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HORMONE ABNORMALITIES IN SOD

A REFERENCE GUIDE



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THE HYPOTHALAMUS AND PITUITARY GLAND



Children with SOD often have **HYPOPI TUITARI SM** (an under activity of the **PITUITARY GLAND**). It is actually an under activity of the pituitary gland's "boss," the **HYPOTHALAMUS**, that causes the hormone problems in this condition.

The **HYPOTHALAMUS** makes hormones called **RELEASING HORMONES** (end in **___RH**) that travel through the brain's blood and tell the pituitary gland to make its hormones. The **PITUITARY** hormones are called **STIMULATING HORMONES** (end in **___SH**) and travel through the body's bloodstream to tell the various glands to produce their own hormones. Unfortunately we cannot measure the levels of the releasing hormones in blood tests, so we generally rely on levels of the stimulating hormones from the pituitary gland and levels of the glands' hormones to make the diagnosis of a **HORMONE DEFICIENCY**.

This guide will outline the different **HORMONES** that can be abnormal in SOD, including their function, signs of under activity in a child, diagnostic tests, medical abbreviations, and the brand names of common medications used to replace these hormones.

While it is intended to serve as a guide to educate you, it is also meant to serve as a tool to ensure that your child is receiving the proper assessment and care from their doctor. Even if they are growing "normally" every child with SOD needs to be evaluated by a hormone specialist, or Endocrinologist!

1. GROWTH HORMONE



The hypothalamus makes GROWTH HORMONE RELEASING HORMONE (**GHRH**), which travels to the pituitary gland and tells it to make GROWTH HORMONE (**GH**). While we used to believe that GH acted directly, we now know that it must go to the liver where it is changed in to another hormone, INSULIN LIKE GROWTH FACTOR 1 (**IGF-1**) that is the active hormone. Another substance called **IGFBP-3** is important to growth hormone's action.

GH is not only necessary for growth in height, but for many other things in our body. It also:

- a. converts fat to muscle
- b. builds muscle strength (tone)
- c. regulates our blood sugar
- d. aids in heart strength
- e. controls our cholesterol

If **GH DEFICIENCY** is present at birth, the baby will have problems with low blood sugar. If it occurs later the child may have poor growth and be overweight, and have developmental delays from poor muscle tone.

Endocrinologists have different opinions about which tests are needed to diagnose GH deficiency. In a newborn, a low level of GH during a time of hypoglycemia is seen. In a child the initial blood tests should include levels of **IGF-1 and IGFBP-3**. If these levels are low this should be sufficient, but some doctors, or more unfortunately insurance companies will have the child undergo **GH STIMULATION TESTS** before they will prescribe GH. In **GH STIMULATION TESTS** the levels of GH in the blood are measured at baseline and then the child is given different medications that are known to normally STIMULATE the pituitary gland to release GH. The blood GH level is then remeasured at different intervals of time and if the level does not rise appropriately the diagnosis of GH deficiency is confirmed.

Growth hormone is currently only available in an injectable form and should be given daily for best results. There are now many different brands of synthetic GH on the market, and they are all comparable. The dose of GH is based on the child's weight, and is increased periodically according to weight

gain. When a child goes through puberty this dose is doubled to ensure the best growth possible.

Brand Names of GH:

- ↪ Nutropin and Nutropin AQ
- ↪ Protropin
- ↪ Humatrope
- ↪ Norditropin
- ↪ Genotropin
- ↪ Saizen

2. THYROID HORMONE



The hypothalamus makes THYROTROPIN RELEASING HORMONE (**TRH**), which travels to the pituitary gland and tells it to make **THYROID STIMULATING HORMONE (TSH)**. **TSH** then travels through the blood to the thyroid gland and causes the release of **THYROID HORMONE (T4)**. **T4** is the main active form of thyroid hormone, but **T4** is also converted in the body to another form of thyroid hormone called **T3**.

