Soft Bones
Finding the Key to HPP

Food for Thought: Dietary Guidelines for Patients with Hypophosphatasia (HPP)

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This guide is meant to help you think about how your food and beverage choices can influence your health. It should also help you and your doctors make common-sense dietary decisions specific to you. In addition to nutrition: exercise, sleep, and socializing have also been shown to be important to physical and mental health. See the resource section at the end for more information

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Overall Nutrition

Is there any nutritional advice that applies to everyone with hypophosphatasia (HPP)?

Yes, people with HPP should follow a healthy diet in general and then make changes with the help of their doctor. Your overall health will be determined by the same health factors that you share with everyone with or without hypophosphatasia.

Eating more vegetables, fruits, and whole grains as well as consuming less salt, saturated and trans fats, added sugars, alcohol, and soda are all important to improving health in everyone. There is a lot of science behind the rules for a healthy diet; suggestions for specific modifications for someone with hypophosphatasia are listed below.

Why should I trust the dietary recommendations from the USDA? It seems like they keep changing.

The recommendations are updated every 5 years. The recommendations "keep changing" because science is doing what science does best: always asking more questions, using information just learned from other areas of science, and testing new ideas with carefully controlled studies.

How are dietary recommendations created for the general population?

Some studies have collected daily food logs from thousands of people for decades and then compared their health outcomes; other studies have compared the current diets of healthy and unhealthy populations; other studies have tested the impact of restricted diets. This research is ongoing. Expect to see improvements with each update.

General Comments About a HPP Diagnosis

Does everyone with a low blood alkaline phosphatase level have HPP?

No, other conditions & medications can cause the alkaline phosphatase level to become lower than normal.

Does everyone with a mutation in the Tissue Nonspecific Alkaline Phosphatase gene (ALPL) have HPP?

No, one can have a mutation in the gene that causes HPP without having disease.
This is called being a carrier of HPP.

General Comments Regarding Supplements and Vitamins

Note: The law defines dietary supplements in part as products taken by mouth that contain a "dietary ingredient" including vitamins, minerals, amino acids, and herbs or botanicals...

It seems like many doctors discourage the use of supplements, why?

There are several reasons. Supplements and natural remedies can contain ingredients that are just as powerful as a "drug", but without having gone through the same level of testing and FDA review. They can have contaminants and/or not actually contain the ingredients listed. Also, supplements can make it harder for the doctor to evaluate and diagnose a patient with any rare disease, including HPP, because supplements might cause additional symptoms or change test results.

(See pages 10–12 for specific comments on vitamins B-6, B-12, C, and D.)

General comments regarding Supplements and Vitamins continues on page 4.

What about vitamins? Do doctors approve of supplemental vitamins?

In HPP there are concerns about taking certain vitamin and mineral supplements (see below). In general, however, doctors tend to be less worried about taking a multivitamin with no more than 100% of recommended daily allowance (RDA) for each vitamin. We know that too much of some nutrients cause disease. For example, excess vitamin A can cause a liver, bone, skin and brain disease. There are many other examples supporting a 'moderation in all things' approach to vitamins, but there is undoubtedly so much more to know.

When the amount of the vitamin in a supplement is greater than 100% RDA, the potential for concern depends on the vitamin and the patient. A vitamin or supplement is not a good substitute for eating a variety of healthy foods. Not only would one likely be missing important nutrients, but nutrients seem to be better absorbed from food instead of from a supplement or vitamins in a pill.

"Anti-inflammatory" and Other Diets

Should patients with HPP follow "anti-inflammatory" diets or spices that reportedly help cut down on inflammation?

There are more than 17,000 articles that show up in a search of scientific literature for "anti-inflammatory" and "diet". And although there are no studies to support any specific diet for HPP, it is worth noting that frequently these "anti-inflammatory" diet studies recommend increasing vegetables and fruits and following a **Mediterranean Diet**, which is a good diet for everyone. Regarding using spices, recognize that spices are another category that the FDA does not evaluate for cure, easing of symptoms, treatment, or prevention of disease.

Fluid Intake

My mom is always after me to drink more water. Is she right?

