ADDISON’S DISEASE SUPPORT GROUP FOR NORTHERN ILLINOIS

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Susan S. Braithwaite, MD
Visiting Clinical Professor
Division of Endocrinology, Diabetes and Metabolism,
University of Illinois at Chicago
What exactly is Addison’s disease?

Is there any research being done on how to prevent us from acquiring additional autoimmune diseases?

What is the best thing to do or say in the emergency room to make sure the ER staff knows how to treat me if I’m in a crisis?

Hydrocortisone dosing for seniors

Should Addison’s patients be under the care of an endocrinologist if one is doing well?
Resources


10. THE NATIONAL ADRENAL DISEASES FOUNDATION, INC. www.nadf.us
What Exactly Is Addison’s Disease?

• How do we get it?

• How is it treated, and how does it differ from person to person?

• How does it affect our daily living, and how does our daily living affect the disease?

• How should medication be managed while traveling?

• How do we know when to increase dosage regarding every day stress?
What exactly is Addison’s disease / primary adrenal insufficiency?

• “Addison's disease is a severe or total deficiency of the hormones made in the adrenal cortex, caused by its destruction....

• the adrenal cortex makes two important steroid hormones, cortisol and aldosterone....

• cortisol mobilizes nutrients, modifies the body's response to inflammation, stimulates the liver to raise the blood sugar, and also helps to control the amount of water in the body. ...

• aldosterone regulates salt and water levels which affects blood volume and blood pressure....”

Within the *adrenal cortex*, cortisol and aldosterone are made in different zones, and their release is regulated differently.

(Catecholamines including adrenaline are made in the adrenal medulla, which is surrounded by the cortex.)
The hypothalamus and pituitary: these normally regulate adrenal cortical production of cortisol

Corticotrophin releasing hormone (CRH) comes from the hypothalamus

Adrenocorticotrophic hormone (ACTH) comes from the pituitary

ACTH normally causes adrenal release of cortisol
Stimuli to the release of corticotrophin releasing hormone (CRH) and adrenocorticotropic hormone (ACTH)

Stress, inflammatory factors, cortisol deficiency, and normal circadian / ultradian rhythmicity drive hypothalamic release of CRH

CRH causes release of ACTH

ACTH normally causes adrenal release of cortisol

Normally, adrenal production of cortisol results in feedback inhibition of the hypothalamus and pituitary, reducing release of CRH and ACTH.

Inability of the adrenal to produce cortisol causes loss of feedback inhibition and results in high ACTH.

Renin- angiotensin- aldosterone

Normally aldosterone causes sodium retention and potassium excretion

*Low aldosterone* results in *sodium loss* from the kidney

Sodium loss causes *low BP* and *increased renin*

*lack of aldosterone causes salt loss*
Diurnal / circadian patterns of cortisol release

- normally, secretion begins to rise between 0200 and 0400
- peaks within 1 hr of waking
- declines gradually to low levels during the evening
- lowest levels at and after midnight

Circadian and ultradian patterns of cortisol release

- there is a pulsatile pattern of release of ACTH and cortisol, embedded within the diurnal pattern
- biologic consequences may be significant
- present treatment modalities do not capture pulsatility of cortisol release

Glucocorticoid-related symptoms

- glucocorticoid therapy is necessary to prevent
  - weight loss, “wasting away”
  - poor response to stress
  - altered consciousness, low blood pressure, shock, death

- insufficiency may result in
  - fatigue
  - muscle weakness
  - loss of appetite, nausea, vomiting
  - diarrhea
  - abdominal or flank pain
  - hyperpigmentation (skin, gums)
  - irritability / depression
  - in women, irregular menses
  - hypoglycemia, especially in children
Addisonian pigmentation
Addisonian pigmentation
Mineralocorticoid-related symptoms and laboratory findings

- mineralocorticoid replacement therapy is necessary to prevent
  - loss of sodium
  - low blood volume
  - high blood potassium

- insufficiency may result in
  - salt craving
  - dizziness standing up
  - low blood pressure standing up
  - low sodium, high potassium and high BUN on blood testing
  - high renin on blood testing
(What Exactly Is Addison’s Disease?)

- How do we get it?
How do we get Addison’s disease / primary adrenal insufficiency?

