

RADIATION INDUCED HYPOPITUITARISM

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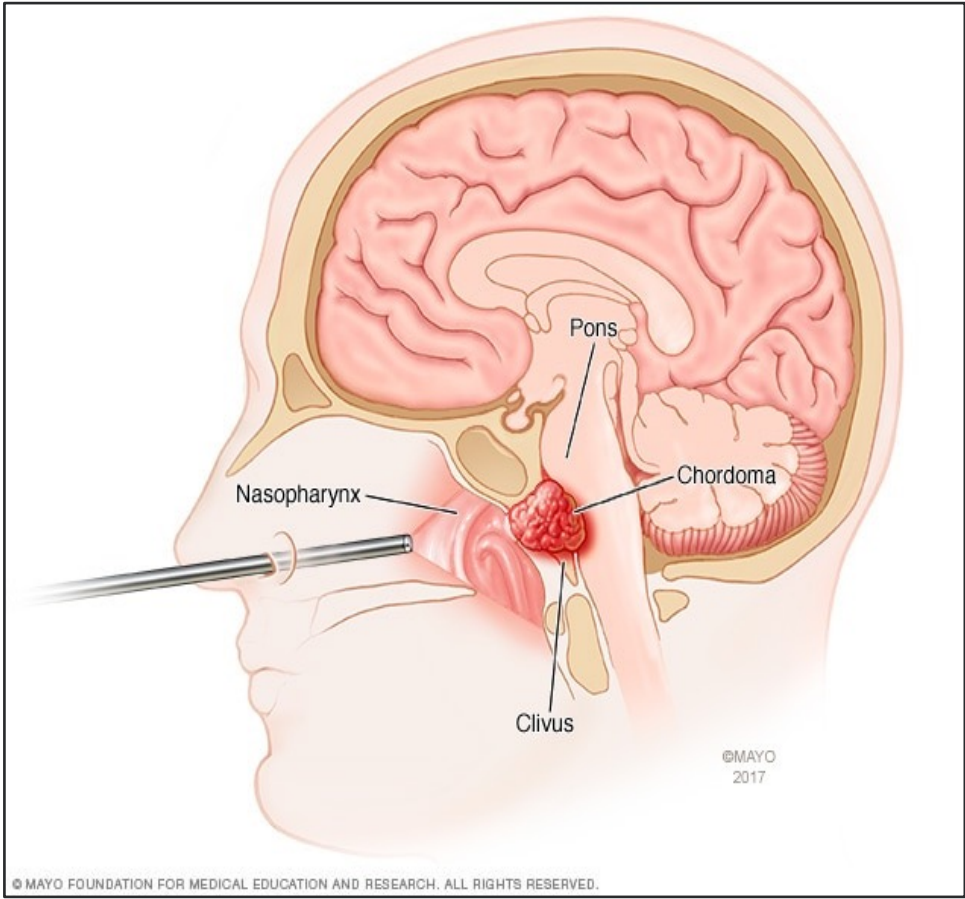
Director, Pituitary Diseases

