



## Endocrine Disease in Mucopolysaccharidosis (MPS)

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The endocrine system is a vast network of glands and hormones that regulate various functions of the body. The pituitary gland is a pea sized gland in the center of the brain that acts as a “control center” of other hormone-secreting glands such as the thyroid gland, adrenal gland, ovaries, and testicles. Although endocrine disease has not yet been well studied in MPS, there are case reports of glycosaminoglycan (GAG) deposition in the pituitary, as well as hormone deficiencies reported in MPS I and II. As a separate risk, bone marrow transplantation, particularly if radiation was used, increases the risk of someone developing certain hormone problems.

The following hormone problems have been seen in patients with MPS:

#### **Thyroid**

The thyroid gland is a butterfly-shaped gland located at the base of the neck just below the “adam’s apple”. This gland secretes thyroid hormones called thyroxine (T4) and triiodothyronine (T3). Thyroid hormone regulates how quickly or slowly the body works. Thyroid hormone affects almost every organ and system in the body.

A low thyroid hormone level, or “hypothyroidism”, is a condition where the thyroid gland does not make enough thyroid hormone. This leads to a general slowing down of body functions. The symptoms of hypothyroidism include weight gain, low energy, increased sleepiness, depressed mood, dry skin, constipation, feeling cold when others are not cold, brittle nails, and hair loss. Girls can have irregular menstrual periods and difficulty becoming pregnant. Hypothyroidism is treated with a once daily pill of thyroid hormone (levothyroxine).

#### **Growth Hormone**

Growth hormone is a hormone that is made in the pituitary gland and is critical for normal growth and adult height. Growth hormone deficiency is when the pituitary gland does not make enough growth hormone. Growth hormone deficiency can be caused by damage to the pituitary gland (for instance, radiation therapy, possibly GAG deposition) or a genetic variation. Besides being short, people with long-term growth hormone deficiency can also have problems with bones, heart, muscle, and too much body fat.

The pituitary needs to make much more growth hormone during childhood than during adulthood. For this reason, not all children treated with growth hormone will need growth hormone treatment as adults. Growth hormone deficiency is treated with recombinant human

growth hormone (hGH) given as a daily injection under the skin. There are possible side effects that should be discussed with a pediatric endocrinologist before starting treatment with hGH.

## **Sex Hormones**

### *Puberty*

Puberty is a period during which the body changes from that of a child to that of an adult. The initiation of puberty is controlled by the pituitary gland: two hormones, LH and FSH, stimulate the ovaries in girls and testicles in boys to make estrogens (female hormones) and androgens (male hormones). Girls typically start puberty between 8 and 13 years of age, and boys between 9 and 14 years of age. The average age for a girl to have her first period is 12.5 years. In girls pubertal changes include the development of breasts, pubic and axillary hair, acne, body odor, growth spurt, and a menstrual cycle. In boys pubertal changes include increasing size of the testicles and penis, development of pubic and axillary hair, acne, body odor, deepening of the voice, growth spurt, and facial hair.

Early or “precocious” puberty is when puberty starts before 8 years of age in girls or before 9 years of age in boys. Precocious puberty is diagnosed by physical examination and laboratory testing showing that the LH, FSH, estrogens or androgens, are higher than would be expected in a child not yet in puberty. There are many causes for precocious puberty, these include injury to the brain (i.e. radiation, brain tumors, period of low oxygen to the brain), environmental exposure to estrogens or androgens, and genetic variations. Frequently, no cause for precocious puberty is found and this is called “idiopathic precocious puberty”. Precocious puberty can be treated by a medication given as a monthly intramuscular injection or yearly subcutaneous implant.

Late or “delayed” puberty is when puberty has not started by 13 years of age in girls and by 14 years of age in boys. Delayed puberty is diagnosed by physical examination and laboratory testing showing that the LH, FSH, estrogens or androgens, are not yet at a level that is found in pubertal children. There are many causes for delayed puberty, similar to precocious puberty; these include injury to the brain, injury to or problem with the ovaries or testicles, and genetic variations. Delayed puberty can be treated by increasing doses of estrogen in girls and testosterone in boys over the course of 2-3 years. Estrogen is given as either a daily pill or patch that is changed twice weekly. Testosterone is given as a monthly injection; a daily gel or patch may be used when adult levels of testosterone are reached.

### *Low Sex Hormones in Adulthood*

For adult men and women, low androgens (male hormones) in men and low estrogens (female hormones) in women can cause osteoporosis, low sex drive and problems with sexual function. Men may notice that they need to shave less often and have lower muscle mass. Women may experience “hot flashes”. Some people with low sex hormones feel a decrease in their sense of well-being. Treatment varies and should be discussed with a physician.

## **Vitamin D Deficiency**

Vitamin D is a hormone that is important for dietary calcium absorption and bone health. Severe vitamin D deficiency results in “rickets”, a condition where weak, under mineralized bone results in a bowing of the legs and easy fracturing. Less severe vitamin D deficiency is very common around the world and has been associated with decreased lung function, increased risk of certain infections, increased blood cholesterol levels and other components of the metabolic syndrome, low mood and energy, and bone pain. Risk factors for vitamin D deficiency are dark skin color, judicious use of sun block, lack of exposure to the sun, and gastrointestinal diseases that cause problems absorbing vitamin D.

Vitamin D can be obtained in the diet in foods such as salmon, tuna, and mackerel, shiitake mushrooms, milk, and fortified juices and cereals. Vitamin D is also available over-the-counter and called ergocalciferol or cholecalciferol. Current recommendations for daily vitamin D intake is 400 IU daily for infants less than 1 year old, 600 IU daily for anyone older than 1 year including adults. However, measurement of the level of 25-OH vitamin D in the blood is the only way to ensure that the vitamin D intake is adequate. The goal 25-OH vitamin D level is between 30 ng/ml and 60 ng/ml.