- autoimmunity
- granulomatous disease (fungal, tuberculous)
- spread of cancer to both adrenal glands
- cytomegalovirus (CMV) in association with AIDS
- hemorrhage - during shock; anticoagulation; anti-phospholipid syndrome
- surgical removal of both adrenal glands
- amyloidosis
- hemochromatosis
- adrenoleukodystrophy
- genetically caused failure of development, function, or capability of synthesis of the cortical hormones of the adrenal glands
- other

NIDDK of the U.S. Department of Health and Human Services, National Institutes of Health, National Endocrine and Metabolic Diseases Information Service.; Bethesda, MD; 2009.
• How is it treated, and how does it differ from person to person?
Equivalencies for glucocorticoid therapy

hydrocortisone is cortisol

1 mg hydrocortisone

  = 1.6 mg cortisone acetate
  = 0.2 mg prednisolone
  = 0.25 mg prednisone
  = 0.025 mg dexamethasone

some countries do not have access to hydrocortisone or cortisone acetate

prednisolone and dexamethasone have considerably longer biological half-lives than hydrocortisone

use of long-acting glucocorticoids is likely to result in unfavorable high night-time glucocorticoid activity

effects may be detrimental on insulin sensitivity and bone mineral density

exception: longer acting glucocorticoids (instead of hydrocortisone) may help smooth out peaks and troughs of blood glucose for patients with insulin-dependent diabetes

Glucocorticoid preparations

- longer-acting synthetic glucocorticoids should be avoided, such as
  - prednisolone
  - prednisone
  - dexamethasone

- the longer duration of action can lead to signs of chronic glucocorticoid excess

Charmandari E, Nicolaides NC, Chrousos GP. Adrenal insufficiency. Lancet. 2014. Published online February 4, 2014 http://dx.doi.org/10.1016/S0140-6736(13)61684-0
Glucocorticoid dose (Arlit)

- primary adrenal insufficiency:
  - start on 20-25 mg hydrocortisone per 24 h

- secondary adrenal insufficiency:
  - 15-20 mg hydrocortisone per 24 h
  - if only borderline failure in cosyntropin test, consider 10 mg, or stress dose coverage only

- administer in two (or three) divided doses with two thirds (or half) of the dose, respectively, administered immediately after waking up, remainder later – for example:
  - 15 mg upon awakening, + 5 mg six hours later
  - 10 mg upon awakening, + 5 mg 4 hr later, + 5 mg again 8 hr after awakening

Glucocorticoid dose (Quinkler)

- recommended daily hydrocortisone doses in primary adrenal insufficiency...
  are lower than estimated before, ranging between 10 and 20 mg

Glucocorticoid dose

- most patients with primary adrenal insufficiency should take 15-25 mg of hydrocortisone daily
- split dose
- the lowest dose compatible with health and a sense of well-being should be used

• primary adrenal insufficiency—
  start on 20- 25 mg hydrocortisone per 24 h

• hydrocortisone should be given in three doses
  with two-thirds or half of the total daily dose given early in the morning

Published online February 4, 2014 http://dx.doi.org/10.1016/S0140-6736(13)61684-0
Summary of provisional daily dose recommendations, to be adjusted as indicated, given in split dose

<table>
<thead>
<tr>
<th>Study</th>
<th>Glucocorticoid as Hydrocortisone</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arlit, 2009</td>
<td>20 - 25 mg</td>
</tr>
<tr>
<td>Quinkler, 2011</td>
<td>10 - 20 mg</td>
</tr>
<tr>
<td>Husebye, 2013</td>
<td>15 - 25 mg</td>
</tr>
<tr>
<td>Charmandari, 2014</td>
<td>20 - 25 mg</td>
</tr>
</tbody>
</table>
Glucocorticoid dose, admonitions to *individualize* (Arlit)

- ? weight-related dosing
- body surface area-adjusted dosing for children
- increased dose for overt hyperthyroidism
- increased dose for 3rd trimester of pregnancy
- concurrent medications

Glucocorticoid dose, admonitions to *individualize* (Quinkler)

- co-medication has to be taken into account... may necessitate up to doubling the dose
- some... recommend weight-adjusted hydrocortisone dosing, thrice daily before food
- dose finding has to be individually adapted....
- to date no reliable laboratory parameter exists for correct assessment of replacement....

