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Independent Study Project

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Department  Nursing
Degree  Master of Science

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Abstract

Vaccination rates in the immunocompromised population remain less than favorable. In patients with rheumatoid arthritis, some studies suggest vaccination rates as low as the following: 45% influenza, 28% pneumococcal, and 4% over age 60 against shingles. This paper reviews current literature and studies of immunosuppressed patients regarding vaccinations. Safety of administration, how and when, along with the efficacy of providing annual influenza vaccination, pneumococcal vaccination, and shingles vaccinations to immunosuppressed patients will be explored. Keeping these immunocompromised patients up to date on immunizations can decrease preventable illnesses in already compromised patients. Historically many of these vaccines were avoided in patients receiving immunosuppressive therapies. As research has developed, studies show it is better to give vaccinations to reduce preventable illnesses, even if the patient’s humoral response is lower. Vaccination rates are influenced by patient beliefs and knowledge of the provider and patient. A team-based approach when caring for compromised patients, by all members of the healthcare team has been found to improve vaccination rates and reduce gaps. Through increased knowledge and awareness, providers are able to keep patients up to date on vaccinations in this immune compromised population and improve patients’ risk of preventable diseases.

Keywords: immunocompromised, vaccinations
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Background

Mr. Foster has history of rheumatoid arthritis and is currently being treated with immunosuppressive drug therapy, consisting of Humira, a TNF blocking agent and methotrexate, an antimetabolite antineoplastic agent for the past year (Dunphy, Winland-Brown, Porter & Thomas, 2015). He denied any complications with these medications and rarely experiences any rheumatic flares.

Rheumatoid arthritis poses many complications for individuals as a chronic, progressive, systemic inflammatory disease, primarily effecting synovial joints but can also affect many organ systems (Dunphy et al., 2015). Other organ systems which can be affected by immunopathology of rheumatoid arthritis are cardiac, hepatic, splenic, pulmonary and ocular systems. With rheumatoid arthritis, there is a notably different distribution of immune cells during inflammatory responses. The peak occurrence is most often seen between ages 40-60 years, with an earlier onset of 20-40 years of age. In the United States, it is the 2\textsuperscript{nd} most common connective tissue disease and most destructive to a person’s joints (Dunphy et al., 2015).

Immunosuppressive and anti-inflammatory medications can pose many adverse effects for patients; therefore, these medications are not usually started until later in the rheumatoid process. Additionally, medication therapies are often based on symptom control during the progressive states of rheumatoid arthritis. One adverse effect is an increased risk for infections due to immunosuppressive agents used in therapy. Due to increased risk of infection, health promotion is especially important with immunocompromised individuals.

Many of the infectious diseases immunosuppressed patients are at higher risk of contracting are vaccine preventable. Unfortunately, there is a gap in vaccinating
immunocompromised patients for reasons of confusion about safety of the vaccine in individuals with compromised immune systems, communication gaps between providers, and patient attitudes on vaccination importance. It is not uncommon for an immunocompromised patient to be cared for by multiple health care providers, which can often lead to providers assuming another department will ensure health maintenance items are up to date in these individuals. Electronic medical records have helped to ensure each provider has access to the patient’s medical record and care history.

Case Report

Mr. Foster is a pleasant 60-year-old gentleman who came to clinic with complaints of fever, chills, headache, cough, joint pain and fatigue, over the past five days. His history was significant for rheumatoid arthritis and hypertension. He used immunosuppressive medications to help control his rheumatoid arthritis. He used Humira 40mg injection every two weeks and Methotrexate 10mg injections weekly. His other medications included Lisinopril 10mg daily and a multivitamin. He had no known drug allergies.

He had been taking ibuprofen 600mg, intermittently, for his fevers of 100°-103°. His cough was dry and continuous, interrupting his sleep. He had clear nasal drainage and he felt congested. His throat was sore and irritated; he had been using throat lozenges but had little to no relief. He was aching, feeling stiff and sore throughout his body. Vital signs were: 142/92, 90, 30, 102.4°. On physical exam, he appeared in no acute distress but it was visible that he was feeling fatigued and not well. He had non-budging, visible tympanic membranes in his ears bilaterally. Hearing was appropriate during exam. His throat was reddened with clear post nasal drainage. Nasal passages were dry and pink. He had S1, S2 heart sounds, with no murmur or rub
present. His lungs were clear to auscultation. Abdomen was soft and non-tender with active bowel sounds present.

