

SHOX Deficiency

Child Growth Foundation

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ABOUT US

The Child Growth Foundation (CGF) is a UK charity, focused on the support, understanding and management of rare growth conditions and concerns.



We work to improve the lives of everyone affected by a growth condition. We support children, young people, adults and their families – whether or not they have a diagnosis.

About this booklet

This booklet is for anyone wanting to know more about SHOX deficiency. Including what it is, and how it is diagnosed and treated.

WHAT IS SHOX DEFICIENCY?

SHOX is a gene (short stature homeobox-containing gene), which plays an important role in bone growth and development. SHOX deficiency resulting from SHOX gene abnormalities causes poor growth in humans, usually in the first few years of life.

SHOX deficiency is now recognised as one of the commonest genetic causes of short stature. Studies suggest that up to 1 in 1,000 children with short stature may have a problem with the SHOX gene, and that SHOX changes may be present in around 2–15% of children who have short stature with no clear cause (idiopathic short stature). However, the exact numbers are uncertain and can vary between different populations.

The SHOX genes are located on the sex chromosomes (the X and Y chromosomes) in humans. SHOX deficiency is more common in females. Changes (mutations) or loss (deletions) of one of the SHOX genes causes growth failure. Changes in the SHOX gene can also cause a type of skeletal dysplasia called Leri-Weill dyschondrosteosis. This a rare genetic condition which results in short stature and shortening of the bones of the arms and legs. The loss of both SHOX genes (complete lack of SHOX), is very rare and causes a very severe skeletal abnormality known as Langer syndrome. This results in extreme short stature and very short, underdeveloped bones.

In contrast, extra copies of SHOX due to abnormal numbers or structure of the sex chromosomes may cause tall stature.



FEATURES OF SHOX DEFICIENCY

The features of SHOX deficiency can vary from person to person but include:

- Short stature
- "Mesomelic" shortening or shortening of the middle parts of limbs (forearms or calves)
- Wrist and forearm changes such as Madelung deformity (curving of the radius, prominent ulna at the wrist, and restricted movement)
- Milder skeletal features - a high-arched palate (roof of the mouth), short fourth and fifth fingers or toes (short metacarpals/metatarsals), increased "carrying angle" at the elbow (the forearm angles out slightly), bowing of the forearms, knock knees, and muscular calves
- Heart or kidney problems or delayed/absent puberty, especially girls with Turner syndrome

HOW IS IT DIAGNOSED?

Genetic testing usually looks for small missing or extra pieces of DNA (deletions or duplications) around the SHOX gene as well as spelling changes (variants) within the gene. In some children, the SHOX gene itself can be normal but changes are found in nearby "regulatory" regions that control how the gene works. A blood sample will be taken to do the genetic testing.

GENETICS

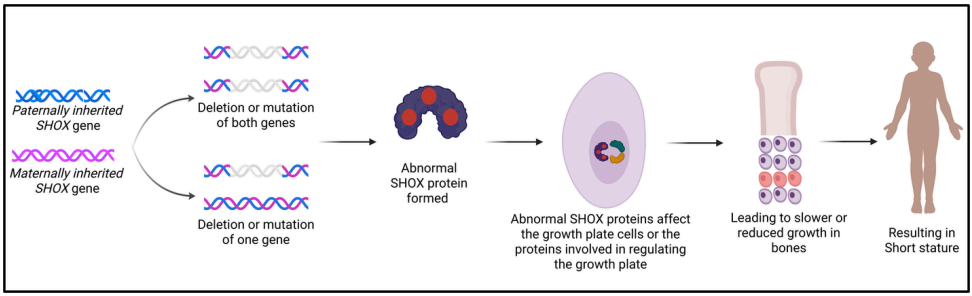


Figure 1. How changes in the SHOX gene affects childhood growth:

A single copy of the SHOX gene is inherited from the mother and the father. Changes in one or both the SHOX genes (mutations or loss) can lead to growth failure. SHOX proteins act directly on the growth plate cells (chondrocytes) or the regulatory network of genes affecting the growth plate (chondrogenesis pathway).

TREATMENT

In the UK, SHOX deficiency is a licenced indication for synthetic growth hormone (GH), a man-made form of GH. GH is given by daily injections just under the skin (subcutaneous) and has been shown to improve the final height of SHOX deficient patients.

SHOX patients are usually prescribed a similar GH dose to that given to patients with Turner syndrome and the effects of treatment are thought to be equivalent.