**Glucocorticoid dose, drug interactions (Arlit)**

**hydrocortisone**

**dose increase**

*(may be 2-3x dose increase)*

- rifampicin
- ketoconazole
- mitotane
- phenytoin
- carbamazepine
- oxcarbazepine
- phenobarbital
- topiramate
- etomidate
- barbiturates
- sunitinib

**possible hydrocortisone**

**dose reduction**

- antiretroviral agents, ritonavir
- fluoxetine
- diltiazem
- cimetidine

adapted from:


It is important to *let the patient experiment* with different timings to find the most suitable regimen for... individual needs.....

- not clear whether thrice daily regimen is preferred over twice daily

*Avoid evening administration* of high doses

- *unfavorable metabolic response* to evening administration
- *disruption of sleep* by high levels of hydrocortisone given in PM
- *fatigue* resulting from previous insomnia

*Adapt to work shifts*, working time, subsequent sleep-wake cycle

Patients on shift work usually report better performance when they adapt their hydrocortisone dose according to the time of awakeness.

Glucocorticoid *timing* (Husebye)

<table>
<thead>
<tr>
<th>Glucocorticoid</th>
<th>Dose range (mg day$^{-1}$)</th>
<th>Typical dose regimen (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hydrocortisone</td>
<td>15–25</td>
<td>Three doses (07:00, 12:00, 16:00 ± 1 h)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>15 + 5 + 5; 10 + 5 + 5; 10 + 5 + 2.5;</td>
</tr>
<tr>
<td></td>
<td></td>
<td>7.5 + 5 + 2.5</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Two doses (07:00, 12:00 ± 1 h)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>15 + 5; 10 + 10; 10 + 5</td>
</tr>
</tbody>
</table>

*Long-shift regimen (mg)$^a$

10 + 5 + 2.5 + 2.5........... + 2.5

$^a$Airline stewardess, postman.

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last dose should be not less than 6 hr before bedtime
lack of appetite or nausea and vomiting in the morning are common symptoms

waking up earlier to take the first dose of hydrocortisone and then going back to sleep may relieve these symptoms

prednisolone may have a role in a few select patients who experience marked fluctuations in energy or well-being over the course of the day

Glucocorticoid timing (Charmandari)

- Hydrocortisone should be given in three doses with two-thirds or half of the total daily dose given early in the morning.

Published online February 4, 2014 http://dx.doi.org/10.1016/S0140-6736(13)61684-0
**Glucocorticoid monitoring**

- when suspecting hydrocortisone under-replacement, a morning test of absorption and elimination could be useful, either as a cortisol serum or saliva day curve

- measure before, 2, 4, and 6 hr following the morning dose

- in patients with rapid disappearance of cortisol, more frequent dosing of hydrocortisone is reasonable

- this approach for routine care is not supported by controlled studies

- timed serum cortisol measurements could be of value however in case of suspected malabsorption or dose omission


Glucocorticoid monitoring

- serum and urine cortisol measurements are usually impossible to interpret
- it is impossible to eliminate all ACTH elevations without over-treating
- therefore, glucocorticoid dose is usually evaluated by clinical evaluation, not by laboratory tests of cortisol or ACTH


Glucocorticoid-related symptoms

- **signs of under-replacement**
  - weight loss
  - fatigue
  - nausea
  - myalgia
  - joint stiffness
  - lack of energy
  - poor mental concentration
  - hyperpigmentation

- **signs of over-replacement**
  - insomnia
  - weight gain
  - central obesity
  - stretch marks
  - osteopenia / osteoporosis (seen with hydrocortisone dose ≥ 30 mg)
  - impaired glucose tolerance
  - hypertension
  - edema


Mineralocorticoid medication
( fludrocortisone, 9-α-fluorohydrocortisone )

• mineralocorticoid is required
  in **primary** (and generally not in secondary) adrenal insufficiency

• fludrocortisone is not required
  at times when hydrocortisone dose ≥ 50 mg per 24 h

• each 40 mg hydrocortisone provides mineralocorticoid effect
  equivalent to 100 mcg fludrocortisone

• prednisolone provides reduced mineralocorticoid activity
  compared to hydrocortisone

• dexamethasone provides no mineralocorticoid activity

Fludrocortisone dose

- start with 100 mcg fludrocortisone (doses vary between 50-250 mcg per 24 h), administered as a single dose in the morning immediately after waking up -- Arlit
- single morning dose of 0.05-0.20 mg fludrocortisone -- Quinkler
- dose is 0.05-0.20 mg taken once daily, in the morning -- Charmandari


Charmandari E, Nicolaides NC, Chrousos GP. Adrenal insufficiency. Lancet. 2014. Published online February 4, 2014 http://dx.doi.org/10.1016/S0140-6736(13)61684-0
Fludrocortisone dose, with co-existent hypertension

