Endocrinal Disorders

**Introduction**

Four systems in the human body are responsible for the integration and coordination of various body functions; these systems are:

1- Nervous system

2- Circulatory system

3- Immune system

4- Endocrine system

The hypothalamus represents the main mediator between the CNS and the endocrine system, which is at the same time an integral part of the central nervous system and an endocrine gland.

The hypothalamus controls the function of the “peripheral” endocrine glands such as adrenal and thyroid glands via the pituitary gland.

**Pituitary Gland**

The pituitary gland is a complex gland consisting of hormone-producing adenoid (glandular) cells (anterior pituitary) and the axon terminals of neurosecretory cells originating in the hypothalamus (posterior pituitary). It is a pea-sized endocrine gland located at the base of the brain, often referred to as the “master gland”.

**Posterior pituitary hormones**

ADH and oxytocin are the two hormones released by the posterior pituitary.

ADH is responsible for osmotic homeostasis (it decreases the free water clearance in kidneys and stimulates thirst) .

Oxytocin mostly acts at the uterine smooth muscle and the smooth muscle in the mammary glands.

**Anterior pituitary hormones**

There are six types of cells in the anterior pituitary, named after the primary peptide/protein hormones they produce:

1- **ACTH** (adrenocorticotropin),  **2- TSH** (thyroid stimulating hormone; thyrotropin), **3,4- FSH** and **LH** (follicle stimulating and luteinizing hormone or gonadotropins),

**5- GH** (growth hormone or somatotropin) **6-prolactin** (lactotropin).

Upon stimulation of the anterior pituitary by hypothalamic hormones, these hormones are released and diffuse into the second portal capillary bed.

**Presenting problems in endocrine disease**

Endocrine diseases present in many different ways and to clinicians in many different disciplines.

Although endocrinal disorders can present as classical syndrome, the presentation is sometimes with non-specific symptoms or with asymptomatic biochemical abnormalities.

Examples of non-specific symptoms that might indicate an endocrinal disorder include:

|  |  |
| --- | --- |
| **Symptom** | **Most likely endocrine disorder(s)** |
| Lethargy and depression | Hypothyroidism, diabetes mellitus, hyperparathyroidism, hypogonadism, adrenal insufficiency, Cushing’s syndrome |
| Weight gain | Hypothyroidism, Cushing’s syndrome |
| Weight loss | Thyrotoxicosis, adrenal insufficiency, diabetes mellitus |
| Polyuria and polydipsia | Diabetes mellitus, diabetes insipidus, hyperparathyroidism, hypokalaemia (Conn’s syndrome) |
| Heat intolerance | Thyrotoxicosis, menopause |

**Thyroid Disorders**

**I- Hyperthyroidism (Thyrotoxicosis)**

Thyrotoxicosis describes a group of clinical features arising from elevated circulating levels of thyroid

hormone (hyper-metabolic state).

**Causes**

1- Grave’s disease (autoimmune disease) 2- toxic multinodular goiter

3- toxic adenoma 4- excess drug intake (thyroxin).

**Clinical features**

1- heat intolerance, sweating, warm skin

2- tachycardia, palpitation, atrial ﬁbrillation

3- increased appetite with weight loss

4- ﬁne tremor, nervousness, anxiety, insomnia

5- weakness, muscle cramps, fatigue, diarrhea

6- eyelid retraction, exophthalmos

7- enlarged thyroid gland (goiter)

8- pretibial myxedema (non-inﬂamed indurated plaque).

**Investigation**

High freT4 and freeT3

Low TSH (except if the cause of hyperthyroidism is TSH secreting tumor)

Anti TSH receptor antibodies

Thyroid ultrasound to assess thyroid nodules.

Radioactive iodine uptake scan shows homogenous high uptake in Grave’s disease.

**Treatment**

1- Symptomatic:Beta-blocker (propranolol) controls tachycardia and decreases T4 to T3 conversion.

2- Blocking T3 and T4: Propylthiouracil (PTU) or Carbimazole to block T3/T4 synthesis.

3- Radioactive iodine ablation

4- Surgical subtotal thyroidectomy

**Dental aspect**

Well controlled thyrotoxicosis is not a problem in dentistry.

Exacerbating sympathetic over-activity by adrenaline in LA is not a significant problem.

Oropharyngeal ulceration from agranulocytosis due to carbimazole is a possibility.

