Agitated patient in ICU- approach & management

Arjun Srinivasan

Agitation

- Extreme arousal, irritability, excess motor activity driven by internal sense of discomfort such as disease, pain, anxiety and delirium

- Acute

- Ongoing

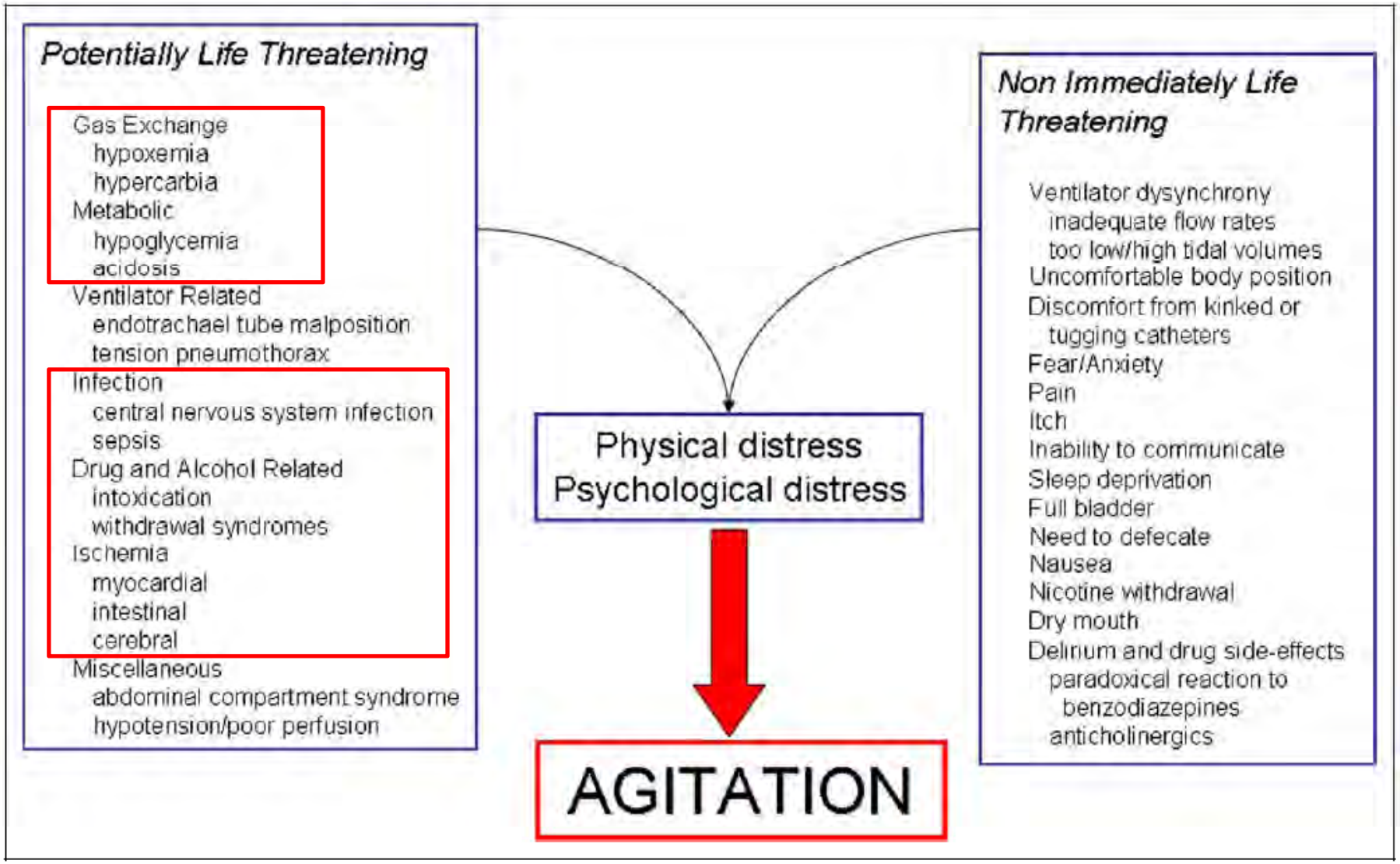
Why bother ?

- Harm to self & staff
- Prolonged & inadequate ventilation
- Inappropriate & overuse of sedation
- Increased ICU cost, morbidity & mortality

