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Management of Glucocorticoids

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Faculty Disclosures

Sarah Wilmsmeyer, PA-C

- There are no relationships to disclose.

Management of Glucocorticoids

Objectives:

- Review indications for use of steroids in rheumatic disease
- Review the mechanism of action of steroids
- Compare different formulations and modes of administration
- Discuss side effects of long-term use of steroids and mitigation strategies of these side effects
- Discuss appropriate doses and tapering schedules
- Compare different approaches to using steroids in several commonly encountered rheumatic diseases

Overview of Glucocorticoids

Indications for Use of Steroids:

- Suppress the inflammatory cascade
- Modify the immune response

Specifically:

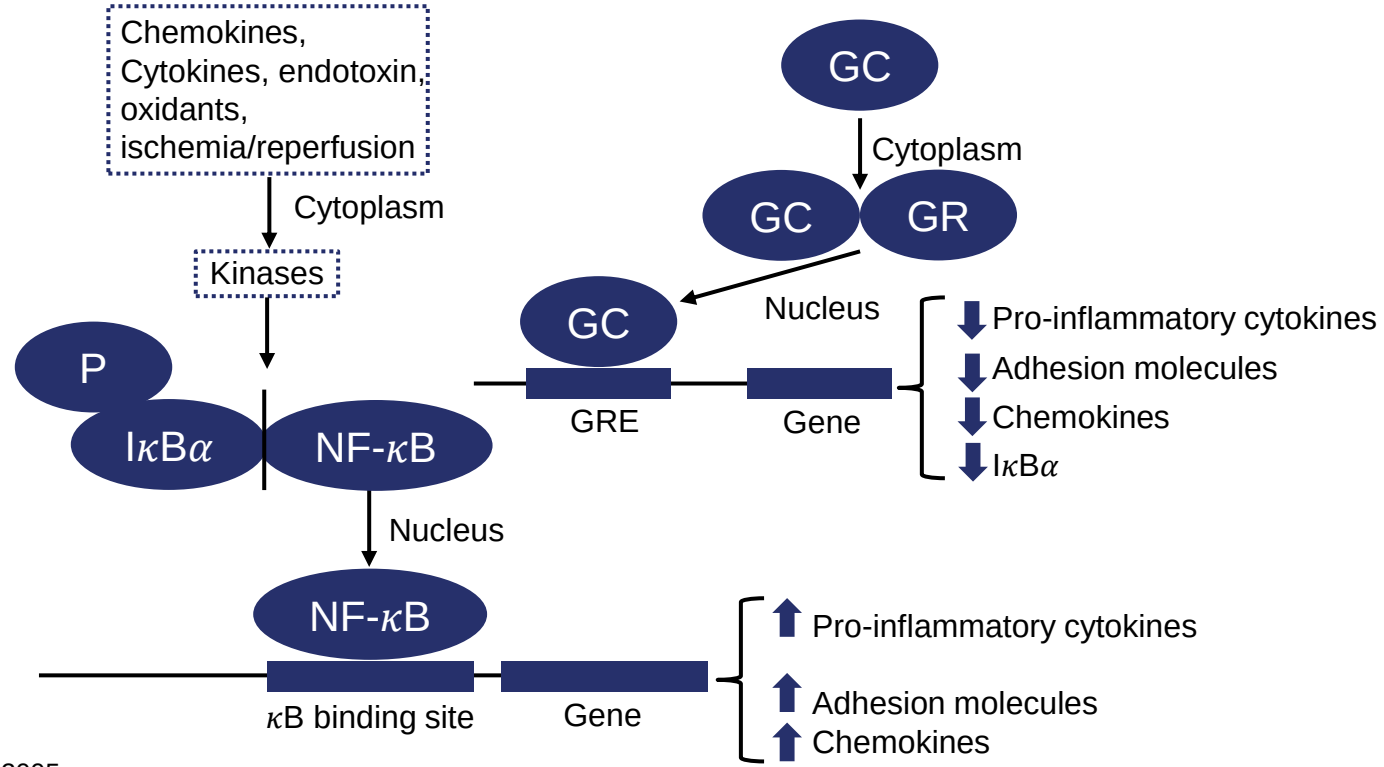
- Rapidly improve signs and symptoms of inflammatory disease while bridging to safer long-term DMARD
- Reduce risk of permanent organ damage or life-threatening inflammatory process

Mechanisms of Action

Steroids...

