Endocrinology in Primary Care

Presentation and Impact

John Marlow- October 2013

Hypothyroidism

Cushing's disease

Type 2 Diabetes Mellitus

Hyperprolactinaemia

Acromegaly

Grave's disease

Hyperthyroidism

Diabetes insipidus

Type 1 Diabetes Mellitus

Polycystic ovarian syndrome

Addison's disease

Hyperparathyroidism

Hypoparathyroidism

Hypogonadism

Conn's syndrome

Phaeochromocytoma

What do I need to know?

The Medical Bits

- Especially to recognise the *presentation* of both common and rare disease
- Most endocrine diseases present to a GP
- Some are exclusively managed in general practice, others you need to understand treatment.

The GP bits

- To understand the *impact* of endocrine disease
- To manage what are usually chronic long term conditions

3.17 Care of People with Metabolic Problems

Key messages:- (RCGP)

- Have understanding of how common disorders present, and rarer and important ones, which can be potentially life-threatening if missed
- GPs should understand the role of good diabetes management in prevention of associated morbidity and mortality
- All GPs should be competent in the recognition and management of primary care emergencies.

Aims and objectives

- Aim

Understand the primary care management of endocrine disease

- Objectives

1) See how some endocrine cases presented

2) Identify the key features of each disease

3) Analyse the impact of the diseases using the 6 RCGP competences and 3 essential features

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Acromegaly

Epidemiology

- Uncommon. Prevalence 40-60/million
- Very uncommon in children. Peak incidence 30-50 years (as with other pituitary tumours)
- Pituitary tumours order of prevalence: Prolactin (relatively common), GH, ACTH, Gonadotrophins, TSH (very rare)

Aetiology

- Usually a benign pituitary tumour
- Predominantly secrete GH (+ prolactin in 30%)

Rarely

- Pituitary carcinoma
- Associated with MEN
- Ectopic GHRH from carcinoid tumour

Clinical Features

- Insidious onset, but early diagnosis important
- **Local effects** of pituitary tumour- headaches, visual field defect, cranial nerve palsy
- **Endocrine** effects

Facial- coarse features, supra-orbital ridges, broad nose, thickening soft tissues. Lips thicken, prognathism, macroglossia, dental separation

Sweating

Hands- enlarge, CTS (may be presentation)

Arthritis- premature OA

CVS- coronary artery disease, hypertension (35%), cardiomyopathy (less common)

