INFANTILE SPASMS

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TARGET POPULATION

Inclusion Criteria:

- Patients less than 24 months of age presenting with suspected or known infantile spasms

Exclusion Criteria:

- Patients older than 24 months of age

BACKGROUND | DEFINITIONS [1]

Infantile spasms (also known as West Syndrome) are an age-specific epilepsy of early infancy and are distinct from myoclonic and tonic seizures. They are characterized by an initial contraction phase followed by a more sustained tonic phase. They can be divided into flexor, extensor, and mixed flexor-extensor spasms; they can also be asymmetrical. All of these spasm types may present in the same patient at different times. The EEG characteristically demonstrates hypsarhythmia (random/chaotic high-voltage slow waves and spikes arising from multiple foci and spreading to all cortical areas), but this pattern is not always present. The onset of spasms is frequently associated with neurodevelopmental regression.

Epidemiology

Infantile spasms (IS) are estimated to occur in 2 to 3/10,000 live births. Onset is typically between 4 to 9 months. IS are slightly more common in males than females [2].

Etiology

- Known causes (70%) - perinatal hypoxic-ischemic encephalopathy (HIE), neurocutaneous disorders, brain malformations, chromosomal abnormalities, and inborn errors of metabolism; more than 200 causes.
- Unknown cause (30%)
- Several conditions, listed alphabetically, are likely to predispose to IS (not all inclusive):
  - Aicardi syndrome
  - Cytomegalovirus (CMV)
  - Hemimegalencephaly
  - Hypoxic ischemic encephalopathy (HIE)
  - Incontinentia pigmenti
  - Lissencephaly
  - Sturge Weber
  - Phenylketonuria (PKU)
  - Tuberous sclerosis complex (TSC)
  - Trisomy 21
  - ARX mutation

INITIAL MANAGEMENT | PRIMARY CARE PROVIDER

Parents will often bring an infant with IS to a primary care provider for episodes that look like colic or may be mistaken for gastroesophageal reflux.

- If the patient is asymptomatic upon PCP examination or H&P is questionable, and if PCP has a low index of suspicion for IS, encourage parents to obtain video footage of episodes.
- If PCP is concerned about possible IS, the patient should be evaluated by a pediatric neurologist within 1-2 days. PCP should call neurology immediately to coordinate care 720-777-6895 or OneCall 720-777-3999.
- Early recognition of IS and prompt initiation of treatment may improve developmental and cognitive outcomes in some patients[3,4].

INITIAL MANAGEMENT | SPECIALIST

Diagnosis [4,5]

- Prior to a diagnosis of infantile spasms, all infants should have an EEG demonstrating hypsarhythmia, modified hypsarhythmia, or ictal EEG manifestations of infantile spasms. Not all patients with IS have hypsarhythmia.
- **EEG should be of sufficient duration to include wake and sleep to accurately rule out a diagnosis of infantile spasms.** In the absence of an established alternative diagnosis, and if initial routine EEG is nondiagnostic, a prolonged overnight video EEG should be performed the same day to capture clinical events and document interictal EEG during wakefulness and all sleep stages.
  - If episodes are clinically suspicious for IS and began within the past 7 days, a nondiagnostic interictal initial EEG does not definitively rule out IS, due to the chance of an early false negative result if no spells are captured. If episodes continue, obtain a repeat EEG with at least one sleep/wake cycle in 3-5 days.
- Case Management should be notified upon admission of any patient with possible spasms. Case Managers are unit specific.

Additional Diagnostic Studies

In some series, etiology is determined in approximately 55% of children by detailed history and exam and MRI. Additional genetic testing demonstrated a cause in 24% of children[6,7]. *Additional tests may be indicated if the results will change the immediate management, prognosis, or clarify etiology. Avoid unnecessarily delaying initiation of treatment when possible.*

LABORATORY STUDIES | IMAGING

Laboratory studies to consider

Further testing for specific metabolic and genetic etiologies may be recommended by the Inpatient Neurology Team or outpatient neurologist, based on associated signs and symptoms. Laboratory testing can often be done after initiation of treatment or potentially by the outpatient neurologist. **It is not necessary to wait for the results of genetic/metabolic testing prior to starting medication.**

Radiology

MRI brain (begin with non-contrast study) should be obtained for ALL patients with IS, ideally within 48 hours of admission. MRI can often identify the etiology of IS. MRI results may influence the choice of treatment and assist with prognosis. **However, it is not necessary to wait for the results of the MRI prior to starting medication.**

