Chapter 31
Acute Thyroid and Adrenal Disorders

P.E. Rama Subrahmanyam

Part A – Acute Thyroid Disorders

Key Points

- Adequate understanding of the aetiology and pathophysiology is the key for prompt management of thyroid disorder.
- Thyroid crisis is a decompensated state of thyroid hormone-induced hypermetabolism due to:
  - Excess thyroid hormone synthesis and release
  - Peripheral effects of thyroid hormone
  - Underlying precipitating event
- Myxoedema coma is usually in elderly with undiagnosed or undertreated hypothyroidism.
- Hydrocortisone in thyroid crisis decreases peripheral conversion of T4 to T3 and in myxoedema coma helps to tide over the adrenal insufficiency.
- Management of the precipitating cause is the main supportive treatment in thyroid crisis and myxoedema coma.

Introduction

Acute thyroid disorders are infrequently observed in clinical practice with a poorly defined incidence. They represent a long-standing dysregulation of thyroid gland, usually precipitated by an acute illness. They are either caused by overt dysfunction

P.E.R. Subrahmanyam, MBBS, FAEM, MCEM
Emergency Medicine, Leicester Royal Infirmary, NHS, UK,
15 Old Westbury, Letchworth Garden City, Hertfordshire SG6 3NB, UK
e-mail: sriramdr@gmail.com

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resulting in myxoedema coma or hyperfunctioning of the gland giving rise to thyrotoxicosis. Despite utmost care, mortality remains high, 30–50 % in myxoedema coma and 30–40 % in thyroid storm thereby necessitating immediate and aggressive intervention in emergency department.

Thyroid Storm

Thyroid storm is a condition in which multiple organ dysfunction results from failure of the compensatory mechanisms of the body owing to excessive thyroid hormone activity induced by some factors in patients with thyrotoxicosis. Although rare, it is a life-threatening condition requiring emergency treatment [1–3].

Aetiology of Thyroid Storm

The excess thyroid hormone is released from the thyroid gland as a result of excess thyroid hormone production or by processes that disrupt the follicular structure of the gland with subsequent release of stored hormone. Table 31.1 shows the precipitating factors for thyroid storm.

Pathophysiology of Thyroid Storm

Thyroid hormone influences almost every tissue and organ system in the body. It increases tissue thermogenesis and basal metabolic rate (BMR) and reduces serum cholesterol levels and systemic vascular resistance. Some of the most profound effects of increased thyroid hormone levels are on the cardiovascular system [4], but even then the pathophysiology of thyroid storm is unclear; the hypothesis suggested is an increase in free T_3 concentrations and increase in β-adrenergic receptor activation. In presence of both a larger availability of adrenergic receptors and a reduction of thyroid

Table 31.1 Precipitating factors in thyroid storm

Precipitating factors in thyroid storm
General
Infection, non-thyroidal trauma or surgery, N psychosis, parturition, myocardial infarction or other acute medical problems
Thyroid specific
Radioiodine, high doses of iodine-containing compounds (e.g. radiographic contrast media), discontinuation of antithyroid drug treatment, thyroid injury (palpation, infarction of an adenoma), new institution of amiodarone therapy

hormone binding to TBG (thyroid hormone-binding globulin), the leak of catecholamine provoked by an acute event (i.e. triggering factor) finally precipitates TS. There is usually a precipitating event that sets off the thyroid storm. There is no clear cut-off level for free T_4 or free T_3 to predict severe thyrotoxicosis. What is important is to recognise the severity of thyrotoxicosis and treat the patient appropriately.

Clinical Features

Thyroid storm has now become a rare entity owing to early detection and treatment of thyrotoxicosis.

Thyroid storm presents with:

- An exaggeration of the features of uncomplicated thyrotoxicosis
- An alteration in mental status
- Irreversible cardiovascular collapse and death if proper treatment is not initiated in the emergency department

Cardinal features include:

- Cardiovascular: severe tachycardia, atrial fibrillation, systolic hypertension and congestive heart failure may occur, particularly in the elderly, and most patients have systolic hypertension.
- Fever (usually 38.5 °C).
- Gastrointestinal dysfunction (vomiting, diarrhoea and occasional jaundice).
- Agitation, confusion, delirium or coma.
- Biochemical: hyperglycaemia, leucocytosis, hypocalcaemia and abnormal liver function tests.

