
بسم الله الرحمن الرحیم

Endocrine shock

Dr zahra mazloum khorasani

Endocrinologist

Mashhad University Of Medical Sciences

1401

INTRODUCTION

Shock is a life-threatening condition of circulatory failure, causing inadequate oxygen delivery to meet cellular metabolic needs and oxygen consumption requirements, producing cellular and tissue hypoxia.

Endocrine shock

- ***Addisonian crisis (adrenal failure due to mineralocorticoid deficiency)***
- ***Myxedema***
- ***Thyrotoxicosis***
- ***Pheochromocytoma (rare)***

- →can be associated with hypotension and states of shock..

- **Addison** :
- In states of mineralocorticoid deficiency
- vasodilatation can occur due to altered vascular tone and aldosterone-deficiency-mediated hypovolemia
- **Secondary adrenal insufficiency:**
- Hypotension

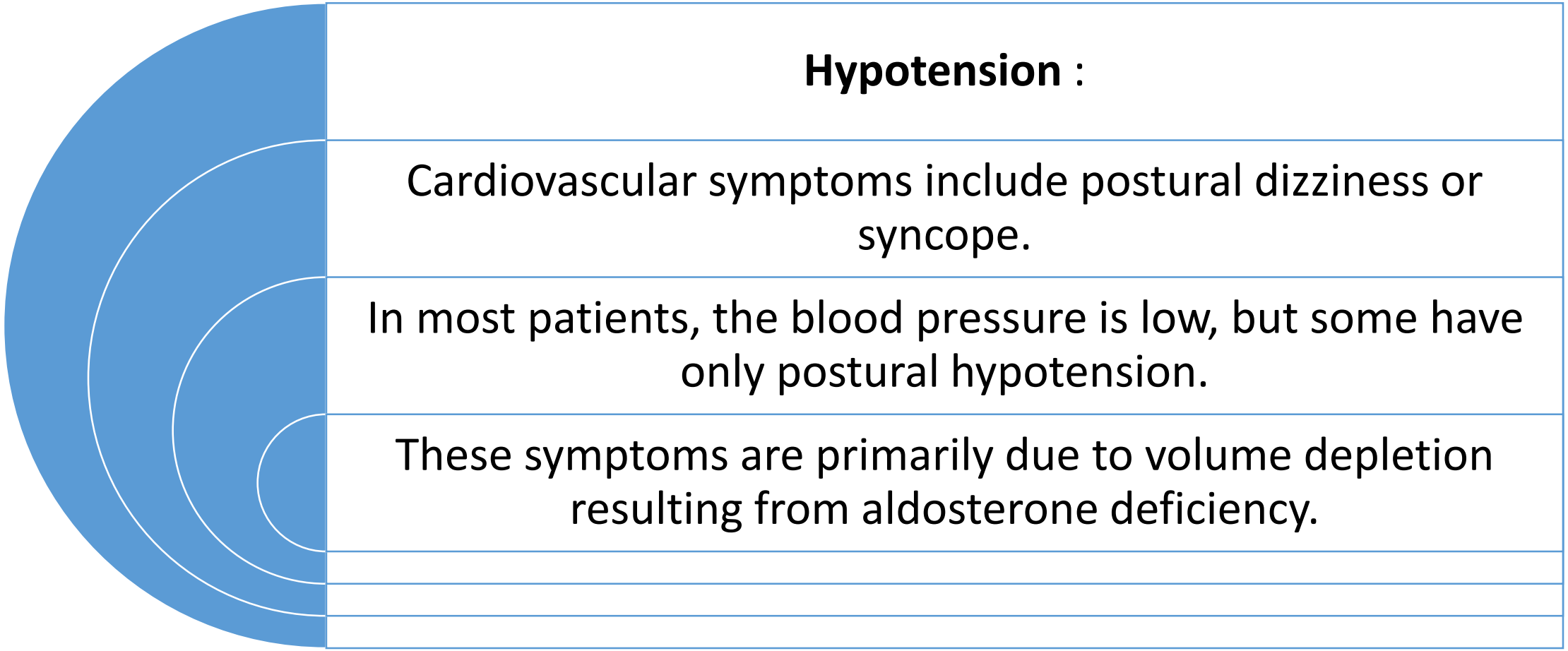
- **Myxedema coma:**
- Exact mechanism of vasodilation in patients with myxedema is unclear???
- Concurrent myocardial depression
- Pericardial effusions likely contribute to hypotension and shock in this population

Hypothyroidism

- ✓**Cardiovascular abnormalities** :
- ✓diastolic hypertension
- ✓narrowed pulse pressure
- ✓bradycardia
- ✓decreased myocardial contractility
- ✓low cardiac output
- ✓***Sometimes hypotension :***
- ✓Pericardial effusion
- ✓ventricular function is rarely compromised.
- ✓All of the cardiac abnormalities are reversible with thyroid hormone therapy

CLINICAL PRESENTATION

- ***Tamponade***
- pericardial effusions are often discovered incidentally during evaluation of other cardiopulmonary diseases.
- patients with a hemodynamically significant pericardial effusion leading to cardiac tamponade usually present with signs and symptoms related to impaired cardiac function (ie, fatigue, dyspnea, elevated jugular venous pressure, edema).


Hypotension :
Cardiovascular symptoms include postural dizziness or syncope.
In most patients, the blood pressure is low, but some have only postural hypotension.
These symptoms are primarily due to volume depletion resulting from aldosterone deficiency.

- Laboratory evaluation
- If the diagnosis of myxedema coma is suspected, a blood sample should be drawn prior to treatment for measurement of:
- ●TSH
- ●Free thyroxine (T4)
- ●Cortisol

Clinical features of myxedema coma

Decreased mental status
Hypothermia
Bradycardia
Hyponatremia
Hypoglycemia
Hypotension
Precipitating illness

Graphic 54836 Version 1.0

Treatment of myxedema coma

Draw serum for T4, TSH, and cortisol.
Administer levothyroxine 200 to 400 mcg intravenously, followed by daily doses of 50 to 100 mcg, and triiodothyronine 5 to 20 mcg intravenously, followed by 2.5 to 10 mcg every eight hours.*
Change to an appropriate oral dose of levothyroxine when the patient can tolerate oral medications. (Oral dose is approximately the intravenous dose divided by 0.75).
Hydrocortisone 100 mg intravenously every eight hours until exclusion of possible adrenal insufficiency.
Supportive measures:
Mechanical ventilation
Fluids and vasopressor drugs to correct hypotension
Passive rewarming
Intravenous dextrose
Consider empirical antibiotic treatment
Monitor for arrhythmias and treat when indicated

T4: thyroxine; TSH: thyroid-stimulating hormone.

* The lower end of the dose ranges is preferred in lower weight and

Thyrotoxicosis

- Usually high-output cardiac failure and do not develop shock per se.
- with progression → left ventricular systolic dysfunction
  →tachyarrhythmia →leading to hypotension

- **Heart failure** :
- Heart failure is most commonly seen as a result of longstanding, often untreated disease with coexistent atrial fibrillation.
- Heart failure in the absence of underlying cardiac disease or arrhythmia is thought to reflect a rate-related cardiomyopathy

- **Pulmonary hypertension** :
- PH has been reported with increasing frequency in patients with overt hyperthyroidism.
- Pulmonary artery pressures average twice normal values (10 mmHg) and may be as high as 30 to 50 mmHg.
- These changes reverse with treatment of the hyperthyroidism .

