

PEDIATRIC DELIRIUM

A PRACTICAL APPROACH

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Child with Pediatric Delirium.
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Many names have been used by different disciplines to describe the clinical entity of delirium, such as “acute confusional state”, “toxic psychosis”, “ICU psychosis”, “organic psychosyndrome”, “encephalopathy” etc. Pediatric delirium was described for the first time in Leo Kanner’s 1935 textbook *Child Psychiatry* in the chapter “Transient cerebral infections”. “Children become delirious so often and quickly that this is of no interest to us” wrote Bleuler (1955) in his *Lehrbuch der Psychiatrie*. After a long period in which pediatric delirium was ignored in textbooks, the topic was dealt with in the 1991 edition of *Lewis’ Textbook of Child and Adolescent Psychiatry*. In DSM-IV, the section devoted to children and adolescents does not have a single mention of pediatric delirium but there is some mention in the section devoted to delirium in adults. Pediatric delirium is not described in DSM-5. However, in the last few years there has been a growing awareness of the clinical importance of pediatric delirium, consistent with an increasing number of publications on the topic (Kudchadkar et al, 2014; Schieveld & Janssen, 2014; Schieveld et al, 2014) and concerns have been expressed about its clinical implications, the lack of systematic evidence and the lack of treatment guidelines (Schieveld & Janssen, 2014; Schieveld et al, 2014).

DEFINITION

Delirium, from the Latin *de-lira* (out of the track), is a neuro-cognitive disorder due to a somatic illness or its treatment. The brain can react to illness, particularly critical illness, with several responses of which the more important are sickness behavior, fever, epilepsy, catatonia, delirium, refractory agitation, and coma.

By *critical illness* it is meant a life-threatening failure of the brain, heart or major organs. *Sickness behavior* is the behavioral repertoire displayed by humans—and other mammal species—in response to infection, trauma, oncological problems, and their treatment. This behavior is characterized by loss of interests and appetite, emotional irritability, tiredness, and an increased need for sleep.

According to DSM-5 (American Psychiatric Association, 2013) the essential features of delirium are:

- A disturbance of attention or awareness
- This disturbance is accompanied by changes in cognition that cannot be better accounted for by another pre-existing neurocognitive disorder (e.g., mental retardation, dementia)
- The condition develops in a short period of time, hours or days, and often fluctuates during the day, typically worsening in the evening (“sundowning”); and
- There are indications from the patients’ history, examination or laboratory results that the disturbance is probably the result of a medical condition or its treatment.

The DSM-5 definition of delirium has been criticized because of the requirement to exclude coma without specifying how this is to be done. Consciousness has two simultaneous aspects:

- Arousal, which goes from clarity of mind to somnolence, stupor, and to coma; and

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Delirium is acute brain failure in man

—Lipowski, 1980)

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- Content of thought, from logical reasoning according to age and education to thought disorder.

Without an appropriate level of arousal thinking is not possible; that is, arousal is necessary for thinking. Arousal allows mental processes and the ability to focus, sustain and shift attention to take place. With somatic disorders, *attention is the first to be lost and the last back.*

ICD-10 (World Health Organization, 2015) defines delirium as an etiologically nonspecific organic cerebral syndrome characterized by concurrent disturbances of consciousness and attention, perception, thinking, memory, psychomotor behavior, emotion, and the sleep-wake schedule. The duration is variable and the degree of severity ranges from mild to very severe.

EPIDEMIOLOGY

Delirium has a high prevalence; it affects 10% to 30% of general hospital patients and up to 80% in tertiary intensive care units (ICUs). Delirium in adults and the elderly is strongly associated with increased length of hospital stay, morbidity and mortality. In the elderly it is associated with a faster cognitive decline, loss of independence, and increased mortality in the year following hospital discharge. Delirium is the most important predictor of the proximity of death in the elderly and in oncological patients, young or old (terminal delirium).

The reported prevalence of delirium in critically ill children varies from 20% to 30%. Rates depend on age (more common in younger children), severity of the illness, number of medications, diagnostic tools used, and group under study (e.g., pediatric ICU patients, general ward). Mental retardation and a previous episode of delirium are also known risk factors.

CLINICAL CHARACTERISTICS

According to seriousness, pediatric delirium can be benign and non-benign. There are two types of benign pediatric delirium: emergence delirium and the common delirium seen in general practice.