Diagnosis of Thyroid Storm

The prerequisite for the diagnosis of thyroid storm is a definite biochemical evidence of thyrotoxicosis along with the scoring system based on the clinical criteria as shown in Table 31.2 [5]. A score between 25 and 44 is suggestive of impending thyroid storm, and a score >44 is suggestive of thyroid storm.

Investigation and Treatment of Thyroid Storm

Prompt recognition and aggressive treatment employing a multifaceted approach are generally effective at correcting the homeostatic decompensation. Routine investigations along with thyroid function tests should be carried out. However, treatment

Table 31.2 The clinical scoring system for diagnosis of thyroid storm

Criteria		Score
Thermoregulatory dysfunction		
Temperature	99–99.9 °F (37.2–37.7 °C)	5
	100–100.9 °F(37.8–38.2 °C)	10
	101–101.9 °F(38.3–38.8 °C)	15
	102–102.9 °F(38.9–39.3 °C)	20
	103–103.9 °F(39.4–39.9 °C)	25
	≥104 °F (40 °C) or higher	30
Central nervous system effects		
Absent		0
Mild agitation		10
Delirium, psychosis, lethargy		20
Seizure or coma		30
Gastrointestinal dysfunction		
Absent		0
Diarrhoea, nausea, vomiting or abdominal pain		10
Unexplained jaundice		20
Cardiovascular dysfunction		
Tachycardia	90–109 beats/min	5
	110–119 beats/min	10
	120–129 beats/min	15
	130–139 beats/min	20
	≥140 beats/min	25
Congestive heart failure	Absent	0
	Mild oedema	5
	Moderate bibasilar rales	10
	Severe pulmonary oedema	15
Atrial fibrillation	Absent	0
	Present	10
History of precipitating event (surgery, infection, etc.)		
Absent		0
Present		10

should be initiated without awaiting the results in clinically suspected cases. Adrenal reserve may be impaired. Infective screening, e.g. urine, chest x-ray, blood cultures and sputum, is essential. ECG should be done to check for arrhythmias.

Thyroid studies: Usually, there is elevated triiodothyronine (T3), thyroxine (T4) and free T4 levels; increased T3 resin uptake; suppressed thyroid-stimulating hormone (TSH) levels; and an elevated 24-h iodine uptake. TSH levels are not suppressed in the rare instances of excess TSH secretion.

The initial stabilisation and management of systemic decompensation are as follows:

- Supplemental oxygen.
- Ventilatory support.

- Intravenous fluids: Dextrose solutions are the preferred intravenous fluids to cope with continuously high metabolic demand.
- Correction of electrolyte abnormalities and cardiac arrhythmia.
- Aggressively control hyperthermia by applying ice packs and cooling blankets and by administering acetaminophen.
- Antiadrenergic drugs (e.g. propranolol) to minimise sympathomimetic symptoms. High doses of β-blocker should be given, and propranolol at a dose of 80–120 mg every 6 h is recommended.

Specific therapy of hyperthyroidism follows several strategies, including:

1. Inhibition of hormone synthesis and release
2. Inhibition of peripheral conversion of T4 to T3
3. Blocking of the systemic effects of excess thyroid hormone

1. Inhibition of thyroid hormone synthesis and release: Inhibition of thyroid hormone can be achieved by either PTU or carbimazole (less useful). PTU inhibits iodine and peroxidase from their normal interactions with thyroglobulin to form T4 and T3. This action decreases production of thyroid hormone. Propylthiouracil can be given by the mouth, nasogastric tube or rectally at a rate of 250 mg every 4–6 h or methimazole 20–30 mg PO q6h.

   Inhibition of thyroid hormone release is achieved by iodine given orally or via a nasogastric tube to block the release of THs (at least 1 h after starting antithyroid drug therapy). This delay allows the antithyroid drug to inhibit thyroid hormone synthesis, which otherwise may be enhanced by unopposed iodide.
2. Inhibition of peripheral conversion of T4 to T3 can be achieved by: Administration of hydrocortisone 100 mg IV q8h or dexamethasone 2 mg IV q6h. Glucocorticoids also serve in preventing relative adrenal insufficiency due to hyperthyroidism and provide vasomotor stability.

Alternative therapies:

Lithium 300 mg PO q8h appears to be actively concentrated in the thyroid follicular cells and inhibits thyroid hormone release [6, 7]. Lithium should be monitored regularly to maintain a concentration of 0.6–1.0 mEq/L.

