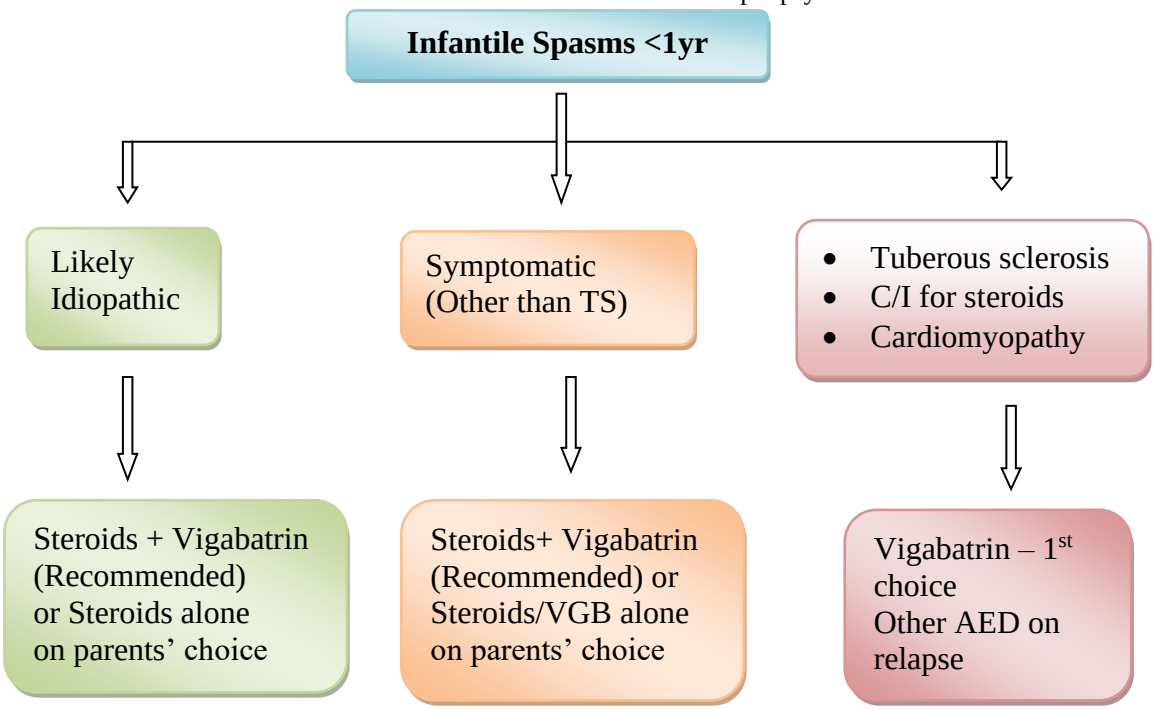
Management of Infantile Spasms in Infants Under One Year of Age

Establishing the Diagnosis

- History consistent with Infantile spasms (symmetric or asymmetric)
- Directly witnessed event /video of seizures seen by a senior clinician
- Developmental regression or arrest
- Classical/modified hypsarrhythmia or compatible EEG findings
- In case of normal EEG and diagnostic uncertainty – obtain sleep EEG
- If clinical or EEG findings are uncertain – discuss with Paediatric neurologist, Addenbrookes Hospital

Before Treatment

- Obtain a thorough history including perinatal brain injury, family history of epilepsy and congenital malformations.
- Clinical examination for congenital malformations, head circumference and evidence of IU infections (microcephaly, hydrocephalus, retinitis, petechiae and hepatosplenomegaly/jaundice)
- Actively look for tuberous sclerosis (Clinical, including wood's lamp examination)
- Refer to ophthalmology for fundus examination if there are signs of TS or IU infections.
- Assess development – document pre-morbid developmental delay
- Arrange investigations (plasma glucose, serum calcium and magnesium, renal and liver function tests, blood and urine cultures, FBC and Array CGH)
- Arrange imaging at a later date (unless TS is highly likely)
- Further investigations for epileptic encephalopathy can be arranged later (refer to list of investigation available at Paediatric Neurology department, Addenbrookes Hospital)
- Provide information about infantile spasms (ICISS trial/Epilepsy action) to the parents. (See appendix 1 and 2)
- Discuss treatment options including side-effects with parents (Prednisolone, ACTH, Vigabatrin alone or in combination). Parents should be made aware of lack of evidence for development and relapse rates with combination treatment.
- Document baseline blood pressure
- Are there any contraindications for steroid?
- Rule out active bacterial infection (clinical +/-investigations)



