



1. Medical Condition

GROWTH HORMONE DEFICIENCY (ADULT)

2. Diagnosis

A. Medical history

Pure GH deficiency in adults may not be clinically obvious. It may however be part of a disorder affecting hyposecretion of all the anterior pituitary hormones and involve a wide constellation of signs and symptoms. Where the patient is an athlete, the diagnosis of such deficiency must be clearly defined within an appropriate clinical context and with the support of an experienced endocrinologist. The particular issue of relative adult GHD must be managed by an experienced specialist and meet strict diagnostic criteria before treatment commences.

B. Diagnostic criteria

- The diagnosis of adult GH deficiency is biochemical. An evaluation for GH deficiency should be considered only in patients with evidence of hypothalamic-pituitary disease, childhood onset of GH deficiency or after cranial irradiation (therapeutic or accidental).
- Because of the fast half life of GH in blood (around 19 min), serum GH levels are frequently very low or even undetectable. For this reason the diagnosis of GH deficiency is established by provocative testing of GH secretion. The insulin tolerance test is the diagnostic test of choice. It should be performed in an endocrine unit where the test is performed frequently. After insulin-induced hypoglycemia most normal subjects respond with a peak of GH in serum **above 5 mcg/L**. A peak of GH to **less than 3 mcg/L** constitutes a severe GH deficiency. In patients with contraindications to the insulin tolerance test, the arginine test combined with GHR can be used as an alternative. One provocative test is sufficient for the diagnosis of GH deficiency in adults with hypothalamic-pituitary disease. To

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diagnose isolated GH deficiency it is recommended that a second biochemical test of GH status be abnormal. The **cut-off point of 5 mcg/L** is used for provocative tests as the current reference, regardless the stimulation test or the GH assay used (see references at the end of the document). It does not vary with age.

C. Relevant medical information

- A serum IGF-1 concentration below the normal range is suggestive but not conclusive proof of GH deficiency. It is recommended that the diagnosis be confirmed by a provocative test of GH release.
- GH and IGF-1 results should be expressed in mass units.
- Currently, the benefits of the treatment of partial GH deficiency remain debatable. Consequently, only patients with documented, severe GH deficiency should be eligible for an exemption to use growth hormone therapeutically.

3. Medical best practice treatment

A. Name of prohibited substance

Recombinant growth hormone

B. Route

Due to the short half-life of GH, daily subcutaneous injections in the evening are recommended. Where practically possible it is recommended that GH administration is carried out and logged daily by an appropriate health professional. However where this is impractical it is strongly recommended that the quantity of GH delivered to the patient be strictly controlled by the physician in charge.

C. Frequency

The current consensus states that the therapy should start with a low dose (0.15-0.30 mg/day; 0.45-0.90 IU/day) and should be increased gradually based on the clinical and biochemical responses at monthly intervals. The normal maintenance dose may vary until 1.0 mg/day (3 IU/day) is achieved, but should never be reached by increments more than 0.1 or 0.2 mg/day each month.

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D. Recommended duration of treatment

The duration of therapy is decided by the consulting specialist in accordance with the current model of best practice. A continuous evaluation of the results of treatment on appropriate serum levels (see below) and clinical benefits must be undertaken.

4. Other non-prohibited alternative treatments?

No alternative for growth hormone substitution in proven cases.

5. Consequences to health if treatment is withheld.

Debatable if only a partial deficiency exists.

6. Treatment monitoring

The best biochemical marker of GH action is serum IGF-1. Values should imperatively be kept in the age-related normal range, in order to avoid any over replacement.

7. TUE validity and recommended review process

Three years as a maximum, with continuous evaluation of results of treatment on serum levels and clinical benefits. Based on the results of monitoring a review should be achieved annually.

8. Any appropriate cautionary matters

Given the potential for the inappropriate use of GH, this is a controversial area that demands strict adherence to diagnostic criteria confirmed by an endocrinologist.

The personal administration of GH is not recommended but in many circumstances is the only practical option. In such cases it is recommended that a log book of administration be maintained by the patient and that this may be subject to review at any time.

Quantities of GH delivered to the patient must be strictly controlled and limited by prescription.

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9. References

1. The Merck Manual, sec 2, Ch. 6, sec 19 Ch 269 Endocrine and metabolic disorders.
2. Journal of Clinical Endocrinology and Metabolism Vol.83, No 2, *Consensus Guidelines for the Diagnosis and treatment of Adults with GH Deficiency.*
3. American Association of Clinical Endocrinologists. *Medical Guidelines for clinical practice for growth hormone use in adults and children.* 2003 update.