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### Role of vaccinations and prophylaxis in rheumatic diseases



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Targeted strategies for reducing the increased risk of infection in patients with autoimmune rheumatic diseases include vaccinations as well as antibiotic prophylaxis in selected patients. However, there are still issues under debate: Is vaccination in patients with rheumatic diseases immunogenic? Is it safe? What is the impact of immunosuppressive drugs on vaccine immunogenicity and safety? Does vaccination cause disease flares? In which cases is prophylaxis against *Pneumocystis jirovecii* required?

This review addresses these important questions to which clinicians and researchers still do not have definite answers. The first part includes immunization recommendations and reviews current data on vaccine efficacy and safety in patients with rheumatic

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diseases. The second part discusses prophylaxis for *Pneumocystis pneumonia*.

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## Introduction

Autoimmune rheumatic diseases (ARDs) are associated with an increased susceptibility to infections [1]. Patients with rheumatoid arthritis (RA) have been shown to have up to twofold higher risk of being hospitalized for infection and higher mortality due to common infections compared with the general population [2]. In several series, infection has been reported as the leading cause of mortality in systemic lupus erythematosus (SLE) patients and as a major cause of early death in patients with vasculitis [3]. The excess mortality from infection along with the frequent occurrence of severe infections suggest that patients with ARDs may be predisposed to develop infections, or infections may run a more severe course in ARDs. The immune system dysfunction in ARDs has been attributed to several parameters such as the immune effects of the disease itself, the immunosuppressive effects of the agents used for ARD treatment, comorbidities, medical/surgical procedures, and frequent clinic visits [4]. Over the years, several policies for reducing this increased risk of infection have been considered. There is little evidence to support that improving general health and nutrition can reduce infection rates. Judicious and careful use of immunosuppressive drugs is recommended; however, significant levels of immunosuppression are unavoidable in severe disease. More targeted strategies include antibiotic prophylaxis with specific antimicrobial agents – for example, co-trimoxazole in the prophylaxis of *Pneumocystis jirovecii* pneumonia, and, finally, immunizations.

## Role of vaccinations in patients with ARDs

Given the increase in infection-related risks in ARD patients, immunizations are the principal preventive care options available to rheumatologists. However, despite the formulation of recommendations, vaccination coverage among ARD patients is lower than in the general population [5]. Possible explanations include controversies about the efficiency and immunogenicity of vaccine administration in ARD patients and its potential hazardous effects on the exacerbation of the underlying disease, or on triggering new autoimmune disorders.

### *Inactivated vaccines*

The majority of published data shows that the administration of inactivated vaccines to ARD patients under immunosuppressive therapy is safe and it is not associated with a higher risk of vaccine reactions, nor with a worsening or reactivation of the underlying disease. However, vaccine immunogenicity may be reduced during the use of corticosteroids, and non-biological and biological disease-modifying anti-rheumatic drugs (DMARDs). Vaccination should preferentially be administered before the initiation of immunosuppressive therapy and during stable disease. Specific inactivated vaccinations that are recommended for ARD patients are listed in Table 1 [6–10]. Data from studies in ARD patients supporting the development of vaccination recommendations are elaborated in the following paragraphs.

### *Influenza vaccine*

*Epidemiology of influenza in ARDs.* The morbidity and mortality due to influenza infection is increased in ARD patients; however, the incidence of influenza in ARD patients is unknown [1]. In a cohort study assessing the risk of hospitalization or death associated with influenza among subgroups of elderly members of managed-care organizations, 4.5–7% of patients with ARDs (including vasculitis), dementia, or stroke who were not vaccinated for influenza were admitted for pneumonia/influenza or

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