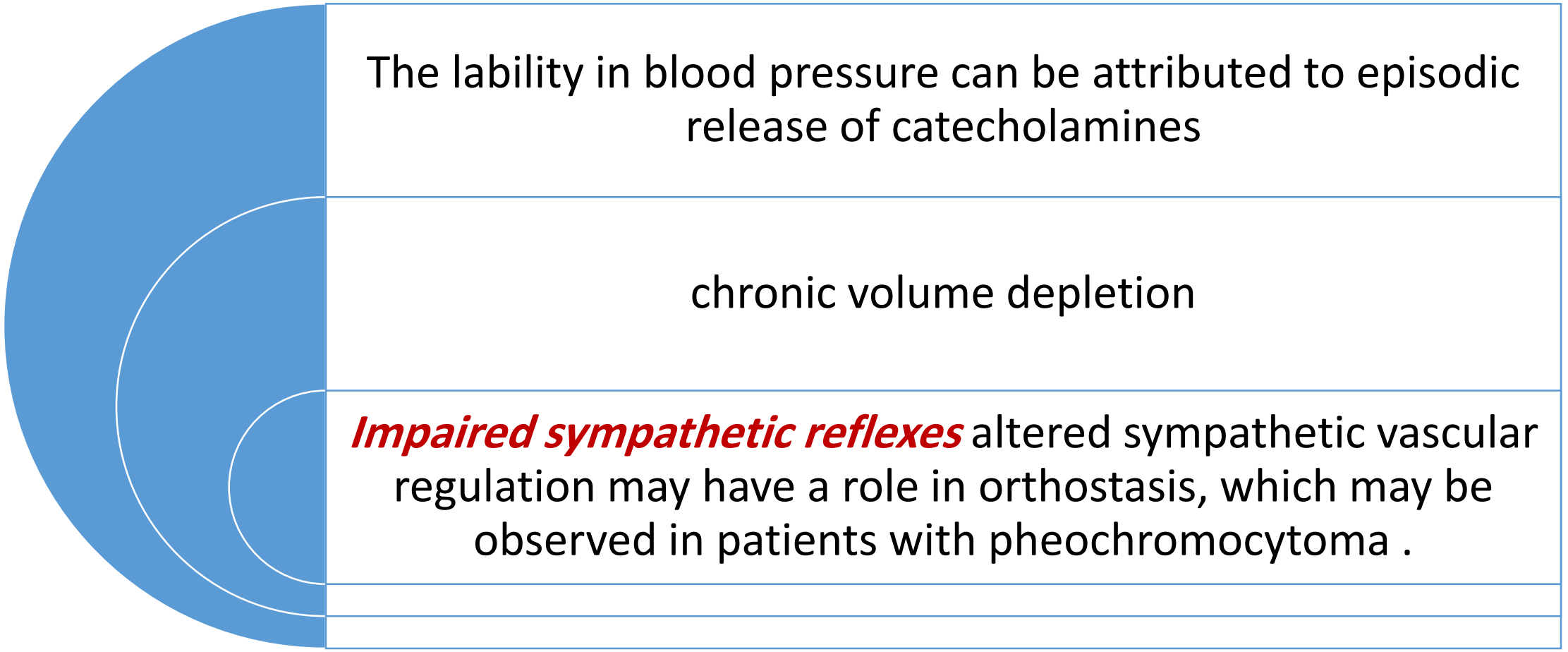
- **Thyrotoxic crisis, or thyroid storm, is rare and presents as a life-threatening exacerbation of hyperthyroidism, accompanied by fever, delirium, seizures, coma, vomiting, diarrhea, and jaundice**

Thyroid storm management

- Large doses of *propylthiouracil* (500–1000 mg loading dose and 250 mg every 4 h)
- If not available, *methimazole* can be used in doses of 20 mg every 6 h.
- One hour after the first dose of propylthiouracil , *stable iodide* (5 drops SSKI every 6 h) is given to block thyroid hormone synthesis via the Wolf-Chaikof effect
- *Propranolol* should also be given to reduce tachycardia and other adrenergic manifestations (60–80 mg PO every 4 h; or 2 mg IV every4 h)

- Additional therapeutic measures include *glucocorticoids* (e.g., hydrocortisone 300 mg IV bolus, then 100 mg every 8 h)
- Antibiotics if infection is present
- Cholestyramine to sequester thyroid hormones
- Cooling
- Oxygen
- IV fluids

Pheochromocytoma (rare)

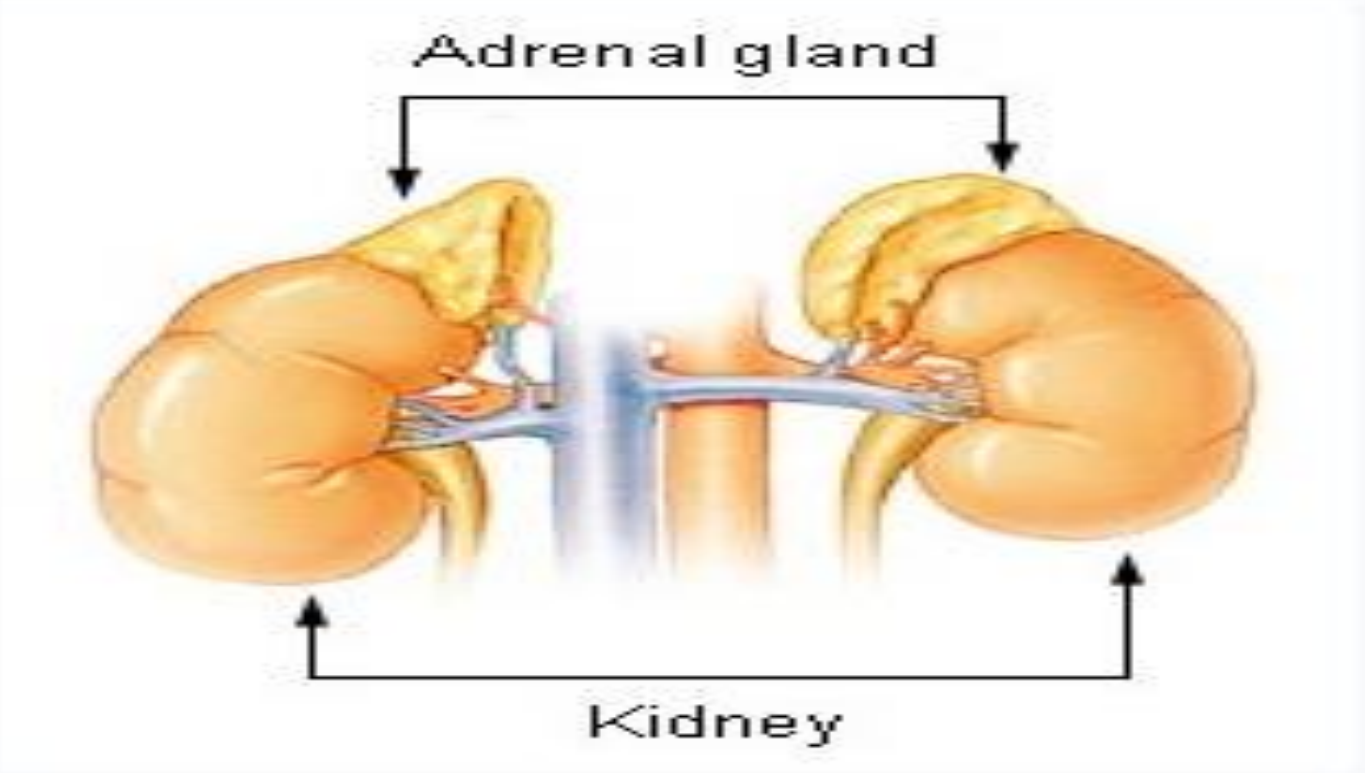


Pheochromocytoma (rare)