(Mitochondrial disorders or inborn errors of metabolism are excluded from this guideline. If these conditions have already been diagnosed or strongly suspected on the basis of other results please discuss treatment options with Addenbrookes paediatric neurology team)

STEROIDS TREATMENT
(Excluding children < 5kg or younger than 2months)

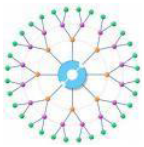
Treatment from Day 1 to Day 14 (Prednisolone or ACTH – not both)

Oral Prednisolone: **10mg** per dose, **four times a day** for **14 days**.
If spasms continue on Day 7 or reappear between Day 8 and Day 14 inclusive, increase the dose to **20mg** per dose **three times a day** for the remaining doses.

Tetracosatrin (ACTH): Intramuscular injection, **0.5 mg on alternate days** for **3 days in a week** (Mon, wed, Fri).
If spasms continue on Day 7 **or** reappear between Day 8 and Day 14 inclusive, increase the dose to **0.75 mg on alternate days** for the remaining doses.

ACTH injection should be given by health care professional who can deal with allergic reactions and in a hospital setting. Keep necessary equipment and drugs to deal with anaphylaxis. Watch for reactions such as marked redness, pain at reaction site, urticaria, pruritus, flushing and dyspnoea. Switch to prednisolone, if reactions are noted.

Weaning Steroid Treatment after Day 14 in those with no spasms



If receiving prednisolone 10mg four times a day/ACTH 0.5mg on Day 14, the dose of prednisolone will be;

30 mg daily for 5 days
20mg daily for 5 days
10mg daily for 5 days
then stop

If receiving prednisolone 20mg three times a day/ACTH 0.75mg on Day 14, the dose of prednisolone will be

40 mg daily for 5 days then
20mg daily for 5 days and finally
10mg daily for 5 days
then stop

Alternatively if on ACTH at Day 14, it can be weaned as below

If receiving 0.5mg during first 2 weeks

0.25mg IM on alternate days (Mon, Wed, Fri)	week 3
0.25mg IM twice in week (Mon, Thu)	week 4
0.25mg IM once in a week	week 5

then stop

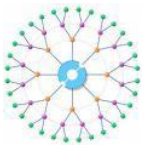
If receiving 0.75mg during first 2 weeks

0.5 mg IM on alternate days (Mon, Wed, Fri)	week 3
0.25mg IM on alternate days (Mon, Wed, Fri)	week 4
0.25mg IM twice in week (Mon, Thu)	week 5
0.25mg IM once in a week	week 6

then stop

Monitoring steroid treatment

- Please add ranitidine or omeprazole/lansoprazole until end of treatment (To avoid gastric irritation).
- Monitor blood pressure every 3 days (At least twice in a week) for 14 days. Monitoring can be discontinued during weaning unless elevated at the end of 14 days (If elevated on day 14 monitoring should be continued until stopping treatment and blood pressure returns to normal range after stopping treatment.
- Treat genuine elevation in blood pressure above the 95th centile for age (usually above 120/90) with thiazide diuretic or nifedipine as per BNF and monitor 48 hourly thereafter until acceptable, being prepared to increase antihypertensive dose as necessary.
- Provide urine dipsticks and ask to check urine sugar at 48 hours and then weekly till end of treatment.
- After 3 days treatment with prednisolone or 2 doses of ACTH, consider child to be immunosuppressed and treat fevers as per local febrile neutropenia protocol.
- Counsel regarding chicken pox exposure - consider zoster immune globulin if exposed, and treat with IV acyclovir if vesicles appear whilst on treatment. The preventive effect of VZIG lasts for about three



weeks. Antibodies degrade after that time. If there is a new contact (after three weeks) or continued contact from the same index patient (household?), VZIG will be needed again after three weeks. The dose for oral aciclovir prophylaxis is 40mg/ kg/ day in four divided doses for one week starting from day seven of contact (contact only once) If there is continued contact start aciclovir from day 7 till the end of contact + 7 more days.

- Arrange open access to paediatric ward for acute febrile illnesses during first 6 weeks.
- Consider the child to have adrenal suppression for 6 weeks after the end of treatment and consider need for hydrocortisone replacement if the child develops an acute illness during this period.

