

Infants and Children - Acute Management of Seizures

Summary This Guideline is a best clinical practice guide for the acute management of seizures in children and infants older than 28 days post term in the acute care setting.

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INFANTS AND CHILDREN - ACUTE MANAGEMENT OF SEIZURES

PURPOSE

This Clinical Practice Guideline provides evidence based direction for clinicians in the acute management of seizures in infants and children older than 28 days. It is aimed at achieving the best possible care including assessment, management and where required escalation to a higher level of care.

KEY PRINCIPLES

This Guideline applies to all facilities where paediatric patients are managed. It requires Chief Executives of all Local Health Districts and Specialty Health Networks to determine where local adaptations are required or whether it can be adopted in its current format in all hospitals and facilities required to manage seizures in infants and children.

This Guideline reflects what is currently regarded as a safe and appropriate approach to the management of seizures in infants and children older than 28 days. However, as in any clinical situation, there may be factors which cannot be covered by a single set of guidelines. This document should be used as a guide, rather than as a complete authoritative statement of procedures to be followed in respect of each individual presentation. It does not replace the need for application of clinical judgement of each individual presentation.

USE OF THE GUIDELINE

Chief Executives must ensure:

- This Clinical Practice Guideline Infants and Children Acute Management of Seizures is adopted or local protocols are developed based on the Guideline
- Local protocols are in place in all hospitals and facilities likely to be required to manage paediatric patients with seizures
- Ensure that all staff treating paediatric patients are educated in the use of the locally developed paediatric protocols.

Directors of clinical governance are required to inform relevant clinical staff treating paediatric patients of this revised guideline.



REVISION HISTORY

Version	Approved by	Amendment notes
	Deputy	Changes to assessment and management of
June 2018	Secretary,	hypoglycaemia, removal of rapid sequence
(GL2018_015)	Strategy and	induction for anaesthesia and revision of dosage for
	Resources	second line antiepileptic drug, levetiracetam.
	Deputy	
February 2016	Secretary,	Third edition
(GL2016_005)	Population and	Changes to medications used in status epilepticus
	Public Health	
	Deputy Director-	
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(PD2009_065)	Strategic	
	Development	
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(PD2006_023)		
December 2004	Director-General	New policy
(PD2005_389)		

ATTACHMENTS

1. Infants and Children - Acute Management of Seizures: Guideline

Infants and Children - Acute Management of Seizures



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1. PURPOSE

1.1 About this document

This guideline presents the current best evidence for acute management of seizures in infants and children. Its purpose is to inform practice for NSW health care providers.

The document should not be seen as a stringent set of rules to be applied without the clinical input and discretion of the managing professionals. Each patient should be individually evaluated and a decision made as to appropriate management in order to achieve the best clinical outcome.

This guideline is primarily targeted to clinicians, caring for infants (after the neonatal period) and children, undertaking any task related to acute management of seizures in paediatric acute healthcare.

In 2017 a targeted review of the 2016 guideline was undertaken to address management of hypoglycaemia and rapid sequence induction. It is recommended that the literature is revisited and this document reviewed in 2020 as the last comprehensive review was undertaken in 2015.

This guideline was developed by a representative group of NSW clinicians with expertise in acute paediatric care and paediatric neurology. No conflict of interest was identified.

In the interests of patient care it is critical that contemporaneous, accurate and complete documentation is maintained during the course of patient management from arrival to discharge.

Parental anxiety should not be discounted.

It is often of significance even if the child does not appear especially unwell.

Respecting the difference – be aware of cultural differences and factors influencing the health of Aboriginal people. Refer to your local Aboriginal Liaison Officer or for further information see <u>NSW Health Communicating positively – A guide to appropriate Aboriginal terminology.</u>

2. CHANGES FROM PREVIOUS CLINICAL PRACTICE GUIDELINE

The following sections have been changed in this version to align with current evidence, standards and expert advice:

Section:

- 4. Algorithm: acute Intravenous (IV) fluid maintenance and rapid sequence induction
- 5. Assessment and Management, 5.7 Glucose: Standard IV fluid maintenance and rates



• **10. Evidence Base for Use of Antiepileptic Drugs**, 10.2 Second line antiepileptics for refractory status epilepticus: IV Levetiracetam dosage.

