Advanced Practice in Endocrinology

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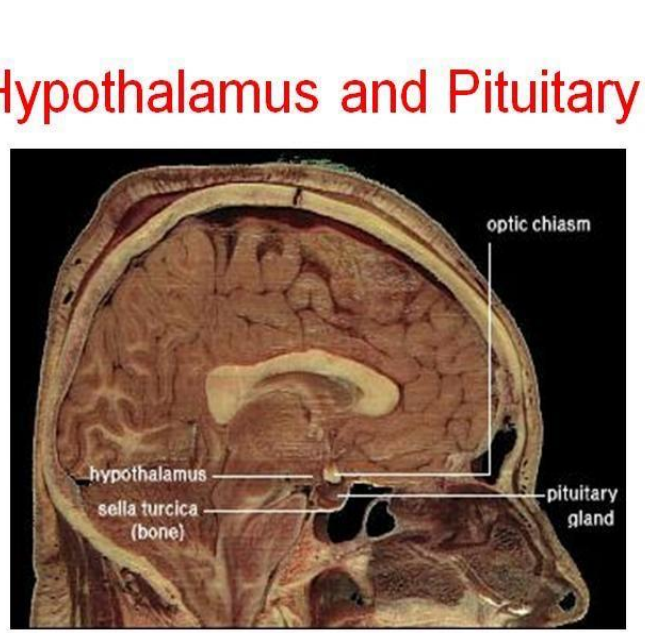
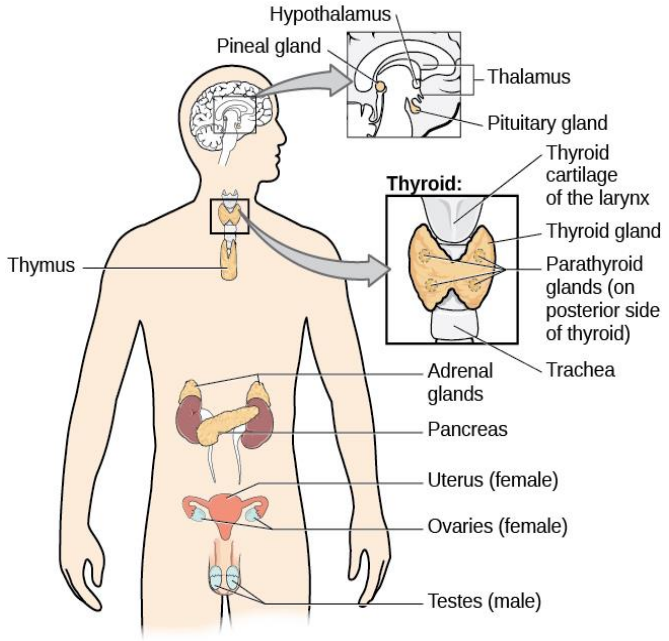
ANP Role in Endocrinology
What do we do?

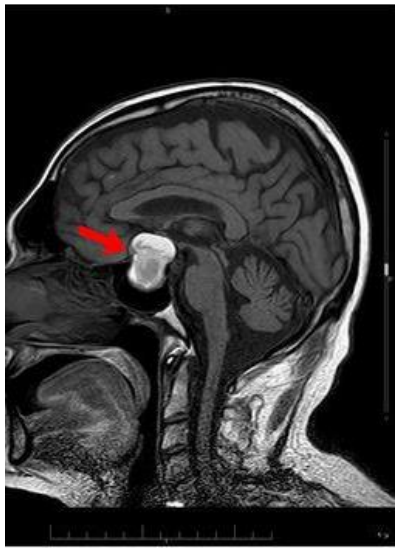




Growth Hormone?
Too much or too little?