Therapeutics [2,8,9]

1. Following confirmation of the diagnosis of infantile spasms, discuss treatment options with primary attending and parents/guardians. First-line treatments include adrenocorticotropic hormone (ACTH), prednisolone, or vigabatrin. If ACTH therapy is being considered, please notify inpatient case management ASAP.
2. Once parents have chosen a treatment, treatment should be initiated immediately. **It is not necessary to wait for the results of the MRI or genetic/metabolic testing prior to starting medication.**

Table 1. Pros and Cons of Possible First-Line Therapeutics

	Pros	Cons
ACTH (Adrenocorticotropin Hormone)	• Likely most effective	• **Adverse effects**: Immune suppressant, edema, gastric bleeding, weight gain, irritability, sleep disturbance, HTN, cortical atrophy, HPA axis suppression, death • Intramuscular injection • Most expensive – only available from specialty pharmacy
Prednisolone	• Least expensive • Oral administration	• **Adverse effects**: Immune suppressant, edema, gastric bleeding, weight gain, irritability, sleep disturbance, HTN, cortical atrophy, HPA axis suppression, death. • Less effective vs. ACTH
Vigabatrin*	• Most effective option for patients with Tuberous Sclerosis Complex (TSC) (treatment of choice) • Oral administration	• **Adverse effects:** 15 to 30% sedation, behavioral changes, sleep disturbance, weight gain, psychosis, 25-50% irreversible peripheral vision loss* (time and dose dependent), reversible MRI changes while taking the medication. • REMS program enrollment required • Less effective vs. ACTH (with exception of patients with TSC)

***Black Box Warning:** >30% of patients will experience irreversible peripheral vision loss dependent on dose and duration of therapy. Because of the risk of permanent vision loss, vigabatrin is available only through a special restricted program under a risk evaluation and mitigation strategy (REMS) called the Vigabatrin REMS program.

3. Patients with IS are at high risk for developmental delay. Consider **physical therapy/occupational therapy evaluation during the admission** and **referral to Early Intervention Services** to ensure that monitoring for/treatment of developmental delay continues after discharge.

Starting Vigabatrin Therapy at CHCO

1. Inpatient admission for diagnostic work-up and parental education is strongly recommended, but not required in rare cases.
2. ***Detailed instructions on how to prescribe vigabatrin can be found on the Neurology Department intranet site, Epilepsy care team page.***

   STEP 1: Provider must be certified with the Vigabatrin REMS. This enrollment form can be found and completed electronically on the vigabatrin REMS website (preferred method).

   STEP 2: Counsel Parent/Guardian. Review 'What You Need to Know About Vigabatrin Treatment: A Patient Guide" with families. This can be found on the vigabatrin REMS website.

   STEP 3: Patient must be enrolled in the Vigabatrin REMS program and prescriptions generated:

   - Notify the Case Manager (inpatient) or Neurology administrative MA (outpatient). They can assist with the paperwork preparation and faxing.
   - Complete Vigabatrin REMS program paperwork (found on vigabatrin REMS website) and prescription.
   - Fill out the Parent/Physician agreement form.
   - Complete prescription/prescription form (found of chosen manufacturer's website).
   - Ensure needed parent/guardian signatures are obtained prior to submission.
   - Consider documenting the up-titration schedule in a patient chart.
   - Inpatient neurology team to fax all forms and give copies to the Case Manager (inpatient) or Neurology administrative MA (outpatient) as soon as possible, who will upload all documents into Epic under the Media tab.
   - Case Manager or MA to call and verify any/all faxes are received.
3. For inpatient initiation, order vigabatrin in Epic utilizing the Infantile Spasm order set. Must include your NPI number with the order. Pharmacy will dispense a 7-day supply directly to the patient's caregiver/guardian and labeled for outpatient use.
4. ***Dosing (Infants and children 1 month – 2 years):***

   - Vigabatrin 25 mg/kg/dose twice a day – increase by 25-50 mg/kg/DAY increments every 3 days for spasm control, to max of 75mg/kg/dose twice a day.
   - Vigabatrin is available as 500 mg tablets or 500 mg powder sachets for making an oral suspension (CHCO stocks the powder sachets only). Any leftover liquid oral suspension must be thrown away and cannot be reused for subsequent doses. Refer to table below for convenient dosing recommendations using the 500 mg/10mL suspension