Your mom is encouraging you to stay hydrated (having enough fluids for normal body function). The amount of water needed can vary based on exercise, the weather, and other things, including, for women pregnancy and nursing. Thirst and drinking liquids at meals is typically enough for the average healthy individual. In infants and in old age, thirst may not be as strong and dehydration becomes a greater risk.

In HPP, staying hydrated can be especially important since dehydration can increase the concentration of minerals in the urine (which can already be elevated in HPP). Your doctor may want you to increase your fluid intake to dilute the excess minerals that may be in your urine. (**See pages 6–10**).

Precision Medicine (treatment tailored to you)

Why do I need to talk to my doctor about dietary recommendations for HPP?

Your doctor will take many factors into account to determine the treatment that is right for you. Your age, disease severity, current complaints, time since a change in treatment as well as current and past treatments, current laboratory results and other factors can each change the appropriate recommendations for the optimal intake of calories, minerals, Vitamin D, fluids, etc. And so, even for one individual, the recommendations can change over time.

What are some of the specific considerations for HPP?

Not all RDA recommendations are appropriate for patients with HPP. The RDA recommendations are a good starting place and, unless you tell your doctors otherwise, they will assume you are following a standard recommended diet (see above). However, people with HPP may benefit from tailored recommendations for **Calcium**, **Vitamin D**, **fluid**, and **sodium** (salt) intake. This will differ from patient to patient and change over time. Some people with HPP have too high or too low a level in the blood (and/or urine) of one or more of the items. If your levels are too high or too low, your doctor will likely want to first make sure you don't have another reason for this problem other than HPP, especially if the severity of your HPP does not match the severity of one of these lab values (there can be other causes for abnormalities in the levels of these items—including lab error).

HPP Specific Dietary Considerations

General Notes About Bones and HPP

- Bone is a live tissue whose job is not only to provide structure, support, and protection for the body, but also acts as a place where minerals such as calcium and phosphorus are stored and easily retrieved when needed.
- Calcium and phosphorus are the two major minerals in bone. The bone disease in HPP occurs from there being too much inorganic pyrophosphate (PPi), which blocks calcium and phosphorus from being deposited properly in bone.
- The minerals and many of hormones that control them can change moment to moment based on your recent food and drink intake.
    - Lab testing: It is wise to eat and drink your usual diet the day before testing. The blood tests are usually done first thing in the morning on an empty stomach. 'Spot urine' tests are also usually collected first thing in the morning on an empty stomach, but if you are requested to bring in a 24-hour urine instead, make sure you do so while on your usual diet; if you collected all of the urine in a 24-hour period, it should be more accurate than a spot urine.
- In this section, treated and untreated refers to whether or not the patient is taking enzyme replacement.
- Many of the comments refer only to patients who have a form of HPP other than odontoHPP.

Minerals (and the hormones that influence them)

General

- Calcium and phosphorus: In untreated patients with HPP and early in treatment there is not enough calcium or phosphorus in the skeleton. With enzyme replacement, the PPi levels decrease, allowing calcium and phosphorus to now enter the bones more easily.
- Mineral handling: blood levels of calcium and phosphorus (and sodium) are controlled by:
  - How much is excreted in the urine (if the body detects an increased need, hormones tell the body not to let as much out in the urine)
  - Absorption from the gut (if the body detects an increased need, hormones tell the gut to bring in more from your diet).
- Hormones: hormones are molecules that travel through the bloodstream to tell other parts of the body how to behave. The body makes many different types of hormones (not just sex hormones). Two of the hormones that influence the use of minerals include parathyroid hormone (PTH) and Vitamin D (which is actually a hormone). Vitamin D plays a role in the absorption and use of calcium and phosphorus. Parathyroid hormone (PTH) responds to and helps control these levels in the body, but PTH also plays a role in bone growth and overall bone health.

Calcium

If there is not enough calcium in the bones of patients with HPP, should they take more calcium in their diets?

This is a good question for your doctor. Most often, unless someone's diet has very little calcium in it, untreated patients with HPP do not need additional calcium and it might be harmful. Many patients with HPP have too much calcium in their urine and/or blood, even though they don't have enough calcium in their bones. When a person is given more calcium than his or her body can use, the body tries to get rid of it through the urine, when that doesn't work, the calcium goes up in the blood as well.