T4 and T3 are important for controlling:

- a. growth
- b. energy
- c. brain development
- d. body temperature
- e. digestion
- f. heart pumping and blood circulation
- g. mood

If **THYROID HORMONE DEFICIENCY (HYPOTHYROIDISM)** is present at birth, the baby will have problems with low body temperature, jaundice, constipation, and low muscle tone. If it occurs later in childhood there may be poor growth, weight gain, constipation, as well as physical and cognitive developmental delays.

The tests needed to diagnosis **HYPOTHYROIDISM** are levels of **TSH** and **free T4**, and **free T3** levels should be measured as well. A level of just TSH is NOT sufficient for diagnosis in SOD, as this level may be “normal” while the levels of thyroid hormones are low.

Thyroid hormone replacement is given orally and there are many different forms available commercially. Some forms are synthetic and others are “natural” (animal products), some contain just T4 or just T3, while others have a combination of both hormones. The dose is adjusted according to periodic blood levels of T4 and T3 – levels of TSH are NOT helpful for this.

Brand Names of Thyroid Hormone:

- ↪ Synthroid (T4)
- ↪ Levothroid (T4)
- ↪ Levoxyl (T4)
- ↪ Unithroid (T4)
- ↪ Cytomel (T3)
- ↪ Armour thyroid (T4 + T3)

3. CORTISOL



The hypothalamus makes CORTICOTROPIN RELEASING HORMONE (**CRH**), which travels to the pituitary gland and tells it to make ADRENOCORTICOTROPIC HORMONE (**ACTH**). **ACTH** then goes through the bloodstream to the two adrenal glands, where it causes the release of **CORTISOL**. Our adrenal glands also make other hormones, including male sex hormones (androgens), adrenaline, and aldosterone, but these hormones are NOT affected in SOD.

CORTISOL is called a “**stress hormone**” as it is released when our body is under any sort of stress (physical or psychological). It raises the blood sugar level, which provides a quick form of energy.

If **CORTISOL DEFICIENCY** is present at birth, the baby will have problems with low blood sugar. If it occurs later the child may have poor growth and be underweight, fatigued, have low blood sugar with fasting (especially in the mornings) or have a difficult time recovering from even mild illnesses. If it goes undiagnosed the child may present in an **ADRENAL CRISIS** with vomiting, low blood sugar (which may cause a seizure), low blood pressure and lethargy. This is a LIFE THREATENING CONDITION.

The blood tests needed to diagnose **CORTISOL DEFICIENCY** are morning, fasting levels of cortisol and glucose.

CORTISOL is given in an oral form (hydrocortisone) and should be dosed twice or three times daily. The dose of is based on the child's surface area, calculated from their weight and height, and is increased periodically accordingly. When a child goes through STRESS this dose is doubled or tripled to prevent **ADRENAL CRISIS**.

GUIDELINES FOR ADJUSTING CORTISOL DOSES DURING STRESS AND ILLNESS:

-DOUBLE DOSE for: fever of 101 - 103 degrees
minor injuries (e.g. sprained ankle)
psychological stress

-TRIPLE DOSE for: fever > 103 degrees
significant injury (e.g. broken bone)
surgery

If the child is vomiting and can not keep down their medication and/or develops signs of adrenal crisis they need to receive this important medication by INJECTION. The dose varies by age and is given in to the muscle in the leg or buttocks.

<u>AGE (years)</u>	<u>DOSE</u>
0-3	25 mg
3-10	50 mg
10 +	100 mg

*Carry your emergency card with you at all times so that if you have the misfortune of having to go to the ER the doctors there will know how to treat a child with cortisol deficiency!

Brand Names of Cortisol:

- ↪ Hydrocortisone
- ↪ SoluCortef
- ↪ Cortef

4. SEX HORMONES



The hypothalamus makes GONADOTROPIN RELEASING HORMONE (**GnRH**), which travels to the pituitary gland and causes release of two different hormones called FOLLICLE STIMULATING HORMONE (**FSH**) and LEUTINIZING HORMONE (**LH**). **FSH** and **LH** travel through the blood to the sex glands (**OVARIES** in a girl and **TESTICLES** in a boy) and stimulate the release of the sex hormones, **ESTROGEN** and **PROGESTERONE** in girls and **TESTOSTERONE** in boys.