- Bind to glucocorticoid receptors in the body
- Interact with DNA elements which affect gene transcription
- Exert non-genomic effects on the innate and adaptive immune system
- Block pro-inflammatory cytokines
- Increase anti-inflammatory cytokines

MOA: Steroids



Fernandes, 2005

Comparison of systemic corticosteroid preparations

	Equivalent doses (mg)	Antiinflammatory activity relative to hydrocortisone*	Duration of action (hours)
Glucocorticoids			
Short acting			
Hydrocortisone (cortisol)	20	1	8 to 12
Cortisone acetate	25	0.8	8 to 12
Intermediate acting			
Prednisone	5	4	12 to 36
Prednisolone	5	4	12 to 36
Methylprednisolone	4	5	12 to 36
Triamcinolone	4	5	12 to 36
Long acting			
Dexamethasone	0.75	30	36 to 72
Betamethasone	0.6	30	36 to 72
Mineralocorticoids			
Fludrocortisone	Not used for an antiinflammatory effect¶. The typical dose of fludrocortisone for mineralocorticoid replacement is 0.1 to 0.2 mg.		12 to 36

The mineralocorticoid effect of commonly administered glucocorticoids may be estimated as follows:

- When given at replacement doses, triamcinolone, dexamethasone, and betamethasone have no clinically important mineralocorticoid activity.
- 20mg hydrocortisone and 25mg of cortisone acetate each provide a mineralocorticoid effect that is approximately equivalent to 0.1mg of fludrocortisone.
- Prednisone or prednisolone given at antiinflammatory doses ≥50mg per day provide a mineralocorticoid effect that is approximately equivalent to 0.1mg fludrocortisone.

*Equivalent anti-inflammatory dose shown is for oral or intravenous (IV) administration. Relative potency for intraarticular or Intramuscular administration may vary considerably.

¶ The antiinflammatory potency is 10 to 15 times that of hydrocortisone; however, fludrocortisone is not used clinically as an Antiinflammatory agent.

Data from: 1. Schimmer BP, Finder JW. ACTH, Adrenal Steroids and Pharmacology of the Adrenal Cortex. In: Goodman & Gilman's: The pharmacological Basis of Therapeutics, 12th ed, Brunton LL, Chabner BA, Knollmann BC (Eds), McGraw-Hill Education 2011; 2. Liu D, Ahmet A, Ward L, et al. A practical guide to the monitoring and management of the complications of systemic corticosteroid therapy. *Allergy Asthma Clin Immunol*. 2013, 9:30.