Emergence delirium, also known as emergence agitation, is a well-documented phenomenon occurring in children—and adults—in the immediate postoperative period, after the withdrawal of anesthetic drugs. It frequently occurs in an otherwise healthy child even after minor surgery or a diagnostic procedure. Clinically, it fulfills all the criteria for pediatric delirium but has a benign course and usually resolves completely—mostly without any intervention—in 30 to 45 minutes.

In general practice pediatric delirium frequently occurs in the context of an infection (febrile delirium). It is characterized by confusion, which can be intense, in a sick child with a waxing and waning course, increasing in the evening and night, usually coinciding with an increase in the fever. Although it can be dramatic, more often than not the underlying infection resolves within two or three days and so does the delirium. In cases of persistent delirium of this kind an emergency medical assessment is indicated.

*The brain is wider than
the sky
For put them side by
side
The one the other will
include
With ease - and you
beside.*

—Emily Dickinson
(1830-1886)



Paul Eugen Bleuler (1857-1939) was a Swiss psychiatrist known for his contribution to the understanding of mental illness. He coined the term "schizophrenia". Bleuler considered pediatric delirium to be unimportant because children became delirious easily and often. Opinion has changed since then.

Case vignette 1

A 6-year-old boy was admitted to the pediatric ICU with respiratory insufficiency due to an asthma attack. Despite asthma treatment he deteriorated and needed intubation and mechanical ventilation with high doses of sedatives and even muscle relaxation for a few hours because of high ventilation parameters. Before intubation he said he was afraid to die because of his breathing difficulty.

After two days his asthma improved and he was weaned from the ventilator. After extubation, on the third day after admission, he became confused, extremely anxious and had hallucinations about flying objects and monsters; he became verbally aggressive (swearing using words his parents believed he did not know). Besides, his parents did not recognize his behavior as that of their child anymore. He was diagnosed as being delirious and treated with lorazepam (because of his extreme anxiety) and haloperidol intravenously.

Twenty-four hours after starting treatment his delirium improved, his behavior normalized and he told his parents that he was feeling well again. This is a typical presentation of *hyperactive* pediatric delirium.

Case vignette 2

A 4-year-old boy was admitted to the pediatric ICU with epiglottitis and was mechanically ventilated for three days. The boy was very agitated during the ventilation period (e.g., fighting with the ventilator, extreme restlessness) and was sedated with midazolam, ketamine, and morphine. After 48-hours he improved and was weaned from the ventilator. On the third day of his admission he no longer required invasive ventilation support and was extubated. The sedatives were tapered off and stopped.

On the fourth day of admission he was scheduled to be transferred to the referring hospital. In the afternoon, two hours before the transfer was due, the boy suddenly became very agitated and anxious. Despite his parents being present, he made no eye contact with them or the nurses. Shortly after he did not seem to be aware of his surroundings (e.g., of his parents' presence) and appeared to "live in his own world". He scored seven on the SOS-PD scale (a score of 4 or higher is consistent with pediatric delirium). A child psychiatrist was consulted who concluded that the boy had developed delirium and advised starting treatment with risperidone. Twelve hours after starting treatment his behavior normalized and he was able to be transferred back to the referring hospital. This is a case of a *combined* type of pediatric delirium (initially hyperactive and then hypoactive).

Case vignette 3

A 3-year-old girl was admitted for tracheal surgery. After surgery she was mechanically ventilated for six days during which she was sedated with midazolam, ketamine, dexmedetomidine, levomepromazine, and morphine in various combinations. She was also treated with dexamethasone. To prepare her for extubation this sedation was tapered off except for the morphine which was changed to methadone. The day after extubation she suddenly became slightly agitated, disoriented and was unable to focus her attention. That same evening she became apathetic and unresponsive. She seemed to look through us with an empty gaze and without making eye contact. She scored 21 points on the CAP-D (a score above 10 is consistent with pediatric delirium) with high scores particularly on the hypoactive delirium criteria. Her parent's remarked: "We do not recognize our daughter anymore". This is a typical case of *hypoactive* pediatric delirium.



Zbigniew J Lipowski (1924-1997) was a Polish-Canadian neuro-psychiatrist who wrote several books on consultation-liaison psychiatry, delirium and psychosomatic illness as well as numerous articles. Lipowski had an abiding interest in and knowledge about the interface of consultation liaison psychiatry and neurology, in particular the problem of delirium. His work culminated with the publication in 1980 of his influential monograph *Delirium: Acute Confusional States*.

Delirium can also be *hyperactive* (children are agitated, irritable and thrash about), *hypoactive* (they appear apathetic, uninterested) and *mixed* (see case vignettes for clinical examples).

