About Growth Hormone

Human growth hormone (GH) is essential for normal growth and development. It enables youths to achieve normal height, and adults to burn fat (lipolysis), regulate insulin and glucose, and synthesize protein. GH also helps support sex steroid and thyroid hormone function.\(^1\)

A moderate-sized peptide secreted in pulses throughout the day, GH is the most abundant of the pituitary hormones.\(^1\) Lipolysis, or fat burning, is a unique function of GH that results in increased circulating levels of free fatty acids and ketone bodies. GH peaks in puberty and starts to decline in early adulthood. It has been estimated that secretion of GH declines by approximately 14% for every decade after entering adulthood.\(^2\)

The decreased GH associated with aging is thought to contribute to the following physiologic changes:

- increased abdominal fat
- decreased bone and muscle mass/strength
- mild depression
- impaired concentration/memory\(^3\)

Clinically, restoring GH to adequate levels has been shown to decrease visceral fat volume.\(^4\) improve mood, and increase muscle.\(^5\)

Why Test GH in Urine?

GH is released from the anterior pituitary approximately every 2 hours throughout the day.\(^6\) Given the cyclic nature of GH release, neither single nor multiple serum collections can reliably capture peak growth hormone levels. Nearly half of daily GH output is secreted overnight during the onset of slow wave (non-REM) sleep. Thus, an overnight or 24-hour urine collection measures the cumulative total of all the GH produced during the collection period. In men, the overnight surge is the dominant source of GH.\(^7\) In addition to their overnight surge, women tend to have higher pulse amplitude throughout the day, making their overall GH levels higher than those of men.

Research shows that urine GH levels correlate with circulating (serum) GH levels, both in the rested state and after exercise.\(^8\)\(^9\) GH is freely filtered out of blood; however, since most is reabsorbed in the kidneys, urine GH is only 0.025% of what is in serum. Rocky Mountain Analytical is the first company in Canada to utilize new technology that enables highly accurate measurement of the low levels of GH found in urine.

Why Test GH?

Because low GH levels have been linked to many symptoms of aging, interest in GH has intensified particularly as the proportion of seniors in Canada increases. Conditions such as fibromyalgia, metabolic syndrome and cardiovascular disease have also been linked to low GH. Consequently, early identification and correction of sub-optimal GH levels may help reduce symptom severity or limit disease progression. Various lifestyle and dietary changes have been shown to improve endogenous GH secretion. (See page 3)

Test Limitations

This urine GH assay is not validated to diagnose GH deficiency in either children or adults. Specimens received from patients under 18 years of age will not be processed.

This assay is not validated to monitor the effectiveness of injectable GH therapy.

Urine growth hormone testing is not appropriate for patients with impaired renal function or those on diuretic medication.

Reference Ranges

Gender-stratified reference ranges were developed using results from a cohort of clinically normal men and women aged 18 years and older. Gender stratification and creatinine normalization are essential to clinically relevant results.
Growth hormone receptors are present in many tissues, which means it can affect a variety of physiologic systems including:

**Metabolic**

Optimal levels of GH may help increase resting energy expenditure (REE) independent of changes in lean body mass.4

Sub-optimal GH may contribute to metabolic syndrome and weight gain via the following:

- Impaired lipolysis, contributing to increased visceral adiposity.
- Impaired conversion of T4 to its active T3 form.
- Impaired conversion of cortisol to its less active cortisone form in adipose tissue, leading to higher cortisol levels.1

The lipolytic effects of GH may be attenuated in women, elderly and in the presence of abdominal obesity.6

**Mood/Memory**

Growth hormone deficiency has been linked with:

- Low energy
- Fatigue
- Depression
- Lower perceived quality of life.5

**Musculoskeletal**

- GH increases protein synthesis and muscle mass.4
- In addition to anabolic effects on muscle and bone, GH has the added effect of switching muscle metabolism temporarily toward burning fat instead of glucose.
- Research suggests that fibromyalgia may be related to a physiologic GH deficiency.10

**Cardiovascular**

Insufficiency of GH is associated with increased risk for thrombosis and atherosclerosis due to increased levels of plasminogen activator inhibitor-1 (PAI-1).5 Other cardiovascular risk factors including LDL cholesterol, total cholesterol and diastolic blood pressure all tend to improve when growth hormone deficient adults are given GH.

Although many of the physiologic changes associated with aging are also linked to low levels of growth hormone, it is important to differentiate between age-related low growth hormone and Adult Growth Hormone Deficiency (AGHD). Patient history consistent with probable AGHD is an indication for diagnostic testing and/or an endocrinological consult. Possible causes of adult-onset GHD include: history of brain injury or infection, autoimmune disease, radiation therapy or pituitary tumor. The insulin tolerance test is commonly used to diagnose GHD in Canada, although the arginine and GHRH stimulation test has fewer false positives.11

Diagnosed growth hormone deficiency requires administration of exogenous growth hormone (somatomedin).

An age-related decline in GH typically results in sub-optimal rather than clinically low GH levels. Other factors that negatively impact GH include: obesity, sex steroid hormone imbalances, excessive alcohol intake, refined carbohydrates and sleep apnea. Fortunately, there are a number of lifestyle factors that positively impact GH secretion including: intermittent fasting, increased body temperature, exercise, and restful sleep. The chart on page 3 lists the promoters and inhibitors of GH in more detail.
### Increases Growth Hormone

**Sleep**: In adults, there is a linear relationship between the duration of slow-wave sleep (SWS or non-REM sleep) and secretion of GH. Decreased total sleep time and fragmented sleep have been noted in growth hormone deficient adults.

