Question 41
A 63-year-old woman presents with weight gain, reduced energy and depression, five years after pituitary surgery and radiotherapy for a non-functioning pituitary adenoma. Current medication are thyroxine 0.15mg/day, hydrocortisone 20 mg/day (equivalent to cortisol acetate 25mg /day) in divided doses, conjugated oestrogen 0.625mg/day, medroxyprogesterone 2.5 mg/day and fluoxetine 20mg day

Examination is unremarkable except for truncal obesity. Her body mass index (BMI) is 30kg/m² [20-25] and her blood pressure is 145/85 mmHg.

Which one of the following is the most likely cause of her weight gain?

A. Inadequate thyroxin replacement dose  
B. Excess hydrocortisone replacement dose  
C. Excess oestrogen replacement dose  
D. **Growth hormone deficiency**  
E. Fluoxetine therapy

I thought this question required quite a lot of information to be confident in the answer actually, much more suited to a clinical application anyway:

What do you need to know?

1. A bit of an understanding of diagnosis and management of pituitary tumours (there are immediate, medium and long term issues)
2. An appreciation of hypopituitarism as a consequence of surgical management, hormones involved and the impact of their deficiency
3. Knowledge of the appropriate medications for deficiency syndromes and doses
4. Fluoxetine therapy

Dosing – from therapeutic guidelines

**Thyroxine** (0.15 mg / dau) – standard maintenance is 100-125 microg / day (start with 50-100) ie dose is not inadequate is at the max maintenance

**Hydrocortisone** (20 mg /day) (15 – 30 mg per day in divided doses)

hydrocortisone, is the glucocorticoid the adrenals make, use in a daily dose according to the patient's weight; suitable doses are approximately 20 mg/day for a patient who weighs 55 kg and 30 mg/day for a patient who weighs 80 kg

so the dose is not excessive

**Gonadotropin**

**Oestrogen** 0.625 mg/day and **medroxyprogesterone** 2.5mg /day

**Medium dose**

- oestrogen 0.625mg/day
- medroxyprogesterone 2.5 – 5

**no growth hormone replacement therapy**

Fluoxetine: starting dose 20mg to max 80mg

**Adverse Reactions:** CNS disturbances incl anxiety, insomnia, mania, seizures, tremor, dizziness; withdrawal reactions; hyponatraemia; GI upset; weight loss; allergy esp rash; asthenia; headache; others, see full PI.

**Children:** headache; decr height gain, weight gain, alkaline phosphatase
Side effect = weight gain but small dose of lack of growth hormone replacement unlikely to be the most important cause

Up to date

<table>
<thead>
<tr>
<th>Mechanism</th>
<th>Symptoms</th>
<th>Signs</th>
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<tbody>
<tr>
<td>Slowing of metabolic processes</td>
<td>Fatigue and weakness, Cold intolerance, Dyspnea on exertion, Weight gain, Cognitive dysfunction, Mental retardation (infant), Constipation, Growth failure</td>
<td>Slow movement and slow speech, Delayed relaxation of tendon reflexes, Bradycardia, Carotenemia</td>
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<tr>
<td>Accumulation of matrix substances</td>
<td>Dry skin, Hoarseness, Edema</td>
<td>Coarse skin, Puffy facies and loss of eyebrows, Periorbital edema, Enlargement of the tongue</td>
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<tr>
<td>Other</td>
<td>Decreased hearing, Myalgia and paresthesia, Depression, Menorrhagia, Arthralgia, Pubertal delay</td>
<td>Diastolic hypertension, Pleural and pericardial effusions, Ascites, Galactorrhea</td>
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Hypopituitarism

GENERAL PRINCIPLES — Damage to the anterior pituitary can occur suddenly or slowly, can be mild or severe, and can affect the secretion of one, several, or all of its hormones. As a result, the clinical presentation of anterior pituitary hormone deficiencies varies, depending upon the following factors:

The rapidity with which a disease affects anterior pituitary cells. Some diseases, such as pituitary apoplexy, develop rapidly, causing sudden impairment of ACTH secretion and, consequently, sudden onset of symptoms of cortisol deficiency. Other insults, such as radiation therapy to the pituitary or hypothalamus, usually act slowly, causing symptoms many months or, more likely, years later."

The severity of the hormonal deficiency. Complete ACTH and cortisol deficiency, as an example, can cause symptoms under basal circumstances, while partial ACTH deficiency may cause symptoms only during times of physical stress.

How many kinds of anterior pituitary cells are affected, leading to impairment in the secretion of one, a few, or all the pituitary hormones (called panhypopituitarism). As a general rule, the secretion of gonadotropins and growth hormone is more likely to be affected than ACTH and thyroid-stimulating hormone (TSH). Many exceptions occur, however, so that one may see a patient who has only isolated ACTH deficiency. Thus, one cannot make an assumption about the status of one pituitary hormone from the status of another; if the physician judges that it is clinically important to know the status of a particular pituitary hormone, the status of that hormone must be tested directly.

ACTH deficiency — The presentation of ACTH deficiency is almost exclusively that of the resulting cortisol deficiency. In its most severe form, cortisol deficiency leads to death due to vascular collapse, because cortisol...
is necessary for maintenance of peripheral vascular tone. A less severe form of the same phenomenon is postural hypotension and tachycardia. Mild, chronic deficiency may result in lassitude, fatigue, anorexia, weight loss, decreased libido, hypoglycemia, and eosinophilia. There are two important clinical distinctions between ACTH deficiency and primary adrenal insufficiency with a secondary increase in ACTH release:

ACTH deficiency does not cause salt wasting, volume contraction, and hyperkalemia, because it does not result in clinically important deficiency of aldosterone.

