ALL ABOUT

Infantile Spasms

Information and guidance for families and medical professionals

www.ukinfantilespasmstrust.org

PRODUCED IN ASSOCIATION WITH CONSULTANT PAEDIATRIC NEUROLOGIST DR ANDREW LUX

UKIST

THE UK INFANTILE SPASMS TRUST

Supporting families & offering hope

This information booklet has been produced by the UK Infantile Spasms Trust (UKIST) primarily to help parents of newly diagnosed children find out about the condition. Since infantile spasms is a rare condition, affecting up to 1 in 2500 children, it may also be useful for primary care clinicians unfamiliar with the disease. The average GP is likely to see only one case in the course of their professional career.

What is infantile spasms?

Infantile spasms has been recognised since Dr West wrote a letter to medical journal The Lancet in 1841 describing the 'bobbing of the head, and heaving of the head forward towards the knees, then relaxing, repeated alternately at intervals' that he observed in his own son, James. The name West syndrome is still used to describe the condition in some children with infantile spasms, and in particular where it is associated with characteristic EEG features (which are discussed below).

Infantile spasms (IS) constitute a form of epilepsy. Epilepsies are conditions that occur because of changes in the way that nerve cells coordinate their signalling, and they are associated with electrical disturbances in the brain.

As Dr West described so vividly, spasms are short in duration (1-2 seconds) and jerky movements that often occur in clusters, with a period of relaxation lasting many seconds in between each spasm. The movements often consist of the head dropping forward, the arms being flung forwards and the legs being drawn up towards the body. They can also be very subtle, sometimes only involving a nod of the head or a movement of the eyes. Video footage of the movements can be very helpful in obtaining a diagnosis. There is

footage of children experiencing spasms on our UKIST video on Youtube.

IS is an age-related condition. Onset of spasms is normally in the first year of life, most commonly between 3 and 6 months of age, though some children will have symptoms starting before 3 months, and onset may occur up to 2 years of age – or even later in very rare cases. Infantile spasms in a child too old to be referred to as an infant are called epileptic spasms, and this term is also used as a more general description of the movement than IS.

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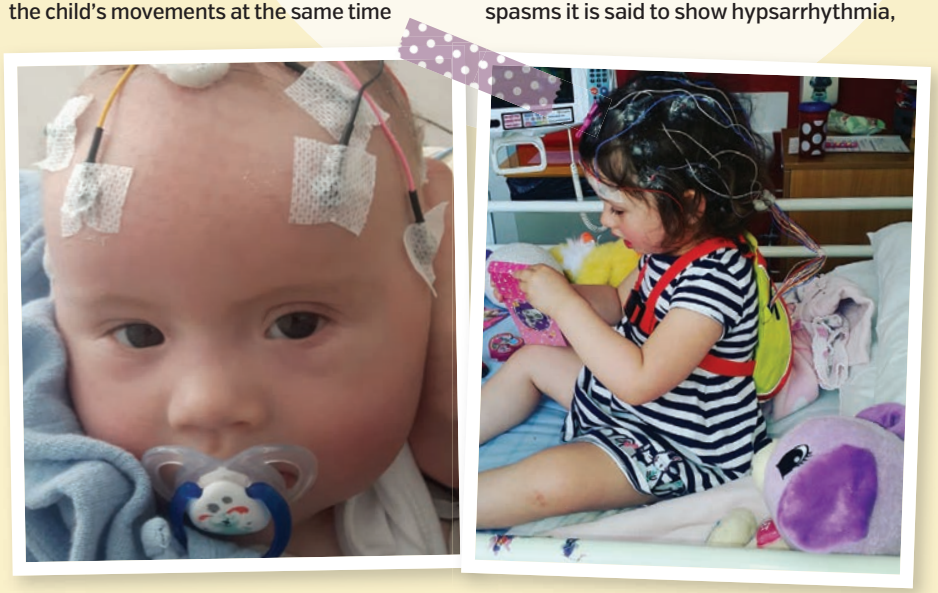
IS can be confused at first with several more common and more benign conditions – for example: colic, startle reflex, tics or Sandifer syndrome (Sandifer syndrome is linked to reflux). The pattern of the same movement being clustered and repeated at a more or less predictable interval should lead to the suspicion of IS rather than these non-epileptic conditions.