Overall, there are more similarities than differences between children, adults and the elderly:

- In general, critically ill children with delirium have a higher resilience (and better prognosis) than adults. This is probably owing to a better vascularization of their brains, hearts, lungs etc. and they mostly have no other comorbidities or polypharmacy
- The negative neuro-cognitive effects of delirium in adults and the elderly are well known, but we do not know yet whether this is also true for children.

ETIOLOGY

Increasing evidence suggests there is a positive association between illness severity and pediatric delirium, that is, severity of disease is a major risk factor for delirium—the most common cause of severe delirium is a critical illness. Depending on the local facilities, the most frequent places to encounter pediatric delirium are hospitals or pediatric ICUs. The differential diagnosis of conditions potentially leading to delirium is summarized by the acronym “I WATCH DEATH” (Wise et al, 1987; see Table I.5.1).

Table I.5.1. Possible causes of delirium, summarized by the acronym ‘I WATCH DEATH’*

I	Infections	Encephalitis, meningitis, urinary tract infection, pneumonia...
W	Withdrawal	Alcohol, barbiturates, benzodiazepines...
A	Acute metabolic	Electrolyte imbalance, hepatic or renal failure...
T	Trauma	Head injury, postoperative...
C	CNS pathology	Stroke, haemorrhage, tumour, seizure disorder...
H	Hypoxia	Anaemia, cardiac failure, pulmonary embolus...
D	Deficiencies	Vitamin B12, folic acid, thiamine...
E	Endocrinopathies	Thyroid, glucose, parathyroid, adrenal...
A	Acute vascular	Shock, vasculitis, hypertensive encephalopathy...
T	Toxic or drugs	Toxins, substance intoxication, medications (alcohol, anaesthetics, anticholinergics, narcotics etc.)
H	Heavy metals	Arsenic, lead, mercury...

*Wise et al, 1987.

The differential diagnosis of *hypoactive delirium*—given its high prevalence and frequently disappointing response to treatment deserves particular attention:

- In the context of withdrawal of medication (too fast)
- When there is an underlying intoxication with psychotropics or a neuroleptic-induced syndrome due to sensitivity to antipsychotics
- The possibility of non-convulsive status epilepticus, major depressive disorder and catatonic inhibition should be excluded.

An EEG may be helpful in these cases, although frequently there is a mix of conflicting or co-occurring signs and potential explanations.

DIAGNOSIS

According to the literature, delirium is underdiagnosed, especially in young, critically ill children (Schieveld & Janssen, 2014; Schieveld et al, 2009). A possible reason is that nurses and physicians do not specifically look for the symptoms of delirium and it is difficult to assess symptoms in pre-verbal patients. A number of delirium symptoms overlap with those observed in other conditions, such as pain, distress, and opioid or benzodiazepine withdrawal (Ista et al, 2007). There are important clinical reasons for assessing pediatric delirium and taking it seriously (Schieveld & Janssen, 2014):

- Delirium is an *acute brain failure* and the consequences of such a failure can be severe
- The neuro-metabolic stress of delirium probably has a negative impact on the outcome and recovery from critical illness
- A hyperactive delirium is accompanied by various risks, such as pulling out of IV lines and catheters, auto-detubation, stepping or falling out of bed etc.
- It is stressful for the patient who may experience terrifying hallucinations or delusions (sometimes without amnesia) that may lead to a post-traumatic stress disorder (PTSD) and
- It can also be very stressful for the child's family and clinical staff (up to 25 % of parents of children who have been in a pediatric ICU may develop PTSD) (Colville & Pierce, 2012).

The acute occurrence of a disturbance of cognition, emotions, consciousness, or a behavioral disturbance in a critically ill child should raise the suspicion of pediatric delirium and the need to consult a child psychiatrist, if available. Nurses and physicians may find it difficult to assess symptoms of delirium, including cognitive changes, especially in pre-verbal and critically ill and mechanically ventilated children. In these children, other aspects, such as behavioral characteristics and non-verbal interactions between parent and child, should be considered.

One of the most challenging issues is how to diagnose pediatric delirium accurately in critically ill children. In adults, tools that rely on neurocognitive parameters can be used. However, because most critically ill pediatric patients are younger than 3 years or may have intellectual disabilities, one has to rely on behavioral symptoms. In principle there is no lower limit to the age in which delirium can occur; the youngest cases described have been in 3-month-olds (Schieveld, 2008; Silver et al, 2012; Turkel & Tavaré, 2003). In the last few years,

steps had been taken to develop observational screening tools—variations on the theme of parents' comment that "this NOW is not my child!"