Type 2 diabetes 20-30% present with this

Hyperprolactinaemia- women, men

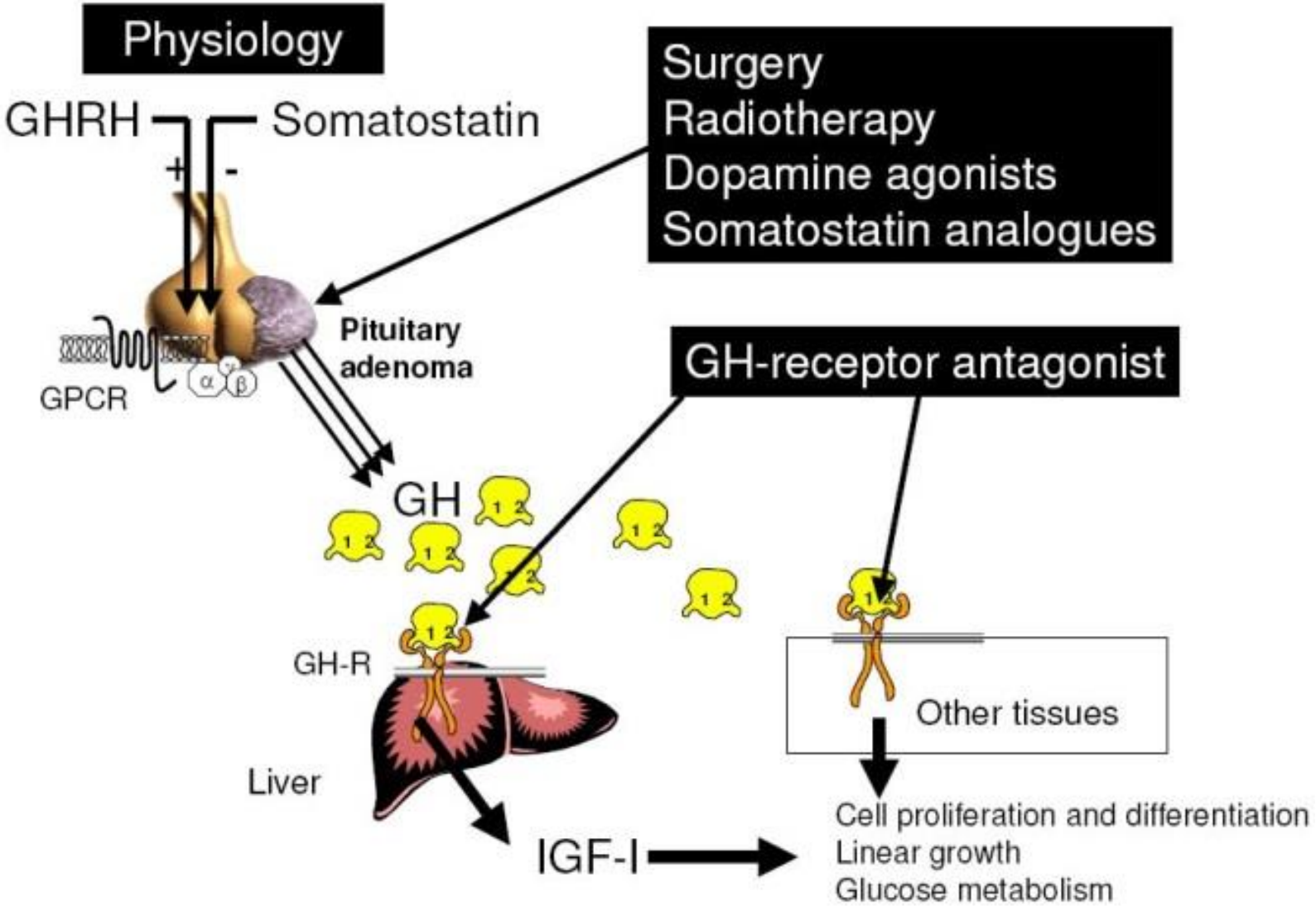
Hypopituitarism-> hypothyroidism, hypo-adrenalism

Investigations

- insulin-like growth factor 1 levels (IGF-1)
- failure of growth hormone to be suppressed by 75 g oral glucose (can measure GH but fluctuates)
- MRI pituitary
- Chest and abdominal radiology
- Hand x-ray: tufting of terminal phalanges, ↑ joint spaces
- Pituitary function tests
- Visual fields
- Urinary calcium

Management

- The aim of treatment should be symptomatic control and a growth hormone concentration of less than 5 mU/l.
- Treatment of choice is usually transphenoidal surgery (60% remission microadenoma)
- If IGF-1 normal, GH <5 then no further treatment
- If not, then radiotherapy and/or drug treatment (e.g. octreotide, bromocriptine, pegvisomant)
- Treat complications e.g. hypopit., BP, DM


Physiology
GHRH
Somatostatin
+
-
Surgery
Radiotherapy
Dopamine agonists
Somatostatin analogues
Pituitary adenoma
GPCR
α
β
γ
GH-receptor antagonist
GH
GH-R
Liver
Other tissues
IGF-I
Cell proliferation and differentiation
Linear growth
Glucose metabolism

Medical Treatment

- Medical treatment does not cause significant shrinkage of the pituitary adenoma. Used to reduce growth hormone concentrations whilst radiotherapy is taking effect, and for those who fail treatment with surgery and radiotherapy.
- Somatostatin anologues- GHRIH (e.g. octreotide) currently the most effective medical treatment of acromegaly and reduces growth hormone concentrations in most cases

Prognosis

- Markedly reduced survival if untreated
- Most deaths from heart failure, coronary artery disease and hypertension related complications
- Increased incidence large bowel tumours

