Are immunizations safe and effective for patients being treated with immunosuppressive agents?

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ABSTRACT

Most immunizations have not been well studied in patients with drug-induced immune suppression. This article reviews strategies for administering vaccines to patients with rheumatoid arthritis who are taking disease-modifying antirheumatic drugs.

Keywords: rheumatoid arthritis, immunization, vaccine, disease-modifying antirheumatic drugs, immune suppression, corticosteroids

According to the CDC, in 2007, about 1.5 million adults in the United States had rheumatoid arthritis (RA).[1] In 2008, the American College of Rheumatology published recommendations for the use of disease-modifying antirheumatic drugs (DMARDs) and biologic agents in patients with RA; this report was updated in 2012.[2] These recommendations demonstrate the increasingly important roles these immunosuppressant agents have for reducing disease progression and improving quality of life for patients with RA. Many of these same agents are also regularly integrated into management plans for patients with other chronic autoimmune diseases, such as lupus erythematosus, inflammatory bowel disease, and psoriatic arthritis.

The safety and efficacy of immunizations in patients with RA and other autoimmune diseases can be a clinical controversy. Patients may have a reduced immunologic response, bringing into question the utility of administering vaccines. Also, researchers do not know if immunizations precipitate clinical worsening in patients with RA or put them at higher risk for vaccine-related adverse reactions. To complicate matters, patients with RA already are at increased risk for infection.[3,4] In fact, patients with RA have an increased age-adjusted all-cause mortality, and frequent opportunistic and common infections contribute to that increased mortality.[5]

The extent of immune suppression that occurs with DMARDs has not been established, but biologic agents carry black box warnings about increased infection risk. In contrast, corticosteroids, when used longer than 2 weeks and at doses greater than or equal to 20 mg/day of prednisone or the equivalent, are known to raise infection risk largely because of impaired T-cell production.[6,7] Administering *live* vaccines to patients who have received long-term, high-dose corticosteroid therapy is not recommended because of the risk of infection coupled with the possibility of an inadequate immune response from the vaccine. Acute risk of a tetanus infection or exposing a neonate to pertussis could be compelling reasons to vaccinate a corticosteroid-exposed individual. If a patient is vaccinated while on high-dose corticosteroid therapy, providers should consider checking antibody titers and revaccinating if necessary. Another option is simply revaccinating after the patient achieves immune competency, although achieving competency can take 6 months to a year depending on the extent of therapy. **Table 1** outlines administration recommendations for selected vaccines.

Most immunizations have not been well studied in immunocompromised patients, particularly those with drug-induced immune suppression. Despite limited evidence, recommendations are available for these populations; however, they require PAs to perform individualized risk and benefit analyses for each immunization. The most effective strategy is to vaccinate patients with RA before they begin taking immunosuppressive agents. In a recent article, Thome offers three reasons to vaccinate first:

- Patients with impaired immune function experience decreased responses to vaccines, thus vaccinating first can improve the odds for a positive immunologic response.

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TABLE 1. Recommendations for administering select vaccines in adults with RA receiving immunosuppressive therapy or DMARDs.[10-12]

Herpes zoster vaccination

- Contraindicated in patients on immunosuppressive therapy.
- Several trials suggest benefits may exist and adverse reactions to immunization are low; thus, future empiric research is needed to better understand risk and benefits for this population.
- Antiviral agents against herpes zoster may interfere with vaccine efficacy. Vaccine-indicated patients taking these antivirals should discontinue these drugs for at least 24 hours before administration of the vaccine and should not restart them for at least 14 days after vaccination.
- The National Advisory Committee on Immunization states that patients taking antivirals at the time of vaccination may benefit from a second dose of vaccine at least 42 days after the first dose and after antiviral therapy discontinuation.

Influenza vaccine

- Annual immunization is recommended.
- Immunize before starting a DMARD, if feasible.
- An inactivated vaccine is preferred for patients on DMARDs.
- Treat confirmed influenza exposures with antiviral medication, such as oseltamivir.

Meningococcal vaccine

- No specific guidance about use in patients on immunosuppressive therapy.
- For patients with functional asplenia or persistent complement component deficiencies, guidance supports administration of two doses of MCV4.

Pneumonia vaccine

- Two vaccines are available for adults (PPSV23 and PCV13); both are recommended for the same indications by the CDC's Advisory Committee on Immunization Practices for immunosuppressed patients.
- Immunize at least 2 weeks before starting a DMARD, if feasible.

Tetanus, diphtheria, pertussis vaccine

- Tetanus-diphtheria (Td) is administered every 10 years during adult life, with a single dose of Tdap substituted for Td once during adult life to protect against pertussis.

• The risk of invasive infection increases when patients become immunocompromised, thus vaccinating first may help avoid serious infection.
• Live vaccines are often contraindicated for patients with both primary and secondary immune deficiency, thus vaccinating first may represent the only opportunity to safely immunize them.[8,9]

Additional research about the safety and efficacy of immunization in patients receiving immunosuppressive therapy is needed. The relevance of this question will increase as the number of patients diagnosed with RA and the number of immunosuppressive drugs available for treatment continue to increase. **JAAPA**

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