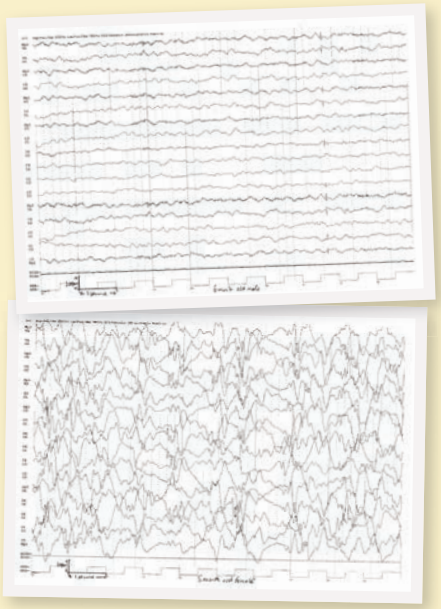
Many parents notice that their child behaves differently once the spasms start. They may lose interest in their surroundings or interact less with caregivers. Some children seem irritable or drowsy. They may also appear to lose skills they had previously mastered. Because of the young age at which they typically occur, the loss of skills is likely to relate to visual function. However, there may also be features such as floppiness.

How is infantile spasms diagnosed?

If an infant is thought to have IS, they need urgent referral to a paediatrician, and probably discussion with, or review by, a neurologist. To diagnose IS in a child with suspicious movement patterns, the brainwaves need to be assessed with an EEG test (electroencephalogram). The EEG is a test that measures electrical activity in the brain by placing a series of sm electrodes on the child's scalp and connecting them to a computer. It often involves taking a video of the child's movements at the same time (video-EEG) to correlate any seizure episodes or movements that might cause an artefact on the trace.

If a child has IS, the EEG is usually very different from normal, even when the spasms are not happening. This is described as an 'interictal' EEG, a term that means 'between attacks'. The electrical activity is much stronger than usual (high voltage) and chaotic or disorganised in quality. If the EEG shows the most typical features of infantile spasms it is said to show hypsarrhythmia,





A normal EEG (top) compared to the EEG of a child experiencing infantile spasms (bottom)

'To diagnose IS in a child with suspicious movement patterns, they need urgent referral to a paediatrician'

but it is not necessary to meet all the criteria for hypsarrhythmia in order to make a diagnosis of IS. In some cases, the EEG is only abnormal during sleep, or only when a spasm cluster occurs. An EEG that captures an attack is referred to as an 'ictal EEG'. Very occasionally the EEG of a child with suspicious movements is completely normal even when a child is asleep, and this is likely to lead to a diagnosis of benign infantile myoclonus. This is not a type of epilepsy and does not require treatment, so it is important to perform the EEG test before starting treatment for IS. The term 'West syndrome' is used when there are epileptic spasms in an infant and the EEG shows hypsarrhythmia.

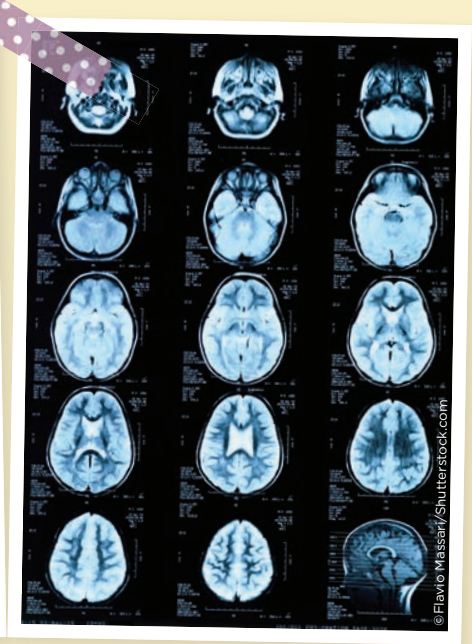
If there are epileptic spasms in an infant and the EEG shows features of epilepsy but not the pattern known as hypsarrhythmia, then the condition is referred to simply as 'infantile spasms', In practice, however, the term 'infantile spasms' is used for both situations, and there appears to be no practical difference in treatment or outcomes.

