Document 00711

Seizures - Emergency Management in Children
Children's Health Queensland Hospital and Health Service

Custodian/Review Officer:
Director, Paediatric Emergency Medicine, Children's Health Queensland

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Medical and nursing staff working in Children's Health Queensland

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Children's Health Queensland Hospital and Health Service

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NSQHS
Standard 1: Governance for Quality and Safety in Health Service Organisations
Standard 4: Medication Safety

1. Purpose

This procedure provides clinical practice guidelines to guide clinicians involved in the emergency management of children with seizures.

2. Scope

This procedure relates to all staff involved in the care and management of children with seizures.

3. Procedure: Introduction

Seizures occur in 4 - 10% of children[1] and may be defined as paroxysmal and involuntary events of altered consciousness, behaviour, motor skills, sensation or autonomic function that result from abnormal rhythmic discharges of cerebral neurons. [2] The majority of seizures are convulsive, involving a change in muscle tone or activity. The lack of a motor component in non-convulsive seizures may make diagnosis difficult without an electroencephalography (EEG). Febrile convulsions are seen in 2 - 4% of children,[3] whereas epilepsy (an idiopathic susceptibility to recurrent seizures) occurs in about 0.5% of children.[4]

Individual convulsive seizures are often broadly classified as focal or generalised, based on their degree of body involvement. Classification may aid diagnosis and direct ongoing treatment in some cases, however the management priority in all seizure types is to protect the airway and terminate the seizure.

The causes of seizures are numerous, but the majority occur in the setting of a pre-existing seizure disorder, febrile illness, central nervous system (CNS) infection, head injury, poisoning or metabolic disturbance.

Status epilepticus is a neurological emergency which has an incidence of 10 - 40/100,000 children per year and has traditionally been defined as seizures lasting longer than 30 minutes or recurring without recovery to baseline consciousness over a 30 minute period.[5] This definition was used particularly for epidemiological studies; however for practical management purposes some have proposed reducing the time limit to 5 - 10 minutes for convulsive seizures.[6] This has been driven by the realisation that as the duration of the convulsion increases, there is an increased risk of status epilepticus becoming refractory to drugs and of irreversible neurological injury or death.[3,7] Convulsive status epilepticus is associated with a high neurological morbidity (10 - 20%) and a significant mortality (3 - 8%) depending on age, seizure duration and aetiology.[8]

Data from specialist children's hospitals in Brisbane reveal that 1 - 2% of all presentations to the children's emergency service each year relate to seizures, with 4 - 6% of these having a Triage Category of 1 and assumed to be actively seizing on arrival.[9] An Australian and New Zealand study[10] found that, in children presenting with ongoing seizure activity of greater than 10 minutes, the median pre-hospital seizure duration was 45 minutes. Almost one half of these had received anticonvulsant treatment by a parent, carer or ambulance officer. This suggests that children who present with ongoing seizures to the emergency service are likely to already be in established (and possibly refractory) status epilepticus and highlights the emergent need to rapidly terminate their prolonged convulsions to minimise adverse events.

4. Assessment

Clinical Assessment

Emergency assessment and management should always involve a rapid primary survey with evaluation of (and immediate management of concerns with) airway, breathing, circulation and disability (ABCD). Pre-hospital treatment should be taken into consideration.

Differential diagnosis

There are other neurological conditions that present with altered level of consciousness and abnormalities of tone, posture or movement that need to be differentiated from convulsive status epilepticus[11]. These include:

- Pseudoseizures
- Extensor posturing due to raised intracranial pressure (ICP)
- Acute movement disorders (chorea, tic)
- Dystonia
- Acute encephalopathy.

A careful history and examination will distinguish between these conditions in most patients.