Treat the underlying cause:

- Broad-spectrum antibiotics if an infection is the precipitating factor.
- Any other medical condition precipitating thyroid storm should be addressed like DKA, HONK, myocardial infarction and hypoglycaemia.

(Note: Cholestyramine, 4 g every 6–8 h, binds thyroid hormone in the gut and thus interrupts the modest enterohepatic circulation of thyroid hormone; its use will lead to a more rapid lowering of circulating thyroid hormones. In exceptional cases, peritoneal dialysis or plasmapheresis may be needed.)

Once the patient is stable, the differential diagnosis of thyroid disease underlying thyroid storm should be accurately investigated, with the aim of distinguishing thyroid hyperfunction, destructive thyroiditis or thyrotoxicosis factitia.

The managemnt algorithm for Thyroid storm can be summarised as in Fig. 31.1

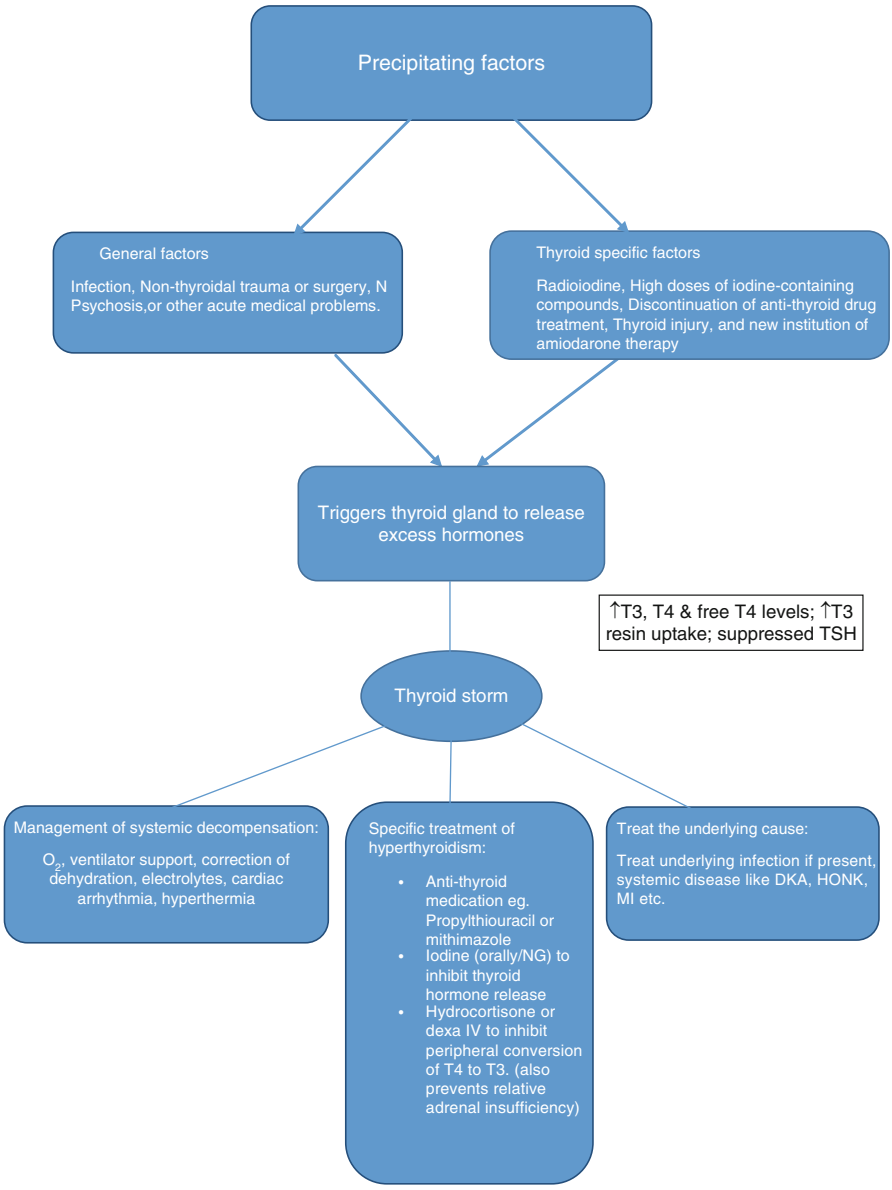

Fig. 31.1 Approach to Thyroid storm (algorithm)

Myxoedema Coma

Myxoedema coma is a rare decompensated state of extreme hypothyroidism with a high mortality rate (25–60 %) [8, 9] even with early diagnosis and appropriate treatment. It is typically found in elderly patients with undiagnosed or undertreated hypothyroidism [10].

