Delirium in Critically ill Children

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Definition and Clinical Presentation

Delirium is a syndrome of **acute brain dysfunction**, characterized by an **acute onset** and **fluctuating course,** with changes in baseline awareness, altered behaviour or cognition. This can manifest as disturbances in attention, orientation, memory, language and can result in disorganized thinking and visual or auditory hallucinations. Parents may say, "*This is not my child*", while healthcare workers may say, "*This child is very difficult to sedate*".

Delirium develops over a short period of time (hours or days), often fluctuates during the day and typically worsens in the evening ("sundowning"). It is not explained by a pre-existing, established or evolving neurocognitive disorder and occurs as a result of an illness or its treatment. It is a **temporary state**, reversing when the underlying condition abates or when iatrogenic triggers are removed.

Patients can have hypoactive, hyperactive or a mixed delirium with features from both types (Table 1). While hyperactive delirium is more readily recognized, it is far less common than hypoactive delirium, which can be easily missed. This highlights the importance of universal screening and reinforces the fact that the presence or absence of delirium in the CICU should be treated as a **vital sign**.

To facilitate this, **ALL patients** in the CICU (whether receiving intravenous analgesics or sedatives or intubated or not) should have routine State Behavioural Scale (SBS) scoring and delirium screening [Cornell Assessment of Pediatric Delirium (CAPD) (Annex A)] performed.

Table 1. Types of Delirium

Subtype	Hypoactive	Hyperactive	Mixed
Incidence	46%	8%	45%
Clinical Features	• Apathy • Decreased responsiveness • Withdrawn from family or familiar items • Slowed / reduced speech and motor activity • Lethargy	• Agitation / Inconsolability • Restlessness • Hypervigilance • Emotional lability • Combative behaviour • Purposeless actions • Sleep-wake disturbance	• Features of both hypoactive and hyperactive delirium
SBS scores	-3 to 0	+1 to +2	Fluctuating scores above and below 0

The prevalence of delirium in critically ill children ranges from 12 to 65%, with a higher incidence in children who undergo cardiopulmonary bypass. Delirium typically has an early onset. **Amongst children who become delirious, about 65% and 80% develop delirium within the first 48 and 72 hours of ICU admission, respectively, with the episode lasting an average of 1-2 days**. Almost 30% of children with delirium develop recurrent delirium (recurrence after a minimum period of 24 hours of normal mental status), ranging from 2 to 14 episodes of delirium within the same admission.

In adults, hypoactive delirium is thought to be the most severe form of delirium, with the worst prognostic implications. It is uncertain if this also holds true in children.

Pathophysiology and Etiology of Delirium

The pathophysiology of delirium is complex and incompletely understood. There are several hypotheses for processes that are thought to contribute to delirium.

(1) The neuroinflammatory hypothesis suggests that systemic inflammation either compromises the blood brain barrier or leads to de novo production of inflammatory mediators in the brain. Inflammation within the central nervous system (CNS) leads to endothelial activation, enhanced cytokine and leukocyte activity and results in local ischaemia and neuronal apoptosis.

(2) The oxidative stress hypothesis suggests that reduced oxygen delivery in critical illness, coupled with increased cerebral metabolism, results in increased reactive oxygen species that cause global CNS dysfunction.

(3) The neurotransmitter hypothesis is based on the observation that delirium follows the use of medications that alter neurotransmitter function. Normal brain activity depends on a balance of stimulatory (e.g., dopamine) and inhibitory (e.g., GABA, acetylcholine) neurotransmissions. Dysregulation of dopamine, acetylcholine, glutamate, norepinephrine, serotonin, histamine, melatonin and GABA have all been implicated in the development of delirium. Commonly used sedatives (benzodiazepines, propofol) act via stimulation of GABA receptors and have also been reported to contribute to delirium.

Although the final common pathway leading to delirium may be the same (alterations in neurotransmission leading to a failure of integration and processing of sensory information and motor response), many different etiologies (Table 2) can trigger and contribute to the delirium cascade, such as the underlying disease process, side effects of treatment and the abnormal critical care environment.

