Resident Responsibilities While on Pediatric Endocrinology

1. The resident must attend all regularly scheduled resident education conferences: grand rounds, morning report.

2. Resident must attend their continuity care clinic each week.

3. Resident must take any scheduled call, such as in the ER.

4. At all other times Monday through Friday, the resident should be working with the pediatric endocrinology section.

5. Residents are expected to do all in-hospital consults during the week, and present these to the pediatric endocrinologist on call.

6. Residents are expected to follow all in-hospital patients on the pediatric endocrinology service.

7. Residents should see all in-patients each morning before morning report.

8. Residents will be given self-assessment exams or reading materials almost every day. It is important to complete these each evening/night, as you will usually be given new materials the next day.

9. Residents are expected to see both new and follow-up patients in the clinic. Green and white flags designate a pediatric endocrine patient, and the face sheet is magnetically attached to the door frame of the room of patient waiting to be seen.

10. Residents may see any of the pediatric endocrine staff’s patients (unless specifically told not to as in the case of a difficult family).

11. Pediatric endocrinology patients are designated with green and white flags. Different colored numbers designate which staff the patient has an appointment with:

   Dr. Rogers: green number on white background
   Dr. Haider: gold number on red background
   Dr. Narasimhan: gold number on green background
   Dr. Kim: yellow number on a blue background
   Dr. Mucci: white number on a purple background
   Dr. Cartaya: white number on a blue background

12. Residents are to never take a day off, even in the unlikely event that no pediatric endocrine staff have patients scheduled. On those rare occasions, residents should read in the library, and be available to see in-patient consults.

13. Residents usually work in clinic with the staff member who is on call for the week. This facilitates communication between the resident and staff regarding inpatient management.

14. The usual weekly clinic schedules are listed below:

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INTRODUCTION.

In pediatric endocrinology we focus on those medical problems caused by hormone abnormalities. I will discuss the nature of hormones, how hormones affect cell function, and how hormones are regulated, especially negative feedback loops.

Actions of hormones can be broken down into 3 broad categories:

1. **Autocrine.** A cell secretes a hormone that binds to a receptor on the same cell and alters the function of that cell. Chondrocytes at the growth plate of long bones can secrete Insulin-like Growth Factor I (IGF-1) that then binds to the IGF-1 receptor on the chondrocyte stimulating the chondrocyte to grow.

2. **Paracrine.** A cell secretes a hormone that binds to neighboring cell receptors, and alters the neighboring cell’s function. Delta cells in pancreatic islets secrete somatostatin, which causes beta cells in the islets to decrease their secretion of insulin.

3. **Endocrine.** A cell secretes a hormone into the bloodstream. The hormone is distributed throughout the body, but will only affect the function of those cells that possess receptors for that hormone.

Hormones can be categorized as either a peptide or steroid hormone.

Steroid hormones are formed from the cholesterol molecule. They affect cells by binding to receptors in the target cell nucleus. The hormone-receptor complex then binds to specific DNA binding sites to regulate the function of a specific gene. The hormone-receptor complex may either down-regulate a gene or up-regulate a gene. Because of their structure, steroid hormones can pass through cell and nuclear membranes unassisted. The effect of exposure to a steroid hormone can require hours before any significant physiologic changes are noted.

Some examples of steroid hormones in humans:

- 1,25 dihydroxy vitamin D
- Testosterone
- Estradiol
- Cortisol
- Aldosterone
- DHEA-S

Peptide hormones are proteins. They bind to receptors on the target cell surface membrane. These cell surface receptors have extracellular, transmembrane, and intracellular domains. By changing the conformation of the cell surface receptor’s extracellular domain, chemical reactions (usually phosphorylations of proteins) are rapidly initiated at the intracellular domain. These chemical reactions then usually increase the concentration of second messengers within the cell, such as cAMP. The increased concentration of second messengers then affects the function of specific enzymes within the cell, altering the cell’s function. Another way that peptide hormones can affect cells is by altering ion channels, usually sodium or calcium. Peptide hormones do not cross cell membranes. Their effects are rapid, and significant physiologic changes can usually be seen in a matter of minutes.
Some examples of peptide hormones in humans:

Insulin
Glucagon
All pituitary hormones
   Luteinizing hormone (LH)
   Follicle stimulating hormone (FSH)
   Thyrotropin (TSH)
   ACTH
   Prolactin (PRL)
   Growth hormone
   Anti-diuretic hormone (ADH)
All hypothalamic hormones
   Gonadotropin releasing hormone (GnRH)
All gut hormones
   Gastrin
   Glucagon like peptide-1 (GLP-1)

Thyroid hormone (T4, T3) is unique in that thyroxin receptors exist on cell surface membranes, and in the nucleus. Thus thyroxin can act like a peptide hormone in regard to some cell functions (rapid alteration) and a steroid hormone (slow alteration) for other cell functions.