Aetiology and Pathophysiology

Myxoedema coma results as a consequence of critical decompensation of a patient due to stress. The stress factors include: infection, hypothermia, intoxication, drugs, cerebrovascular accident, congestive cardiac failure and trauma. More than 95 % of patients have primary thyroid disease like autoimmune thyroid disease or hypothyroidism secondary to ablative procedures on the thyroid.

Thyroid hormone is essential for cellular metabolism, and all organ systems are affected if hypothyroidism is severe and prolonged. Decreased thyroid function results in:

- Depressed basal metabolic rate
- Decreased oxygen consumption
- Impaired energy production

The cardiovascular system is particularly susceptible leading to depressed myocardial contractility and bradycardia resulting in low cardiac output and profound hypotension resulting in decreased cerebral perfusion.

Clinical Features

Patients with myxoedema coma classically demonstrate features of severe hypothyroidism, which includes dry skin, thin hair, periorbital swelling, non-pitting oedema of the hands and feet, hoarse voice, macroglossia and delayed tendon reflexes along with central nervous system features including respiratory depression secondary to a decreased hypoxic ventilatory drive and an impaired response to hypercapnia [11–13]. This will eventually lead to myxoedema coma characterised by altered mental status in the form of confusion, lethargy, obtundation or frank psychosis.

Hypothermia is universal and often the first clinical indication of myxoedema coma. Body temperatures lower than 94 % and a core body temperature lower than

88 % have been reported [14]. The mortality of myxoedema is directly correlated with the degree of hypothermia. The lower the temperature, the worse is the prognosis.

Other features include bradycardia, depressed cardiac contractility, anorexia, nausea, abdominal pain, constipation, respiratory depression, respiratory muscle weakness, respiratory acidosis and hypoxaemia.

Diagnosis and Treatment

The diagnosis of myxoedema coma is based on the presence of clinical characteristics in a known patient of hypothyroidism, and this suspicion should be confirmed by thyroid function tests.

Thyroid function studies demonstrate:

- Low total and free thyroxine (T4)
- Low total and free triiodothyronine (T3)
- TSH: increased in primary hypothyroidism but normal or decreased in central pathology

Other biochemical studies show hyponatraemia, hypoglycaemia, hypoxemia, hypercapnia, elevated lactate dehydrogenase (LDH), creatine phosphokinase (CPK) and cholesterol.

Enlarge cardiac silhouette due to pericardial effusion on chest x-ray.

ECG demonstrates profound bradycardia and low-voltage complexes.

The three principles of management are:

1. Rapid institution of thyroid hormone replacement
2. Treatment of the precipitating cause
3. Supportive treatment providing adequate ventilation and correcting biochemical parameters

Thyroid hormone therapy administers T3, T4 or combination.

- T3 is given as an initial dose of 10 mcg, followed by 10 mcg every 8–12 h until there is clinical improvement and patient is able to take it orally. T4 is given in a loading dose of 200–300 mcg intravenously, followed by 100 mcg 24 h later and then a daily dose of 50 mcg. Thereafter, the daily dosage can be adjusted according to the laboratory results.
- The second most important drug is hydrocortisone because thyroid replacement may unmask coexisting adrenal insufficiency and precipitate adrenal crisis dosage: 100 mg IV q6–8 h given along with thyroid replacement for several days later tapered and stopped after assessment of adrenal function.

Supportive treatment:

IV fluid boluses for hypotension: Pressor agents should be avoided in such patient as they precipitate an arrhythmia, and also response to pressors is poor until thyroid replacement is initiated.

Consider hypertonic saline for severe hyponatraemia.

Hypothermia should be treated with space blankets, since active rewarming leads to circulatory collapse.

Part B – Acute Adrenal Disorders

Key Points

- Sudden withdrawal of steroids and precipitation by intercurrent illness are by far the most common causes of adrenal crisis in ED.
- Patients with adrenal crisis manifest with profound shock, hypoglycaemia, hyperkalaemia and hyponatraemia.
- Hydrocortisone 100 mg IV should be initiated even before awaiting the results of serum cortisol and ACTH.
- Blood pressure control in pheochromocytoma is the mainstay of management, and phenoxybenzamine is the drug of choice.