Approach

- Onset & organ dysfunction
- Etiology & reversibility
- Therapy

Etiology



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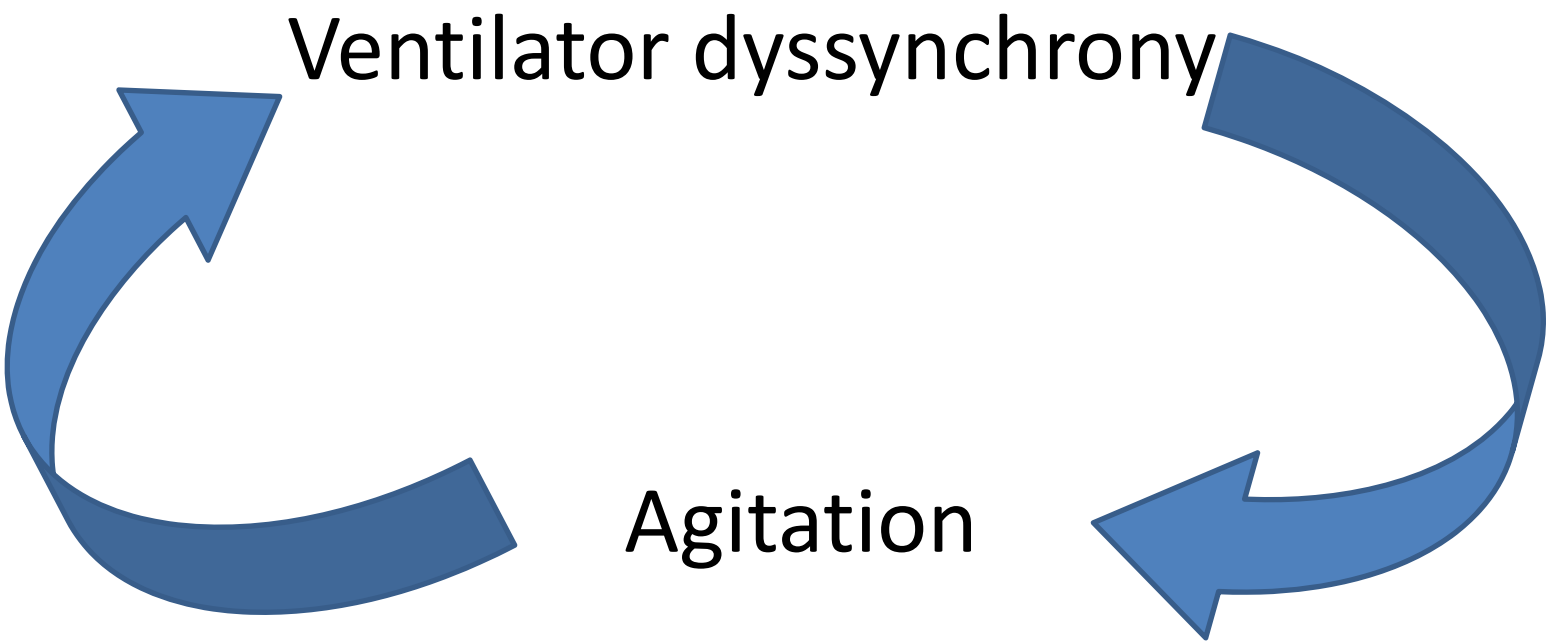

Ventilator dyssynchrony
Agitation

Patient ventilator dyssynchrony

- Ventilator should cycle in synchrony with pt's respiratory drive
- Indirectly proportional degree of support
- Dyssynchrony arises frequently
  - Trigger
  - Rest of inspiration (flow dependent)
  - Cycle
  - End of expiration

Physical signs

Failed trigger

- Chest wall & abdominal effort in spite of no breath delivery

Trigger delay

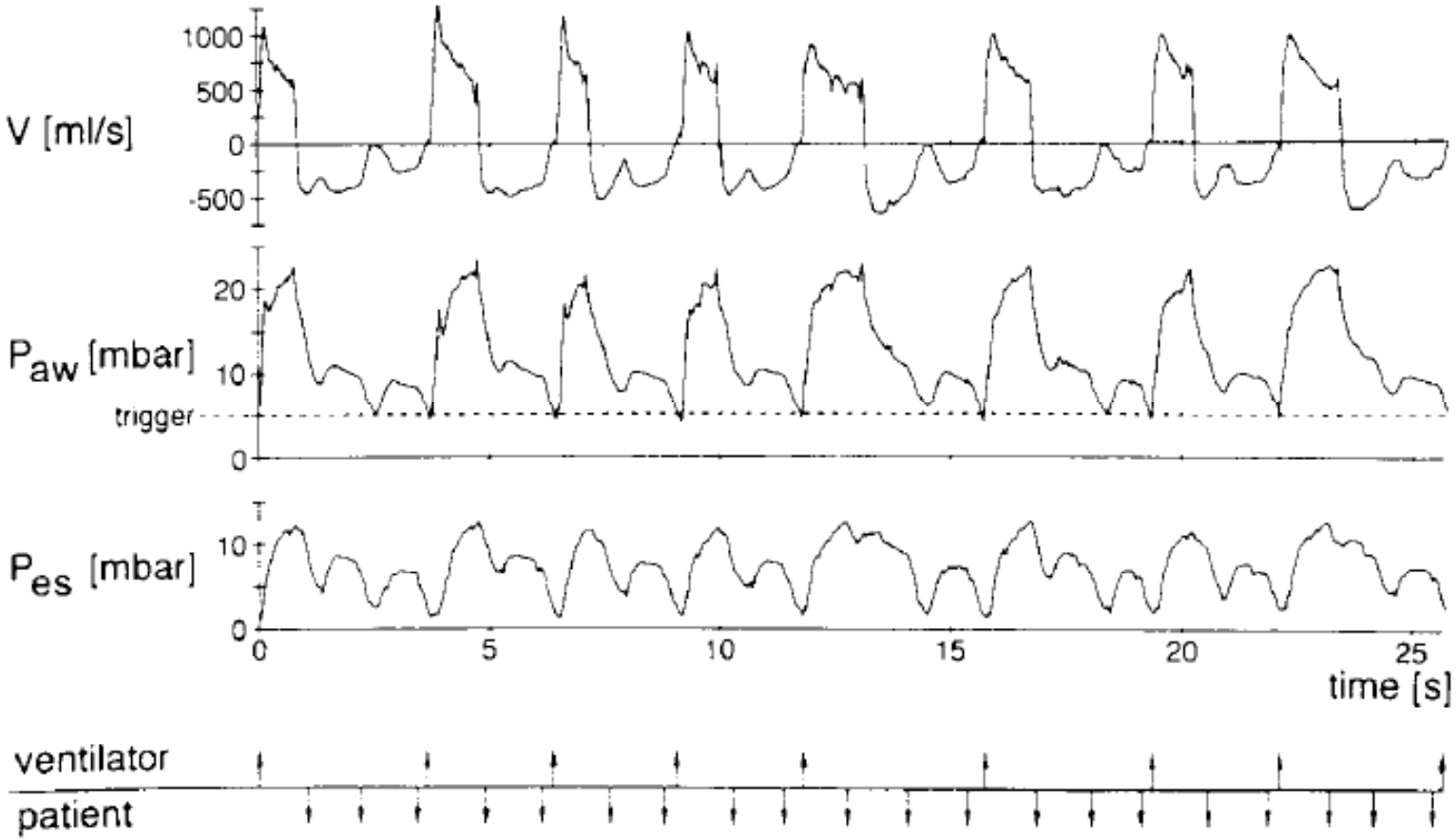
- Appreciable delay between effort & breath delivery

