Infants and Children: Acute Management of Seizures

Summary This Guideline represents a best practice guide for the acute management of seizures in children and infants in the acute care setting. Further information may be required in practice. Key changes from the previous edition are outlined in the introduction.

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Audience Emergency departments; nursing; medical; clinical staff
INFANTS AND CHILDREN: ACUTE MANAGEMENT OF SEIZURES

PURPOSE
The Infants and Children: Acute Management of Seizures, third edition Clinical Practice Guideline provides direction to clinicians and is aimed at achieving the best possible paediatric care in all parts of the state. The Clinical Practice Guideline was prepared for the NSW Ministry of Health by an expert clinical reference group under the auspice of The Office of Kids and Families.

KEY PRINCIPLES
This Guideline applies to all facilities where paediatric patients are managed. It requires the 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 Clinical Practice Guideline format in all hospitals and facilities required to manage seizures in infants and children.

The Clinical Practice Guideline reflects what is currently regarded as a safe and appropriate approach to the management of seizures in infants and children. 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 the application of clinical judgement to each individual presentation.

USE OF THE GUIDELINE
Chief Executives must ensure:
- This Guideline is adopted or local protocols are developed based on the Infants and Children: Acute Management of Seizures, third edition Clinical Practice 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

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<tr>
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<th>Approved by</th>
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ATTACHMENT

1. Infants and Children: Acute Management of Seizures, 3rd Edition: Guideline
Infants and Children - Acute Management of Seizures
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Rescinded
1 PURPOSE

This guideline is aimed at achieving the best possible care in NSW. This guideline presents the current best evidence for *Acute Management of Seizures in infants and children*. Its purpose is to inform practice for Australian 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 and children undertaking any task related to acute management of seizures in paediatric acute healthcare.

The systematic review underpinning this guideline was completed in 2014. The guideline was revised between October 2014 and September 2015. Public consultation occurred during July and August 2015. It is recommended that the literature is revisited and this document is reviewed in 2020.

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.

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**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 of Aboriginal people. Refer to your local Aboriginal liaison or for further information see NSW Health Communicating positively – A guide to appropriate Aboriginal terminology.

2 CHANGES FROM PREVIOUS CLINICAL PRACTICE GUIDELINE

The following outlines changes to the document:

- Definitions of hypoglycaemia vary between 2.2 and 3.5 mmol/L. Advanced Paediatric Life Support (APLS) recommends administration of 2 mL/kg of 10% glucose for a BGL < 3.0 mmol/L⁴

- IV levetiracetam has been included in the management of seizures as a second line therapy

- It is important to attempt to control the seizure without delay as the longer the seizure continues the more difficult it becomes to control

- This guideline is for infants and children. The first line treatment for neonates with seizures (first 28 days) remains phenobarbitone.
• Rectal diazepam has been removed as a first line choice. Midazolam, administered by buccal, nasal or intramuscular route is more effective \(^1,2\).

• Paraldehyde has been removed as second line therapy based on recent product information that it contains low levels of crotonaldehyde which is known to be genotoxic and carcinogenic. The recommended maximum life-time dose of paraldehyde is now 30 mL. Its use in status-epilepticus should only be under the direction of a Paediatric Neurologist or Intensivist.

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, and 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 control is likely to become.

Given that most acute seizures in children stop spontaneously, usually during transit to hospital, it should be assumed that if a child were 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 were 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. A recent review reported 0-2% mortality from the seizure itself for seizures lasting longer than 30 minutes.\(^3\) Neurological sequelae of Convulsive Status Epilepticus (CSE), (epilepsy, motor deficits, learning difficulties, and behaviour problems) are age dependent, occurring in six per cent of those over the age of three years but in 29% of those under one year.

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. However, 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 anti-epileptic 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 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 anti (e.g. phenytoin/levetiracetam/phenobarbitone) should be introduced early (i.e. at 20 minutes from onset of seizure).^{4}

4 **ALGORITHM**

See next page.
ACUTE MANAGEMENT OF SEIZURES FOR INFANTS AND CHILDREN

**Establish airway and apply oxygen**
Seek senior advice and assistance if necessary.
Include pre-hospital doses of Midazolam or Diazepam given within 1hr prior to presentation

**Attempt intravenous access**
Collect blood (as below) Check blood glucose DON'T EVER FORGET GLUCOSE
If BGL <3.0 mmols give 2 mL/kg 10% glucose IV (as bolus)
Then commence 5 mL/kg/hr 10% glucose IV infusion and REPEAT BGL within 5 mins