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Grave’s disease

Grave's disease

- 70-80% of all cases hyperthyroidism (most of rest are toxic multi-nodular goitre and toxic adenoma)
- Caused by production of antibodies that stimulate the TSH receptor
- Female > Male 5:1
- 50% monozygotic twin concordance

Clinical Features- thyroxtoxicosis

- - weight loss, increased appetite, heat intolerance, sweating, fatigue, weakness, hyperactivity, irritability, dysphoria, insomnia, tremor, depression, oligomenorrhoea, pruritis, diarrhoea, polyuria, periodic paralysis, chorea
- - signs: tremor, hyper-reflexia, tachycaridia, AF, muscle weakness, proximal myopathy, cardiac failure, warm skin, hair loss, onycholysis

Specific for Grave's disease

- FH or personal history autoimmune disease
- Ophthalmopathy- grittiness, increased tear production, periorbital oedema, conjunctival oedema, proptosis, corneal ulceration
- Pretibial myxoedema 1-2%
- Thyroid acropachy (periosteal bone formation, looks like clubbing)

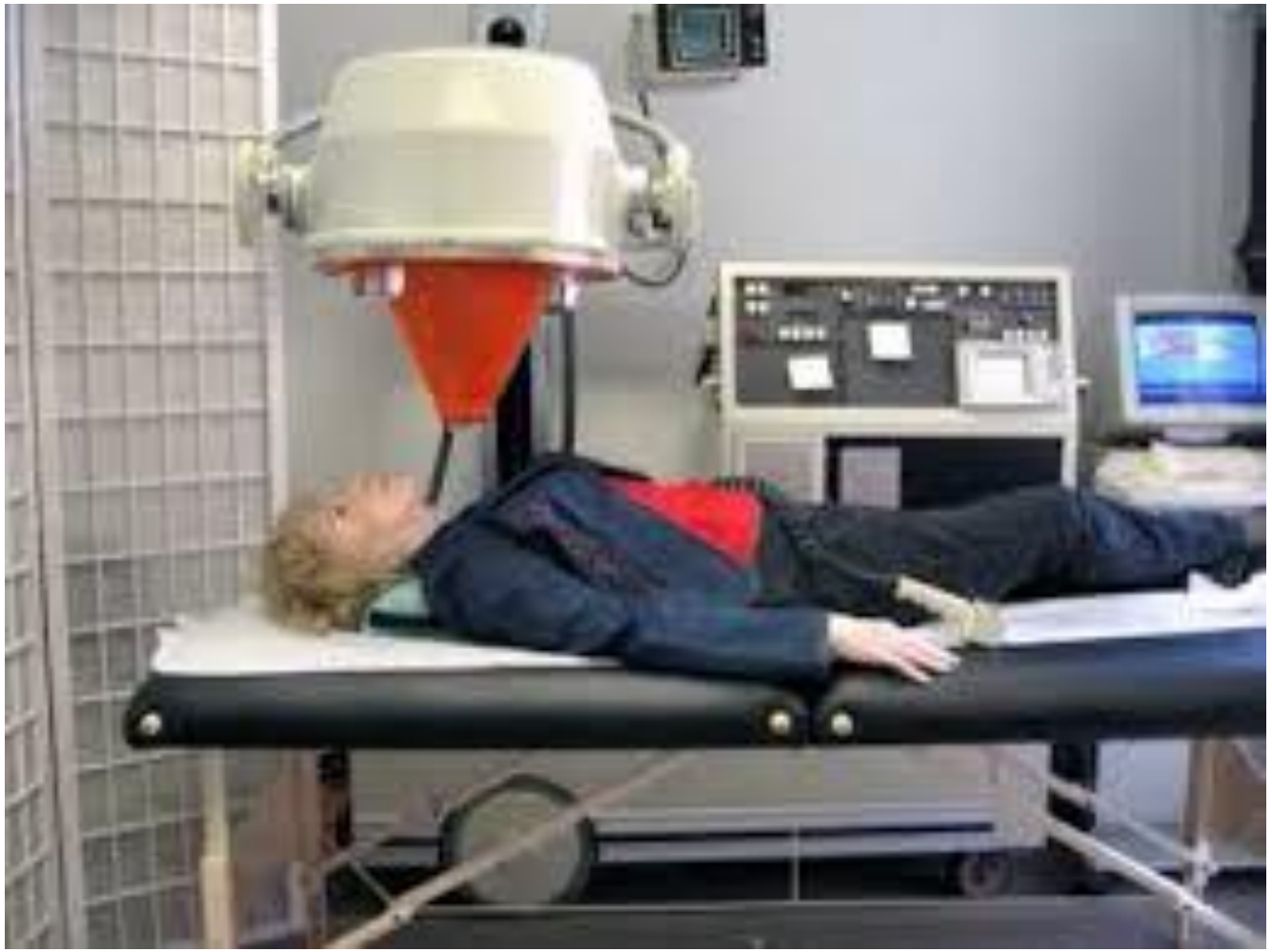
Investigations

- TSH, free T3 and T4
- Auto-antibodies against thyroglobulin and thyroid peroxidase (80%, but false +ve)
- Isotope scan of thyroid if doubt about nature of goitre

Management

- Anti-thyroid drugs- carbimazole, propylthiouracil
- Beta blockers
- Radioiodine
- Subtotal thyroidectomy
- Symptomatic management of ophthalmopathy

- 40-50% success with medication, of relapses 70% happen in first year.



Side effects & Complications