Symptoms of orthostatic hypotension (e.g., lightheadedness, presyncope, syncope) may dominate the presentation, especially in patients ***with epinephrine-predominant or dopamine-predominant tumors***

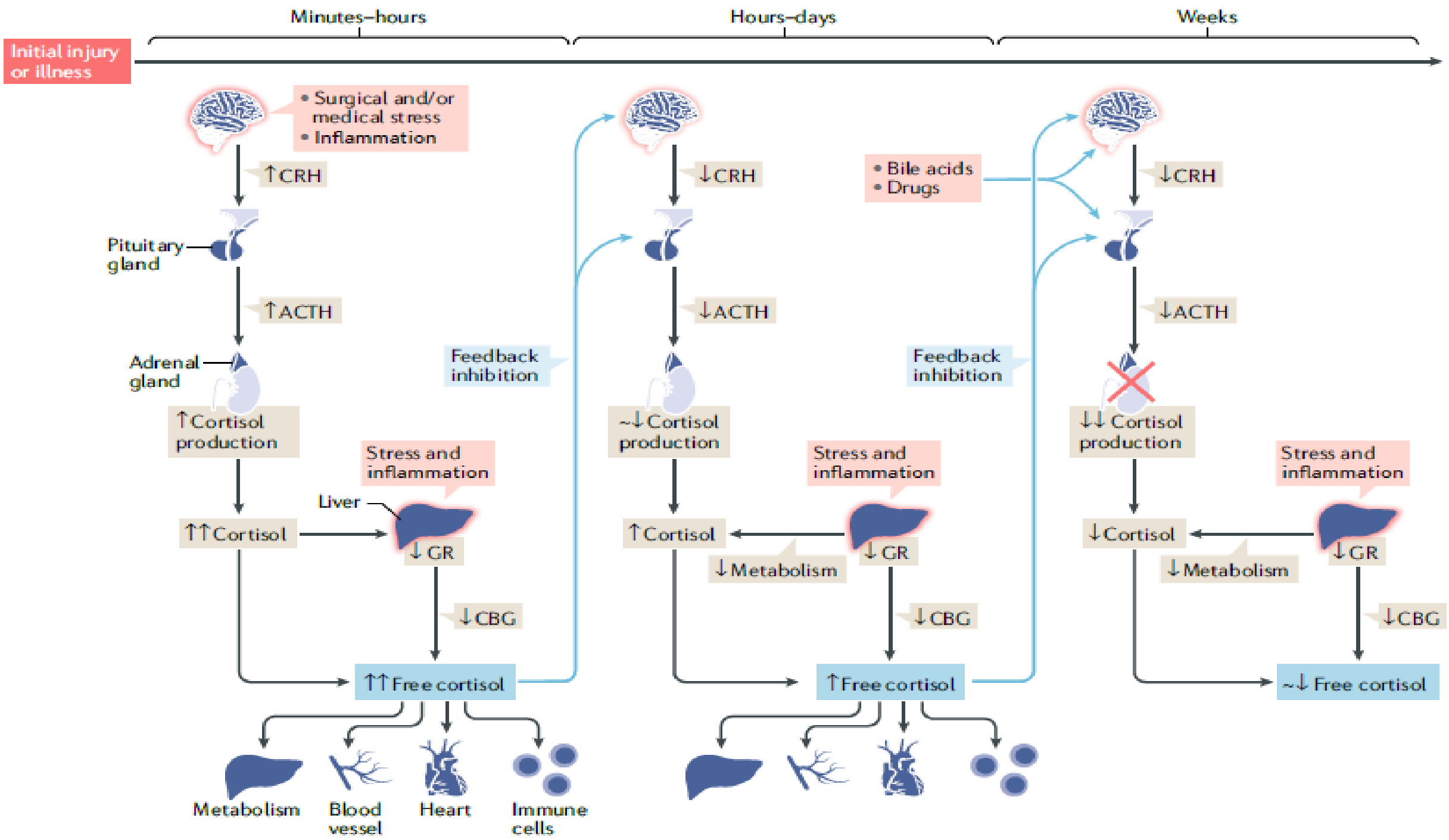
Adrenal insufficiency

Adrenal insufficiency

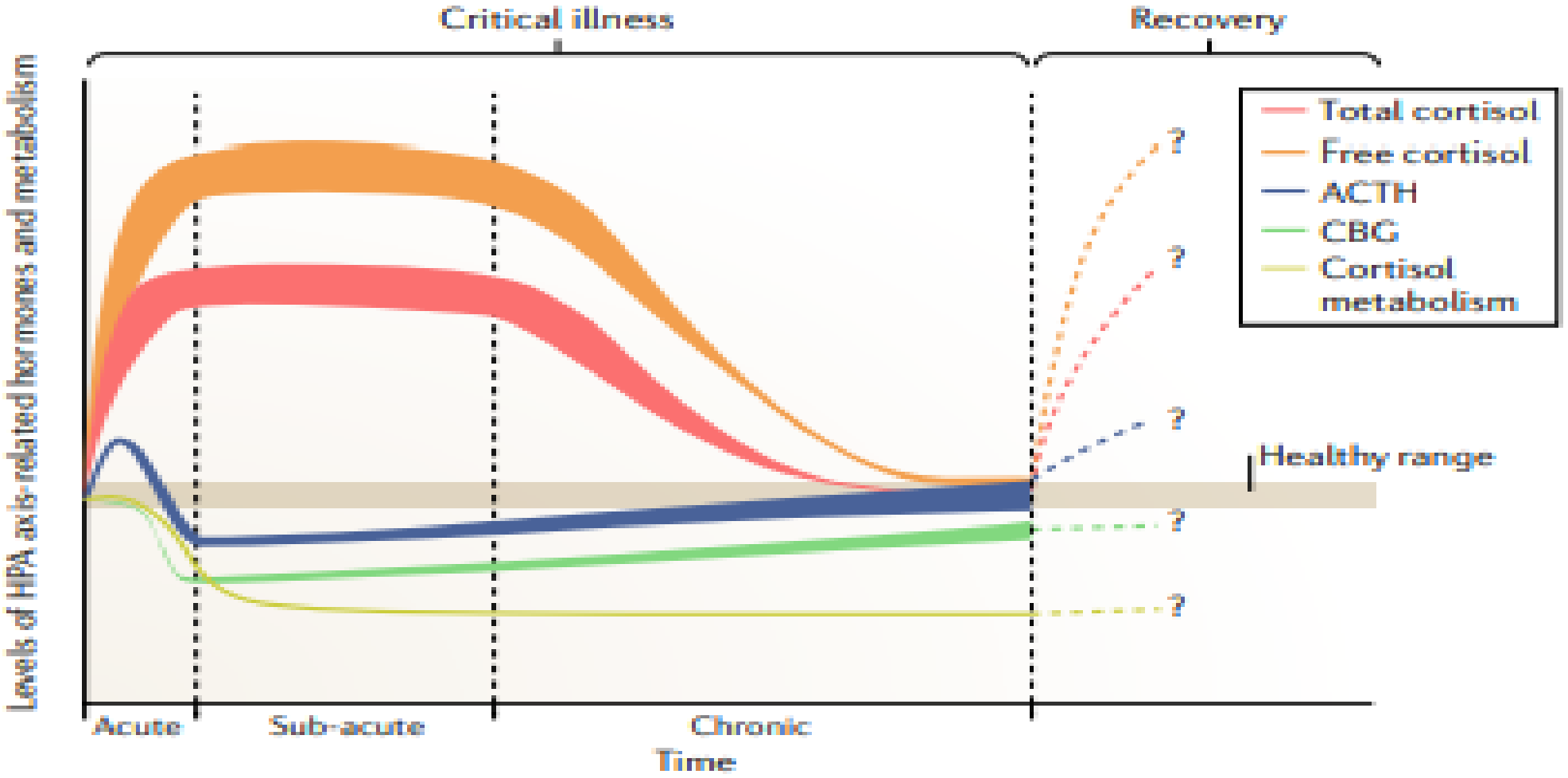


Adrenal gland

Source of pathology	CRH	ACTH	DHEA	DHEA-S	cortisol	aldosterone	renin	Na	K	Causes[5]
hypothalamus (tertiary)[1]	low	low	low	low	low[3]	low	low	low	low	tumor of the hypothalamus (adenoma), antibodies, environment (i.e. toxins), head injury
pituitary (secondary)	high[2]	low	low	low	low[3]	normal	low	low	normal	tumor of the pituitary (adenoma), antibodies, environment, head injury, **surgical removal**[6], Sheehan's syndrome