- **Vascular access obtained**
  - **YES**
    - Midazolam 0.15 mg/kg IV (max 10 mg) OR Diazepam 0.25 mg/kg IV (max 10 mg)
  - **NO**
    - Midazolam 0.3 mg/kg Buccal or Intranasal (max 10 mg) OR Midazolam 0.15 mg/kg IM (max 10 mg)

5 minutes still fitting

- **Vascular access obtained**
  - **YES**
    - Repeat either:
      - Midazolam 0.15 mg/kg IV (max 10 mg) OR Diazepam 0.25 mg/kg IV (max 10 mg)
  - **NO**
    - Repeat either:
      - Midazolam 0.3 mg/kg Buccal or Intranasal (max 10 mg) OR Midazolam 0.15 mg/kg IM (max 10 mg)

5 minutes still fitting

- **Vascular access obtained**
  - **YES**
    - Give either:
      - Phenytoin 20 mg/kg IV/Intraosseus (over 20 mins*) OR
      - Levetiracetam 20 mg/kg IV/Intraosseus (over 15 mins) OR
      - Phenobarbitone 20 mg/kg IV/Intraosseus (over 20 mins)
      - If already on phenytoin or phenobarbitone halve the above loading dose of that antiepileptic drug.
  - **NO**

5 minutes still fitting

**If still fitting obtain vascular access, if necessary by intraosseous route**

**Escalation as per local Clinical Emergency Response System or consult NETS 1300 36 2500.**
Phenytoine should only be administered under advice of Paediatric Neurologist

**Maintain continuous monitoring of ECG, respiratory rate, and oximetry whilst child is still fitting or unconscious. NOTE: 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**

**Rapid sequence induction with thiopentone (2-5mg/kg) if still fitting**

*Phenytoin - Do not exceed 1–2mg/kg/minute infusion rate or maximum rate of infusion 50 mg/minute whichever is slower.*
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.

5.1 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 maneuver 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 anti-epileptics 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 help summoned.

**Prolonged seizures and/or repeated doses of anti-epileptic 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 anti-epileptics 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 Paediatric Sepsis Pathway.

Give a broad spectrum antibiotic (third generation cephalosporin) to any child in whom a diagnosis of meningitis or septicaemia is suspected. If possible blood should be collected first for culture but this should not delay administration of antibiotics. Refer to the Therapeutic Guidelines (eTG) 2015, the Bacterial Meningitis Clinical Practice Guideline and the Paediatric Sepsis Pathway.

Check blood pressure as soon as the seizure has finished.

5.4 Disability

Assess the following for adequacy of neurological function:

- The AVPU (Alert, Voice, Pain, Unresponsive) 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 intra- cranial pressure. Very small pupils suggest brainstem injury or opiate poisoning, large pupils suggest amphetamines, atropine, or tricyclic antidepressants
- 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 anti-epileptic 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 Standards for Paediatric IV Fluids: NSW Health (Second Edition).

5.7 Glucose

“Don’t Ever Forget Glucose”. Take blood glucose stick test and laboratory test. Give 2 mL/kg of 10 percent glucose to any hypoglycaemic patient (BGL < 3mmol/L). If possible, take 10 mLs of clotted blood before giving the glucose for later investigation of the hypoglycaemic state.

The response to the initial management of hypoglycaemia should be monitored by frequent repeat BGL measurements. Inborn errors of metabolism where the seizure may be a consequence of hypoglycaemia will usually respond to 5% glucose +/- 0.9% sodium chloride at a rate of 10mL/kg/hr (8mg/kg/min). 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 Infants and Children: Acute Management of Altered Consciousness in Emergency Departments (1st Edition). 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 anti-epileptic 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 \(^1.6\) where 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 Mucosol Atomiser Device (MAD) into one or both nostrils.

