Addison's disease

Addison's disease, also known as primary adrenal insufficiency and hypocortisolism, is a long-term endocrine disorder in which the adrenal glands do not produce enough steroid hormones.

**Common features:**

1. Fatigue
2. Weight loss, the weight loss is primarily due to anorexia, but dehydration may contribute. The amount of weight lost can vary from 2 to as much as 15 kg and may not become evident until adrenal failure is advanced.
5. Skin hyperpigmentation.
6. Postural hypotension.
7. Salt craving.

**Lab findings:**

1. Hyponatremia.
2. Hyperkalemia.
3. Anemia.
### Treatment of chronic primary adrenal insufficiency in adults

#### 1. Glucocorticoid replacement

Hydrocortisone 15 to 25 mg orally in two or three divided doses (largest dose in morning upon awakening; typically 10 mg upon arising in morning, 5 mg early afternoon, 2.5 mg late afternoon) or

- Prednisone 5 mg (range: 2.5 to 7.5 mg) orally at bedtime; or
- Dexamethasone 0.75 mg (range: 0.25 to 0.75 mg) orally at bedtime

Monitor clinical symptoms and morning plasma ACTH.

#### 2. Mineralocorticoid replacement

Fludrocortisone 0.1 mg (range: 0.05 to 0.2 mg) orally.

Liberal salt intake.

Monitor lying and standing blood pressure and pulse, edema, serum potassium, and plasma renin activity.

- Hydrocortisone 20 mg and prednisone 50 mg provide a mineralocorticoid effect that is approximately equivalent to 0.1 mg of fludrocortisone, so fludrocortisone replacement (if needed) must be decreased appropriately. Dexamethasone lacks mineralocorticoid effect.
- Mineralocorticoid replacement to prevent sodium loss, intravascular volume depletion, and hyperkalemia

#### 3. Androgen replacement

Dehydroepiandrosterone (DHEA) initially 25 to 50 mg orally (only in women with impaired mood or sense of well-being despite optimal glucocorticoid and mineralocorticoid replacement).

#### 4. Patient education

Educate patient about the disease, how to manage minor illnesses and major stresses, and how to inject dexamethasone or other glucocorticoid intramuscularly or subcutaneously.
Glucocorticoids equivalency

<table>
<thead>
<tr>
<th>Glucocorticoids</th>
<th>Equivalent doses* (mg)</th>
<th>Relative anti-inflammatory activity</th>
<th>Duration of action (hours)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Short acting</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hydrocortisone (cortisol)</td>
<td>20</td>
<td>1</td>
<td>8 to 12</td>
</tr>
<tr>
<td>Cortisone acetae</td>
<td>25</td>
<td>0.8</td>
<td>8 to 12</td>
</tr>
<tr>
<td>Intermediate acting</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prednisone</td>
<td>5</td>
<td>4</td>
<td>12 to 16</td>
</tr>
<tr>
<td>Prednisolone</td>
<td>5</td>
<td>4</td>
<td>12 to 16</td>
</tr>
<tr>
<td>Methylprednisolone</td>
<td>4</td>
<td>5</td>
<td>12 to 16</td>
</tr>
<tr>
<td>Tixocortol</td>
<td>4</td>
<td>5</td>
<td>12 to 16</td>
</tr>
<tr>
<td>Long acting</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dexamethasone</td>
<td>0.75</td>
<td>30</td>
<td>36 to 72</td>
</tr>
<tr>
<td>Betamethasone</td>
<td>0.6</td>
<td>30</td>
<td>36 to 72</td>
</tr>
<tr>
<td>Mineralocorticoids</td>
<td></td>
<td>Not used for an anti-inflammatory effect</td>
<td>12 to 16</td>
</tr>
</tbody>
</table>

The mineralocorticoid effect of commonly administered glucocorticoids may be estimated as follows:
- 20 mg hydrocortisone provides a mineralocorticoid effect that is approximately equivalent to 0.1 mg fludrocortisone.
- 25 mg of cortisone acetate provides a mineralocorticoid effect that is approximately equivalent to 0.1 mg fludrocortisone.
- Prednisone or prednisolone given at anti-inflammatory doses 250 mg per day provide a mineralocorticoid effect that is approximately equivalent to 0.1 mg of fludrocortisone.
- When given at replacement doses, the other glucocorticoids listed in this table have minimal or no clinically relevant mineralocorticoid effect.

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


- Use the lowest glucocorticoid dose that relieves symptoms of glucocorticoid deficiency and avoids signs and symptoms of glucocorticoid excess.

- The dose may be too low if symptoms of apparent glucocorticoid deficiency are present. If, however, increasing the dose does not promptly relieve the symptoms, then they have other causes and the lower steroid dose should be resumed.
• The dose may be too high if excessive weight gain, facial plethora or other symptoms or signs of Cushing's syndrome are present.