Source: UpToDate

Benefits vs Risks

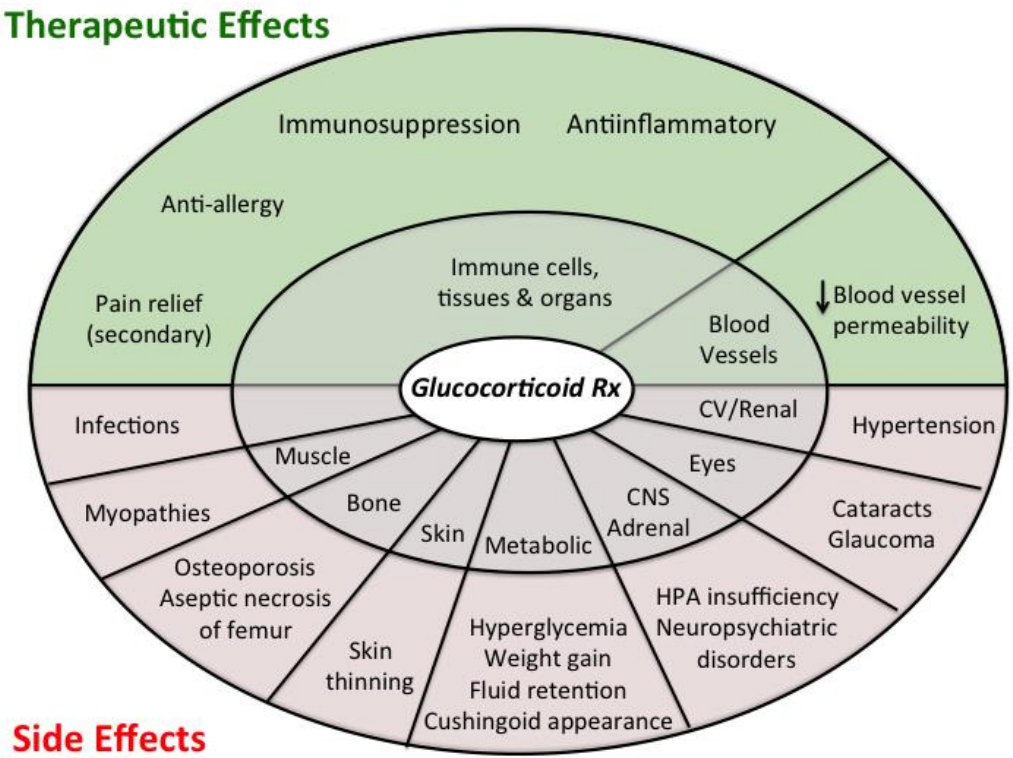


Image credit:
http://tmedweb.tulane.edu/pharmwiki/doku.php/glucocorticoid_pharmacology

Minimizing Risks of Steroids

- Use the lowest possible dose for the shortest duration necessary
- Encourage physical exercise and healthy diet
- Calcium (1000-1500mg) and Vit D (1000IU)
- Bisphosphonate if dose >7.5mg/d for >3 mos
- Appropriate vaccinations
- Infection precautions

Dosing Considerations

- Organ damage/life-threatening scenario:
  - Start high PO/IV dose, maintain until inflammation is suppressed, then slow taper to avoid relapse
- Treating pain/swelling:
  - Low-moderate PO dose with faster taper
  - Consider single IM dose in office, no need to taper

Dosing of Prednisone

Low dose	≤7.5mg/day
Medium dose	7.5mg/d to <40mg
High dose	≥40mg to 100mg
Very high dose	>100mg/day

Tapering Considerations

Why taper?

- Adrenal insufficiency
- Reduce risk of disease flare

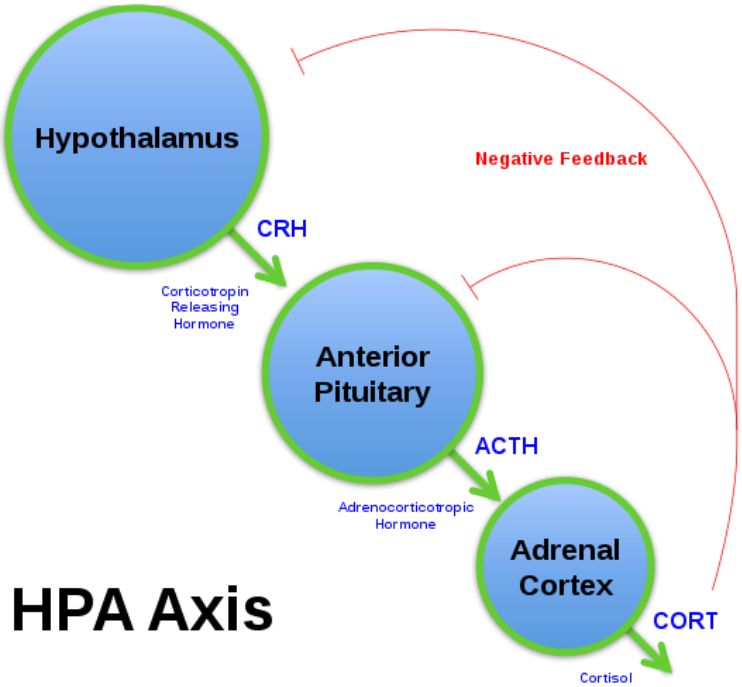


Image credit: Sweis. 2012.

