Repeated hypoglycaemic episodes in a diabetic patient whose insulin dosage has been decreasing may indicate the development of renal insufficiency, adrenal failure, hypothyroidism or hypopituitarism.

**Clinical features**

Patients may complain of weakness, lassitude, incoordination and confusion. This may ultimately progress to seizures and coma. Rapid falls in blood sugar levels produce adrenergic symptoms such as tremulousness, sweating, palpitations and anxiety, which are attributable to the increased sympathetic drive. Faintness and sweating with tachycardia, variable blood pressure and pupillary dilatation are easily overlooked or mistaken for alternative pathologies. Measurement of blood glucose is therefore essential in any patient presenting with ‘funny turns’, hypothermia or altered consciousness.

It has been suggested that the warning signs of hypoglycaemia are less well appreciated by patients receiving human insulin than by those using animal insulins. This phenomenon, which is probably related to more rapid absorption of human insulin, was extensively investigated, but no clear differences between the hypoglycaemic effects of human and animal insulin emerged (Gale, 1989). It is also important to appreciate that loss of awareness of hypoglycaemia occurs over time in many diabetics, regardless of the type of insulin prescribed.

Hypoglycaemia from the long-acting sulphonylureas is especially dangerous because glucose levels can be suppressed for many hours. Chlorpropamide is excreted mainly unmetabolized by the kidney and coexisting renal insufficiency greatly prolongs its half-life, thereby increasing the risk of hypoglycaemia. It is no longer recommended.

**Management**

Simultaneously with the usual resuscitative measures, any insulin infusion should be discontinued and 25 mL 50% dextrose (or 50 mL 20% dextrose) injected intravenously. This usually produces an immediate improvement in conscious level and vital signs. The circulating blood glucose level can then be maintained by the continuous administration of 10% or 20% dextrose. To avoid superficial thrombophlebitis concentrated dextrose solutions should be administered via a central vein.

Accidental or deliberate overdose with sulphonylureas can be refractory to an infusion of concentrated dextrose alone and may require the additional administration of hydrocortisone, glucagon or diazoxide. Glucocorticoids increase glucose levels by stimulating gluconeogenesis and antagonizing the effects of insulin. Glucagon is a polypeptide hormone produced by the alpha cells of the islets of Langerhans, which increases plasma glucose concentration by mobilizing glucose from hepatic glycogen stores. Diazoxide acts directly on the pancreas to decrease insulin secretion. Haemodialysis is not helpful since sulphonylureas are protein-bound.

Intentional overdosage with intravenous insulin injections may prove impossible to reverse, especially when there is significant delay in discovering the collapsed hypoglycaemic patient. Parenteral administration of insulin has, nevertheless, been successfully treated by surgical resection of the subcutaneous tissue into which the insulin had been injected.

Mallnourished alcoholic patients are susceptible to hypoglycaemia as a consequence of alcohol-induced suppression of gluconeogenesis. Furthermore, glucagon administration is usually not effective in reversing hypoglycaemia in such patients since liver glycogen stores are often depleted.

Prolonged coma despite treatment of hypoglycaemia should prompt consideration of other potential causes of unconsciousness such as hypoxic cerebral injury, intracerebral haemorrhage, drug or alcohol intoxication, meningitis or hypothermia.

Clearly, whatever the aetiology of hypoglycaemia, subsequent treatment and investigations should be aimed at the primary disorder.

**Prognosis**

The prognosis after severe prolonged hypoglycaemia depends on the duration of coma and corresponding cerebral injury.

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**THYROID EMERGENCIES**

**THYROID CRISIS (Ringel, 2001)**

**Causes**

Thyroid crisis (or ‘storm’) is a life-threatening hypermetabolic condition which can involve every organ/system (Jiang et al., 2000). A precipitating event such as infection, surgery, trauma or other intercurrent illness (e.g. stroke, DKA) can usually be identified in a patient with partially treated or untreated hyperthyroidism. Thyroid crisis may also follow massive overdose of thyroid hormone preparations, radiiodine therapy and the administration of iodinated contrast dyes.

The mechanism underlying thyroid crisis remains unclear, but may involve an increase in β-adrenergic receptor numbers.

**Clinical presentation**

In thyroid crisis, the characteristic features of hyperthyroidism are accentuated. The clinical presentation may include palpitations, tachycardia, arrhythmias, tremor, sweating, profuse sweating, heat intolerance, tachycardia, atrial fibrillation, heart block and cardiac failure. There may be profuse sweating, tachycardia, arrhythmias, and profuse sweating. Fever is invariable and sets the scene for thyroid crisis apart from hyperthyroidism, but makes the distinction from sepsis extremely difficult. Leukocytosis is also well recognized in thyrotoxicosis, even in the absence of...
infection. Myopathy is common in both hyper- and hypothyroidism and rhabdomyolysis has been reported.

Amphetamine overdose also resembles severe thyrotoxicosis and a toxicology screen should be undertaken when drug abuse is suspected, especially if the thyroid gland is not palpable. Pheochromocytoma can also present in a similar fashion, but severe hypertension and paroxysmal attacks usually dominate the clinical presentation of this condition.