Investigations

All children presenting with a seizure should have blood glucose checked. Other investigations are usually directed by history and examination findings:

- Electrolytes should be done in children with a history of vomiting or diarrhoea.
- Calcium & magnesium should be considered in those children with afebrile seizures, particularly infants.
- Septic screen should be considered in the febrile child (with lumbar puncture deferred if any contraindications are present).
- Antiepileptic drug (AED) levels are not usually helpful unless adherence is thought to be an issue.
- Neuroimaging is indicated when trauma is considered or there are focal neurological signs.
- Electroencephalography (EEG) is not usually indicated in the acute phase but may be requested as an outpatient investigation following a seizure.

5. Management

The goals in the management of status epilepticus are to maintain vital functions whilst stopping the seizure as soon as possible and to identify and treat any underlying cause[9].

First line agents

Benzodiazepines are widely used to stop seizures. They work by binding to GABA (gamma-aminobutyric acid) receptors in the central nervous system, which in turn hyperpolarises the neuronal membrane – making it more difficult for the neuron to be activated[12]. Two benzodiazepines are routinely used in the management of status epilepticus — Midazolam and Diazepam.

Midazolam

Midazolam has a rapid onset, with its anti-seizure effect often observed within 1 minute of IV administration.[13] It can reliably be given via the buccal, intranasal, IM, IV, or IO routes (**Table 1**). Oral absorption is much less reliable than either Lorazepam or Diazepam.

Buccal Midazolam has largely replaced PR Diazepam for the management of seizures by parents and caregivers because of its greater effectiveness.

This medication has a short duration of action so a number of children who stop convulsing after an initial Midazolam dose will require further doses to maintain seizure control.[12] Respiratory depression is a relatively common side effect of Midazolam. This is particularly seen with repeated dosing.

Table 1: Midazolam dosages for management of seizures

MEDICATION	DOSAGE
Midazolam Buccal / IN	0.2 - 0.3 mg/kg (up to 10 mg)
Midazolam IV / IO	0.15 mg/kg (up to 10 mg) [16]
Midazolam IM	0.2 mg/kg (up to 10 mg)

Adapted from: Paediatric Pharmacopoeia. 13th ed. RCH, Melbourne[14] and Therapeutic Guidelines, 2011[15]

Diazepam

Diazepam has a rapid onset of action, with its anti-seizure effect seen within a median of two (2) minutes after IV administration.[13] Midazolam is more effective as an anti-seizure agent when compared with Diazepam. Diazepam can be given via the PR, IV or IO routes (**Table 2**). It *should not* be given via IM injection due to slow and erratic absorption.[14] Oral absorption is effective however the oral route is usually not appropriate in the child with ongoing seizure activity.

Diazepam has a long elimination half-life but only a relatively short-lasting anti-seizure effect of between 15 - 30 minutes. Respiratory depression is relatively common with Diazepam.

Table 2: Diazepam dosages for management of seizures

MEDICATION	DOSAGE
Diazepam IV / IO	0.1-0.3 mg/kg (up to 20 mg)
Diazepam rectal	0.3-0.5 mg/kg (up to 10 mg)

Adapted from: Paediatric Pharmacopoeia. 13th ed. RCH, Melbourne[14] and Therapeutic Guidelines, 2011[15]

Second Line Agents

Second line agents are traditionally used after seizure continues despite appropriate doses of rapid acting first line agents. These drugs require administration by infusion over 20 - 30 minutes and have the advantage (over first line agents) of having a longer duration of action.

Phenytoin

Phenytoin has been available since 1938 and is the drug of choice following administration of benzodiazepines. The dose is 20mg/kg (up to 1g) intravenously administered over a minimum of 20 minutes (do not exceed rate of 1mg/kg/min or 50 mg/min).[15] Phenytoin load should be administered more slowly (over 60 minutes) if the child's seizure activity has ceased. The effects of Phenytoin demonstrate less respiratory depression than Phenobarbitone, however there is a risk of arrhythmias. Cardiac monitoring should occur during the infusion period[16].