3. OVERVIEW

Seizures are a common occurrence in children: about eight per cent will have at least one seizure by 15 years of age. A seizure may be defined as a sudden attack of altered behaviour, consciousness, sensation or autonomic function produced by a transient disruption of brain function. The result of this altered brain function is most commonly a tonic (stiffening) or tonic-clonic (stiffening-jerking) seizure. When the seizure has motor accompaniments, it is also known as a convulsion. Non-convulsive seizures, i.e. those not associated with motor phenomena may also occur, but are rare and occur usually in the context of a child with a previous diagnosis of epilepsy.

Many underlying conditions and neurological challenges may provoke seizures. In over 50% of children, seizures are isolated events associated with either a fever (febrile seizures or febrile convulsions) or minor head injury in early childhood. Most acute seizures in children are brief, terminating spontaneously and do not need any treatment. Seizures that persist beyond five minutes may not stop spontaneously. Seizure control then becomes a matter of urgency, as the longer the seizure the more difficult it is to obtain control of the seizure.

Given that most acute seizures in children stop spontaneously, usually during transit to hospital, it should be assumed that if a child is still convulsing on arrival in the Emergency Department the seizure would continue unless treated. In this situation the child should be treated as if they are in 'established' status epilepticus.

The term status epilepticus means prolonged seizures, however, there are differences in the definition of prolonged. Regardless, it is important to promptly treat seizures lasting for more than five minutes as the longer the duration of the seizure, the more difficult it is to control. For operational purposes, in particular clinical management and administration of anti-seizure medications, a seizure lasting more than five minutes is considered status epilepticus.

A child whose conscious state is not improving as expected after apparent termination of the seizure may be in subclinical status and require further treatment according to the algorithm.

Mortality in convulsive status epilepticus is less common in children than adults. Amongst those whose seizures lasted longer than 30 minutes, 0-2% mortality has been reported due to the seizure itself.³

In some children with a diagnosis of epilepsy, a previously individualised acute seizure management plan devised by the child's paediatrician may be followed and may be administered at home or at school. In most children who have acute prolonged seizures, the seizure will be managed by ambulance or hospital staff.

Please note:

 In the algorithm, the timing is from onset of seizure, and not from the arrival to the Emergency Department



- Prolonged seizures and/or repeated doses of antiepileptic medications especially benzodiazepines, may lead to a compromise of breathing requiring on-going respiratory support, including intubation
- In assessing medication load, one needs to consider benzodiazepines given by carers and ambulance personnel as part of the total dosage
- Midazolam or diazepam administered <1 hour prior to presentation to emergency departments should be regarded as 'initial doses already given' in the algorithm
- After no response to two doses of midazolam, appropriate second line antiepileptics i.e. a long acting antiepileptic (e.g. phenytoin, phenobarbitone, levetiracetam) should be introduced early (i.e. at 20 minutes from onset of seizure).⁴

4. ALGORITHM

See following page.



ACUTE MANAGEMENT OF SEIZURES FOR INFANTS AND CHILDREN





5. ASSESSMENT AND MANAGEMENT

The first step in the management of the patient who is having a seizure is to assess and support airway, breathing and circulation. This will ensure that the seizure does not compromise supply of oxygenated blood to the brain and is not secondary to hypoxia and/or ischaemia.⁵

5.1 Airway

A clear airway is the first requisite. If the airway is not clear, it should be opened and maintained with a head tilt/chin lift or jaw thrust manoeuver while the child is in a supine position.

An oropharyngeal or nasopharyngeal airway may be used.