PEEPi

- Inward chest wall movement persisting up to next inspiration
- Audible expiratory sound during next inspiration

Trigger dyssynchrony

- Too little
  - Inappropriate setting
  - Dynamic hyperinflation & PEEPi
  - Decreased effort / drive
  - Increased resistance (ET tube / tubing / pt's respiratory mechanics)
- Time delay
  - Ventilator design anomaly
- Too much
  - Inappropriate setting
  - Water / secretions in tubing
  - Leak / expiratory valve fault



Chest 1995;107:1387–1394.

Strategies for Optimizing trigger synchrony

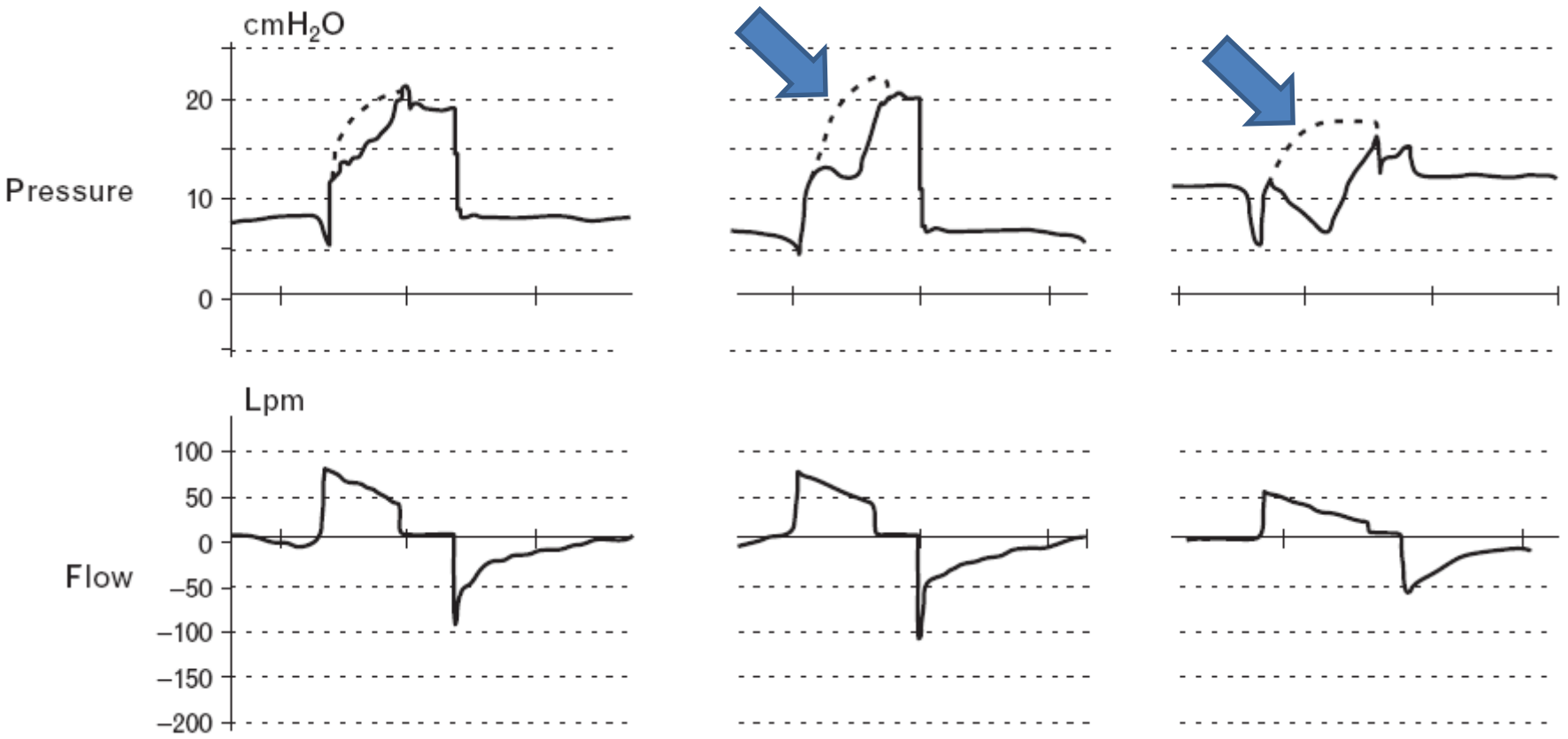
Manifestation	Cause	Treatment	Potential Consequences
Trigger dyssynchrony (including untriggered breaths)	Intrinsic positive end-expiratory pressure ($PEEP_I$) (dynamic hyperinflation, DH)	Treat airflow obstruction	
		↓ Minute ventilation (V_E)	May not work in spontaneously breathing patient
		↑ Inspiratory flow rate (IFR)	May lead to ↑ RR
		Add extrinsic PEEP	If $PEEP_E$ > 85% $PEEP_I$, DH may worsen
	Improper trigger sensitivity	Decrease trigger pressure to 0.5–1.0 cmH_2O	Autocycling
		Δ to FT or ↑ Flow sensitivity	
	↓ Respiratory drive	Minimize sedation	
	Respiratory muscle weakness	Correct electrolytes, nutrition	
	↑ Endotracheal tube resistance	Δ Endotracheal tube	

