

**SOTOS SYNDROME  
FAMILY INFORMATION LEAFLET**

## **WHAT IS SOTOS SYNDROME?**

Sotos syndrome is a genetic condition characterised by four cardinal features (table 1):-

1. Increased height above that expected for the family.
2. Increased head circumference
3. Learning difficulties
4. Characteristic facial appearance

### **I- Increased height**

In general, the height of children with Sotos syndrome is  $>2$  standard deviations above the mean. That is the same as a height equal to or greater than the 98<sup>th</sup> centile on the height charts shown below which are the same as those included in the “red book”.

We currently have limited data on final adult height. However, through a preliminary study of 32 adults, we showed a broad range of final adult heights ranging from the 25<sup>th</sup> centile to  $> 99.6$  centil. Further prospective studies are being undertaken to clarify adult height in Sotos syndrome and to try to determine what factors influence it.

### **II- Increased head circumference**

Many children and adults with Sotos syndrome have a head circumference  $>2$  standard deviations above the mean.

### **III- Learning difficulties**

Nearly all children and adults with Sotos syndrome have some degree of learning difficulty. However, the severity of the learning difficulties can vary greatly from one individual to the next. Approximately 25% of children with Sotos syndrome have “mild”

learning difficulties, - 50% have moderate learning difficulties and 25% have severe learning difficulties.

#### **IV- Characteristic facial appearance**

Most children and adults with Sotos syndrome have a characteristic facial appearance with a long thin face prominent chin and prominent forehead. Often children have ruddy cheeks (malar flushing) a high hairline and thin hair over their temple area (bi-temporal hair sparsity).

#### **V- Associated clinical features (table 1)**

A number of different clinical features have been associated with Sotos syndrome and are described in the published literature as “major features”. The four most important associations are:

**Scoliosis-** this is evident in about 30% of individuals with Sotos syndrome. Scoliosis may be diagnosed at any age from infancy to adulthood and varies greatly in severity from individual to individual.

**Cardiac problems-** approximately 20% of individuals with Sotos syndrome have a problem with their heart. Again Sotos syndrome is associated with a broad spectrum of complexity and severity.

**Seizures-** approximately 25% of individuals with Sotos syndrome have a form of seizures.

**Kidney problems-** approximately 25% of individuals with Sotos syndrome have a form of renal abnormality. The most common renal problem is vesico-ureteric reflux (VUR) where the urine refluxes from the bladder up into the kidneys.

In addition, more than 2/3 of individuals with Sotos syndrome have had jaundice, poor feeding or were described as “floppy” in the newborn period.

Other medical problems have been described in Sotos syndrome but we do not yet know whether these are real associations of the condition or incidental findings. This may be clarified with further research.

**Table 1: Clinical features associated with Sotos syndrome**

<b>Cardinal features</b>	<b>Major features</b>
<input type="checkbox"/> height	Scoliosis
<input type="checkbox"/> head circumference	Heart problems
Learning difficulties	Seizures
Characteristic facial appearance	Kidney problems

### **MANAGEMENT OF SOTOS SYNDROME**

There is still much debate about the correct protocol for the management of Sotos syndrome. A suggestion is that at initial diagnosis every child should receive:

- Detailed examination with particular attention being paid to growth parameters and examination of the back

  - Blood pressure measurement

  - Urine dipstick

  - Baseline echocardiogram

  - Baseline renal ultrasound scan

Children should then followed up every 1-3 years depending upon the complexity of their problems. A clinical geneticist should see all young adults with Sotos syndrome to discuss the inheritance of the condition.

## **WHAT CAUSES SOTOS SYNDROME?**

Sotos syndrome is a genetic condition inherited as an autosomal dominant trait. It is caused by alterations in a gene called NSD1.

### **GENES**

Our bodies are made up of millions of cells, each of which contains a complete set of genes (approximately 30,000) which in turn are made from a chemical called deoxyribonucleic acid, or DNA for short.

We inherit two copies of most genes, one copy from our mother and one from our father. Genes act like a set of instructions, controlling our growth and how our bodies work. Any alteration to these instructions is called a mutation (or change). Mutations (or changes) can stop a gene functioning correctly.

Genes are carried in thread like structures called chromosomes. We each have 46 chromosomes, and, like our genes, these are arranged in pairs. We therefore have 23 pairs of chromosomes in most of our cells. The only exceptions to this are the sperm and egg cells which have half the normal number – i.e. 23 rather than 46 chromosomes. This is so that when the sperm (carrying 23 chromosomes) fertilises the egg (also carrying 23 chromosomes) the resultant baby will have 46 chromosomes.

### **Autosomal dominant inheritance**

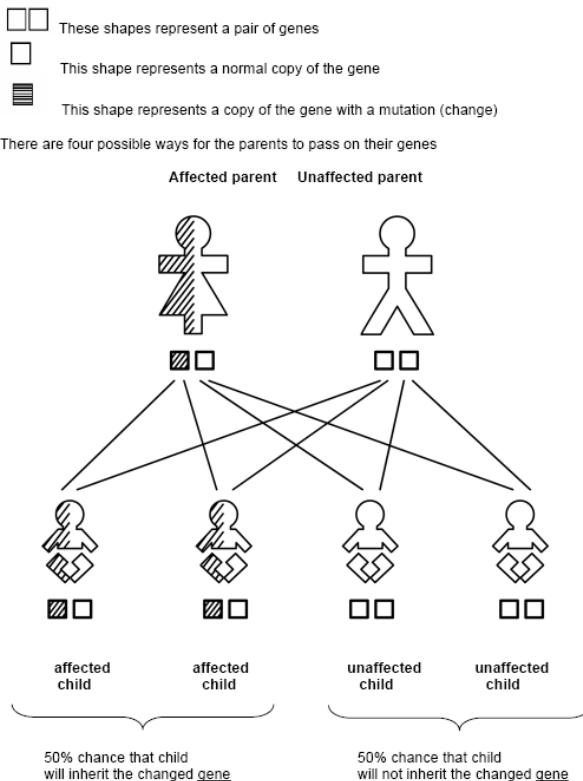
If one gene in a pair has a change (mutation) the other normal gene can sometimes compensate for it but this is not the case for all of our genes. Some disorders are caused by a change in one copy of a gene. These are called dominant disorders as the gene change dominates the normal change.

### **How our dominant genes inherited?**

When individuals with a dominant disorder have children, they pass on either the normal gene or the gene with the change (mutation). This occurs randomly and so there is a 50% chance

that the child will receive the disrupted gene and therefore the disorder from their parent. This chance remains the same in each pregnancy and is the same for boys and girls. There is also a 50% chance that a child will receive a normal copy of the gene. In this case the child will not be affected with the disorder and will not pass it on to any of his or her children (picture 1).

**Picture 1. How dominant genes are passed on from parent to child**



## NSD1

NSD1 stands for Nuclear receptor SET domain containing protein 1. The name is derived from the structure of the protein that NSD1 encodes. We currently do not understand exactly what NSD1 does and why, if an individual has one disrupted copy of the gene, they have Sotos syndrome.