If the airway is compromised due to the seizure, controlling the seizure with antiepileptics will generally control the airway.

Even if the airway is clear, the oropharynx may need secretion clearance by gentle suction. After initial airway clearance, the airway should continue to be observed and protected as required. Post seizure a child should be positioned on his or her side (recovery position).

5.2 Breathing

Assess the following for adequacy of breathing by the 'look, listen and feel' method:

- Effort of breathing:
 - recession
 - respiratory rate
 - grunting. This may be caused by the convulsion and not be a sign of respiratory distress in this instance.
- Efficacy of breathing:
 - breath sounds
 - chest expansion/abdominal excursion
 - monitor oxygen saturation with a pulse oximeter
- Effects of breathing:
 - heart rate
 - skin colour

All fitting children should receive high flow oxygen through a face mask with a reservoir as soon as the airway has been demonstrated to be adequate.

If the child's breathing is inadequate, respiration should be supported with oxygen via a bag-valve-mask device and experienced senior clinical help summoned.

Prolonged seizures and/or repeated doses of antiepileptic medications may lead to compromise of airway and breathing requiring ongoing support, including



intubation. Help from senior clinicians, if necessary using telehealth, should be obtained for intubation.

5.3 Circulation

Assess the following for adequacy of cardiovascular status:

- Heart rate: the presence of an inappropriate bradycardia or hypertension will suggest raised intracranial pressure
- Pulse volume: assess the adequacy of circulation by palpation of central pulses (femoral, brachial)
- Capillary refill: capillary refill should be three seconds or less and is measured by applying cutaneous pressure on the centre of the sternum for 5 seconds
- Blood pressure: significant (>97th percentile for age) hypertension indicates a possible aetiology for the seizure
- Effects of circulatory inadequacy on other organs pale, cyanosed or cold skin.
- Gain intravenous access. If vascular access is not readily obtained, initial doses of antiepileptics should be given by the buccal, intra-nasal or intramuscular route.

Intraosseous access should be obtained immediately in children with signs of shock if intravenous access is not readily obtained. Intraosseous access may be needed for administration of long-acting antiepileptics if there is no intravenous access after two doses of a benzodiazepine.

Give 20 mL/kg rapid bolus of 0.9% sodium chloride to any patient with signs of shock or sepsis - see <u>Paediatric Sepsis Pathway</u>.

Give antibiotics to any child with suspected meningitis or sepsis according to the NSW <u>Bacterial Meningitis Clinical Practice Guideline</u> or the CEC <u>Paediatric Sepsis</u> <u>Pathway</u>. If possible, blood should be collected for culture first, but this should not delay administration of antibiotics.

Check blood pressure as soon as the seizure has finished.

5.4 Disability

Assess the following for adequacy of neurological function:

- The Alert, Voice, Pain, Unresponsive (AVPU) score cannot be measured meaningfully during a seizure as a generalised seizure depresses the level of consciousness
- Pupillary size, reaction and symmetry should be noted. Pupillary changes can occur during a seizure but may also result from poisoning or raised intracranial pressure. Very small pupils suggest brainstem injury or opiate poisoning, large pupils suggest amphetamine, atropine, or tricyclic antidepressant poisoning
- Note the child's posture. Decorticate or decerebrate posturing in a previously normal child should suggest raised intracranial pressure. These postures can sometimes be mistaken for the tonic phase of a seizure. Consider also the



possibility of a drug-induced dystonia that is distinguishable from tonic-clonic status epilepticus

• Assess for neck stiffness in a child and a bulging fontanelle in an infant, which suggests meningitis.

Document any focal neurological signs, either during or after the seizure. Prolonged seizures and/or repeated doses of antiepileptic medications may cause prolonged depression of consciousness and lead to compromise of airway and breathing, requiring ongoing support including intubation.

5.5 Exposure

- Look for rash and bruising as signs of sepsis or injury
- Measure temperature.