The most frequently described early symptoms are subtle: cognitive (e.g., they do not remember what they have just been told, are unable to concentrate, do not know where they are), perceptual (e.g., visual hallucinations), thought (e.g., delusions), language, emotional (e.g., may be frightened, irritable) and psychomotor disturbances (e.g., restless, agitated, unable to be still). Answering the following questions (based on the CAP-D; Silver et al, 2012) can be helpful in raising the possibility of delirium:

- Does the child make eye contact with the parents?
- Are the child's actions purposeful?
- Is the child aware of their surroundings?
- Does the child communicate needs and wants?
- Is the child restless?
- Is the child inconsolable?
- Is the child underactive (moves very little while awake)?
- Does the child take a long time to respond to interactions?

The diagnosis of delirium in children older than 5 years with normal development is based on DSM-5 or ICD-10 criteria. Accurately diagnosing pediatric delirium requires using a reliable, valid and clinically suitable bedside tool that may also serve for screening and to guide treatment such as the Pediatric Anesthesia Emergence Delirium Scale (PAED; Sikich & Lerman, 2004); the pediatric Confusion Assessment Method for ICU (pCAM-ICU; Smith et al,



Child with pediatric delirium.
Roel Seidell, with permission.

Table I.5.2 Characteristics of validated tools for the assessment of delirium in critically ill children

	PAED	pCAM-ICU	CAP-D	SOS-PD
Age group	1-17 years	> 5 years	0-21 years	0-16 years
Variables assessed	<ul style="list-style-type: none"> • Eye contact with caregiver • Purposeful actions • Awareness of surrounding • Restlessness • Inconsolability 	<ol style="list-style-type: none"> 1. Acute change or fluctuating course of mental status 2. Inattention 3. Altered level of consciousness 4. Disorganized Thinking 	<ul style="list-style-type: none"> • Eye contact with caregiver • Purposeful actions • Awareness of surroundings • Ability to communicate needs • Restlessness • Inconsolability • Underactivity • Response to interaction 	<ul style="list-style-type: none"> • Agitation (restlessness), anxiety, eye contact, grimacing • Impaired attention • Speech • Tremor • Muscle tone • Purposeful actions • Sleeplessness • Hallucinations • Disorientation • Sweating • Acute change / fluctuation.
Score range (cut off point)	0-25 (10)	Delirium* if 1, 2 and 3 or 4 present	0-40 (9)	0-15 (4)
Reliability data	+	+	+	+/-
Forms of validity established	Criterion	Criterion	Criterion	Face (criterion pilot)
Sensitivity	91%	83%	94%	91%
Specificity	98%	99%	79%	97%
Clinical utility	Feasibility and utility established bedside	Feasibility	Utility established bedside	Feasibility

PAED: Pediatric Anesthesia Emergence Delirium scale (Janssen et al, 2011).

pCAM-ICU: Pediatric Confusion Assessment Method-Intensive Care Unit (Smith et al, 2011).

CAP-D: Cornell Assessment of Pediatric Delirium (Silver et al, 2012; Traube et al, 2013);

SOS-PD: Sophia Observation withdrawal Symptoms-Pediatric Delirium scale (van Dijk et al, 2012; Ista et al, 2014).

*There is no score range.

2011); the Cornell Assessment Pediatric Delirium tool (CAP-D; Silver et al, 2012; Traube et al, 2013); and the Sophia Observation Withdrawal Symptoms-Pediatric Delirium scale (SOS-PD; van Dijk et al., 2012, Ista et al, 2014). No tool stands out; therefore the choice is a matter of context and personal preference. The characteristics of the better studied rating scales are summarized in Table I.5.2.

It must be emphasized however that the right diagnosis and treatment for pediatric delirium cannot be made merely on the basis of scores on an observational screening tool. It is also necessary to evaluate all other possible diagnostic explanations of a sudden emotional or behavioral disturbance in a critically ill child (as listed in Table I.5.1). After a positive score on a pediatric delirium rating scale and before starting treatment one should answer three questions to exclude other explanations for a positive delirium score (e.g., as described by Esseveld et al, 2013). Only after a negative response to these questions a diagnosis of delirium would be made and treated accordingly. These questions are:

- Are symptoms the manifestation of a somatic complication developing (e.g., pneumonia)?
- Has there been a change of medication?
- Is there physical discomfort (a full bladder, full bowel, stomach distension, hunger, thirst, itching, pain due to lines, IV lines, catheters, etc.?)