Tapering Considerations

Goal: Maintaining control of disease, reducing risks of severe disease complications, and minimizing the risks of steroids

General rule of thumb: reduce steroid dose at a steady rate of change, such as 10% dose reduction every 1-4 weeks

Case #1 – Early RA

45yoF with pain and swelling in multiple joints of the hands and feet for the past 3 months. Difficulty making fists, gripping, opening jars, fastening buttons. Pain with walking. Pain 8/10. AM stiffness 3 hours. Has been taking otc ibuprofen around the clock without significant relief. Physical exam reveals significant synovitis to wrists, MCPs, PIPs, ankles, and MTPs. Lab workup shows +RF, CCP. Xrays do not show any erosions.

Patient says, “I cannot live like this anymore. I have to have some relief ASAP! I’ll try anything!”

Case #1 Treatment Options

Start oral DMARD?

Start steroids?

What dose? What method of administration?

Case #1- Early RA

Steroid options:

- Administer single IM dose in the office (100mg triamcinolone), +/- subsequent oral steroid at low dose
- Begin oral prednisone at moderate-high dose with fast taper over 1-2 weeks
- Begin low dose of prednisone daily and taper slowly over 3-6 months
- IV pulse dosing?

Case #1 – Early RA

Safety concerns:

- If single IM dose or short duration (<3 weeks) of oral steroids- don’t need to worry too much about side effects
- If longer than 3 weeks – discuss need for taper, avoid abrupt cessation, monitor for infections, discuss appropriate vaccinations, calcium/vit D, exercise/diet
- This 45yoF patient is still menstruating so would not add bisphosphonate

Case #2 – Established RA

65yoM with 30 year history of RA. Has been on methotrexate, hydroxychloroquine, sulfasalazine in the past, eventually tried and failed multiple biologics/JAKs. He has been kept on 20mg methotrexate weekly plus the latest available biologic therapy to try to slow disease progression, but he still has moderate-high disease activity scores at each visit. He has had a good response to short courses of steroids in the past for flares and wants to know if he can just stay on prednisone to help maintain his quality of life.

Is this an acceptable treatment option?

What dose would you use?

Case #2 – Established RA

- Start at 5-10mg daily dose.
- Maintain for 2-4 weeks or longer until symptoms and disease activity improve.
- Discuss very gradual taper, (ex: 1mg/month) but maintain/slightly increase dose if symptoms worsen significantly.
- If pt unable to completely taper off steroids, then leave on lowest possible dose that controls symptoms.
- Document discussion of risk/benefit ratio with use of long-term steroids. Review this discussion periodically at future visits.

Case #3 – SLE

35yoF who was diagnosed with lupus 6 months ago. Clinical presentation involves +ANA 1:160, polyarthritis, mild photosensitive rashes, intermittent oral ulcers, and fatigue. She has not had any manifestations of severe organ involvement. Has been on hydroxychloroquine for 6 months and does feel somewhat better but still complains of AM stiffness of at least an hour, 5/10 joint pain which is affecting her daily activities, and fatigue. The rashes and oral ulcers have decreased in frequency and severity. The addition of stronger immune suppressants/biologics has been discussed but she is nervous about the possible side effects. Has a cousin with SLE who talked about “the miracle drug prednisone” and wonders if she can try this option first.

How would you prescribe steroids for this patient?

Case #3 – SLE Without Organ Involvement

Steroid options:

- Administer single IM dose in the office (100mg triamcinolone), +/- subsequent oral steroid at low dose
- For mild symptoms, use low dose (< 7.5mg pred daily)
- For moderate symptoms, can use between 5-15mg daily with relatively short-term taper
- Taper slowly within 3-6 months
- IV pulse dosing? Not indicated

Case #3 – SLE

Case continued…

The patient feels better after completing short-term treatment with low dose prednisone and she continues on hydroxychloroquine.

