



What I tell my patients about the importance of calcium and phosphate

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Calcium and phosphate are two minerals found in abundance in the body, and they are both vital for the maintenance of good health. If blood levels of calcium and phosphate become either too high or too low, this can affect normal bodily functions.

Problems with calcium, phosphate, and a chemical messenger in the blood called parathyroid hormone (or PTH for short) can occur in people whose kidney function is 40% or less of normal. In many cases, these problems can start without the patient having any symptoms, and can slowly cause irreversible damage to the bones, the heart or the blood vessels over a period of years.

What is calcium?

Calcium is the most abundant mineral that is found in the human body. The average body contains approximately 1 kg of calcium in total, about 99% of which is stored in bone tissue. The remaining 1% of the body's calcium circulates in the blood and other body fluids.

Calcium plays an important role in the development and maintenance of bones and, together with phosphate, it provides the main strength within the bones. Calcium is also needed in the formation of teeth, and has an important role in other body functions; for example, calcium is carried around the body in the bloodstream, where it plays an important role in blood clotting. Calcium is also needed in the body to enable muscles to contract, for the transmission of nerve impulses, and to help the heart function properly.

The level of calcium in the blood must be kept very tightly controlled for the body to work normally. The normal total calcium level is 2.2–2.6 mmol/l (millimoles per litre), and if the level goes outside this range, it can have important consequences for health.

Very low calcium levels in the body can result in adverse effects such as muscle twitching and spasms, especially in the face and arms, whereas



A crystal of calcium phosphate. If their levels rise too high, calcium and phosphate can deposit in the blood vessels, requiring medical management

high calcium levels can cause agitation, gritty eyes and abdominal pain.

Calcium gets into the body from food, the major source of calcium being dairy products; for example, milk, cheese and yoghurt. Eggs, green leafy vegetables (for example, broccoli, spinach, kale), legumes, nuts, and whole grains also provide calcium, but in smaller amounts than dairy products (see Box 1).

Only about 10–30% of the calcium in food is absorbed into the body, and calcium must be broken down by the digestive system before the body can use it. Calcium is absorbed into the body in the small intestine, and your body needs several other nutrients for calcium to be absorbed and used properly, including magnesium, phosphorous, and especially vitamin D and vitamin K.

The amount of calcium absorbed also depends on the level of calcium already present in the bloodstream. One interesting fact is that the 'fizz' in fizzy drinks like champagne, lemonade and



cola inhibits the absorption of calcium and can take calcium out of the bones.

What is phosphate?

Phosphate (which is phosphorus bound together with oxygen) is the second most abundant mineral found in the body after calcium. Together with calcium, phosphate is needed to build and repair bones and teeth, and it is also used in many other ways by the body; for example, helping nerves to function, and making muscles contract. It also helps reduce muscle pain after exercise. It plays an essential role in how the body stores and uses energy. Phosphorus is needed for the growth, maintenance and repair of all tissues and cells, for the production of the genetic building blocks, DNA and RNA, and to help balance and use other vitamins and minerals, including vitamin D, iodine, magnesium and zinc.