5.6 Fluids

Correct any fluid or electrolyte imbalance according to established protocols. See: <u>Standards for Paediatric IV Fluids: NSW Health (Second Edition)</u>.

5.7 Glucose

"Don't Ever Forget Glucose". Take blood glucose stick test and laboratory test. Give a bolus of 2 mL/kg of 10% glucose to any hypoglycaemic patient (BGL < 3 mmol/L⁴). If possible, take 10 mL of clotted blood before giving the glucose for later investigation of the hypoglycaemic state.

Following initial bolus:

- Check BGL
- Commence standard IV fluids, 0.9% sodium chloride with 5-10% glucose in accordance with the NSW Standards for Paediatric IV Fluids at standard rates
- Frequently measure BGL.

Hypoglycemia due to an inborn error of metabolism will usually respond to increased amounts of glucose, for example, sodium chloride with 10% glucose at a rate of 5mL/kg/hr (providing 8mg/kg/min). Even larger amounts of glucose may be required to correct hypoglycaemia associated with hyperinsulinism.

Children who present with hypoglycaemia associated seizures should have serum insulin, cortisol and metabolic work-up as per the <u>Infants and Children: Acute Management of</u> <u>Altered Consciousness in Emergency Departments (1st Edition)</u>. Early advice should be sought from a metabolic or endocrine paediatrician.

5.8 Ongoing monitoring and reassessment of A - G

In addition to continuous visual observation and monitoring with ECG and oximetry, the vital signs and neurological status should be reassessed and documented frequently on



the relevant Standard Paediatric Observation Chart/Standard Paediatric Emergency Department Observation Chart:

- After each dose of antiepileptic medication
- Every 5 minutes while the seizure continues
- Every 15 minutes after a seizure until level of consciousness returns to normal.

6. MEDICATION USED IN ACUTE SEIZURES

Buccal or intranasal midazolam can be administered in the emergency management of prolonged seizures^{1,6} when intravenous access cannot be obtained. Buccal or intranasal midazolam may be used in combination with other antiepileptic drugs. Midazolam or diazepam <1 hour prior to presentation should be regarded as initial doses already given.

Technique for Intranasal and Buccal Administration of Midazolam

Buccal administration of midazolam can be achieved by trickling the appropriate dose between the lower cheek and gum with the patient in the recovery position. This technique aids absorption directly through the buccal mucosa, providing more rapid absorption than if the midazolam was swallowed.

Intranasal administration can be achieved by instilling the appropriate dose into the nasal passage a few drops at a time or by using a Mucosal Atomiser Device (MAD) into one or both nostrils.

Medication Name: Route(s)	Dose and administration
Midazolam: buccal/intranasal	0.3 mg/kg (maximum 10 mg) Off label use - see special considerations
Midazolam: intravenous/intraosseous/intramuscular	0.15 mg/kg (max 10 mg)
Diazepam: intravenous/intraosseous	0.25 mg/kg (max 10 mg)
Phenytoin: intravenous/intraosseous	20 mg/kg in 0.9% sodium chloride If ≤ 50 kg infuse over 20 minutes * For adolescents >50kg administer at a rate of 50 mg/minute or slower. ECG and BP monitoring required. * For more information see page 15 or the Australian
	Injectable Drugs Handbook

