Age and the Immune System

Canna Jagdish Ghia[1], Madhura Naik[2], Jignesh Ved[3], Gautam Rambhad[4]

Introduction

Vaccination, which started with Edward Jenner's smallpox vaccine more than 200 years ago, has been an important advance in improving public health and decreasing morbidity and mortality from infectious disease. Its success, however, has only been possible because of the dynamic nature of the immune system. Factors such as young or older age, and the presence of concomitant medical conditions, can profoundly impact both the ability of a person's immune system to respond and the effectiveness of certain vaccines.

Alteration of an immune mechanism can expose the body to a much greater risk of infection for which the other layers of immunity may not be able to fully compensate. For example, an alteration that leads to slower clearance of bacterial invaders can allow these organisms to proliferate, gain a foothold in lungs, and cause pneumonia.

Generally, the functioning of the immune system can be altered by age related variations, immunodeficiency, hypersensitivity and autoimmunity. Every individual goes through a period in life in which the immune system is not fully operational[1-5].

Infants and Young Children

The immature immune systems of young children do not produce a full battery of antibodies at first. One consequence is that children under 2 years of age do not respond to most polysaccharide antigens. This makes the young children vulnerable to infection with bacteria such as *S pneumoniae, H. influenzae,* and meningococcus, which are coated with polysaccharides. This limitation also means that polysaccharide vaccines do not induce effective immunity in infants.

Table 1: Changes in Natural Immunity Associated with Older Age[1-5]

Element	Changes
Dendritic cells	Uptake and presentation of antigen is impaired
Macrophages	A reduced phagocytic capacity means that the rate of antigen clearance is decreased
Natural killer cells	Pathogen killing ability is decreased
Neutrophils	Reduced phagocytic capacity and reduced ability to attract other immune cells to the site of infection

Older Children and Adults

After the age of 2 years, the immune system continues to mature. For example, adult levels of some immunoglobulins are not achieved until 12 years of age. The thymus reaches adult size by about 6 years of age, increases in size during the prepubertal years, and then undergoes involution at the time of puberty. Regression of the thymus steadily continues into middle age, and it is this age-related change that is considered responsible for the decrease in T-lymphocyte-mediated immunity associated with aging.

Immunosenescence[6]

Changes occur in immune system as one ages that result from a loss of some immunological activities and a simultaneous increase in others. Immunosenescence leads to inappropriate, inefficient, and sometimes detrimental immune responses. Age-related changes in the natural immune system are shown in Table 1.

Table 2: Changes in Acquired Immune Response Associated with Older Age[1-5]

Element	Changes
Cellular immunity	Activation and proliferation of T- and B-lymphocytes are decreased Number of naïve T-lymphocytes is decreased, and number of memory T-lymphocytes is increased T-helper and T-cytotoxic activities are both decreased, especially to novel pathogens
Humoral immunity	Number of antigen-responsive B-lymphocytes is decreased Production of antibodies to specific antigen is decreased Production of high-affinity antibodies is decreased

Some of the age-related changes in the acquired immune response are shown in Table 2.

Taken together, the changes in T-lymphocyte activity mean that the protective immune response decreases as one ages, and changes in B-lymphocyte activity mean that the humoral immune response is generally impaired both qualitatively and quantitatively. With age, B-lymphocytes produce antibodies that are less protective because they fail to opsonize effectively i.e. they typically bind to antigens less well. It has been shown that despite having a similar concentration of antibodies to that of individuals less than 45 years of age, the effectiveness of those antibodies is significantly reduced in individuals over the age of 65 years ($p<0.05$).[1-5]

Immunocompetent Adults

Increasing age is associated with changes in the immune system which diminish the immune response. This age-related effect

[1]Medical Advsior, Pfizer Ltd.; [2]Senior Resident, TNMC and BYL Nair Ch Hospital, Mumbai; [3]Senior Medical Advisor, [4]India Vaccines Medical Lead, Pfizer Ltd.

means that apparently healthy immunocompetent individuals will, over the years, become less immunocompetent.[1-5] The ability to fight infection and respond optimally to immunization therefore diminishes as one ages. This is one reason for the high incidence and high mortality of infections such as pneumonia and influenza among older people. For instance, the incidence of pneumonia among older persons is double that seen in younger individuals.

