



NORTHWEST AIDS EDUCATION AND TRAINING CENTER

Clinical Consequences of Glucocorticoid/ Antiretroviral Interaction

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Risk Factors for Cushing's Syndrome Due to Exogenous Glucocorticoids

Supraphysiologic dose for >2 weeks

Use of long-acting preparations or multiple daily doses

Nighttime administration

Systemic (versus topical or inhaled) use

AIDS. 1999 Sep 10;13(13):1803.

Ritonavir-induced Cushing's syndrome in a patient treated with nasal fluticasone.

Hillebrand-Haverkort ME, Prummel MF, ten Veen JH.

PMID: 10509596 [PubMed - indexed for MEDLINE]

REVIEWS IN ANTIRETROVIRAL THERAPY

Adrenal suppression and Cushing's syndrome secondary to an interaction between ritonavir and fluticasone: a review of the literature

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Cushing's Syndrome Due to Fluticasone/ Ritonavir Interaction

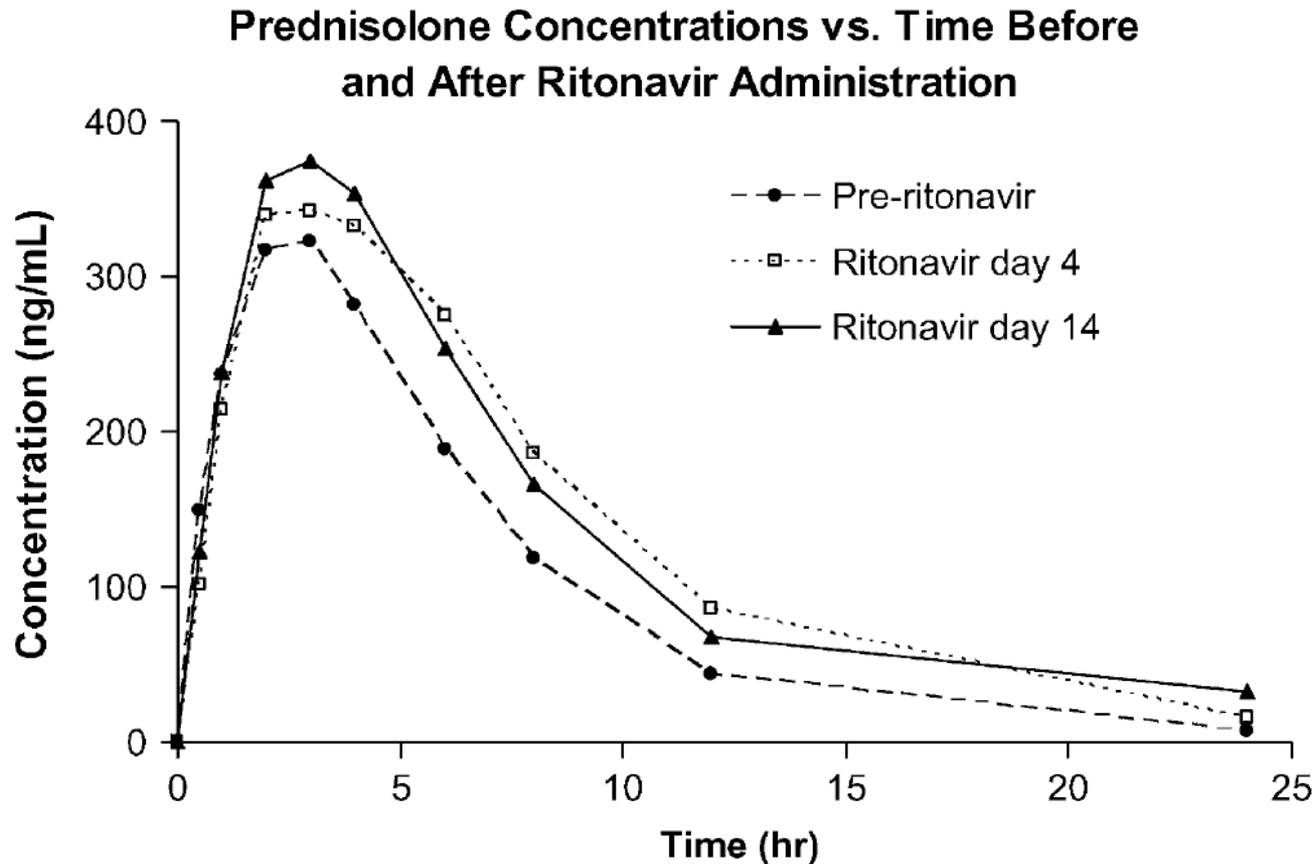
Seen with inhaled and intranasal fluticasone