Table 1: Medications used in acute seizures 7,14,15, 21



Medication Name: Route(s)	Dose and administration
Phenobarbitone: intravenous/intraosseous	20 mg/kg (maximum 1 g) If ≤30kg infuse over 20 minutes For patients >30kg infuse at a rate of 30mg/min See Australian Injectable Drugs Handbook, for more information
Levetiracetam: intravenous/intraosseous (limited evidence available see pg. 13)	20 mg/kg (maximum dose 1.5 g) <i>Further dosing may be required and should be based</i> <i>on recommendations from a paediatric neurologist.</i> Dilute in 100mL of 0.9% sodium chloride or 5% glucose and give over 15 minutes. If necessary a more concentrated solution of 5mg/mL may be used. <i>See Australian Injectable Drugs Handbook, for</i> <i>more information</i>
Pyridoxine: intravenous/ oral enteral	Should be used only after discussion with a paediatric neurologist. Give 50–100 mg as a single initial dose (i.e. not in mg/kg) Dose may be repeated after 10 minutes. A maximum total dose up to 500 mg. If intravenous route is used, give as a slow injection. Special monitoring and ward requirements-see page 15.
Thiopentone: intravenous/intraosseous	Now rarely indicated and should only be considered in consultation with an intensivist 2-5 mg/kg



Medication Name: Route(s)	Dose and administration
Sodium Valproate: Intravenous/intraosseous	Should only be considered in consultation with a paediatric neurologist 20-40 mg/kg over 3-5 minutes, then 1-5 mg/kg/hour infusion. Dilute in 0.9% sodium chloride or 5% glucose. *Caution use in the child less than 3 years ⁷ OR mitochondrial disorder OR family history of liver failure because of the risk of acute encephalopathy and hepatic failure.

7. FOCUSED HISTORY

Whilst the primary assessment and resuscitation are being carried out, a focused history of the child's health and activity over the previous 24 hours and any significant previous illness should be gained. Specific points for history taking include:

- Current febrile illness
- Neurologic state prior to the seizure
- Recent trauma. Consider non-accidental injury
- History of epilepsy
- Current medication and allergies
- Recent immunisation
- Poison ingestion including lead, tricyclic antidepressants, benzodiazepines, antipsychotics and salicylates. Antiepileptic toxicity may also exacerbate seizures
- Past medical history, immunisations.

8. SPECIALIST CONSULTATION/TRANSFER

If in doubt or unsure about a child's clinical condition, signs or symptoms, consult with someone more experienced such as a paediatric specialist. If a specialist is not available, escalate as per local **Clinical Escalation Response System (CERS)** policy or call **NETS** (the NSW Newborn and paediatric Emergency Transport Service) on **1300 36 2500**. **NETS** will set up a conference call which includes a paediatrician and other relevant paediatric specialists as well as organise urgent transfer of a child to a paediatric centre if necessary.



The treating doctor should consult with a specialist about:

- Children with compromise of vital functions:
 - Airway compromise requiring intubation
 - Breathing compromise e.g. persistent hypoventilation, aspiration
 - Circulatory compromise e.g. requiring more than 20 mL/kg fluid bolus
 - Neurological compromise e.g. localizing signs focal fit, asymmetry of movement, asymmetry of reflexes; prolonged depression of level of consciousness
- Prolonged seizures
- Seizures continuing after two doses of a benzodiazepine
- Suspected serious underlying cause of seizures e.g. meningitis, metabolic abnormality, head injury.

9. POST SEIZURE CARE

- Position child in recovery position, on left side
- Maintain airway (jaw thrust, chin lift, suction)
- Maintain continuous monitoring of pulse, respiratory rate, oximetry and neurological status until child is fully recovered.

Bloods:

Calcium, magnesium, glucose level and venous blood gas should be measured in any child who is continuing to fit, or has not regained full consciousness at presentation. Electrolytes, Urea, Creatinine (EUC) should be collected if there has been repeated diarrhoea or vomiting. Carbon dioxide (CO₂) will usually be high during and shortly after a seizure. This can be tolerated if oxygenation is adequate, the seizure is controlled, and the level of consciousness is improving. Antiepileptic drug levels should be measured if previously regularly administered. Blood count and culture should be collected if a child has prolonged seizure with fever, or if sepsis is suspected. Cerebral imaging should be arranged if the seizure was focal. If meningitis is suspected intravenous antibiotics must be administered promptly according to the Bacterial Meningitis Clinical Practice Guideline and/or Paediatric Sepsis Pathway. Lumbar Puncture should be considered if meningitis is suspected and there are no contraindications.