SEMINARS IN RESPIRATORY AND CRITICAL CARE MEDICINE/VOLUME 22, NUMBER 2 2001

Flow dyssynchrony

- Frequently due to low fixed flow setting in volume cycled flow controlled ventilation
- Pt has breath to breath variability
- Mismatch especially in cases of ARDS & COPD
- Patient's requirement may exceed set parameters
  - Minute ventilation
  - Tidal volume
  - Hypoxemia
  - Flow rate
- Elicits sensation of dyspnea & increases WOB

“Pulled down” pressure tracing



Current Opinion in Critical Care 2010, 16:261–268

Strategies for optimizing flow synchrony

- Increase flow rate
  - Pros
    - Decreases inspiratory time
    - Allows more expiratory time
    - Decreases dynamic hyperinflation & PEEPi
  - Cons
    - Increases PIP
    - Causes tachypnea
- Increase MVe & TV
  - Not always possible
- Decrease CO2 production
  - Treating fever & sepsis

Cycle dyssynchrony

- Cycling
  - Parameter determining the switch from inspiration to expiration
  - It is volume / time in ACMV & flow in PSV
- Synchrony
  - Patient's Ti (neural Ti) = machine Ti
- Dyssynchrony
  - Neural Ti > machine Ti or neural Ti < machine Ti

Does cycle dyssynchrony occur in PSV?

- Usually no
- Can occur in presence of severe obstruction
  - Ventilators use flow for cycling in PSV
  - Usually < 25% of PF or 5 Ltrs/min
  - Rate of decrease of flow is slow & inspiratory time prolonged
- Tackled by
  - Increasing inspiratory rise time % or changing cycling parameters
  - Decreasing PS (may increase WOB)

Last difficult to ventilate pt needed….

- 18 days of ventilation
- ~ 5 grams of midazolam
- ~ 12 grams of propofol
- ~ 4 grams of vecuronium
- ~ 200 mg of haloperidol
- ~100 mg of morphine

What if no cause is identified ?

- Structured ICU sedation algorithm
- Target specified, patient focused
- Incorporating scales for assessing
  - Pain
  - Sedation need
  - Delirium

Pain

- Whether present ?
- If yes, then why ?
- Management

Whether present ?

- Omnipresent
  - Day to day procedures (suctioning / dressing changes / turning)
  - Improper positioning
  - Immobilization
  - Full bladder
  - Post operative / wound site pain
  - Cardiac / visceral pain (constipation / ileus)

How to detect ?

- Able to communicate
  - Verbal or non verbal localization
  - Quantification by appropriate scales
    - Visual analog scale
    - Numeric scales
    - Verbal descriptive rating
- Unable to communicate
  - Inferred by observable behaviors & vital parameters
  - Limited by lack of specificity
  - BPS & CPOT have been used and validated recently

Behavioral Pain Scale Tool

Item	Description	Score
Facial expression	Relaxed	1
	Partially tightened (e.g. brow lowering)	2
	Fully tightened (e.g. eyelid closing)	3
	Grimacing	4
Upper limbs	No movement	1
	Partially bent	2
	Fully bent with finger flexion	3
	Permanently retracted	4
Compliance with ventilation	Tolerating movement	1
	Coughing with movement	2
	Fighting ventilator	3
	Unable to control ventilation	4

