How do age and biological sex influence vaccine responses and public health guidelines?

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Introduction

Vaccines are essential to maintain a functioning, healthy community. Vaccines are biological agents that are usually injected through a small needle into an intramuscular part of your body to promote immunity against viral infections. They mimic viral infections by presenting an aspect of the virus to your immune system that is not infectious. This enables your immune system to create a response that can be leveraged during a real exposure to that virus. One major way the immune system responds to vaccines is by producing antibodies that interact with viral antigens to prevent or combat infection (1). Some of the antibodies produced by vaccines are Immunoglobulin G, which is the most common, and sometimes Immunoglobulin A. In this way, vaccines train your body to protect you from future viral infections. Therefore, vaccines behave as a first line of defense that plays a role in immune regulation.

Variolation is a historic method of vaccination where patients were deliberately infected with mild forms of viral or bacterial pathogens. This started in China and India in the 1500s.

Both countries had discoveries that contributed to the evolution of vaccines. Doctors in China found that smallpox could be weakened by placing it in the sun. Doctors in India found that transferring pus from a pustule of a person infected with a virus, to a healthy person, provided protection from contracting that viral infection. With this information in mind, Edward Jenner, a scientist in England, developed the first official vaccine against smallpox disease in 1796. Jenner had taken material from a cowpox sore, a blister from the infectious disease called cowpox disease, on a milkmaid in England and then injected it into James Phipp's arm, the son of Edward Jenner's gardener (2). A few months after he was inoculated with the cowpox sore, Jenner exposed him to the variola virus several times and he never developed smallpox. This allowed for the first vaccine to be created with cowpox, then later switched to vaccinia virus to provide immunity against smallpox disease. The research about smallpox contributed to the creation of all of the vaccines we have today (3).

Vaccines have since become a topic of public health. Today, mandated vaccine schedules are required for children that participate in the U.S. public school system. The schedule was developed starting with the smallpox vaccine in the early 1950s, and is still evolving to this day. There are 32 mandated vaccines in the vaccination schedule from ages 0-18 (4). Newborns all the way to senior citizens need vaccinations to keep the community from spreading deadly viruses. This is important because if we do this, we can reach herd immunity, meaning a large part of the community will be immune to a disease, allowing our communities to be better protected. Vaccination is relevant to all ages and studies have found that age affects vaccine side effects, severity, and efficacy.

Another factor that affects vaccination is biological sex. Biological sex is the reproductive traits you are born with. This can be female, male, or intersex depending on chromosomes, organs, and other traits. Males and females have different hormones and genetics. Females produce estrogen and men produce testosterone from different organs. The sex chromosomes between males and females are also different. Males have a XY chromosome, while females just have two X chromosomes. Studies have demonstrated that females have greater inflammatory, antiviral, and stronger adaptive immune systems compared to men. This is thought to be because estrogen activates the immune system in the female body (5).

Both age and biological sex have various impacts and effects on the immune system. In this report, these factors will be discussed and compared; specifically, we will cover side effects, severity, and vaccine uptake of biological sex and age. Additionally, we will discuss age and biological sex as essential factors of vaccinations and immuniztions because these apply to everyone in public health society.

Vaccines confer immune protection against viral and bacterial pathogens

Vaccines imitate an infection by allowing your body to create antibodies from the weakened virus. Some immune cells that are responsible for fighting the weakened virus, and diseases in general, are T-lymphocytes, B-lymphocytes, and macrophages. These ensure your body knows how to fight the bacterial infection or virus in the future. After getting a vaccine, you might experience symptoms like a fever, chills, etc. Minor symptoms are normal, as the body is building up immunity. We might experience side effects because our bodies recognize something as being foreign and want to "attack" it. Some vaccines require multiple doses to ensure the immunity remains the same and it does not fade after a while. For example, it is recommended

that we receive two doses for the COVID-19 vaccine and later we need boosters. Additionally, since multiple strains of influenza arise every year, the influenza vaccine is reformulated to combat whichever strain is predicted to be the most present. We also have two different vaccination schedules; one ranges all the way from birth to 18, and the other is 19+. Each schedule has specific immunizations to take in a certain time frame to make sure you are protected against the virus. We get vaccinated so we are protected from many of the diseases and viruses always circulating in the air. Everywhere you go, you are being exposed to new stimuluses and new diseases (6). These vaccines help your immune system combat illness to protect your body.

Biological sex affects vaccine responses, uptake, and attitudes towards vaccination

At Oregon Health and Science University (OHSU), they found that women have stronger immune systems than men. This can be from hormones, genetics, or even the environment (7). Hormones are chemical messengers in the body that help with metabolism, growth, sexual reproduction and function, and mood. Women produce estrogen and men produce testosterone hormones. The hormone estrogen in women has been found to stimulate the immune system to drive stronger immune responses. This connection and system provides stronger immunity towards viruses and bacteria. Differences in vaccine responses against COVID-19 vaccination for women and men have been recorded (8). Early on in the pandemic, scientists reported that men were dying at rates as high as twice that of women (9). This could be a result of differences in immune responses between men and women. Women's stronger immune system may have played a favorable role in protection.