Phenobarbitone

Phenobarbitone has been used since 1912 and the dose is 20 mg/kg (up to 1g) intravenously administered over a minimum of 20 minutes (do not exceed rate of 100 mg/min to avoid respiratory and/or circulatory impairment).[15] It is traditionally the second line agent in infants or when the patient has a contraindication to Phenytoin use or is already on maintenance Phenytoin therapy. In combination with benzodiazepines, there is an increased risk of respiratory depression with Phenobarbitone.[16]

Latest agents in Australia

There are a number of anticonvulsants administered in other parts of the world as either first or second line agents in the treatment of convulsive status epilepticus. These are not yet licensed for use in Australia however, depending upon availability, may be considered in consultation with a paediatric neurologist.

Lorazepam (Ativan)

Lorazepam is the benzodiazepine of choice as a first line agent across North America, U.K. and Europe. Lorazepam has rapid infiltration (1 - 2 minutes after IV injection) across the blood-brain barrier and a relatively long half-life with an effective duration of action of 4 - 6 hours.[17,18] It also has fewer side effects than other benzodiazepines[7]. Lorazepam can be administered via several routes including buccal, rectal and intranasal. It is available in Australia, however, is currently only licensed for rapid tranquilisation for patients with acute agitation and disturbed behaviour. The status epilepticus dose for children is 0.05-0.1 mg/kg (maximum of 4 mg/dose) slow intravenous administration over 2 - 5 minutes (maximum rate 2mg/minute). A repeat dose may be given 10 - 15 minutes later if needed.[19]

Intravenous Valproate (Epilim)

Intravenous Valproate is currently being used in a number of centres across the world as either a second line agent or a third line agent following Phenytoin. Multiple small case series have been published, however at this time, no prospective randomized control trial has been set. A number of studies have shown that 60 - 80% of seizures not responding to benzodiazepines and Phenytoin will cease with administration of IV Valproate [20,21]. It does not appear to have significant adverse effects acutely with stable haemodynamic parameters following administration.[2] It is less commonly used in children due to the risk of hepatotoxicity in infants and young children.

The IV Valproate loading dose is 30mg/kg (up to 800 mg) by slow IV injection over 3 - 5 minutes[14].

Intravenous Levetiracetam (Keppra)

Intravenous Levetiracetam is another new agent which appears to be effective in terminating seizures which are not responsive to benzodiazepines and Phenytoin. A number of studies have shown its safety and efficacy in terminating refractory convulsive status epilepticus thereby avoiding intubation and ventilation.[23-27] It also appears to have no acute side effects relating to hypotension or respiratory depression and does not have any known drug interactions.[24,25]

The IV Levetiracetam loading dose is 30 mg/kg.[15]

Rapid Sequence Induction

Rapid sequence induction (RSI) is a sequence of events designed to safely and quickly protect the airway and breathing of severely ill children. For convulsive status epilepticus (CSE) the primary goal is to maintain oxygenation to the brain and vital organs. RSI also allows the use of larger doses of anti-epileptic medications whose primary adverse effects are hypoventilation and apnoea (e.g. benzodiazepines and barbiturates). RSI facilitates the expeditious investigation (e.g. CT), treatment and management requirements of causes of CSE.

The steps of RSI include (6 "P"s):

- Preparation (equipment and staff)
- Pre-oxygenation (bag mask and FiO_2 100%)
- Pre-Medication
- Paralysis and sedation (Induction)
- Passing airway tube and placement (including failed intubation plan)
- Post-intubation management

Paralysis and Sedation (induction). Paralysis will lead to apnoea and is painful in awake individuals and therefore should follow induction with a sedation and analgesic agent. Thiopental is the agent of choice as it is also an effective anti-epileptic medication, however, it may cause hypotension. Higher doses of midazolam may also be effective. Fentanyl is an analgesic and sedative agent which may be substituted when there is concern regarding hypotension. Ketamine is an agent that produces a dissociative anaesthesia with less airway issues and less hypoventilation concerns, and may be first choice in a difficult airway situation. Propofol is a common induction agent in emergency services, however has no known anti-epileptic effects. The choice of induction agent to be administered is made by the airway doctor.

