Congenital sideroblastic anaemia (CSA): information for patients and parents

What is inherited sideroblastic anaemia?

Sideroblastic anaemia is a group of rare inherited conditions in which the bone marrow cannot use iron properly to make haemoglobin – the protein inside red blood cells that carries oxygen around the body.

The iron itself is not the problem. You absorb it normally, and there is usually plenty of it. The problem is that the developing red blood cell cannot put the iron to work. So the iron arrives, finds the production line broken, and simply stays there – building up inside the cell in a ring around the centre.

Under the microscope these are called ring sideroblasts, and they are what gives the condition its name.

Sideroblastic anaemia is not iron deficiency. It is almost the opposite: there is too much iron in the wrong place, and the red blood cells cannot use it. This is why iron tablets do not help and in fact contribute to the harm.

What causes sideroblastic anaemia?

Several different genes can be involved, and which one matters more than you might expect – it changes the treatment and the outlook considerably.

ALAS2 is the commonest. This gene makes the enzyme that starts the haem-making process. It sits on the X chromosome, so this form is called X-linked sideroblastic anaemia (XLSA). It usually affects boys and men, but it can genuinely affect women too – if that applies to you, please see our separate leaflet on ALAS2 mutations in women, because the picture in women is different and often missed.

SLC25A38 is the second commonest. This gene makes a transporter that carries a building block into the part of the cell where haem is made. It is inherited in an autosomal recessive pattern, meaning both parents must pass on a changed copy.

Other genes – including GLRX5, HSPA9 and others – account for a smaller number of cases.

There are also syndromic forms, where the anaemia comes alongside problems in other par of the body – muscles, the pancreas, the nervous system, or hearing. These are caused by different genes again, and they are managed by more than just a haematology team.

Why does the gene matter so much?

This is the part that is worth understanding properly, because it is not obvious.

The two commonest forms – ALAS2 and SLC25A38 – look almost identical under the microscope. Same small pale red cells, same ring sideroblasts, same anaemia on the blood count. A doctor looking only at the blood film often cannot tell them apart.

But they lead to very different lives.

XLSA (ALAS2) is usually milder. Most people respond well to vitamin B6, and many never need transfusions at all. SLC25A38 anaemia is severe, does not respond to vitamin B6, and usually needs regular transfusions from infancy – a course much more like thalassaemia major (also called TDT, transfusion dependent thalassaemia). Genetic testing is what tells these apart, and it changes everything about the treatment.

If you or your child has been diagnosed with sideroblastic anaemia but nobody has said which gene is involved, that is a reasonable and important thing to ask.

What are the symptoms?

The anaemia itself can range from very mild to severe enough to need regular transfusions.

Anaemia causes tiredness, weakness and a lack of energy, breathlessness on exertion, dizziness, headaches, and difficulty concentrating. Skin may look pale, and for people with darker skin this is often seen best inside the mouth, on the lips or the tongue. In children, severe anaemia can slow growth and development.

Iron overload is the other half of the picture, and it deserves its own explanation.

Why does iron build up, even without transfusions?

This surprises almost everyone, and it is one of the most important things in this leaflet. Your body senses that there are not enough red blood cells and responds sensibly – for the wrong problem. It cannot tell that the difficulty is a broken production line rather than a shortage of raw materials, so it turns up iron absorption from food.

The result is that iron keeps arriving, keeps not being used, and keeps accumulating. You can be anaemic and iron-overloaded at the same time. They are not opposites.

If you are also receiving transfusions, iron arrives that way too, and the build-up is faster.

Iron overload causes no symptoms for years. By the time it does, damage may already have been done to the liver, heart or hormone glands. This is why it is monitored with blood tests and scans long before you would notice anything, and why treatment may be recommended while you feel perfectly well. See our leaflets on iron overload for more.

How is it diagnosed?

A full blood count shows anaemia, usually with small, pale red blood cells – though in women with ALAS2 mutations the cells may be normal-sized, large, or a mixture.

Iron studies typically show iron is plentiful rather than lacking. This is often the first real clue, and the point at which someone realises this is not iron deficiency.

Some people have a test called a bone marrow biopsy, and this is taking a sample of the blood factory to look at it under the microscope. A special test looks for ring sideroblasts using a stain that turns iron blue. **However, many people do not need a bone marrow biopsy done if the genetic test has been checked first- please speak to your medical team if you do not think you have had genetic testing yet and you are being told you need a bone marrow biopsy.**

Genetic testing identifies the specific gene, and as described above, this is what determines the treatment. It may be done as a panel testing several genes at once. This is called the R92 panel and your haematologist should know how to order it.

Your team may also review your family history and offer testing to relatives.

What is the treatment?

Pyridoxine (vitamin B6) The ALAS2 enzyme needs a helper molecule made from vitamin B6 to work. In many people with ALAS2 mutations, flooding the system with extra B6 partly overcomes the fault – and the response can be excellent, sometimes correcting the anaemia almost completely.