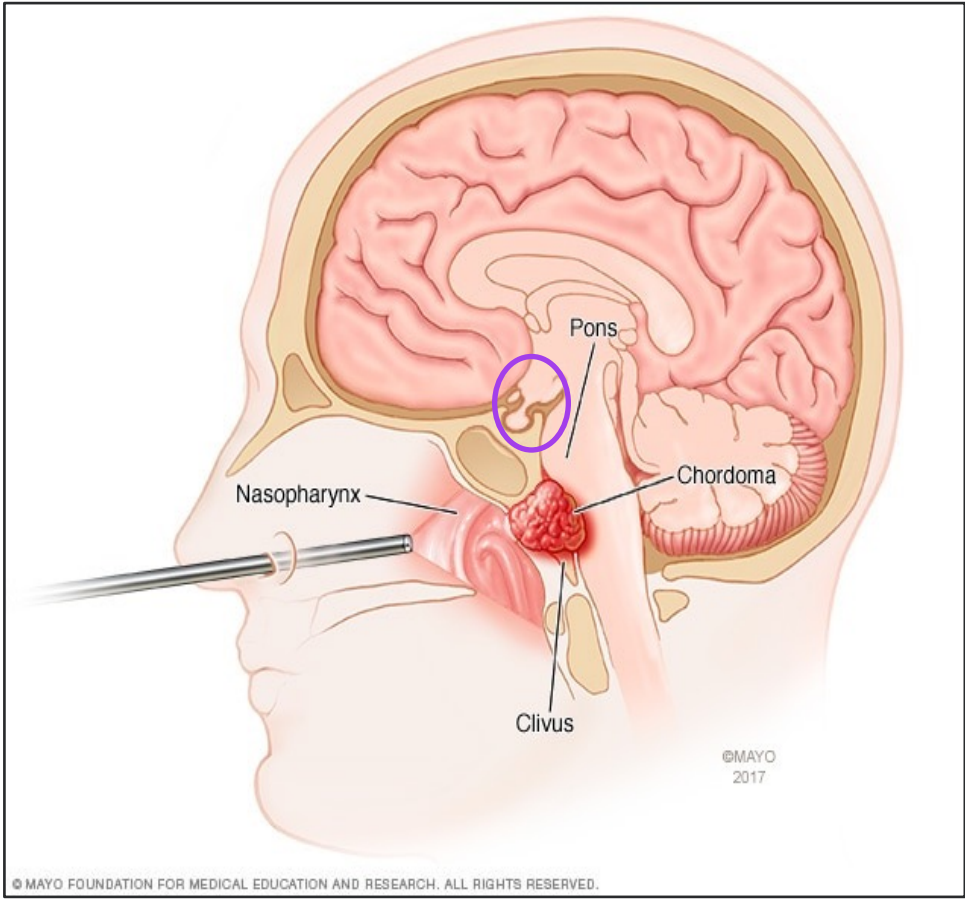
Division of Diabetes, Endocrinology and Metabolism



Definition

- Pituitary is a tiny pea sized gland (master gland) which releases and stores different hormones
- Hormones are chemicals that coordinate different functions in your body by carrying messages through your blood to your organs, muscles and other tissues.
- **Hypopituitarism** is a condition in which there's a lack (deficiency) of one, multiple or all of the hormones made by the pituitary



