## Gigantism

This rare condition occurs if GH hypersecretion begins in childhood, before closure of the epiphyses. Skeletal growth velocity and ultimate stature are increased, but little bony deformity occurs. However, soft-tissue swelling occurs, and the peripheral nerves are enlarged. Delayed puberty or hypogonadotropic hypogonadism is also frequently present, resulting in a eunuchoid habitus.

## Acromegaly

### Summary

Acromegaly is a condition in which benign pituitary adenomas lead to an excess secretion of growth hormone (GH) and insulin-like growth factor 1 (IGF-1). In adults, whose epiphyseal plates are closed, the disease causes enlarged hands and feet, coarsened facial features, and pathological growth of internal organs. If the condition occurs in children, before epiphyseal plate closure, it is known as gigantism, which is discussed in a separate learning card. The first step in diagnosing acromegaly is to measure IGF-1 levels. Further testing includes an oral glucose tolerance test (OGTT) with assessment of GH levels, and evaluation of pituitary tumors via cranial MRI. Management consists of transsphenoidal adenomectomy for operable tumors, or GH-inhibiting medication and radiotherapy if surgery is contraindicated or unsuccessful. Adequate treatment is vital to reduce the risk of complications, such as cardiovascular disease and cerebral aneurysms, as these may considerably increase mortality.

### Etiology

- Benign growth hormone-secreting pituitary adenoma (> 95% of cases)
- Very rare: neuroendocrine or hypothalamic tumors, paraneoplastic syndromes

### Pathophysiology

- **Physiology of GH and IGF-1**
- Hypothalamus secretes GHRH → ↑ secretion of GH → GH induces IGF-1 synthesis → ↑ serum IGF-1 :
- → binds to IGF-1 and insulin receptors → stimulation of cell growth and proliferation, inhibits programmed cell death

- Proliferative effects especially on bone, cartilage, skeletal muscle, skin, soft tissue, and organs
- Pathological glucose tolerance caused by binding to insulin receptors
- → ↑ secretion of somatostatin from the hypothalamus → ↓ serum GH and IGF-1 (negative feedback)
- **Effects of a pituitary adenoma**
- Overproduction of GH → abnormally high serum IGF-1 levels → **overstimulation of cell growth and proliferation** → symptoms of acromegaly
- Tumor mass compresses neighboring structures (e.g., optic nerve) → symptoms of mass effect
- Impaired secretion of other pituitary hormones possible, especially gonadotropins → ↓ LH and FSH → ↓ estrogen and testosterone

**Clinical features**

- **Tumor mass effects**
- Headache, vision loss (**bitemporal hemianopsia**), cranial nerve disorders
- ♀: Oligomenorrhea, secondary amenorrhea, galactorrhea, vaginal atrophy
- ♂: Erectile dysfunction, decreased libido, ↓ testicular volume
- **Soft tissue effects**
- Doughy skin texture, hyperhidrosis
- Deepening of the voice, macroglossia, obstructive sleep apnea
- Carpal tunnel syndrome
- **Skeletal effects**
- Large skull, coarsened features: **enlarged nose, forehead, and jaw** (macrognathia) with diastema
- **Widened hands, fingers, and feet**
- Painful arthropathy (ankles, knees, hips, spine)
- **Cardiovascular disease**: hypertension (~ 30% of cases), left ventricular hypertrophy, cardiomyopathy
- **Organ enlargement**: especially kidneys and thyroid gland
- Effects of diabetes mellitus (up to 50% of cases)