ACTH deficiency does not result in hyperpigmentation.

Both forms of adrenal insufficiency can cause hyponatremia. This abnormality is due to inappropriate secretion of antidiuretic hormone (vasopressin) that is caused by cortisol (not aldosterone) deficiency.

**TSH deficiency** — The clinical presentation of TSH deficiency is exclusively that of thyroxine deficiency, which might include fatigue, lethargy, cold intolerance, decreased appetite, constipation, facial puffiness, dry skin, bradycardia, delayed relaxation phase of the deep tendon reflexes, and anemia. The degree of symptoms and abnormal physical findings usually parallels the degree of thyroxine deficiency, but, as the case with ACTH deficiency, some patients with marked TSH deficiency have few or no symptoms.

**Gonadotropin deficiency** — Deficient secretion of the gonadotropins follicle-stimulating hormone (FSH) and luteinizing hormone (LH) causes hypogonadism in both women and men.

In women, hypogonadism means ovarian hypofunction, which results in the inability to ovulate, infertility, and decreased estradiol secretion. The latter may be responsible for a variety of symptoms including oligo- or amenorrhea, vaginal dryness and atrophy, and fatigue. Estradiol deficiency due to hypopituitarism causes hot flashes, like estradiol deficiency due to ovarian disease. No physical findings of hypogonadism are detectable initially, but after several years, breast tissue decreases, fine facial wrinkles appear, and bone mineral density declines.

Serum androgen concentrations in women with hypopituitarism (particularly those with both gonadotropin and ACTH deficiency) are lower than those in normal control women [2], and appear to be correlated with bone mineral density [3]. The clinical significance of this decrease has yet to be determined.

In men, hypogonadism means testicular hypofunction, which results in infertility and decreased testosterone secretion. The latter causes decreased energy and libido, and hot flashes if sufficiently severe, within weeks to months, but does not cause decreased muscle mass (and perhaps strength) for several years. Testosterone deficiency also causes decreased bone mineral density.

**Growth hormone deficiency** — Growth hormone deficiency in children typically presents as short stature. For many years, growth hormone deficiency beginning in adulthood was not thought to have any adverse consequences. However, evidence suggests that lack of growth hormone in adults might have a number of adverse effects. The evidence is of two kinds.

1. The demonstration that patients who have growth hormone deficiency have a greater frequency of certain diseases than expected. Interpretation of this kind of evidence is confounded by the simultaneous deficiencies of other pituitary hormones and the variability of their replacement.
2. The improvement these patients experience when they are treated with growth hormone. Interpretation of this kind of evidence is made difficult by the lack of placebo controls in most studies of growth hormone treatment.

With the above qualifications, we should consider the possibility that growth hormone deficiency may result in the following:

- Diminished muscle mass and increased fat mass. This effect is the best documented.
- Increased serum low-density-lipoprotein (LDL) cholesterol.
- Decreased bone mineral density.
Year 2003 Paper one: Questions supplied by Tricia

- Diminished sense of well being.
- Increased risk of cardiovascular disease] and increased inflammatory cardiovascular risk markers (IL-6 and C-reactive protein).

**Prolactin deficiency** — The only known presentation of prolactin deficiency is the inability to lactate after delivery.

**Treatment of hypopituitarism**

**SUMMARY** — Treatment of patients with hypopituitarism is the sum of the treatments of each of the individual pituitary hormonal deficiencies detected when a patient with a pituitary or hypothalamic disease is tested. The treatments of corticotropin (ACTH), thyroid-stimulating hormone (TSH), and luteinizing hormone (LH) and follicle-stimulating hormone (FSH) deficiencies are in many ways the same as the treatments of primary deficiencies of the respective target glands, but in other ways they differ.

1. Lack of ACTH primarily induces cortisol deficiency. Treatment consists of the administration of hydrocortisone or other glucocorticoid in an amount and timing to mimic the normal pattern of cortisol secretion.
2. TSH deficiency, which results in thyroxine (T4) deficiency, is treated with L-thyroxine. The goal of therapy should be a normal serum T4 value. T4 should not be administered until adrenal function, including ACTH reserve, has been evaluated and either found to be normal or treated. Measurement of serum TSH cannot be used as a guide to the adequacy of L-thyroxine replacement therapy.
3. 
4. In men with gonadotropin deficiency, testosterone replacement is indicated when fertility is not desired. Men with secondary hypogonadism who wish to become fertile may be treated with gonadotropins, if they have pituitary disease or with either gonadotropins or gonadotropin-releasing hormone (GnRH) if they have hypothalamic GnRH deficiency.
5. In women with gonadotropin deficiency, treatment depends upon the patient's goals. Estrogen and progestin replacement is indicated in women who are not pursuing fertility, while gonadotropin or pulsatile GnRH therapy may be used when ovulation induction and fertility are the goal.
6. We currently do not recommend recombinant human growth hormone as routine treatment for all patients with adult-onset growth hormone deficiency. This issue is reviewed in detail elsewhere.
   a. **GROWTH HORMONE DEFICIENCY** — The availability of several recombinant human growth hormone preparations (Humatrope®, Nutropin®, Serostim®, and Genotropin®) for treating adults with growth hormone deficiency allows physicians in the United States to prescribe this treatment. Patients with GH deficiency acquired as an adult must meet at least two criteria for therapy: a poor GH response to at least two standard stimuli; and hypopituitarism due to pituitary or hypothalamic damage. The criteria are different in children in whom GH is required for normal growth.