• A low normal or suppressed morning plasma adrenocorticotropic hormone (ACTH) concentration indicates excessive glucocorticoid replacement in patients with primary adrenal insufficiency.

Adrenal Crisis

<table>
<thead>
<tr>
<th>Clinical and laboratory findings suggesting adrenal crisis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dehydration, hypotension, or shock out of proportion to severity of current illness</td>
</tr>
<tr>
<td>Nausea and vomiting with a history of weight loss and anorexia</td>
</tr>
<tr>
<td>Abdominal pain, so-called &quot;acute abdomen&quot;</td>
</tr>
<tr>
<td>Unexplained hypoglycemia</td>
</tr>
<tr>
<td>Unexplained fever</td>
</tr>
<tr>
<td>Hyponatremia, hyperkalemia, azotemia, hypercalcemia, or eosinophilia</td>
</tr>
<tr>
<td>Hyperpigmentation or vitiligo</td>
</tr>
<tr>
<td>Other autoimmune endocrine deficiencies, such as hypothyroidism or gonadal failure</td>
</tr>
</tbody>
</table>
# Treatment of acute adrenal insufficiency (adrenal crisis) in adults

## Emergency measures

1. Establish intravenous access with a large-gauge needle.
2. Draw blood for immediate serum electrolytes and glucose and routine measurement of plasma cortisol and ACTH. Do not wait for lab results.
3. Infuse 2 to 3 liters of isotonic saline or 5 percent dextrose in isotonic saline as quickly as possible. Frequent hemodynamic monitoring and measurement of serum electrolytes should be performed to avoid iatrogenic fluid overload.
4. Give 4 mg dexamethasone as intravenous bolus over one to five minutes and every 12 hours thereafter. Dexamethasone is the drug of choice because it does not interfere with the measurement of plasma cortisol. If dexamethasone is unavailable, intravenous hydrocortisone, 100 mg immediately and every six hours thereafter, may be used.
5. Use supportive measures as needed.*

## Subacute measures after stabilization of the patient

1. Continue intravenous isotonic saline at a slower rate for next 24 to 48 hours.
2. Search for and treat possible infectious precipitating causes of the adrenal crisis.
3. Perform a short ACTH stimulation test to confirm the diagnosis of adrenal insufficiency if patient does not have known adrenal insufficiency.
4. Determine the type of adrenal insufficiency and its cause if not already known.
5. Taper parenteral glucocorticoid over one to three days, if precipitating or complicating illness permits, to oral glucocorticoid maintenance dose.
6. Begin mineralocorticoid replacement with fludrocortisone, 0.1 mg by mouth daily, when saline infusion is stopped.

* Electrolyte abnormalities may include hypernatremia, hyperkalaemia or rarely hypercalcemia. Hypernatremia is rapidly corrected by cortisol and volume repletion.

## Treatment of minor febrile illness or stress

Increase glucocorticoid dose two- to threefold for the few days of illness. Do not change mineralocorticoid dose. Patient is instructed to contact clinician if illness worsens or persists for more than three days. No extra supplementation is needed for most uncomplicated, outpatient dental procedures under local anesthesia.

Glucocorticoid supplement for surgical stress:

- Minor (e.g., herniorrhaphy): hydrocortisone 25 mg IV (or equivalent) on day of procedure
- Moderate (e.g., orthopedic surgery): hydrocortisone 50 to 75 mg IV (or equivalent) on day of surgery and postoperative day 1
- Major (e.g., cardiac bypass): hydrocortisone 100 to 150 mg IV (or equivalent) in two or three divided doses on day of surgery and postoperative days 1 and 2

Then return to usual daily glucocorticoid dose.

## Emergency treatment of severe stress or trauma

Each patient should have an injectable glucocorticoid (e.g., 4 mg vials of dexamethasone or 100 mg vials of hydrocortisone) and vials of sterile 0.9% normal saline and syringes.

Instruct patient/caregivers on how to reconstitute the vial and to inject entire dose intramuscularly or subcutaneously in event of severe stress or trauma and get medical help immediately after injection.
• Treatment of patients who present in possible adrenal crisis should not be delayed while diagnostic tests are performed. Blood for serum cortisol, adrenocorticotropic hormone (ACTH), aldosterone, renin, and serum chemistry should be drawn and therapy initiated immediately.

• In contrast to glucocorticoid replacement, mineralocorticoid replacement is not necessary acutely because it takes several days for its sodium-retaining effects to appear, and adequate sodium replacement can be achieved by IV saline alone.

• After the initial bolus, hydrocortisone 50 mg IV bolus is administered every eight hours until stabilization of vital signs and capacity to eat and take medication orally.

• Unless there is a major complicating illness, parenteral glucocorticoid therapy can be tapered over one to three days and changed to an oral stress or maintenance dose.

• After initial treatment, the precipitating cause of the adrenal crisis (as an example, bacterial infection, and viral gastroenteritis) should be sought and appropriately treated.

References:


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