Introduction

Acute adrenal disorders are rare life-threatening situations, requiring prompt clinical suspicion and immediate replacement of fluids, electrolytes and hormones. The disorders of adrenal cortex result in various manifestations, such as severe deficiency of corticosteroids in adrenal crisis in turn leading to fluid-electrolyte disturbances, whilst excessive unregulated production of steroids results in Cushing's syndrome. Pheochromocytomas on the other hand are functional tumours of adrenal medulla presenting with hyperadrenergic spells.

This section is aimed to channelise the thought process of the emergency physician to recognise the subtle clinical manifestations at tip of the iceberg and dwell deep towards the endocrine abnormalities and deal with the appropriate management of these potentially life-threatening conditions.

Acute Adrenocortical Insufficiency

Adrenal insufficiency results from inadequate adrenocortical function and may be due to Addison's disease, previous bilateral adrenalectomy, pituitary disorders, hypothalamic dysfunction or sudden withdrawal of long-term oral steroids in people with chronic diseases.

Table 31.3 Causes of adrenal insufficiency

Primary adrenocortical insufficiency (Addison's disease)	Secondary adrenocortical insufficiency
Anatomic destruction of adrenal gland	Disease of the hypothalamic-pituitary axis
Idiopathic – probably autoimmune	Tumour
Infective – TB, AIDS, disseminated fungal infection	Apoplexy
Haemorrhage – anticoagulant therapy, Waterhouse	Granulomatous disease
Friderichsen syndrome	Suppression of the hypothalamic-pituitary axis
Infiltration – carcinoma, lymphoma, sarcoidosis, amyloidosis	Exogenous steroids
Metabolic failure of the adrenal gland	
Congenital adrenal hyperplasia	
Drugs, e.g. ketoconazole, etomidate	

Aetiology of Adrenal Insufficiency

The adrenal insufficiency can be divided into two major categories, primary and secondary adrenal insufficiency (Table 31.3).

- Primary adrenal insufficiency: both glucocorticoid and mineralocorticoid functions are lost.
- Secondary adrenocortical insufficiency: only glucocorticoid function is lost due to disease or suppression of the hypothalamic-pituitary axis, but mineralocorticoid function is preserved. The causes of adrenal insufficiency are listed in Table 31.4.

Acute Adrenocortical Insufficiency (Adrenal Crises)

Acute adrenal crisis is a life-threatening state caused by insufficient levels of cortisol from an acute insult in a patient with chronic insufficiency or more commonly from withdrawal of exogenous steroids (Table 31.4).

Clinical Features

The onset is gradual with features including weight loss, lethargy, weakness, vague abdominal pain, nausea, vitiligo, oligomenorrhoea and pigmentation of buccal mucosa, palmar creases, elbow and knees. In adrenal crises, the patient can be profoundly shocked (tachycardia, hypotensive, vasoconstricted, oliguric) and hypoglycaemic.

Table 31.4 Precipitating factors for acute adrenal crises (in alphabetical order)

Alcohol
Asthma
Exogenous steroid withdrawal/reduction
Hypothermia
Infection
Myocardial infraction
Stroke
Trauma

Table 31.5 Emergency approach of adrenal crisis

Clinical features: anorexia, nausea, vomiting, craving for salt, headaches, memory loss, postural hypotension, tachycardia, abdominal pain, shock, unexplained pyrexia
Step 1: Take blood for urea, electrolytes, glucose and cortisol (low serum cortisol <200 nmol/L indicates adrenal insufficiency. If ACTH is raised, it indicates primary and a low ACTH suggests secondary adrenal insufficiency. High serum cortisol>550 nmol/L excludes adrenal insufficiency. Intermediate serum cortisol 200–550 nmol/L requires Synacthen test)
Step 2: Commence an IV infusion of 0.9 % saline (to reverse fluid and sodium deficiency). Correct hypoglycaemia
Step 3: 100 mg IV hydrocortisone bolus should be administered immediately followed by 100 mg of IV hydrocortisone six hourly for 24–48 h or until oral therapy can commence

Investigations

In the early phases of adrenal destruction, the laboratory investigations may not be abnormal but adrenal reserve is decreased; hence, adrenal stimulation with ACTH is necessary to uncover the abnormalities at this stage of the disease.