Score of 3 = no pain & 12 = maximum pain

Intensive and Critical Care Nursing (2006) 22, 32–39

Critical-Care Pain Observation Tool

Indicator	Score		Operational definition
Facial expressions	Relaxed, neutral	0	No muscle tension observed
	Tense	1	Presence of frowning, brow lowering, orbit tightening, and levator contraction or any other change (e.g., opening eyes or tearing during nociceptive procedures)
	Grimacing	2	All previous facial movements plus eyelid tightly closed (the patient may present with mouth open or biting the endotracheal tube)
Body movements	Absence of movements or normal position	0	Does not move at all (doesn't necessarily mean absence of pain) or normal position (movements not aimed toward the pain site or not made for the purpose of protection)
	Protection	1	Slow, cautious movements, touching or rubbing the pain site, seeking attention through movements
	Restlessness	2	Pulling tube, attempting to sit up, moving limbs/thrashing, not following commands, striking at staff, trying to climb out of bed
Compliance with the ventilator (intubated patients)	Tolerating ventilator or movement	0	Alarms not activated, easy ventilation
	Coughing but tolerating	1	Coughing, alarms may be activated but stop spontaneously
	Fighting ventilator	2	Asynchrony: blocking ventilation, alarms frequently activated
OR			
Vocalization (extubated patients)	Talking in normal tone or no sound	0	Talking in normal tone or no sound
	Sighing, moaning	1	Sighing, moaning
	Crying out, sobbing	2	Crying out, sobbing
Muscle tension: Evaluation by passive flexion and extension of upper limbs when patient is at rest or evaluation when patient is being turned	Relaxed	0	No resistance to passive movements
	Tense, rigid	1	Resistance to passive movements
	Very tense or rigid	2	Strong resistance to passive movements, incapacity to complete them
TOTAL		___ / 8	

Pain Management Nursing, Vol 11, No 2 (June), 2010: pp 115-125

Agitation- sedation scales

- First used by Ramsay et al in 1974
- Titrate sedation – target specific end points
- Shown to decrease
  - Over sedation & costs
  - Dose of sedatives & analgesics
  - Duration of mechanical ventilation & early weaning
  - Nosocomial infections

Various scales in use

- Ramsay Sedation Scale (RSS)
- Richmond Agitation-Sedation Scale (RASS)
- Sedation Agitation Scale (SAS)
- Motor Activity Assessment Scale (MAAS)
- Adaptation to the Intensive Care Environment (ATICE) instrument
- Minnesota Sedation Assessment Tool (MSAT)
- Vancouver interaction and calmness scale (VICS)

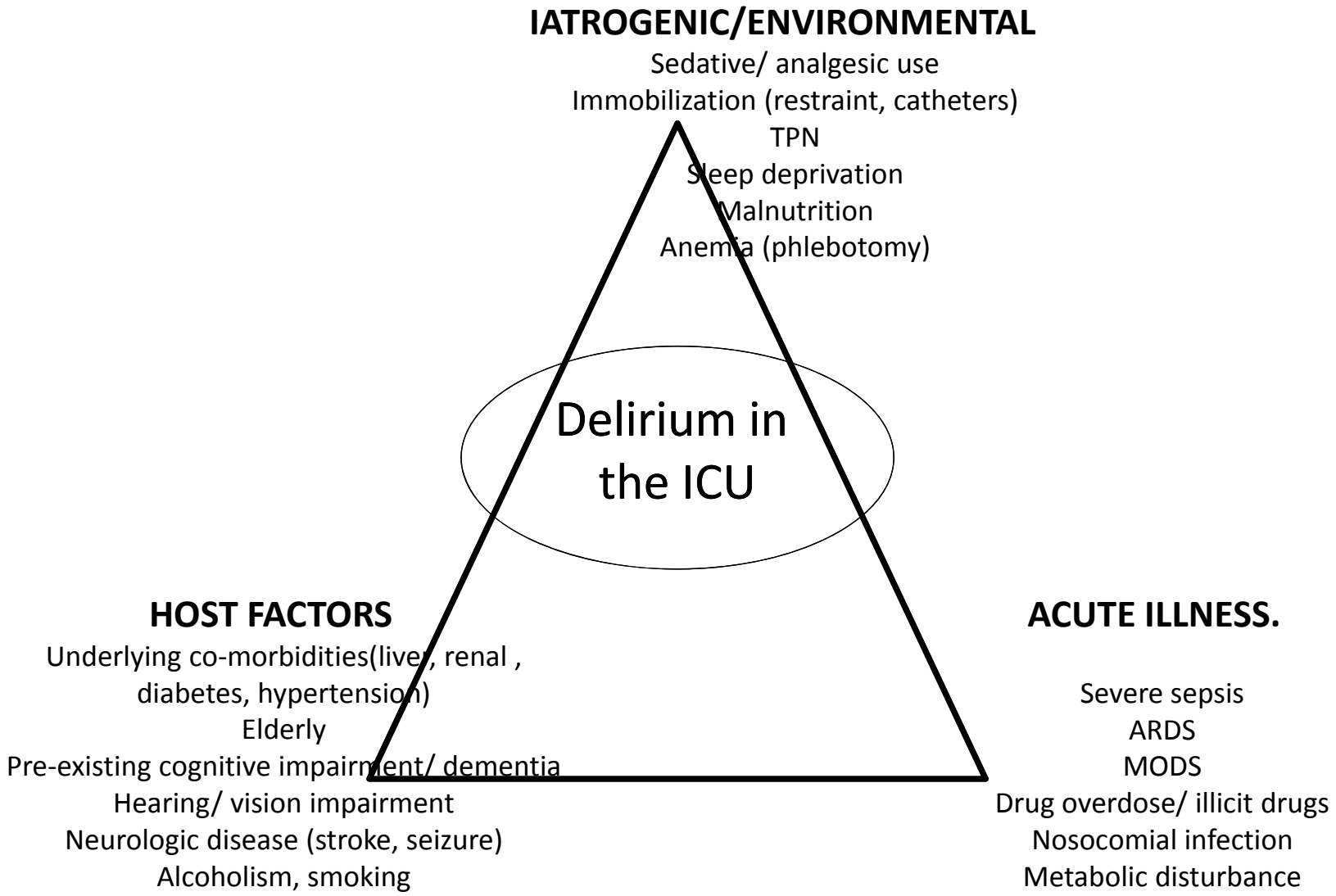
Delirium

- Present in 35-80% of critically ill patients
- Independent predictor
  - longer hospital stay
  - Higher hospital costs
  - Higher mortality
- Not easily recognized by treating physicians
- Caused by interplay of multiple factors