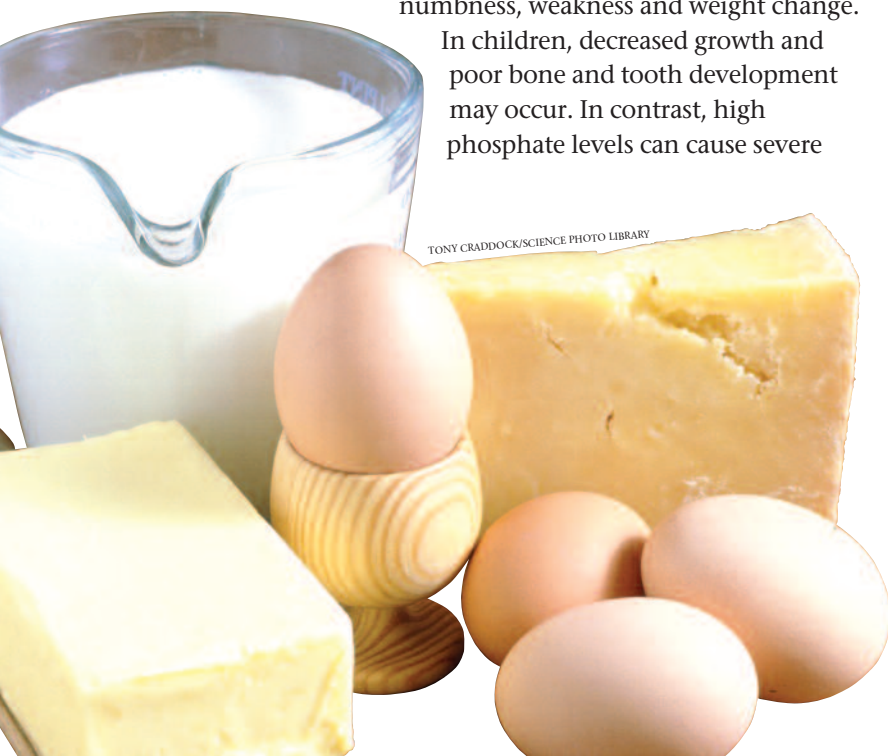
Phosphate enters the body from the diet, and protein-rich foods, such as meat, poultry, fish, eggs, dairy products, nuts and legumes, are good dietary sources of phosphate. Other sources include whole grains, potatoes, dried fruit, garlic cloves and carbonated drinks (see Box 1).

Approximately 85% of all the phosphate in the body is stored in bones, while the rest of it is stored in other tissues throughout the body. Your kidneys help to control the amount of phosphate in the blood. Any excess phosphate that the body does not require is filtered out of the blood by the kidneys and passes out of the body in the urine. The normal level of phosphate in the blood is 0.8–1.4 mmol/l.

Symptoms of phosphorus deficiency include loss of appetite, anxiety, bone pain, fragile bones, stiff joints, fatigue, irregular breathing, irritability, numbness, weakness and weight change.

In children, decreased growth and poor bone and tooth development may occur. In contrast, high phosphate levels can cause severe

High-protein foods, such as eggs and dairy products, are also high in phosphate



Box 1. Calcium and phosphorus in foods

Foods high in calcium

- Cheese, malt drinks, green vegetables, seaweed, tofu, fortified breakfast cereals, hot chocolate drinks, milk (especially condensed milk/evaporated milk/powdered milk), shrimps/prawns, sardines, eggs, yoghurt

Foods high in phosphorus

- Yoghurt, cheese, wheat (wheat bran, wheat germ, wholemeal bread), poultry, meat, fish and shellfish (eg prawns), eggs, mushrooms, malt drinks, nuts and seeds, tofu and other soya products

As taken from McCance and Widdowson's *The Composition of Foods*
(www.food.gov.uk/science/dietarysurveys/dietsurveys/)

Box 2. Ways of balancing calcium and phosphate in chronic kidney disease

- Dietary phosphate restriction
- Use of phosphate binders
- Vitamin D may be limited by hypercalcaemia
- Aim to maintain parathyroid hormone level up to 4 x normal
- Use of calcimimetics

generalised itching, and can lead to calcium phosphate (calcium bound together with phosphorus) being deposited in tissues around the body.

What happens to calcium and phosphate in chronic kidney disease?

As someone develops chronic kidney disease, the following sequence of events might occur:

1. The kidneys can no longer convert vitamin D to its active form, so the body can no longer absorb calcium from food in the gut, which means the level of calcium in the blood falls.
2. At the same time, because the kidneys are not working as efficiently as normal, they are unable to excrete excess phosphate into the urine. Thus the level of phosphate in the blood rises, which can cause intense itching all over the body.
3. The low levels of calcium in the blood cause PTH to be produced in large quantities. The PTH tries to restore the calcium level in the blood to normal by increasing the amount of calcium absorbed from food. However, it also takes calcium out of the bones, which in turn causes weakening of the bones, and renal bone disease, or, as it is now called, metabolic bone disorder of chronic kidney disease.



