# Endocrinology – growth hormone (GH)

*Rudolf Cardinal, 18 Oct 98*

## Nature

GH is a 191-amino acid polypeptide released by somatotrophs in the anterior pituitary. It is species-specific (humans only respond to human GH). It acts directly on target tissues, but also stimulates the release of **somatomedins** from the liver (see below).

## Functions

GH has two main types of effect.

1. **Direct metabolic actions.** These *antagonise insulin* and are synergistic with cortisol – they are "diabetogenic". That is, GH inhibits glucose uptake by muscle and adipose tissue, increases hepatic glucose output and reduces the sensitivity of muscle and adipose tissue to insulin. If glucose tolerance was poor in the first place, an unpleasant cycle can ensue: insulin resistance → elevated plasma glucose → pancreas releases more insulin → raised insulin levels → downregulation of insulin receptors → insulin resistance worsens… → eventual exhaustion of pancreatic β cells.
2. **Indirect growth-promoting actions.** These are "insulin-like" in that, like insulin, they promote growth.[1] These actions are mediated via the **somatomedins** (see below).

**Growth** is a term covering a variety of physiological processes. It may be defined simply as an increase in size, and may result from cellular *hypertrophy* (enlargement) or *hyperplasia* (increase in number), or increased production of *extracellular matrix*. GH has all these effects.

## Control

- The hypothalamus releases **growth hormone-releasing hormone (GHRH)** which stimulates GH release, and **somatostatin** which is inhibitory. It is the GHRH:somatostatin ratio that determines the level of GH secretion.
- GH release is *episodic*, not tonic. There is a clear 24-hour rhythm. Secretion is increased by sleep (stages III and IV, i.e. deep sleep – REM sleep diminishes secretion).
- Levels are highest in children aged 15–19 years.
- Levels are **increased** by a protein meal; by exercise; acute fear/stress; acute hypoglycaemia; for the first few days of fasting. Various drugs and neurotransmitters may also stimulate GH release (e.g. dopamine, β-endorphin). Secretion is **decreased** by chronic emotional stress in children, by hyperglycaemia and by a rise in plasma FFAs.
- **Negative feedback:** GH inhibits its own release (probably via somatomedins).

## Disease

- **Deficiency** of GH causes **growth failure (dwarfism)** in children. Little effect of deficiency in the adult, except increased sensitivity to insulin. Replacement must be with human GH – pituitary extracts carried risk of prion infection before synthetic GH was available. African pygmies have low circulating IGF-1.
- GH excess in children is rare, but causes **gigantism** – individuals are large but of normal proportions. In adults, whose epiphyses are fused, stimulation of skeletal growth causes overgrowth and thickening of bones and the characteristic appearance of **acromegaly**. There is also a tendency to develop diabetes mellitus.

## The somatomedins

- A class of growth factors, also known as the **insulin-like growth factors (IGFs),** including IGF-I and IGF-II. They are structurally similar to insulin and have some affinity for insulin receptors; similarly, insulin has some action at somatomedin receptors. This accounts for the metabolic effects of somatomedins, the growth-promoting effects of insulin, and the rather confusing terminology!
- Somatomedins stimulate the growth of cartilage and the incorporation of sulphate into cartilage (accounting for yet another term for them, "sulphation factor").
- GH stimulates somatomedin synthesis by the liver.

## Other growth factors

There are many agents that promote growth – some hormonal, some paracrine. They include GH, somatomedins, insulin (esp. in the fetus[2]), prolactin, placental lactogen, nerve growth factor, fibroblast growth factor, steroids…

---

[1] Insulin has these action because it provides glucose substrate for muscle and independently increases amino acid uptake, promoting protein anabolism.

[2] Babies of diabetic mothers are large. Insulin doesn't cross the placenta, but glucose does: the baby therefore makes more insulin to keep its glucose levels down and grows as a result. This isn't good for the baby.