Chemically

- Increased dopamine
- Decreased acetyl choline
- Serotonin imbalance
- Endorphin hyperactivity

DELIRIUM


IATROGENIC/ENVIRONMENTAL
Sedative/ analgesic use
Immobilization (restraint, catheters)
TPN
Sleep deprivation
Malnutrition
Anemia (phlebotomy)
Delirium in the ICU
HOST FACTORS
Underlying co-morbidities(liver, renal , diabetes, hypertension)
Elderly
Pre-existing cognitive impairment/ dementia
Hearing/ vision impairment
Neurologic disease (stroke, seizure)
Alcoholism, smoking
ACUTE ILLNESS.
Severe sepsis
ARDS
MODS
Drug overdose/ illicit drugs
Nosocomial infection
Metabolic disturbance

Can these scales be implemented ?

Large-scale implementation of sedation and delirium monitoring in the intensive care unit: A report from two medical centers*

Objective: To implement sedation and delirium monitoring via a process-improvement project in accordance with Society of Critical Care Medicine guidelines and to evaluate the challenges of modifying intensive care unit (ICU) organizational practice styles.

Design: Prospective observational cohort study.

Setting: The medical ICUs at two institutions: the Vanderbilt University Medical Center (VUMC) and a community Veterans Affairs hospital (York-VA).

Subjects: Seven hundred eleven patients admitted to the medical ICUs for >24 hrs and followed over 4,163 days during a 21-month study period.

Interventions: Unit-wide nursing documentation was changed to accommodate a sedation scale (Richmond Agitation-Sedation Scale) and delirium instrument (Confusion Assessment Method for the ICU). A 20-min introductory in-service was performed for all ICU nurses, followed by graded, staged educational interventions at regular intervals. Data were collected daily for compliance, and randomly 40% of nurses each day were chosen for accuracy spot-checks by reference raters. An implementation survey questionnaire was distributed at 6 months.

Measurements and Main Results: The implementation project involved 64 nurses (40 at VUMC and 24 at York-VA). Sedation and delirium monitoring data were recorded for 711 patients (614 at VUMC and 97 at York-VA). Compliance with the Richmond Agitation-Sedation Scale was 94.4% (21,931 of 23,220) at VUMC and 99.7% (5,387 of 5,403) at York-VA. Compliance with the Confusion Assessment Method for the ICU was 90% (7,323 of 8,166) at VUMC and 84% (1,571 of 1,871) at York-VA. The Confusion Assessment Method for the ICU was performed more often than requested on 63% of shifts (5,146 of 8,166) at VUMC and on 8% (151 of 1871) of shifts at York-VA. Overall weighted-κ between bedside nurses and references raters for the Richmond Agitation-Sedation Scale were 0.89 (95% confidence interval, 0.88 to 0.92) at VUMC and 0.77 (95% confidence interval, 0.72 to 0.83) at York-VA. Overall agreement (κ) between bedside nurses and reference raters using the Confusion Assessment Method for the ICU was 0.92 (95% confidence interval, 0.90–0.94) at VUMC and 0.75 (95% confidence interval, 0.68–0.81) at York-VA. The two most-often-cited barriers to implementation were physician buy-in and time.

Conclusions: With minimal training, the compliance of bedside nurses using sedation and delirium instruments was excellent. Agreement of data from bedside nurses and a reference-standard rater was very high for both the sedation scale and the delirium assessment over the duration of this process-improvement project. (Crit Care Med 2005; 33:1199–1205)

KEY WORDS: delirium; sedation; implementation; mechanical ventilation; protocols; monitoring; intensive care; nursing; quality improvement; process improvement; clinical practice guidelines

General measures

- Reassurance (for fear, anxiety)
- Writing board if unable to communicate
- Re-positioning the patient
- Repositioning ET > 2 cms from carina
- Treatment of withdrawal state
- Correcting metabolic derangements
- Catheterization
- Music therapy
- Hypnosis

How drug use in ICU is different ?