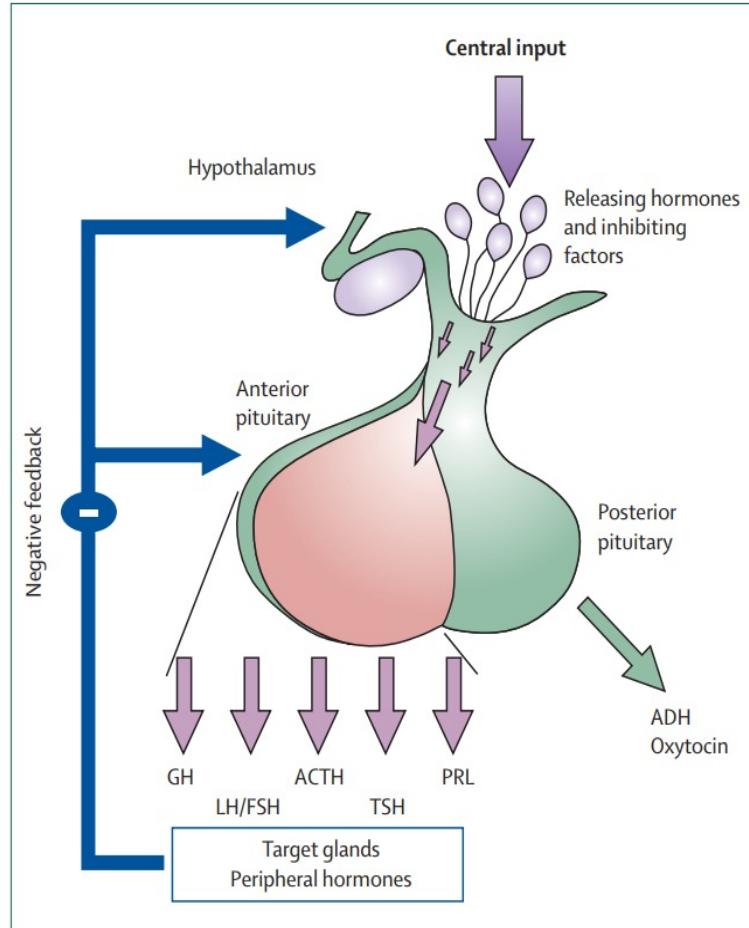


Causes of Hypopituitarism

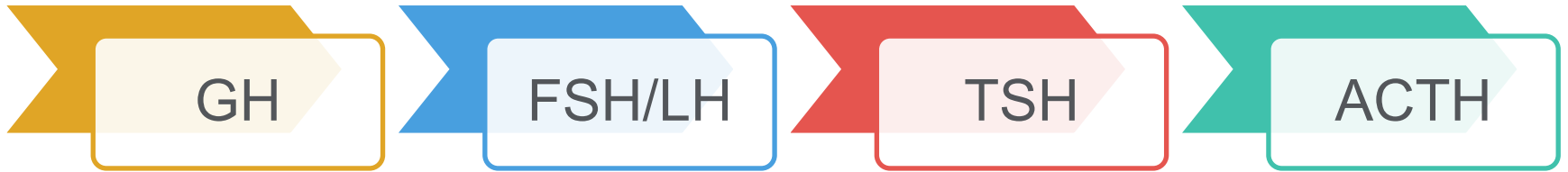
- Tumors in or near the pituitary gland (which are usually benign, meaning not cancerous)
- **Radiation treatment, which can destroy pituitary gland tissue**
- Pituitary surgery
- Traumatic brain injury, such as with a head injury from an accident
- Certain infections such as tuberculosis or meningitis
- Hypophysitis (inflammation of the pituitary gland)
- Conditions that can infiltrate the pituitary gland (example, histiocytosis, lymphoma, hemochromatosis)
- Sometimes, the cause is unknown (called idiopathic).

Radiation induced Hypopituitarism

- Radiation-induced hypopituitarism is insidious, progressive and largely nonreversible.
 - Direct neuronal rather than vascular damage to the hypothalamus (more radiosensitive)
 - Altered neurotransmitter input from other brain centers
- Hypopituitarism
- ~30% of cases following SRT at 5-10 years
- ~30–50% following CRT at 5-10 years