adrenal glands (primary)[7]	high	high	high	high	low[4]	low	high	low	high	tumor of the adrenal (adenoma), stress, antibodies, environment, Addison's disease, trauma, surgical removal (resection), miliary tuberculosis of the adrenal


Minutes–hours
Hours–days
Weeks
Initial injury or illness
• Surgical and/or medical stress
• Inflammation
↑CRH
Pituitary gland
↑ACTH
Adrenal gland
↑Cortisol production
↑↑Cortisol
Liver
Stress and inflammation
↓GR
↓CBG
↑↑Free cortisol
Feedback inhibition
↓CRH
↓ACTH
~↓Cortisol production
↑Cortisol
↓Metabolism
↑Free cortisol
• Bile acids
• Drugs
↓↓Cortisol production
↓Cortisol
~↓Free cortisol
Metabolism
Blood vessel
Heart
Immune cells

Time-dependent and dose-dependent changes in plasma concentrations of key components during critical illness



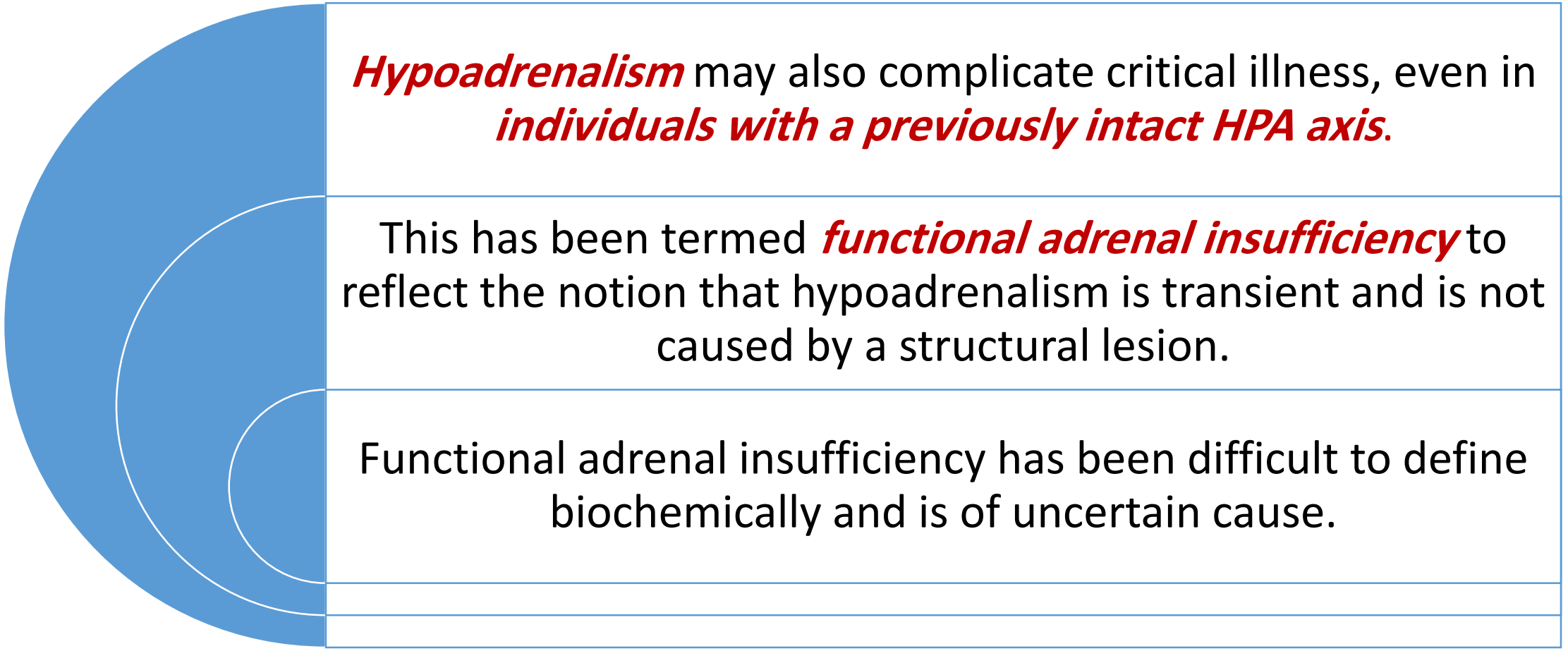
Box 1 | Commonly used intensive care unit-related terms and definitions