Succinylcholine is the most common agent administered due to its rapid onset (15 - 30 seconds) and short duration of action (5 - 10 minutes). Succinylcholine has an increased risk of causing life-threatening malignant hyperthermia (MHT), particularly in children with neuromuscular diseases, some of whom will present with seizures. Rocuronium is another agent that also has rapid onset (30 - 60 seconds) and is not associated with MHT but has a longer duration of action (30 - 60 minutes). Sugammadex is the antidote which allows the safe reversal of paralysis due to Rocuronium. For CSE, Rocuronium would appear to be the superior choice, when available.

See flowchart Appendix 1: Emergency management of children with seizures

6. Disposition

Prior to discharge from the emergency service the child should meet certain discharge criteria and have relevant discharge plans completed. Suggested follow up depends upon a number of factors including the seizure type (first or subsequent seizure, febrile or afebrile seizure, focal or generalised seizure) and whether the episode represents a change in seizure control. Outpatient follow up plans and need for investigations should be discussed with the local paediatric service.

If the child is not suitable for discharge, admission to the children's inpatient services is required. The decision to admit a child following presentation of a seizure/s is made after initial treatment and observation. (See flowchart Appendix 2: Admission / discharge criteria for children presenting with seizures).

When a decision is made to transfer a child to a higher level facility (Level 6), referral must be made through RSQ.[30]

Activation of the QLD emergency medical system coordination centre (QCC)

Further information on the preparation of a infant prior to transport can be obtained through *RSQ Clinical Guidelines paediatric* section (pages 31-35).[30]

Statewide RSQ clinical guidelines — Paediatrics

7. Abbreviations

Term	Definition
AED	Antiepileptic drug
BP	Blood pressure
Children	0-14 years of age
CHQ	Children's Health Queensland
CNS	Central nervous system
CSE	Convulsive status epilepticus
CT	Computed tomography
EEG	Electroencephalography
GABA	Gamma-aminobutyric acid
GCS	Glasgow coma scale
HR	Heart rate
ICP	Intracranial pressure
IO	Intraosseous
IM	Intramuscular
IV	Intravenous
MHT	Malignant hyperthermia
PREDICT	Paediatric research in emergency departments international collaborative
PICU	Paediatric Intensive Care Unit
PO	Per oral (oral route)
PR	Per rectum (rectal route)
QCC	Queensland Coordination Centre
RSI	Rapid sequence induction
RR	Respiratory rate
RSQ	Retrieval Services Queensland

8. Supporting Documents

- Appendix 1: Emergency management of children with seizures
- Appendix 2: Admission / discharge criteria for children presenting with seizures
- For those children diagnosed with a febrile convulsion and discharged home, please provide the carer / parent with the Febrile convulsion in children fact sheet,

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10. Consultation

Key stakeholders who reviewed this version are:

- Director of Paediatric Emergency Medicine, Children's Health Queensland
- Clinicians (medical, nursing, allied health) working within Level 4, Level 5 and Level 6 Children's Health and Metro Children's Queensland in emergency, inpatient and ambulatory services
- Children's Health Services District clinical leaders — medical, nursing and allied health
- District Chief Executive Officers — Children's Health Queensland, Metro South, Metro North and West-Moreton Health Queensland
- Queensland Ambulance Services — Manager Clinical Standards.