**Investigations**

Blood should be collected for thyroid function tests and a cortisol level before commencing therapy. A toxicology screen should be performed and specimens should be sent for microscopy, culture and sensitivity. Liver function tests may be abnormal.

**Management** *(Table 17.6)*

In these extremely ill patients therapy for thyrotoxicosis must precede laboratory confirmation of the diagnosis. Treatment is aimed at decreasing the synthesis and secretion of thyroid hormone and countering the effects of thyroid hormone already in the circulation, as well as identifying and treating any precipitating illness and providing supportive therapy. A combination of antithyroid drugs and iodine may decrease serum triiodothyronine (T<sub>3</sub>) levels in days but the metabolic response lags behind.

**GENERAL MEASURES**

Supplemental oxygen should be given to an unobstructed airway. Many patients are dehydrated and will require intravenous fluid and electrolyte replacement. A cooling blanket or tepid sponging can be used to decrease body temperature. Salicylates should not be used since they displace thyroid hormone from binding proteins and may worsen hypermetabolism.

**Chlorpromazine** (25–50 mg intramuscularly) can be given to reduce agitation and anxiety and may also facilitate cooling. Standard antiarrhythmic drugs can be used, including digoxin for atrial fibrillation, after correction of hypokalaemia (see Chapter 9). If sepsis is a possibility antibiotics should be given.

**SPECIFIC MANAGEMENT**

*Carbimazole* and *propylthiouracil* (PTU) impede formation of thyroid hormone and block peripheral conversion of thyroxine (T<sub>4</sub>) to the metabolically active hormone T<sub>3</sub>. A 500-mg loading dose followed by 250 mg of PTU every 6 hours is recommended and can be given by nasogastric tube or rectally if the patient is unable to take oral medication.

The administration of *iodine*, which blocks the synthesis and release of thyroid hormone, should be delayed for approximately 1 hour following the first dose of PTU to minimize the possibility of massive hormone release following iodination. Traditional preparations include *potassium iodide* (60 mg orally three times daily), Lugol’s iodine (use 10 drops of a solution containing 130 mg of iodine/ml diluted in milk or water twice daily), or *sodium iodide* (250 mg intravenously every 6 hours). *Radiographic contrast dyes* containing iodine have also been used in place of traditional preparations (Burger and Philippe, 1992).

Lithium carbonate may be used to block thyroid hormone release in those with iodine sensitivity. There is a considerable risk of serious cardiovascular and central nervous system side-effects because of the narrow therapeutic ratio. The initial dose of 300 mg 6-hourly should be adjusted to maintain plasma lithium levels of approximately 1 mmol/L. Lithium should be avoided in those with cardiac failure or renal insufficiency.

*Propranolol* (80 mg orally 8-hourly or 2 mg intravenously as required) blocks the sympathetic effects of thyroid hormone and is especially useful to reduce sinus tachycardia (Hellman et al., 1977). It inhibits release of thyroid hormone, impairs conversion of T<sub>4</sub> to T<sub>3</sub> and blocks sympathetic hyperactivity, which is responsible for many of the psychomotor and cardiovascular features of thyrotoxicosis. β-blockers are relatively contraindicated in patients with moderate or severe cardiac failure, as well as in peripheral vascular disease, and should not be used in those with reversible airflow limitation. More specific β-blockers such as atenolol can be used in such cases. *Dexamethasone* 2 mg

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**Table 17.6 Guidelines for the management of thyroid crisis**

<table>
<thead>
<tr>
<th>General measures</th>
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<tbody>
<tr>
<td>Oxygen administration</td>
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<tr>
<td>Intravenous fluids</td>
</tr>
<tr>
<td>Cooling blanket and/or tepid sponging</td>
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<tr>
<td>Chlorpromazine (25–50 mg intramuscularly)</td>
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<tr>
<td>Treat arrhythmias and cardiac failure</td>
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<table>
<thead>
<tr>
<th>Specific treatment</th>
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</thead>
<tbody>
<tr>
<td>Carbimazole (15–40 mg daily)</td>
</tr>
<tr>
<td>Propylthiouracil (500 mg loading dose followed by 250 mg every 6 hours PO, NG or PR)</td>
</tr>
<tr>
<td>Iodine preparations should be delayed for approximately 1 hour following the first dose of propylthiouracil. e.g.:</td>
</tr>
<tr>
<td>Potassium iodide (60 mg orally 8-hourly)</td>
</tr>
<tr>
<td>Lugol’s iodine (10 drops of a solution containing 130 mg of iodine/ml 12-hourly)</td>
</tr>
<tr>
<td>Sodium iodide (250 mg intravenously 6-hourly if available)</td>
</tr>
<tr>
<td>Radiographic contrast dyes</td>
</tr>
<tr>
<td>Lithium carbonate (initially 300 mg 6-hourly) can be used in those with iodine sensitivity</td>
</tr>
<tr>
<td>Propranolol (80 mg orally 8-hourly or 2 mg intravenously as required) or atenolol</td>
</tr>
<tr>
<td>Dexamethasone (2 mg intravenously 6-hourly) or hydrocortisone 100 mg i.m. 6-hourly</td>
</tr>
<tr>
<td>Plasmapharesis in severe, unresponsive cases</td>
</tr>
</tbody>
</table>

NG, nasogastric; PO, orally; PR, per rectum.
intravenously every 6 hours, or hydrocortisone (100 mg intramuscularly 6-hourly), can also be used to reduce the conversion of \( T_4 \) to \( T_3 \), and may be useful because severe hyperthyroidism can cause relative hypoadrenalism due to accelerated cortisol metabolism.