In advanced stages, there are obvious manifestation of hyponatraemia and hypokalaemia; hence, serum sodium, potassium, chloride and bicarbonate should be checked along with other causes identifying the cause of the acute adrenal insufficiency (e.g. infective screen). In all the suspected cases of adrenal crisis, serum cortisol and ACTH should be sent but should not delay the treatment with hydrocortisone.

Management of Adrenal Crises

Management of suspected case of adrenal crisis should be done in a stepwise manner as shown in the Table 31.5 and the algorithm Fig. 31.2.

- Intravenous fluids should be continued till oral therapy is commenced.
- Patient may require several litres of fluids for resuscitation if the crisis was preceded by severe dehydration secondary to nausea or vomiting, but cardiac status should be the guide for further fluid resuscitation.
- Fludrocortisone is only required in primary adrenocortical insufficiency and is not commonly given in the emergency department.

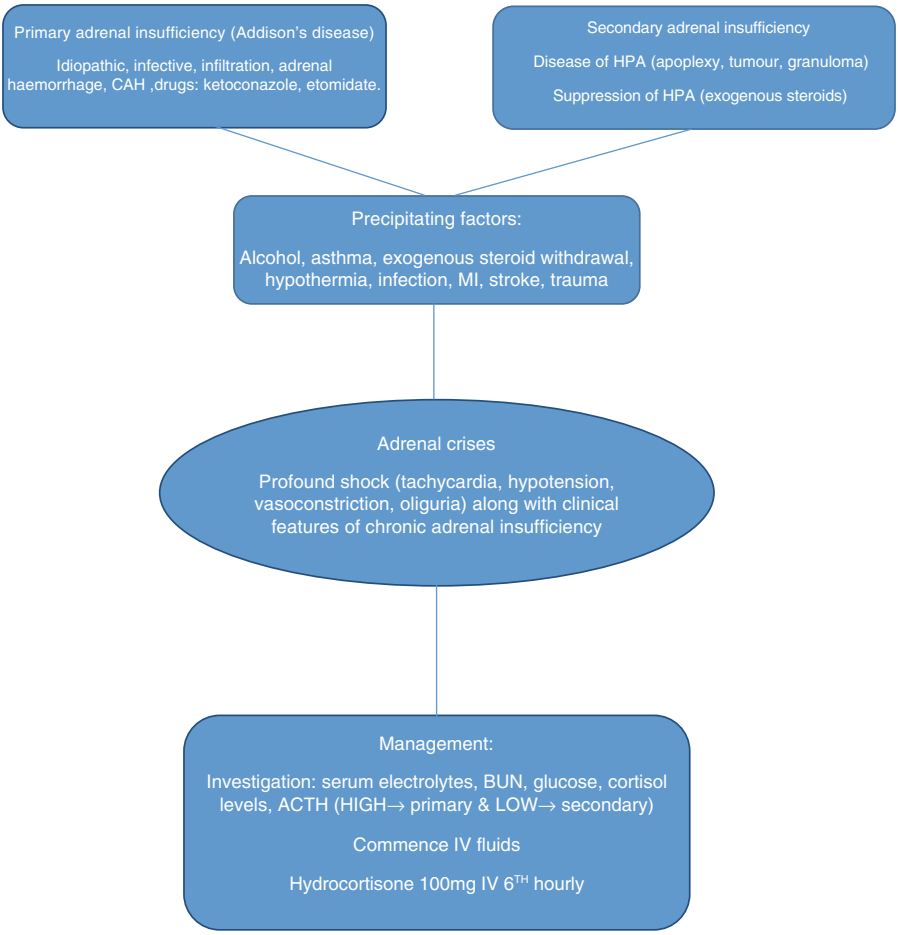

Fig. 31.2 Adrenal insufficiency: algorithm

- Monitor for hypoglycaemia and treat with 10 % glucose IV if necessary.
- Underlying infections should be screened and treated with appropriate antibiotics.

Cushing's Syndrome

Cushing's syndrome and Cushing's disease are the complex metabolic disorders that result in excess glucocorticoids in the body and are associated with impairment of circadian oscillation [15, 17]. This is most commonly caused by patients taking exogenous steroids for other medical conditions. Excluding the exogenous causes, adrenocorticotropic hormone-secreting pituitary adenomas account for nearly 70 % of all cases of Cushing's syndrome [16].

