Clinical reviews in allergy and immunology

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# Glucocorticoid-induced osteoporosis: An update on effects and management

Bjoern Buehring, MD,[a,b]* Ravi Viswanathan, MD,[c]* Neil Binkley, MD,[a,b] and William Busse, MD[c] *Madison, Wis*

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**List of Design Committee Members:** Bjoern Buehring, MD, Ravi Viswanathan, MD, Neil Binkley, MD, and William Busse, MD

**Activity Objectives**

1. To summarize the epidemiology and pathophysiology of glucocorticoid-induced osteoporosis (GIO) and the role of oral and inhaled corticosteroids in asthmatic adults and children.
2. To review the clinical effect of GIO therapies on bone health in children and adults.
3. To review the American College of Rheumatology (ACR) GIO guidelines, including diagnostic and therapeutic measures, to reduce the risk of glucocorticoid-induced fragility fractures.

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**Glucocorticoids remain a cornerstone of guideline-based management of persistent asthma and allergic diseases. Glucocorticoid-induced osteoporosis (GIO) is the most common iatrogenic cause of secondary osteoporosis and an issue of concern for physicians treating patients with inhaled or oral glucocorticoids either continuously or intermittently. Patients with GIO experience fragility fractures at better dual-energy x-ray absorptiometry T-scores than those with postmenopausal or age-related osteoporosis. This might be explained, at least in part, by the effects of glucocorticoids not only on osteoclasts but also on osteoblasts and osteocytes. Effective options to detect and manage GIO exist, and a management algorithm has been published by the American College of Rheumatology to provide treatment guidance for clinicians. This review will summarize GIO epidemiology and pathophysiology and assess the role of inhaled and oral glucocorticoids in asthmatic adults and children, with particular emphasis on the effect of such therapies on bone health. Lastly, we will review the American College of Rheumatology GIO guidelines and discuss diagnostic and therapeutic strategies to mitigate the risk of GIO and fragility fractures. (J Allergy Clin Immunol 2013;132:1019-30.)**

***Key words:*** *Glucocorticoid, inhaled and oral corticosteroid, asthma, growth, osteoporosis, bisphosphonates*

Glucocorticoids remain an effective therapeutic option commonly used by clinicians and researchers in the treatment of many inflammatory and autoimmune diseases. However, moderate-to-high doses of glucocorticoids have multiple adverse effects.[1] This review will focus on glucocorticoid-induced osteoporosis (GIO),

From [a]the University of Wisconsin Osteoporosis Research Program, Division of Geriatrics and Gerontology, University of Wisconsin School of Medicine & Public Health; [b]GRECC, William S. Middleton Memorial Veterans Hospital, Madison; and [c]the Department of Medicine, Section of Allergy, Pulmonary & Critical Care, University of Wisconsin School of Medicine & Public Health.

*These authors contributed equally to this manuscript and are joint first authors.

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Corresponding author: Bjoern Buehring, MD, University of Wisconsin Osteoporosis Research Program, Section of Geriatrics and Gerontology, Department of Medicine, University of Wisconsin School of Medicine & Public Health, 2870 University Ave, Suite 100, Madison, WI 53705. E-mail: bbuehring@medicine.wisc.edu. Or: Ravi Viswanathan, MD, Division of Allergy, Pulmonary & Critical Care, Department of Medicine, University of Wisconsin School of Medicine & Public Health, H4/612 CSC, 600 Highland Ave, Madison, WI 53792. E-mail: rviswanathan@medicine.wisc.edu.

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*Abbreviations used*
ACR: American College of Rheumatology
AFF: Atypical femur fracture
ASBMR: American Society for Bone Mineral Research
BDP: Beclomethasone dipropionate
BMD: Bone mineral density
CAMP: Childhood Asthma Management Program
DXA: Dual-energy x-ray absorptiometry
FDA: US Food and Drug Administration
GIO: Glucocorticoid-induced osteoporosis
ICS: Inhaled corticosteroid
LABA: Long-acting β-agonist
OCS: Oral corticosteroid
OR: Odds ratio

outline the pathophysiology and epidemiology of GIO, summarize the literature on the effect of inhaled and oral glucocorticoids on bone health, and discuss the American College of Rheumatology (ACR) guidelines for GIO management[2] and the commentary on these guidelines by the American Society for Bone and Mineral Research (ASBMR).[3]