Table 2. Risk Factors and Causes of Delirium

Non-modifiable (Predisposing factors)		
• Age ≤ 2 years • Baseline developmental delay or cognitive dysfunction • Pre-existing emotional, behavioural or psychological disorder • Higher illness severity • Poor nutritional status (Low albumin < 30g/L)		
Modifiable (Precipitating factors)		
Underlying Disease	**Side Effects of Treatment**	**Environmental Factors**
• Infection • Hypoxia • Pain • New organ dysfunction (CNS, cardiac, respiratory, renal, hepatic, endocrine) • Metabolic derangements (hyper/hyponatremia, hyper/hypokalemia, hyper/hypocalcemia, hypoglycemia, acidosis/alkalosis)	• Use of benzodiazepines, anticholinergics, ketamine and propofol • High doses of opioids • Deep sedation / Prior coma • Withdrawal syndrome • Red blood cell transfusion • Mechanical ventilation • Cardiopulmonary bypass / ECMO	• Immobilization / Restraints • Sleep-wake cycle disturbance • Lighting schedules • Loud sounds • Unfamiliar people / environment

Impact of Delirium

Delirium can have significant impact on morbidity, mortality and financial costs.

In paediatric literature, delirium has been found to be associated with:

- Increased durations of mechanical ventilation, ICU and hospital stay
- Higher exposure to sedatives and increased risk of long-term cognitive impairment
- Increased healthcare costs
- Increased mortality
- Increased post-traumatic stress symptoms in survivors
- Uncertain impact on long term complications – preliminary studies suggest decreased spatial and verbal memory, decreased attention, longer school absences, increased maladaptive behaviour (anxiety, eating disorders, aggression, apathy)

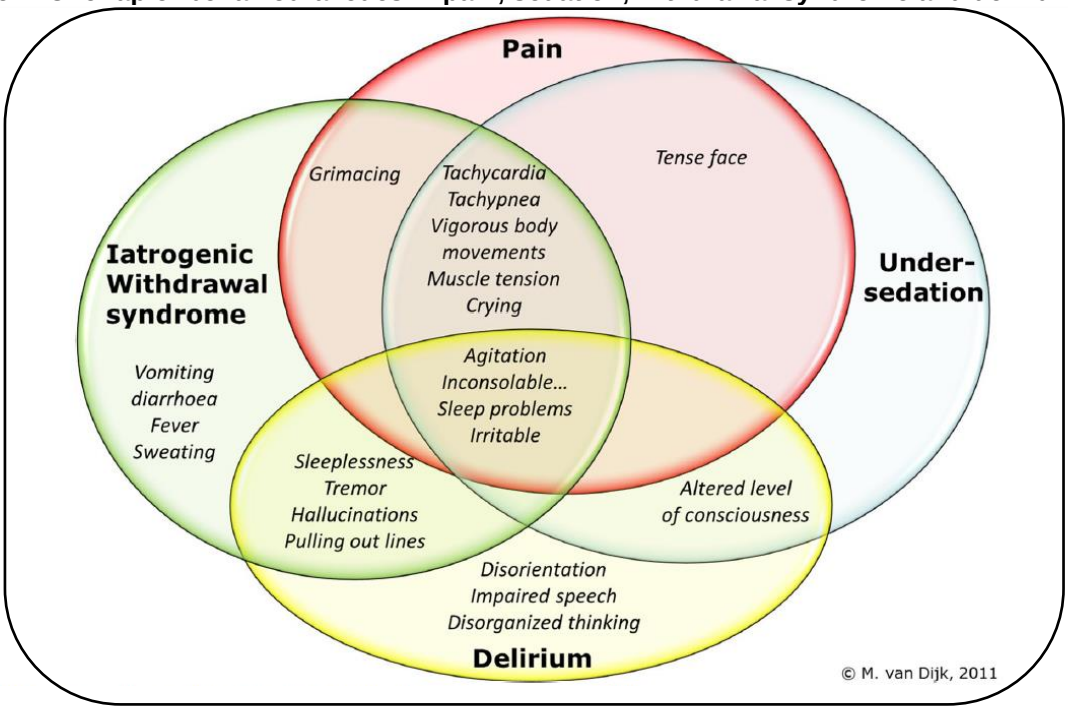
In adults, delirium has also been associated with long term cognitive, emotional and behavioural impacts, with an increased incidence of post-intensive care syndrome. The risk of post-traumatic stress in families and healthcare workers must also be considered.