Table 2. Dosing Recommendations for Vigabatrin

Weight (kg) - Round to nearest 0.1 kg	Starting dose	Maximum dose
	25 mg/kg/dose twice a day	75 mg/kg/dose twice a day
≤3.2	1.5 mL (75 mg) twice a day	4.5 mL (225 mg) twice a day
3.3-4	2 mL (100 mg) twice a day	5 mL (250 mg) twice a day
4.1-4.6	2 mL (100 mg) twice a day	6 mL (300 mg) twice a day
4.7-5.6	2.5 mL (125 mg) twice a day	7 mL (350 mg) twice a day
5.7-6.7	3 mL (150 mg) twice a day	8.5 mL (425 mg) twice a day
6.8-8.2	3.5 mL (175 mg) twice a day	10 mL (500 mg) twice a day
8.3-9.9	4 mL (200 mg) twice a day	12.5 mL (625 mg) twice a day
10-11.6	5 mL (250 mg) twice a day	15 mL (750 mg) twice a day
11.7-13.2	5.5 mL (275 mg) twice a day	17.5 mL (875 mg) twice a day

13.3-14.9	6 mL (300 mg) twice a day	20 mL (1000 mg) twice a day
15-16.5	7.5 mL (375 mg) twice a day	22.5 mL (1125 mg) twice a day
16.6-19.9	8 mL (400 mg) twice a day	25 mL (1250 mg) twice a day
≥20	10 mL (500 mg) twice a day	30 mL (1500 mg) twice a day

Note: The attending neurologist must verify vigabatrin dosing for all patients.

- At conclusion of treatment, vigabatrin should be tapered off by 25-50 mg/kg/DAY every 3-4 days.
- ***Treatment failure***: If vigabatrin treatment has failed after 2 weeks (see "Follow-up for all Therapies" section), consider switching to an alternative agent with a different mechanism of action (i.e. ACTH or prednisolone). Vigabatrin should be weaned by 25-50 mg/kg/DAY every 3-4 days while simultaneously beginning an alternative agent.

5. ***Duration of therapy***
   - If vigabatrin is successful, optimal duration of treatment is unknown. Common practice is 6 months.
6. ***Monitoring***
   - Per the Vigabatrin REMS program, baseline eye exams **within 4 weeks** of vigabatrin initiation, every 3 months during therapy, and at 3-6 months following discontinuation of therapy are recommended for vigabatrin therapy. Pre-existing visual impairment is not a contraindication for vigabatrin treatment.
   - Baseline MRI is encouraged due to vigabatrin-associated changes on MRI.
7. ***Patient/Caregiver education***
   - Administration: If child is receiving vigabatrin powder for oral suspension, mixing and administration education must be provided. Mixing instruction handouts are available on vigabatrin REMS website.
   - Monitoring for adverse effects: Vigabatrin is NOT associated with hypertension, hyperglycemia, immunosuppression, stomach irritation, increased appetite, or adrenal crisis. Patients taking vigabatrin do NOT require frequent monitoring of blood pressure/blood glucose, PJP prophylaxis, GI prophylaxis, immunization delay, or stress dose steroids. The most common and/or serious side effects associated with vigabatrin include:
     - Sedation
     - Behavioral changes
     - Sleep disturbance
     - Weight gain
     - Permanent vision changes. Vision loss typically occurs only after 6 or more months of therapy. In these patients, there is a 40% risk for peripheral visual field loss. However, given difficulties in monitoring visual development in infants and the potential harm to myelin, the risks and benefits of treatment remain somewhat unclear and should be discussed with family[10]
     - Magnetic resonance imaging (MRI) changes. These are typically signal abnormalities in the thalamus and subcortical regions thought to be consistent with intra-myelinic edema. Changes are usually transient and resolve after cessation of medications. Patients are typically asymptomatic.
   - Parent Education Handout:
     - Infantile Spasms Safety – English and Spanish
     - Ensure that parents/caregivers get the Vigabatrin Parent packet