Epidemiology

In general, CS is a rare disease. The reported incidence of endogenous CS worldwide ranges from 0.7 to 2.4 cases per million per year [18]. Commonly affected age group ranges from 20 to 50 years with a marked female preponderance (1:5 ratio of male vs. female).

Causes

CS is a heterogeneous disorder that arises from prolonged exposure to elevated levels of either endogenous or exogenous glucocorticoids resulting in a broad spectrum of eventually fatal comorbidities such as diabetes and hypertension (Table 31.6).

Clinical Features

CS comprises of numerous general and endocrine symptoms and side effects, some of which might be entailed with fatal outcome.

Excess cortisol levels result in:

- Facial plethora
- Hirsutism
- Gonadal dysfunction
- Menstrual irregularities
- Depression
- Infections due to generalised immune suppression
- Striae
- Vascular fragility
- Hypokalaemia, muscle weakness
- Osteoporosis and eventually fractures

The metabolic consequences of cortisol excess include weight gain, central obesity, skin atrophy, glucose intolerance entailed by diabetes and insulin resistance, dyslipidaemia, hypertension and clotting disorders (eventually even hypercoagulability) [19].

Table 31.6 Causes of Cushing's syndrome

Endogenous causes of Cushing's syndrome		Exogenous causes of Cushing's syndrome
ACTH-dependant Cushing's syndrome	ACTH-independent Cushing's syndrome	Intake of steroids in high doses over an extended period of time Iatrogenic administration of ACTH
Pituitary adenoma (Cushing's disease) Ectopic tumours secreting ACTH or corticotropin-releasing hormone (CRH)	Adrenocortical tumours or hyperplasia	

Investigations

Obtain a thorough drug history to exclude exogenous glucocorticoid exposure leading to iatrogenic Cushing's syndrome before conducting biochemical testing. The clinical suspicion should be followed by a step-by-step diagnostic workup. The diagnostic studies involved in the evaluation of patients with suspected Cushing's syndrome fall into two categories:

1. Confirming the presence of true hypercortisolism
2. Establishing the precise aetiology

Diagnosis of hypercortisolism (irrespective of its origin) comprises the following:

- Complete blood count including serum electrolytes and blood sugar
- Urinary free cortisol (UFC) from 24 h urine sampling and circadian profile of plasma cortisol, plasma ACTH, dehydroepiandrosterone, testosterone itself and urine steroid profile, low-dose dexamethasone test and high-dose dexamethasone test, after endocrine diagnostic tests
- Magnetic resonance imaging (MRI), ultrasound, computed tomography (CT) and other localization diagnostics

The laboratory findings suggestive of Cushing's syndrome include: hyperglycaemia, hypokalaemia and hypocalcaemia. Ectopic Cushing's syndrome should always be ruled out in patients with severe hypertension and hypokalaemia [20].

Management of Cushing's Syndrome

Cushing's syndrome may occasionally present as an acute emergency. In suspected cases of Cushing's syndrome caused by exogenous glucocorticoid exposure, the following steps should be carried out:

- A detailed drug history and any relevant drug-drug interactions.
- In an emergency situation, treatment should focus on management of severe metabolic disturbances, followed by rapid resolution of the excess glucocorticoid exposure, and subsequent confirmation of the cause and its treatment.
- If the cause of Cushing's syndrome is exogenous steroids, these may be gradually tapered off and eventually stopped, if possible.
- The definitive treatment for endogenous Cushing's syndrome is selective removal of the tumour from the affected organ.
- Pharmacotherapy is an option in the case of failure of surgery for Cushing disease or in ectopic ACTH secretion where the source cannot be identified.

Medical therapy can be categorised in three different groups:

Inhibition of steroidogenesis: The drugs which inhibit steroidogenesis either by enzyme inhibition or by destroying the adrenal cells include mitotane,

aminoglutethimide, metyrapone, trilostane and ketoconazole. Etomidate is one of the parenteral drugs which can be used in case of emergency situations and is commenced at 2.5 mg/h and titrated subsequently according to cortisol levels [21].

Suppression of adrenocorticotropic hormone: Somatostatin receptor ligands like pasireotide [22] and dopamine agonists like cabergoline can lower ACTH secretion caused by a pituitary adenoma.

Antagonism of the glucocorticoid receptor: Mifepristone binds to the glucocorticoid receptor with a fourfold higher affinity than dexamethasone and an 18-fold higher affinity than cortisol and hence acts as antagonist.