The duration of delirium and magnitude of CAPD scores are both indicators of severity of delirium. However, the **duration of delirium is a more important prognosticator and a longer duration of delirium has a greater impact on clinical outcomes**. In addition, a recurrence of delirium is frequently a warning sign of new intercurrent illness.

Screening and Diagnosis of Paediatric Delirium

The diagnosis of paediatric delirium is made more challenging due to the variability of neurodevelopment in children. This is especially so in neonates and infants, where an understanding of normal development and illness behaviours is required. It can also be challenging to discriminate delirium from pain, under-sedation or withdrawal syndrome (typically manifesting as the 3 “Ds”, dilated pupils, diaphoresis and diarrhoea) (Figure 1).

Figure 1. Overlap of behavioural cues in pain, sedation, withdrawal syndrome and delirium



CHAPTER Delirium

The gold standard for diagnosing delirium is a psychiatric evaluation. However, given the significant incidence of delirium in critically ill children and the need for serial monitoring, it is imperative to have delirium screening tools for non-psychiatrists to use routinely at the bedside.

In recent years, several screening tools have been developed for screening paediatric delirium. These include the:

- Cornell Assessment of Pediatric Delirium (CAPD) (for 0-21 years of age)
- Pediatric Anesthesia Emergence Delirium Scale (PAED) (for >5 years)
- Pediatric Confusion Assessment Method for the ICU (pCAM-ICU) (for 5-17 years of age)
- PreSchool Confusion Assessment Method for the ICU (psCAM-ICU) (for <5 years)

The CAPD and PAED are observational tools which are easy to administer, while pCAM and psCAM are interactive in nature and require more extensive training. The pCAM and psCAM are both not validated for use in children with developmental delay. The PAED tool was originally designed for post-anaesthesia use to detect hyperactive or emergence delirium, while the CAPD is suitable for detecting hypoactive and mixed types of delirium, which are the most common forms of delirium in critically ill children. For the above-mentioned reasons, as well as its applicability for use in a wide age range and in children with developmental delay, our unit has elected to use the CAPD tool to screen for delirium.

The Cornell Assessment of Pediatric Delirium

The CAPD is a quick, observational, screening tool that is able to detect all subtypes of delirium. It has been validated for use in children from birth to 21 years of age and in critically ill children or in post-operative states. The CAPD tool was designed as a screening tool, but it also works reasonably well as a diagnostic tool in developmentally normal children. However**, the clinical team can always disagree with the CAPD score, as an experienced clinical opinion is more important than the tool in diagnosing delirium**.

How is CAPD scoring performed and where is it charted?

1. CAPD scores should be performed at the end of each nursing shift (at least Q12H, at 0600hrs and 1800hrs)

2. SBS scores are first established:
    a. If the patient was unarousable to verbal stimulation for the ENTIRE nursing shift (SBS is -2 to -3) → do not proceed to assess the CAPD score (the patient is too sedated), consider weaning sedation if clinically appropriate
    b. If the patient was arousable AT ANY POINT during the nursing shift (SBS is -1 or higher) → proceed to score the CAPD
    c. The CAPD tool is meant to be a “period-of-time” screen, NOT a “point-in-time” screen and should be scored based on observations of the child’s behavior during the course of a nursing shift
    d. “Score it as you see it” – Questions should be answered exactly as the child behaves. For example, if a patient is blind, always score question 1, “Does the child make eye contact with the caregiver?” as “Never”. Don’t rationalize that the child would have made eye contact if he/she could see.