However, 6 months later she comes back for follow up and reports “just not feeling well.” You recheck labs and she now has elevated +dsDNA, low C3/C4, creatinine of 2.0, and proteinuria 1.5g/d.

You refer for kidney biopsy which reveals diffuse lupus nephritis (Class IV).

Treat with steroids?

Dose?

Case #3 – SLE With Nephritis

High dose steroids are indicated for severe internal organ involvement:

- Renal (nephritis classes III-V)
- CNS
- Hematologic (plts <30,000, hemolytic anemia)
- Lung (acute pneumonitis, diffuse alveolar hemorrhage)
- Vasculitis

Case #3 – SLE With Nephritis

High dose steroid protocol:

- IV pulse methylprednisolone 0.5-1gm/d x 3 days followed by high dose (60mg) oral prednisone
- Taper oral prednisone to lowest effective dose over 1-6 months
- Steroids used in conjunction with CYC or MMF

Case #4 – Giant Cell Arteritis

70yoF referred for 2 week history of headache, scalp tenderness, jaw claudication, and double vision. ESR is high at 70mm/hr.

You refer for temporal artery biopsy and initiate steroid treatment.

Low dose vs high dose steroids in this patient?

Case #4: GCA

Prednisone 20mg TID for 2-4 weeks, until symptoms improve and ESR normalizes then gradual taper.

Monitor for relapses (symptoms, elevated esr/crp) and increase dose until symptoms improve then begin tapering again.

Actemra studies: Add Actemra SC 162mg weekly + 26-52 wk steroid taper.

Case #4 – GCA

Slow taper from high dose prednisone:

- 5 to 10 mg/day every two weeks from an initial dose above 40 mg of prednisone or equivalent per day.
- 5 mg/day every two weeks at prednisone doses between 40 and 20 mg/day.
- 2.5 mg/day every two to three weeks at prednisone doses between 20 and 10 mg/day.
- 1 mg/day every two to four weeks at prednisone doses between 10 and 5 mg/day.
- 0.5 mg/day every two to four weeks at prednisone doses from 5 mg/day down.

Case #5 – Polymyalgia Rheumatica

60yoM with onset of pain and stiffness in hips and shoulder girdle, progressively worsening over the past 4 weeks. Profoundly stiff in the morning and can hardly move for the first hour of the day. Physical exam reveals reduced and painful ROM of shoulders and hips but no significant synovitis of other peripheral joints. ESR is elevated at 50mm/hr (normal <20) and crp elevated at 15mg/L (normal <8.0).

Initiate steroids?

Case #5 – PMR

PMR usually responds quickly and dramatically to relatively low doses of prednisone (10-20mg/d)

Continue initial dose for 4-8 weeks. If symptoms have resolved, then begin slow taper

Taper over 1-2 years

Relapses are common and require increase in dose

Case #6 – Myositis (IIM)

50yoF with 3 month history of progressive weakness in arms and difficulty lifting arms overhead. Also finding it difficult to get up from seated position without using arms for assistance. Experiencing rash to eyelids and anterior chest, as well as new DOE. Unintentional weight loss of 15lbs in the last 2 months. Denies any pain in muscles or joints.

Physical exam reveals muscle strength ⅗ to proximal UE and LE without pain, erythematous rash to anterior chest and violaceous rash to eyelids. Pt has difficulty getting from chair to exam table.

Markedly elevated muscle enzymes and +jo-1 antibody, interstitial disease noted on CXR.

Case #6 – Myositis

Steroids are the mainstay of treatment to reduce muscle damage and potentially life-threatening heart/lung involvement

High dose induction regimen followed by slow taper

- Prednisone 1 to 1.5mg/kg/d (up to 80mg) or IV pulse methylprednisolone 1gm/d x 3 days

Add immunosuppressant to help with steroid tapering

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Questions/Discussion?

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