- in case of co-existent hypertension, *consider dose reduction of fludrocortisone but avoid cessation*  
  -- Arlt

- in case of fludrocortisone dose reduction, *supervise serum potassium levels*  
  -- Arlt

- data is lacking concerning use of medications influencing the renin-angiotensin system  
  -- Quinkler

- diuretics and drugs that affect blood pressure and electrolytes may require dose adjustments; *avoid diuretics; consider vasodilators*  
  -- Husebye


Fludrocortisone dose, *individualization and adjustment*

- *children*, in particular neonates and infants, have higher dose requirements
- temperature, humidity, Mediterranean or tropical climates may require a 50% dose increase due to *perspiration* -- Arlit
- dose might have to be increased in the *summer*, especially at temperatures higher than 29°C -- Charmandari


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**Fludrocortisone under- treatment and over- treatment**

### under- treatment
- symptoms of low blood pressure upon standing
- postural drop of blood pressure $\geq 20$ mm Hg
- weight loss
- dehydration
- high potassium
- low serum sodium
- increased renin

### over- treatment
- high blood pressure
- weight gain
- swelling of legs
- fluid on the lungs
- low potassium
- suppressed renin

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Fludrocortisone monitoring

- monitor *supine and erect blood pressure*,
- serum *sodium* and *potassium*
- plasma *renin* activity at least every 2-3 yr, upon clinical suspicion of fludrocortisone over- and under-replacement, and after significant changes in the hydrocortisone dose -- Arlt
- electrolytes within the normal range, normal blood pressure without evidence of postural hypotension, and a plasma renin in the upper normal range indicate adequate mineralocorticoid replacement -- Quinkler
- dose is titrated individually on the basis of blood pressure, sodium and potassium blood tests, plasma renin -- Charmandari


Charmandari E, Nicolaides NC, Chrousos GP. Adrenal insufficiency. Lancet. 2014. Published online February 4, 2014 http://dx.doi.org/10.1016/S0140-6736(13)61684-0
Other interactions

- avoid NSAIDS
- licorice and grapefruit juice potentiate the mineralocorticoid effect of hydrocortisone and should be avoided

Sodium / salt

- eat sodium salt and salty foods without restriction
- avoid potassium-containing salts (may be billed as a health food)
- recognize salt craving as a sign of insufficient treatment

Sodium supplementation

• high *salt intake* may slightly reduce fludrocortisone dose requirement
  -- Arlit

• In case of hot climate or strong perspiration, it is necessary to increase the fludrocortisone dose (0.1-0.2 mg/day) and/or the *salt intake*
  -- Quinkler


Sodium supplementation in case of unusual losses
( What Exactly Is Addison’s Disease? )

- How does it affect our daily living, and how does our daily living affect the disease?
Exercise and Addison’s disease

- for strong and prolonged physical activity, *an additional hydrocortisone dose of 5-10 mg* is recommended
  - intensive fitness training
  - running for several hours
- extra dose is *not* needed for brief physical activity

Carbohydrate-rich food and Addison's disease

need for hydrocortisone dose increase in 3rd trimester is controversial
• fludorocortisone dose increase is likely to be needed due to the anti-mineralocorticoid effect of progesterone
• judge by serum potassium and blood pressure
• renin is not helpful during pregnancy
DHEA and Addison’s disease

Random-effects meta-analysis of DHEA on HR QOL, depression, anxiety, and sexual function (libido and satisfaction with sex)

General well-being with Addison’s disease

Persons having Addison’s disease, despite standard treatment, do not always enjoy freedom from symptoms

- fatigue, lack of “get-up-and-go”
- insomnia
- possibly daytime somnolence
- consequences of other autoimmune conditions

New approaches to delivery and monitoring of hydrocortisone may prove helpful in the future
Subjective health status questionnaire, in Norwegian patients with Addison's disease

79 patients compared with general population:

• general *health and vitality* perception -- *impaired* with Addison’s
• scores on physical functioning -- low in women
• autoimmune polyendocrine syndromes -- lower scores than solitary Addison’s
• level of *fatigue* -- higher than normal
• working *disability* at ages 18-67 years -- 26%, compared with 10% in the corresponding general Norwegian population, higher in subgroups with concomitant endocrine diseases