3. For children aged between 0 to 2 years of age, a set of developmental anchor points serves as a reference for age-appropriate behavior for each of the 8 CAPD questions (Annex B)

4. CAPD scores are then charted within the “NUR ICU KKH” vital signs flowsheet

How to interpret and use CAPD scores?

1. **A CAPD score ≥ 9 is meant to trigger a patient assessment**, the medical team should:
    a. review medical history and hospital course
    b. review medication history
    c. perform a clinical + neurological examination + assess for pain/itch/other discomforts
    d. obtain parent/multi-disciplinary input
    e. consider targeted investigations based on suspicion of contributing etiologies

2. **In a developmentally normal child, a CAPD score ≥ 9 has good sensitivity and specificity and can be considered diagnostic of delirium**

3. **In a child with developmental delay or abnormal baseline neurological function, CAPD scores should be paired with the trend of SBS scores to improve diagnostic accuracy**
    a. There is a need to establish an acute change from cognitive baseline with a fluctuating level of awareness over the course of the day before diagnosing delirium
    b. A CAPD score ≥ 9 and the presence of fluctuating SBS scores of ≥ 2 points in the last 24 hours, is highly suggestive of delirium

4. The duration of delirium is the most important indicator of severity of delirium. An increasing trend/magnitude of CAPD scores is also an indicator of worsening delirium

5. Due to the fluctuant course of delirium, it is common to see fluctuating CAPD scores

6. The trend and magnitude of CAPD scores within an individual patient is important and gives an idea of the trajectory of the patients’ delirium. However, CAPD scores across different patients shouldn’t be compared

7. CAPD scores should be assessed and routinely discussed during ward rounds

Management of Delirium

The complex pathophysiology of delirium makes a one-size-fits-all approach to treatment unrealistic. When assessing a patient, it is necessary to identify the discrete etiologies of delirium in order to determine the best treatment strategy (Table 3).

In other words, when a child is diagnosed with delirium, one should consider not only ***how*** to treat the delirium, but ***why*** the child is delirious. When suspicious of delirium, a careful neurological examination should be performed to exclude a primary CNS disease.

Table 3. The 3-pronged approach to Delirium Treatment (Non-pharmacological)

Address underlying disease	Minimize iatrogenic factors	Optimize environment
• Address infections • Address hypoxia • Prioritize and optimize pain control over sedation (consider paracetamol, NSAIDS, intermittent opioids rather than infusions) • Correct metabolic derangements • Optimize nutrition and hydration	• Minimize sedatives, opioids, ketamine and propofol • Consider dexmedetomidine in place of benzodiazepines • Prevent withdrawal • Avoid anticholinergics • Avoid polypharmacy • Avoid restraints • Encourage early mobilization • Bundle cares to allow for uninterrupted sleep • Remove unnecessary indwelling catheters	• Address the child by name • Introduce care members • Frequently re-assure and re-orient the child • Communicate calmly, clearly and concisely in an age-appropriate manner • Explain care activities simply • Create a quiet, well-lit space with familiar objects from the child's home • Provide spectacles or hearing aids if needed • Facilitate sleep-wake cycle: Encourage being awake in the day and longer stretches of sleep at night • Provide a clock/calendar • Engage parents' help!

As much as possible, all patients in the ICU should be receiving non-pharmacologic interventions to minimize the risk of delirium. Depending on the trigger for delirium and how long it takes for the trigger to be reversed, response to interventions for delirium may take at least 24 to 48 hours. The majority of patients with delirium may be managed via non-pharmacological interventions, with only a small proportion of patients (<10%) requiring pharmacological therapies for symptom management.

One of the most challenging types of delirium that lasts for long durations of time is withdrawal-associated delirium, where delirium only resolves after all opioids and sedatives are stopped. This requires a balance of timely weaning of opioids and sedatives so that withdrawal symptoms are controlled. Weaning too quickly may precipitate withdrawal while weaning too slowly may prolong delirium.