- Carbimazole- maculopapular rash (often settles), arthralgia, N&V, pruritus, cholestatic jaundice, hepatitis, Agranulocytosis < 0.1% usually in first 3 months
- Radioiodine- CI pregnancy/breastfeeding. Can take 4-6 months to judge response
- Surgery- laryngeal nerve palsy, transient hypocalcaemia, hypothyroidism.

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Hypopituitarism

Pituitary hormone deficiency

- Usually GH, FSH, LH, ACTH, TSH in order
- ADH and Oxytocin rarely affected unless hypothalamus involved
- Can get increased prolactin instead of low prolactin (related to loss of dopamine inhibition)

Causes

- Pituitary tumour (haemorrhage into tumour can cause pituitary apoplexy)
- Cerebral tumours
- Vascular (post-partum necrosis- Sheehan's, infarction, severe hypotension, cranial arteritis)
- Trauma- basal skull fracture
- Infection (e.g. TB meningitis, syphilis)
- Iatrogenic (surgery, radiation, drugs e.g. steroids)
- Infiltration (sarcoidosis, haemochromatosis)
- Hypothalamic disorders- anorexia, starvation

Clinical Features

- GH: ↓growth, ↓muscle bulk, ↓glucose
- FSH/LH: delayed puberty, ↓libido, ↓body hair

  F oligomenorrhoea, infertility

  M E.D., azoospermia, testicular atrophy
- ACTH: features of glucocorticoid deficiency, decreased skin pigmentation
- TSH: hypothyroidism
- ADH: thirst, polyuria

Investigations

- Pituitary function tests
- Visual fields
- MRI pituitary
- Others depending on suspected cause

Replacement hormone treatment

- Hydrocortisone
- Thyroxine (can precipitate adrenal crisis)
- Testosterone, oestrogen, progesterone
- Growth hormone
- Desmopressin
- For fertility- HCG, FSH, pulsatile LHRH