Due to Mr. Foster’s history of rheumatoid arthritis, which alters his immune system, along with his immunosuppressive medications Humira and Methotrexate, he was at an increased risk of infections. Infections in an immunocompromised individual can be serious, even life threatening. Based on Mr. Foster’s symptoms of body aches, elevated fever and cough, treatment with Tamiflu should be started. Treating him immediately was important due to his immunocompromised state and risk for secondary infection. A work-up ruling out acute bacterial infection, including laboratory work consisting of CBC, AST, and ALT. Obtainment of a chest x-ray, even though his lungs were clear on auscultation, would rule out any consolidations or pneumonia. Instructing Mr. Foster, about the importance of rest and hydration during his illness was important for his recovery. Discussion of his increased infection risk due to his immunosuppressive medications, while also encourage him to take protective measures such as hand hygiene during high cold and flu seasons, as he was still employed as a retail worker. It would also be important to discuss his immunization history with Mr. Foster, ensuring he was up to date on his immunizations, such as, yearly influenza, pneumococcal and shingles. These vaccinations can help prevent many disease states Mr. Foster is at added risk for, due to his immunocompromised state. He will be followed up with the next day regarding results of his tests, as well as checking on his health status.

**Literature Review**

As previously stated, immunosuppressive mediations, such as treatment for rheumatoid arthritis, put patients at an increased risk of infections. Many of these infectious diseases are presumably preventable with vaccinations. “The safety and efficacy of immunizations in patients
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with rheumatoid arthritis and other autoimmune diseases can be a clinical controversy” (Bushardt & Winter, 2013, p.12). It is important to become familiar with each patient and his or her healthcare beliefs and behaviors. Many of these individuals have reduced immune response, further provoking the question rather to administer vaccinations, but also examining their attitudes and knowledge of vaccinations.

In this study, Mr. Foster was at an increased risk of infectious disease being on immunosuppressive medications for his rheumatoid arthritis. He still worked as a retail salesman, so he was around the general public and exposed to many people and organisms. Many infectious diseases can be avoided through vaccination, which is why it is important to ensure immunocompromised patients receive vaccinations.

Vaccination rates in immunocompromised patients are low. It is important to examine attitudes towards vaccinations among immunocompromised patients. Sandler et al. (2016) completed a study which used a Behavioral Risk Factor Surveillance System survey and addressed the following areas: 1.) self-reported receipt of vaccinations 2.) attitudes about these vaccinations, including reasons for non-vaccination when applicable 3.) provider recommendations about vaccinations. In this study, they used open ended questions to promote participant responses. Non-vaccinated responses were placed into categories of: a.) no recommendation for the vaccine b.) no thought of needing vaccination c.) against vaccination (Sandler et al., 2016). This (2016) study found that 75% of respondents noted their physician had told them they were at an increased risk for infection, while only 64% recalled discussion of importance of vaccinations by their providers (Sandler et al.). Further results of the study showed: 96.1% reported their provider recommended the influenza vaccination, 60.8% were told to get the pneumococcal vaccine and only 16.7% reported shingle vaccination being
recommended (Sandler et al., 2016). Lack of physician recommendation, per the patient, appears to be the leading cause of non-vaccination. Looking at these results, as healthcare providers we have room to improve vaccination numbers in immunocompromised patients. Due to many questions of safety and efficacy regarding administration of vaccinations in immunocompromised patients, the European League Against Rheumatism (EULAR), created and published guidelines in 2011, about vaccination in patients with rheumatoid arthritis, after completing an expert panel literature review. (Muller-Ladner & Muller-Ladner, 2013).

In 2015, The American College of Rheumatology updated their guidelines regarding pharmacologic treatment for patients with rheumatoid arthritis. These guidelines consisted of six major topics, number four being related to use of vaccines along with DMARDs or biologics treatments in patients with rheumatoid arthritis (Singh et al., 2016). Both of these guidelines, were created for a reference for health care providers to refer to due to changing options and national standards in treatment specifications in these areas. The 2015 guidelines recommend killed vaccines to be safe for immunosuppressive patients. Looking into the live attenuated vaccines, it was recommended as a guideline to administer these vaccinations to a patient with rheumatoid arthritis over the age of 50 years, as benefits outweigh the risks, although vaccination prior to initiating immunosuppressive therapy is still preference (Singh et al., 2016).