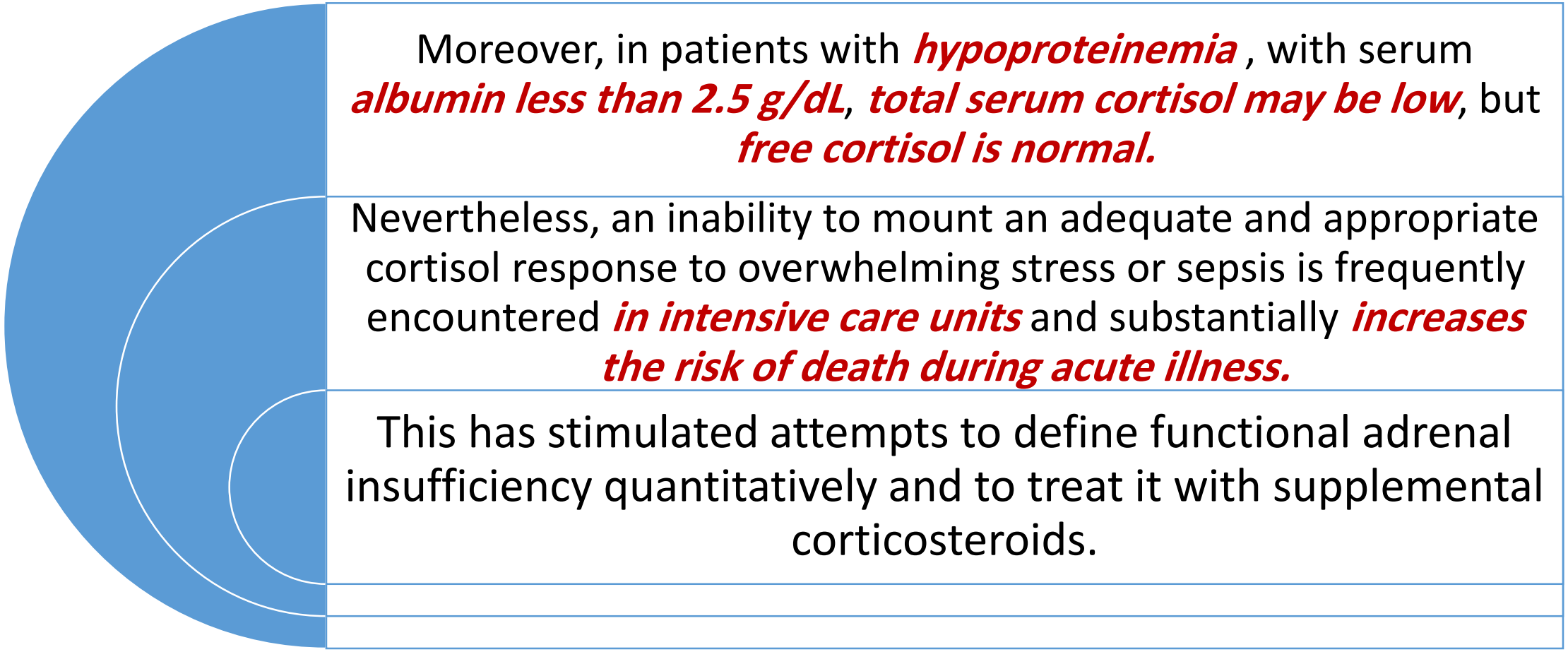
- Hyperinflammation: this is an updated term for the state of inflammation in critically ill patients that was previously defined by the systemic inflammatory response syndrome criteria[128].
- Sepsis*: this is defined as life-threatening organ dysfunction, which is caused by a dysregulated host immune response to infection. Sepsis is diagnosed when a patient has an increase in the sequential (sepsis-related) organ failure assessment[129] score of >2 points; such an increase is associated with an in-hospital mortality of >10%.
- Septic shock*: this is defined as a condition that develops in patients with sepsis, in which profound circulatory, cellular and metabolic abnormalities are associated with a greater risk of death than that from sepsis alone. Septic shock is present when there is a vasopressor requirement to maintain a mean arterial pressure of ≥65 mmHg and serum lactate level of >2 mmol/l (>18 mg/dl) in the absence of hypovolaemia. Septic shock is associated with an in-hospital mortality of >10%.

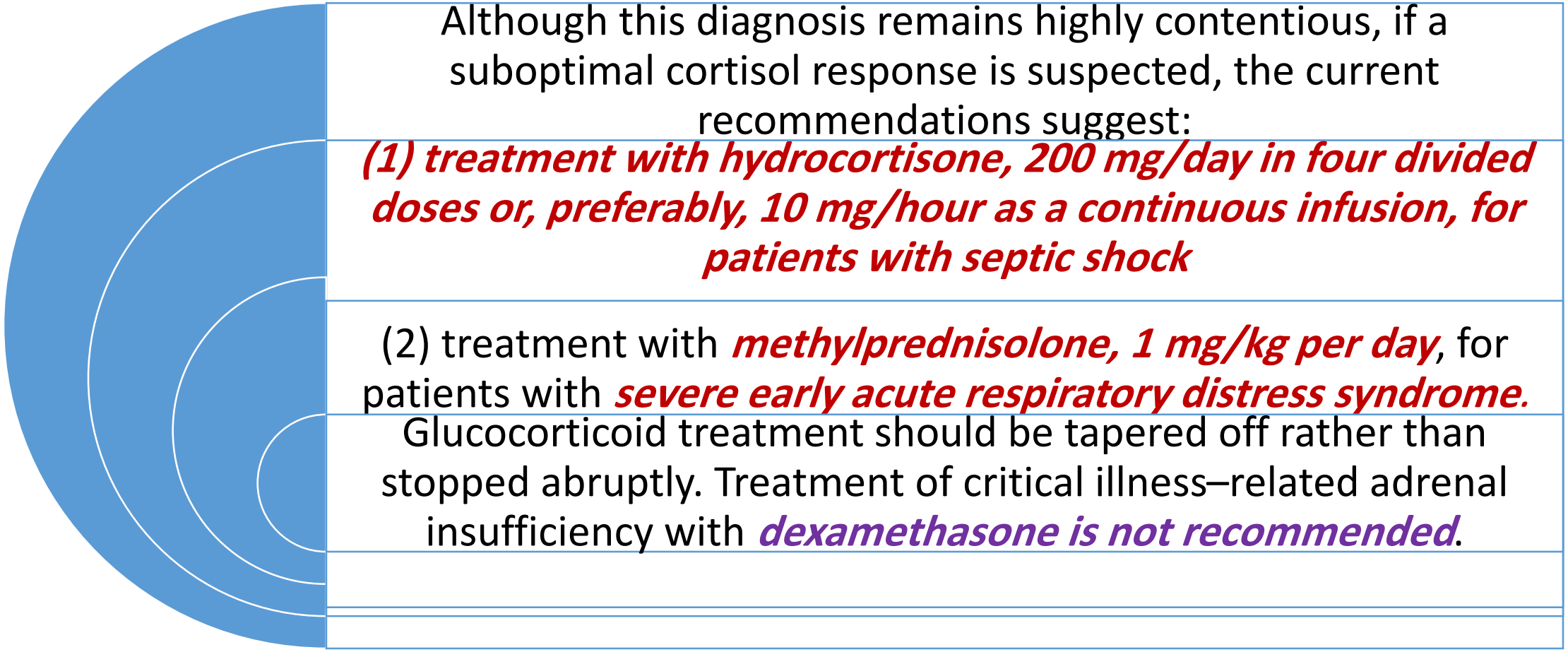
*Definitions of both sepsis and septic shock were updated in 2016 in the 'The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3)'[130].

Adrenal function and dysfunction in critically ill patients
*Arno Téblick , Bram Peeters, Lies Langouche and Greet Van den Berghe **
Nature Reviews | **Endocrinology**
2020

Hypoadrenalism During Critical Illness




Moreover, in patients with hypoproteinemia , with serum albumin less than 2.5 g/dL, total serum cortisol may be low, but free cortisol is normal.
Nevertheless, an inability to mount an adequate and appropriate cortisol response to overwhelming stress or sepsis is frequently encountered in intensive care units and substantially increases the risk of death during acute illness.
This has stimulated attempts to define functional adrenal insufficiency quantitatively and to treat it with supplemental corticosteroids.


