosomes fuse with Primary lysosomes to form secondary lysosomes. Primary lysosomes are decided from the Golgi complex and contain a large of degradative enzymes, including proteases, nucleases, lipases and other hydrolytic enzymes in secondary lysosomes, the ingested macromolecules are then digested into small break down Products (e.g., Peptides, nucleotides, and Sugars) which eventually are eliminated from the Phagocytosis involves the ingestion of particulate including material, whole pathogenic microorganisms. In phagocytosis, the plasma membrane impanels around the particulate material to form large vesicles called phagosomes. These vesicles are roughly 10-20 times larger than endocytic vesicles. The membrane expansion in phagocytes requires the participation of microfilaments, which do not participate in

endocytosis. Another difference between the two processes is that only specialized cells can be phagocytes, whereas virtually phagocytic cells include blood monocytes, neutrophils, and tissue macrophages <sup>25</sup>.

**Inflammatory Barrier:** Inflammatory barrier is generally involved in another innate immune mechanism, which provides complex sequences of events that occur collectively at the site of infection and tissue injury caused by the microbes. The series of events involving inflammatory response are given below <sup>26</sup>.

- 1. Vasodilation,
- 2. Increased capillary permeability
- **3.** Extravasation of phagocytes.

Vasodilation: The vasodilation procedure generally occurs at the site of injury, whereas blood vessels show an increase in their diameter, especially the arteries carrying the blood toward the site of infection. On the other hand, blood vessels (vein) carrying blood away from the site constrict, resulting in the engorgement of capillaries with blood. The engorged capillaries are responsible for tissue redness, erythema, and increased tissue temperature. Increased blood supply increases tension at the site of infection, and increased temperature hinders microbial growth. prevents the spreading of infection <sup>27</sup>. This

**Increased Capillary Permeability:** Increased capillary permeability mechanism facilitates the influx of fluids and defense cells, such as neutrophils and monocytes, from the engorged capillaries into the tissue at the site of infection. The fluid that accumulates has higher protein content than intravascular fluid (*i.e.*, blood plasma).

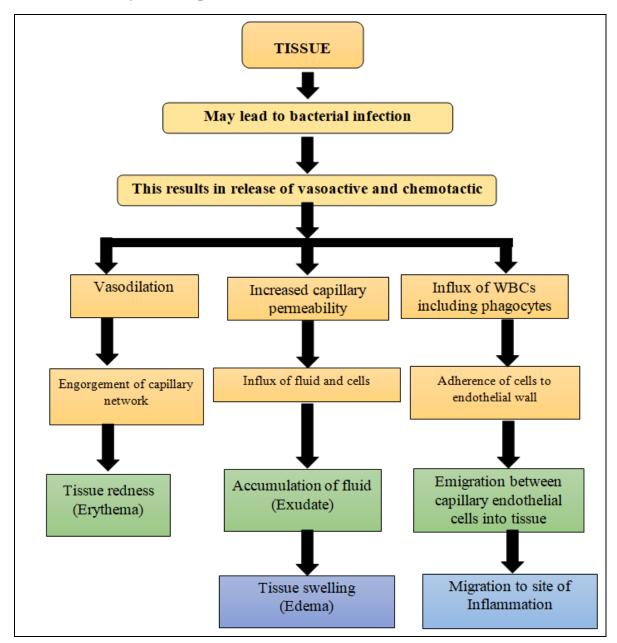
The accumulation of fluid contributes to tissue swelling or edema <sup>28</sup>.

**Extravasation of Phagocytes:** Extravasation or diparesis of phagocytes from the blood capillaries into the tissue is facilitated by increased capillary permeability. The permittee of phagocytes from the intravascular space to the extravascular space involves complex series of events. First, adherence of the phagocytic cells to the endothelial lining of

the blood vessels is called margination. Second, the emigration of phagocytes between the endothelial linings into the tissue is called extravasation.

Finally, the migration of phagocytes to the site of infection is called chemotaxis <sup>29</sup>.