One of the risks of having too much calcium in the blood or urine is having it deposit in the wrong places such as in the kidney (nephrocalcinosis). Your doctor may want to measure your mineral levels in blood and urine as well as hormones that help control calcium and phosphate levels in the body. From looking at these levels, your doctor can give you up to date information regarding how or whether to modify your calcium intake. The amount of calcium that a person needs varies from one patient to another and can also change over time for the same individual. It may fluctuate with growth spurts, medication adjustments, or shifts in overall health.

Phosphorus

Unlike patients with other forms of rickets or osteomalacia, blood (serum) phosphorus levels are often above the normal range in patients with HPP. Also note: The normal range for blood phosphorus differs across childhood.

Should patients with HPP increase phosphorus intake because it is needed for bone mineralization?

Increasing one's phosphorus intake would not be expected to increase the amount of phosphorus going into the bones. The poor mineralization of the bones in HPP is from there being too much PPi, a mineral blocker, not a lack of phosphorus. In fact, phosphorus levels in the blood are generally above the normal range in patients with HPP.

But, unlike an occasional recommendation from a doctor to increase calcium intake (based on blood and urine results—see above) in a patient with HPP, a similar recommendation is even less likely for phosphorus not only because phosphorus does not become low in the blood in HPP but also because it is so plentiful in food and drinks. [Note: if a patient with HPP ever had a low blood phosphorus, one would need to carefully question whether there was a lab error, a wrong normal range or the wrong diagnosis.]

Should patients with HPP restrict phosphorus intake to try to bring their blood phosphorus back into the normal range?

Trying to lower a blood phosphorus to bring it back into the normal range by changing a healthy diet is unlikely to work in HPP and may not be safe. Phosphorus is in so many healthy foods that trying to limit it might jeopardize the intake of other nutrients that are known to be important to overall health. However, if you consume much more than the RDA for phosphorus (e.g., you drink dark colas or eat a lot of fast foods or processed meats), it would be logical to eliminate (or at least reduce) the amount of drinks or foods you consume that have phosphate added (check the ingredient labels).

What about taking a low phosphate diet and a phosphate binder to lower a high blood phosphorus level in HPP?

In HPP, some of the molecules that control the blood level of phosphorus are present at abnormal levels, so long-term attempts to lower the phosphorus intake would likely be unsuccessful even if one could safely decrease the phosphorus intake of a healthy diet. Taking a phosphate binder to lower the blood phosphorus level has been tried in HPP for a 3 day period of time, but would not be expected to be helpful in HPP.

Sodium

My doctor told me to decrease my salt intake, why?

There is too much salt in a typical Western diet. There are a number of reasons that a doctor might tell a patient to decrease salt intake. One of the most common is to decrease a high blood pressure. In patients with HPP, another reason is that a high urine sodium concentration can pull calcium out into the urine with it and lead to an increased concentration of calcium in the urine (which may increase the risk of calcium deposits). Your doctor might include a measurement of urine sodium in your urine studies to see if this is something you should be doing.

Zinc and Magnesium

Zinc (Zn) and Magnesium (Mg) have many functions in the body. Among their functions, they are both part of the structure of the alkaline phosphatase (ALP) protein and necessary to it working properly.

When I first saw the doctor for the diagnosis of HPP, he measured my blood levels of magnesium (Mg) and Zinc (Zn) but hasn't measured them since. Why?

It is unusual to have a deficiency of Mg or Zn (there is typically enough available from a normal diet), but since a deficiency in either Zn or Mg is associated with a low ALP activity, it is sometimes measured at a first visit to make sure that both were present in your blood in normal concentrations (and not the reason for your low ALP) or to understand the severity of your HPP.

If Zn and Mg are necessary for the function of ALP, wouldn't extra Zn and Mg be a good idea in HPP?

Since both Zn and Mg are cofactors for alkaline phosphatase it is important to have normal amounts of each. If your blood levels of Zn or Mg are low, reviewing your dietary record with a nutritionist might help identify why you are not getting enough of these minerals from diet alone. However, you do not want to take anything in excess (e.g., too much Zn can lead to stomach problems).