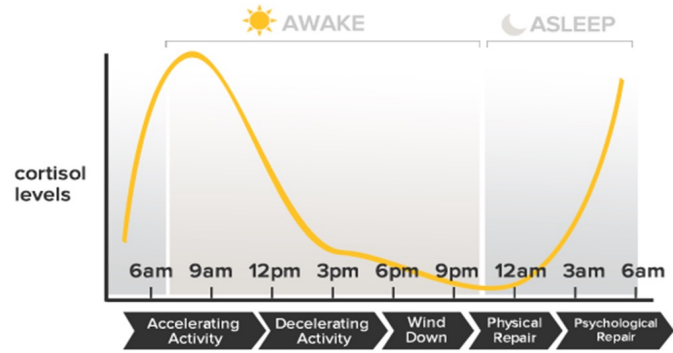


Hypopituitarism: Sequence of hormonal decline



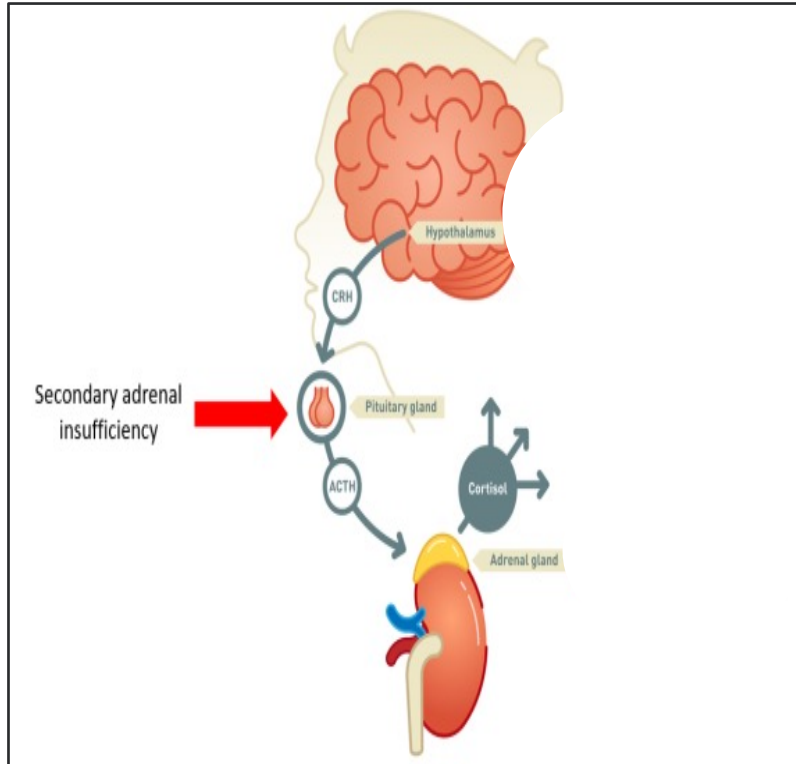
Biochemical Work-up

- Morning blood test to check your cortisol
- Thyroid hormone levels
- Morning blood test for testosterone in men
- IGF-1; this reflects your GH levels - not a great screening test
- Pituitary hormone levels such as LH, FSH, prolactin



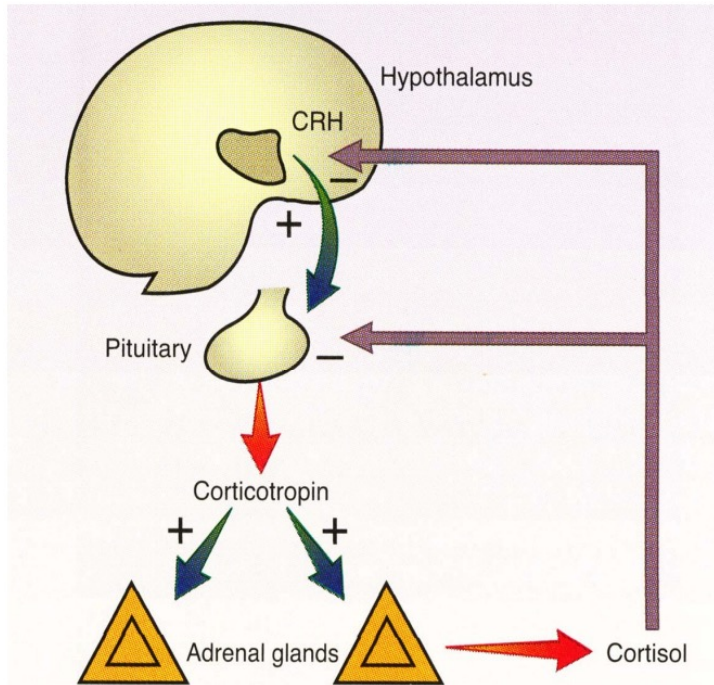
ACTH DEFICIENCY

Secondary Adrenal Insufficiency



- Fatigue malaise
- Postural dizziness and presyncope
- Gastrointestinal symptoms
 - Nausea
 - Vomiting
 - Diarrhea, abdominal pain
- Joint pain,
- Weight loss
- Loss of libido and irregular cycles

ACTH Stimulation Test



- 250 mcg ACTH[1–24]
 - Baseline, 30 mins, 60 mins
- Testing when AM cortisol levels between 5 and 15 mcg/dl (3-16 mcg/dl*)
- Testing any time of the day
- The cortisol response to ACTH stimulation tests
 - 14 to 15 $\mu\text{g/dL}$ (assay)

*Munro V The effect of time of day testing and utility of 30 and 60 minute cortisol values in the 250 mcg ACTH stimulation test. Clin Biochem. 2018

Stefan R. Bornstein Diagnosis and Treatment of Primary Adrenal Insufficiency: An Endocrine Society Clinical Practice Guideline, *The Journal of Clinical Endocrinology & Metabolism* 2016

Management

- Hydrocortisone usually 15–20 mg total daily dose in single or divided doses (extra for travel)
- “Sick day rules”
- Stress-dose and emergency steroid administration
- Emergency card/ bracelet/necklace regarding AI and an emergency kit containing injectable steroids
- Vaccinations