TREATMENT

Non-pharmacological interventions

Minimizing risk factors

Many risk factors for delirium have been identified. These can be classified as relating to the patient, iatrogenic, and environmental (e.g., hospital, ward, pediatric ICU). The conditions for which children are admitted to the ICU often predispose them to delirium, for example infections, metabolic disorders, hypertension, pain, and withdrawal from medications. Iatrogenic factors that precipitate delirium in ICU patients include mechanical ventilation, restraints, sleep disturbance, catheters, and IV lines.

Minimizing these factors is a logical and important approach in preventing the onset of pediatric delirium. Non-pharmacological interventions appear to have been successful in several studies (Tabet & Howard, 2009). For example, a 40% decrease in the incidence of delirium was achieved in adults using a multi-component approach, which included repeated reorientation, early mobilization, noise reduction, and a non-pharmacological sleep management (Marcantonio et al, 2001). In adults, the effectiveness of preventive interventions such as early mobilization, ear plugs, and staying in a single room is well established (Colombo et al, 2012; van Rompaey et al, 2012; Zaal et al, 2013).

Can these findings from adults be extrapolated to children? There is limited evidence that this is the case. However, common sense suggests that these interventions (for example promoting orientation and day-night rhythm, and avoiding overstimulation by light and sounds) may be effective for children as well.



Click on the image (and select "Multidisciplinaire Richtlijn pediatrisch delier") to access the Dutch Multidisciplinary Guideline for Pediatric Delirium (in Dutch)

Table I.5.3 Non-pharmacological interventions for delirium in children*

- Constant presence of a parents and a soothing stimulation of all the five senses:
- A dim nightlight, day/night lighting schedule
- Familiar music/ sounds/ voices, or smells
- Favorite toys, pets, blankets, and familiar photographs on the bedside
- Staff psycho-education (to give reassurance and improve orientation)
- Information leaflet for parents on pediatric delirium
- Optimization of the level of sensory stimulation (in case of hyperactive delirium move to single quiet room; if hypoactive delirium, increase social interaction)
- If possible, discontinuation of drugs that reinforce delirium
- Early mobilization

*Hatherill et al, 2010; Schieveld et al, 2007.

The role of parents

Apart from involvement in the daily care of their hospitalized child, parents can have a major role in the prevention, detection and treatment of delirium. A model that recognizes and respects the uniqueness of each family and empowers and encourages them to partner with health care providers is useful. Opinions are asked, values are respected and family members are viewed as key elements in their child's health care. With this partnership one seeks to create a soothing environment for the child in order to prevent or mitigate the onset of delirium and to optimize the child's chances of recovery.

Symptoms associated with delirium, such as delusions or hallucinations, may come as a complete surprise, something the family has never encountered before, and can be very frightening for both child and parents. This may lead to parents not recognizing their child's behavior, becoming afraid that neurological damage has occurred or that their child is going to die (Schieveld et al, 2007). Not knowing how to cope with these behaviors in their child makes parents insecure and anxious; this in turn can influence the child, causing the delirium to worsen. A soothing stimulation of all the five senses of the child with delirium is advocated. The constant presence of one parent during the hospitalization, hearing parents' voices, readily visible photographs of parents or other well-known family members, and favorite toys decrease the severity of delirium (Kim et al, 2010; Hatherill et al, 2010; Schieveld et al, 2007). Therefore it is essential that parents and family members are informed extensively about all aspects of pediatric delirium and are allowed to be close to the child as much and as often as possible.



It is equally important to recognize that a critically ill child is a major burden for the parents, can exhaust them and lead to arguments between them and with the multidisciplinary team, affecting the parents' relationship, their relationship with the care team, the care of their other children, and neglect of their work. These issues should be approached within the multidisciplinary team with an open mind and heart. A leaflet providing information for parents and relatives may be of help. An example is presented in the Appendix.

Intensive care units are scary places.

Photo: Dayton Children's

Pharmacological prevention

Prevention of pediatric delirium by pharmacological means is not advised in children, although it is sometimes recommended in adults, especially in patients that have experienced delirium previously. There are no studies on pharmacological prevention of delirium in children although there are studies on prevention of emergence delirium in children. These studies are very variable in quality and no firm conclusions for the prevention of pediatric delirium can be drawn from them.

Pharmacological treatment

Hyperactive delirium

Medication may be considered to reduce symptoms such as anxiety, agitation, hallucinations and disturbed sleep. Pharmacokinetics in children is different from adults. Before starting pharmacological treatment the risk of side effects and interactions with other medications and the route of administration have to be considered and weighed against the potential benefits of treatment.

