1. **How common is glucocorticoid-induced osteoporosis (GIOP)?**

Glucocorticoid-induced osteoporosis (GIOP) is currently the most common cause of drug-induced osteoporosis. Significant bone loss and skeletal fractures may occur within 6 months of starting glucocorticoid therapy, and up to 50% of people on chronic glucocorticoid treatment develop osteoporotic fractures.

2. **What are the important determinants of bone loss with glucocorticoid therapy?**

Bone loss is related mainly to the dose and the duration of glucocorticoid therapy. Glucocorticoid doses of 7.5 mg or higher of prednisone (or equivalent) are associated with the greatest risk. However, a large cohort study showed a significantly increased fracture risk even in those whose median prednisolone doses had been as low as 2.5 mg per day. Decreased bone mass and an increased fracture risk have even been demonstrated in patients using only inhaled glucocorticoids.

3. **Explain the pathogenesis of GIOP.**

Glucocorticoids adversely affect both phases of bone remodeling. They impair bone formation by promoting cell death (apoptosis) of existing osteoblasts and by reducing the recruitment of new osteoblasts, partly through inhibitory effects on local growth factors such as IGF-1. At the same time, they increase bone resorption through various mechanisms, such as decreasing the production of sex steroids and osteoprotegerin, an endogenous inhibitor of bone resorption (Fig 9-1).

![Figure 9-1. Pathophysiology of glucocorticoid induced osteoporosis.](image-url)
4. What are the BMD criteria for a diagnosis of GIOP?
The ideal BMD criteria for the diagnosis of GIOP are still being debated, but the best existing evidence suggests that the fracture risk per BMD decrement is higher in GIOP than in primary osteoporosis. The same BMD criteria are currently used to diagnose osteoporosis in these patients as in those who are not taking glucocorticoids, but active treatment should be considered at an earlier stage (T-score $\leq -1.0$) because of the rapidity of bone loss in GIOP.

5. In which patients on glucocorticoids should BMD be tested?
Patients starting glucocorticoid therapy (prednisone dose $\geq 5$ mg/day or equivalent) with planned duration of treatment 3 months or more or on existing treatment for 3 months or more.

6. When should BMD be tested?
- BMD (spine and hip) should be measured at initiation of glucocorticoid therapy or as soon as possible thereafter.
- BMD should be repeated every 6 to 12 months as long as glucocorticoid therapy is continued.

7. What measures should be instituted in all patients on glucocorticoids?
All glucocorticoid-treated patients should be advised to consume adequate calcium (1500 mg/day; combination of dietary intake plus supplements) and vitamin D (800–1200 U/day), exercise regularly (aerobic and resistance), stop smoking, and limit alcohol and caffeine consumption.

8. Which medications are effective in preventing and treating GIOP?
Bisphosphonates and teriparatide have been shown to increase bone mass significantly and to prevent fractures in patients with GIOP. The dose regimens for these agents are discussed in the chapter on osteoporosis (Chapter 8). These are currently the most effective agents for this condition.

9. Which glucocorticoid-treated patients should receive active intervention?
- Postmenopausal women (all)
- Men and premenopausal women with T-score $\leq -1.0$

10. When should gonadal steroids be considered?
Gonadal steroids may be considered, usually in combination with other agents, in postmenopausal women and hypogonadal men (men with low serum testosterone).

11. List the indications for thiazide diuretics
- If urine calcium $> 300$ mg/day in men.
- If urine calcium $> 250$ mg/day in women.

**KEY POINTS: PREVALENCE AND PATHOPHYSIOLOGY OF GIOP**

1. Glucocorticoid-induced osteoporosis is the most common type of drug-induced osteoporosis.
2. High doses and prolonged use of glucocorticoids produce greater risk, but all doses of oral glucocorticoids and even inhaled steroids appear to increase the risk of osteoporotic fractures.
3. The pathophysiology of glucocorticoid-induced osteoporosis involves both suppressed bone formation and enhanced bone resorption, which account for the rapid bone loss often seen in glucocorticoid-treated patients.
KEY POINTS: PREVENTION AND TREATMENT OF GIOP

1. Bone mineral density (BMD) testing is recommended before initiation of glucocorticoid therapy in patients who will receive $\geq 5 \text{ mg/day of prednisone (or equivalent)}$ for $\geq 3$ months duration and every 6 to 12 months thereafter as long as glucocorticoid therapy is continued.

2. Treatment is recommended for all postmenopausal women regardless of initial BMD and for men or premenopausal women with a BMD T-score of $\leq -1.0$ who are treated or will be treated with $\geq 5 \text{ mg/day of prednisone (or equivalent)}$ for 3 months or more.

3. Both antiresorptive and anabolic agents improve BMD in patients with glucocorticoid-induced osteoporosis; alendronate, risedronate, and teriparatide have also been shown to reduce the occurrence of fragility fractures.

BIBLIOGRAPHY


