Updates in the prevention of glucocorticoid-induced adverse effects

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To the Editor:

Oral corticosteroids are mainstays in the management of several dermatologic and multisystem disorders, though their use is associated with numerous well-known adverse effects. In 2017, Caplan et al. published a series of articles in the *Journal of the American Academy of Dermatology* reviewing prophylaxis and management of glucocorticoid side effects [1,2]. Since this publication, the American College of Rheumatology has released updated guidelines for the prevention and management of corticosteroid-induced osteoporosis [3]. The present article aims to update and remind the practicing dermatologist regarding the prevention of, and therapy for important glucocorticoid-related complications with focus on osteoporosis and infections.

Although there is no clinical threshold under which glucocorticoid therapy can be considered safe, risk is especially associated with daily dosing and duration greater than six months of use. Glucocorticoid-induced osteoporosis (GIOP) affects up to 30-50% of patients utilizing glucocorticoids and osteoporosis-related fractures may occur within the first three months of treatment; thus, preventive measures should be implemented from the outset of therapy [1]. Factors increasing risk of GIOP include advanced age, low body mass index, underlying disease, previous fractures, smoking, excessive alcohol use, falls, family history of fracture, low bone mineral density, and hypovitaminosis D. If therapy is anticipated to exceed three months, a dual energy X-ray absorptiometry scan is recommended [3].

Basic efforts for the prevention of GIOP include ensuring adequate calcium (800-1200mg daily) and vitamin D (800-2000 units daily), [1]. Bisphosphonates are first-line therapies for the prevention of GIOP in postmenopausal women and men >50 years of age with established osteoporosis taking ≥7.5mg/day prednisone for ≥3 months, or with osteopenia taking <7.5mg/day prednisone who are considered high risk [1,3]. In patients who are younger or lower risk, consider long-term risk and potential teratogenicity [2]. For patients who cannot tolerate bisphosphonates or whose glomerular filtration rate is <35ml/min, other potential agents include teriparatide, a parathyroid hormone analog, denosumab, a monoclonal antibody against RANKL, and calcitonin, a parathyroid hormone antagonist [1,3,4].

Two newer osteoporosis-directed therapies discussed in the 2022 American College of Rheumatology guidelines are abaloparatide and romosozumab [3]. Abaloparatide is a parathyroid hormone-related protein for patients at very high risk for fractures [3]. Romosozumab, a monoclonal antibody that inhibits sclerostin, is used to treat osteoporosis in postmenopausal women. However, its use is reserved for very high-risk patients who are

Box 1. *Pneumocystis jiroveci pneumonia prophylaxis consideration*.

Those receiving the equivalent of 20mg of prednisone daily for ≥4 weeks
AND a second risk factor such as:

- Hematologic malignancy
- Interstitial lung disease
- An additional immunosuppressive agent (i.e., chemotherapy, rituximab, TNF alpha inhibitor, alemtuzumab)

intolerant to other options given risk for thrombosis, stroke, and cardiovascular events [3,5].

Screening and prophylaxis for certain infections should be considered in patients on chronic systemic corticosteroids. *Pneumocystis jiroveci* pneumonia is a life-threatening infection and there is evidence for the underutilization of *Pneumocystis jiroveci* pneumonia prophylaxis in prolonged corticosteroid use [2,6,7]. In patients with a secondary risk factor (**Box 1**) and glucocorticoid use greater than or equal to four weeks, prophylaxis should be considered. Administration of trimethoprim-sulfamethoxazole 160-800mg daily or three times weekly, regular tuberculosis testing, and *Strongyloides* screening are recommended in populations at increased risk of infection. Screening for hepatitis B, hepatitis C, and HIV may be indicated. Clinicians should also review the patient's vaccine history to ensure thorough coverage (**Box 2**), [2].

Box 2. *Vaccinations to review and update prior to initiation of prolonged steroid use.*

Haemophilus influenzae B	
Hepatitis A and Hepatitis B	
Human Papillomavirus	
Influenzae	
Neisseria Meningitidis	
MMR* (for women of childbearing age)	
Streptococcus Pneumoniae	
Tetanus Toxoid	
Varicella Booster* or Shingles	Vaccine* if >50 years old

*live vaccines should be given at least 2-4 weeks before initiation of immunosuppressive agents.

Glucocorticoids continue to be a valuable tool for healthcare providers. Their initiation, maintenance, and adverse effects as well as the preventive and therapeutic measures to manage the latter should be thoughtfully considered. Risk factors for glucocorticoid-induced osteoporosis and infections should be assessed and appropriate prophylactic measures taken, if warranted.

Potential conflicts of interest

The authors declare no conflicts of interest.

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