Mean inhaled fluticasone dose 992 $\mu\text{g}/\text{d}$ and
both low and high dose ritonavir

Mean time to onset 2.75 months

May resolve when inhaled beclomethasone
is substituted for fluticasone

Ritonavir Inhibits CYP3A4-Mediated Metabolism of Exogenous Glucocorticoids



Other Glucocorticoids Causing Cushing's Syndrome in the Presence of Ritonavir

Triamcinolone (single intra-articular or intramuscular injection)

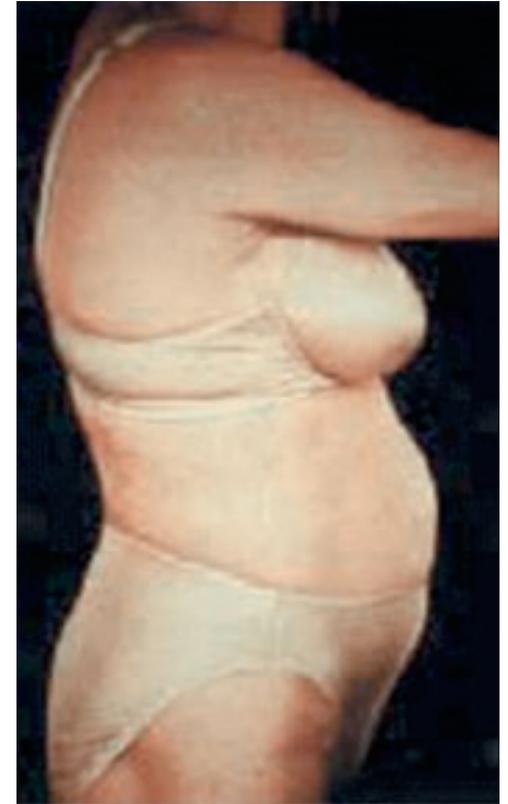
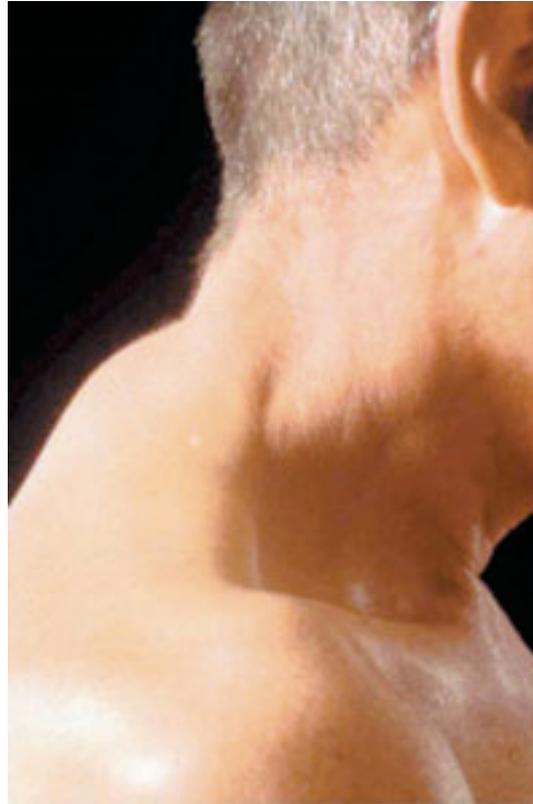
Dexamethasone and betamethasone eye drops