Outbreaks of influenza, pneumonia and shingles can pose a threat to anyone, but especially immunocompromised patients. Patients with rheumatic diseases are prone to different infections, this risk of infection is about 2-fold higher than the normal population (Muller-Ladner & Muller-Ladner, 2013). The Advisory Committee on Immunization Practices (ACIP) recommends immunocompromised adults receive an annual influenza vaccination, the pneumococcal vaccination 13-strain conjugated vaccine followed by the 23-strain polysaccharide
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vaccine, and herpes zoster vaccination, which is more complex and will be discussed further (Sandler et al., 2016). Even with these recommendations, vaccination rates remain low among immunocompromised patient population. Friedman and Winthrop (2016) found that in the United States, only 28.5% of patients with rheumatoid arthritis were vaccinated for pneumococcal pneumonia and 48.5% had received their yearly influenza vaccination. Their study also found only 4% of patient with rheumatoid disease over the age of 60, had been vaccinated against herpes zoster (Friedman & Winthrop, 2016).

Patient education is important for immunocompromised patients regarding increased risk of infections, prevention of secondary infections, risks associated with secondary infections along with health maintenance preventative measures. A study by Sandler et al. (2016), examined patient beliefs on infections while taking immunosuppressive therapies, only 41% of patients worried at all about getting an infection due to immunocompromised states. According to Winthrop et al. (2017), patients with rheumatoid arthritis are known to respond less strongly to certain vaccines. Reduced response is likely due to disease activity along with immunosuppressive therapy treatments. Three vaccinations: influenza, pneumococcal, and shingles were examined regarding administration and efficacy of each vaccination in immunocompromised patients.

**Influenza**

The American College of Rheumatology (ACR) recommends the intramuscular influenza vaccine annually for all patients with rheumatoid arthritis regardless of immunosuppressive therapies, with the exception of rituximab (Friedman & Winthrop, 2016). Rituximab does significantly reduce humoral response; thus, influenza vaccine should be given prior to starting therapy or as long after therapy administration in conjunction with influenza season (Friedman &
Winthrop, 2016). In 2014, Hue, Barnetche, Combe, and Morel, completed a systematic literature review along with a meta-analysis to achieve a better understanding of the effects of different rheumatoid arthritis medications on the immune response to influenza and pneumococcal vaccinations. Results of this study showed the immune response being affected, but not significantly, with anti-TNF α therapy. In this same study, methotrexate was shown to have a negative impact on the humoral response (2014).

While rituximab and methotrexate have been found to reduce humoral response, all other immunosuppressive therapies have been found to have little effect on the influenza vaccination. According to Ward, Flowers, Gansler, Omer, and Bednarczyk (2017), influenza vaccination effectiveness may be lower in immunocompromised patients, thus it is strongly encouraged for family members, as well as all health care providers to be vaccinated. Although, immunocompromised patients may not have as high of a response to vaccinations, it is safe to administer and may potentially reduce their risks of severe infections along with complications (Ward et al., 2017). Thus, the influenza vaccination is recommended for patients, families and healthcare workers, due to the protective effects it could hold for those immunocompromised.

Immunocompromised patients should be administered the inactivated version of the vaccine, rather than the live attenuated influenza vaccine. According to Muller-Ladner and Muller-Ladner (2013), the inactivated influenza vaccination has reduced hospital admissions as well as number of deaths. They further found no safety concerns with the influenza vaccine and demonstrated sufficient immunogenicity along with protection against both influenza and secondary complications. Immunocompromised patients are at a higher risk for adverse reactions and infections given a live vaccination. It is important to note that immunocompromised patients should avoid contact with persons who have received a live vaccine for a period of 7 days post
vaccination, due to compromised immune system states and increased risk of illness or infection (Ward et al., 2017).

Recommendations suggest treatment with antivirals for adults with rheumatoid arthritis on immunosuppressive therapy following any influenza exposure, regardless of vaccination status (Bushardt and Winter, 2013). Mr. Foster did not remember any specific exposure to any illness, although, he worked in retail with the public and was exposed to many things daily. He had symptoms of influenza, so antiviral treatment was started, in hopes to reduce severity of his symptoms.

**Pneumonia**

Immunocompromised patients are at increased risk for developing invasive pneumococcal disease. Overall incidence rates of invasive pneumococcal disease remain high for those with at-risk conditions. Ward et al. (2017) provided that in 2009, incidence rate of invasive pneumococcal disease per 100,000 persons was 8.8 in healthy adults and 34.9 in those who high-risk, including people who were immunocompromised. That was almost a 4-fold increase in occurrence for those at high-risk.