REGULATION OF HORMONE SECRETION AND ACTIVITY.

Negative Feed Back Loops.

Because hormones are powerful little molecules, their concentration in the blood must be tightly regulated. This is usually accomplished by a negative feed back loop. We will examine the regulation of T4 as an example of a simple feed back loop. A certain level of T4 must be maintained in the blood. As the level of T4 starts to fall, this fall is detected by receptors in the hypothalamus and pituitary gland. In response to the fall, the production of thyrotropin releasing factor (TRF) from the hypothalamus, and TSH production from the pituitary gland increase. The increasing level of TSH then stimulates the thyroid gland to increase its production of T4.

If a patient were to develop microsomal antibodies to the thyroid gland (Hashimoto’s disease) the thyroid gland may have difficulty producing adequate amounts of T4. In response to this, the pituitary gland will increase production of TSH, to the point where TSH levels are above the “normal” range. This may occur even while the T4 level is still within the “normal” range.

If a patient were to develop thyroid stimulating immune globulins (Grave’s disease) the thyroid gland would produce an excessive amount of T4. The pituitary gland would respond by stopping production of TSH entirely. Thus the T4 level would be above the “normal” range, while the TSH level would fall below the level of detection for the assay.

The above two examples involve abnormal gland function that is primarily in the thyroid gland. Disorders of the pituitary gland may secondarily affect the thyroid gland. A child who is born with septo-optic dysplasia frequently develops an underactive pituitary gland. Thus the ability to increase TSH secretion as T4 levels fall may be compromised. Blood test may reveal a T4 level that is just below the “normal” range, while the TSH level remains in the “normal” range. The TSH did not rise as expected when the T4 level became low.
Hormone Receptors.

The effect a hormone has is proportional to the product of the hormone concentration times the sensitivity of receptors to the hormone. If an individual were to gradually lose sensitivity to a particular hormone, increasing the concentration of the hormone in the blood may compensate for this and maintain “normal” hormone function. As an example, in the development of Type 2 Diabetes Mellitus, the initial insulin insensitivity (resistance) is compensated for by higher levels of circulating insulin.

A genetic mutation of the testosterone receptor may cause a complete lack of sensitivity to testosterone. In these cases, a fetus can not masculinize because the tissues will never be affected by the circulating testosterone. Thus a 46 XY fetus will develop as female. These girls with complete androgen insensitivity may present having had breast development for many years, but no menarche. No uterus would be found on pelvic ultrasound.

Endocrinopathies.

Endocrine disease results when an individual can not make adequate amounts of a hormone (lack of insulin in type 1 diabetes), makes too much hormone (excessive insulin secretion in nesidioblastosis), or lacks adequate sensitivity to a hormone (Type 2 Diabetes).

Quiz:

Q1. A fourteen-year-old girl has some axillary hair, Tanner 2 pubic hair, but no breast development. Her LH and FSH levels are high. Which of the following is the most likely diagnosis?

1. Complete androgen insensitivity.
3. Kallman’s syndrome
4. Prolactinoma

Q2. A fourteen-year-old girl has some axillary hair, Tanner 2 pubic hair, but no breast development. She can not identify odors like coffee or garlic. Her LH and FSH levels are unmeasurable. Which of the following is the most likely diagnosis?

5. Complete androgen insensitivity.
7. Kallman’s syndrome
8. Prolactinoma

Q3. A fourteen-year-old girl has Tanner 5 breast development, but no axillary hair or pubic hair. She has never menstruated. Her LH is elevated but her FSH level is normal. Which of the following is the most likely diagnosis?

9. Complete androgen insensitivity.
10. Mosaic Turner syndrome.
11. Kallman’s syndrome
12. Prolactinoma

The above three examples illustrate cases of: primary gland failure (Q1), secondary gland failure due to hypothalamic dysfunction (Q2), and hormone insensitivity (Q3).