History/examination:

Search for an underlying cause (head injury, sepsis, meningitis, metabolic), and include localisation of infection when febrile (when appropriate refer to other Clinical Practice Guidelines e.g. <u>Fever</u>, <u>Meningitis</u>, <u>Recognition of the Sick Child</u>. Poisoning may be suggested by the history, clinical features of toxidromes (anticholinergic, serotonin,



sympathomimetic), a widened QRS complex or hypoglycaemia. Contact the Poisons Information Centre on 131126 for advice.

Antibiotics:

Consider antibiotics if bacterial sepsis cannot be excluded.

10. EVIDENCE BASE FOR USE OF ANTIEPILEPTIC DRUGS

In choosing an antiepileptic drug, the desired outcome of most rapid cessation of acute seizures, with smallest possible incidence of side effects, at minimal cost was chosen. Consideration was also given to variation in regional availability of antiepileptic drugs. Early treatment is essential, as once seizures are established for more than 15 minutes, they become more difficult to control.

For refractory seizures the second line antiepileptic drug should be compatible with the first line agent. Second line agents should ideally work synergistically without contributing to side effects and be more effective in preventing ongoing seizures. Phenytoin and phenobarbitone remain the cornerstone of second line therapy. Experience of levetiracetam as a second line drug for continuing seizures is limited.

Several antiepileptic drugs presented in this guideline are considered off label. The term "off label" refers to registered medications being used in ways other than specified in the Australian Therapeutic Goods Administration (TGA) such as for a patient outside the age/gender of the registered use, via an alternate route, at a different dose or for another indication.²² Off label use of medicines generally have less supporting evidence and guidance regarding efficacy, safety and cost effectiveness.²²

In determining the justified clinical need for off label use of medicines in this guideline, the working party considered:

- the current evidence
- opinion of paediatric neurologists
- paediatric pharmacists guidance

to represent the best available options in the acute management of seizures in infants and children.

10.1 First line therapies

Midazolam - has replaced rectal diazepam as the drug of first choice before venous access has been obtained, because of improved efficacy, preferred route of administration (buccal vs. rectal).¹ As a first line antiepileptic, the majority of seizures are stopped within one minute after IV injection of 0.1–0.3 mg/ kg and within 5-10 minutes after IM midazolam. Intramuscular midazolam has superior absorption in comparison with diazepam and lorazepam because of its water solubility. Intranasal and IM midazolam has been adopted by the NSW Ambulance Service as the drug of first choice in status epilepticus.⁴



Widely used, buccal and intranasal route of administration remain off label. In practice, the injection solution is used for buccal and intranasal administration, commonly in the form of 5mg/mL plastic ampoules. The solution is bitter and acidic, and may cause nasal irritation when given via the intranasal route⁷.

Midazolam and other benzodiazepines may lead to respiratory depression, with a more marked effect in patients receiving multiple doses. A single dose of buccal or intranasal midazolam 0.5 mg/kg has been shown to carry minimal risk of respiratory depression. If there has been no response to TWO doses of midazolam via any route of administration, appropriate second line antiepileptics i.e. a long acting antiepileptic (e.g. phenytoin, phenobarbitone, levetiracetam) should be introduced within 20 minutes.

Diazepam - has been used both intravenously and rectally for first line control of status epilepticus. Intravenous administration produces rapid control of seizures in approximately 80 % of patients. Rectal diazepam is no longer recommended as midazolam, administered by buccal, nasal or intramuscular route is more effective.^{1,13}

Lorazepam - no significant difference in effectiveness has been demonstrated between intravenous lorazepam and intravenous diazepam in children with convulsive status epilepticus. Lorazepam is only available on the Therapeutic Goods Administration (TGA) Special Access Scheme in Australia.

