

Infantile Spasms and West Syndrome Guideline

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1. Definitions

1.1 Infantile Spasms - axial movements longer than myoclonus and shorter than tonic seizures that occur either in clusters or periodically.

1.2 West Syndrome - an epilepsy syndrome consisting of epileptic infantile spasms, developmental delay or 'plateauing' and a supportive EEG (e.g. 'hypsarrhythmia' - see below)

2. Scope

This guideline is for paediatric health professionals in a secondary and tertiary care setting in the Trent region.

3. Diagnosis

3.1 Children presenting with possible Infantile Spasms (IS) should have an urgent EEG within < 3 days, ideally capturing sleep. (Acute admission is usually required to achieve this and to coordinate appropriate initial investigations and treatment).

3.2 If 'hypsarrhythmia' or 'modified hypsarrhythmia', or a 'hypsarrhythmia-like' EEG is demonstrated, the diagnosis is made and treatment should be started promptly (within the same day if possible).

3.3 If EEG is reported as 'normal', and no part of the EEG was recorded during sleep, arrange for a sleep EEG (e.g. after a feed at usual nap time). If normal in sleep and awake, repeat EEG in 10-14 days. This is an issue because the awake EEG can be normal in early phases of the illness.

3.4 If the EEG is normal while awake, in sleep, inter-ictal and ictal, and on follow-up, the diagnosis of non-epileptic movements can be made (e.g. benign infantile myoclonus).

3.5 Other epilepsies may be diagnosed if other epileptiform EEG patterns are demonstrated.

3.6 All children with probable infantile spasms or West syndrome should be discussed with the paediatric neurology team.

4. Treatment

4.1 First-line treatment to discuss with the family or carers. Commence as soon as possible (within 3 days of supportive EEG; ideally same day).

4.2 If not tuberous sclerosis, offer inclusion in the International Collaborative Infantile Spasms Study (ICISS) if running locally, via the local research representative.

4.3 If ICISS not running or inclusion declined, consider Prednisolone or Vigabatrin. Prednisolone has in general a better chance of working. However in Tuberous Sclerosis there is some evidence that Vigabatrin may have a better chance of working. If the first treatment fails consider the other first line treatment next.

4.4 Prednisolone 10 mg qds oral or NGT, increase to 20 mg tds if spasms continue into or reappear in the second week. After 2 weeks of treatment tail off the Prednisolone over 2-3 weeks (total duration of Prednisolone approximately 5 weeks). Usually treatment is started as an in-patient.

Example 1: Spasms disappear by 7 days		Example 2: Spasms don't disappear by 7 days or reappear in week 2	
Week 1	Prednisolone 10 mg qds	Week 1	Prednisolone 10 mg qds
Week 2	10 mg qds	Week 2	20 mg tds
Then:		Then:	
Week 3	10 mg tds	Week 3	20 mg bd
Week 4	10 mg bd	Week 4	20 mg od
Week 5	10 mg od	Week 5	10 mg od
Week 6	stop	Week 6	stop

4.5

- Check, and if present treat, for oral and peri-anal candidiasis
- Check BP e.g. Day 2 and 7. Mild elevation (less than 120/90) is usual but rarely needs treatment
- Check urine for glycosuria daily if possible while inpatient
- Check U&E for hypokalaemia at 5-10 days
- Repeat EEG at 2 weeks (10-15 days) after commencing treatment
- Consider prescribing a proton pump inhibitor (e.g. omeprazole) for children taking prednisolone

If there are no epileptic seizures and EEG is normal or improved to an acceptable degree and therefore no longer diagnostic of West syndrome this would indicate remission. Children achieving remission should continue to tail off their prednisolone. They do not need subsequent anti epilepsy drug treatment if remission is maintained.

4.6 Vigabatrin 25 mg/kg/dose bd (50 mg/kg/day) 24 hours, then 50 mg/kg/dose bd (100 mg/kg/day). If no clinical remission by end of 4th day of Vigabatrin increase to 75 mg/kg/dose bd (150 mg/kg/day). If no clinical remission by 7th day of Vigabatrin consider increasing to 100 mg/kg/dose bd (200 mg/kg/day)^{7.4} after discussion with paediatric neurologist. Repeat EEG at 2 weeks (10-15 days).

Check visual fields when old or mature enough (e.g. at about 10 years of age using standard perimetry, or earlier if special techniques are available; Department of Vision Sciences, Aston University may be able to offer field specific VEP from 4 years of age).

If IS in remission (no epileptic seizures and EEG normal or improved i.e. no longer diagnostic of West syndrome (3.2), continue Vigabatrin for 3 months if tolerated then wean off over 1 month.

4.7 Children not achieving remission by 14 days. If children do not achieve remission on prednisolone then vigabatrin should be tried. If children do not achieve remission on vigabatrin then prednisolone should be tried.

4.8 Second line treatments

When Prednisolone and Vigabatrin fail or cannot be used, consider second line treatments in discussion with the paediatric neurology team:

4.9 Pyridoxal phosphate Give two doses of oral pyridoxal phosphate (10 mg/kg/dose) 2 h apart. (if the epilepsy persists try two doses of folinic acid 5 mg, 6 hours apart). If remission achieved continue maintenance pyridoxal phosphate at 30–50 mg/kg/day.^{7.5}

Pyridoxine is an alternative to pyridoxal phosphate. 30 mg/kg/day oral/NG for 7 days then stop if no remission. If remission continue maintenance at 15 mg/kg/day.^{7.6}

4.10 Valproate oral 20mg/kg/day increasing to 50mg/kg/day if necessary.

4.11 Nitrazepam oral 0.25 mg/kg/day increasing to 1 mg/kg/day if necessary.

4.12 Tetracosactide IM. 500 microgrammes alternate days for 14 days. If no remission by 7 days, or spasms reappear, increase to 750 microgrammes alternate days for the second week. Stop after 2 weeks and give prednisolone tail (as in 4.4).