Thus, there might be *potential for further refinement of replacement therapy*

Innovative approaches to glucocorticoid therapy designed to capture diurnal rhythmicity

- infusion pump
- modified-release or dual-release hydrocortisone preparations


Charmandari E, Nicolaides NC, Chrousos GP. Adrenal insufficiency. Lancet. 2014. Published online February 4, 2014 http://dx.doi.org/10.1016/S0140-6736(13)61684-0
Normal diurnal rhythm
reference group
32 males
had peak
around 8:32 AM
with two smaller peaks
at meal times

Treatments during
dex suppression
regimens were studied
among 20 subjects
during 1 mg dexamethasone
suppression of HPA axis
(subjects did not have Addison’s)

Cortisol blood levels with dual-release formulation of hydrocortisone

Other findings with dual-release formulation of hydrocortisone

In a pilot study enrolling 64 patients with primary adrenal insufficiency, 11 having concomitant diabetes, after 12 weeks there were favorable results with use of the once-daily dual-release formulation:

- reduction of mean weight (difference 0.7kg, P =0.005)
- reduction of systolic blood pressure (difference 5.5 mm Hg, P =0.0001) and diastolic blood pressure (difference: 2.3 mmHg; P =0.03),
- reduction of glycated hemoglobin hemoglobin by 0.6% in patients with concomitant DM (P=0.004)

How do we know when to increase dosage regarding every day stress?
Dr. Paul Margulies’ guidelines for stress dosing with glucocorticoid

- extra 5 mg of hydrocortisone for mild stress, such as a mild cold without fever, a mild injury, or emotional stress
- extra 10 mg for infection with mild fever
- double the usual dose for significant fever or any illness that includes vomiting, diarrhea or dehydration
- all these doses should be continued until the stress has diminished
- then return to the normal dose without a need to taper

Psychological stress and Addison’s disease

- An additional hydrocortisone dose should be considered in situations of severe and prolonged psychological stress, such as
  - death of a relative
  - acute depression
- Reduce back to standard dose in a timely manner
- Short-acting stressors usually do not routinely require dose adaptation

Glucocorticoid stress doses

• hydrocortisone dose should be doubled during intercurrent illness, such as a respiratory infection with fever, until clinical recovery  
  -- Arlt

• in case of minor physical stress (infectious diseases with fever, stress, surgery under local anaesthesia) or major and prolong psychic stress, the daily hydrocortisone replacement dose should be doubled or tripled to approximately 40-50 mg/day  
  -- Quinkler

• during minor illness or surgical procedures, the dose of glucocorticoid can be increased to up to three times the usual maintenance dose  
  -- Charmandari


Charmandari E, Nicolaides NC, Chrousos GP. Adrenal insufficiency. Lancet. 2014. Published online February 4, 2014 http://dx.doi.org/10.1016/S0140-6736(13)61684-0
Being prepared for an emergency

- review “sick day rules” and emergency guidelines at visits with healthcare provider
- involve family or partner
- update bracelet / steroid card as required

Self- injection of hydrocortisone

- a hydrocortisone emergency kit is prescribed
- patients (together with relatives) are educated in *self-administration* of hydrocortisone as *intramuscular injection* in emergency situations

-- Quinkler

• How should medication be managed while traveling?
Traveling

- when traveling, people with adrenal insufficiency should carry a needle, syringe, and an injectable form of cortisol for emergencies
  --NIDDK

- preferably all patients, but at least patients traveling or living in areas with limited access to acute medical care, should receive a hydrocortisone emergency self-injection kit
  --Arlt

Adrenal Insufficiency and Addison's Disease.

What is the best thing to do or say in the emergency room to make sure the ER staff knows how to treat me if I’m in a crisis? 

In other words, talking with emergency room personnel / doctors:

• who don’t know you
• to get the care you need
• in an urgent timeframe
Symptoms of crisis (from Husebye consensus statement):
malaise, fatigue, nausea, vomiting, abdominal pain, muscle pain or cramps, dehydration, impaired cognitive function, confusion, loss of consciousness, coma

glucocorticoid crisis

- nausea
- vomiting
- abdominal pain
- weakness
- low blood pressure
- shock
- fever
- hypoglycemia (especially children)

mineralocorticoid crisis

- low blood pressure
- shock
- high potassium
- low serum sodium
- poor kidney perfusion (high creatinine)
Being prepared for an emergency

• people with adrenal insufficiency should always carry identification stating their condition in case of an emergency