10.2 Second line antiepileptics for refractory status epilepticus

Phenytoin, as a single 20 mg/kg dose IV provides good seizure control in 60–80% of children within 20 minutes. It is less likely to cause respiratory depression than phenobarbitone, particularly following benzodiazepine administration. There are few acute side effects when administered in recommended doses. Consideration should be given to obese children. There are no standard recommendations for phenytoin dose adjustment in obesity an adjusted body weight has been suggested (i.e. Adjusted body weight (kg) = Ideal Body Weight (IBW) + 1.33 (measured weight – IBW) for loading doses up to the adult maximum²³. Ideal Body Weight should be used for subsequent maintenance doses with appropriate therapeutic drug monitoring and dose adjustment.

Phenytoin is poorly soluble and should be diluted in 0.9% sodium chloride only. After inspection for signs of precipitation (haze or cloudiness) the prepared product should be administered immediately. Caution must be taken to ensure the prepared product is not inadvertently mixed with other medications or incompatible fluids. A 0.22-0.55 micron filter should be used if available. See Australian Injectable Drugs Handbook, for additional advice on administration.

Phlebitis is probably the most common minor effect, a flush with 0.9% sodium chloride before and after the infusion, and administration via a large vein are recommended. The catheter insertion site should also be closely monitored.

The main risk of rapid acute therapy with phenytoin is asystole; this is rare when administered at the prescribed administration rate (Table 1). If hypotension or bradycardia



is observed, the infusion rate should be halved and keep the patient closely monitored. Additives such as propylene glycol and alcohol may contribute to this side effect.

The close relative fosphenytoin is not available in Australia and there is little evidence of its superiority over phenytoin.

Phenobarbitone has been used in seizure control since 1912 and is used worldwide. It is well established, cheap and highly effective. After intravenous loading there is a biphasic distribution and highly vascular organs, excluding the brain, benefit first. Although penetration to the brain has been reported to occur 12–60 minutes after administration, this may happen faster in status epilepticus because of increased cerebral blood flow. In combination with prior administration of benzodiazepines, there is a risk of respiratory depression. In children already on phenobarbitone as maintenance therapy, the widespread strategy of giving a 5–10 mg/kg loading dose even without knowing current levels is often used with benefit.

Levetiracetam, a newer antiepileptic medication, has been widely used for prophylactic treatment of a wide variety of seizure types for a number of years. An IV formulation of levetiracetam has been used as an alternative to IV phenytoin for treating convulsive status epilepticus with success reported in retrospective cohorts.²⁰ In second line treatment, current evidence suggest an initial dose of 20mg/kg is safe.²¹ Further dosing may be required and should be based on recommendations from a paediatric neurologist.

Levetiracetam use in status epilepticus is "off label". Evidence on the efficacy of levetiracetam in status epilepticus is sparse, and the preferred dosage is not yet established. A prospective study is currently being undertaken to compare the efficacy of IV phenytoin and levetiracetam as second line treatment for continuing status epilepticus. In the absence of robust evidence the initial doses in this guideline are based on expert guidance.

Levetiracetam has a favourable pharmacokinetic profile with linear kinetics, minimal protein binding, and has 1:1 oral : IV bioavailability.⁶ Half-life in children is approximately 4-8 hours.⁹ Levetiracetam is not hepatically metabolised, and is eliminated primarily unchanged by renal excretion.⁷ A dose adjustment has been suggested for patients with renal impairment.

The adverse effects of IV levetiracetam include drowsiness, behavioural disturbances, lethargy, headache, dizziness and increased pharyngitis infections.¹¹

Sodium Valproate use in the treatment of focal and generalized epilepsies is well established. The drug has been available as an injectable formulation since 1993. A systematic review evaluating the efficacy and safety of intravenous sodium valproate for the treatment of status epilepticus found that the overall response rate in terminating status epilepticus was 70.9%.¹⁷ Studies on the use of sodium valproate in children with status epilepticus have reported efficacy of between 80 to 100% with loading doses of 25 to 40mg/kg.¹⁸ In children, IV sodium valproate appears to be equivalent to midazolam, and diazepam.¹⁹ Its use in status epilepticus is "off-label".