Pharmacologic Therapy of Delirium

Antipsychotic drugs may be indicated for symptom control and can be considered when:

- Symptoms are distressing to the child or family
- A child is deemed to be at risk of self-harm or dislodging medical devices
- The course of delirium is protracted (> 5 days)

Table 4. Pharmacologic Agents for Symptom Control in Delirium

Medication	Route	Formulation available	Indication
Haloperidol*	IV/IM	Vial (5mg/ml)	Agitation, if strictly NBM, for Hyperactive & Mixed delirium
Quetiapine^	PO	Tablet (25mg & 100mg)	Hyperactive, Mixed & Hypoactive delirium
Risperidone	PO	Solution (1mg/ml) Tablet (1mg)	Use solution for weight <12.5kg, for Hyperactive, Mixed & Hypoactive delirium
Olanzapine	PO	Conventional tablet (5mg) Orally disintegrating tablet (5mg)	Not recommended as first line therapy. For Hypoactive & Mixed delirium
Melatonin	PO	Tablet (3mg)	Sleep disturbance

**Haloperidol is a typical antipsychotic drug (use with caution in patients with / at risk of QTc prolongation). Unless strictly NBM, atypical antipsychotics (Quetiapine, Risperidone) are preferred.*
^Quetiapine is poorly soluble in water, but can be cut into quarter or half tablets and mixed with water for administration → Hence, the lowest dose that can be served is a quarter tablet (6.25mg).

Antipsychotic drugs may not directly reverse delirium, but can alleviate its symptoms (relief of agitation, perceptual disturbances, sleep-wake cycle abnormalities and behavioural dysregulation). **Thus, antipsychotic drugs should be used only when the benefits outweigh the risks.**

If antipsychotic therapy is initiated, baseline investigations should be performed (Table 5) and patients must be monitored for adverse effects, which include prolonged QTc interval, tachycardia, hypotension, sedation, extrapyramidal side effects (dystonia, oculogyric crisis, hyperpyrexia), anticholinergic effects (dry mouth, constipation, urinary retention), reduced seizure threshold, photosensitivity, hyperglycemia, elevated cholesterol/triglycerides, leukopenia, transaminitis and rarely, neuroleptic malignant syndrome. All antipsychotic agents are sedating and if served once daily, are preferably served at night (ON dosing).

Table 5. Monitoring Parameters while using Antipsychotic Drugs

Parameter	Baseline	After Initiation and Subsequent Dose Increase(s)	Maintenance (if continued)
ECG	X	48 hours	Monthly (Oral agents) Weekly (IV haloperidol)
Renal Panel	X		
Mg	X		
FBC	X	Twice a week	Monthly
CK	X		
LFT	X		
Triglycerides	X	Monthly	Monthly

After starting drug therapy, the patient's mental status should be reviewed daily and doses can be up-titrated every 1 – 2 days based on clinical status. Consider reducing the dose or frequency of administration if significant adverse effects occur. Extrapyramidal side effects are seen when doses for antipsychotics are increased rapidly and should improve by reducing the dose and frequency of administration. Cessation of antipsychotics must be considered if there is significant QTc prolongation, new T wave abnormalities, marked bradycardia or a Brugada phenotype (Table 6).

In general, if pharmacologic therapy is started for delirium, evaluate the ability to wean therapy within 5 – 7 days of initiation, especially if the underlying disease process is improving and behaviours are well controlled. Antipsychotics should **not** be discontinued suddenly and weaning should be carried out gradually, over 5 – 7 days.