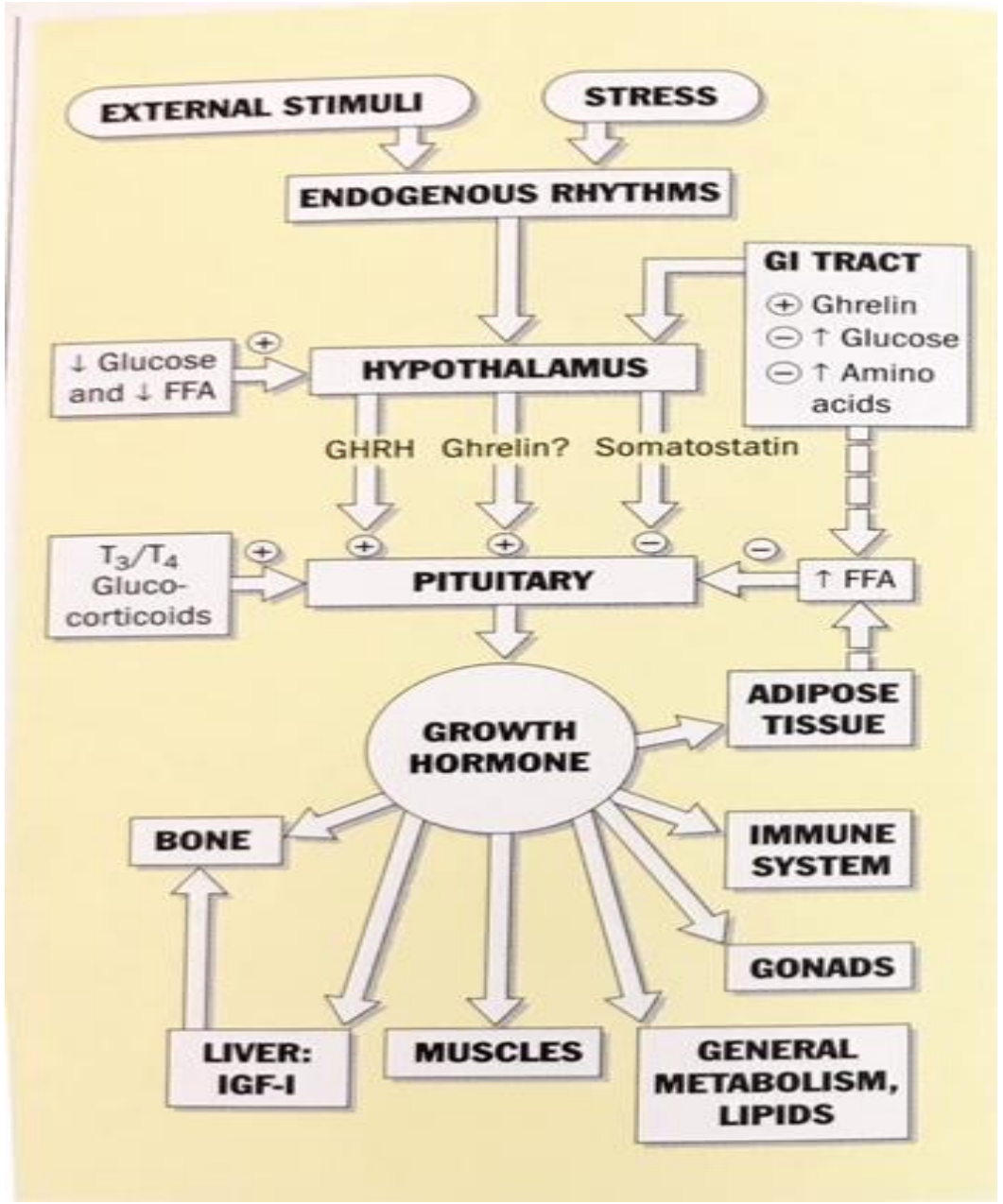
- Acromegaly
- Gigantism
- Achondroplasia
- Abuse in elite sport
- Pituitary Tumor
- Different Aetiology

Figure 1 - Familial gigantism in the two Hugo brothers. Top row: Battista Ugo (Baptiste Hugo), 1876–1916, reached a height of 2.30 m (7 ft, 7 in) and Paolo Antonio Ugo (Antoine Hugo), 1887–1914, reached a height of 2.25 m (7 ft, 5 in). Bottom row: the parents of the Ugo brothers, Teresa Chiardola (1849–1905) and Antonio Ugo (1840–1917), and their sister, Maddalena Ugo (1885–1960). Picture from the collection of Dr. W. W. de Herder.