**II- Hypothyroidism**

A condition with reduced metabolic state resulted from deﬁciency of thyroid hormones.

**Causes**

1- Hashimoto’s thyroiditis (autoimmune disease) 2- iodine deﬁciency 3- thyroidectomy

4- hypopituitarism 5- drugs (amiodarone).

**Clinical features**

1- cold intolerance, hair loss, thin eyebrow

2- bradycardia, dry cold skin, weight gain

3- fatigue, weakness, slow thinking, poor memory, constipation

4- slow speech, with hoarse voice

5- menorrhagia

6- periorbital edema and myxedema (non-pitting thick skin).

**Investigation**

Low T4, increased TSH in primary hypothyroidism and reduced in secondary hypothyroidism.

Diminished radioactive iodine uptake.

Positive antithyroglobulin and anti-thyroid peroxidase antibodies in Hashimoto’s thyroiditis.

**Treatment**

Levothyroxine tablet

**Dental aspect**

Sedative drugs should be avoided in poorly controlled hypothyroidism as they may precipitate myxedematous coma.

Well controlled hypothyroidism carries no significant risk in dental procedures.

Many medical conditions may be present in association with hypothyroidism and may carry significant risk, these include:

1- anemia 2- hypotension 3- heart failure

4- Addison’s disease 5- hypopituitarism 6- Sjogren's syndrome.

**Disorders of adrenal gland**

The adrenals comprise several separate endocrine glands within a single anatomical structure.

The adrenal medulla is an extension of the sympathetic nervous system which secretes catecholamines into capillaries rather than synapses.

Most of the adrenal cortex is made up of cells which secrete cortisol and adrenal androgens.

**Presenting problems in adrenal disease**

**I- Adrenal insufficiency**

Adrenal insufficiency results from inadequate secretion of cortisol and/or aldosterone. It is potentially fatal and notoriously variable in its presentation. A high index of suspicion is therefore required in patients with unexplained fatigue, hyponatremia or hypotension.

**Causes**

Adrenal failure could be:

A- primary defect in adrenals called Addison’s disease due to:

1- autoimmune disease

2- tuberculosis

3- septicemia

B- secondary defect due to suppression of hypothalamic- pituitary-adrenal axis by exogenous steroids, or pituitary- hypothalamic disease.

**Clinical features**

1- weakness, weight loss, anorexia, nausea, vomiting

2- hypotension, hypoglycemia

3- diarrhea, abdominal pain, dehydration

4- hyperpigmentation of mucosa (tongue, gingiva), hand crease, and elbows and knees.

**Investigation**

Low serum cortisol before and after ACTH stimulation

Increased ACTH in primary defect and reduced in secondary defect.

High serum potassium, low serum sodium, hypoglycemia, and anemia.

**Treatment**

Hydrocortisone and ﬂudrocortisone.

**Addisonian or adrenal crisis**

A critical clinical condition caused by acute adrenal insufficiency characterized by shock, dehydration, confusion, weakness, nausea, vomiting, and hypoglycemia. It is precipitated by stress like sepsis, hemorrhage, or trauma.

**Treatment**

Immediate ﬂuid resuscitation and IV hydrocortisone.

**Dental aspect**

To prevent Addisonian crisis, before performing dental surgery under LA, the patient should be given 100 mg hydrocortisone 1 hour pre-operatively followed by 100 mg every 6 hours for one day post-operatively then return to the usual dose.

For major surgery, the patient should be given 100 mg hydrocortisone 1 hour pre- operatively followed by 100 mg every 6 hours for 3 days post-operatively then return to the usual dose.

**Cushing’s syndrome**

A group of clinical manifestations caused by excess cortisol. By far the most common cause is iatrogenic, due to prolonged administration of synthetic glucocorticoids such as prednisolone. Non-

iatrogenic Cushing’s syndrome is rare.

**Causes**

1- Adrenal neoplasm 2- ectopic ACTH secretion (lung cancer)

3- pituitary tumor 4- steroid therapy

**Clinical features**

weight gain, hypertension, facial plethora, “moon face”, truncal obesity, buffalo’s hump, thin limbs, easy bruising, purple striae, DM, proximal muscle weakness, hirsutism, acne, emotional liability, osteoporosis, growth retardation, and hyperpigmentation (hyperpigmentation occurs in Cushing’s disease only).