The same antipsychotics (typical antipsychotics, such as haloperidol, and atypical antipsychotics, such as risperidone) are used in children as in adults. Benzodiazepines and clonidine are used in the treatment of delirium due to benzodiazepine withdrawal; clonidine and methadone are used in the treatment of delirium due to opiate withdrawal.

Table I.5.4. Recommended dose of intravenous (IV) haloperidol for hyperactive pediatric delirium

Age (years)	Weight (kg)	Maximum loading dose (IV)	Maintenance dose (IV)	Maximum dose (IV)
0-1	3,5-10	<ul style="list-style-type: none"> 0.05 mg in 30 minutes 	<ul style="list-style-type: none"> Dose not exactly known 0.01-0.05 mg/kg/day, divided into 2-4 times daily 	<ul style="list-style-type: none"> Unknown
1-3	10-15	<ul style="list-style-type: none"> 0.15 mg in 30 minutes 	<ul style="list-style-type: none"> 0.025 mg/kg/day divided into 2-4 times daily 	<ul style="list-style-type: none"> Unknown
3-18	> 15 kg	<ul style="list-style-type: none"> 0.3-0.5 mg in 30 minutes 	<ul style="list-style-type: none"> 0.05 mg/kg/day divided into 2-4 times daily 	<ul style="list-style-type: none"> Unknown in children younger than 16 years In children aged 16 years or older: 5 mg per day divided into 2-4 doses

Studies on the pharmacological treatment of pediatric delirium are scarce and have serious methodological flaws: small numbers of patients with large age differences and very different physical illnesses, interventions or outcomes are poorly described, and the studies often have no control group. Therefore recommendations are based on consensus rather than on evidence. However, there are suggestions that haloperidol and risperidone are effective in reducing symptoms of pediatric delirium in seriously ill children.

Haloperidol is mostly given intravenously; risperidone is only available orally. In a sophisticated pediatric ICU setting the IV route is preferable because it is faster and easier to control. The oral administration of haloperidol or risperidone is also acceptable. Dosage varies in the different studies. The recommended dosages are summarized in Tables I.5.4 and I.5.5. Benzodiazepines are not usually recommended due to their potential delirigenic effects in adults and the elderly.

Most experts recommend to start pharmacological treatment of pediatric delirium when, in spite of non-pharmacological interventions, the child shows extreme agitation or anxiety, hallucinations or delusions, especially when this leads to discomfort, stress or danger to the child (e.g. loss of IV catheters or endotracheal tubes), when delirium leads to extreme stress in parents or when it interferes seriously with the care of other patients in the ICU or ward. When the child is comfortable, it is easier for the parents to take care of their child. Some studies indicate that patients who are treated pharmacologically may be more comfortable and weaned earlier from the ventilator than patients that are not treated.

Adverse effects are extrapyramidal symptoms, such as dystonia, oculogyric

Table 1.5.5 Recommended dose of haloperidol or risperidone orally (PO) for hyperactive pediatric delirium. Oral doses of haloperidol and risperidone are the same.

Weight (kg)	Loading dose (mg) (PO)	Maintenance dose (mg) (PO)	Maximum dose (mg) (PO)
<45 kg	<ul style="list-style-type: none"> 0.02 mg/kg 	<ul style="list-style-type: none"> 0.01-0.08 mg/kg/day divided into 2 to 4 doses 	<ul style="list-style-type: none"> 4 mg/day divided into 2 to 4 doses
>45 kg	<ul style="list-style-type: none"> 0.5-1 mg Maximum 2 mg/day, divided into 2 to 4 doses 	<ul style="list-style-type: none"> 0.01-0.08 mg/kg/day divided into 2 to 4 doses 	<ul style="list-style-type: none"> 6 mg/day divided into 2 to 4 doses. Dosages >6mg have not been studied

crisis, akathisia, and hyperpyrexia. Extrapyramidal symptoms are seen frequently, particularly if antipsychotics are increased rapidly. *Start low and go slow* is an important principle. It can take 24 to 48 hours before an adequate response is achieved. To cover this time-window of ongoing agitation the short term addition of levomepromazine (also known as methotrimeprazine) has been described (with a total starting dosage of 1 to 3 mg/IV slowly in 30 minutes and then titrating according to the clinical response, up to a maximum dosage of 1mg/kg/IV in 24 hours).