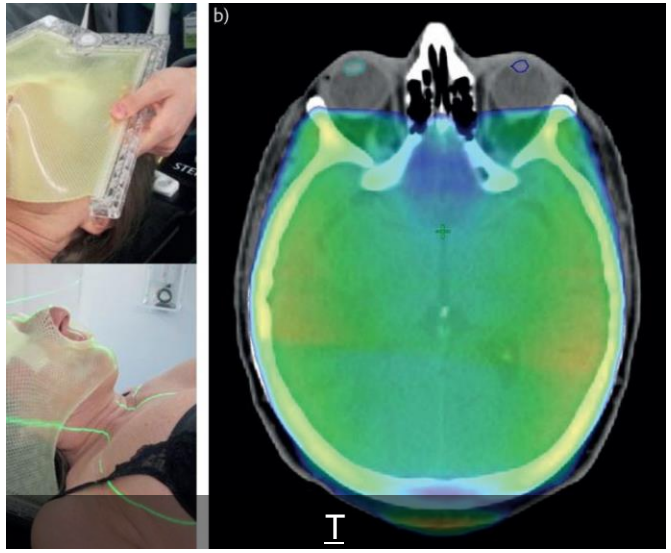
Action of Growth Hormone

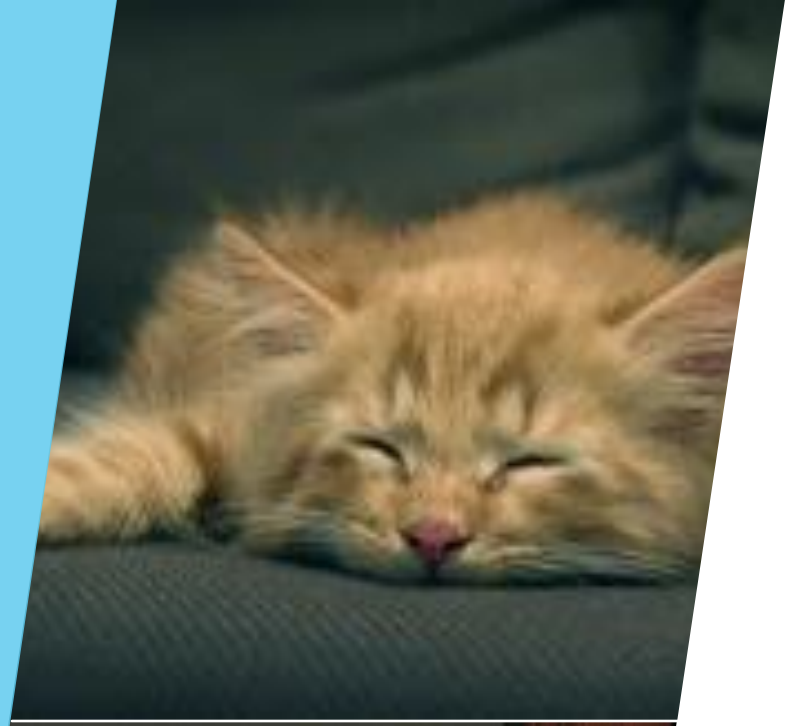
- Growth Hormone belongs to a family of hormones which are thought to have evolved from a common precursor.
- Members of the GH family are encoded by genes that span approximately 2.0kb, contain 5 exons and 4 intervening sequences.
- hGH gene family consists of the 191-amino acid hGH molecule, human chorionic somatomammotrophin and human prolactin,all located on the long arm of chromosome 17.
- Major function is growth promotion-in vertebrates hyposecretion leads to dwarfism-hypersecretion before puberty leads to gigantism.
- 2 major kinds of metabolic activity-early insulin and late insulin like activities