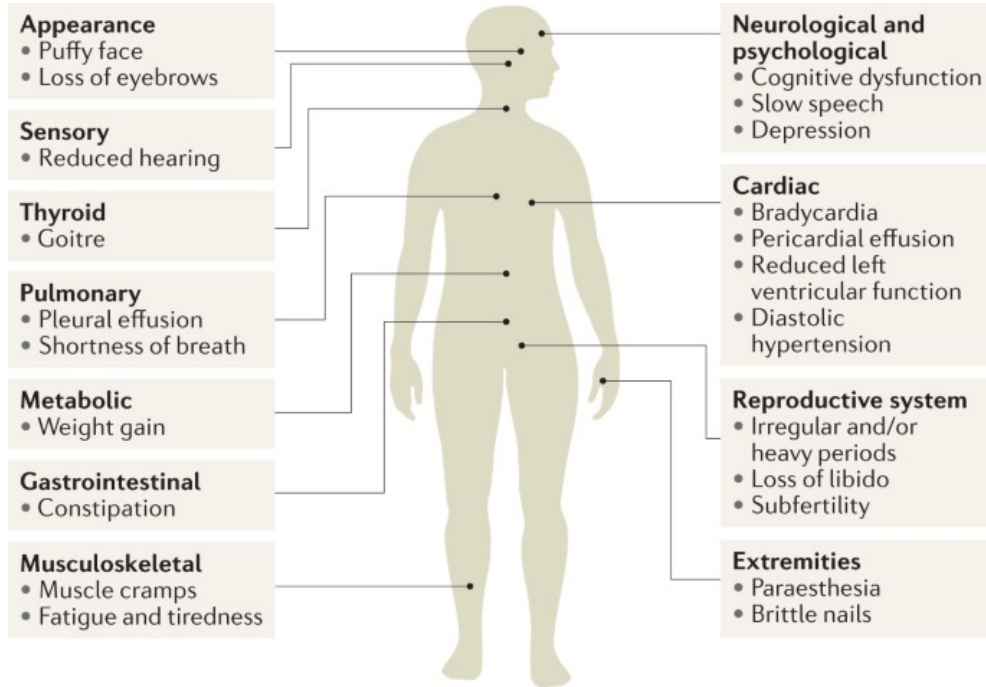
Table 4. Dose Equivalence for GCs

Equivalent Dose	GCs
20 mg	HC
5 mg	Prednisone
0.75 mg	Dexamethasone
4 mg	Methylprednisolone
5 mg	Prednisolone
25 mg	Cortisone

[Derived from S. Melmed and J. L. Jameson: Disorders of the anterior pituitary and hypothalamus. In: Jameson JL, ed. *Harrison's Endocrinology*. 2nd ed. Chap 2. New York, NY: McGraw-Hill Professional; 2010:16–49 (65); Webb R, Singer M. Oxford handbook of Critical Care. Oxford; New York: Oxford University Press, 2005, with permission, © Oxford University Press (88).]

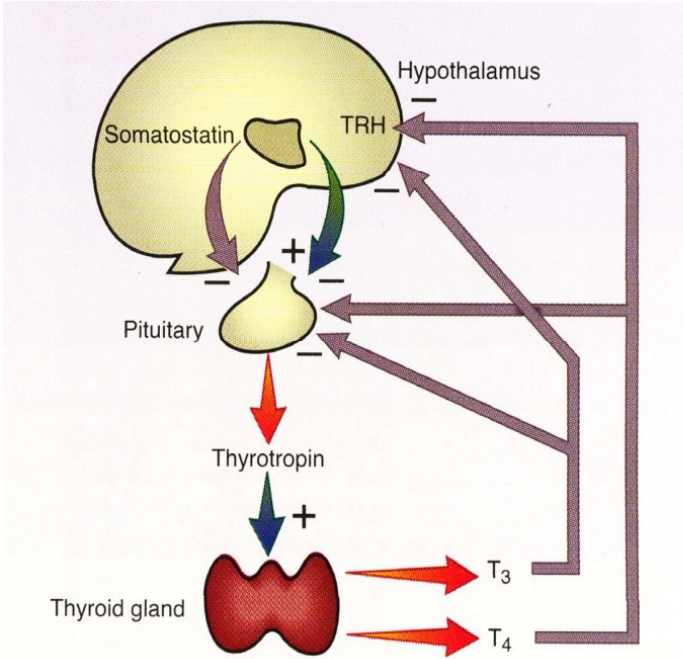
TSH DEFICIENCY

Secondary Hypothyroidism



- Tiredness
- Mental depression
- Sluggishness
- Feeling cold
- Weight gain (~5-10 pounds)
- Dry skin and hair
- Constipation
- Menstrual irregularities