It is well worth trying if your form might respond. If it works, a response usually shows within a few weeks, and treatment continues lifelong because the anaemia returns if it stops. Your team will use the lowest dose that keeps you well: high doses over long periods can damage nerves, causing numbness and unsteadiness, so this is not a vitamin to take more of than advised or to buy over the counter and self-manage.

Pyridoxine does not work in SLC25A38 anaemia, and generally does not help in the other forms. A trial may still be offered, because occasionally there is a partial response.

Blood transfusions For SLC25A38 anaemia and other severe forms, regular transfusions are usually needed from early childhood. Others may need them only occasionally – during an illness, around surgery, or through a pregnancy.

Treating iron overload This is a central part of care, not an afterthought.

If you are not too anaemic, iron may be removed by **venesection** – taking off a unit of blood, exactly like donating. This is simple, effective, and is often the approach in pyridoxine-responsive XLSA once the haemoglobin allows it.

If you are too anaemic for venesection, or you are being transfused, **iron chelation** medicines are used instead. These bind iron and remove it from the body.

Stem cell transplant (bone marrow transplant) is the only treatment that can cure severe sideroblastic anaemia, and it is considered mainly for children with transfusion-dependent disease such as SLC25A38. It is a major undertaking with real risks, and the timing matters – outcomes are better when it is done before years of iron overload have accumulated. If this is raised with you, ask for a proper discussion of the risks and benefits in your own situation. It is not a decision to rush, but it is also not one to postpone indefinitely without a reason.

Folic acid is usually recommended, as the bone marrow is working hard.

Why iron tablets are the wrong treatment

If your anaemia is caused by inherited sideroblastic anaemia, iron tablets will not help – and taking them adds to a load your body cannot get rid of. Do not take iron supplements, or multivitamins containing iron, unless your haematologist has specifically told you to.

This matters more than it sounds. Anaemia usually does mean iron deficiency, so a doctor who does not know your diagnosis will reasonably reach for iron. Check the labels of over-the-counter supplements, as iron appears in many products that are not obviously iron tablets. If another doctor prescribes you iron, check back with your haematology team before starting.

What does it mean for my family?

This depends on which gene is involved, so the answer needs to come from your own genetic results rather than a leaflet.

ALAS2 (X-linked): sons of a woman carrying the mutation have a 1 in 2 chance of inheriting it and would usually be affected.

Daughters have a 1 in 2 chance of inheriting it, and whether they are affected is much harder to predict – some are entirely well, some are significantly anaemic. See our leaflet on ALAS2 mutations in women.

SLC25A38 (autosomal recessive): both parents carry one changed copy and are themselves well. Each pregnancy carries a 1 in 4 chance of an affected child. Brothers and sisters of an affected child have a 1 in 2 chance of being carriers.

A referral to a genetic counsellor is worth asking for. Once a mutation is identified in one person, relatives can be tested – and in a condition that is this easily mistaken for something else, that can end years of unexplained anaemia for a family member. Our leaflet on preimplantation genetic diagnosis (PGD) covers options for people planning a pregnancy.

What can I do to help myself or my child?

Ask which gene is involved, if you do not already know. It shapes everything else.

Keep up with iron monitoring, including scans, even when you feel well. This is the part that is easiest to let slide and hardest to undo.

Be careful with alcohol, which interferes with the same haem-making pathway and adds to liver strain.

Ask your team before taking vitamin C supplements, as vitamin C affects how iron is handled. Fruit and vegetables in a normal diet are fine.

Ask whether your care should involve a specialist centre for inherited anaemias. These conditions are rare enough that few doctors see many of them.

If your child has this condition, tell their school – both about the tiredness and about the appointments. Children who need regular transfusions miss a lot of school in ways that are easy to underestimate.

Having sideroblastic anaemia does not mean giving up on living a full and active life.

When to seek medical advice

Contact your team if you notice:

- Worsening tiredness or breathlessness
- Numbness, tingling or unsteadiness on your feet, if you are taking pyridoxine
- Joint pain, abdominal pain, palpitations, or increased thirst
- In children: slowing growth, or delayed puberty
- That you are pregnant or planning a pregnancy
- That another doctor has prescribed you iron

Can we help?

CAN (Congenital Anaemia Network) is a charity specifically for patients with inherited anaemias. It was started by a group of patients and doctors, working together to tackle some of the problems of having an inherited anaemia – the lack of information and the loneliness of not knowing anyone else with your condition. We run events for patients to meet each other, as well as provide some additional information, support and services for patients who need that extra bit of help.

If you want to know more visit www.togetherwecan.uk or email us: info@togetherwecan.uk

Do you know your care should involve a specialist centre for inherited anaemias? These conditions are rare enough that few doctors see many of them and all patients with rare inherited anaemias should be under the care of a haemoglobinopathy specialist. Please read our 'How red cell services are organised in England' information sheet. If you don't know who your specialist service should be, please get in touch with us so we can help you find out.