Protein and Calories

Protein/calorie malnutrition can cause a low ALP even for those without HPP.

My mom has adult HPP with fractures, and is heavy. My toddler has infantile HPP and is underweight. My toddler's doctor is trying to get our toddler to eat more protein to help him gain weight. He says it will help with his bone strength. Wouldn't more protein help my mother as well?

Your son being underweight is not surprising. Young children with infantile HPP may need a lot of calories. Eating a well-balanced, nutritious diet, enough to attain/maintain a normal weight for height, would be good for both your son and your mother. Your son needs to gain weight to achieve this; your mother needs to lose weight.

Both need to achieve this with a healthy, balanced diet. Being underweight or overweight at any age can lead to an increased risk of fractures, even in people without HPP, and may be harder on the skeletons of those with HPP. Being underweight as a child can also interfere with growth. As an aside, being overweight as a child with HPP might also increase the risk of knock-knee deformity or bowing.

Protein and Calories continues on page 10.

I have a friend whose son is short, has poor weight gain, a low ALP, and was recently diagnosed with gluten-sensitive enteropathy (celiac disease). They said he doesn't have an ALP mutation and have put him on a gluten-free diet. Should he be retested for HPP?

I can't tell you if he should be retested, but I can tell you that celiac disease (gluten-sensitive enteropathy) can interfere with the absorption of necessary nutrients. Anything that interferes with one's nutritional status might lead to a low ALP.

If a gluten-rich diet causes a low ALP in someone with celiac disease, would a gluten-free diet increase the ALP of people with HPP?

Gluten does not interfere with nutrition unless you have celiac disease. Any unnecessary change from a standard recommended diet may lead to difficulty maintaining a balanced diet (and is doing an uncontrolled experiment on yourself)

Vitamins

Vitamin D

As mentioned previously, Vitamin D is actually a hormone, not a vitamin. It has many effects including influencing calcium and phosphorus uptake by the gut and by the bone. Otherwise healthy children and adults can get rickets or osteomalacia (not enough mineral in their bones) by having too little Vitamin D.

If too little Vitamin D causes another form of rickets, shouldn't my child be given extra Vitamin D so that he/she doesn't have two forms of rickets?

Asking your doctor if your child's (or your) blood level of Vitamin D is in the normal range, is a good idea, for the reason you mentioned. Having a low level of Vitamin D is surprisingly common throughout the world. However, as with anything, too much of Vitamin D carries risks of its own, including being one of the causes of a low ALP in people without HPP.

Vitamin B-6 (PLP)

Vitamin B6 is elevated in virtually everyone with HPP.

So, if Vitamin B-6 is elevated, should we limit intake of Vitamin B6?

It may seem counterintuitive, but not only do you not need to restrict dietary intake of Vitamin B6, but it is also used to treat the seizures that occur in perinatal HPP. Vitamin B6 is metabolized by alkaline phosphatase (ALP). In perinatal HPP, with very limited ALP activity, Vitamin B6 can't be broken down to the molecules that can cross from the blood into the brain, so infants with B6-dependent HPP-related seizures are prescribed Vitamin B6, which helps decrease the difficulty with seizures.

Vitamin B-6 (PLP) *continued*

So, if Vitamin B6 is helpful for the most severe of patients with HPP, would others with HPP benefit from supplemental Vitamin B6?

This does not seem wise. A Vitamin B6 overdose can cause significant symptoms, Vitamin B6 levels are already elevated in the circulation of people with HPP and there is no evidence that this is needed in those patients without seizures.

Regarding the infants with perinatal HPP and seizures, if the reason for the seizures is inadequate ALP activity, can you stop the Vitamin B6 supplementation, after the enzyme is restored (with enzyme replacement therapy)?

This needs to be decided on a case-by-case basis with your doctor. There are patients in whom this has been successfully done, but it has not been well enough studied to make general recommendations about when and if Vitamin B6 supplementation can be stopped.

Vitamin C

Vitamin C deficiency causes scurvy (bleeding, tooth loss, and bone disease) and a low ALP.