However, the majority of common drugs are not available for parenteral administration, which may evoke a management problem in emergency settings or in patients unable to tolerate oral medication.

Pheochromocytoma

Introduction and Epidemiology

Pheochromocytomas are the catecholamine-secreting functional tumours that arise from the chromaffin cells in the adrenal medulla (80–85 %) or extra-adrenal chromaffin cells (15–20 %) and can originate in either the parasympathetic or sympathetic ganglia [23].

Aetiology and Pathophysiology

Pheochromocytomas were known as the 10 % tumours, meaning that 10 % of cases were familial, 10 % bilateral, 10 % malignant and 10 % extra-adrenal [24]. They may arise sporadically or be inherited as features of multiple endocrine neoplasia type 2 or several other pheochromocytoma-associated syndromes. They account for 0.1–0.2 % of cases of systemic hypertension; 35 % of them are hereditary in adults [25–27] and up to 40 % are hereditary in children [28]. The prevalence is equal in men and women and is reported in people of all races.

Clinical Features of Pheochromocytoma

The clinical presentation of pheochromocytoma is variable (Table 31.7). The clinical suspicion of pheochromocytoma should arise if one or more of the following features are present:

Table 31.7 Signs and symptoms associated with catecholamine-secreting tumour

Spell-related signs and symptoms
Anxiety and fear of impending death, diaphoresis, dyspnoea, epigastric and chest pain, headache, hypertension, nausea and vomiting, pallor, palpitation, tremor
Chronic signs and symptoms
Weight loss, tremor, dyspnoea, cold hands and feet, anxiety, headache, hypertension, orthostatic hypotension, fever, fatigue, nausea, vomiting
General increase in sweating
Nontypical of pheochromocytoma: flushing

- Hyper adrenergic spells (e.g. self-limiting spells of nonexertional palpitations, diaphoresis, headache, tremor, pallor).
- Resistant hypertension.
- A familial tumour that predisposes to catecholamine-secreting tumours (e.g. multiple endocrine neoplasia (MEN) 2).
- Labile hypertension and paroxysms of hypertensions and tachycardia.
- In emergency situations, it should be noted, however, that most patients do not have tachycardia but have bradycardia due to reflex cardiac slowing in response to norepinephrine-mediated vasoconstriction.
- Sustained tachycardia would suggest an epinephrine-secreting tumour.

Diagnosis of Pheochromocytoma

The three key elements for the diagnosis of pheochromocytoma are clinical suspicion, biochemical testing and localization studies.

Biochemical studies: documentation of catecholamine excess can be difficult because hormonal activity of tumours fluctuates, resulting in considerable variation in serial catecholamine measurements. Thus, there is some value in obtaining tests during or soon after a symptomatic crisis. On the other hand, most tumours continuously leak O-methylated metabolites, which are detected by metanephrine measurements. The following biochemical tests can be performed:

- The plasma-free metanephrine levels and normetanephrines
- Twenty-four hours urinary free catecholamine level in the initial screening test
- Plasma catecholamines

Emergency physician should also look for evidence of hypertensive end-organ damage (e.g. renal failure, proteinuria, left ventricular hypertrophy, retinopathy and papilloedema).

Localization studies involve imaging (CT/MRI), radio-labelled catecholamine precursors to localise the tumour and genetic testing.

Treatment

Hypertensive crises (systolic BP >250 mmHg): Blood pressure control is the mainstay of the treatment when the patient arrives to the emergency department. First step is to block the effects of catecholamine excess by controlling HTN and expanding intravascular volume. Establish adequate alpha blockade and subsequently instituting a beta-blocker or a calcium channel blocker if needed to control blood pressure and heart rate. A hypertensive crisis may be precipitated by drugs that inhibit catecholamine uptake, such as tricyclic antidepressants and cocaine, opiates, anaesthesia induction and x-ray contrast media; hence, a thorough history should be retrieved from the patient.

- Intravenous phentolamine (a potent alpha-2 blocker) 1 mg followed by 5 mg bolus infusions.
- IV nitroprusside not more than 3 μg/kg/min can be started as the initial rescue to control hypertension.
- Hydration and a high-salt diet (>5 g/day) are given to offset the effects of catecholamine-induced volume contraction associated with alpha blockage.
- Provide volume expansion with isotonic sodium chloride solution
- Initiate a beta-blocker only after adequate alpha blockade, to avoid precipitating a hypertensive crisis from unopposed alpha stimulation [29].

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