**Investigation**

Increased plasma and urinary cortisol.

High ACTH in Cushing’s disease and low in Cushing’s syndrome

Dexamethasone suppression test to distinguish between causes of high ACTH.

Radiology: CT and MRI are useful to exclude tumors.

**Treatment**

Surgical resection or radiotherapy of hormone secreting tumors.

Minimize exogenous steroids

The patient must carry warning card and told about the dangers of withdrawal and about side effects.

**Dental aspect**

The complication of long-term use of systemic corticosteroids should always be kept in mind during dental treatment, these include:

- DM - psychosis - vertebral collapse - activation of latent TB

- osteoporosis - hypertension - peptic ulceration - immunosuppression

- wound infections - poor wound healing

Acute adrenal insufficiency crisis can be precipitated by any significant trauma.

Long-term profound immunosuppression may lead to oral complications like: hairy leukoplakia, Kaposi sarcoma, lymphomas, lip cancer, and oral keratosis.

Monitor blood pressure before, during, and after surgery and intravenous hydrocortisone must be immediately available for use if the blood pressure falls or the patient collapses.

Susceptibility to infection predisposes the patient to HSV and HZV which could be fulminant disease, so passive immunization with immunoglobulin against varicella zoster is indicated within 3 days of exposure to chickenpox or zoster.

Careful aseptic surgery and prophylactic antimicrobials may be indicated.

Avoid aspirin and NSAIDs.

**The recommended Steroid cover for dental patients on long-term steroid medication:**

|  |  |
| --- | --- |
| **Dental procedure** | **Steroid supplement** |
| Dental care | No supplement steroid and continue regular steroid dose |
| Minor surgery under LA | 50 mg hydrocortisone 1 hour pre-operatively followed post-operatively by continuing on the regular dose**.** |
| Major surgery under GA | Physician consultation.  Schedule the patient operation in the morning.  100 mg hydrocortisone injection 1 hour pre-operatively and every 6 hours post-operatively for 1-3 days.  Then return to regular dose |

It is essential to know the equivalent doses of various types of steroids which are:

|  |  |
| --- | --- |
| **Equivalent Dose** | **Steroid** |
| **1.2 mg** | **Betamethasone (long-acting)** |
| **1.5 mg** | **Dexamethasone (long-acting)** |
| **8 mg** | **Methylprednisolone (intermediate-acting)** |
| **8 mg** | **Triamcinolone (intermediate-acting)** |
| **10 mg** | **Prednisone (intermediate-acting)** |
| **10 mg** | **Prednisolone (intermediate-acting)** |
| **40 mg** | **Hydrocortisone (short-acting)** |
| **50 mg** | **Cortisone (short-acting)** |

**Rickets and Osteomalacia**

Rickets is a disease of growing bone that is unique to children and adolescents. It is caused by a failure of osteoid to calcify in a growing person. Failure of osteoid to calcify in adults is called osteomalacia.

**Causes**

1- dietary deﬁciency of vitamin D and calcium 2- malabsorption

3- hepatobiliary and pancreatic diseases 4- renal failure (renal osteodystrophy)

5- drugs (phenytoin) 6- familial hypophosphatemia

**Clinical features**

Rickets: weak deformed bones (bowing of legs), fragile bones (greenstick fractures), weak irritable hypotonic muscles, bone pains, and rachitic rosary (swellings at costochondral junctions).

Osteomalacia: persistent bone pain, weakness, difﬁculty in walking (waddling gait), thoracic kyphosis.

**Investigation**

Skeletal X-ray: diffuse osteopenia, biconcave vertebrae, pseudofractures.

Low serum calcium, low urinary calcium

Low - normal serum phosphate

High alkaline phosphatase

High PTH

**Treatment**

Calcium and vitamin D supplement

Treat underlying cause

**Dental aspect**

Severe form of rickets may be associated with orofacial features: retarded dental eruption, dental defects in severe cases, and radiolucent jaws

There is no association between dental caries and rickets or osteomalacia.

In cases of malabsorption, consider possibly associated vitamin K deﬁciency and related bleeding tendency

In cases with familial hypophosphataemia, the skull sutures are wide with frontal bossing and the teeth have large pulp chambers with abnormal dentine calciﬁcation, and are liable to pulpitis and multiple dental abscesses due to minimal caries or attrition, so preventive care with ﬁssure sealing or prophylactic occlusal coverage are needed.