4.13 Topiramate oral 1 mg/kg/day increasing to 20 mg/kg/day if necessary.

4.14 Zonisamide oral 5mg/kg/day increasing to 10 mg/kg/day if necessary.

4.15 Ketogenic diet

4.16 Epilepsy surgery (rarely indicated).

5 Information for families

5.1 Infantile Spasms & West Syndrome. An Explanatory Booklet for Parents & for Professionals (2007)^{7,7} (www.iciss.org.uk)

5.2 AED drug information leaflets (www.cewt.org.uk)

6 Investigations

6.1 In addition to those in 3 and 4 above all will need:

- **Brain MRI (epilepsy protocol)**, (Occasionally a CT is indicated after discussion with neuroradiologist and neurologist)
- **Woods light (UV-light) skin examination**
- **ophthalmology exam.**
- **varicella serology**

6.2 Those under 3 months should have a

- **cardiac ECHO** for TS (and possibly a renal USS for TS)
- **tests for congenital infection** "TORCH screen": urine for CMV, throat swab for viral culture, blood for: toxoplasma, rubella, CMV, and possibly hepatitis, herpes, syphilis, HIV.

6.3 Metabolic and genetic diseases should be considered although rarely identified:

- **Blood:** chromosomes; lactate, glucose, U&E, LFT, Ca, Mg, urate, blood gas, anion gap, ammonia, biotinidase, plasma amino acids; and possibly VLCFA, transferrin electrophoresis for Congenital Disorders of Glycosylation (CDGs); copper & caeruloplasmin; pipercolic acid
- **Urine:** aminoacids, organic acids, GAGs, oligosaccharides, pipercolic acid, thiosulphate
- **Fasting CSF and parallel blood:** lactate, glucose, protein, glycine and serine, microscopy and culture

6.4 Other tests:

May be considered in some cases in discussion with the paediatric neurology team.

7 References & Resources

- 7.1 Osborne JP *et al.* *Infantile Spasms & West Syndrome* 2007. Quarriers. www.quarriers.org.uk
- 7.2 Lux AI *et al.* UKISS RCT. *Lancet* 2004; 364: 1773-78.
- 7.3 ICISS. www.iciss.org.uk.
- 7.4 Fejerman *et al.* Vigabatrin as a First-Choice Drug in the Treatment of West Syndrome. *Child Neurology* 2000;15:161-165
- 7.5 Surtees R. Treatable neonatal epilepsy. *Arch. Dis. Child* 2007;92;659-661
- 7.6 Baxter P . Pyridoxine dependent and pyridoxine responsive seizures. In Baxter P (Ed.) *Vitamin responsive conditions in paediatric neurology*. 2001. International Review of Child Neurology Series. Mac Keith Press, London. pp108-165.
- 7.7 Infantile Spasms & West Syndrome. An Explanatory Booklet for Parents & for Professionals.
<http://www.bath.ac.uk/health/research/iciss/index.php>

8 Disclaimer

Clinical guidelines are guidelines only. The interpretation and application of clinical guidelines will remain the responsibility of the individual clinician. Caution is advised when using guidelines after a review date.

Appendix 1 Infantile Spasms & West Syndrome Flowchart

(see full guideline for specific details)

Initial assessment and Diagnosis

- History and full examination (include OFC, BP, Wood's light)
- Developmental assessment
- Urgent awake & sleep EEG (< 3 days after presentation) to confirm 'hypsarrhythmia' or 'modified hypsarrhythmia', or 'hypsarrhythmia-like'
- Repeat initial EEG (necessary if first EEG 'normal' and no sleep captured)
- Discuss with paediatric neurologist if diagnostic doubt or uncertainty about treatment



Investigations

Urine	Blood	Radiology	CSF
<ul style="list-style-type: none"> • Amino acids and organic acids • Thiosulphate • GAGs • Oligosaccharides • Pipecolic acid • CMV (<3 months) 	<ul style="list-style-type: none"> • TORCH (<3 months) • Chromosomes • Lactate • Glucose • FBC, U&E, LFT, Ca, Mg, urate • Blood gas & anion gap • Ammonia • Biotinidase • Plasma amino acids Consider: <ul style="list-style-type: none"> • VLCFA, • Transferrins (CDGs) • Copper & caeruloplasmin • Pipecolic acid 	<ul style="list-style-type: none"> • MRI brain (Epilepsy Protocol) <p><3 months</p> <ul style="list-style-type: none"> • ECHO • renal USS 	<p>Consider:</p> <ul style="list-style-type: none"> • MC&S • Glucose (fasting) • Lactate • Protein • Glycine • Serine



First Line Treatments

- Commence soon (< 1 day if possible) after confirmation of supportive EEG
- Prednisolone PO/NG initial dose 10mg qds (see main text for subsequent dosage plan) (Monitor BP, urine dipstick, U&E; steroid information)

OR

- Vigabatrin PO (particularly if evidence of Tuberous Sclerosis) initial dose 25 mg/kg/dose bd (50 mg/kg/day) (see main text for subsequent dosage plan)



Subsequent Treatment and Follow-up

- Aim initially for seizure freedom and improvement of EEG
- Repeat EEG at 10-15 days after commencing treatment
- Ophthalmology assessment
- If seizure freedom not achieved, will need to work through successive AEDs with close monitoring and frequent inpatient or outpatient review
- Neurodevelopmental follow up etc
- Paediatric neurology review if not already involved
- Patient information regarding West Syndrome and appropriate AEDs