

Hypoparathyroidism and DiGeorge Syndrome



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Hypoparathyroidism

Hypoparathyroidism occurs when the body does not produce enough parathyroid hormone (PTH). This hormone is made in 4 or 5 parathyroid glands, located behind the thyroid tissue in the neck area. They are very small—the size of peas. Their only job is to produce PTH, which keeps the calcium levels in the blood in the right range.

The name “hypo-parathyroid-ism”, means a condition of low parathyroid hormone.

What does PTH do?

PTH balances the calcium level in the blood, keeping it in the right range. When the calcium level is low, PTH is produced and it raises the calcium level by:

1. Moving calcium from the bones into the blood.
2. Decreasing how much calcium is eliminated from the blood into the urine by the kidneys.
3. Activating vitamin D to increase the amount of calcium and phosphorus absorbed from the intestines into the bloodstream.

What causes hypoparathyroidism?

In some situations, hypoparathyroidism is present from birth (congenital), such as occurs with DiGeorge syndrome and other rare inherited conditions (see next section). In others, hypoparathyroidism develops later in life as an acquired condition.

Acquired hypoparathyroidism can be a result of:

1. An autoimmune process which destroys

the parathyroid cells. The body has developed cells that destroy some of its own tissue. This may include other organs and endocrine glands, causing type 1 diabetes, Addison disease or other autoimmune diseases.

2. Surgery or radiation to the thyroid gland which damages the parathyroid glands.
3. Iron deposits in the parathyroid glands, a side-effect of repeated transfusions to treat thalassemia or other blood diseases

How is hypoparathyroidism diagnosed?

Something will have happened to make your doctor request special blood tests. Perhaps a heart problem is discovered during a routine pregnancy ultrasound or at birth, or perhaps your baby or child became very sick with symptoms of low blood calcium (see handout *Disorders of Calcium and Phosphorus*). Blood tests will be taken, and if the tests confirm low calcium and PTH levels in the blood, the diagnosis of hypoparathyroidism is made. There is no easy way to scan the parathyroid glands.

How is hypoparathyroidism treated?

The parathyroid hormone is generally not replaced—it is an extremely expensive medication and must be given by injection. The low calcium level is treated by taking calcium pills or liquid. However, the calcium itself will not be absorbed into the digestive system unless the activated form of vitamin D is taken as well. Both calcium and the activated form of vitamin D, calcitriol (Rocaltrol®) or alfacalcidol (One-Alpha®), must be replaced in just the right amounts (see Appendix). The calcium must be taken

frequently, possibly four times each day. If the child isn't taking enough calcium, the level can become so low that the child becomes extremely sick with seizures. This is an emergency, and the calcium will need to be given by intravenous.

Blood and urine tests must be done frequently at first (daily or weekly) to be sure that the calcium level is in the right range. Even after doses are just right, tests will be done every 2–3 months. Urine tests for calcium will show if extra calcium is being flushed from the body through the kidneys into the urine. Extra calcium and activated vitamin D can be harmful, as they can lead to side-effects such as calcium deposits in the kidneys (called nephrocalcinosis) or even calcium deposits in the blood vessels. Ultrasound scans of the kidneys may be recommended every year or two to watch for this problem.

Hypoparathyroidism is almost always a permanent condition, but it tends to be most difficult to treat during periods of rapid bone growth, for example, during infancy and during puberty.

There are many reasons for low calcium.

Regardless of cause, the treatment is usually the same

affected child has congenital hypoparathyroidism, with low calcium and PTH levels.

Dr. Angelo DiGeorge, an endocrinologist in Philadelphia, was the first doctor to describe a group of patients with these characteristics. This was reported in the mid 1960's.

What other problems can be seen in DiGeorge syndrome?

Other midline parts of the body may not be formed normally in DiGeorge syndrome. These can include:

1. The roof of the mouth, leading to cleft palate with feeding, hearing and speech difficulties.
2. The heart, leading to a number of serious cardiac malformations.
3. The thymus (an organ that assists the body with immunity), leading to repeated serious infections.
4. Learning difficulties, particularly with math and conceptual thinking.
5. Certain facial features are characteristic of DiGeorge syndrome: small, wide-set eyes; small, cup-shaped, low-set ears; small lower jaw; and a blunted nose with a bulbous tip.

As a result, many children with DiGeorge syndrome are often followed by a number of specialists (craniofacial experts, speech therapists, cardiologists, and immunologists). There are also specialists in non-verbal learning disorders (NVLD) who can offer guidance for the child having school problems. It is important to know that DiGeorge syndrome is quite variable from child to child.