What is calciphylaxis?

Calciphylaxis is a medical term for the deposition of calcium and phosphate in parts of the body other than the bones. There can be a build-up of a kind of 'chalk' formed from calcium and phosphate in blood vessels, heart valves or other parts of the body. One of the reasons for achieving good control of phosphate levels is to avoid calciphylaxis. Calcium deposition in the blood vessels may occur rapidly in people on haemodialysis who have high phosphate levels.

Although the calcium is deposited in a manner that is different from the narrowing of the arteries that cause heart attacks, there can still be other serious problems with the arteries. One of these is to make it impossible to have a kidney transplant, since it is extremely difficult to attach a kidney graft to highly calcified blood vessels at the time of surgery, and maintain a good blood supply to the kidney.

What is the treatment for calcium, phosphate and PTH problems?

There are several types of treatment used to manage calcium, phosphate and PTH (see Box 2). No specific treatment is completely effective, but a combination of therapies can achieve good calcium and phosphate control. These include:

- Good-quality dialysis
- Vitamin D medication
- Medication to reduce phosphate absorption (phosphate binders)
- Medication to lower blood calcium levels (calcimimetics).

Dialysis

Good-quality dialysis means more effective removal of waste products from the blood. Unfortunately, phosphate is not removed from the body very efficiently by dialysis, so even good dialysis does not always remove enough phosphate. Therefore, it is always necessary to restrict phosphate levels in the diet, and it is usually necessary to take phosphate-binding drugs.

Vitamin D

Since vitamin D deficiency is one of the main causes of calcium and bone problems in people with kidney disease, vitamin D replacement therapy can be given.

This is not quite as simple as it might sound, because vitamin D needs to be converted to an active form, first in the skin by the effects of sunlight, and second in the kidneys. In severe kidney disease, the final conversion step does not

Quick reference glossary

- Calcimimetics – Drugs that mimic calcium in the body, leading to a reduction in calcium levels
- Calciphylaxis – This is where high levels of calcium and phosphate mean they build up and become deposited in the body; causing tissue and blood vessels to calcify
- Calcium – A mineral that is essential in the body for bone strength and is also important in many other systems, including blood clotting, muscles and the nervous system
- Chronic kidney disease – A condition where the kidneys no longer filter the blood as well as they should, which can lead to too much calcium and phosphate being retained in the body
- DNA/RNA – Deoxyribonucleic acid and ribonucleic acid; these carry the genetic information that is essential in the development and growth of cells
- Iodine – A chemical element that is needed in small amounts in the body for the production of certain hormones
- Magnesium – A chemical element that is needed for many functions of the body, including providing energy for cells
- Millimoles – A unit of measurement that describes the concentration of a substance within a liquid
- Parathyroid hormone – A hormone that regulates the amount of calcium and phosphate in the blood and helps to process vitamin D
- Phosphate – A mineral that, in the body, works with calcium for bone and tooth strength, and is also important in how the body uses energy
- Phosphate binders – Drugs that prevent the body from absorbing phosphate from food, reducing phosphate levels
- Vitamin D – A vitamin that regulates the concentration of calcium and phosphate in the blood
- Vitamin K – The name for a group of vitamins that are required for proper coagulation (clotting) of the blood
- Zinc – A chemical element that is necessary in the body and is found in many enzymes, as well as the eye and brain

happen, so a special form of vitamin D, which has already undergone this activation process, has to be given.