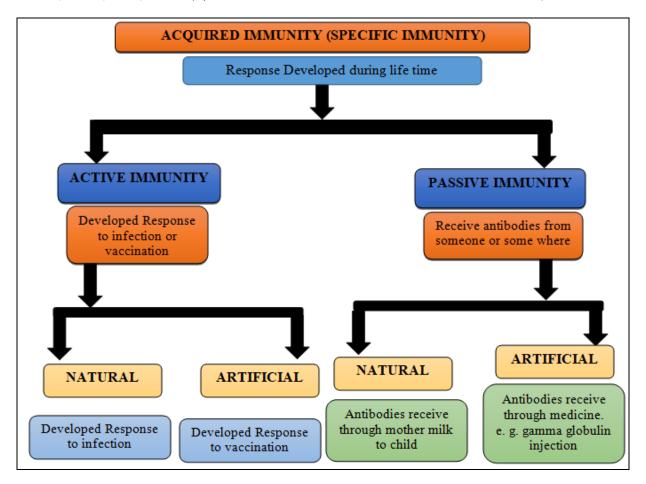
#### **Procedure of Immune System Response:**



Acquired **Immunity** (Specific **Immunity):** Acquired immunity is also known as adaptive immunity, which mainly occurs immune response. It follows a natural or artificial stimulation of the antibody-producing mechanism. Natural stimulation is imparted by the infection through microorganisms, contracting a disease, recovering from it. This will usually result in a long-lasting immunity to another attack of the same

organisms. It reflects a functional immune response capable of specifically recognizing and selectively eliminating foreign antigens of microbial or tissue origin. Acquired immunity can be of the active or passive type, which can be schematically represented as follows <sup>30</sup>.

- ✓ Active immunity
- ✓ Passive immunity



**Active Immunity:** Active Immunity is very important for the human body which is generally classified as given below.

- a) Natural
- b) Artificial

Naturally Acquired Active Immunity: Active immunity is obtained from natural infections caused by bacteria and viruses. Most cases are obtained by sub-clinical infections, which are saved unnoticed. Active immunity has many advantages over passive immunization, mainly because the individual's immune system is stimulated to produce antibodies and cellular immune responses against the pathogen or antigen. Antibody production occurs through humoral immune response, and T-cells help in cellular immune response and immunologic memory to boost the response in case of subsequent exposure to the same antigen. Antibodies formed as a result of active immunity are longer lasting as compared to passively acquired immunoglobulins <sup>31</sup>.

Artificially Acquired Active Immunity: Artificial active immunity is usually taken by vaccination or

in case the organisms, which produce potent exotoxins, by administration of toxoid.

Vaccines are generally made up by killed or live attenuated microorganisms, which is done by heat killing or growing them in unnatural hosts or aging them in culture or treating the microorganisms with detergents *etc*.

The toxoids are formulate to toxins, which are decomposed or non-activated by certain chemical treatment and some modification in toxin property is brought about so as to make it non-toxic. At the same time toxoid will retain antigenic potency and thus like toxin can induce antitoxin (antibody) formation. Therefore, they are used for artificial immunization to protect against toxic effects brought about by the infection of certain strain of bacteria <sup>32</sup>.

**Passive Immunity:** Passive immunity is also very important which generally by developed during mother lactation and taken some medicine that are following two types are available.

a) Natural

#### **b)** Artificial

Naturally Acquired Passive Immunity: This occurs due to transfer of antibodies (IgG) from mother to fetus and lasts for nearly six months after antibodies birth. Maternal to diphtheria, streptococci, tetanus, rubella, mumps. rubeola and poliovirus protect developing fetus through passive immunity. Secretory antibodies (IgA) present in mother's milk also provide local immunity in the gastrointestinal tract of breastfed infants. Human colostrum is rich in macrophages and lymphocytes. These macrophages can process antigens, and the lymphocytes are of T cell type, which can survive in the intestine of suckling infants for some time and can penetrate the intestinal wall to reach mesenteric lymph nodes. These cells (T-cells) can transfer cell-mediated immune response <sup>33</sup>.

**Acquired Passive Immunity: Artificially** specific Administering antibodies (immunoglobulins) or serum containing specific antibodies or sensitized lymphocytes from an individual who possesses specific immunity to a particular pathogen achieves this for example, an individual who gets wounded is immediately administered with horse antiserum to tetanus toxin, if the individual has not been immunized against tetanus toxin. The preformed horse antibodies against the toxin of Clostridium tetany neutralize the toxin produced at the site of wound <sup>34</sup>.

Routine passive-immunization is done against botulinum, diphtheria, hepatitis, measles and rabies. Protection against snakebites and black widow spiders is provided by passive immunity by injecting horse antivenin. Usually, antibodies against a pathogen or its antigens or toxin are raised in a suitable animal by repeated injection of antigens. The serum or suitable immunoglobulin from the plasma is used as a therapeutic measure in treating the diseases caused by the infective agent or as a prophylactic measure to prevent infection in individuals likely to suffer from the disease. Immunizing horse obtains antitetanus, anti-diphtheria, and anti-cholera antibodies with corresponding toxoids 35-36.

