# Prevention and management of glucocorticoid-induced side effects: A comprehensive review

## Infectious complications and vaccination recommendations

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**Learning objectives**
After completing this learning activity, participants should be able to describe important infectious complications of chronic glucocorticoid therapy and implement preventative strategies, including appropriate use of prophylactic agents and routine vaccinations.

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Part 3 of this 4-part continuing medical education series reviews several important infectious complications of corticosteroid use, including a focus on pneumocystis pneumonia (PCP) prophylaxis, tuberculosis, viral hepatitis, and other infections, followed by a discussion of vaccination recommendations in immunosuppressed patients. (J Am Acad Dermatol 2017;76:191-8.)

***Key words:*** glucocorticoids; infections; pneumocystis pneumonia; side effects; steroids; vaccines.

## GLUCOCORTICOIDS AND IMMUNITY

### Key point

- **Glucocorticoids cause significant impairment in immune function, necessitating prophylactic considerations and vaccination recommendations**

Glucocorticoid use affects both adaptive and innate immunity, increasing the risk for acquiring pathogens, reactivating chronic infections, and impacting vaccine recommendations. Adaptive immunity refers to the part of the immune system that produces lymphocytes (B and T cells) and antibodies. The adaptive immune system works in conjunction with the innate immune system (ie, the part of the immune system that is always present, such as inflammatory proteins, antimicrobial peptides, phagocytic cells, natural killer cells, and physical barriers) to defend against infection and create immunologic memory. Glucocorticoids affect the function of phagocytic cells, downregulate mechanisms involved in antigen presentation, and decrease the effective number of antigen-presenting

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Please note that bone health and gastrointestinal and endocrinologic side effects of glucocorticoid were discussed in the first two installments of this Continuing Medical Education feature in the January 2017 issue of the JAAD.

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cells (macrophages and dendritic cells) and circulating T and B cells. Patients who are taking glucocorticoids are at increased risk for infection by commonly encountered viruses, bacteria, fungi, and less commonly encountered pathogens. Increased vigilance for specific infections and vaccination recommendations relevant to patients who are taking glucocorticoids are reviewed below.

## PNEUMOCYSTIS PNEUMONIA PROPHLAXIS

### Key points

- **The risk for pneumocystis pneumonia is related to total dose and duration of glucocorticoids; however, the best available evidence suggests that additional risk factors should be present before prescribing pneumocystis pneumonia prophylaxis**
- **Trimethoprim-sulfamethoxazole is an effective prophylactic agent against pneumocystis pneumonia, and it is associated with an acceptably low risk of side effects**

### Overview

Pneumocystis pneumonia (PCP) is a life-threatening complication of immunocompromised patients. It is most commonly seen in patients with HIV/AIDS, but it is also seen in patients who are undergoing high-dose corticosteroid therapy and patients with other significant iatrogenic immunosuppression. Concern for this infection has resulted in the widespread use of PCP prophylaxis in patients with HIV/AIDS. Published guidelines exist regarding the timing and duration of PCP prophylaxis in hematopoietic and solid organ transplant recipients. Special populations—those with certain primary immunodeficiencies, acute lymphoblastic leukemia, and those receiving certain highly immunosuppressive combination chemotherapies or the anti-CD52 monoclonal antibody alemtuzumab—are at substantial risk of PCP and should also receive prophylaxis.

### Estimating risk

Data guiding the use of PCP prophylaxis in dermatologic and rheumatologic patients receiving high-dose corticosteroids and other immunosuppression are less clear. In general, such patients are less immunosuppressed, and ultimately the risk of PCP must be balanced against potential adverse effects of the prophylaxis itself. Accounting for this issue, a metaanalysis concluded that PCP prophylaxis is warranted when the risk of PCP exceeds 3.5%.[1]

Unfortunately, there is no existing risk equation or means of quantifying risk numerically in this way. Among collagen vascular diseases, only granulomatosis with polyangiitis (ie, Wegener granulomatosis), which is treated with combination high-dose steroids and cyclophosphamide, is associated with a PCP risk >2.5%.[2] Similar incidence data pertaining to dermatologic diseases are lacking, but what is available suggests that the risk in most such patients is low. In 1 study, only 1 (0.5%) of 198 unselected patients receiving immunosuppressive medications for dermatologic conditions developed PCP.[3] In another, 7 of 3921 dermatology patients with connective tissue or immunobullous disease developed PCP, while 327 developed pneumonia due to other causes.[4]

Nonetheless, the mortality associated with PCP infection in non–HIV-infected patients is high (approximately 40%[5]), and prophylaxis is highly effective.[2] While routine PCP prophylaxis in all patients taking glucocorticoids or other immunosuppressive medications may not be justified by the available data, it should be considered on a case by case basis. Dermatology patients who develop PCP tend to represent a highly selected population. This includes patients with systemic lupus erythematosus (SLE), dermatomyositis, or immunobullous disease who are taking ≥1 immunosuppressive agent in addition to moderate- or high-dose corticosteroids and who frequently have other serious comorbidities, such as active cancer, organ transplantation, or interstitial lung disease.

Therefore, in patients taking the equivalent of ≥20 mg of prednisone daily for ≥4 weeks,[6] PCP prophylaxis should be considered, particularly if a second risk factor, such as hematologic malignancy, interstitial lung disease, or another immunosuppressive agent, is present. Alkylating agents, such as cyclophosphamide, are particularly problematic, but other intensely immunosuppressive regimens, such as rituximab or tumor necrosis factor (TNF)–$\alpha$ inhibitors combined with steroids should receive similar consideration.

### Prophylactic regimens

Trimethoprim-sulfamethoxazole 160/800 mg (double-strength) dosed either daily or thrice weekly is the medication of choice. In HIV-negative patients, the rate of adverse events necessitating cessation of the medication is low, about 3.1%.[2] Alternative regimens include atovaquone 1500 mg daily or dapsone 100 mg daily. Some data suggest that sulfonamide antibiotics can exacerbate systemic lupus, so some favor using an alternative agent in these patients. PCP prophylaxis should be continued until the immunocompromised state has resolved; in some cases, this may be some time after the final dose of immunosuppressive medication is given.

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