**Table 1:**

<table>
<thead>
<tr>
<th>Medications used in acute seizures&lt;sup&gt;7,14,15&lt;/sup&gt;</th>
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<tbody>
<tr>
<td>Midazolam: buccal/intra-nasal</td>
<td>0.3 mg/kg (max 10 mg)</td>
</tr>
<tr>
<td>Midazolam: intravenous/intraosseous/intramuscular</td>
<td>0.15 mg/kg (max 10 mg)</td>
</tr>
<tr>
<td>Diazepam: intravenous/intraosseous</td>
<td>0.25 mg/kg (max 10 mg)</td>
</tr>
<tr>
<td>Phenytoin: intravenous/intraosseous</td>
<td>20 mg/kg in 0.9% sodium chloride over 20 minutes with ECG monitoring. Do not exceed 1–2 mg/kg/minute in children (or maximum rate of infusion 50 mg/minute whichever is slower). See Australian Injectable Drugs Handbook, 6&lt;sup&gt;th&lt;/sup&gt; Edition.</td>
</tr>
<tr>
<td>Levetiracetam: intravenous/intraosseous</td>
<td>20mg/kg (maximum dose 1 g) in infants and children. 40mg/kg (maximum dose 3 g) for adolescents and adults. Infusion time is 15 minutes. May be diluted in 0.9% Sodium Chloride or glucose 5%.</td>
</tr>
<tr>
<td>Phenobarbitone: intravenous/intraosseous</td>
<td>20 mg/kg (maximum 1 g)</td>
</tr>
<tr>
<td>Pyridoxine: Slow IV injection (not above 200 mg) or oral/enteral route.</td>
<td>50–100 mg/dose</td>
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<tr>
<td>Thiopentone: intravenous/intraosseous</td>
<td>2-5 mg/kg</td>
</tr>
<tr>
<td>Sodium Valproate: Intravenous/intraosseous</td>
<td>20-40 mg/kg over 3-5 minutes, then 1-5 mg/kg/hour infusion. <em>Caution use in the child less than 3 years</em>&lt;sup&gt;7&lt;/sup&gt; OR mitochondrial disorder OR family history of liver failure because of the risk of acute encephalopathy with hepatic dysfunction.</td>
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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 anti-depressants, benzodiazepines, anti-psychotics and salicylates. Anti-epileptic toxicity may also exacerbate seizures
- Past medical history, immunisations.

8  SPECIALIST CONSULTATION/TRANSFER

If in doubt or confused 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. They 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. EUC should be collected if there has been repeated diarrhoea or vomiting. The 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. Anti-epileptic 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 seizure has been focal. If meningitis is suspected intravenous antibiotics must be administered promptly Bacterial Meningitis Clinical Practice Guideline and Paediatric Sepsis Pathway. Lumbar Puncture should be considered if meningitis is suspected and there are no contra-indications.

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. Fever, Meningitis, Recognition of the Sick Child. Poisons may be suggested by the history, clinical features of toxidromes (anticholinergic, serotonin, sympathomimetic), a widened QRS 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 ANTI-EPILEPTIC DRUGS

In choosing anti-epileptic drug, the desired outcome of most rapid cessation of acute seizures with smallest possible incidence of side effects at minimal cost was chosen. Requirements of such medications include ease of administration and rapid appearance in the CSF. Consideration was also given to variation in regional availability of anti-epileptic drug. Early treatment is essential, as once seizures are established for more than 15 minutes, they become more difficult to treat.

Second line anti-epileptic drug, for refractory seizures, should be compatible with such first line anti-epileptic drug, 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 but encouraging.

10.1 First line therapies
Midazolam has now replaced diazepam as drug of first choice before venous access has been obtained, because of improved efficacy and preferred route of administration (buccal vs rectal).¹ It is highly effective as a first line anti-epileptic stopping the majority of seizures within one minute after IV injection of 0.1–0.3 mg/ kg and IM within 5–10 minutes. It has superior absorption in comparison with diazepam and lorazepam when given IM because
of its water solubility. Intra-nasal and IM midazolam has been adopted by the NSW Ambulance Service as the drug of first choice in status epilepticus.4

A single dose of buccal or intranasal midazolam 0.5 mg/kg has been shown to carry minimal risk of respiratory suppression.

Midazolam and other benzodiazepines may lead to respiratory depression. The effect could be more marked in patients receiving multiple doses. After no response to two doses of midazolam, appropriate second line anti-epileptics i.e. a long acting antiepileptic (e.g. Phenytoin/Levetiracetam/Phenobarbitone) should be introduced early (i.e. within 20 minutes).

**Diazepam** has been used both intravenously and rectally since 1965 for the first line control of status epilepticus. Intravenous administration produces rapid control of seizures in approximately 80 per cent of patients. Rectal administration of Diazepam is no longer recommended as Midazolam, administered by buccal, nasal or intramuscular route is more effective.¹,¹³

**Lorazepam** IV is used in North America and the UK. There is evidence of longer duration and reduced need for repeated doses. There is suggestion of more success over IV diazepam in control of acute seizures with a similar side effect profile although this did not reach statistical significance. There is significant difference in comparison with diazepam in the reduced need for second dose. Although there is evidence for advantage in adults, the evidence is less convincing in children, it is currently available on SAS scheme only in Australia. There may be more resistance to its effects in children on regular benzodiazepines.