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Addison's Disease

Addison's Disease

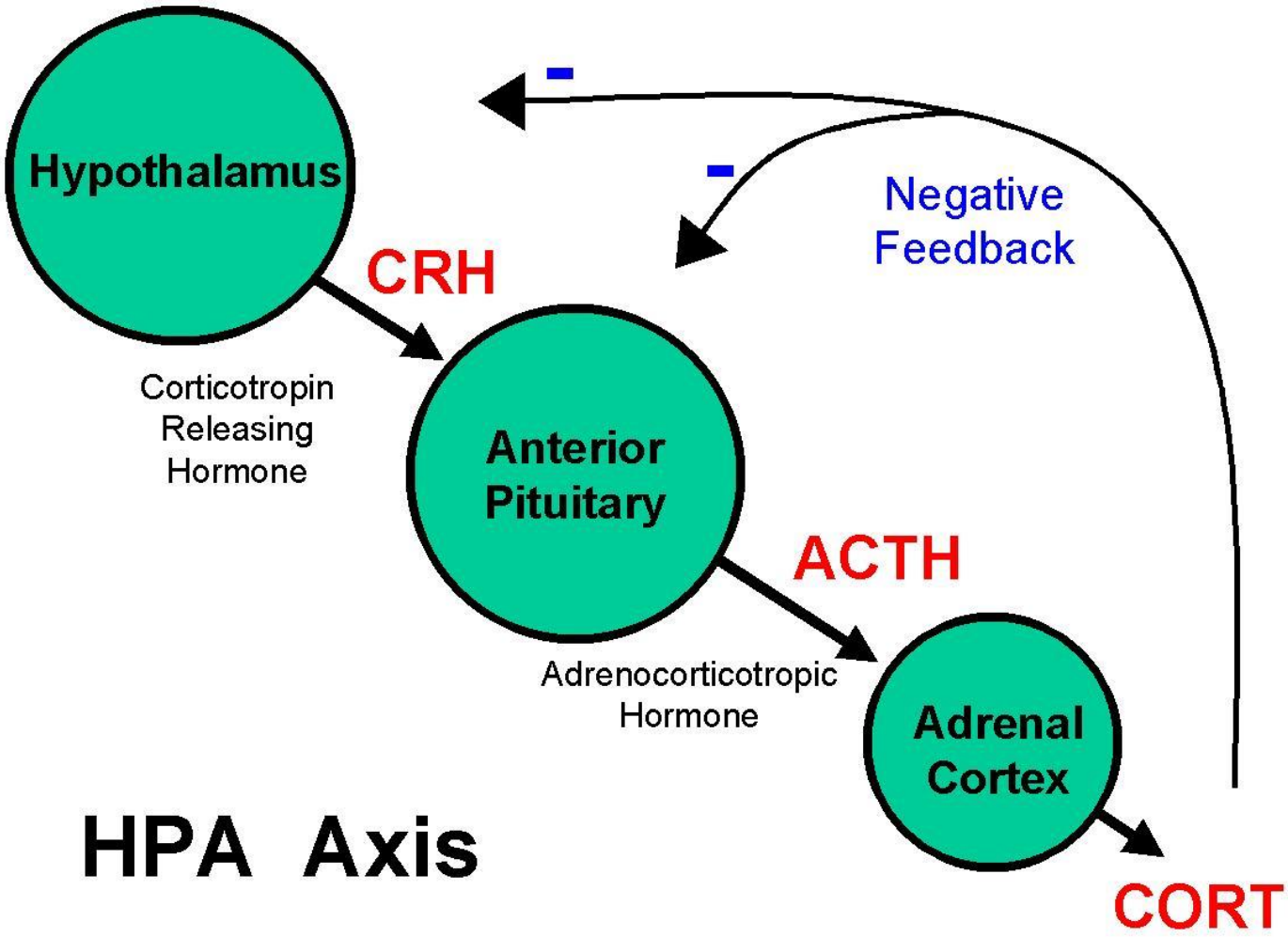
- = primary adrenal failure
- Life threatening condition

Incidence

- 1/100,000/year

Adrenal gland

- Cortex is essential to life, secreting 3 classes of steroid hormone- glucocorticoids, mineralocorticoids and androgens
- In Addison's get lymphocytic infiltration and destruction entire adrenal cortex
- Medulla isn't essential- secreting NA and A
- CRH, ACTH, glucocorticoids –ve feedback loop