GIO is the most common form of iatrogenic osteoporosis and also the most common form of secondary osteoporosis[4-7] but remains a complex and often confusing issue for clinicians not intimately involved with osteoporosis treatment. Fragility fractures, the negative consequence of osteoporosis, occur in 30% to 50% of patients taking long-term systemic glucocorticoids. Fracture risk increases markedly in the first 3 months after glucocorticoid initiation and decreases after discontinuing glucocorticoid therapy, but the risk appears to never return to baseline. Hip fracture risk increases up to 7-fold and vertebral fracture risk increases up to 17-fold with treatment with prednisone equivalent doses of 10 to 12 mg/d for more than 3 months. Fracture risk appears to be increased with prednisone doses as small as 2.5 to 3 mg/d.[4-11] Vertebral fractures occur at higher bone mineral density (BMD) values in those receiving glucocorticoids compared with nontreated patients.[8] Hip and vertebral fractures are associated with significant morbidity, reduced quality of life, mortality, and health care costs.[12]

Limited data are available on the prevalence of GIO and GIO-related fractures in children.[13-21] The incidence of vertebral fractures in children with systemic autoimmune diseases receiving glucocorticoids was estimated to be 6% after 1 year of treatment.[22] The relative fracture risk increases by approximately 30% but can be up to twice as high (humerus fractures) in children receiving glucocorticoids (>4 courses of glucocorticoids per year) compared with the general pediatric population.[17] Thus, glucocorticoid therapy increases fracture risk in both adults and children and is of clinical interest and importance to physicians involved in the care of asthma and allergic diseases, in which glucocorticoid use is fundamental to treatment.

## OSTEOPOROSIS OVERVIEW

Osteoporosis is defined as follows: a systemic skeletal disease characterized by low bone mass and microarchitectural deterioration of bone tissue, resulting in increased bone fragility and susceptibility to fracture. This definition highlights 4 important aspects. First, osteoporosis is systemic, affecting the

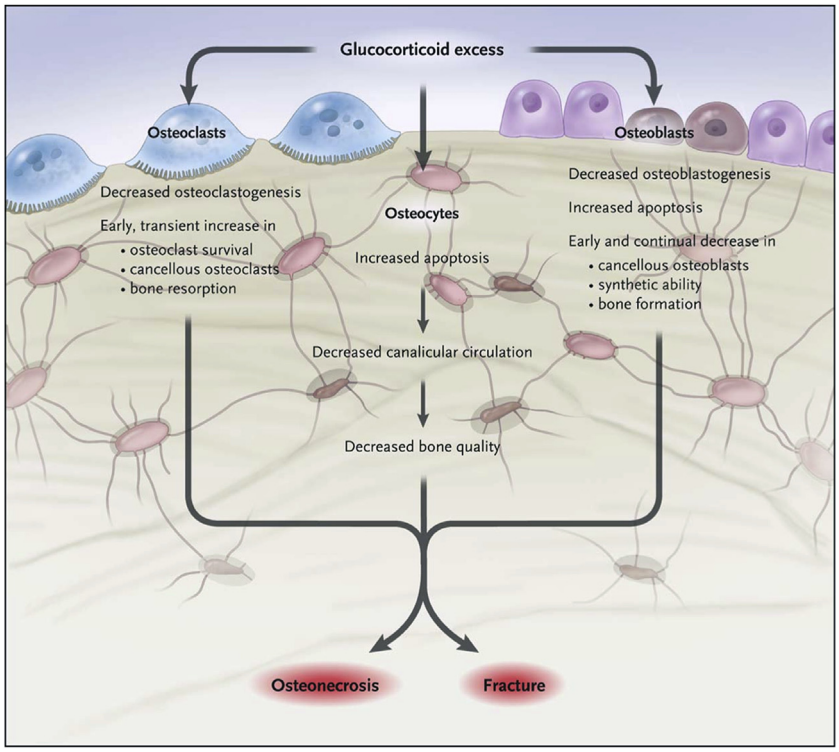


**FIG 1.** Direct effects of glucocorticoids on bone cells. Shown are the adverse skeletal changes that result from an excess of glucocorticoids and lead to osteoporosis and osteonecrosis. The *brown* condensed cells are apoptotic osteoblasts and osteocytes. Apoptotic osteocytes disrupt the osteocyte-lacunar-canalicular network. Reproduced with permission from Weinstein.[7]