VIGABATRIN TREATMENT

Route: Oral
Dose: Day 1 25mg/kg/dose, twice a day
Day 2 50mg/kg/dose, twice a day
If no spasms: continue the same dose until weaned.
If spasms continued until day 4 or reappeared between Day 5 and 14 increase the dose to 75mg/kg/dose, twice a day before day 14.

Practical information: Each sachet of 500 mg of Vigabatrin is made up in 10 ml of water making a mixture containing 50 mg per ml water. The dosage will be given to the nearest 25 mg dose (0.5 ml), i.e. round up or down to the nearest 0.5 ml.
Duration of treatment: 3 months, withdraw at 3 months (Dose adjusted as per weight gain, increasing as the body weight increases, in increments of 25 mg per dose (50 mg per day) as required until 3 calendar months from Day 0). Duration may be less than 3 months on clinician's discretion when early remission is observed.
Monitoring: Watch for drowsiness and feeding failure initially (may require NG tube feeds). Visual field defects are not possible to monitor.
Weaning: Gradual reduction in 4 weeks and then stop.

Combination treatment:
Doses, escalation and weaning with both agents would be same as for individual agents, which, means 2 weeks of steroids and 3 months of Vigabatrin followed by weaning as advised for each agent.

Side Effects:

Steroids	Vigabatrin
Irritability Hypotonia/Hypertonia Increased appetite Weight gain Gastro- intestinal upset. Fluid and electrolyte disturbance, including systemic hypertension	Drowsiness Hypotonia Increased appetite Weight gain Visual field constriction Susceptibility to infection Gastro-intestinal upset

Hyperglycaemia Neuropsychiatric disturbance including sleep disturbance Immuno suppression with infection susceptibility Allergic rash (tetracosactide depot only) or anaphylaxis	Neuropsychiatric disturbance including sleep disorder Basal ganglia calcification can occur

Further considerations:

- ACTH is not recommended as first choice, because of difficulties with Injections
- Contact Paediatric Neurology for advice regarding relapse off treatment or non-responders to initial treatment.
- Usually the first step following relapse after steroid course alone will be combination treatment.
- Consider other agent if used steroids/Vigabatrin vice versa.
- Pyridoxine treatment should be considered in patients who are refractory to first-line treatment and in whom the etiology is not apparent.
- Alternative treatments to be considered are Sodium Valproate (caution is required in those with suspected mitochondrial disease), Benzodiazepines, Topiramate, Levetiracetam and Ketogenic diet
- Epilepsy surgery should be considered in those with atypical, asymmetrical spasms, or other suggestion of focality in seizure semiology, supported by lesional identification on neuroimaging and localisation on EEG.
- Repeat EEGs are not recommended unless relapse or unclear as to clinical remission.

Please contact Paediatric Neurology Registrar at Addenbrookes on 01223 245151 pager 157488 or CDC on 01223 216662.

Appendix

1. Infantile Spasms & West Syndrome; An Explanatory booklet for parents and for professionals; Written by Professor John P. Osborne,Dr Eleanor Hancock, Dr Colin Kennedy, Dr Andrew Lux, Dr Richard Newton, Dr Finbar O'Callaghan and Dr Christopher Verity http://www.bath.ac.uk/health/research/iciss/index.php (QUARRIERS_Infantile_Spasms_Booklet-2.pdf)
2. Information leaflet on West Syndrome (infantile spasms) from Epilepsy Action website; https://www.epilepsy.org.uk/info/syndromes/west-syndrome-infantile-spasms

References:

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2. Infantile spasms – Treatment - Step-by-Step – BMJ Best Practice; May 2016. http://bestpractice.bmj.com/best-practice/monograph/752/treatment/step-by-step.html
3. Hancock EC, Osborne JP, Edwards SW. Treatment of infantile spasms. Cochrane Database of Systematic Reviews 2013.
4. Lux AL, Edwards SW, Hancock E, Johnson AL, Kennedy CR, Newton RW, O'Callaghan FJ, Verity CM, Osborne JP. The United Kingdom Infantile Spasms Study comparing vigabatrin with prednisolone or tetracosactide at 14 days: a multicentre, randomised controlled trial. Lancet. 2004 Nov 13-19; 364(9447):1773-8
5. Daniel G Glaze. Management and prognosis of infantile spasms. Uptodate. https://www.uptodate.com/contents/management-and-prognosis-of-infantile-spasms#H36
6. ICISS Protocol; http://www.bath.ac.uk/health/research/iciss/index2.php (ICISS_Protocol_v1_3.pdf)

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