If too little vitamin C causes another bone disease along with a low ALP, shouldn't I take extra Vitamin C to help my bones?

No, if you follow the general recommendations of a healthy diet for everyone, you should be getting enough Vitamin C. Too much Vitamin C can cause gut problems and high doses of Vitamin C have been associated with kidney stones in the general population.

I heard you only needed to worry about taking too much of the fat-soluble vitamins (Vitamin A, Vitamin D, Vitamin E, Vitamin K), because the extra gets stored in your fat and can get released later. If all the other vitamins leave your body in your urine why do I have to worry about taking too much Vitamin C or any of the other water-soluble vitamins?

See above. And moderation in all things.

Vitamin B12

Low Vitamin B12 can cause gut and neurologic symptoms and people who can't absorb vitamin B12 (those with pernicious anemia) can have a low blood level of ALP. Vitamin B12 is found in many meats and dairy products. As many as 3 out of 20 older adults can have a low or low normal Vitamin B12 blood level. If you an older individual, or follow a vegetarian diet, your doctor might order a vitamin B12 blood level.

Foods & Food Components to Limit




Dietary Guidelines Recommend Limiting Consumption of the Following

- **SALT.** Adults and children ages 14 years and over should limit sodium to less than 2,300 mg per day, and children younger than 14 years should consume even less. Use the Nutrition Facts label to check for sodium, especially in processed foods like pizza, pasta dishes, sauces, and soups.
- **SATURATED AND TRANS FATS.** Less than 10% of your daily calories should come from saturated fats. Foods that are high in saturated fat include butter, whole milk, meats that are not labeled as lean, and tropical oils such as coconut and palm oil. Saturated fats should be replaced with unsaturated fats, such as canola or olive oil.
- **ADDED SUGARS.** Less than 10% of your daily calories should come from added sugars. ChooseMyPlate.gov provides more information about added sugars, which are sugars and syrups that are added to foods or beverages when they are processed or prepared. This does not include naturally occurring sugars such as those consumed as part of milk and fruits.
- **If ALCOHOL is consumed**, it should be consumed in moderation—up to one drink per day for women and up to two drinks per day for men—and only by adults of legal drinking age.

Resources

The 144 page full **2015-2020 Dietary Guidelines** includes resources about exercise and nutrition and summaries of:

- Age-Sex Groups Based on Dietary Reference Intakes & Dietary Guidelines (appendix 7) and Daily Nutritional Goals (Table A7.1)
- Federal Resources for Information on Nutrition & Physical Activity (appendix 8)
- Calorie Needs per Day, by Age, Sex, & Physical Activity Level (appendix 2; table A2-1)
- Body Mass Index & Corresponding Body Weight Categories for Children & Adults (table A6-1)
- Food Sources of Potassium, Calcium, Vitamin D, Dietary Fiber (appendix 10-13) Ranked by Amounts of Potassium, Calcium, Vitamin D, Dietary fiber & Energy per Standard Food Portions & per 100 Grams of Foods (Table A10-1, A11-1, A12-1. A13-1)
- Examples of Vegetables in Each Vegetable Subgroup (table 2-1)
- Healthy Eating for three types of diets: U.S.-Style, Mediterranean-Style, or Vegetarian (appendix 3-5; tables 1.1-1.2); Recommended Amounts of Food From Each Food Group (for each of the three diet types) at 12 Calorie Levels (Tables A3-1, A4-1, A5-1))
- Alcohol (appendix 9) Alcoholic Drink-Equivalents of Select Beverages (Table A9-1)
- Hidden Components in Eating Patterns (figure 1-3)
- Cup- & Ounce-Equivalents (figure 1-1
- Executive Summary of the **2015-2020 Dietary Guidelines in English** and **Spanish**.
- Recommendations At-A-Glance in **English** and **Spanish**.
- Handouts on making healthy **shifts** and cutting down on added **sugars**.

References

U.S. Department of Agriculture and HHS. 2015-2020 Dietary Guidelines for Americans. January 2016. Available at: **http://health.gov/dietaryguidelines/2015/**.

For more information, please contact the Soft Bones Foundation
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