

# Primary IGF-1 Deficiency (PIGFD)

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## WHAT IS PIGFD

Children with short stature may have low levels of the hormones associated with normal growth. Children with low levels of growth hormone (GH) are said to have growth hormone deficiency (GHD) and this results in growth failure (see the Growth Hormone Deficiency & MPHD page). GHD leads to low levels of insulin-like growth factor-1 (IGF-1), a hormone made primarily in the liver. IGF-1 regulates the growth-promoting effects of GH by acting on 'target' body tissues such as the growth plates of the bones.

Some children have growth failure, despite normal or even high levels of GH. In some of these children we find abnormally low levels of IGF-1 and this condition is called Primary Insulin-like Growth Factor Deficiency (PIGFD). Here the term 'primary' means that no secondary cause of low IGF-1 levels (e.g. a chronic medical illness) can be identified.

Severe primary IGF-1 deficiency (SPIGFD) is a medical term used when IGF-1 levels are extremely low or undetectable in the blood. The classical (most well recognised) form of SPIGFD is a genetic condition called Laron syndrome. Patients with Laron syndrome have an abnormal growth hormone receptor (GHR) which does not function properly. The GHR is vital for normal growth, as it recognises and binds GH, triggering release of IGF-1 and stimulating growth in the individual cells of the body. In Laron, the abnormal GHR makes patients resistant to the effects of GH and as a result, the IGF-1 levels are low or



undetectable. A number of other genetic abnormalities in the GH - IGF-1 pathway are known to cause SPIGFD and short stature.

## DIAGNOSIS

A diagnosis of Primary Insulin-like Growth Factor Deficiency (IGFD) is made by identifying:

- Growth failure or short stature
- Normal growth hormone production
- Low levels of IGF-1
- No other underlying disease or causes of poor growth e.g. chronic diseases, poor nutrition

When all of these criteria are met, a doctor may diagnose PIGFD. PIGFD may be divided into moderate and severe forms based on how short the child is and how low the IGF-1 levels are relative to other children of the same age. As some children with PIGFD have an underlying abnormality in their genes, genetic testing is sometimes offered as part of the initial investigations.

## TREATMENT

In the UK, PIGFD can now be treated with Increlex, a recombinant (man-made) form of IGF-1. This is also called mecasermin. It has the same chemical structure and acts in the same way as naturally produced IGF-1. Increlex is used to treat children who have growth problems due to low levels of IGF-1 in their blood. Growth hormone therapy is not useful in PIGFD because GH levels are normal, and the body is resistant to the effects of GH. Increlex is given as an injection just under the skin (subcutaneous), twice each day. It must be given shortly before or just after a meal. This is because it has effects similar to insulin and can reduce the blood sugar levels.

In order to fulfil the criteria for Increlex treatment in the UK, children must be aged 2-18 years and have severe primary IGF-1 deficiency (SPIGFD). In the UK, this is defined as height  $< -3$  standard deviation scores (SDS) below the mean, serum IGF-1  $< 2.5$ th centile and normal GH production.

**Increlex patient and physician leaflets can be downloaded here:**

<https://www.medicines.org.uk/emc/product/384/rmms>

**The BSPED supported guideline 'Recombinant IGF-1 Therapy in Children with Severe Primary IGF-1 Deficiency (SPIGFD)' can be accessed here:**



<https://www.bsped.org.uk/media/1448/uk-igf1-users-group-guidelines-2018.pdf>

## INSULIN LIKE GROWTH FACTOR DEFICIENCY

Insulin like growth factor one (IGF-1) is a hormone that is produced by the liver and skeletal muscles. This process is the response to levels of Growth Hormone. (GH)

IGF-1 along with GH helps promote normal bone and tissue growth.

Patients with severe primary insulin-like growth factor-1 deficiency (IGFD), called Laron syndrome, may be treated with either IGF-1 alone or in combination with IGFBP-3. Mecasermin (brand name Increlex) a synthetic analogue of IGF-1 which is approved for the treatment of growth failure.

## TYPES OF IGF-1 DEFICIENCY

### 1. Idiopathic short stature / Growth Hormone Insensitivity Disorder

In this case the child may have normal levels of GH, but low, to no levels of IGF-1. This may be treated with synthetic GH.

### 2. Severe Primary IGF-1D. Also called Laron Syndrome.

In this case the child will have very low to undetectable levels of IGF-1. This may be treated with a synthetic IGF-1.

## SYMPTOMS OF IGF-1D / ISS

Slow growth

Short stature

Reduced muscle strength

Reduced exercise tolerance

Fatigue



## ACKNOWLEDGEMENTS

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## FURTHER INFORMATION

If you have any questions regarding the information contained in this sheet, then please contact:

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## 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](mailto:info@childgrowthfoundation.org)

## FUNDING

The Foundation funds research into many aspects of growth conditions such as the causes, effects, treatments and psychological impact. It also offers essential advice and experience to parents of children who have been diagnosed with growth problems. The annual convention provides a great forum for people to get together to discuss problems and solutions with others in a similar position. It also provides a chance to meet and learn from the doctors and professors dealing with child growth in the UK.

The CGF is entirely self-sufficient and is an independent charity. It relies on donations and membership subscriptions to keep going. If you have found this information leaflet helpful, please consider becoming a member and/or making a donation - [www.childgrowthfoundation.org](http://www.childgrowthfoundation.org).