Pneumococcal vaccination rates among immunosuppressed patients are low, 19%-54% in those with rheumatoid arthritis (Desai et al., 2013). Pneumococcal vaccination is important for all adults over age 65, but especially important for those who are immunocompromised; although, many studies suggest the majority of patients are not vaccinated. Data from the National Health Interview Survey in 2014, reported pneumococcal vaccine coverage, meaning both PSV-13 and PSV-23, among adults aged 19-64 with high risk conditions was 21.3% overall (Ward et al., 2017).
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These were low rates, with all the threat the illness can pose on an immunocompromised immune system. One quality improvement project by Desai et al. (2013) focused on increasing the number of patients vaccinated with pneumococcal in a rheumatology practice setting. It was found that using a simple point-of-care reminder form significantly increased the rate to 67.6-80% of patients receiving immunosuppressive therapies to be up to date on their vaccinations. This point-of-care reminder system was a simple piece of paper which was applied to each patient as they checked in for an appointment. The nurse verified the patient’s vaccination status with the patient. If the patient had not been vaccinated, they discussed the vaccination together and vaccinated the individual that day if they agreed.

Hue et al. (2014) completed a systematic review along with a meta-analysis, examining immunosuppressive therapies and effects on pneumococcal vaccine. This 2014 study concluded that methotrexate may reduce the immune response of the pneumococcal vaccination, much like the effects on influenza vaccination. In addition, TNF-α blockers showed no effect on the humoral response of pneumococcal vaccine, as well as the influenza vaccine (Hue et al., 2014). Another study by Friedman and Winthrop (2016), also recommended that TNF inhibitors, such as Humira, have little or no effect on the pneumococcal vaccine PCV-23. Bushardt and Winter (2013) suggested that, if a patient is vaccinated while taking high-dose corticosteroids, it would be advisable for health providers to check antibody titers for immune response to vaccination and revaccinate if needed. Another option provided is simply waiting until the patient finishes treatment and reaches immune competency (Bushardt & Winter, 2013).

The Center for Disease Control (CDC) recommends pneumococcal PCV-13 followed by PCV-23 at least 8 weeks later. The American College of Rheumatology guidelines suggest pneumococcal vaccines should be given prior to starting therapy for rheumatoid arthritis, if
possible; yet it is better to give the vaccine during therapy rather than non-vaccination (Friedman & Winthrop, 2016). Therefore, looking at Mr. Foster’s medications of Humira and methotrexate, it is advised to ensure he receives a pneumococcal vaccination due to his immunocompromised state. Both the pneumococcal and influenza vaccines are inactivated, thus should pose no risk of viral reactivation after vaccination in immunocompromised patients (Hue et al., 2014). Contraindications for the pneumococcal vaccination are similar for all patients, primarily history of severe reaction after a previous dose or component of vaccine.

**Shingles**

Shingles is common in older adult patients and those with immunocompromised systems. The CDC estimated that the lifetime incidence for developing herpes zoster is almost 1 in 3 people in the United States (Ward et al., 2017). This data included all populations, not only immunocompromised patients. Patients with immunosuppression have an increased risk of herpes zoster. According to Cheetham et al. (2015) “patients with diseases such as rheumatoid arthritis, are at an increased risk of herpes zoster” (p.866), while immunosuppressive therapy increases their risk even further.

Zostavax is a live vaccine, which has been shown to reduce the incidence of herpes zoster and post herpetic neuralgia, yet it is not recommended for all individuals, especially those with compromised immune systems or those on high-dose immunosuppressive therapy (Müller-Ladner & Müller-Ladner, 2013). Live shingles vaccines have historically been contraindicated with immunosuppressive therapy. The vaccine be used safely with methotrexate (<0.4mg/kg/week) and low-to-moderate doses of glucocorticoids (<20mg/day prednisone), according to the CDC (Friedman and Winthrop, 2016). The CDC and the Infectious Disease Society of America, both recommend avoiding vaccination if using biologics or high-dose
corticosteroids and waiting at least one month following discontinuation of these before vaccinating against shingles (Friedman & Winthrop, 2016).

A study completed during 2006-2009, by Cheetham et al. (2015) examined Zostavax, a live vaccination administered to patients with current or remote history of immunosuppressive therapy. Immunosuppressed individuals have the risk of the vaccine virus disseminating to other organs, such as the lungs, liver, or even central nervous system (Cheetham et al., 2015). Their results showed during a 42-day risk window following vaccination, no cases of disseminated vaccine virus were identified, in current or remote users of immunosuppressive therapy. Further results showed an increased risk of herpes zoster during current immunosuppression versus remote therapy, which validated incidence of adverse events following vaccination while immunocompromised (Cheetham et al., 2015). Due to increased risk of dissemination of the vaccine virus, recommendations include vaccinating before initiating immunosuppressive therapy.