**Osteoporosis**

Metabolic bone disease characterized by reduced bone mass with normal mineralization leading to increased bone fragility (fractures of femoral neck, distal radius and humerus).

**Causes**

- Smoking - alcoholism - renal failure - hyperthyroidism

- multiple myeloma - heparin - chronic steroid use - age

**Clinical features**

Typically, an old lady without symptoms or with chronic low back pain, loss of height, progressive kyphosis and sometimes vertebral compression fractures after bending or lifting followed by acute lumbar pain radiate to the ﬂanks and downward to one leg. Sometimes presented with fractures after minor trauma.

**Investigation**

Normal serum calcium and phosphorus, high urinary calcium.

Normal alkaline phosphatase but increased after fracture only.

Skeletal x-ray: biconcave vertebral bodies with compression fractures.

Reduced bone density by dual x-ray absorptiometry (DEXA) scan.

**Treatment**

Adequate dietary calcium and vitamin D supplement.

Weight bearing exercise (walking, running, jogging).

Hormone replacement therapy in menopausal women.

Raloxifene: selective estrogen receptor modulator

Bisphosphonates (alendronate) increases bone density of spinal bone and decreases incidence of fractures.

Intranasal calcitonin decreases bone reabsorption.

Denosumab: monoclonal antibody

**Dental aspect**

Osteoporosis increase the risk of fractures when handling the patient.

Oro-facial feature: excessive alveolar bone loss, Jaw osteoporosis, bisphosphonate-related osteonecrosis of Jaws (BRONJ)

**BRONJ**

Bisphosphonate-related osteonecrosis of the jaw (BRONJ) is a condition found in patients who have received intravenous and oral forms of bisphosphonate therapy for various bone-related conditions. BRONJ manifests as exposed, nonvital bone involving the maxillofacial structures.

BRONJ is thought to be caused by trauma to dentoalveolar structures that have a limited capacity for bone healing due to the effects of bisphosphonate therapy.

Area of exposed necrotic bone in maxillofacial region that did not heal within 8 weeks after identiﬁcation by dentist in patient receiving or received bisphosphonate and not had radiation therapy to the craniofacial region.

**Clinical examination**

Exposed bone, loose teeth, foul discharge, pain, and ﬁstula.

X-ray: sclerosis or loss of lamina dura and wide periodontal ligament space

**Prevention**

Oral surgery to be done before starting bisphosphonate or after drug stopping for 6 months and in emergency surgery, use prophylactic antibiotic.

**Treatment**

* Antimicrobial rinses
* Systemic antibiotics
* Systemic or topical antifungals
* Discontinuation of bisphosphonate therapy
* No dental therapy or minimally invasive dental therapy (ie, root canal therapy instead of extraction)

**Gigantism and acromegaly**

Clinical condition results from overproduction of growth hormone by anterior pituitary adenoma causing gigantism before the time of epiphyseal fusion and acromegaly thereafter.

**Clinical features**

Gigantism: tall stature, thick soft tissue with prominent supraorbital ridges, coarse oily skin, thick spade like ﬁngers and deep voice.

Acromegaly: enlarged mandible (prognathism), thick facial features, large spade like hands.

**Complications**

DM, hypertension, heart failure, arrhythmia, sleep apnea, hypercalcemia, osteoarthritis, hypopituitarism, visual ﬁeld defect, and raised intracranial pressure.

**Investigation**

Raised serum GH.

Lack of GH suppression by glucose load.

High serum IGF-1 (Insulin-like growth factor-1)

Radiography: X-ray, CT, and MRI show evidence of pituitary enlargement

**Treatment**

Surgery (trans-sphenoidal resection of pituitary adenoma).

Radiation therapy

Dopamine agonist (bromocriptine) or somatostatin analogue (octreotide).

GH receptor blocker (pegvisomant).

**Dental aspect**

Consider possible associated complications (HT, DM, HF, hypopituitarism, and arrhythmia).

GA may be hazardous from associated kyphosis and associated difﬁcult intubation.

Both gigantism and acromegaly could be associated with following orofacial features:

thickened skull, enlarged paranasal sinuses, mandibular enlargement with prognathism (class III malocclusion), teeth spacing, thickening of facial soft tissue and sialosis may develop.

^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^^