Starting Adrenocorticotropic Hormone (ACTH, aka Corticotropin) Therapy at CHCO

1. Inpatient admission for diagnostic work-up, injection teaching, and timely medication access is strongly recommended, but not required in rare cases. Patients generally remain hospitalized until medication delivery to home has occurred, to ensure prompt and consistent treatment.
2. Adrenocorticotropin Hormone (also called ACTH, Corticotropin, orActhar Gel) for home use is only available from specialty pharmacies. ACTH order processing (for home use/delivery) is typically unavailable on Saturday and Sunday. However, under some circumstances, delivery might occur on a Saturday. Always complete paperwork as soon as possible during business hours, to avoid unnecessary delays.
    - Please notify CHCO Inpatient RN Case Manager ASAP and provide the Acthar Referral/Prescription Form (found on the ACTHAR.com website) with the following sections completed:
        - HCP Information (section3) – the attending neurologist is the HCP
        - Prescription: H.P. ACTHAR Gel (section 4)
        - Prescription Consent & Statement of Medical Necessity (section 5)
        - Diagnosis & Medical Information (section7)
        - Relevant Treatment History (section8)
        - History of Corticosteroid Use (section9)
        - HCP Signature
    - CHCO RN Case Manager will complete other sections, attach supporting documents, fax information and contact ACTHAR Support Team.
    - CHCO RN Case Manager will follow up with the ACTHAR Support Team and inform the managing medical team and parent regarding the progress of ACTH delivery.
    - **FOR KAISER PATIENTS**:
        - Please notify CHCO Inpatient RN Case Manager ASAP.
        - Case Manager will contact Kaiser Neuro Pharmacists:
            - Shilpa Kinikar: 303.861.3314 office/ 303.907.3521 cell
            - Nikki Hahn: 303.764.4758 office/ 303.902.0520 cell
            - Rachel Heilmann (supervisor): 303.764.5049/ 720.390.2159 cell
        - The Kaiser Neuro Pharmacist will determine the pharmacy benefits for the patient and work in conjunction with the inpatient CHCO Case Manager to obtain ACTH.
        - FYI: Some Commercial Kaiser Insurance Patients do not have a pharmacy benefit. Others have a high deductible or copay. Some Medicaid patients are managed by Kaiser. ACTH is obtained via ACTHAR Support for Kaiser Medicaid Patients.
        - For all Commercial Kaiser Patients, CHCO will obtain the Kaiser Medication Request Form from the Kaiser Neuro Pharmacist and work with the primary team to complete the documentation.
        - Parents must pick up ACTH at a Kaiser Pharmacy. The case manager will work with parents to determine the most convenient pharmacy for pick up.
        - Kaiser will order ACTH once the medication is authorized and approved; however, the drop ship will take 48-72 hours.
        - CHCO RN Case Managers shall serve as point person for communicating the status of the ACTH order with the medical team, Kaiser attending and parents.
3. **Pre-treatment Screening:** Consider whether the patient could have a pre-existing illness or tuberculosis (TB) exposure

- Evaluation for infectious etiology (e.g., CBC and UA) is only necessary if clinically indicated. Routine workup is not needed for an otherwise healthy appearing child. Hold initiation of ACTH if there is clinical suspicion for infection.
- For patients considered at high risk of TB (history of travel or potential exposure), place PPD skin test at least 48 hours prior to the anticipated start of the ACTH, and confirm negative results before first dose. If PPD is positive (induration of 10 mm or greater, or 5mm or greater among children with clinical evidence of TB or in close contact with contagious people with TB), obtain chest X-ray and Infectious Disease consult, and hold initiation of ACTH until cleared by Infectious Disease. Note: PPD is preferable to the Quantiferon-Gold (IGRA) because the IGRA blood test may not be accurate in children less than 2 years of age.

4. **Dosing (Infants and children < 2 years**): There are two ways to give ACTH – either high dose or low dose protocol. There is no clear consensus in the literature as to which treatment protocol is the best. High dose ACTH is felt to possibly be more effective, but with higher side effects. Low dose ACTH is also felt to be effective (perhaps less so) but with fewer side effects. High dose ACTH, with the following tapering schedule, is currently the recommended dose on the package insert (i.e. FDA-approved dosing regimen; 75 units/m2/dose twice a day or BID).

Table 3. High dose ACTH Protocol: dosing based on body surface area of child (requires weight and height)

Schedule	**Dosing – administered via intramuscular injection**
Day 1-14 (weeks 1 and 2)	75 Units/m^2 /dose twice a day Note – it is acceptable for the patient to receive only one dose on Day 1
Taper over two weeks (weeks 3 and 4) as below:	
Day 15-17	30 Units/m^2 /dose every morning
Day 18-20	15 Units/m^2 /dose every morning
Day 21-23	10 Units/m^2 /dose every morning
Day 24-30	10 Units/m^2 /dose every other morning (Days 25, 27, and 29). On Day 30, treatment is complete.