Interestingly, although deficiencies of these hormones, and therefore a LACK of PUBERTY is the usual case, some children with SOD will actually have **PRECOCIOUS PUBERTY**, or the production of these hormones at too young an age (before 8 years old in girls, before 9 in boys). If **PRECOCIOUS PUBERTY** occurs there may be accelerated growth, weight gain, moodiness, and development of breasts in girls. The development of pubic or armpit hair in a girl is NOT always a sign of puberty.

The tests needed to diagnosis the presence or absence of puberty are levels of **FSH**, **LH** and **estradiol** or **testosterone**. As these levels can be low early on in puberty a **GNRH STIMULATION TEST** may need to be performed to confirm the diagnosis. Levels of **FSH** and **LH** are drawn at baseline, then **GnRH** (Factrel) is given IV and repeat levels of the hormones are performed at different time intervals to look for a characteristic increase.

If a child has **PRECOCIOUS PUBERTY** it can be treated with a once monthly injection called **Lupron Depot**, which is continued until the time of expected normal puberty. Once this is stopped puberty will progress normally.

If a child fails to enter puberty on their own (**HYPOGONADISM**), sex hormone replacement is given orally in girls and by injections in boys. Adults can use patches or creams that allow the hormones to be absorbed through the skin, but it difficult to control the amount of hormone a child receives in this way so it is not recommended. Again, there are many different forms of these hormones available commercially. Some forms are synthetic and others are “natural” (animal products). The doses are increased with age according to a set protocol, and it is not necessary to monitor the levels of these hormones in the blood.

Brand Names of Sex Hormones (abbreviated list)

<u>Estradiol</u>	<u>Progesterone</u>	<u>Testosterone</u>
↗ Estrace	↗ Provera	↗ T. enanthate
↗ Premarin	↗ Medroxy P	↗ T. cypionate
↗ Depot E		↗ Depot T

Girls are given only estrogen replacement for the first two years, then progesterone is added for ten days each month to initiate menstrual cycles. Once a girl is on these hormones for several years she can be switched to OCPs (oral contraceptive pills) to allow for easier doses and regular predictable menstrual periods. Boys are given testosterone injections every two to four weeks.

5. ANTIDIURETIC HORMONE



The hypothalamus makes ANTIDIURETIC HORMONE (**ADH**), which travels to the pituitary gland and is stored there; unlike the other hypothalamic

hormones it does not cause the release of a second hormone from the pituitary gland.

ADH is critical for maintaining the balance of salt (**SODIUM**) and water in our body. Namely it keeps water in our body preventing the kidneys from losing it in the urine, and keeps sodium in our body as needed.

If **ADH** deficiency is present the condition is called **DIABETES INSIPIDUS or DI**. Children with this condition have extreme urination because they can not hold on to the water. Their urine is very dilute, and is said to have a **LOW SPECIFIC GRAVITY**. To prevent dehydration they will drink extreme amounts of fluids, and may "crave" water.

Endocrinologists also may have different opinions about the test needed to diagnose ADH deficiency. Most doctors will have the child undergo a **WATER DEPRIVATION TEST**, but the length of this may vary. Usually an overnight fast (i.e. no fluids) is done, and measurements of the blood sodium level and concentrations of the urine are tested. In the prolonged **WATER DEPRIVATION TEST** the level of sodium in the blood and urine concentration are measured at baseline and then the child is not allowed anything by mouth for several hours. Levels are remeasured at different intervals of time and the child is also weighed. If a child has **DI** they will continue to urinate large amounts of dilute urine despite becoming dehydrated, and will lose weight during the testing.

ANTIDIURETIC HORMONE is currently available under the name **DDAVP** in an oral form but traditionally is given through a nose spray. The oral dose may be as high as 20 times the intranasal dose, and is not as easy to regulate. The dose can be difficult to judge during times of stress or illness.