



Sitosterolaemia

What is sitosterolaemia?

"Sterol" is a general term for a group of naturally occurring waxy solids. Sitosterols and cholesterol are both sterols, but they have slightly different structures. Unlike cholesterol, our bodies do not make sitosterols; they only come from plants.

Sitosterols are often referred to as plant sterols or phytosterols. Sitosterolaemia may also be called phytosterolaemia.

Sitosterolaemia is a very rare condition. The exact number of people with sitosterolaemia is unknown. Although less than 100 cases have been reported worldwide it is likely that many cases remain undiagnosed.

What causes it?

Sitosterolaemia is caused by a gene alteration in either the ABCG5 gene or the ABCG8 gene. Inheriting one copy of the altered gene is not enough to cause the condition but inheriting two altered genes, one from each parent, results in the condition. This pattern of inheritance is called autosomal recessive.

Inheriting two copies of the identical gene alteration is referred to as homozygous sitosterolaemia. Inheriting different alterations, in either the same or different genes, is referred to as compound heterozygous sitosterolaemia. Both the homozygous and the compound heterozygous form lead to very high concentrations of sitosterols in the blood and a build-up of sterols in the tissues.

How do sitosterols get into our bodies?

When you eat foods that contain sitosterols they are absorbed by our intestine. Two of our genes (ABCG5 and ABCG8) are responsible for the production of a transporter protein which is involved in sterol transport. These transporters sit in the cells that line the intestines and pump any sterols that are absorbed back into the intestine; just like a taxi service. As a second protective mechanism the liver also excretes sterols back into the intestines in bile, which is needed for digestion.

In sitosterolaemia these mechanisms are not working properly. This means that too much sitosterol is absorbed from our food and builds up in tissues and the blood. Cholesterol levels may also be increased but not markedly.

How are people with sitosterolaemia affected?

The effects of having sitosterolaemia are very similar to having high cholesterol levels and may start from early childhood. Excess sitosterols are deposited in the soft tissues of the body, particularly the tendons. Some of these deposits may be visible, for example as a white ring around the iris (the coloured part of the eye), in the skin around the eyes, on the finger like tendons on the backs of the hands and feet, the tendons at the back of the ankle and the elbow and knee joints. These deposits are called xanthomas and are similar to those caused by raised cholesterol. But not everyone with sitosterolaemia or high cholesterol will have these. Some people with sitosterolaemia may develop early atherosclerosis (the furring up of the arteries) which can cause early cardiovascular disease.

In some people with sitosterolaemia there may also be a problem with the production of healthy blood cells. This can result in too few functioning red blood cells or platelets.

Red blood cells carry oxygen around the body. Too few red blood cells can result in a condition called anaemia. Typical symptoms in people with anaemia are tiredness, shortness of breath, an increased heart rate and a pale appearance to the skin.

Platelets are involved in normal clotting mechanisms. Abnormal platelets can result in prolonged clotting times; for example, after a minor injury or cut there could be excessive bruising and/or bleeding.

How is sitosterolaemia diagnosed?

Diagnosis is not simple but should be suspected in people who respond poorly to statins but better than expected to other types of treatments such as ezetimibe and bile acid sequestrants.

The diagnosis of sitosterolaemia is usually made by measuring the amount of sitosterols in the blood. Normally blood levels of sitosterols are 100 times lower than those of cholesterol. But in untreated people with sitosterolaemia the amount of sitosterols in the blood and tissues is very high, typically 50-200 times what is considered normal.

In children with sitosterolaemia this increase in the plasma concentration of sitosterol does not happen until the child starts a

mixed diet including fruits, vegetables and cereal foods, all of which contain sitosterols. So diagnosis of sitosterolemia is difficult when the child is only breast or formula feeding or in the initial stages of weaning. Testing should be delayed until the child is routinely eating foods that contain sitosterols.

Are there other people who might be affected by high levels of sitosterols?