Treatment failure: If ACTH treatment has failed after 2 weeks (see "Follow-up for all therapies" section), consider switching to an alternative agent with a different mechanism of action (i.e. vigabatrin). Taper ACTH according to the protocol above, while simultaneously beginning an alternative agent. If an expedited taper is necessary, discuss dosing with endocrine.

5. **Gastrointestinal prophylaxis**: H2 blocker or proton pump inhibitor is required during the full course of ACTH treatment (e.g. ranitidine, omeprazole, or lansoprazole). GI prophylaxis can be stopped when ACTH is stopped.
6. **PJP prophylaxis:** Patients will be immunosuppressed while on ACTH and for weeks after ACTH treatment. PJP prophylaxis is needed with Bactrim 2.5 mg/kg/dose two times a day or BID on three consecutive days each week (preferred practice is Monday, Tuesday and Wednesday) during ACTH treatment and for an additional 4 weeks after ACTH treatment is stopped.
7. **Immunizations:** Consult the Red Book for latest recommendations. In general, children receiving high dose systemic corticosteroids (such as ACTH or prednisolone) should NOT receive LIVE-virus vaccines until 4 weeks after discontinuation of steroids. Inactivated vaccines may be temporarily deferred until corticosteroids are discontinued or may be given during corticosteroid treatment if caregiver adherence with follow-up is not likely.
8. **Stress dose steroids**: At the cessation of steroids or with illness, there may be a need for stress dose steroids. Patients will have adrenal insufficiency after the course of ACTH for as long as they received the medication, (e.g. a patient treated with 4 weeks of ACTH will have adrenal insufficiency for 4 weeks following cessation of therapy). They should be evaluated by a physician for any signs of illness including fever, vomiting, diarrhea, or with trauma to assess for hypoglycemia and hypotension.

9. **Monitoring**: Common side effects from ACTH include hypertension, hyperglycemia, irritability, immunosuppression, stomach irritation, increased appetite, and adrenal crisis (especially if stopped abruptly).
    - Hypertension:
        - Blood pressure monitoring is required 2-3 times per week. This is generally performed by the PCP but can also be arranged via Neurology RN office visits. Ensure that appropriate size BP cuff is available.
        - Sustained hypertension is defined as systolic blood pressure (SBP) greater than 95th% (in children <12 months of age, SBP>100 is >95th%) on 3 consecutive days.
        - Sustained hypertension can be a sign of steroid-induced endocrine dysfunction or cardiomyopathy (septal hypertrophy), which can develop after 5+ days of ACTH treatment. BP monitoring and prompt attention to hypertension is critical. Follow the hypertension algorithm in Appendix A.
    - Hyperglycemia:
        - Weekly glucose monitoring is required. Consider either blood glucose monitoring or use of urine glucose dipsticks.
        - Educate family to notify PCP of increased urine output.
        - If hyperglycemia occurs (glucose is >200), ensure the patient's PCP is involved. Draw a BMP to check for hypokalemia. Insulin treatment may be required. Endocrinology may be paged at 303 201-0927 to assist with a treatment plan.
10. **Caregiver/Parent Education**
    - Administration: Parent education on IM injection of medication, rotating sites, and general care
        - See Intramuscular ACTH injection handout – English and Spanish
    - Infantile Spasms Safety – Infantile Spasms Safety – English and Spanish
    - Monitoring for adverse effects:
        - Instruct caregivers to note increased urine output (possible elevated glucose) and notify PCP.
        - Warn families of the risk of thrush and that patient may not develop fever even if ill.
    - As much as possible, keep patient away from other children or individuals who have been ill, due to potential for immunosuppression.
    - Instruct caregivers to NOT give patient any cold or allergy medications without first consulting their PCP as this may cause a rapid and dangerous rise in blood pressure.
    - Create an emergency letter for families to carry to alert providers to the risk of adrenal insufficiency and immunosuppression. The FYI adrenal phrase should be included in their emergency letter with dates listed, and can be added to their EPIC chart as an FYI.