What causes infantile spasms?

In our experience, the questions that most parents ask are, 'Why did my child develop IS?' and 'What are the likely long-term effects?' There are at least 200 known conditions affecting the brain that can lead to infantile spasms, including structural problems with the brain, genetic diseases, and metabolic diseases. Some parents may already know or suspect that their child has an underlying problem, either because of concerns about development or because of other pre-existing seizures, but for many parents an IS diagnosis comes apparently out of the blue. After initial investigations, an underlying cause will be found in about 70% of cases. Such cases have often been referred to as falling into the category known as 'symptomatic', although this term is now used less often. The remaining 30% have often been referred to as 'cryptogenic' (meaning of 'hidden cause') or idiopathic (meaning that it occurs by itself). As knowledge and technologies develop, especially in the field of clinical genetics, underlying causes are identified in a higher proportion of cases. The underlying cause has a strong influence on outcomes and this should be discussed with your doctor.

In the days and weeks following an IS diagnosis, your doctor will begin a process of looking for an underlying condition.

'There are at least 200 known conditions affecting the brain that can lead to infantile spasms'



Your child will need to have a brain scan following diagnoses – either a CT scan or MRI

THE HISTORY, EXAMINATION AND TESTING IS LIKELY TO INCLUDE:

- **History**
  Questions about the pregnancy and birth, any problems in early life and any family history of epilepsy.
- **Examination of your child**
  For any features that might suggest a genetic problem, head circumference, stage of development.
- **Examination of the skin with an ultraviolet light**
  This is to check for white patches that are suggestive of a condition called tuberous sclerosis.
- **Eye drops**
  Putting drops in the eye to dilate the pupils to examine the retina (back of the eye).
- **Blood and urine tests**
  For blood counts, basic organ function and testing for metabolic diseases. Metabolic diseases are a group of conditions that affect how the body deals with nutrients from food.
- **Imaging of the brain**
  Your child will need to have a brain scan, either with CT (computed tomography – uses X-rays to form images of the brain)

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or MRI (magnetic resonance imaging – uses electromagnetism to form the images). These scans look for issues with the structure of the brain, either in how it formed, or for problems such as strokes, which can be an issue stemming from premature birth or from problems around the time of childbirth. These images can show areas of damage, but they can only tell doctors whether or not the structure of the brain is normal. They do not show how well the brain is working. Sedation or a general anaesthetic may be needed for the scan to be performed safely.

- **CSF**
  Doctors may need to collect a sample of cerebrospinal fluid (the fluid that bathes the brain and spinal cord) by putting a needle into the tissues around the spine. This procedure is called a lumbar puncture.

- **Genetic tests**
  Blood is often taken for genetic testing, of which there are several levels:
  - The first level is to examine the chromosomes (this test is called karyotyping. This would detect for example Down Syndrome – an extra copy of chromosome 21).
  - The second and more sensitive test is a microarray CGH (comparative genomic hybridisation). In this test, the child’s DNA is compared to a known sample to detect small sections that are duplicated or missing. Because of its greater sensitivity, many centres perform the microarray in place of the karyotyping test. In many cases, it is preferable to also test the DNA from one or both parents in order to assess the likely significance of any unusual finding.
  - The third is an epilepsy gene panel – where the genes linked to epilepsy syndromes are sequenced to see if there are any ‘spelling mistakes’.
  - Where there is a high suspicion of there being a genetic cause, it might be possible to perform more extensive genetic tests that search for variants in any part of the human genome. Whole-genome or whole-exome testing currently takes a long time. Also, since many of the findings are new, interpretation of the findings can be difficult.

Once an IS diagnosis is made, doctors will be keen to start treatment as soon as possible, because allowing the spasms to continue untreated can be detrimental to the child’s future development.