DiGeorge syndrome

DiGeorge syndrome is also known as chromosome 22q11.2 deletion syndrome, or CATCH-22. The velocardiofacial or Shprintzen syndrome is a closely related condition. In DiGeorge syndrome, a small genetic area is missing from chromosome 22. This area is responsible for some midline development when the baby isn't born yet—in fact very early in development—between the 2nd and 10th weeks. When this midline development does not occur properly, the parathyroid glands are not formed. As a result, there is no PTH production, and the

How is DiGeorge syndrome diagnosed?

When DiGeorge syndrome is suspected clinically, the diagnosis can be confirmed by a DNA test.

How is DiGeorge syndrome treated?

The low calcium levels in DiGeorge syndrome are treated the same as for simple hypoparathyroidism (see above), using calcium supplementation and either calcitriol (Rocaltrol®) or alfacalcidol (One-Alpha®).

Is DiGeorge syndrome hereditary?

In some cases, DiGeorge syndrome is familial (inherited from one parent), but in many cases, it happens by chance. If this is suspected, your child's doctor can refer your family to a Medical Geneticist for further evaluation and counselling.

Note: Since DiGeorge syndrome can include so many possible aspects, you may want to start a binder to collect the information. It is very hard to remember so many specialists and so much information.

Questions from families

Q: How do you give calcium to a baby?

A: There are many forms of calcium which may be used (see Appendix). Your doctor is planning to give your child a certain amount of elemental calcium per day.

Calcium may be in a pre-mixed solution. **NOTE THE INFORMATION ON THE CONTAINER AND SHAKE WELL IF INSTRUCTED.** This means shaking hard for 2–3 minutes while watching the clock. Otherwise, the calcium settles out, and you are giving your child less than the recommended dose.

Calcium may be in the form of antacid tablets such as Tums®. Cut the tablet to the required size, crush and dissolve in milk or formula.

Q: Can I change my child's calcium to a cheaper product?

A: Talk with your doctor and pharmacist before making a change. Each calcium product (see Appendix) has a different amount of elemental calcium. Some products have a low percentage of elemental calcium, and your child would have to take a large amount. Some products may have more side-effects, such as diarrhea.

The calcium that your child takes has to be given 4 times each day, before each meal and at bedtime, to provide the body with a steady supply of calcium. It cannot be taken all at one time.

Q: My baby seems very fussy after I give her calcium.

A: Some forms of calcium may be upsetting the stomach. Give the calcium as part of the feeding, not at the very beginning. It is also possible that your baby has a lax muscular connection between the esophagus (the food pipe) and the stomach, allowing the acid stomach contents to come up into the esophagus. This is called reflux. Your doctor may recommend a medication for this.

Q: Can I use non-prescription vitamin D instead of calcitriol (Rocaltrol®) or alfacalcidol (One-Alpha®)?

A: No! Vitamin D from the drugstore doesn't work in the body until it is turned into the activated form of vitamin D. Because of his or her medical condition, your child's body is not able to convert vitamin D into the activated form.

Q: My son is booked for a surgical procedure soon. I've been told he should have nothing to eat or drink before the surgery. Does this include the calcium and calcitriol (Rocaltrol®) or alfacalcidol (One-Alpha®)?

A: Speak with your endocrinologist about this— it can be dangerous to miss any doses. If

the calcium level drops too low, the surgery will be cancelled. Often the doctor recommends taking all doses of medication with just a tiny sip of water.

Q: What should I do if my child is vomiting and can't keep his medicine down?

A: *Since it can be dangerous to miss doses, you should speak to your endocrinologist about this.*

Q: I don't like giving my child medicine. Can I give her a special diet instead of the calcium and Rocaltrol® or One-Alpha®?

A: *Every day a child's body needs calcium—between 700 and 1300 milligrams a day. While it remains important to have a diet with lots of calcium (dairy products, fortified soy milk, and green vegetables), that unfortunately won't be enough for your child, because her body cannot absorb calcium normally. Much of calcium in the foods she eats is lost through the digestive system, and so she needs supplements as well. One of the activated forms of vitamin D, either calcitriol (Rocaltrol®) or alfacalcidol (One-Alpha®), is also needed in order for the calcium from the diet and from supplements to be absorbed by the digestive system.*

As you can see, the process of treating your growing child with a disorder of calcium or phosphorus involves taking medications regularly and checking blood and urine to be sure the amounts are right for her. At first, it will take a lot of care, but soon it will become part of your everyday life, and you will be able to enjoy your child for the unique child that he or she is.