Starting Prednisolone Therapy at CHCO

1. Inpatient admission for diagnostic work-up and parental education is strongly recommended, but not required in rare cases. Patients can be discharged once diagnostic work-up is complete, and prednisolone prescription has been filled.
2. **Pre-treatment Screening**: Consider whether the patient could have a pre-existing illness or tuberculosis (TB) exposure
    - Evaluation for infectious etiology (e.g., CBC and UA) is only necessary if clinically indicated. Routine workup is not needed for an otherwise well- appearing child. Hold initiation of prednisolone if there is clinical suspicion for infection.
    - For patients considered at high risk of TB (history of travel or potential exposure), place PPD skin test at least 48 hours prior to the anticipated start of the prednisolone and confirm negative results before first

dose. If PPD is positive (induration of 10 mm or greater, or 5mm or greater among children with clinical evidence of TB or in close contact with contagious people with TB), obtain chest X-ray and Infectious Disease consult, and hold initiation of prednisolone until cleared by Infectious Disease. Note: PPD is preferable to the Quantiferon-Gold (IGRA) because the IGRA blood test may not be accurate in children less than 2 years of age.

3. **Dosing:** Prednisolone is the active metabolite of prednisone and may have better bioavailability.

   Oral prednisolone protocol**:** There are two ways to give prednisolone, either high dose (4 mg/kg/DAY; UKISS trial[8]) or very high dose protocol (8 mg/kg/DAY; UCLA study[9]). There is no clear consensus in the literature as to which treatment protocol is the best. Very high dose prednisolone may be more effective, but possibly with higher side effects. At CHCO, we recommend the very high dose prednisolone protocol (8mg/kg/DAY or ~2.6mg/kg/dose three times a day or TID).

Table 4. Oral Prednisolone Protocol – Schedule and Dosing

Note: The attending neurologist must verify prednisolone dosing for all patients.

Schedule

Days	Dose
1-14	2.6mg/kg/dose three times a day (~8mg/kg/DAY). Max 60 mg/DAY (see next table for convenient oral dosing by weight)
15-21	2.6mg/kg/dose twice a day
21-28	2.6mg/kg/dose once a day
29	stop prednisolone

Dosing (15mg/5ml suspension)

Weight (kg)*	mg per dose	mL per dose
≤3.3	7.5 mg	2.5 mL
3.4-3.9	9 mg	3 mL
4-4.4	10.5 mg	3.5 mL
4.5-5	12 mg	4 mL
5.1-5.5	13.5 mg	4.5 mL
5.6-6.1	15 mg	5 mL
6.2-6.7	16.5 mg	5.5 mL
6.8-7.4	18 mg	6 mL
≥7.5	19.8 mg	6.6 mL

*round up to nearest 0.1 kg

Example: 5 kg baby would receive 12 mg (4 mL) three times a day x 2 weeks. To taper, give 12 mg (4 mL) twice a day x 1 week, then 12 mg (4 mL) daily x 1 week, then stop.

Treatment failure: If prednisolone treatment has failed after 2 weeks (see "Follow-up for all therapies" section), consider switching to an alternative agent with a different mechanism of action (i.e. vigabatrin). Taper prednisolone according to the protocol above, while simultaneously beginning an alternative agent. If an expedited taper is necessary, discuss dosing with endocrine.

4. **Gastrointestinal prophylaxis:** H2 blocker or proton pump inhibitor is required during the full course of prednisolone treatment (e.g. ranitidine, omeprazole, or lansoprazole). GI prophylaxis can be stopped when prednisolone is stopped.
5. **PJP prophylaxis:** Patients will be immunosuppressed while on prednisolone. PJP prophylaxis is needed with Bactrim 2.5 mg/kg/dose BID on three consecutive days each week (preferred practice is Monday, Tuesday and Wednesday), during prednisolone treatment and **for an additional 4 weeks** after prednisolone treatment is stopped.
6. **Immunizations:** Consult the Red Book for latest recommendations. In general, children receiving high dose systemic corticosteroids (such as ACTH or prednisolone) should NOT receive LIVE-virus vaccines until 4 weeks after discontinuation of steroids. Inactivated vaccines may be temporarily deferred until corticosteroids are discontinued or may be given during corticosteroid treatment if caregiver adherence with follow-up is not likely.