**Fasting**: Intermittent fasting (14 to 20 hours one to three times per week) has been shown to amplify GH secretion. During fasting, GH increases while IGF-I and insulin both decrease. Fasting also stimulates GH mediated lipolysis and protein preservation.

**Exercise**: High-intensity interval training stimulates growth hormone release, with circulating GH peaking at about 30 minutes post-exercise, and remaining elevated for 2 hours. Resistance training may also stimulate GH, particularly when the lactate threshold is reached. Chronic endurance exercise may inhibit GH release.

**Hormone Balance**: Circulating sex steroid hormone levels help regulate the synthesis and secretion of GH from the anterior pituitary. Elevated estrogens are associated with increased GH. There is a positive relationship between testosterone levels and GH secretion.

**Stress and Critical Illness**: Growth hormone levels increase in the acute phase of critical illness or stress, but decline with chronic stress/protracted illness.

**Supplements**: The table below lists a number of natural interventions that may help stimulate GH secretion.

### Decreases Growth Hormone

**Visceral Adiposity**: Increased visceral fat inhibits the release of growth hormone. There is a linear relationship between increased waist circumference and decreased levels of stimulated GH in serum. About 1/3 of patients with a BMI >30 given a stimulation test for diagnosis of growth hormone deficiency could be considered deficient.

**Aging**: In men, growth hormone levels are estimated to drop by 50% every seven years after the age of 25. In women, declining estradiol levels are thought to be largely responsible for GH decline with age.

**Traumatic brain injury (TBI)**: GH is the first hormone to deplete following pituitary trauma. A 2005 study found approximately 6% of patients with TBI had a clinical growth hormone deficiency (GHD). Furthermore, almost one-quarter of participants (n=170) had a pituitary hormone deficiency of some type.

**Simple Carbohydrates**: Sugar and other refined carbohydrates stimulate the release of insulin, which suppresses growth hormone secretion. Late evening carbohydrate consumption may attenuate the overnight GH surge.

**Alcohol**: Research shows that alcohol consumption suppresses GH release.

### Interventions and Evidence

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>GH secretagogues</strong></td>
<td>GH secretagogues stimulate pituitary gland GHRH receptors to secrete GH. Secretagogues include both synthetic and naturally occurring peptides (6 to 10 amino acids). Ghrelin is an example of a natural GH-releasing agent. Canada has an NHPD approved synthetic GH secretagogue.</td>
</tr>
<tr>
<td><strong>Amino Acids</strong></td>
<td>Amino acids signal brain that muscle repair is needed and stimulate growth hormone release. Studies of the effects of amino acids on growth hormone release have typically been small, but produced generally positive results. Combinations of GH promoting amino acids also appear beneficial. Canada has NHPD approved multi-amino acid products.</td>
</tr>
<tr>
<td><strong>L-arginine</strong></td>
<td>Suppresses somatostatin, although GH stimulating effects appear most effective at night.</td>
</tr>
<tr>
<td><strong>Other amino acids</strong></td>
<td>Administration of L-ornithine, GABA, glycine, lysine, leucine, L-dopa, ornithine alpha-keoglutarate, and/or glutamine have all resulted in increased growth hormone levels <em>in vivo</em>.</td>
</tr>
<tr>
<td><strong>Melatonin</strong></td>
<td>A 5mg melatonin dose increased GH secretion independent of exercise.</td>
</tr>
<tr>
<td><strong>Timing of Meals</strong></td>
<td>In the fasting state, growth hormone acts alone to promote lipolysis. Immediately after meals, insulin acts alone in promoting glucose storage. In between meals, insulin and growth hormone act synergistically to promote IGF-I production which ultimately aids protein synthesis. Although bodybuilding sites frequently recommend specific meal protocols to promote growth hormone release (e.g. carb back loading), there is no scientific evidence in favour of one protocol over another.</td>
</tr>
</tbody>
</table>
As illustrated in Figure 1, liver synthesis and secretion of IGF-I is dependent on GH. In circulation, IGF-I is bound to one of six IGF binding proteins, which prolong its half-life and provide more consistent levels throughout the day. Consequently, many clinicians use total IGF-I as a surrogate marker for growth hormone. Most often, total IGF-I (free IGF-I + IGFBP3) is measured, however the secretion of IGF binding protein can vary independent of growth hormone. The following are examples of when IGF-I and growth hormone levels do not correlate well:

- 30 to 40% of growth hormone deficient patients have normal IGF-I for their age.24  
- In young adults, serum IGF-I is fairly reliable as a means of assessing GH deficiency or insufficiency, but it is less reliable over age 40.25  
- Circulating IGF-I decreases during fasting while GH increases.3,4  
- IGF levels may be normal in obesity, but GH is suppressed.2  
- IGF-I binds to protein and can therefore be affected by protein status/malnutrition.4  
- Tissue resistance to GH leads to declining IGF-I levels.1  
- IGF-I has no lipolytic effects and there are no functional IGF-I receptors found in adipocytes.26  

References