Although the live zoster vaccine is currently contraindicated in patients receiving high dose steroids (>20mg/day prednisone) or methotrexate (>25mg/week), it is recommended they be vaccinated prior to starting therapy or when therapy is stopped for at least one month. Patients receiving lower dose therapies, below these thresholds are thought to be safe and effective for receiving the vaccine, although Winthrop et al. (2017) suggested this has been based on expert opinion with little data available. In 2016, United States Medicare data was used to identify over 600 patients who had inadvertently vaccinated while taking biologic therapy for rheumatoid arthritis and, over the long-term the vaccinated patients showed about 40% reduction in risk of shingles (Friedman & Winthrop, 2016).
In 2017, Winthrop et al. conducted a study examining the safety of live zoster vaccine. The preformed a placebo-controlled trial with patients 50 years and older who had active rheumatoid arthritis and were receiving methotrexate. Participants were then randomized to receive tofacitinib 5mg twice daily or a placebo, both which started 2-3 weeks following vaccination. During the study, no negative side effects were observed, and after starting tofacitinib 2-3 weeks post vaccination, great immune responses were developed to this vaccine (Winthrop et al., 2017). Winthrop et al. (2017) suggested further research was necessary to understand long term effectiveness of live zoster vaccine in this high-risk population.

Fortunately, through new medical advances, a proven, more effective shingles vaccination was developed. Shingrix, an inactivated vaccine for shingles, was licensed in 2017. The Advisory Committee for Immunization Practices (ACIP) recommended Shingrix for prevention and reduction of complications of herpes zoster for immunocompetent adults aged 50 and older, regardless of prior vaccination with live vaccine, Zostavax (Resnick, 2018). Most insurance plans will cover Shingrix for patients starting at age 50 and older; while Zostavax is approved for those 60 years of age and older. In clinical trials the Shingrix vaccine was shown to reduce the risk of shingles by 97% in healthy people (Jacobsen & Brickley, 2018). Currently, there is little known information about potential benefit in people with compromised immune systems, but Mayo Clinic recommends Shingrix for the immunocompromised population (Jacobsen & Brickley, 2018). The only absolute contraindication for Shingrix vaccine is previous history of allergic reaction to any component of the vaccine.

Since, Mr. Foster had not yet received his Zostavax, it is important he get vaccinated with the new Shingrix vaccine, helping reduce potential threat of herpes zoster virus and post-herpetic neuralgic pain due to his increased risk related to immunosuppressive therapies.
Conclusions

After examining literature reviews for safety and efficacy of these vaccinations, it is evident that further patient education and administration efficacy protocols are needed to protect the immunosuppressive population. Illnesses such as influenza, pneumococcal, and shingles are prevalent among all populations, especially as we age. It is particularly important for immunosuppressed patients to be protected from these vaccine-preventable illnesses. These patients often have a primary care provider, along with multiple specialist all providing health care. Too often, each healthcare provider focuses on the patient’s acute issues during visits and assumes another provider has educated the patient on preventative health maintenance. Lack of current, easily access immunization records, as well as insufficient knowledge and awareness of vaccines have been barriers to vaccination, as electronic medical records evolve, accessing vaccination records is becoming easier.

Literature review showed there are recommendations and guidelines available for the immunocompromised population, yet it is still important to preform individualized risk and benefit analysis for each patient and vaccination. Studies have shown that low doses of immunosuppressive medications are safe with most vaccinations. As new vaccines evolve, most vaccines are created as inactivated vaccine forms making them even safer for the immunocompromised population. Ideally, the provider would be able to administer as many vaccinations needed before beginning the immunosuppressive therapy. We know patients on immunosuppressive therapies are at an increased risk of infection due to alterations in their immune system. Development of vaccines has remarkably saved countless lives during the 20th century and vaccinations should be an essential part of immunocompromised patient care.
Low vaccination rates among immunocompromised populations are related to unnecessary suffering, even death of individuals, as well as increased costs for health care systems. Patient education on risks for infections and vaccination importance is essential part of healthcare. Increased communication between healthcare teams caring for immunocompromised patients, ensuring the whole person is being cared for, providing optimal care and support through all stages of life. High immunization rate is critically important to protect immunosuppressed patients from vaccine-preventable diseases.

**Learning Points**

- There are many gaps in vaccinating immunosuppressed patients today – with much room for improvement in vaccination rates for this population
- Vaccines such as influenza, pneumococcal and shingles are an important part of caring for immunocompromised patients, reducing risks and side effects preventable illnesses
- Team care approach is important for patients, ensuring all parts of health are met
- It is crucial for health care providers to stay up to date on latest news and education on vaccinations, providing accurate patient education to patients and families
- Be in tune to patient attitudes, beliefs and barriers of vaccinations
References