The vitamin D most commonly used is called alfacalcidol (available unbranded and as One-Alpha[®], LEO, UK), although others, such as calcitriol (unbranded; Rocaltrol[®], Roche, UK; and Calcijex[®], Abbott, UK) and paricalcitol (Zemplar[®], Abbott, UK), are also available. An unwanted side-effect of alfacalcidol is that the level of calcium in the blood can go too high, so regular blood tests are necessary to monitor the blood calcium and PTH levels.

Phosphate binders

Phosphate binders are a group of medicines that 'trap' the phosphate consumed in food and prevent the body from absorbing it. They only



work effectively in combination with a controlled diet, and the dose that you will need to take will vary according to the phosphate level in your blood.

There are several types of phosphate binder available. Your doctor, dietitian and pharmacist will help to decide which one is best for you to take depending on blood results and how easy you find it to take your tablets. Alu-Cap® (3M, UK) (aluminium hydroxide) is a phosphate binder that contains aluminium. It is very effective at binding phosphate, but if taken over a long period of time, aluminium can build up in the body, which can potentially cause memory problems. Your doctor will measure your aluminium levels if you take Alu-Cap.

Calcichew-D3®, CalciheW-D3® Forte (both Shire, UK) and Adcal-D3® (ProStrakan, UK) (calcium carbonate) are phosphate binders that contain calcium; Phosex® (Vitaline, UK) (calcium acetate) contains calcium in another form.

Renagel® (Genzyme, UK) (sevelamer hydrochloride) is a phosphate binder that does not contain either calcium or aluminium. Fosrenol® (Shire, UK) (lanthanum carbonate), too, is an alternative phosphate binder – it does not contain calcium or aluminium.

Phosphate binders should be taken with meals or snacks that include meat, fish, eggs, cheese, milk or pulses. They need not be taken with meals or snacks that do not include protein foods, such as toast, jam or salad sandwiches, biscuits or fruit. The most common side-effects with these medications are constipation or diarrhoea, feeling sick and a chalky taste in the mouth.

Key points

- Calcium and phosphate are the two most abundant minerals in the body and are both important for the maintenance of good health.
- In chronic kidney disease, the levels of calcium and phosphate in the body can be disturbed.
- Calcium and phosphate can be controlled in various ways, including good-quality dialysis, vitamin D medication, phosphate binders (to reduce phosphate absorption) and calcimimetics (to lower blood calcium).

Box 3. Information on calcimimetics

- Phosphorus, vitamin D, and calcium all regulate production of parathyroid hormone by the parathyroid glands in the neck
- The level of calcium in the blood is a key regulator of parathyroid hormone, acting through a calcium-sensing receptor (CasR)
- Calcimimetic agents are a new class of small molecules that mimic the action of calcium on the CasR and thereby reduce parathyroid hormone secretion

Calcimimetics

A class of drug known as ‘calcimimetics’ has recently been developed; calcimimetics mimic the action of calcium, and may be useful in people on dialysis with severe PTH problems (see Box 3).

The first drug in this class to become available in the UK is called cinacalcet (Mimpara®, Amgen, UK). This drug makes the body ‘think’ that there is more calcium in the blood than there actually is. This in turn reduces the production of excessive PTH, and as a result, the blood calcium and phosphate levels fall.

A reduction in the blood calcium level can also allow a higher dose of calcium-containing phosphate binders to be used to control the blood phosphate level, without at the same time causing a high blood calcium level.

Although cinacalcet can potentially cause mild-to-moderate nausea and sickness, it is generally easy to take.

What is the conclusion?

We have seen that calcium and phosphate are two very important minerals necessary for good health, and that their regulation by the body becomes very disturbed in people with chronic kidney disease, leading to the development of bone disease and tissue calcification.

Regular blood tests can be used to identify problems, and preventive treatment with the medicines described will help to reduce the chances of irreversible damage to bones and soft tissues occurring.

Understanding your treatment, and discussing your diet and medicines with your doctor, pharmacist and dietitian are the keys to you managing these complex problems successfully ■



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