### 10.2 Second line anti-epileptics for refractory status epilepticus

**Phenytoin**, a single dose of 20 mg/kg 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. Side effects in doses and levels within the therapeutic range, and at prescribed administration rates, are circumscribed. Consideration should be given to obese children. A loading dose based on Total Body Weight should be given while Ideal Body Weight should be used for subsequent maintenance doses. Consider the clinical condition and extent of obesity when determining loading doses.¹⁶

The main theoretical risk of rapid acute therapy is asystole although with administration rates of 1 to 2mg/kg/min (up to a maximum of 50 mg/min) this is rare in children. If hypotension or bradycardia is seen the infusion rate should be reduced to no more than 25 mg/minute. Additives such as propylene glycol, alcohol may contribute to this side effect. Phlebitis is probably the most common minor effect, caution must be taken to ensure the prepared product is not mixed with other medications or incompatible fluids and remains free of precipitation at all times.

Concurrent use of phenytoin with benzodiazepines results in a faster onset of therapeutic effect. Although several combination regimes were compared albeit in adults there was no significant difference.

The advantage of its close relative fosphenytoin is the reduced potential for cardiac dysrhythmia and hypotension as well as less severe extravasation consequences. Whilst it may be infused more rapidly than phenytoin, time to peak levels is identical and the cost
is very significantly higher. The small advantage for a relatively high cost excludes it from our recommendations.

**Levetiracetam**, a newer antiepileptic medication, has been widely used for prophylactic treatment of a wide variety of seizure types for a number of years and more recently in status epilepticus. Levetiracetam has a favourable pharmacokinetic profile with linear kinetics, minimal protein binding, and has 1:1 oral:IV bioavailability. Half-life in children is approximately 4-8 hours.

Levetiracetam is not hepatically metabolised, and is eliminated primarily unchanged by renal excretion. It has been given safely by rapid IV infusion (5 minutes) and has an excellent safety profile however we recommend infusion over 15 minutes.

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. However, prospective data describing the use of levetiracetam in infants and children is limited. A prospective study is being undertaken to compare the efficacy of IV phenytoin and levetiracetam as second line treatment for continuing status epilepticus despite two doses of benzodiazepines.

The side effects of IV levetiracetam are similar to oral preparation and include drowsiness, behavioural disturbances, lethargy, headache, dizziness and increased pharyngitis infections.

**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. It is used as the second line anti-epileptic drug of choice in the neonatal period. In addition, it can be given after a load of phenytoin, often with additive effect. The converse is true.

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. A similar strategy is seen in high dose protocols which use sequential phenobarbitone loading as high as 130 mg/kg. Cumulative loads of at least 40 mg/kg are regularly tolerated without respiratory depression.

**Sodium Valproate** The effectiveness of sodium valproate 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 to abrogate Status Epilepticus was 70.9 %. 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. In children, IV sodium valproate appears to be equivalent to midazolam, and diazepam. 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 3 years of age, or those with underlying
metabolic disorders and may be associated with hepatic abnormalities and hyperammonaemia.

**Pyridoxine** dependent seizures appear most often postnatally and rarely (1 in 1,000,000) later in the first two years of life. Accordingly, it has been indicated that intravenous therapy ought to be considered in children with resistant status epilepticus under the age of two.\(^\text{12}\)

A slow intravenous injection of pyridoxine 50–100 mg/dose (not/kg and not above 200 mg as a single dose) is accepted practice.\(^\text{13}\) There is risk of cardiovascular collapse with apnoea when administered by intravenous injection and resuscitation facilities must be available. Continuous monitoring of heart rate, respiratory rate and blood pressure is recommended. However, infants administered the same dose of pyridoxine but by oral/enteral route for brief periods (days) rarely have side effects.

IV pyridoxine is not widely available, and its administration is not without potential for exacerbating seizures. It 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. Education should be provided, both verbal and written 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 **Seizures and Epilepsy Fact Sheet** and the **Febrile Convulsions Fact Sheet**.

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


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

12.1 Appendix One – Reference list


20 Wheless JW, Treiman DM. The role of the newer antiepileptic drugs in the treatment of generalized convulsive status epilepticus. Epilepsia 2008;49 (Supplement 9):74-78.
12.2 Appendix Two – Recommended resources and other references


NSW Health Department CIAP website, Managing Young Children and Infants with Seizures in Hospitals at:  
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12.3 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:


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.
12.4 Appendix Four – Working party members

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