People with only one of the altered genes that causes sitosterolaemia may occasionally have mildly elevated plasma concentrations of sitosterol or a higher sitosterol to cholesterol ratio.

Patients with liver disease (especially with cholestasis or obstruction of the bile ducts) or who are on intravenous (parenteral) nutrition which contains sitosterols may have elevated concentrations of sitosterol but the sitosterol to cholesterol ratio is usually normal.

Genetic testing, with sequencing of the ABCG5 and ABCG8 genes is recommended when test results are atypical or the diagnosis is uncertain.

How is sitosterolaemia treated?

Sitosterolaemia is treated by a combination of medicines and by avoiding certain foods.

Ezetimibe, a sterol absorption inhibitor medicine, is often used because it works in the intestines to help prevent the absorption of both sitosterols and cholesterol into the body.

The liver can also be helped to get rid of more sitosterol. This is done using a medicine that reduces the re-absorption of the sitosterol rich bile salts that the liver excretes. These medicines are called bile acid sequestrants.

Statins, which reduce the amount of cholesterol made by the liver, have no effect on sitosterols but they can lower cholesterol levels if raised.

A healthy diet, low in sitosterols and cholesterol, is recommended to help minimise their absorption into the body.

Tell me more about sitosterols and food

Sitosterols that present in food are usually referred to as plant sterols or phytosterols. They are well known for their cholesterol-lowering effects and are often added to foods to produce special cholesterol-lowering spreads, yogurt drinks and other cholesterol-lowering products.

Normally only a very small amount (< 5%) of the plant sterols that we eat get into our body; but in sitosterolaemia this could be much higher - as high as 15-60%. This is because the transporter proteins (or taxis) that normally remove them are not working.

It is possible that people who have sitosterolaemia, but have not been diagnosed, will take large quantities of plant sterols with a view to lowering their blood cholesterol without knowing that plant sterols are "toxic" for them. Foods fortified with plant stanols are not normally a concern.

Which foods contain plant sterols?

Plant sterols are found naturally in a wide range of plant foods such as vegetable oils, nuts, seeds, whole grains, wheat germ, avocado,

chocolate, vegetable spreads, shellfish, seaweed, fruits and vegetables. Most diets provide around 0.3g of plant sterols per day but vegetarian diets may contain twice as much as this.

People diagnosed with sitosterolaemia should have regular checks with a doctor who is an expert in managing blood fat conditions. These doctors are usually called lipidologists, endocrinologists or clinical biochemists. Dietary advice ideally given by a dietitian, is important to help reduce the amount of plant sterols that are eaten. The dietitian will also help ensure they are able to have a healthy balanced diet overall; this is particularly important in children because of their rapid growth and development.

Foods with the amount of plant sterols they typically contain:

Plant sterol fortified foods Spreads, yogurts, mini yogurt drinks etc.	A single portion may provide between 0.5g and 2g of plant sterol.
Vegetable oils (per 30ml – 2 tablespoons)	
Corn oil	215-286 mg
Rapeseed oil	75-219 mg
Soyabean oil	66-98 mg
Olive oil	43-45 mg
Palm oil	15-18 mg
Other foods	
Peanuts (100g)	119 mg
Wholemeal bread ((3 slices)	86 mg
Broccoli (100g)	39 mg
Orange (1 small)	24 mg
Carrot (100g)	16 mg
Apple (1 small)	13 mg
Tomato (100g)	5 mg

What are the main sources of dietary cholesterol?

Cholesterol is an "animal sterol" so it is found in animal foods.

Rich sources include:

- Organ meats - liver, kidney, sweetbread and other offal, pate
- Egg yolk
- Some shellfish – prawns, crabs, lobster, squid, octopus and cuttlefish
- Full fat dairy foods including butter
- Fish roe/caviar

Moderate sources include

- Red meat
- White meats
- Fish – both white and oily
- Lard
- Processed meats

Low cholesterol sources (also low in plant sterols)

- Low fat dairy foods
- Egg white
- Refined carbohydrates – white rice, white bread, pasta