Recognizing and treating adverse effects is important. Treatment consists in reducing the dose of antipsychotic and administration of an anticholinergic drug such as biperiden (50 micrograms/kg/IV in 15 minutes). In adult patients lengthening of the QTc interval has been reported with the possibility of Torsades de Pointes. This has not been reported in children. Experts, however, recommend performing an ECG before starting treatment with haloperidol when the child has other risk factors for increased QTc interval (e.g., electrolyte abnormalities, other medications that can lengthen the QTc interval, or medications that influence CYP2D6 or CYP3A4 metabolism).

More adverse effects have been reported for haloperidol than for risperidone. Therefore risperidone is the treatment of choice when symptoms are not extreme and oral administration is possible. When no benefit is obtained with one of them, a switch to the other should be considered.

The consensus is that a pediatric delirium rating scale should be used at least three times daily, to score delirium when medication is started and for as long as the patient receives medication. It is not known for how long treatment should continue. Experts advice to continue treatment at least until symptoms have disappeared and until risk factors that possibly led to the delirium have lessened. Medication should be weaned gradually, over a few days.

Hypoactive delirium

There are no studies and no consensus on the pharmacological treatment of hypoactive pediatric delirium.

SEQUELAE OF DELIRIUM IN CHILDREN AND PARENTS

There are no studies on the long term sequelae of pediatric delirium. The published studies—on long term sequelae in children that had a hospital admission—have been performed in premature-born children admitted to neonatal intensive care units, children with cancer, or children admitted to a pediatric ICU. PTSD symptoms are often reported in these children and their parents. Some studies describe an association between psychological and psychiatric problems after discharge and the occurrence of “delusional memories” (possibly a symptom of delirium) about their ICU stay and invasive procedures during the ICU admission (Colville et al, 2008; Colville & Pierce, 2012)

In adults, there is evidence that some cognitive problems after ICU discharge are related to benzodiazepine use and delirium. Possible causes of cognitive problems in children after pediatric ICU admission are hypoxia, hypoperfusion, infection, and trauma. Long term effects of medications such as benzodiazepines, opioids and anesthetics have not been studied in children. Animal studies, show that these drugs can be neurotoxic, especially to the developing brain.

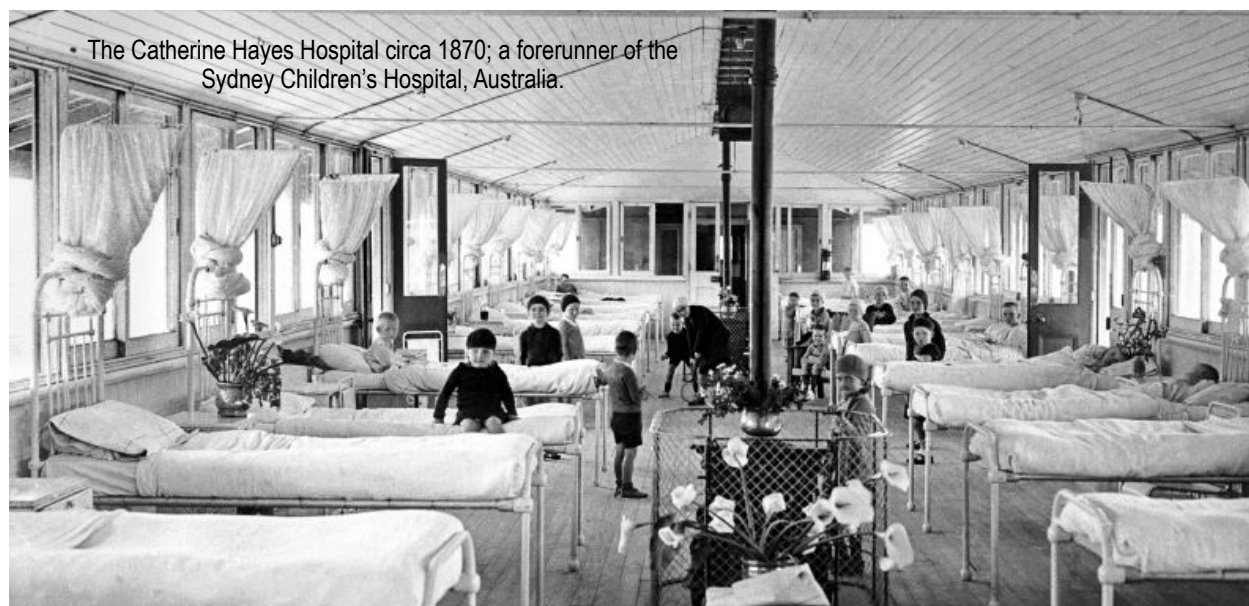
- Do you have questions?
- Comments?