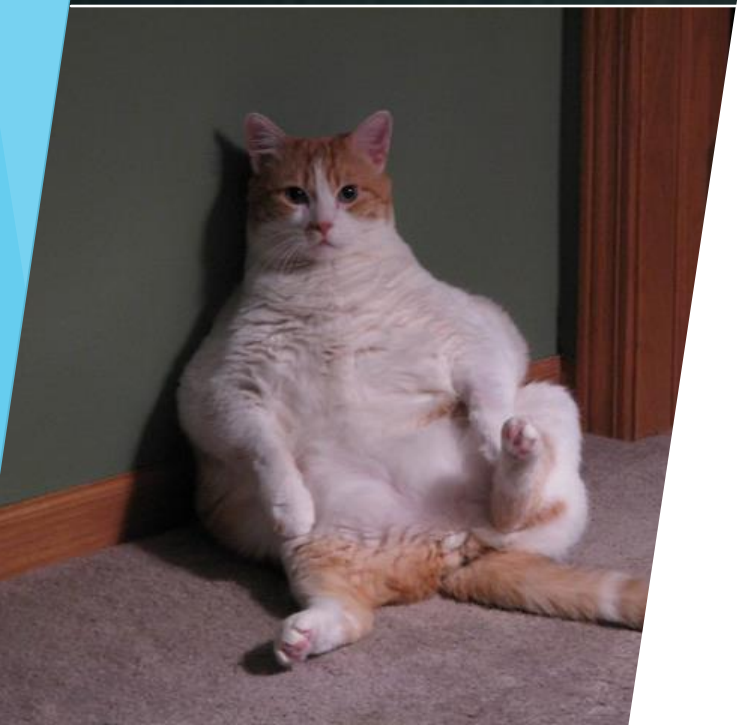

EXTERNAL STIMULI
STRESS
ENDOGENOUS RHYTHMS
GI TRACT
⊕ Ghrelin
⊖ ↑ Glucose
⊖ ↑ Amino acids
↓ Glucose and ↓ FFA
HYPOTHALAMUS
GHRH
Ghrelin?
Somatostatin
T_3/T_4 Gluco-corticoids
PITUITARY
↑ FFA
ADIPOSE TISSUE
GROWTH HORMONE
BONE
IMMUNE SYSTEM
GONADS
LIVER: IGF-I
MUSCLES
GENERAL METABOLISM, LIPIDS

Adult Growth Hormone Deficiency

- Adult GH deficiency may be of adult onset or childhood onset, and may occur as isolated GH deficiency or as part of multiple pituitary hormone deficiency. In adult onset, GH deficiency is commonly due to pituitary tumours or their treatment, and to cranial irradiation. Childhood-onset GH deficiency is often idiopathic, and may continue into adulthood. Also, iatrogenic GH deficiency may occur in childhood or adulthood in survivors of childhood malignancy, as a result of previous cranial irradiation and/or chemotherapy.







Clinical need

- GH deficiency in adults may be associated with the following adverse features to a variable degree in any individual: reduced quality of life (QoL) especially reduced energy levels; altered body composition (reduced lean mass and increased fat mass, especially in the trunk); osteopenia/osteoporosis (reduced bone mineral density); dry skin (reduced sweating); reduced muscle strength and exercise capacity; lipid abnormalities (especially elevated LDL cholesterol); insulin resistance; increased levels of fibrinogen and plasminogen activator inhibitor; reduced extracellular fluid volume; increased thickness of the intima media of blood vessels; and impaired cardiac function.

Diagnosis of Adult GH Deficiency

Patients with severe GH deficiency in adulthood are defined as patients with known hypothalamic pituitary abnormality and at least one known deficiency of another pituitary hormone excluding prolactin.

These patients should undergo a single diagnostic test in order to diagnose the presence of GH deficiency.

In patients with childhood onset isolated GH deficiency (no evidence of hypothalamic pituitary abnormality or cranial irradiation), two diagnostic tests should be recommended, except for those having low IGF-1 (a marker of GH response) concentrations (standard deviation score less than -2) who may be considered for one test.

Several tests are available for the diagnosis of GH deficiency. The ITT is regarded as the „gold standard" test for adults.

A general definition of severe GH deficiency in adults is a peak concentration of less than 9 mU/litre (3 ng / ml) in response to insulin-induced hypoglycaemia

When the ITT is contraindicated other tests – such as response to GH-releasing hormone, arginine or glucagon – can be used.

When to test and clinical assessment

- Diagnostic test after stabilised treatment of other pituitary deficiencies
- Diagnostic test at least one month after pituitary surgery
- Childhood treatment should be interrupted for a period of 2-3 months before retesting of growth hormone level status.
- Current medical history
- Full history of hypothalamic-pituitary disease
- Surgical and radiological history
- Number of pituitary hormone deficiencies
- Current replacement regimen
- Previous growth hormone treatment (if any)
- Quality of life assessment using the disease-specific „Quality of life assessment of growth hormone deficiency in adults" (QoL-AGHDA) questionnaire.

Prescribing

Treatment is self-administered by a daily subcutaneous injection. The initial dose is 0.2–0.3 mg (0.6–0.9 IU) daily (typically 0.27 mg [0.8 IU] daily).