Although this diagnosis remains highly contentious, if a suboptimal cortisol response is suspected, the current recommendations suggest:
(1) treatment with hydrocortisone, 200 mg/day in four divided doses or, preferably, 10 mg/hour as a continuous infusion, for patients with septic shock
(2) treatment with methylprednisolone, 1 mg/kg per day, for patients with severe early acute respiratory distress syndrome.
Glucocorticoid treatment should be tapered off rather than stopped abruptly. Treatment of critical illness–related adrenal insufficiency with dexamethasone is not recommended.

Box 2 | Contradicting guidelines and our proposed novel conceptual framework

- Surviving sepsis campaign[131] (2016) guidelines advise against using intravenous hydrocortisone to treat patients with septic shock if adequate fluid resuscitation and vasopressor therapy are able to restore haemodynamic stability. If this is not achievable, 200 mg of intravenous hydrocortisone per day is suggested (weak recommendation and low quality of evidence).
- Critical-illness-related corticosteroid insufficiency guidelines[14] (2017) suggest using up to 400 mg of hydrocortisone per day in patients with septic shock that is not responsive to fluids and who require moderate-dose to high-dose vasopressor therapy (conditional recommendation, low quality of evidence).
- Our proposed novel conceptual framework suggests that the proposed doses of intravenous hydrocortisone (200–400 mg per day) do not take the suppressed cortisol metabolism during critical illness into account and may therefore be too high. In addition, the administration of such high doses of hydrocortisone to patients with septic shock does not bring about the expected mortality benefit and may have long-term adverse events.

Adrenal function and dysfunction in critically ill patients
*Arno Téblick , Bram Peeters, Lies Langouche and Greet Van den Berghe **
Nature Reviews | **Endocrinology,2020**

Key points

- The amount of cortisol that is produced by patients during critical illness is not much higher, if at all, than that produced when healthy.
- Increased systemic cortisol availability during critical illness is largely driven by decreased cortisol-binding proteins in the circulation, by the reduced binding affinity of these proteins and by suppressed cortisol breakdown.
- Circulating free cortisol that is elevated via such peripheral mechanisms may partially explain why adrenocorticotropic hormone (ACTH) levels are low in patients with critical illness, owing to feedback inhibition.
- Low ACTH levels that are present for an extended period of time may negatively affect adrenocortical integrity and function.

Adrenal function and dysfunction in critically ill patients

*Arno Téblick , Bram Peeters, Lies Langouche and Greet Van den Berghe **

Nature Reviews **| Endocrinology**

2020

- An ACTH stimulation test is invalid for assessing adrenocortical integrity and function in critically ill patients, as the test results are confounded by the increased cortisol distribution volume.
- Doses of hydrocortisone currently advised for treating critically ill patients do not take the substantially increased half-life of cortisol into account, are thus likely too high and may further increase central adrenocortical suppression via feedback inhibition.
- Future research should focus on patients who are critically ill for an extended period, on patients who may be at risk of developing central hypoadrenalism and on novel strategies to prevent and treat this complication.

Adrenal function and dysfunction in critically ill patients
*Arno Téblick , Bram Peeters, Lies Langouche and Greet Van den Berghe **
Nature Reviews **| Endocrinology**
2020

Hypothyroidism and Adrenal Insufficiency in Sepsis and Hemorrhagic Shock

Hao Chih Ho, MD; Alyssa D. Chapital, MD; Mihae Yu, MD

Hypothesis: We hypothesized that hypothyroidism and adrenal insufficiency frequently occur together in critically ill patients.

Design: A prospective observational study.

Setting: Surgical intensive care unit of a university-affiliated tertiary referral center.

Patients: Sixty-six consecutive patients with severe sepsis, septic shock, and hemorrhagic shock who required pulmonary artery catheterization for resuscitation were studied.

Interventions: Thyrotropin and baseline cortisol levels were obtained at 3 AM followed by intravenous injection of 250 µg of cosyntropin, a synthetic adrenocorticotropic hormone derivative. A second measurement of the cortisol level was performed 1 hour later.

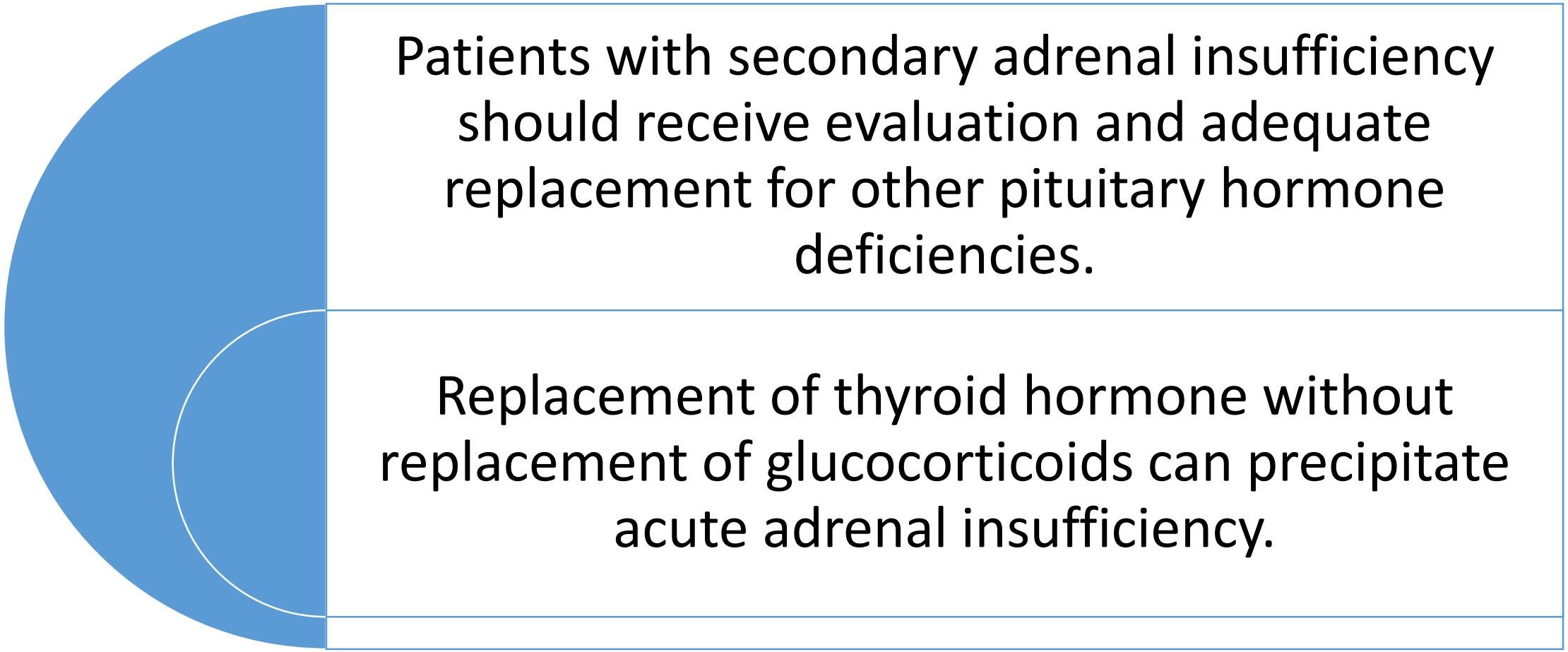
Main Outcome Measures: Incidence of hypothyroidism and adrenal insufficiency and mortality.