Oral budesonide for colitis

Cushing's Syndrome vs Lipodystrophy



Cushing's Syndrome vs Lipodystrophy

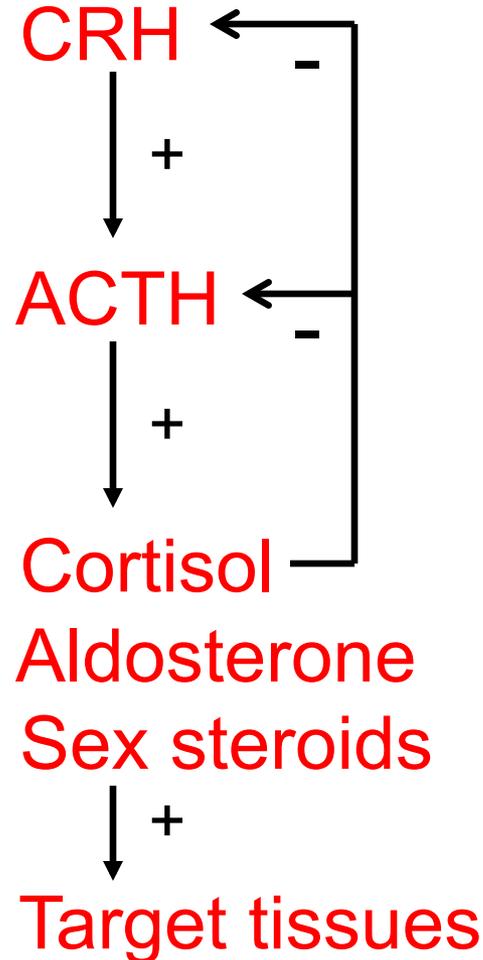


Adrenal Insufficiency in HIV Infected Individuals

Hypothalamus:

Anterior Pituitary:
(2° disease)

Adrenal Gland:
(1° disease)



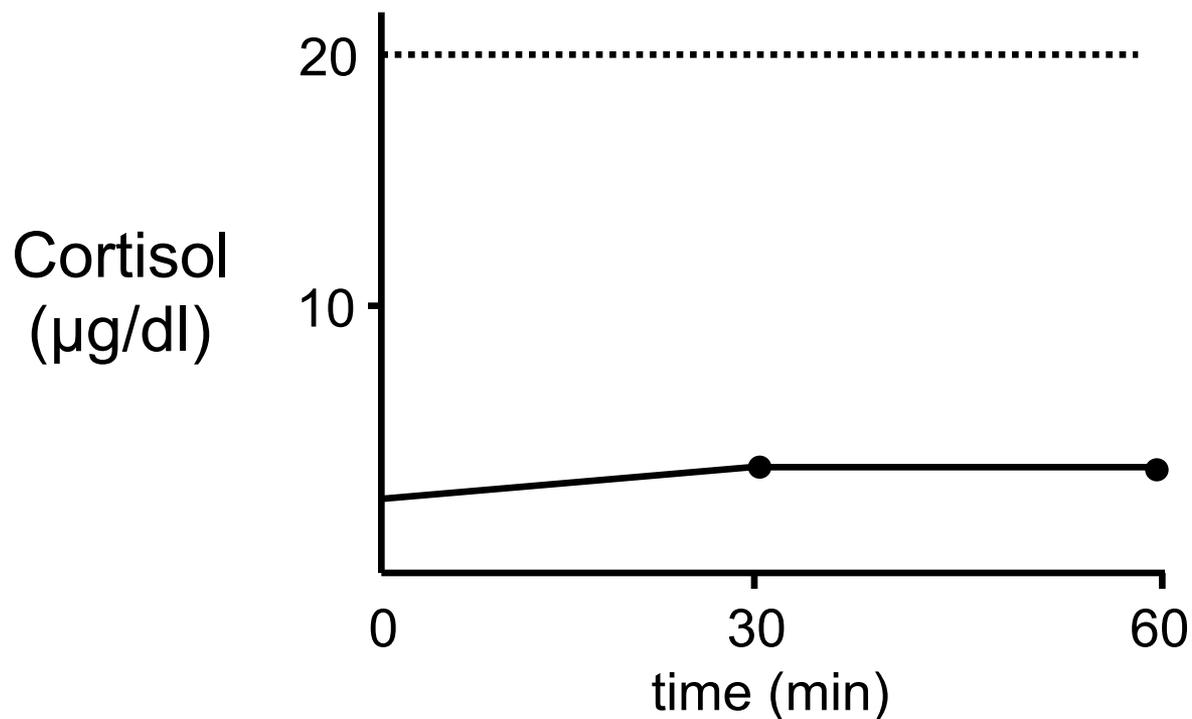
Clinical Presentation of Adrenal Insufficiency