Click here to go to the Textbook's Facebook page to share your views about the chapter with other readers, question the authors or editor and make comments.

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Appendix I.5.1

INFORMATION ABOUT PEDIATRIC DELIRIUM FOR FAMILY, OTHER CAREGIVERS, AND INTERDISCIPLINARY MEDICAL AND NURSING TEAM*

Introduction

Your child has been admitted to hospital due to one or more physical conditions, accidents or operations, which have led your child to become seriously ill. You may have noticed that your child's reactions are not the same as usual and you may have been worried by your child's condition. The child you know is now behaving differently from usual, is agitated or apathetic and it is difficult to make contact or have a conversation with him/her. This state of confusion is called *delirium*. This leaflet gives information about delirium, its origin and how to deal with it best.

What is delirium?

Delirium is a state of confusion that can suddenly appear when a child has an illness. Children with delirium behave differently than usual; they are agitated or apathetic and may act strangely. A delirious state is transitory. When the physical illness improves the confusion usually disappears. The confused state can last from several hours to days or even weeks depending on:

- The severity of the illness
- Your child's age
- Your child's physical condition.

Causes

A delirious state can have many causes. For example, in adults alcohol withdrawal is a common cause of delirium. Children who have

never drank alcohol can also become delirious because of an infection (for example an ear infection, pneumonia), a major operation, heart or lung diseases, brain disorders, infections etc. Acute confusion can also be caused by trauma to the head. Stopping some medications such as strong painkillers, or drugs used in anesthesia, or too little sleep can sometimes cause delirium.

Children with acute confusion or delirium can show some of the following:

- Agitation or apathy
- Not being as clear-minded as usual, like if everything just passes them by, and not recognizing where they are. Establishing contact with them can be difficult in these circumstances
- They may not remember things they have just been told and may not be aware of this lack of memory
- Because sometimes they do not recognize their surroundings, their reactions can be different from usual. They may appear watchful, suspicious, angry or even aggressive. They may want to pull off intravenous lines or other medical instruments. Some children may withdraw into themselves when they would not normally do that
- It is important to realize that very ill children, especially if delirious, regress, behaving like when they were much younger, and should be approached as if they were younger

- They may have a distorted view of reality, for instance seeing or hearing things that aren't there. For them, however, these experiences are very real, can be frightening, and it is better not to argue with the child about them
- Often the symptoms vary during the day usually getting worse in the evening; periods of agitation may alternate with periods of calm or sleepiness.

How to handle delirious children

Children suffering from delirium have difficulty communicating or responding emotionally. Hearing familiar voices and seeing familiar people helps them. You can give your child your utmost support by:

- Speaking calmly in clear, short sentences
- Telling your child who you are and what you are doing there, repeating it if necessary
- Explaining where they are and why they are there
- Trying to involve your child in what is happening now
- Bringing pictures from home, close family and friends
- Asking simple, single questions (e.g.: "did you sleep well?" instead of "did you sleep well, or were you often awake?").
- When people ask too many questions these children can become agitated. It is often enough to just being there
- Visiting is important, but make sure there are not too many visitors at once. If more than two people visit at the same time, remain to one side of the child, so that your child can focus on one point
- Making sure that, if possible, your child wears their glasses, hearing aids etc.
- If children have unusual experiences (e.g., seeing things that are not there) it is better not to go along with it. Do

not argue but reassure them and make clear that you perceive things differently. Try to change the subject to actual events and real people.

Medical treatment

Before treatment, the attending physician will try to determine the medical causes of the delirium as quickly as possible (delirium after anesthesia is very common and can be worrying but almost always disappears in less than one hour without treatment other than reassurance).

Non-medication treatment tries to orient the child and reduce stress and discomfort by stimulating all senses in a soothing way, as described in the section "How to handle delirious children".

There are medications that can reduce or even remedy the delirium although they can also have side effects, usually mild. The two medications more often used are haloperidol and risperidone. Preferably a child psychiatrist, if available, or other medical or nursing specialist with expertise in delirium is involved in these circumstances.

If children are agitated, it is often necessary to take precautions to prevent them from hurting themselves, for example by falling out of bed or pulling out an intravenous line. In case of severe agitation, it may be necessary to immobilize the child to prevent injuries.

It is difficult to predict how long the symptoms of delirium will last. It varies from hours to days. Some children may have symptoms for some time.

If you have further questions after reading this leaflet, you can ask them to the attending physician or nurse.

*Modified from: *Leaflet on Pediatric Delirium*, Jan NM Schieveld et al, 2009. internal publication MUMC+.