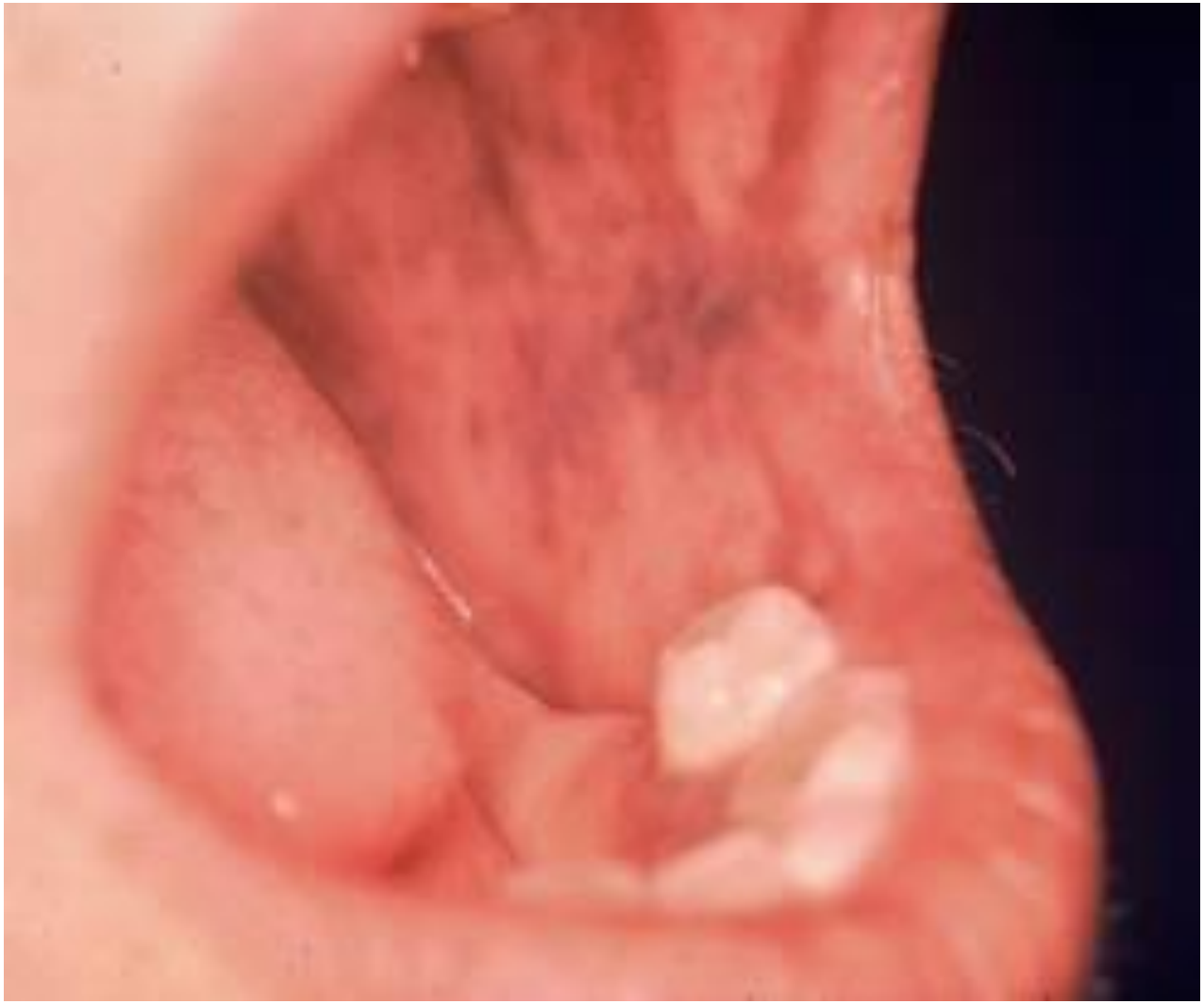

Hypothalamus
CRH
Corticotropin
Releasing
Hormone
Anterior
Pituitary
ACTH
Adrenocorticotropic
Hormone
Adrenal
Cortex
CORT
Negative
Feedback
-
-
HPA Axis

Aetiology

- Autoimmune adrenalitis is most common cause in UK (70-90% cases)
- Other causes: TB infiltration (commonest cause worldwide), malignant infiltration, haemorrhage from meningococcal infection (Waterhouse-Friderichsen syndrome), amyloidosis, haemochromatosis, CMV in HIV, inherited adrenoleukodystrophies.