Table 6. Management of Adverse Drug Events

Adverse Event	Recommendation
QTc > 500 ms OR ↑ by > 60 ms	Stop antipsychotic drug. Weigh risks and benefits of resuming at 50% of the previous dose
QTc ↑ by > 30 ms	Weigh risks and benefits of decreasing antipsychotic dose by 50%
Extrapyramidal side effects (e.g., muscle stiffness or abnormal movements)	Serve IV/PO Diphenhydramine 1mg/kg/dose Q6-8H PRN (Max 50mg/dose) (To rule out neuroleptic malignant syndrome (NMS) before serving)
NMS (fever, muscle rigidity, tremor, altered consciousness, autonomic instability, ↑creatine kinase)	Stop antipsychotic drug. Consider cooling measures if temperature > 39 °C. Refer to "Management of Malignant Hyperthermia versus Neuroleptic Malignant Syndrome in PICU setting" on the intranet

When in doubt regarding challenging or refractory cases of delirium or the initiation of antipsychotic medications, consider consulting our Child & Adolescent Mental Wellness Service.

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Annex A

Cornell Assessment of Pediatric Delirium (CAPD) revised						
SBS Score ____ (if -2 or -3 do not proceed) **Please answer the following questions based on your interactions with the patient over the course of your shift:**						
	Never **4**	**Rarely** **3**	**Sometimes** **2**	**Often** **1**	**Always** **0**	**Score**
1. Does the child make eye contact with the caregiver?						
2. Are the child's actions purposeful?						
3. Is the child aware of his/her surroundings?						
4. Does the child communicate needs and wants?						
	Never **0**	**Rarely** **1**	**Sometimes** **2**	**Often** **3**	**Always** **4**	
5. Is the child restless?						
6. Is the child inconsolable?						
7. Is the child underactive –– very little movement while awake?						
8. Does it take the child a long time to respond to interactions?						
					TOTAL	

Annex B

Developmental Anchor Points For Youngest Patients

	NB	4 weeks	6 weeks	8 weeks	28 weeks	1 year	2 years
1. Does the child make eye contact with the caregiver?	Fixates on face	Holds gaze briefly Follows 90 degrees	Holds gaze	Follows moving object/caregiver past midline, regards examiner's hand holding object, focused attention	Holds gaze. Prefers primary parent. Looks at speaker	Holds gaze. Prefers primary parent. Looks at speaker	Holds gaze. Prefers primary parent. Looks at speaker
2. Are the child's actions purposeful?	Moves head to side, dominated by primitive reflexes	Reaches (with some discoordination)	Reaches	Symmetric movements, will passively grasp handed object	Reaches with coordinated smooth movement	Reaches and manipulates objects, tries to change position, if mobile may try to get up	Reaches and manipulates objects, tries to change position, if mobile may try to get up and walk
3. Is the child aware of his/her surroundings?	Calm awake time	Awake alert time Turns to primary caretaker's voice May turn to smell of primary care taker	Increasing awake alert time Turns to primary caretaker's voice May turn to smell of primary care taker	Facial brightening or smile in response to nodding head, frown to bell, coos	Strongly prefers mother, then other familiars. Differentiates between novel and familiar objects	Prefers primary parent, then other familiars, upset when separated from preferred care takers. Comforted by familiar objects especially favorite blanket or stuffed animal	Prefers primary parent, then other familiars, upset when separated from preferred care takers. Comforted by familiar objects especially favorite blanket or stuffed animal
4. Does the child communicate needs and wants?	Cries when hungry or uncomfortable	Cries when hungry or uncomfortable	Cries when hungry or uncomfortable	Cries when hungry or uncomfortable	Vocalizes /indicates about needs, eg. hunger, discomfort, curiosity in objects, or surroundings	Uses single words, or signs	3-4 word sentences, or signs. May indicate toilet needs, calls self or me
5. Is the child restless?	No sustained awake alert state	No sustained calm state	No sustained calm state	No sustained calm state	No sustained calm state	No sustained calm state	No sustained calm state
6. Is the child inconsolable?	Not soothed by parental rocking, singing, feeding, comforting actions	Not soothed by parental rocking, singing, feeding, comforting actions	Not soothed by parental rocking, singing, feeding, comforting actions	Not soothed by parental rocking, singing, comforting actions	Not soothed by usual methods eg. singing, holding, talking	Not soothed by usual methods eg. singing, holding, talking, reading	Not soothed by usual methods eg. singing, holding, talking, reading (May tantrum, but can organize)
7. Is the child underactive—very little movement while awake?	Little if any flexed and then relaxed state with primitive reflexes (Child should be sleeping comfortably most of the time)	Little if any reaching, kicking, grasping (still may be somewhat discoordinated)	Little if any reaching, kicking, grasping (may begin to be more coordinated)	Little if any purposive grasping, control of head and arm movements, such as pushing things that are noxious away	Little if any reaching, grasping, moving around in bed, pushing things away	Little if any play, efforts to sit up, pull up, and if mobile crawl or walk around	Little if any more elaborate play, efforts to sit up and move around, and if able to stand, walk, or jump
8. Does it take the child a long time to respond to interactions?	Not making sounds or reflexes active as expected (grasp, suck, moro)	Not making sounds or reflexes active as expected (grasp, suck, moro)	Not kicking or crying with noxious stimuli	Not cooing, smiling, or focusing gaze in response to interactions	Not babbling or smiling/laughing in social interactions (or even actively rejecting an interaction)	Not following simple directions. If verbal, not engaging in simple dialogue with words or jargon	Not following 1-2 step simple commands. If verbal, not engaging in more complex dialogue