Results: Mean (SD) age was 62 (19) years. The mean (SD) Acute Physiology and Chronic Health Evaluation II score was 21 (5). Twenty-seven patients (40.9%) had severe sepsis, 31 (46.9%) had septic shock, and 8 (12.1%) had hemorrhagic shock. Five patients (7.6%) had hypothyroidism alone and 35 (53.0%) had only adrenal insufficiency. Eight patients (12.1%) had both hypothyroidism and adrenal insufficiency. All patients with endocrine abnormalities were treated. Mortality for the total group was 15 (22.7%) of 66 patients.

Conclusion: There is a 12% incidence of simultaneous hypothyroidism and adrenal insufficiency in our study and the routine testing for both may be indicated in this population of critically ill patients.

Arch Surg. 2004;139:1199-1203

Considerations in secondary adrenal insufficiency



Considerations in secondary adrenal insufficiency

- Patients with hypopituitarism who have partial or total ACTH deficiency and are receiving suboptimal cortisol or cortisone replacement may be at risk of developing symptoms of cortisol deficiency when growth hormone therapy is initiated. This is due to the ***inhibitory effect of growth hormone on 11-betahydroxysteroid dehydrogenase type 1***, the enzyme that converts cortisone to cortisol.

TABLE 15.19 Clinical and Laboratory Features of an Adrenal Crisis

Dehydration, hypotension, or shock out of proportion to severity of current illness
Nausea and vomiting with a history of weight loss and anorexia
Abdominal pain, so-called acute abdomen
Unexplained hypoglycemia
Unexplained fever
Hyponatremia, hyperkalemia, azotemia, hypercalcemia, or eosinophilia
Hyperpigmentation or vitiligo
Other autoimmune endocrine deficiencies, such as hypothyroidism or gonadal failure

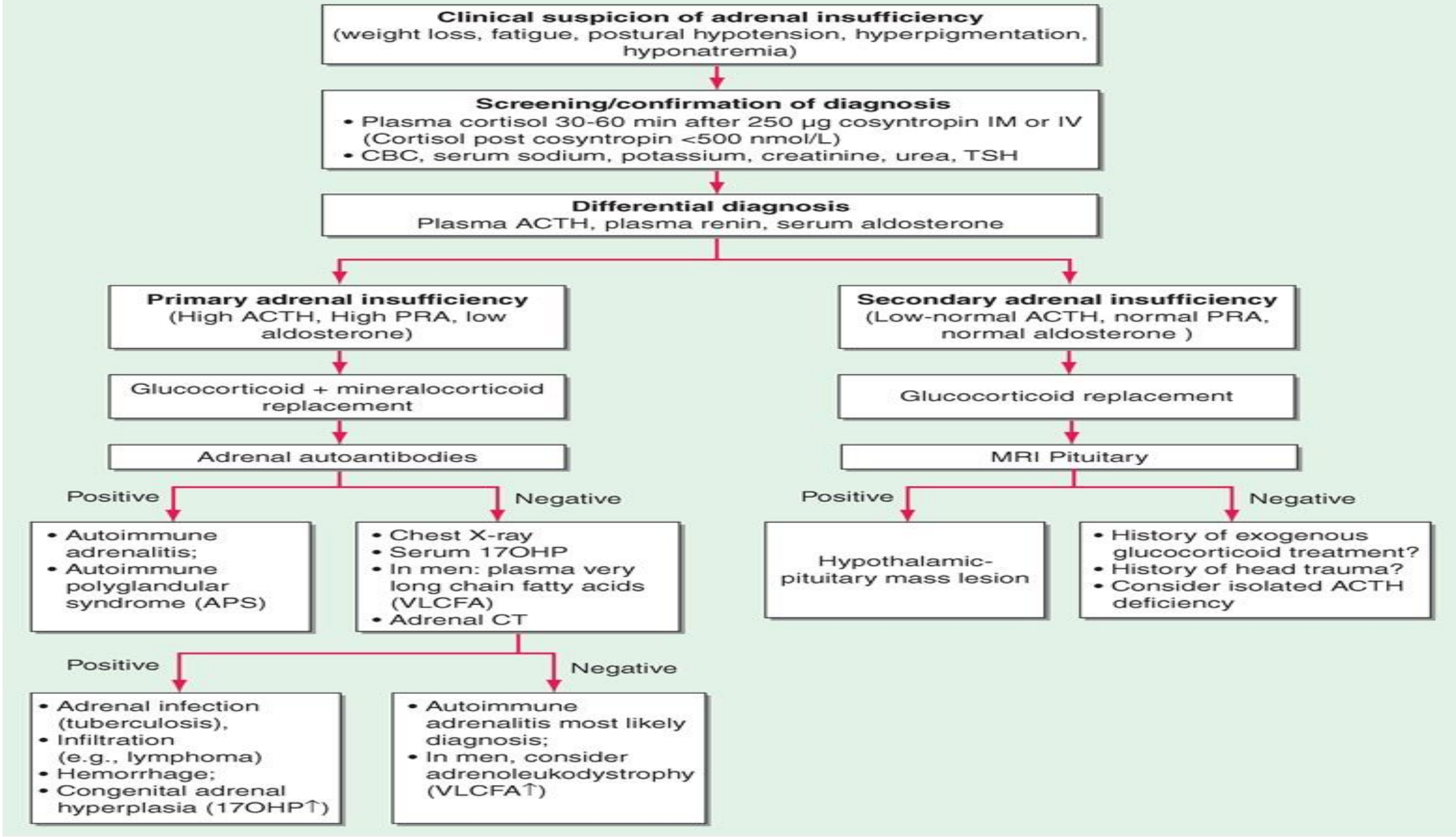
TABLE 15.17 Suggested Plan for Steroid Replacement in Patients Withdrawing From Chronic Corticosteroid Therapy