7. **Stress dose steroids:**
    - At the cessation of steroids or with illness, there may be a need for stress dose steroids. Patients will have adrenal insufficiency after the course of prednisolone for as long as they received the medication, (e.g. a patient treated with 4 weeks of prednisolone will have adrenal insufficiency for 4 weeks following cessation of therapy).
    - They should be evaluated by a physician for any signs of illness including fever, vomiting, diarrhea, or with trauma to assess for hypoglycemia and hypotension.
    - Create an emergency letter for families to carry to alert providers to the risk of adrenal insufficiency and immunosuppression (can use the EPIC smartphrase DOTACTHADRENALLETTER).
    - An FYI should be placed in the patient's EPIC chart.
8. **Monitoring:** Common side effects from prednisolone include hypertension, hyperglycemia, irritability, immunosuppression, stomach irritation, increased appetite, and adrenal crisis (especially if stopped abruptly).
    - Hypertension:
        - Blood pressure monitoring is required 2-3 times per week. This is generally performed by the PJP but can also be arranged via Neurology RN office visits. Ensure that appropriate size BP cuff is available.
        - Sustained hypertension is defined as systolic blood pressure (SBP) greater than 95th% (in children <12 months of age, SBP>100 is >95th%) on 3 consecutive days.
        - Sustained hypertension can be a sign of steroid-induced endocrine dysfunction. BP monitoring and prompt attention to hypertension is critical. Follow the hypertension algorithm in the ACTH section. Note that prednisolone is NOT associated with septal hypertrophy, therefore ECHO is not required.
    - Hyperglycemia:
        - Weekly glucose monitoring is required. Consider either blood glucose monitoring or use of urine glucose dipsticks.
        - Educate family to notify PCP of increased urine output.
        - If hyperglycemia occurs (glucose is >200), ensure the patient's PCP is involved. Insulin treatment may be required. Draw a BMP to check for hypokalemia. Endocrinology may be paged at 303-201-0927 to assist with a treatment plan.
9. **Caregiver/Parent Education**
    - Infantile Spasms Safety – English and Spanish
    - Giving Prednisolone for Infantile Spasms – English and Spanish
    - Monitoring for adverse effects:
        - Instruct caregivers to note increased urine output (possible elevated glucose) and notify PCP.
        - Warn families of the risk of thrush and that patient may not develop fever even if ill.
    - As much as possible, keep patient away from other children or individuals who have been ill, due to potential for immunosuppression.
    - Instruct caregivers to NOT give patient any cold or allergy medications without first consulting their PCP as this may cause a rapid and dangerous rise in blood pressure.