Clinical Features

- Tiredness, generalised weakness and lethargy
- Anorexia, nausea, vomiting, weight loss, abdominal pain, diarrhoea
- Dizziness and postural hypotension
- Pigmentation
- Loss of body hair
- Crisis: hypotension, vomiting and coma



Investigations

- Synacthen test- im, measure cortisol at 30 mins and 1 hour
- High ACTH
- Cortisol (really only useful if presenting with crisis)
- Adrenal antibodies
- Low sodium, high potassium
- Apparent hypothyroidism
- CXR/AXR for TB/calcification adrenals

Management

- Emergency- fluid resuscitation (saline), iv hydrocortisone, correct hypoglycaemia, treat cause, may need ITU, iv HC 6 hourly
- Maintenance- hydrocortisone 20-30mg in 3 divided doses e.g. 20/5/5 (short half life)
- Fludrocortisone 50-200mcg/day

Long term

- Patient education- if vomiting or severe diarrhoea and unable to take hydrocortisone for more than a few hours, need parental HC, usually in hospital.
- Double hydrocortisone during intercurrent illness (not if mild cold, stress)
- Alert bracelet, steroid card
- Peri-operative, pregnancy.

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Hypothyroidism

Epidemiology

- Prevalence 1-2%
- Female: Male 10:1
- Disease register 3%

Depression

Cold intolerance

Change in appearance

Poor memory

Deafness

Menorrhoagia

Tiredness/Malaise

Psychosis

Weight gain

Poor libido

Puffy eyes

Dry, brittle hair

Anorexia

Arthralgia

Myalgia

Constipation

"Peaches and cream" complexion

Mental slowness

Dry, thin hair

Psychosis/dementia

Ataxia

Raised BP

Bradycardia

Dry skin

Slow relaxing reflexes

Hypothermia

Poverty of movement

Heart failure

Large tongue

Deep voice

Carpal tunnel syndrome

Anaemia

Common causes

- Autoimmune hypothyroidism
  - atrophic hypothyroidism
  - Hashimoto's thyroiditis
- Previous radio-iodine or surgery
- Iodine deficiency (common worldwide)
- Anti-thyroid drugs
- Other drugs (e.g. lithium, amiodarone)
- Subacute, silent, or postpartum thyroiditis

Uncommon causes

- Infiltrative disease
- Secondary thyroid failure (hypothalamus or pituitary disease)
- Congenital

Autoimmune hypothyroidism

- Lymphoid infiltration of thyroid
- Atrophic -> atrophy and fibrosis
- Hashimoto's -> atrophy and regeneration (goitre)
- Associated with other auto-immune conditions (vitiligo, pernicious anaemia, type 1 diabetes, Addison's disease, premature ovarian failure)
- Increased incidence in Down's or Turner's syndrome

Investigations

- Low T4 with raised TSH
- Raised TSH, normal T4 = subclinical hypothyroidism
- Low TSH and low T4 suggests hypothalamic or pituitary disease
- Antithyroid antibodies (help indicate cause rather than diagnosis)
- Anaemia, ↑ AST, CK, cholesterol, ↓ sodium

Management

- Levothyroxine 100-150mcg daily
- Clinical improvement 2-3 weeks
- TSH takes ~6 weeks to normalise
- Up to 25% of patients are undertreated. Some are overtreated (increased CVS risk)
- Increased dose needed in pregnancy
- Some drugs increase clearance or decrease absorption of thyroxine

“Subclinical” hypothyroidism

- Raised TSH (<10) with normal T4
- 2-5% progression/year to hypothyroidism
- If +ve TPO antibodies, up to 80% progress to over hypothyroidism in 4 years
- Repeat 3-6 months
- Negative antibodies, repeat every 3 years
- Therapeutic trial levothyroxine if symptomatic

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