- Advanced age
- Malnutrition
- Altered renal & liver function
- Effects of underlying disease
- Polypharmacy
- Slowed metabolism
- High body water/ increased volume of distribution
- Decreased protein binding

Pharmacotherapy

- Opiate analgesics
- Sedatives
- Anti psychotics

Analgesics

Drug/Class	Elimination	Onset/Duration	Dosing (IV)	Concentration	Advantages
Morphine sulfate/opioid analgesic	Conjugation; active metabolite excreted renally	5–10 min/2–4 h	LD: 2–4 mg IV push MD: 2–30 mg/h for ventilated patients	100 mg/100 mL NS or D5W	Reduces tachypnea
Fentanyl/opioid analgesic	Cytochrome P450 3A4	1–2 min/2–4 h (longer in liver failure)	LD: 25–50 μg IV push MD: 0.7–10 μg/kg/h for ventilated patients	1.25 or 2.5 mg/ 250 mL NS or D5W	Less hypotension than morphine
Hydromorphone/opioid analgesic	Hepatic	5–10 min/2–4 h	LD: 0.2–0.6 mg IV push MD: 0.5–3 mg/h	100 mg/100 mL NS or D5W	May work if patients are tolerant to morphine/fentanyl
Alfentanil/opioid analgesic	Hepatic; active metabolites excreted renally	1 min/30–60 min (dose dependent)	LD: 50–75 μg/kg slowly over 3 5 min; MD: 0.5 3 μg/kg/ min (usual 1–1.5 μg/kg/min)	10 mg/250 mL NS or D5W	Very short-acting agent
Remifentanil/opioid analgesic	Tissue esterases	1–3 min/10–20 min	LD: 1 μg/kg over 1 min MD: 0.6–15 μg/kg/h for MV (unlabeled use); use ideal body weight if > 30% over ideal body weight	5 mg/250 mL NS or D5W	No accumulation in hepatic or renal failure
Sufentanil/opioid analgesic	Hepatic	1–3 min/dose-dependent duration	LD: 1–2 μg/kg slowly over 3–5 min; MD: 8–50 μg as needed	250 μg/250 mL D5W; variable stability in NS	

(CHEST 2008; 133:552–565)

Sedation

Drug/Class	Elimination	Onset/Duration	Dosing (IV)	Concentration
Lorazepam/ benzodiazepine	Hepatic conjugation to inactive metabolite	5–20 min/6–8 h; up to 24–72 h in elderly/cirrhosis/ ESRD	LD: 2–4 mg IV push MD: 2–6 mg IV q4h-q6h; infusion: 1–10 mg/h; start low in elderly	100 mg/100 mL D5W only
Midazolam/ benzodiazepine	Cytochrome P450 3A4; active metabolite excreted renally	5–10 min/1–4 h (longer in ESRD/ CHF/liver failure)	LD: 2–5 mg IV push MD; 1–20 mg/h; start low in elderly	100 mg/100 mL NS or D5W
Propofol	Conjugation	30–50 s/ approximately 3–10 min (dose dependent)	MD: 5–150 μg/kg/min	Premixed (10 mg/mL)
Dexmedetomidine	Hepatic Cytochrome P450 and glucuronidation	Immediate/ approximately 6 min (longer in	LD: 0.5–1 μg/kg over 10 min; MD: 0.2–0.7 μg/kg/h for 24 h	100 μg/50 mL NS only

Which drug ?

How to titrate ?

(CHEST 2008; 133:552–565)

Midazolam vs. lorazepam

- Midazolam
  - Faster onset of action- bolus dosing
  - Less duration of action – repeated doing
  - Accumulates in renal / hepatic dysfunction
  - Expensive (10 mg ~ Rs 50)
- Lorazepam
  - Long duration of action (4-6hrs) – prolonged therapy
  - Cheaper (4 mg ~ Rs 15)
  - Carrier toxicity (propylene glycol – anion gap acidosis)
- Time to come off sedation
  - Data conflicting

Propofol

- The active ingredient in Propofol is 2,6-diisopropylphenol in 10% soybean oil, 2.25% glycerol, and 1.2% purified egg phosphatide.
- Disodium EDTA (0.05 mg/ml) or sodium metabisulfite (0.25 mg/ml) is added to inhibit bacterial growth.
- Is hepatically modified & renally excreted
- Key benefits include
  - Rapid onset & offset of action
  - Easy titration
  - Metabolism independent of hepatic & renal function
  - Sedative-hypnotic with anxiolytic & amnestic properties
  - Bronchodialtor, anti-epileptic,muscle relaxant and anti-oxidant

Adverse events

- Hypotension
- Hypertriglyceridemia
- Sepsis due to contamination
- Pancreatitis
- Metabolic acidosis
- Adrenal insufficiency
- Immune dysfunction
- PRIS
- Is very expensive
- Practically no benefit over Midazolam in terms of earlier extubation and shorter stay

Dexmedetomidine

- Is an α2 agonist
- Increasing role, especially in post-operative patients
- Advantages include
  - Maintenance of respiratory drive
  - Rapid awakenings
  - Analgesia
  - Amnesia
  - Good hemodynamic tolerance
  - Decreased requirement for other medications

- Recent meta-analysis of 24 studies
  - Decreased ICU stay
  - Trend towards decreased mortality & delirium
  - Heterogeneity of data
  - Higher incidence of bradycardia

Intensive Care Med (2010) 36:926–939

How to give sedation ?

- Intermittent boluses preferred
- Consider continuous infusion
  - Requirement more frequent than every 2 hours
  - Unable to achieve target sedation
  - Check for pain / delirium
- If on continuous infusion
  - Titrate dose to target
  - Reassess every few hours
  - Daily interruption of sedation (DIS) & restart at half dose
  - Empiric downward titration after 48 hrs

DIS

- “Wake up & breathe” protocol
  - Earlier extubation
  - Less morbidity
  - Less cost
  - No increase in adverse events (PTSD, recall or cardiac events)
- Should be practiced in all except pt s with increased risk for cardiac events

Co-sedation / A1 strategy

Sedation during mechanical ventilation: A trial of benzodiazepine and opiate in combination*

Objective: To compare the efficacy of continuous intravenous sedation with midazolam alone vs. midazolam plus fentanyl ("co-sedation") during mechanical ventilation.