FOLLOW-UP FOR ALL THERAPIES

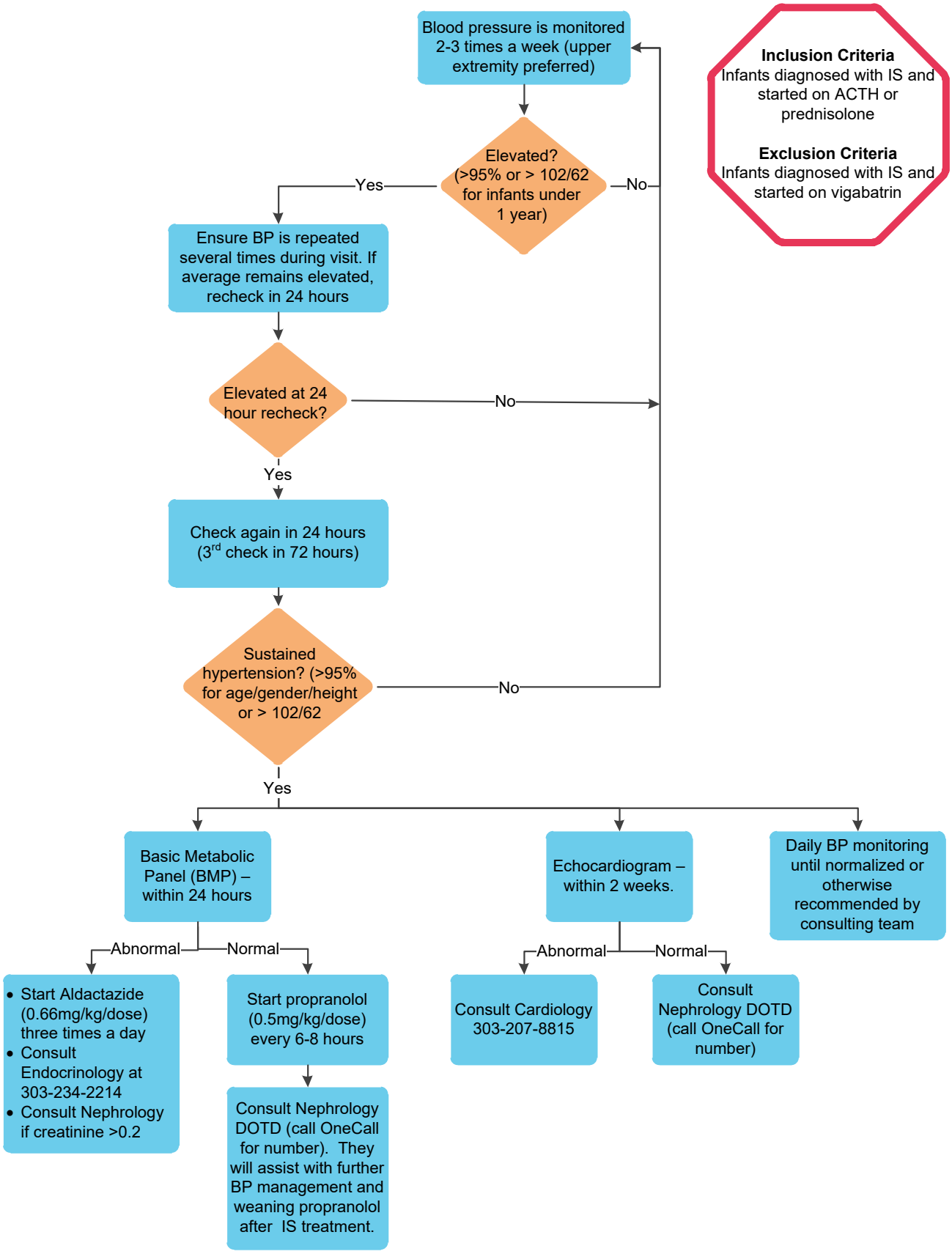
Following the initiation of any first-line treatment, efficacy of therapy should be assessed **by 2 weeks**. Short-term outcomes include cessation of spasms and EEG confirmation of treatment response showing resolution of hypsarhythmia.

- EEG should be used to assess for resolution of spasms and hypsarhythmia at 12-16 days. EEG should be of sufficient duration to include wake and sleep. Contact EEG department directly to arrange (720-777-5402).
- Clinic visit with pediatric neurology should occur at the same time frame as repeat EEG.
- If spasms or hypsarhythmia persist at 2 weeks:
  - Many children will respond to an alternative first-line therapy. Consider switching treatment to an alternative first-line treatment with a different mechanism of action. Follow the weaning protocols outlined for the specific first-line agent.
  - Efficacy of the alternative therapy should also be assessed at 2 weeks, as above.
  - In patients without a clear etiology for IS, consider vitamin B6 diagnostic challenge.
- If spasms or hypsarhythmia persists or recur 2 weeks after treatment with an alternative first-line medication, consider prompt referral to an epileptologist to pursue additional treatment options.
- Consider repeat EEG 1-4 weeks after completion of treatment to confirm sustained efficacy. Also consider repeat EEG if there is concern for developmental plateau/regression or clinical seizures.
- If spasms or hypsarhythmia abnormalities persist or recur in the absence of an established etiology, or if the child does not follow the expected treatment course based on the established etiology, the etiology should be further investigated, to include at least 1 of the following: repeat video EEG monitoring, MRI, or genetic/metabolic studies.
- PCP and neurology should monitor neurodevelopment closely and involve Early Intervention services when appropriate. A diagnosis of IS qualifies for Early Intervention.
- Neuropsychological testing is recommended within the first two years of life.

RELATED DOCUMENTS

Vigabatrin: Risk Evaluation and Mitigation Strategy (REMS)

APPENDIX A. HYPERTENSION ALGORITHM



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Pharmacy & Therapeutics Committee – June 1, 2017

Clinical Pathways and Measures Committee – June 13, 2017

MANUAL/DEPARTMENT	Clinical Care Guidelines/Quality
ORIGINATION DATE	January 1, 2015
LAST DATE OF REVIEW OR REVISION	June 13, 2017
APPROVED BY	 Lalit Bajaj, MD, MPH Medical Director, Clinical Effectiveness

REVIEW | REVISION SCHEDULE

Scheduled for full review on June 13, 2021

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