Biological sex also appears to play a role in vaccination outcomes, specifically, severe symptoms and side effects. During the COVID-19 pandemic, several different types of vaccines were available and we found that different vaccines were associated with different rare side effects for females and males. For example, in a recent study by the Centers for Disease Control and Prevention (CDC), they found that the Moderna COVID-19 vaccine is associated with a rare blood-clotting side effect for females. This was prominent in females and less common for males. This is from the higher estrogen levels in the female body. Males did not experience this because their estrogen levels are lower than females. When COVID-19 was first discovered in China, estrogen was being injected into males in order to help their immune systems fight infection (10). Interestingly, the CDC found that males are more likely to develop myocarditis and pericarditis in response to Moderna and Pfizer COVID-19 vaccines. Myocarditis is inflammation of the heart muscle and pericarditis is the swelling and irritation of the thin tissue surrounding the heart. In males, among ages 5-11, 12.6-17.6 cases out of 100,000 were found to have either myocarditis or pericarditis. At this age, women were found to have 5.4-10.8 cases out of 100,000 people. As age increased, the severity and number of cases increased in males and stayed the same in females (11).

Research shows that men have a higher intention to vaccinate than women do. Studies on the COVID-19 vaccination included 58.3% of men to get vaccinated or have intentions on getting vaccinated (12). This may be because men have been shown to be more dominant in the workforce, allowing them to have greater access to vaccines and take more initiative to get vaccinated. Although men are more dominant in the workforce, many women have filled certain positions. For example, in the United States, 86% of nurses are women (13). Interestingly,

COVID-19 vaccination rates were low among nurses (57%) in the United States despite having priority access to vaccines at the onset of the pandemic (14). Nurses who were hesitant to get the COVID-19 vaccine said they are unsure about the long-term effects and had mistrust about the vaccine trials, development, and approval. Nursing is a female dominant profession and thus, led to the low vaccination rates. This comes to show that biological sex and misinformation can impact if you get a vaccine or not (15).

Vaccine responses and requirements evolve with aging

When getting the vaccine administered, infants and young children tend to cry, throw their hands in the air, and sometimes try to move away. Before the age of one, it is important that we receive 16-18 vaccines; this does not include multiple doses. Some side effects infants have from receiving vaccines are pain, headaches, and fevers. In adults, common side effects tend to be chills, pain, headaches, muscle or joint aches, and fatigue. Although it is challenging to administer vaccinations to children, it is important to have immunity against those 18 viruses or bacteria early in life (16). Researchers found that getting certain vaccines, like the Hepatitis B vaccine, have better long term effects when administered earlier. In every state, public schools have different vaccine mandates. When children go to school, they are exposed to more viruses and diseases than they ever have been before. Children are also prone to touching everything they see and putting their hands in their mouths. This transmits the virus or bacteria from their hand into their mouth, and their immune system has to fight against it. The most prominent vaccines children across the country need to get are those against polio, measles, mumps, tetanus, and rubella diseases (17).

As you age, your immune system weakens. This is from the reduced production of B and T-cells in our bone marrow and diminished function of fully matured lymphocytes. This delays the response to foreign viruses in our body, slowing down the antibodies and antigens trying to fight off the virus, and we get sick. This process of reduced B and T-cells in our bone marrow starts around age 60 and continues to degenerate as we age (18).

During the COVID-19 pandemic, older people had more of a struggle with handling and overcoming the virus. They were more likely to catch the virus when exposed to it because of their weakened immune systems. When the vaccines were released, elderly were able to have it administered first, as they were the most susceptible. According to the CommonWealth Fund, about 97% of the elderly and older adults were vaccinated against COVID-19 in the United Kingdom in 2021. In the US, only 19% of adults age 65 and older had gotten the COVID-19 vaccine in 2021 (19). This study also showed that the COVID-19 virus killed about 800,000 people from 2020-2022 in the United States (20). During the 2020-2021 flu season, 20,342 people in the United States died from the influenza virus. About 11,945 of those people were ages 65 and up. Elderly people get the same flu shot as the rest of the population, but they get a higher dose. We can protect the elderly population from a lot of viruses by encouraging vaccination in our community, cleaning and disinfecting our belongings frequently, and encouraging those who are sick to stay home (21).

These statistics show how important it is for both older people and younger children to get vaccinated for as many pathogens as possible. Infants who are nursed or breast fed have immune systems called passive immunity because the immunity from their mother is passed on to the child. This only protects the child for a few weeks and in these weeks, the child is still not

fully protected against the viruses (22). Infants who are repeatedly getting introduced to new environments and stimuli, as well as older adults with weaker immune systems are more likely to get sick. For the majority of your lifetime, you are getting vaccinated at least annually. According to the CDC, the vaccination schedule was made to help show us when and how many vaccinations we get (23).

Conclusions

In this report, we demonstrated that widespread vaccination administration prevents the spread of diseases. Biological sex and age are important factors influencing side effects, vaccine uptake attitudes, symptoms, and more. Biological sex can impact our ability to respond to a vaccine and plays a part in if we are able or want to get a vaccine. Additionally, newborns and the elderly community are especially vulnerable to disease, so it is important to understand how your age might affect how well you react to vaccinations. These two factors are important to consider before getting a vaccine. Vaccination is a building block of public health. By deciding to get vaccinated, you are not only protecting yourself, but you are protecting those around you by building an extra layer of immunity that helps to prevent the spread of infection and severe disease. They allow your body to produce an immune response, minimizing disease severity. Vaccination is the best practice to protect our bodies from diseases, and important aspects like age and biological sex are certainly factors that can contribute to outcomes.

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