Screening and Management of Delirium in the Children's ICU

Order **SBS Q4H** and **CAPD Q12H** (0600hrs and 1800hrs) for **ALL CICU patients**

SBS -2 to -3 → **DO NOT ASSESS CAPD**
Consider reducing sedatives if within clinical goals

SBS -1 and above
(At any point during a nursing shift) → **PROCEED TO ASSESS CAPD**

SUSPECT DELIRIUM IF:
- **CAPD ≥ 9 in a developmentally normal child**
- **CAPD ≥ 9 + SBS fluctuation of ≥ 2 points in 24hrs in a child with developmental delay or abnormal neurological baseline**

ASSESS THE PATIENT FOR CAUSES OF DELIRIUM
- **Review medical history and hospital course**
- **Review medications**
- **Perform clinical / neurological examination**
- **Obtain parent/multi-disciplinary input**
- **Consider targeted investigations based on suspicion of contributing etiologies**

MANAGEMENT OF DELIRIUM
- **Non-pharmacological interventions**
- **Directly address any underlying causes**
- **Consider antipsychotic drugs when severe symptoms persist despite optimal non-pharmacologic therapy:**
  - **Symptoms distressing to patient or family**
  - **Patient at risk of self-harm or device dislodgement**
  - **Delirium is protracted (> 5 days)**

CAPD ≤ 8 → **Continue routine monitoring for delirium**

CAPD ≥ 9 and Severe Symptoms → **Consider Antipsychotic Drugs**

Causes of Delirium

Underlying Disease	Side Effects of Treatment	Environmental Factors
• Infection • Hypoxia • Pain • New organ dysfunction (CNS, cardiac, respiratory, renal, hepatic, endocrine • Metabolic derangements	• Use of benzodiazepines, anticholinergics, ketamine and propofol • High doses of opioids • Deep sedation / Prior coma • Withdrawal syndrome • Red blood cell transfusion • Mechanical ventilation • Cardiopulmonary bypass / ECMO	• Immobilization / Restraints • Sleep-wake cycle disturbance • Lighting schedules • Loud sounds • Unfamiliar people / environment

Non-pharmacological Management of Delirium

Address Underlying Disease	Minimize Iatrogenic Factors	Optimize Environment
• Address infections • Address hypoxia • Prioritize and optimize pain control over sedation (consider paracetamol, NSAIDS, intermittent opioids rather than infusions) • Correct metabolic derangements • Optimize nutrition and hydration	• Minimize sedatives, opioids, ketamine and propofol • Consider dexmedetomidine in place of benzodiazepines • Prevent withdrawal • Avoid anticholinergics • Avoid polypharmacy • Avoid restraints • Encourage early mobilization • Bundle cares to allow for uninterrupted sleep • Remove unnecessary indwelling catheters	• Address the child by name • Introduce care members • Frequently re-assure and re-orient the child • Communicate calmly, clearly and concisely in an age-appropriate manner • Explain care activities simply • Create a quiet, well-lit space with familiar objects from the child's home • Provide spectacles or hearing aids if needed • Facilitate sleep-wake cycle: Encourage being awake in the day and longer stretches of sleep at night • Provide a clock/calendar • Engage parents' help!

