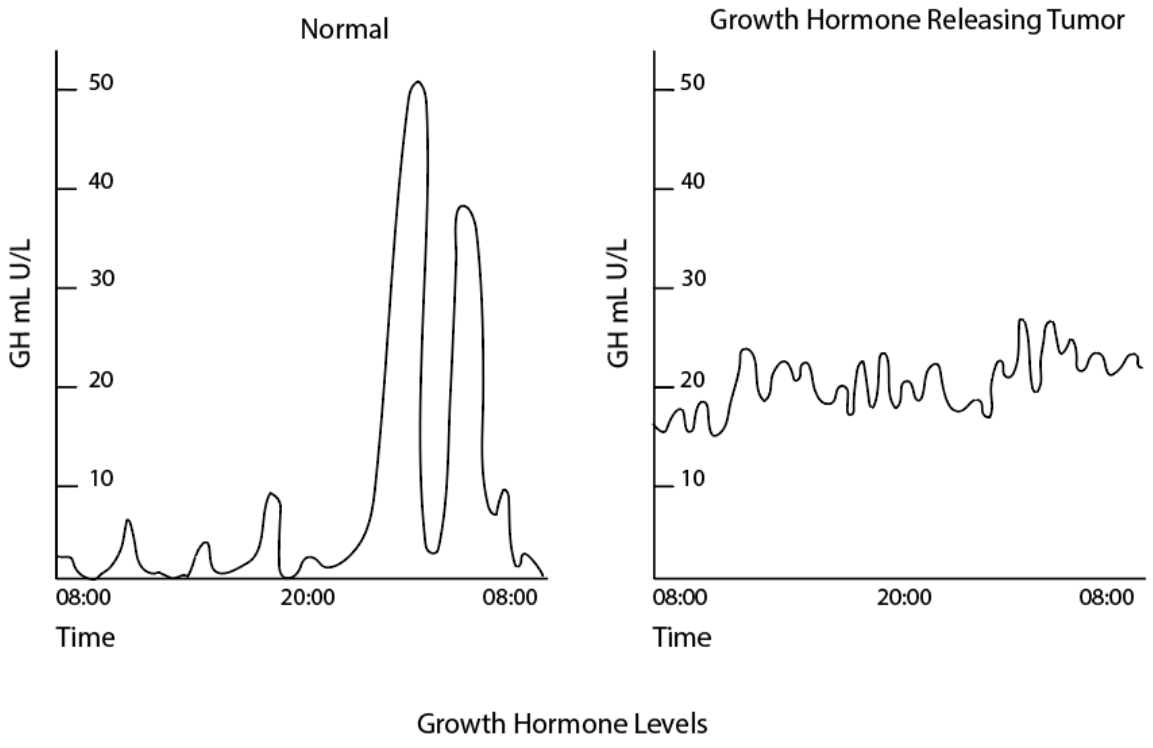
5.1.4

Growth Hormone Disorders

Growth hormone affects most tissues. It functions to increase blood glucose levels, mobilize fatty acids for fuel, increase lipids in the blood, increase the rate of protein synthesis, and increase muscle mass.

Many of the functions of growth hormone are mediated by **insulin-like growth factors (IGFs)** which are produced by the liver and get their name because they have similar structure to proinsulin (a precursor of insulin made in the pancreas). GH stimulates the liver to make IGFs. A specific example is **IGF-1 (somatomedin C)**, which is known to be the hormone responsible for stimulating overall height gains as well as increasing the growth of many tissues including bone, cartilage, body organs, and muscle. Because of its function, IGF-1 is measured in lab tests for children with excessively short stature for their age. IGF-binding proteins (IGFBPs) bind to IGFs in the blood and help to transport the hormones as well as increase their half-life.

As mentioned previously, growth hormone is regulated by GHRH and GHIH from the hypothalamus. It is also regulated by **ghrelin**, which is a hormone released from the fundus of the stomach when GH levels are low or during fasting when blood sugar is low. Ghrelin stimulates the release of GH and also acts as an appetite stimulating signal. Some other common stimulators of growth hormone release are hypoglycemia, fasting, starvation, and stress. Common inhibitors of growth hormone include hyperglycemia, free fatty acid release, cortisol, and obesity. During a 24-hour period, GH levels are highest in the blood 1-4 hours after the onset of sleep. Nocturnal sleep bursts of GH occur more often in children than adults.



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Short Stature in Children

Short stature in children is relatively common and has many possible causes including GH deficiency, hypothyroidism, celiac disease, malnutrition, excessive glucocorticoids, psychosocial dwarfism, and Laron-type dwarfism. **Psychosocial dwarfism** occurs when a child is somehow abused emotionally and they end up being shorter because of decreased growth hormone release. **Laron-type dwarfism** is an extreme resistance to GH due to abnormalities in the growth hormone receptors on the liver. Affected individuals tend to be obese and have high levels of GH and low levels of IGF-1. Treatment is hormone replacement therapy (HRT) with IGF-1, which is now produced by recombinant DNA technology.

Calculating mid-parental height is an easy way to predict the future height of a child. 95% of normal children are within three inches of mid-parental height. For boys, add 5 inches to the height of the mother and add to the father's height and divide by 2. For girls, subtract 5 inches from the father's height and add to the mother's height and divide by 2.

Gigantism and Acromegaly

Gigantism and acromegaly are usually caused by a hypersecretion of growth hormone that is normally due to a pituitary tumor. With a GH-secreting adenoma, the normal GH secretion pattern and nocturnal GH peaks are lost and an unpredictable pattern develops with consistently high GH. GH levels in acromegaly are never completely suppressed, and even small (but chronic) rises in GH and IGF-1 will stimulate growth. **Gigantism** is characterized by a hypersecretion of growth hormone as a child before the growth plates fuse during puberty. It results in extreme growth and height. **Acromegaly** is characterized by a hypersecretion of growth hormone after the growth plates have fused. The highest incident rate of acromegaly is between the ages of 40-59. Because the bones have stopped growing at this age, individuals do not become taller. However, some common manifestations of acromegaly are thickening of bones in the face and jaw to become quite pronounced, increased bone and connective tissue growth causing joint pain, and in some cases nerve entrapment can occur and carpal tunnel is common. An enlarged heart is also possible with both gigantism and acromegaly and can lead to heart failure. CNS symptoms can also develop due to the increased growth

of the pituitary tumor. Symptoms of this may include nausea/vomiting, tunnel vision, papilledema, and headaches. Growth hormone does increase blood sugar, so an excessive secretion of GH generally leads to symptoms of diabetes. This increases the patient's risk of atherosclerosis and heart disease. Death from gigantism and acromegaly often results from heart failure, atherosclerosis, diabetes mellitus, or malignancy (commonly found in the colon or lungs).

A positive diagnosis for acromegaly or gigantism includes observing the characteristic clinical features of the disease and measuring GH and IGF-1 levels. A glucose tolerance test may be performed to diagnose diabetes due to excessive GH release. During this diagnostic test the patient will drink 75 grams of a glucose solution. In healthy individuals, this lowers blood GH levels to less than 1 nanogram per milliliter (ng/ml). In those with acromegaly, this decrease does not happen and in some cases GH levels may even rise. An MRI can also be performed to confirm the existence of an anterior pituitary adenoma. Most all GH secreting adenomas (90%) are macroadenomas.

Treatment of choice for a GH pituitary adenoma is transsphenoidal surgery to remove the tumor. Somatostatin analogs like octreotide (Sandostatin) and lanreotide are also useful for the medical management of GH pituitary adenomas. Pegvisomant (Somavert) reduces serum levels of IGF-1 by blocking the GH receptor on the liver.