THE 100,000 GENOMES PROJECT

In 2018 the NHS supported a major research project that used the whole-genome technologies – the 100,000 Genomes Project. These projects may not give any answers for some years, and are not guaranteed to find an explanation but it is likely that, in the future, these new genomic technologies will become established NHS investigations with faster turnaround times.

How is infantile spasms treated?

Infantile spasms do not generally respond to the types of anti-epileptic drugs (AEDs) used to treat most other forms of epilepsy. Two types of medication have proved to be most effective and they are likely to be recommended, singly or in combination, as the initial treatment.

1. Hormonal treatment with ACTH or prednisolone

a. ACTH (adrenocorticotrophic hormone) is a naturally occurring hormone made in the pituitary gland in the brain. It signals the adrenal glands (small glands near the kidneys) to make the steroid hormone called cortisol. A synthetic form of ACTH can be administered as a course of injections.

b. Prednisolone is a steroid medication that acts in the body in a similar way to cortisol. It is administered by mouth as soluble tablets or a liquid. Earlier studies used low doses of steroids which were much less effective than ACTH, but more recent studies have shown that at high doses (>4mg/kg, with a usual starting dose of 40mg a day) they are similarly effective. Both of these treatments are administered for a short period of time, usually a few weeks of high doses followed by a weaning period of several weeks.

'Two types of medication have proved to be most effective and they are likely to be recommended, singly or in combination, as the initial treatment'

There are some significant side effects associated with these hormonal treatments but they are also the most successful treatment for IS.
Side effects include:

- Suppression of the immune system causing the infant to be more vulnerable to infection for the duration of treatment, and for some months afterwards. You should be given advice on reducing the risks of infection, and about what to do if the baby is exposed to serious infections, such as chickenpox or measles. The immune suppression may also alter the body's response to scheduled vaccinations. You will need to discuss this with your doctor because the vaccinations may need to be rescheduled.
- High blood pressure – this should be monitored during treatment and it is fairly common to require additional medication to control BP if it becomes too high.
- Potential to develop diabetes or high blood sugar – blood or urine glucose should be monitored during treatment.
- Less serious side effects are common and include: increased thirst and hunger.

leading to rapid weight gain, crankiness, poor sleep, and reduced smiling. It is important for parents to know that such side effects are temporary.

- When weaning off steroids, many babies will dramatically drop their food and fluid intake, and this may go on for some weeks. It is important to ensure they stay hydrated and have wet nappies in much the way as before treatment. If they seem unwell during or after the weaning period, then seek medical advice as some children's adrenal glands are slow to start working again having been suppressed by the treatment. In many cases, an investigation called a 'Short Synacthen test' is performed to check the adrenal gland's response to a signal from ACTH.

2. Treatment with vigabatrin (Sabril)

Vigabatrin is a medicine that was designed to increase the level of the neurotransmitter GABA in the brain. GABA is a substance that allows the nerve cells to rest in a more stable electrical state. This inhibitory action makes seizures less likely but also tends to cause a degree of sedation. Vigabatrin is available in powder or tablet form. It can be dissolved in liquid so that a more precisely measured amount may be given based on the basis of your baby's weight. It is usually started at a low dose that can be increased in steps up to a maximum dose over a period of several days. If treatment is successful it will be continued for several months. The main side effects of vigabatrin are:

- Loss of peripheral vision – this has been shown to be an issue in adult patients on vigabatrin. It is thought to be rare in children, who are usually on the drug for a relatively short period of time. The risk is thought to be related to the cumulative dose, and so is higher if the drug is given at higher doses and for longer periods. Most adult patients with measurable visual field loss are not aware of it in everyday activities.

'There is a long list of other AEDs that may work for cases of IS where the first line medications are not successful; your doctor will discuss which treatment may be appropriate'

- Other side effects that parents frequently report include sleepiness and low tone (especially in the first few weeks), and disturbed sleep.

- A large research study published at the end of 2017 (ICISS) showed that combining a hormonal treatment with vigabatrin was significantly more successful at stopping infantile spasms at two weeks of follow-up than either treatment alone. However, what is less clear is whether that effect is also associated with better developmental outcomes. It is likely that your doctor will recommend either starting both treatments together or adding the second in a short timeframe (typically a fortnight) if a single treatment has not been successful.