• a card or medical alert tag should notify emergency health care providers of the need to inject cortisol if the person is found severely injured or unable to answer questions

• the card or tag should also include the name and telephone number of the person’s doctor and the name and telephone number of a family member to be notified

Adrenal Insufficiency and Addison's Disease. 
Seek precipitating cause while treating adrenal crisis

<table>
<thead>
<tr>
<th>Precipitating factors for adrenal crisis</th>
<th>PAI</th>
<th>Percentage of cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gastrointestinal infection</td>
<td>59</td>
<td>32.6</td>
</tr>
<tr>
<td>Other infectious disease/fever</td>
<td>44</td>
<td>24.3</td>
</tr>
<tr>
<td>Surgery</td>
<td>13</td>
<td>7.2</td>
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<tr>
<td>Unknown</td>
<td>12</td>
<td>6.6</td>
</tr>
<tr>
<td>Strenuous physical activity</td>
<td>14</td>
<td>7.7</td>
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<tr>
<td>Cessation of glucocorticoid substitution by patient</td>
<td>9</td>
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<tr>
<td>Neglected glucocorticoid intake</td>
<td>9</td>
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<tr>
<td>Psychic distress</td>
<td>6</td>
<td>3.3</td>
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<tr>
<td>Accident</td>
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<td>2.8</td>
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<tr>
<td>Cessation of glucocorticoid substitution by attending physician</td>
<td>2</td>
<td>1.1</td>
</tr>
<tr>
<td>Other reasons</td>
<td>8</td>
<td>4.4</td>
</tr>
</tbody>
</table>

Intravenous hydrocortisone treatment

- in case of diarrhea / vomiting, hydrocortisone needs to be substituted intravenously (100-150 mg/24h) --Quinkler

- if vomiting or dehydration cannot be controlled, or there is a severe illness or injury, go to the nearest medical facility for intravenous steroids and saline -- Dr. Margulies

- visit the nearest emergency department if vomiting persistently and unable to tolerate oral hydrocortisone

- inform medical staff about the need for early admission to the hospital and IV hydrocortisone treatment in case of a severe illness --Chamandari


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The first dose of hydrocortisone by injection in an emergency

- the dose of hydrocortisone needed may vary with a person’s age or size
- for example, a child younger than 2 years of age can receive 25 mg
- a child between 2 and 8 years of age can receive 50 mg
- and a child older than 8 years should receive the adult dose of 100 mg

Adrenal Insufficiency and Addison's Disease.
Saline infusion for volume losses

- if vomiting or dehydration cannot be controlled, or there is a severe illness or injury, go to the nearest medical facility for intravenous steroids and saline -- Dr. Margulies


COMMENT:

- glucocorticoid and mineralocorticoid administration in an adrenal crisis will not result in volume replacement

- to replace volume losses urgently, saline infusion is needed
FOR EMERGENCIES/EXTREME STRESS SITUATIONS
(TO AVOID OR CORRECT ADDISONIAN CRISIS)

Conditions which must be treated immediately:
- severe injury of any type
- blood loss
- fluid and/or electrolyte loss
- infection
- severe vomiting
- diarrhea.

Treatment protocol prior to Emergency Room arrival:
- Give Hydrocortisone 100 mg. IM (intramuscularly) in buttock or upper thigh.
- Patient then should be immediately admitted to the nearest Emergency Room, where adrenal crisis treatment should begin promptly.
- If transportation to emergency medical facility is impossible, treat patient on site as listed below.

Protocol for treatment of adrenal crisis in emergency room:

1.) I.V. hydrocortisone.
2.) Administer I.V. isotonic saline.
3.) Continue I.V. hydrocortisone until oral medication is tolerated.
Is there any research being done on how to prevent us from acquiring additional autoimmune diseases?

I already have several.....
Molecular immunopathogenesis of primary adrenal insufficiency

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Autoimmune Polyglandular Syndrome (APS)

- the cause, in 90% of persons having primary adrenal insufficiency in North American and European countries, is autoimmune adrenalitis
  - 40% isolated autoimmunity
  - 60% part of an autoimmune polyglandular syndrome (APS)

- two principal types of APS are recognized
  - type 1 autoimmune regulator gene AIRE (15%)
  - type 2 a genetically - complex trait, having loci within the major histocompatibility complex and distinct susceptibility genes

- vitiligo and alopecia are markers of autoimmunity

Autoimmune Polyglandular Syndrome (APS)

- type 1 APS
  ( autoimmune polyendocrinopathy- candidiasis- ectodermal dystrophy )

- type 2 APS is much more common than type 1 APS

- with Type 2 APS, thyroid disease is the most frequent accompanying autoimmune condition

Vitiligo
Alopecia
Mucocutaneous candidiasis: diaper rash and adult onychomycosis
What constitutes appropriate screening for other autoimmunity?