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- Dr Adrian Bonsall — Fellow, Emergency Services, Mater Children's Hospital
- Dr Andrew Blanch — Director of Emergency Medicine, Royal Children's Hospital
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11. Procedure Revision and Approval History

Version No	Modified by	Amendments authorised by	Approved by
1.0	Director, Paediatric Emergency Medicine, Children's Health Queensland	■ Greater Brisbane metropolitan area clinical procedures editorial group ■ CE, CHQ	General Manager Operations

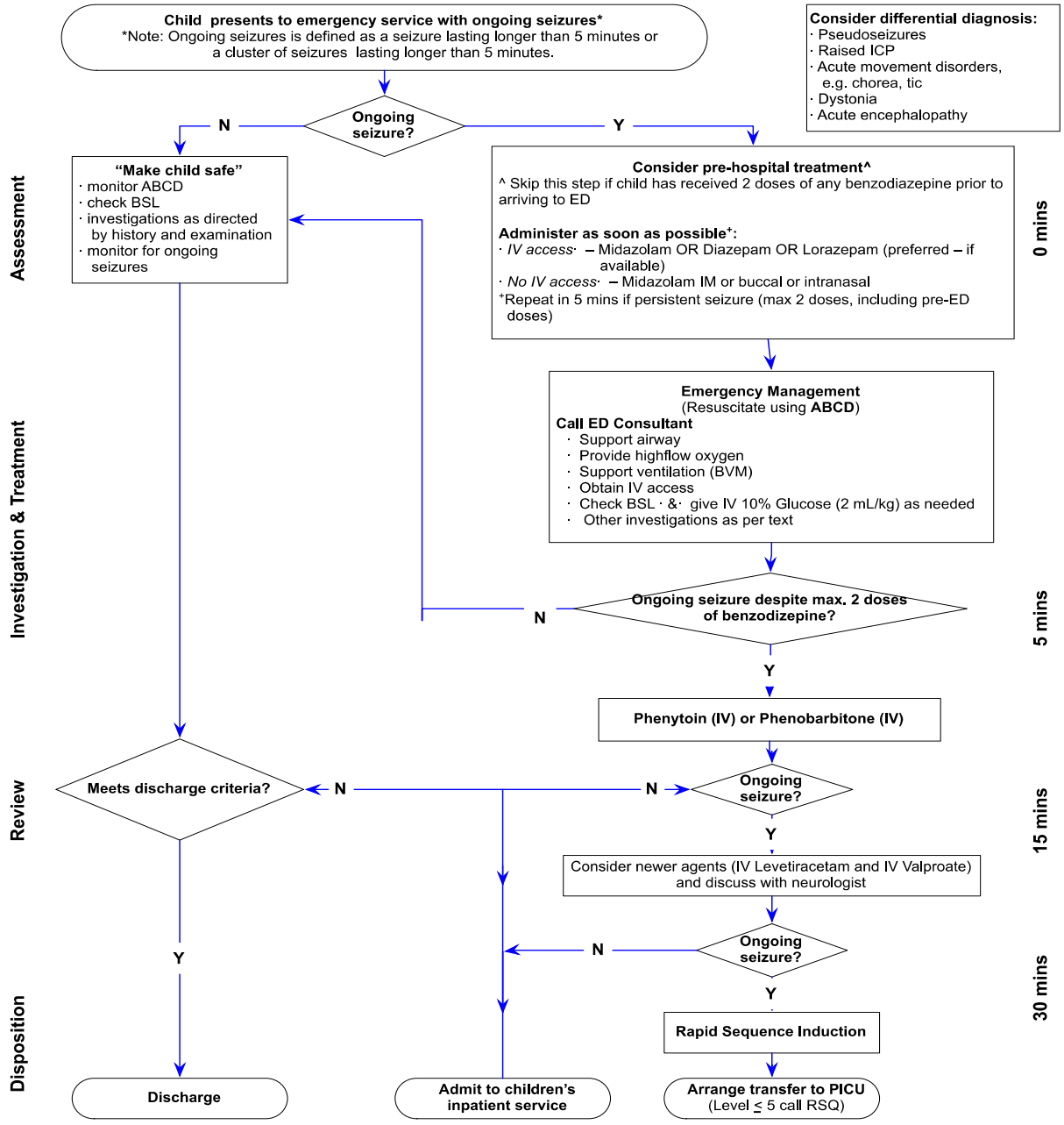
12. Audit / Evaluation Strategy

Level of risk	Medium
Audit strategy	1. Staff survey to evaluate awareness of procedure and emergency management practices 2. Observe practice 3. Review documentation, i.e. chart audit, to evaluate compliance with procedure
Audit tool attached	Nil
Audit date	Annual snapshot review (August)
Audit responsibility	Individual Greater Brisbane Metropolitan hospitals, i.e. Ipswich, Logan, Redland, MCH, RCH, TPCH, Redcliffe, Caboolture
Key Elements / Indicators / Outcomes	KPI 1 — greater than 80% staff awareness of procedure KPI 2 — greater than 80% compliance with procedure

13. Appendices

- Appendix 1: Emergency Management of Children with Seizures
- Appendix 2: Admission / Discharge Criteria for Children Presenting with Seizures

14. Appendix 1 – Emergency Management of Children with Seizures



Medications

Diazepam (Valium)	IV/IO Rectal	0.1 - 0.3 mg/kg (up to 20 mg) 0.3 – 0.5 mg/kg (up to 10 mg)
Levetiracetam (Keppra)	IV	Loading dose 30 mg/kg (up to 800 mg) by slow IV injection over 3 – 5 mins
Lorazepam (Ativan)	IV	0.05 – 0.1 mg/kg (up to 4 mg) slow IV injection over 2-5 mins (maximum rate 2 mg/minute). A repeat dose may be given 10-15 mins later if needed
Midazolam (Hypnovel)	Buccal/IN IV/IO IM	0.2-0.3 mg/kg (up to 10 mg) 0.15 mg/kg (up to 10 mg) 0.2 mg/kg (up to 10 mg)
Phenobarbitone	IV	Loading dose 20 mg/kg (maximum 1 gram) usually given over 20 minutes (maximum rate no greater than 100 mg/min)
Phenytoin (Dilantin)	IV	Loading dose 20 mg/kg (maximum 1 gram) usually given over 20 minutes (maximum rate no greater than 1mg/kg/min or 50 mg/min)
Valproate (Epilim)	IV	Loading dose 30 mg/kg (up to 800mg) slow injection over 3-5 mins