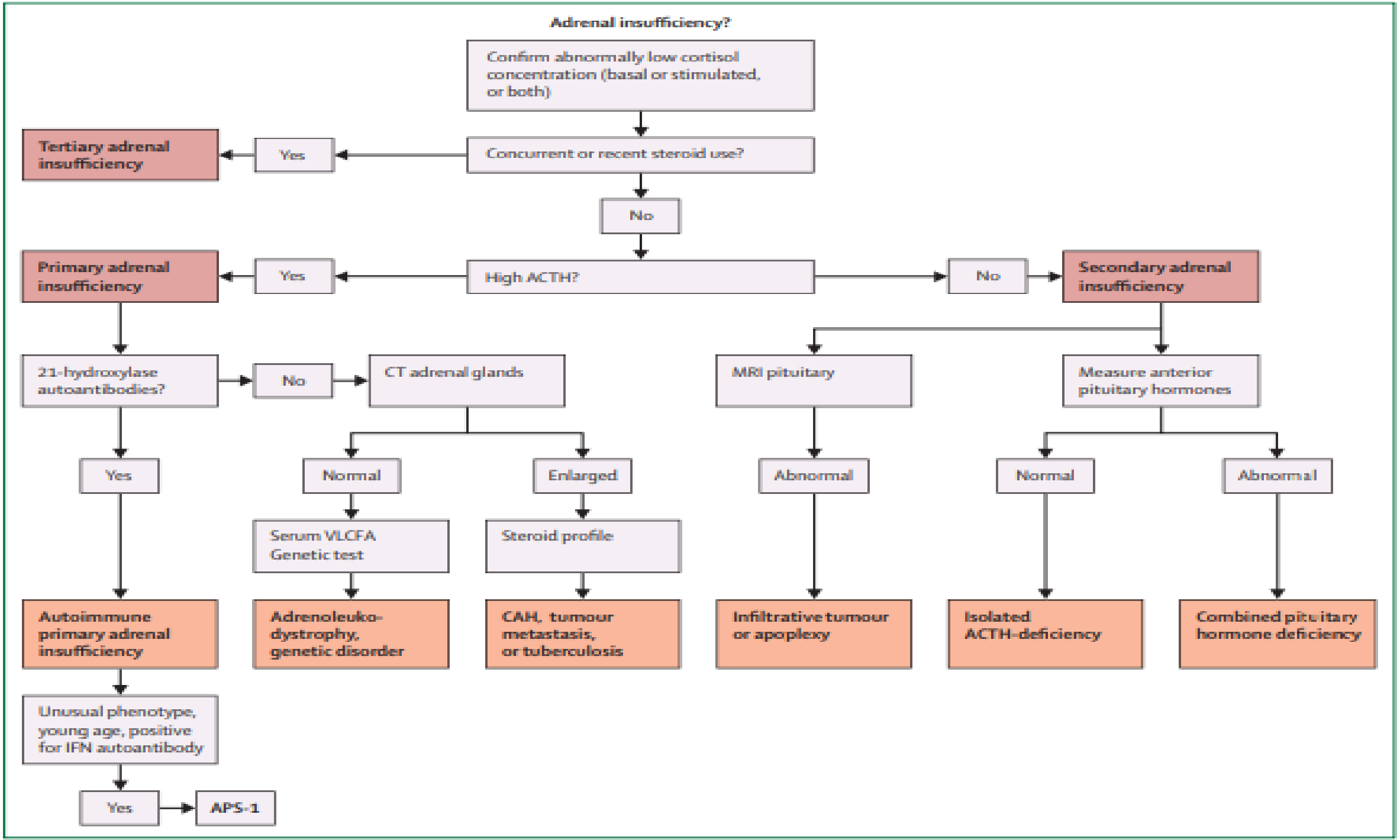
	DURATION OF GLUCOCORTICOID TREATMENT			
Pred Dose (mg/day)	≤3 wk[a]		>3 wk	
≥7.5	Can stop	↓ rapidly (e.g., 2.5 mg q3-4d)		
		THEN		
5–7.5	Can stop	↓ 1 mg q2-4 wk	OR	Convert 5 mg pred to 20 mg HC, then ↓ 2.5 mg/wk to 10 mg/day
		THEN		THEN
<5	Can stop	↓ 1 mg q2-4 wk		After 2-3 mo HC 10 mg/day, administer SST/ITT: Pass → Withdraw Fail → Continue

[a]Beware of frequent steroid courses (e.g., in asthma).

HC, Hydrocortisone; *ITT*, insulin tolerance test; *pred*, prednisolone; *SST*, short synacthen test. Basal 0900h ACTH can be used to monitor for recovery of HPA axis and levels may be above the normal range ahead of a "pass" on an SST.

Algorithm for the Management of the Patient with Suspected Adrenal Insufficiency




Adrenal insufficiency?
Confirm abnormally low cortisol concentration (basal or stimulated, or both)
Concurrent or recent steroid use?
Yes
Tertiary adrenal insufficiency
No
High ACTH?
Yes
Primary adrenal insufficiency
No
Secondary adrenal insufficiency
21-hydroxylase autoantibodies?
Yes
No
CT adrenal glands
Normal
Enlarged
Serum VLCFA
Genetic test
Steroid profile
Autoimmune primary adrenal insufficiency
Adrenoleuko-dystrophy, genetic disorder
CAH, tumour metastasis, or tuberculosis
Unusual phenotype, young age, positive for IFN autoantibody
Yes
APS-1
MRI pituitary
Abnormal
Infiltrative tumour or apoplexy
Measure anterior pituitary hormones
Normal
Abnormal
Isolated ACTH-deficiency
Combined pituitary hormone deficiency

Treatment: Acute Adrenal Insufficiency

TABLE 15.20 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 laboratory results.
3. Infuse 2–3 L of 154 mmol/L NaCl (0.9% saline) solution, or 50 g/L (5%) dextrose in 154 mmol/L NaCl (0.9% saline) solution, as quickly as possible. Monitor for signs of fluid overload by measuring central or peripheral venous pressure and listening for pulmonary rales. Reduce infusion rate if indicated.
4. Inject intravenous hydrocortisone (100 mg immediately and every 6 hours).
5. Use supportive measures as needed.

Subacute Measures After Stabilization of the Patient

1. Continue intravenous 154 mmol/L NaCl (0.9% saline) solution at a slower rate for next 24–48 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 glucocorticoids to maintenance dosage over 1–3 days, if precipitating or complicating illness permits.
6. Begin mineralocorticoid replacement with fludrocortisone (0.1 mg by mouth daily) when saline infusion is stopped.

TABLE 15.21 Treatment of Chronic Primary Adrenal Insufficiency In Adults

Maintenance Therapy

Glucocorticoid Replacement

- Hydrocortisone 15–20 mg on awakening and 5–10 mg in early afternoon
- Monitor clinical symptoms and morning plasma ACTH.

Mineralocorticoid Replacement

- Fludrocortisone 0.1 (0.05–0.4) mg orally
- Liberal salt intake
- Monitor lying and standing blood pressure and pulse, edema, serum potassium, and plasma renin activity.
- Educate patient about the disease, how to manage minor illnesses and major stresses, and how to inject steroid intramuscularly.
- Obtain MedicAlert bracelet/necklace, Emergency Medical Information card.

Treatment of Minor Febrile Illness or Stress

- Increase glucocorticoid dose twofold to threefold for the few days of illness; do not change mineralocorticoid dose.
- Contact physician if illness worsens or persists for more than 3 days or if vomiting develops.
- No extra supplementation is needed for most uncomplicated, outpatient dental procedures with local anesthesia. General anesthesia or intravenous sedation should not be used in the office.

Emergency Treatment of Severe Stress or Trauma

- Inject contents of prefilled dexamethasone (4-mg) syringe or contents of hydrocortisone hemisuccinate rapid reconstitution vial (100-mg) intramuscularly.
- Get to physician as quickly as possible.

Steroid Coverage for Illness or Surgery in Hospital

- For moderate illness, give hydrocortisone 50 mg bid PO or IV. Taper rapidly to maintenance dose as patient recovers.
- For severe illness, give hydrocortisone 100 mg IV q8h. Taper to maintenance level by decreasing by half every day. Adjust dose according to course of illness.
- For minor procedures under local anesthesia and most radiologic studies, no extra supplementation is needed.
- For moderately stressful procedures such as barium enema, endoscopy, or arteriography, give a single 100-mg IV dose of hydrocortisone just before the procedure.
- For major surgery, give hydrocortisone 100 mg IV just before induction of anesthesia and continue q8h for first 24 hours. Taper dose rapidly, decreasing by half per day, to maintenance level.

Take home message:

- ***Endocrine shock : Addisonian crisis ,myxedema ,Thyrotoxicosis, Pheochromocytoma (rare)***
- ***Hypoadrenalism During Critical Illness***
- ***Glucocorticoid tapering***
- ***Acute adrenal insufficiency***
- ***Chronic adrenal insufficiency***