Various injection devices on the market

For the first 2–3 months dosage adjustments are made after monthly assessments of serum levels of IGF-1, and in response to the presence of adverse effects, until a maintenance dose is achieved.

The currently used median maintenance dose is 0.4 mg (1.2 IU) daily.

GH requirements may decrease with age, mirroring the physiological production of growth hormone

Contraindications

GH treatment is contraindicated in people with any evidence of tumour activity, with proliferative diabetic retinopathy, in critically ill patients (for example, after complications following open heart or abdominal surgery, multiple trauma, acute respiratory failure or similar conditions) and also in patients with known hypersensitivity to GH or to any of the excipients.

In patients with tumours, anti-tumour therapy must be completed before starting GH therapy.

Pregnancy and lactation . GH treatment is contraindicated during pregnancy and lactation.

Drug interactions (refer also to BNF)

Corticosteroids: The growth promoting effect of somatropin may be inhibited by corticosteroids

Oestrogens: Increased doses of somatropin may be needed when given with oestrogens (when used as oral replacement therapy)

Monitoring

A recognised technique for monitoring the dose is to take regular measurements of insulin-like growth factor I (IGFI). IGF-I levels should increase during therapy. IGF-I levels should normally be maintained within the upper normal range during therapy. The aim is to find the dose of GH which moves IGF-I levels into the upper normal range.

IGF-1 mediates many of the actions of GH which is produced in the liver, bone and other tissues in response to GH

The patient will require one or two monthly IGF-I blood tests until the optimum maintenance dose is reached. This is normally carried out in secondary care.

Under shared care guidelines this is the common practice

Monitoring and Outcome

- Height, Weight and BMI-TANITA Bioimpeadence
- Waist/hip ratio
- Blood Pressure
- HbA1c/Lipid profile
- AGHDA
- Overall health and well- being
- Adjustment of dose as required
- Discussion with patient of any adverse events
- Check on injection device and compliance
- NICE assessment

Adverse effects

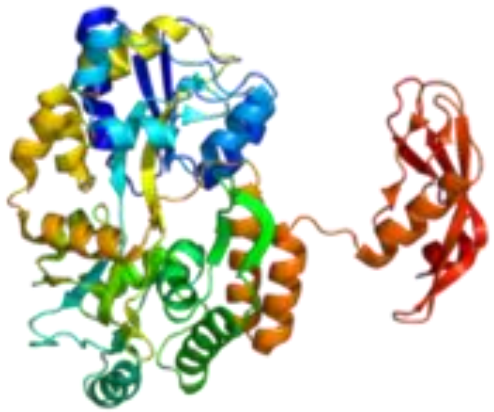
Fluid retention (peripheral oedema) is the most commonly reported “side effect” of GH replacement therapy. Fluid retention, with occasional mild ankle oedema, is a normal part of growth hormone action. This tends to decrease as therapy continues but may occasionally require dose reduction.

Hyperglycaemia and hypoglycaemia have been reported. GH therapy has also been shown to reduce insulin sensitivity in these patients by antagonising the action of insulin – this could increase the risk of diabetes.

Headache;- persistent headaches require investigation with fundoscopy for papilloedema being recommended if severe or recurrent headache, visual problems or nausea and vomiting occur and if papilloedema is confirmed consider benign intracranial hypertension (rare cases reported) This is usually recognised shortly after commencement of therapy. Usually a temporary cessation of treatment resolves the symptoms. A severe and persistent headache should be reported immediately to the endocrinology department.

Adverse events cont……

- Arthralgia (joint pain), myalgia (muscle pain), carpal tunnel syndrome and paraesthesia can occur. These effects, if they occur, are usually mild and self-limiting. A reduction in the GH dose may be required while they persist.
- Hypothyroidism can occur
- Reactions at injection site – these are unusual and may also be due to unnecessary use of a spirit-based skin cleanser.
- Antibody formation can be detected but is rarely of physiological relevance.
- Other side effects may include mild hypertension, visual problems and nausea and vomiting.
- All of these possible side-effects will have been discussed with the patient by the endocrine team before treatment is started and an information leaflet provided.
- There is no evidence to suggest that GH therapy will increase the risk of abnormal or neoplastic growth, either a new growth or a resurgence of an old tumour.



Summary

- Reviewed Growth Hormone and Growth Hormone deficiency
- Diagnosis
- Treatment
- Management
- Monitoring
- Outcome