CASE 7.2
Hypothyroidism | Level 2

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1. Using Figures 1 through 3, what are the patient's current weight, height, and BMI percentiles?

Utilizing the CDC Growth Charts, this patient's weight percentile is below the 25th for his age and gender (see **Figure 4**). His height percentile is below the 5th (see **Figure 5**). The patient's calculated BMI is17.l kg/m^2. Per the CDC Growth Charts, this BMI falls at the 90th percentile (see **Figure 6**), which would categorize the patient as overweight.

2. What subjective and objective evidence supports the diagnosis of secondary hypothyroidism?

SUBJECTIVE FINDINGS: The patient presented with a chief complaint of increased fatigue; weight gain; constipation; increased difficulty with movement; gait, and balance problems; cold intolerance; and delayed growth as noted by the patient's mother.

OBJECTIVE FINDINGS: On physical exam, the patient appears to have significant growth delay, below 5th percentile for height according to his age (see Figure 5). He has a small thyroid gland on palpitation and muscle weakness of lower extremities. Laboratory findings show low free T_4 levels and thyroid-stimulating hormone (TSH) within normal range, which is consistent with findings of secondary hypothyroidism. He also has gait disturbance. Imaging studies rule out other causes of present illness, such as pituitary tumors or lesions.

3. Devise a pharmacologic regimen for the treatment of hypothyroidism that is best suited for this patient.

The recommended treatment of hypothyroidism is thyroid hormone replacement with levothyroxine due to decreased production of free T_4 by the thyroid gland. The dose of levothyroxine replacement is age and weight dependent and requires close monitoring of free T_4 levels and dose adjustments to maintain reference range levels. The recommended dose range for children 1 to 5 years old is 5 to 6 mcg/kg/day; if the initial serum T_4 is below 5 mcg/dL, treatment should begin at higher doses of 50 mcg/day. The goal serum free T_4 level is the upper third of normal range. Based on the patient's weight and age, the appropriate dosing regimen would be 88 mcg daily given in the morning on an empty stomach. Although an extemporaneous suspension can be prepared, the suspension is only stable for 8 days, which would neces-

sitate picking up the prescription weekly from a pharmacy. Therefore, in most instances, the 88 mcg tablet can be dispensed. If administration on an empty stomach becomes a challenge, the American Thyroid Association recommends administering with the same meal daily and avoiding foods containing calcium, soy, or iron. The tablet can be crushed and mixed with 10 to 15 mL of water or apple juice.

The goal of therapy for the patient is to normalize thyroid function to avoid complications of either hypo- or hyperthyroidism. Low T_4 may decrease intellectual development and linear growth and lead to poor school performance due to impaired concentration and slowed mentation. Hyperthyroidism may adversely affect brain maturation, accelerate bone age, leading to premature closure of the epiphyses and reduced adult height. The patient may experience a period of catch-up growth that is expected with treatment. Monitoring of thyroid function tests should be done every 3 months until the patient is euthyroid and then every 6 months for monitoring and adjusting levothyroxine dose as necessary.

4. Assess the pharmacologic therapy for the patient's GH deficiency and appropriate monitoring for clinical and biochemical responses to treatment.

Panhypopituitarism is characterized by decreased production of most pituitary hormones, including growth hormone (GH), gonadotropins, and thyroid hormones. In a child with short stature or a slow growth velocity, low baseline measurements of insulin-like growth factor 1 (IGF-1), insulin-like growth factor 2 (IGF-2), and insulin-like growth factor–binding protein 3 (IGFBP-3) in the presence of deficiency of at least three pituitary hormones, suggests GH deficiency. In this patient, below-normal velocity of growth, decreased concentrations of IGFBP-3, IGF-1, TSH, and follicle-stimulating hormone (FSH), as well as delayed bone age, indicate a diagnosis of severe GH deficiency, which warrants the initiation of replacement therapy.

The goal of therapy for treatment of GH deficiency is to exogenously supplement GH to allow the patient to reach as close to normal expected adult height. Therapy includes physiologic replacement of GH using a purified polypeptide hormone of recombinant DNA origin. In children whose epiphyses are not yet fused, which is determined by radiologic examination of the hands, GH replacement usually increases growth velocity (averaging 10 to 11 cm/yr during first year of therapy). GH replacement with somatropin should be administered at a recommended dose of 0.18 mg/kg/week subcutaneously divided into equal daily doses on either 3 alternative days (0.06 mg/kg/dose) or 6 times per week (0.03 mg/kg/dose). The individualized dose for this patient would be 0.42 mg of somatropin injected subcutaneously every day, for a total weekly dose of 3 mg. Response to recombinant human growth hormone (rhGH) in pediatric patients tends to decrease over time; however, the failure to increase growth rate, particularly during the first year of therapy, indicates the need for close assessment of adherence. The injection is administered via a delivery device in an outpatient setting under the supervision of an adult caregiver. Various delivery devices are available with the various rhGH products, including automated dose delivery and needle-free devices.

The dose should be adjusted gradually based on clinical and biochemical responses assessed at monthly intervals, including body weight, height, growth velocity, waist circumference, serum IGF-1, IGFBP-3, serum glucose, lipids, thyroid function, and whole body dual-energy x-ray absorptiometry. Doses may be titrated upward if there is not an adequate response to GH therapy. An adequate response is defined as an increase in the standard deviation score (SDS) between 0.3 to 0.5, an increase in height velocity of more than 3 cm/yr in the first year, or a height velocity SDS of more than +1. Treatment should be continued until final height or epiphyseal closure or both are evident or if no response is seen at a higher dose after a 1- to 2-year trial of therapy.