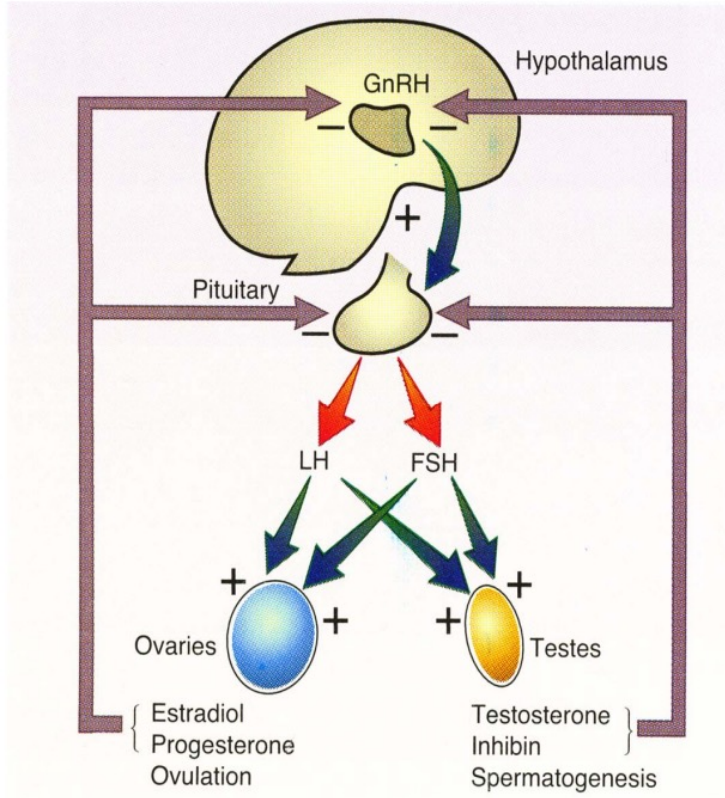
Secondary hypothyroidism



- TSH may be low/ normal (inappropriately normal)
- FT4 needed for diagnosis
- Levothyroxine early morning fasting, daily medication- **monitor FT4 not TSH**
- Treat adrenal insufficiency before hypothyroidism- adrenal crisis
- Goal: FT4 in the mid-normal range

FSH/LH DEFICIENCY

Secondary hypogonadism



- Due to abnormal GnRH, FSH, LH
- Women: Amenorrhea, infertility, dyspareunia, hot flashes
- Men: Decreased libido, impotence, infertility
- Diagnosis:
 - Estrogen levels in women
 - Testosterone levels in men
 - FSH low or inappropriately normal

Treatment of Hypogonadism

- **Men**

- Gonadotropin therapy if fertility desired
- If not, different formulations of testosterone
- Target different with age, comorbidities, elderly, cardiovascular disease



- **Women**

Reproductive age: estrogen/
progesterone birth control

Post menopausal age: consider HRT



GH DEFICIENCY

Adult Growth Hormone Deficiency



- Impaired QOL
- Reduced exercise capacity
- Abnormal lipids, atherosclerosis
- Increased fat mass, decreased lean body mass
- Reduced bone density

NORMAL BONE



OSTEOPOROSIS



Safety of growth hormone replacement in survivors of cancer and intracranial and pituitary tumours: a consensus statement

Moreover, there is a paucity of data related to rare tumours involving the hypothalamic-pituitary area, such as chordoma, pituicytoma, optic gliomas, and germinomas.

JOURNAL ARTICLE

Hormonal Replacement in Hypopituitarism in Adults: An Endocrine Society Clinical Practice Guideline FREE

Maria Fleseriu, Ibrahim A. Hashim, Niki Karavitaki, Shlomo Melmed, M. Hassan Murad, Roberto Salvatori, Mary H. Samuels

CONCLUSION

- Radiation-induced anterior pituitary hormone deficiencies are irreversible and progressive.
- Regular testing is mandatory to ensure timely diagnosis and early hormone replacement therapy
- Baseline pituitary hormone assessment, and dynamic testing for GH deficiency should begin one year after RT
- ACTH deficiency though delayed maybe life threatening
- GH replacement is controversial

Thank you for your
attention!