The presence of chronic conditions may also compromise immune function, increasing the risk for infection. For example, individuals who smoke cigarettes and those with underlying chronic disease involving the heart, lung, liver, or kidneys, as well as those with diabetes mellitus or alcoholism are at increased risk for developing infections such as pneumococcal disease.

The Immunocompromised and Immunodeficient States[1-5]

If any of the immune elements are defective, the body might not be able to mount an effective response against invading pathogens. For example, individuals with haematological malignancies, such as the leukaemias or lymphomas, and those receiving immunosuppressive therapy (anti-cancer treatment, systemic corticosteroids, or drugs to prevent organ rejection following transplant), are all at increased risk of infection.

Being immunocompromised is not the same as having an immunodeficiency. An immunodeficiency occurs when there is a defect in 1 or more elements of the immune system. In clinical practice, the defects manifest as 2 common themes: defects in B-lymphocytes/antibody, complement, or phagocytes increase the risk of recurrent infections with encapsulated bacteria (eg, *Streptococcus pneumoniae, Haemophilus influenzae*) and defects in T-lymphocytes increase the risk of opportunistic infections and infections with intracellular bacteria, such as *Salmonella* and *Mycobacterium tuberculosis.*

Individuals, who are immunodeficient, whether it is a primary or secondary immunodeficiency, are especially susceptible to infections and should therefore receive vaccinations, as appropriate. However, these same individuals may be more susceptible to the adverse effects of some vaccines and may respond poorly to other vaccines. In general, vaccines that contain live organisms are not recommended for immunodeficient patients. Vaccines that contain killed and attenuated (live, but weakened) organisms are safe, although the efficacy of these vaccines may be less than in healthy individuals.

Disclosure

The information contained in the manuscript reflects independent, evidence-based opinions and views of the contributing expert authors; it does not suggest or endorse the opinions or views of Pfizer Ltd., directly or indirectly. Some of the information contained herein, may be off-label in nature. Pfizer Ltd. does not promote / suggest / recommend any such off-label use of its product(s).

References

1. Abbas AK, Lichtman AH, Pillai S. Appendix 1: glossary. In: Abbas AK, Lichtman AH, Pillai S, eds. *Cellular and Molecular Immunology*. 6th ed. Philadelphia, PA: Saunders Elsevier; 2007:489-518.
2. Abbas AK, Lichtman AH, Pillai S. B cell activation and antibody production. In: Abbas AK, Lichtman AH, Pillai S, eds. *Cellular and Molecular Immunology*. 6th ed. Philadelphia, PA: Saunders Elsevier; 2007:215-241.
3. Abbas AK, Lichtman AH, Pillai S. Cells and tissues of the adaptive immune system. In: Abbas AK, Lichtman AH, Pillai S, eds. *Cellular and Molecular Immunology*. 6th ed. Philadelphia, PA: Saunders Elsevier; 2007:47-71.
4. Abbas AK, Lichtman AH, Pillai S. Congenital and acquired immunodeficiencies. In: Abbas AK, Lichtman AH, Pillai S, eds. *Cellular and Molecular Immunology*. 6th ed. Philadelphia, PA: Saunders Elsevier; 2007:463-488.
5. Abbas AK, Lichtman AH, Pillai S. Properties and overview of immune responses. In: Abbas AK, Lichtman AH, Pillai S, eds. *Cellular and Molecular Immunology*. 6th ed. Philadelphia, PA: Saunders Elsevier; 2007:3-17.
6. Gruver AL, Hudson LL, Sempowski GD. Immunosenescence of ageing. *J Pathol* 2007;211:144–156.