Muscular weakness, fatigue, weight loss
Altered mental status (lassitude to coma)
GI symptoms (nausea, abdominal pain)
Orthostatic hypotension
Hyperpigmentation*
Hypoglycemia
Hyponatremia
Hyperkalemia*

*Absent in 2° adrenal insufficiency

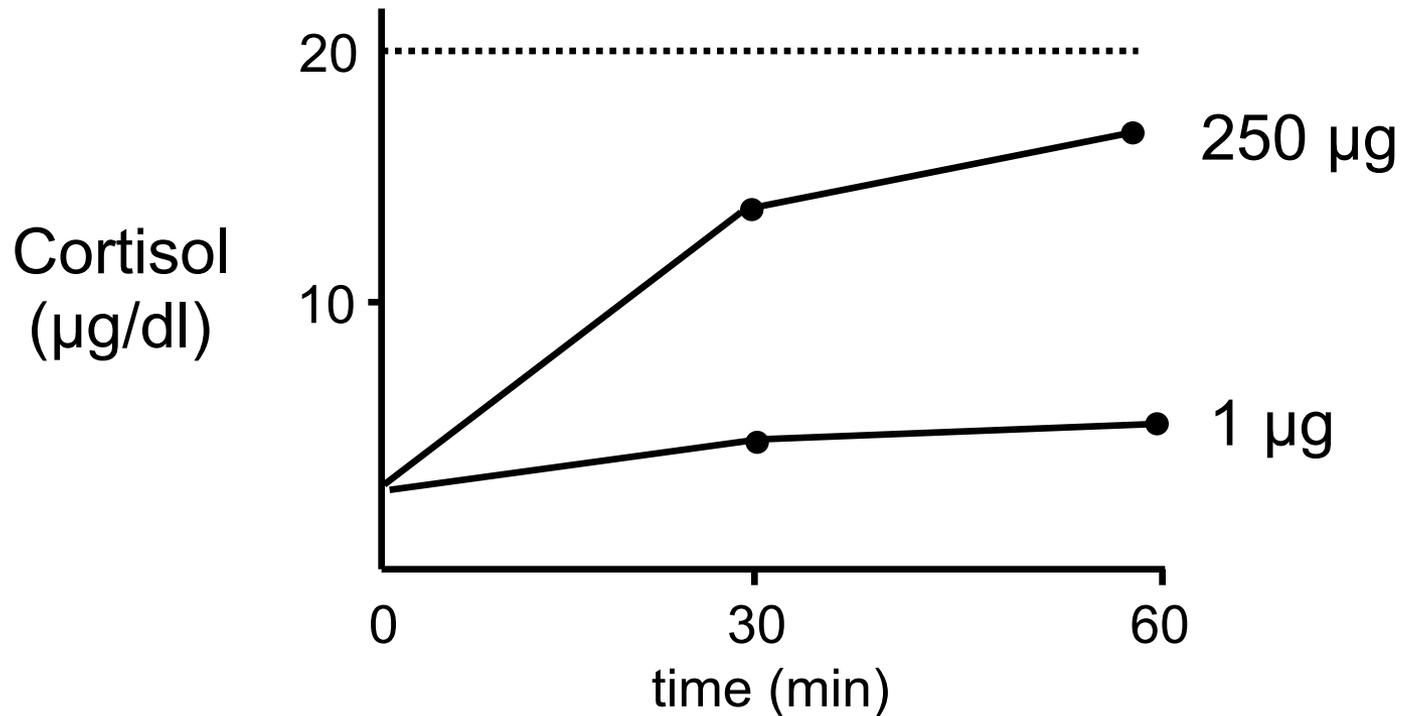
Diagnosis of Primary Adrenal Insufficiency

Plasma cortisol $<5 \mu\text{g/dl}$ at 0800 suggestive
Flat response to $250 \mu\text{g}$ ACTH iv:

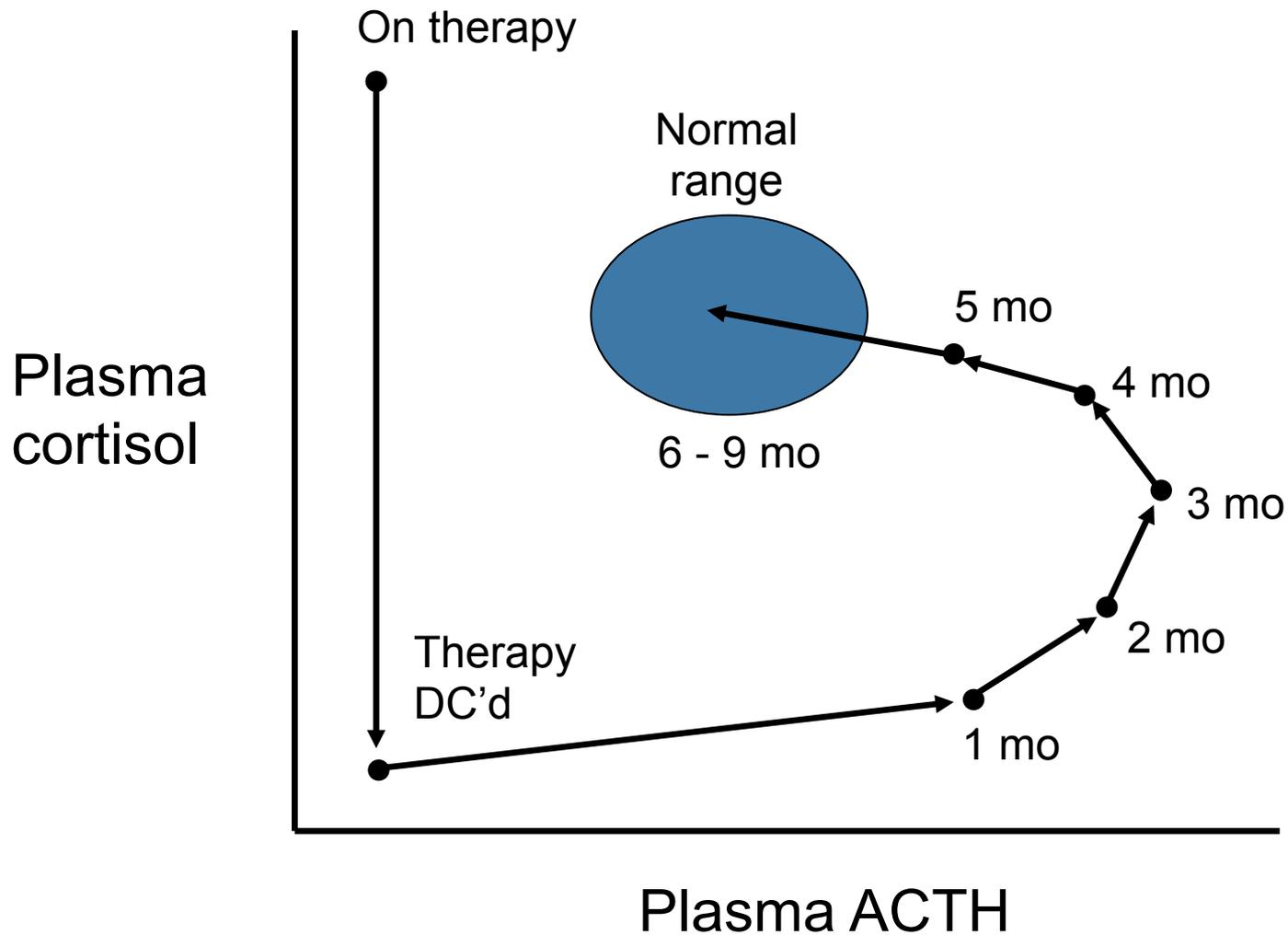


Diagnosis of Secondary Adrenal Insufficiency

Response to iv ACTH:



Recovery From Glucocorticoid Suppression



Treatment of Secondary Adrenal Insufficiency

Treat coexisting endocrine deficiencies

Mineralocorticoid usually NOT required

Glucocorticoid replacement:

- Permanent for irreversible pituitary disease

- 1 - 9 mo following glucocorticoid withdrawal

 - Rapid taper to physiologic dose

 - Slower taper until DC

 - Increase dose for intercurrent stress

Summary

Ritonavir (and other potent CYP3A4 inhibitors) can potentiate the effects of glucocorticoids, even when given by routes that do not usually cause systemic side effects

This potentiation can cause Cushing's syndrome followed by secondary adrenal insufficiency when the glucocorticoid is discontinued

Glucocorticoid and antiretroviral regimens should be chosen to minimize this interaction