To fulfil the criteria for GH treatment in the UK, children must have SHOX deficiency confirmed by DNA (genetic) analysis.

FURTHER INFORMATION

Facebook groups

The CGF maintains and oversees a number of closed Facebook groups covering the conditions we support. These offer peer support, which can be vital in helping those living with rare conditions.

SHOX deficiency Facebook group:
facebook.com/groups/shox or scan the black QR code.

More information about SHOX or growth hormone therapy can be found on the following websites:

https://childgrowthfoundation.org/conditions/shox/

NHS England: https://www.genomicseducation.hee.nhs.uk/genotes/knowledge-hub/shox-related-haploinsufficiency/

British Society for Paediatric Endocrinology and Diabetes (BSPED): Under growth hormone - https://www.bsped.org.uk/clinical-resources/patient-information/

NICE Guidance on Growth Hormone: https://www.nice.org.uk/guidance/ta188

GLOSSARY OF TERMS

We hope you have found this booklet easy to understand and that the medical terminology has been explained simply within each section. Below are further explanations of some of the terms used. However, if you have any questions or would like to speak to someone about the content of this booklet, please don't hesitate to get in contact with the CGF (details on page 9).

Chondrocytes - Chondrocytes are the cells that build and maintain cartilage in the body.

Chondrogenesis pathway - Chondrogenesis is the process by which cartilage is formed from stem cells. In growing bones, cartilage eventually becomes bone.

DNA - short for deoxyribonucleic acid, is the molecule that contains the genetic code of all living organisms.

Genes - a gene is a segment of DNA that contains the instructions for making a specific protein or trait.

Gene mutation - an alteration in the genetic code found in DNA (The molecule that encodes genetic information) that changes the specific instructions of the gene.

Gene deletion - loss of genetic material from the genome (a genome is a complete set of genetic material) is known as a deletion.

Gene duplication - Where a section of the genome has been copied.

Idiopathic - means cause unknown.

Mesomelic - means the middle parts of the limbs are shortened.

Radius -the radius is one of the two bones in your forearm — it's the one on the thumb side.

Skeletal dysplasia - means a group of a conditions where bones don't grow in the usual way, especially the bones in the arms, legs, and spine.

Subcutaneous - describes something that is just below the skin.

Ulna - is one of the two bones in your forearm — it's the one on the little-finger side.

GET IN TOUCH

If you have any questions regarding the information contained in this booklet, or any other queries, please get in touch with our friendly team.

How to contact our nurse led Support Line:

-Call our dedicated Support Line number: 020 8995 0257
-Complete our Support Line online contact form: childgrowthfoundation.org/supportline
-Email us at: support@childgrowthfoundation.org
-Book a slot at: childgrowthfoundation.org/bookings
-Scan the QR code, below:

Our charity supports hundreds of children, young people, adults and families each year through our in-person and virtual events, and we help thousands of people in the UK and beyond with our online information, guidance and support.

We provide peer support including our Virtual Cuppa & Chats run by our nurses and involving parents and carers, alongside closed Facebook groups, and also opportunities to meet other families in the child growth community through our in person Meet Ups and convention - and much more! See our full range of support at: childgrowthfoundation.org

By contacting the Child Growth Foundation Support Line, you are providing consent for us to collect, process and store your data to provide you with the information or services you are contacting us about, in line with our Support Line Privacy Statement childgrowthfoundation.org/supportlineprivacy and our charity's Privacy Policy at: childgrowthfoundation.org/privacy

GET INVOLVED

The CGF is an independent charity that depends entirely on your support to continue it's work. If this resource has helped you, we'd be grateful if you'd please consider becoming a member or making a donation via the QR codes below.

Make a donation

Become a member

Fundraise



Volunteer



Help us continue making a difference wherever growth is a concern. Find out more on how to get involved at: childgrowthfoundation.org/get-involved

FURTHER INFORMATION

Acknowledgements

With thanks to:

- Professor Helen Storr and Dr Uttara Kurup

Disclaimer

We have taken every care to ensure the accuracy of the information contained in this booklet. The information enclosed should not be used as a substitute for the advice from a clinician, GP or other healthcare professional.

Feedback

Your feedback helps us to ensure we are delivering information to the highest standard. If you have any comments or suggestions, please contact us at info@childgrowthfoundation.org or on 020 8798 2139.

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