Adult GHD

Optimal Management of Adult Growth Hormone Deficiency Across the Spectrum, From Transitions in Care to Recent Treatment Advances

TRANSITION FROM PEDIATRIC TO ADULT CARE

The transition period starts in late puberty after achieving final stature and ends with full adult maturation.

Why continue rhGH treatment during the transition period?

If GHD persists, treatment with rhGH can help optimize body composition, BMD, QoL, and metabolic and cardiovascular health; delaying continuation of GH therapy may have a negative impact

Attainment of adult height

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Assess requirement for testing

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Stop rhGH treatment for 1 to 3 months ("washout" phase)

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Select a GH stimulation test (ITT, GST, macimorelin)

↓

Evaluate outcome

↓

Reinitiate treatment if indicated

↓

Monitor and follow-up

GH THERAPY

Goals of GH therapy

Children: growth promotion to normalize final adult height

Adults: reverse the negative metabolic consequences of hormone deficiency; improve QoL

Initiation, titration and monitoring

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Dose adjustments

↓

Continuation of treatment

Diagnosing aGHD

Assess contributing factors and associated conditions

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Identify clinical features of aGHD

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Assess requirement for testing

↓

Select a GH stimulation test (ITT, GST, macimorelin)

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Perform test and initiate treatment if indicated

What's available in the US for aGHD?

- Short-acting somatropin agents (daily administration) agents: Genotropin, Humatrope, Norditropin, Nutropin, Omnitrope, Saizen, Zomacton
- Long-acting agent (weekly administration): Sogroya (somapacitan-beco)

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TRANSITION FROM PEDIATRIC TO ADULT CARE

The transition period starts in late puberty after achieving final stature (usually 15 to 18 years of age) and ends with full adult maturation (5 to 9 years after full adult height is reached).

Impact of rhGH treatment during the transition period

If GHD persists, treatment with rhGH can help optimize body composition, BMD, QoL, and metabolic and cardiovascular health; delaying continuation of GH therapy may have a negative impact

- Height increase velocity <2.0 cm/year
- Bone age 14 to 15 years (girls), >16 years (boys)

- **Idiopathic isolated GHD and serum IGF-1 SDS < 0:** testing required before resuming rhGH treatment
- **Idiopathic GHD and serum IGF-1 ≥ 0 SDS:** retesting and continued rhGH therapy not required; observe
- **High probability of persistent GHD[a]:** testing not required; continue rhGH without interruption

- Ensure all other pituitary hormone deficiencies have been addressed
- Conduct comprehensive clinical evaluation: height, weight, BMI, waist and hip circumference, bone mineral density, fasting lipids, glucose profile, and QoL appraisal

Initiation

- 0.4 to 0.5 mg/day
- 50% of childhood dose
- Increased dose required with oral estrogen

Titration

- Increase by 0.1 to 0.2 mg/month
- **Monitor** serum IGF-1 levels to avoid exceeding upper limit of normal range (IGF-1 > 2 SDS)
- **Modify** dose based on clinical response, serum IGF-1 levels, side effects, patient considerations

- **Side effects:** paresthesia, joint stiffness, peripheral edema, arthralgias, and myalgias
- **Every 6 months:** fasting glucose, A1C, lipid profile
- **Every 12 months:** QoL
- **Every 18 to 24 months:** DXA
- *If a pituitary lesion is present, baseline and periodic MRIs*

Testing during transition

- Attainment of adult height
- Assess requirement for testing
- Stop rhGH treatment for 1 to 3 months (“washout” phase)
- Select a GH stimulation test (ITT, GST, macimorelin)
- Evaluate outcome
- Reinitiate treatment if indicated
- Monitor and follow-up

Set the stage for successful transition

[a] Deficits in ≥ 3 additional pituitary hormones, hypothalamic–pituitary structural defect, causal genetic mutation, tumor-related organic GHD, low serum IGF-1 (< -2.0 SDS).

A1C, glycated hemoglobin; BMI, body mass index; DXA, dual-energy X-ray absorptiometry; GH, growth hormone; GHD, growth hormone deficiency; GST, glucagon-stimulation test; IGF-1, insulin-like growth factor; ITT, insulin-tolerance test; MRI, magnetic resonance imaging; QoL, quality of life; rhGH, recombinant human growth hormone; SDS, standard deviation score.