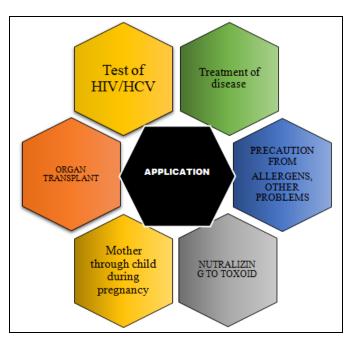
**Immunity Boosters:** Immunity Boosters are extremely popular for individuals wanting to supercharge their immune system.

- Vitamins,
- Minerals
- Antioxidants

Such as glutathione, cysteine, arginine, Vitamin C, and zinc; the treatment work quickly and efficiently to boost the immune system, regenerating the body and protecting against infection.

Remember, washing hands and a healthy immune system is for life, so integrating and maintaining these changes will give you the best chance of keeping well <sup>37-39</sup>.

**Applications:** The following applications are given below  $^{41-43}$ .



#### **Advantages of Strong Immunity:**

- 1. Protection from toxoids.
- 2. Treatment of untreated disease.
- **3.** Help to maintain body growth.
- **4.** Provide an easy diagnosis of the disease.

#### **Disadvantages of Hyperactivated Immunity:**

- 1. Transplant rejection and tolerance.
- **2.** Immune response may lead to malignancy.
- **3.** Biomarker discovery is a very tough task.

**4.** Autoimmune diseases repertoire.

- **5.** Asthma and allergy also caused by hyperimmune response.
- **6.** Vaccine development and their efficacy is a major challenges.
- 7. Cancer immunotherapy are not successful.
- **8.** Infectious diseases treatment are not very effective <sup>14-18</sup>.

**Some Commonly Used Toxoid Vaccines:** Diphtheria and tetanus, Cholera toxin B subunit in combination with killed Vibrio cholera organisms.

**Killed Vaccines:** The following vaccine is available, which are given below.

- a) Bacterial Vaccines: Typhoid, cholera, plague, and pertussis.
- **b) Viral Vaccines:** Rabies, hepatitis B, influenza, poliomyelitis (Salk vaccine).

The pathogen is inactivated by heat or chemicals; hence, it can no longer replicate in the host. During the inactivation process, it is critically important to maintain the structures of epitopes on surface antigen <sup>44</sup>.

Live Attenuated Vaccines: Some live attenuated vaccines are also available, which are given below.

**Bacterial:** BCG (Bacilli, Chalmette, Guerin), a live attenuated *Mycobacterium* bovis for tuberculosis Ty21a-live oral attenuated mutant typhoid bacilli.

Viral: Live vaccinia virus for smallpox, rubella, measles, mumps, yellow fever, polio (Sabin vaccine). Live attenuated vaccines have an advantage over killed preparation of vaccines because attenuated vaccines mimic the natural behavior of the organisms without causing disease. The immunity developed against the attenuated vaccines is superior because actively multiplying organisms provide sufficient antigen supply.

**Recombinant Vaccines:** Recombinant DNA technology is also being used to produce attenuated viruses such as influenza, hepatitis, Herpes, *etc.* Here viral genome is trimmed to remove the virulence coding segment of the gene, and only replication and protein coat coding gene is allowed

to remain. In addition, many viral genome mutations are introduced to prevent it from reverting to a virulent state by reverse mutations. An ingenious approach is using a viral genome to carry the genes of another virus that cannot be grown successfully or is deadly. Large DNA viruses such as vaccinia can act as carriers for one or many foreign genes in its chromosome (DNA) while retaining infectivity for animal and cultured cells <sup>45</sup>.

E-ISSN: 0975-8232; P-ISSN: 2320-5148

CONCLUSION: Immunity is a promising part of protecting the human body from the environment, hazardous material, and infectious or viral bacteria. The future of immunity with artificial immunity has greater physical and chemical stability and is potentially scalable for commercial viability. The delivery system is also very effective as a treatment and protection against viruses, bacteria, fungi, and environmental factors like dust and foreign body particles. Various types of protection and treatment can be possible using an immunity-based vaccine, like targeting, ophthalmic, topical, parenteral, oral, etc. More research is carried out in this field to know the potential of this immunity as beneficial effects on the human body.

**ACKNOWLEDGMENTS:** The authors thank the Institute of Pharmacy, Bundelkhand University Jhansi Uttar Pradesh. To provide the facilities for compiling this review article.

**CONFLICTS OF INTEREST:** The authors have no conflict of interest

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#### How to cite this article:

Saddam, Suman and Alok S: An overview of immunity and immune system related effects on human health. Int J Pharm Sci & Res 2023; 14(8): 3742-52. doi: 10.13040/JJPSR.0975-8232.14(8).3742-52.

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