3. Ketogenic diet

The ketogenic diet is a carefully calculated high fat, very low carbohydrate diet that has been used as a successful treatment for children with some forms of epilepsy, including IS. It is considered a frontline (first) treatment choice in some centres. Its use as a first treatment is limited by access to appropriately trained dieticians and waiting lists to initiate the diet.

4. Epilepsy surgery

Surgery can be a very successful treatment for IS if the spasms are symptomatic of a localised brain lesion. If your child has abnormalities on the MRI or CT scan, then discuss with your doctor if they are a potential candidate for epilepsy surgery.

5. Other AEDS

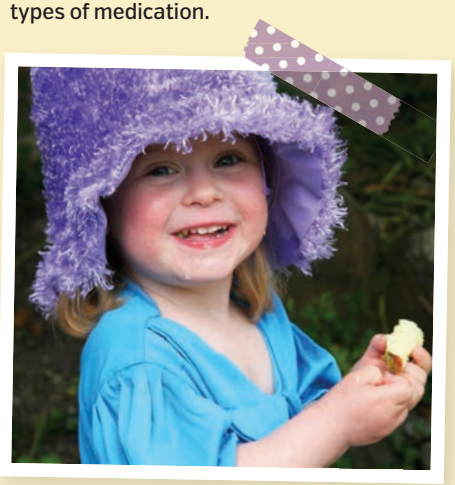
There is a long list of other AEDs (antiepileptic drugs) that may work for cases of IS where the first line medications are not successful. Your doctor will discuss which treatment may be appropriate for your child.

More questions answered

How will we know if treatment has worked?
The aim of treatment is to stop visible spasms and to eliminate the EEG features that confirmed the diagnosis. The aim would be to stop spasms as quickly as possible, ideally within the first two weeks of a treatment. If spasms are still present after two weeks of treatment, it is time to consider adding another medication. If the spasms seem to have stopped, then the EEG test will be repeated to see if there has been improvement in that also. The EEG is often not completely normal at this stage because of residual epileptic activity or because of changes due to the underlying condition, but doctors are looking for the chaotic activity to have reduced or disappeared.

What happens after initial treatment is successful?
Hormonal treatment is usually given for only a short period of several weeks. If your child responded to vigabatrin it will normally be continued for several months. Your doctor will discuss with you whether a 'maintenance' medication is required, and this will depend on the pattern of the post-treatment EEG, the risk of relapsing spasms or developing other seizures, and the nature of any known underlying condition.

Will the spasms come back?
Sometimes spasms are successfully treated and are never seen again. Spasms come back in about a third of children who respond to initial treatment, usually in the first few months after treatment stops. A 'relapse' is upsetting and disappointing, but it may be that the spasms will respond to another round of treatment. Overall, about 60% of children with IS will develop other types of seizures at some stage. How likely this is in your individual child will depend a great deal on the underlying condition. Different seizures may require different types of medication.



'Parents are always a child's most passionate advocates; learn all you can and never be afraid to ask questions'

Will my child develop normally?
Unfortunately, all children with IS are at risk of having slow development. It is because of this risk that it is important to get a prompt diagnosis and to start treatment quickly. When the spasms are stopped quickly, it is thought that the child has a better chance of having normal or near normal development. Any underlying condition also has a large influence on how the child will progress.

How can developmental progress be monitored?
Ask what services are available in your area. Your child's development should be monitored by either your neurologist, a community paediatrician or an early intervention service. These professionals can arrange referrals to services like physiotherapy or speech therapy as necessary.

What support is available for parents?
Firstly, please come and join our private Facebook support group for affected families (see page 16), where you can ask anything and where we celebrate every milestone. We may be able to put you in touch with local families who have been through something similar.

Many parents need extra support after going through a very stressful time, so please contact your health visitor or GP if you are struggling.

Remember that parents are always a child's most passionate advocates. Learn all you can about this new diagnosis, and never be afraid to ask questions or challenge decisions where appropriate.

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More information and support

To find out more about the support available through UKIST visit:

www.ukinfantilespasmstrust.org

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