At minimum, screening tests for:

- thyroid function, on a regular basis (get TSH every 12 months)
- B12
- celiac disease
- HbA1C or blood glucose
- menstrual regularity, consider ovarian autoantibodies

As suggested by clinical evaluation:

- other autoimmunity individually
- family screening


Mission Statement
To consolidate the voice of autoimmune disease patients and to promote increased education, awareness, and research into all aspects of autoimmune diseases through a collaborative approach.
Hydrocortisone Dosing for Seniors
Risk for osteoporosis

- bone mineral density at the femoral neck and lumbar spine is reduced in primary adrenal insufficiency.
- It is believed that bone loss is not influenced by duration or type of steroid treatment, but rather by the glucocorticoid dose.

Osteoporosis
Summary of counseling recommended in the NOF Guide for men and postmenopausal women age 50 yr and older who are not yet on therapy

- advise on adequate amounts of calcium (at least 1200 mg/d, including supplements if necessary) and vitamin D (800–1000 IU/d of vitamin D for individuals at risk of insufficiency)
- recommend regular weight-bearing and muscle-strengthening exercise to reduce the risk of falls and fractures
- advise avoidance of tobacco smoking and excessive alcohol intake

The diagnosis of osteoporosis is established by measurement of BMD or by the occurrence of adulthood hip or vertebral fracture in the absence of major trauma (such as a motor vehicle accident or multiple story fall).
Typical DEXA scan report

Monitoring of bone mineral density

- consensus statement advises DEXA every 3-5 years for persons having primary adrenal insufficiency
Fragility fracture *also* identifies osteoporotic patients needing treatment, despite potentially normal or osteopenic-range BMD.

<table>
<thead>
<tr>
<th>Classification</th>
<th>T-score</th>
</tr>
</thead>
<tbody>
<tr>
<td>normal</td>
<td>-1.0 or higher</td>
</tr>
<tr>
<td>osteopenia</td>
<td>between -1.0 and -2.5</td>
</tr>
<tr>
<td>osteoporosis</td>
<td>-2.5 or lower</td>
</tr>
<tr>
<td>established or severe osteoporosis</td>
<td>-2.5 or lower with one or more fractures</td>
</tr>
</tbody>
</table>
Prevention of glucocorticoid induced osteoporosis

- 1200-1500 mg of calcium per day including diet
- 800-1000 units of vitamin D
- treat with bone drugs if ≥ 7.5 mg/day prednisone for at least 3 months
- use alendronate, risedronate, zoledronic acid, or teriparatide

In the absence of osteoporosis or other indications, there is no evidence that medication to prevent fractures is needed with occasional dose-pack prescriptions, annual short-term (e.g., 7 to 10 days) high-dose intravenous or oral therapy (<1 g of cumulative exposure), or replacement therapy for patients with hypopituitarism, adrenal insufficiency, or congenital adrenal hyperplasia, provided that the replacement doses are not excessive.

Correlation between weight-adjusted hydrocortisone doses and femoral neck Z-scores in Norwegian patients

Bone loss is one of the major reasons for downward revision of hydrocortisone dosing guidelines compared to historical advice.

Should Addison’s patients be under the care of an endocrinologist if one is doing well?
Improvements over time

- prior to the 1940’s, primary adrenal insufficiency always was fatal
- synthesis of corticosteroids made life-saving treatments possible and transformed Addison’s disease into a fully treatable chronic condition
- quality of life may be imperfect
- treatments and followup care patterns vary greatly
- methods of improved delivery of needed treatment are under study

from Husebye et al.
Advice on specialty care

• “Because of the rarity of the disease, an endocrinologist will have more training and experience in properly diagnosing and treating Addison's disease than most physicians.” -- Margulis

• “Regular follow-up in specialist center every 6 to 12 months…” -- Arlit

• Annual follow-up by an endocrinologist is recommended with focus on replacement therapy and detection of new autoimmune diseases -- Husebye

• “Regular follow-up in outpatient endocrinology clinic every 6 months…” -- Charmandari