Websites and support groups for disorders of calcium and phosphorus

The Hypoparathyroidism Association:

<http://www.hypoparathyroidism.org>

Endocrine Web: Hypoparathyroidism:

<http://www.endocrineweb.com/hypopara.html>

22qfamiliesbc (blog)

<http://22qfamiliesbc.blogspot.ca/>

22q11.2 Society

<http://www.22qsociety.org/>

The Dalglish Family 22q Clinic (for adults, Toronto)

<http://www.22q.ca/>

The 22q and You Center (Philadelphia):

<http://www.chop.edu/centers-programs/22q-and-you-center>

22q Central

<http://www.22qcentral.com>

Chromosome 22 Central: VCFS

<http://www.c22c.org/vcfs.htm>

International 22q11.2 Deletion Syndrome Foundation, Inc.:

<http://www.22q.org>

HealthLink BC: Food Sources of Calcium and Vitamin D:

<https://www.healthlinkbc.ca/healthlinkbc-files/sources-calcium-vitamin-d>

Medic Alert Canada:

<http://www.medicalert.ca>

More links are available from the

BC Children's Hospital Endocrinology & Diabetes Unit:

<http://endodiab.bcchildrens.ca>

Children with low blood calcium levels should wear a Medic Alert bracelet, to tell emergency personnel about potential calcium deficiency.

Appendix

Selected Canadian Calcium Products		Normal Levels of Common Lab Tests for a Child 6–12 Months of Age*	
Generic Name / Brand Name	Elemental Calcium	Test	Normal Range
Tums® Regular 500 mg	200 mg/tab	calcium*	1.87–2.50 mmol/L
Tums® Extra Strength 750 mg	300 mg/tab	ionized calcium*	1.10–1.30 mmol/L
Tums® Chewy Bites	300 mg/chew	phosphorus*	1.29–2.58 mmol/L
Tums® Ultra Strength 1000 mg	400 mg/tab	magnesium*	0.78–1.03 mmol/L
Tums® Chewies	470 mg/chew	intact PTH	1.0–5.5 pmol/L
Viactiv® Chews	500 mg/chew	alkaline phosphatase	110–320 U/L
BCCH Pharmacy suspension	80 mg/mL	25-hydroxy-vitamin D	25–110 nmol/L
Note: The regular Tums® tablet, for example, is called Tums® 500 mg. Since calcium carbonate is 40% elemental calcium, Tums® 500 mg actually only contains 200 mg of elemental calcium.		1,25-dihydroxy-vitamin D	40–190 nmol/L
		urinary calcium/creatinine ratio*	<1.69 mmol/mmol
		*Normal levels vary depending on the age of the child and the lab method used.	

Canadian Vitamin D Products		Canadian Phosphorus Products	
Generic Name	Trade Name and Dosages Available	Generic Name	Trade Name and Dosage Available
Cholecalciferol (vitamin D ₃)	Multivitamins: most contain 400 IU Supplements: usually 400 IU or 1000 IU <ul style="list-style-type: none"> Baby Ddrops®: 400 IU/drop Kids Ddrops®: 400 IU/drop Adult Ddrops®: 1000 IU/drop XS Ddrops®: 2500 IU/drop prescription: 10,000 and 50,000 IU tabs/caps 	Sodium phosphate monobasic	JAMP-Sodium Phosphate fizzy tablets: 500 mg or 16.1 mmol elemental phosphorus per tab
		Sodium phosphate monobasic, dibasic	Phoslax® oral solution, 45-mL bottle: 129 mg or 4.15 mmol elemental phosphorus per mL
Alfacalcidol (1-hydroxy-vitamin D)	One-Alpha®: <ul style="list-style-type: none"> 0.25-microgram capsules 1-microgram capsules 2 microgram/mL (0.1 microgram/drop) 	Potassium phosphate monobasic (Health Canada Special Access Programme)	K-Phos® Original 500-mg tabs: 114 mg or 3.68 mmol elemental phosphorus per tab
Calcitriol (1,25-dihydroxy-vitamin D)	Rocaltrol®: <ul style="list-style-type: none"> 0.25-microgram capsules 0.5-microgram capsules 	Potassium phosphate monobasic, dibasic	Potassium Phosphates Injection USP, 50-mL vial: 93 mg or 3.0 mmol elemental phosphorus per mL