Adverse events include dizziness, thrombocytopenia, and mild hypotension, independent of infusion rates. Of note, good cardiovascular and respiratory tolerability has been observed in these studies, even at high doses and fast infusion rates. The most serious concern relates to the possibility of acute encephalopathy often in children less than 2 years of age, or those with underlying metabolic disorders and may be associated with hepatic abnormalities and hyperammonaemia.

Pyridoxine dependent seizures appear most frequently in the neonatal period. Incidence is rare after the neonatal period, with only 1 in 1,000,000 infants between 3 months to 2 years old experiencing pyridoxine dependent seizures.¹² A single initial test dose of pyridoxine 50–100 mg (note: not mg/kg) is accepted practice with close monitoring and dose adjustment.¹³ There is risk of cardiovascular collapse with apnoea when pyridoxine is administered by intravenous injection and resuscitation facilities must be available. Continuous monitoring of heart rate, respiratory rate and blood pressure is recommended. While apnoeic episodes have been reported after a single dose of oral pyridoxine, Infants administered the same dose of pyridoxine but by oral/enteral route for brief periods (days) rarely have side effects.

Pyridoxine use in the management of seizures is considered "off label". IV pyridoxine is not widely available and its administration is not without potential for exacerbating seizures. Its use is not recommended without prior discussion with a Paediatric Neurologist.

11. DISCHARGE

Patients should not be sent home without regaining full consciousness and having a clear plan about management of any recurrence. Both verbal and written education should be provided on the first aid management and care of the child during a seizure. Written material for the family/caregiver should be given and can include the relevant fact sheets <u>Seizures and Epilepsy Fact Sheet</u> and the <u>Febrile Convulsions Fact Sheet</u>.

If the child has a diagnosis of epilepsy it may be helpful to inform the family/caregiver about the following useful resources:

- The Paediatric Epilepsy Network NSW http://www.pennsw.com.au/
- Epilepsy Action Australia <u>http://www.epilepsy.org.au/</u>

A follow up appointment with a specialist may be required and should be arranged prior to discharge. Regardless, follow up arrangements should always be made for the child and parents/carers to attend their local GP for further monitoring and management.



12. APPENDICES

Appendix One – Reference list

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Appendix Two – Recommended resources and other references

Paediatric Epilepsy Network NSW <u>http://www.pennsw.com.au/</u> (accessed August 2015)

Epilepsy Action Australia <u>http://www.epilepsy.org.au/</u> (accessed August 2015)

NSW Health Department CIAP website, Managing Young Children and Infants with Seizures in Hospitals at: <u>http://www.ciap.health.nsw.gov.au.acs.hcn.com.au/</u>

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Appendix Three – Parent information

A Seizures Fact Sheet jointly developed by John Hunter Children's Hospital, Sydney Children's Hospital and Children's Hospital at Westmead is available at:

http://www.schn.health.nsw.gov.au/parents-and-carers/fact-sheets/seizures-and-epilepsy

Disclaimer: The fact sheet is for educational purposes only. Please consult with your doctor or other health professional to ensure this information is right for your child



Appendix Four – Glossary

AVPU Alert, Voice, Pain, Unresponsive BGL Blood glucose level CERS Clinical escalation response system CSE Convulsive status epilepticus CSF Cerebrospinal fluid ECG Electrocardiogram **Emergency department** ED Electrolytes, urea, creatinine EUC eTG Therapeutic guidelines QRS Combination of three graphical deflections seen on a typical electrocardiogram IM Intramuscular IV Intravenous MAD Mucosal atomiser device



Appendix Five – Working party members

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