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Diagnosing aGHD

Potential causes and contributing factors associated with aGHD

Childhood-onset

- Congenital
  - Idiopathic
  - Genetic
  - Embryologic defect
- Cranial irradiation for brain tumor, lymphoma, leukemia
- Head trauma
- CNS tumors
- Infiltrative diseases
- Perinatal insults

Adult-onset

- Pituitary/hypothalamic tumors and treatment
- Perasellar tumors
- Cranial irradiation
- Brain injury/subarachnoid hemorrhage
- Head trauma
- Sheehan's syndrome
- Hypophysitis
- Infiltrative/granulomatous/infectious diseases
- Empty sella syndrome

No testing required

- Organic hypothalamic-pituitary disease, MPHD (≥ 3 PHDs) and low serum IGF-1 levels (< -2.0 SDS)
- Genetic defects affecting hypothalamic-pituitary axes
- Hypothalamic-pituitary structural brain defects

Testing required

- ≤ 2 PHDs, low serum IGF-1 levels (< -2.0 SDS)
- Structural hypothalamic-pituitary lesions
- History of traumatic brain injury
- Cranial irradiation
- Empty sella
- Pituitary apoplexy
- Hypothalamic-pituitary tumors
- Rathke's cleft cysts
- Autoimmune hypophysitis
- Subarachnoid hemorrhage
- Hypophysitis

	Accurate?	Considerations
ITT, intravenous	**Gold standard**	Hypoglycemia symptoms may occur, precluding use in patients with seizure disorder, CVD, pregnant women, and patients > 65 years old; test requires close medical supervision
GST, intramuscular	✓	Nausea, vomiting, headache, and delayed hypoglycemia may occur; diagnostic accuracy is unclear in those with glucose intolerance
Macimorelin	✓	Some patients may experience transient dysgeusia. Avoid concomitant use with drugs known to prolong QT interval; hypothalamic disease may not be accurately diagnosed

Assess contributing factors and associated conditions

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Identify clinical features of aGHD

↓

Assess requirement for testing

↓

Select a GH stimulation test (ITT, GST, macimorelin)

↓

Perform test and initiate treatment if indicated

aGHD, adult growth hormone deficiency; CNS, central nervous system; CVD, cardiovascular disease; GH, growth hormone; GHD, growth hormone deficiency; GST, glucagon-stimulation test; IGF-1, insulin-like growth factor; ITT, insulin tolerance test; MPHD, multiple pituitary hormone deficiencies; PHD, pituitary hormone deficiency; SDS, standard deviation score.

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GH THERAPY

Goals of GH therapy

Children: growth promotion to normalize final adult height

Adults: reverse the negative metabolic consequences of hormone deficiency; improve QoL

Benefits and safety profile of GH therapy

What's available in the US?

- 7 short-acting (daily administration) agents: Genotropin, Humatrope, Norditropin, Nutropin, Omnitrope, Saizen, Zomacton (all somatropin)
- 1 long-acting agent (weekly administration): Sogroya (somapacitan-beco)

Initiation, titration, and monitoring

Dose adjustments

Starting Dose by Age

- **< 30 years:** 0.3 to 0.4 mg/day
- **30 to 60 years:** 0.2 to 0.3 mg/day
- **> 60 years:** 0.1 to 0.2 mg/day
- Increased dose required with oral estrogen
- Lower dose required with diabetes, older age or obesity

Titrate

- **Every 1 to 2 months**
- **Increase dose by 0.1 to 0.2 mg/day based on:**
  - Response
  - Side effects
  - Serum IGF-1 levels
  - Other individual considerations (eg, glucose intolerance)
- Reaching maintenance dose can take up to 12 weeks; typically takes longer in women

Monitor

- **Every 6 to 12 months**
- If initial bone DXA is abnormal, repeat at 2- to 3-year intervals
- If sellar mass, periodic MRIs
- Conduct assessments and evaluations at appropriate intervals
- Assess biochemistry, body composition, and QoL for treatment response

Continuation of treatment

Addressing adherence and persistence challenges in aGHD treatment

Shared decision-making

Increase rhGH dose if patient:

- Is young
- Has low serum IGF-1 levels
- Has recently added oral estrogen or switched from transdermal to oral estrogen

Decrease rhGH dose if patient:

- Is older
- Has high serum IGF-1 levels
- Has discontinued oral estrogen or switched from oral to transdermal estrogen
- Has adverse events due to fluid retention

Continue treatment indefinitely

Significant QoL benefits reported
and/or:
Objective improvements in clinical parameters (eg, cardiovascular risk markers, BMD, body composition, or physical activity tolerance)

Discontinuing treatment can be discussed with patients

No subjective or objective benefits of treatment after ≥ 12 to 18 months

If discontinued, arrange follow-up appointment at 6 months (some may consider resuming GH replacement if they feel QoL was better when on treatment)

aGHD, adult growth hormone deficiency; BMD, bone mineral density; DXA, dual-energy X-ray absorptiometry; GH, growth hormone; IGF-1, insulin-like growth factor; MRI, magnetic resonance imaging; QoL, quality of life; rhGH, recombinant human growth hormone.