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Pharmacological Management of Delirium in the Children's ICU

CAPD ≥ 9 and severe symptoms persistent despite optimal non-pharmacologic therapy

- **Determine Delirium subtype**
- **Is patient strictly NBM?**
- **Perform baseline investigations**

Strictly NBM

- **HYPERACTIVE DELIRIUM / MIXED DELIRIUM** → **IV/IM Haloperidol** → **Oral Drugs Allowed**

Tolerating Orally

- **HYPERACTIVE DELIRIUM / MIXED DELIRIUM** → **PO Quetiapine OR if < 12.5kg, PO Risperidone solution**
- **HYPOACTIVE DELIRIUM** → **Rarely requires drug therapy**; **Consider PO Quetiapine or Risperidone if VERY prolonged or severe**

Subtype	Hypoactive	Hyperactive	Mixed
Clinical Features	• Apathy • Decreased responsiveness • Withdrawn from family or familiar items • Slowed / reduced speech and motor activity • Lethargy	• Agitation / Inconsolability • Restlessness • Hypervigilance • Emotional lability • Combative behaviour • Purposeless actions • Sleep-wake disturbance	• Features of both hypoactive and hyperactive delirium
SBS scores	-3 to 0	+1 to +2	Fluctuating scores above and below 0

Monitoring Investigations while using Antipsychotic Drugs

Parameter	Baseline	After Initiation and Subsequent Dose Increase(s)	Maintenance (if continued)
ECG	X	48 hours	Monthly (Oral agents) Weekly (IV haloperidol)
Renal Panel	X		
Mg	X		
FBC	X	Twice a week	Monthly
CK	X		
LFT	X		
Triglycerides	X	Monthly	Monthly

Dosing Recommendation for IV/IM Haloperidol*	
0 – 1-year-old / 3.5-10kg	0.01 – 0.05mg/kg/day Q6H PRN
1 – 3-year-old / 10-15kg	0.025 – 0.05mg/kg/day Q6H PRN
3 – 18-year-old / >15kg	0.05 – 0.1mg/kg/day Q6H PRN (Max 5mg/day)

*Start at low doses and up-titrate as needed.

Dosing Recommendation for PO Quetiapine
0.5mg/kg/dose Q8H (Regular) AND 0.5mg/kg/dose Q8H PRN^ for breakthrough agitation

^PRN doses can be served 30 mins after regular dose is served

Dosing Recommendation for PO Risperidone	
< 12.5kg	0.05 – 0.1 mg/dose Q12H – Q24H

Up-titration for Quetiapine:
Incorporate previous days PRN doses with regular doses to arrive at next day's total daily dose

Weaning for Quetiapine:
Reduce frequency every 2-3 days (e.g., Q8H → Q12H → ON → ½ of ON dose or stop)

Management of Adverse Drug Events

Adverse Event	Recommendation
QTc > 500ms OR ↑ by > 60ms	Stop antipsychotic drug. Weigh risks and benefits of resuming at 50% of the previous dose
QTc ↑ by > 30ms	Weigh risks and benefits of decreasing antipsychotic dose by 50%
Extrapyramidal side effects (e.g., muscle stiffness or abnormal movements)	Serve IV/PO Diphenhydramine 1mg/kg/dose Q6-8H PRN (Max 50mg/dose) (To rule out neuroleptic malignant syndrome (NMS) before serving)
NMS (fever, muscle rigidity, tremor, altered consciousness, autonomic instability, ↑creatine kinase)	Stop antipsychotic drug. Consider cooling measures if temperature > 39 °C. Refer to "Management" of Malignant Hyperthermia versus Neuroleptic Malignant Syndrome in PICU setting" on the intranet

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