In known or suspected causes of thyroid hormone overdose gastric lavage with charcoal, perhaps combined with the administration of cholestyramine to increase faecal elimination, may be indicated.

The response to treatment can be monitored by observation of clinical signs (e.g. pulse, temperature and agitation) and by regular serum \( T_3 \) estimations.

In extreme cases that are unresponsive to conventional therapy plasmapharesis has been undertaken.

**Prognosis**
When treated, thyroid crisis is associated with a mortality of 20–40%, mainly due to cardiac failure, arrhythmias or hyperthermia.

**MYXOEDEMA COMA** (Fliers and Wiersinga, 2003)
Myxoedema coma is an extreme decompensated form of hypothyroidism associated with a high mortality.

**Causes**
Frequent precipitating causes include:
- exposure to cold;
- surgery;
- trauma;
- infection (e.g. respiratory);
- cerebrovascular accident;
- drug administration (e.g. chlorpromazine, narcotics, \( \beta \)-blockers).

Coma may be secondary to the metabolic deficit induced by profound hypothyroidism, carbon dioxide narcosis, accentuated effects of sedative drugs or hypoglycaemia.

**Clinical presentation and diagnosis**
Myxoedema coma usually occurs in older patients with long-standing unrecognized hypothyroidism, most commonly caused by autoimmune thyroiditis, radioiodine therapy or thyroidectomy. A failure of thyrotrophin (thyroid-stimulating hormone: TSH) secretion due to pituitary disease is termed secondary hypothyroidism, while hypothalamic dysfunction is a tertiary disorder also associated with a low TSH level. There may be a history of previous thyroid disease or antithyroid, lithium or amiodarone therapy. A family history of thyroid or organ-specific autoimmune disease may be elicited.

Recognition of myxoedema coma may be difficult because of its low prevalence and non-specific symptoms. The classical manifestations of hypothyroidism are usually present and may include:
- characteristic facies;
- extreme bradycardia;
- hypotension;
- jeopardized respiratory function, including hypventilation and upper-airway obstruction by tongue enlargement;
- delayed or absent relaxation of the tendon reflexes;
- paralytic ileus, megacolon and urinary retention;
- seizures and cerebellar signs.

Altered mental status, defective thermoregulation and a precipitating event or illness are the three essential elements in making a diagnosis of myxoedema coma. In fact most patients are not comatose, but altered mental status may manifest as disorientation, extreme lethargy, confusion or, occasionally, psychosis.

_Hypothermia_, due to an inability to produce heat and defective hypothalamic function, and _hyponatraemia_ secondary to diminished free water clearance are common. Body temperature may be normal in those harbouring an infection. Occasionally the patient is _hypoglycaemic_. Routine investigations may also reveal a normocytic, normochromic or megaloblastic _anaemia_ and _hypercholesterolaemia_. Raised enzymes (creatine phosphokinase; lactate dehydrogenase; aspartate aminotransferase) may cause confusion with an acute myocardial infarction or reflect a cardiac event in a susceptible patient. In myxoedema coma, however, these enzymes may remain high for several days, unlike the acute transient changes seen after a myocardial infarction, and troponin levels will not be elevated. An ECG is helpful in the differential diagnosis; typical changes in hypothyroidism include small voltages and a prolonged QT interval. Blood gas analysis often reveals _hypercapnia_ and _hypoxia_. A chest X-ray should be obtained and specimens sent for culture and sensitivity.

Thyroid function tests should be requested urgently together with a serum cortisol. Most commonly the tests reveal a primary thyroid disorder (low \( T_4 \) and \( T_3 \), high TSH), but occasionally show secondary (pituitary) or tertiary (hypothalamic) hypothyroidism (low \( T_4 \), low TSH). Some patients may also have adrenal insufficiency. In some cases interpretation may be complicated by the presence of non-thyroidal illness syndrome (NTIS) (see below), in which case TSH may be inappropriately normal or low.

**Management** (Table 17.7)

**GENERAL MEASURES**
Myxoedema coma is an endocrine emergency. Once suspected, treatment can be life-saving and should start promptly, without waiting for laboratory confirmation of the diagnosis. Impaired myocardial performance and hypotension should be managed in accordance with the usual principles and patients with carbon dioxide retention or type II respiratory failure may require ventilatory support. The circulating volume should be expanded cautiously because these patients are at risk of congestive cardiac failure. It must be remembered that patients in myxoedema...


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