15. Appendix 2: Admission / Discharge Criteria for Children Presenting with Seizures

Criteria for discharge from the emergency service

Criteria for discharging a child with a presentation of seizure from the emergency service include:

- certain diagnosis of seizure - The clinical decision as to whether an epileptic seizure has occurred should then be based on a careful history, examination and investigations undertaken (where appropriate). Diagnosis should not be based on the presence or absence of single features.[27] There are a number of conditions which may mimic a seizure in a child and knowledge of the range of differential diagnoses of paroxysmal events in children is important when making the diagnosis.[28]
- nil further seizures whilst in emergency service
- child is alert and responding normally
- all observations are within normal ranges (GCS, pupil reaction, BP, PR)
- follow up care arranged – referral made to paediatrician/neurologist and letter also sent to General Practitioner
- parent information sheet given and discussed

When discharging a child with a diagnosis of seizures, their social circumstances need to be considered and appropriately addressed after the initial assessment and observation period:

- time of day
- parents/carers comprehension and compliance
- access to transport should return be required
- distance to local hospital.

Criteria for admission to children's inpatient service

Criteria for the admission to the children's inpatient service for a child with seizures include:

- does not meet discharge criteria
- required medication to cease seizures with nil further seizures occurring
- observations (GCS, pupil reaction, BP, PR) have returned to pre seizure state
- re-presentation to the emergency service within 24hours
- underlying illness requires treatment.

Criteria for admission to a Level 6 emergency or PICU service

Consultation with paediatric speciality team in the current facility and/or discussion with a Level 6 children's health service via Retrieval Services Queensland (RSQ) is required when:

- seizures are continuing despite ongoing medication
- intubation has been required due to continuing seizures and medication.