Design: A randomized, prospective, controlled trial.

Setting: A ten-bed medical intensive care unit at a university hospital.

Patients: Thirty patients with respiratory failure who were expected to require >48 hrs of mechanical ventilation and who were receiving a sedative regimen that did not include opiate pain control.

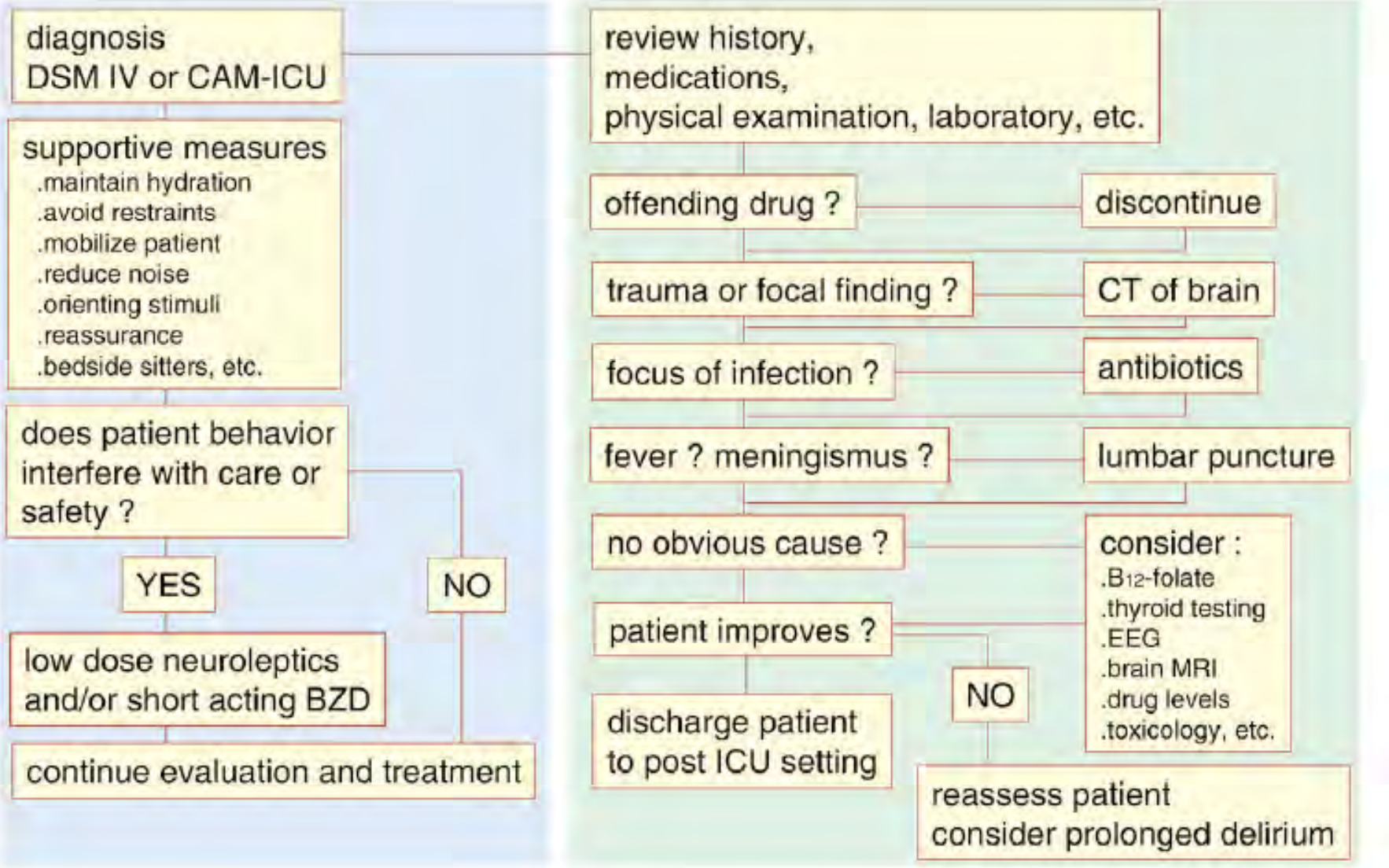
Interventions: An intravenous infusion of either midazolam alone or co-sedation was administered by a nurse-implemented protocol to achieve a target Ramsay Sedation Score set by the patient's physician. Study duration was 3 days, with a brief daily "wake-up."

Measurements and Main Results: We recorded the number of hours/day that patients were "off-target" with their Ramsay Sedation Scores, the number of dose titrations per day, the incidence of patient-ventilator asynchrony, and the time required to achieve adequate sedation as measures of sedative efficacy. We also recorded sedative cost in U.S. dollars and adverse events including hypotension, hypoventilation, ileus, and coma. Compared with the midazolam-only group, the co-sedation group had fewer hours per day with an "off-target" Ramsay Score (4.2 ± 2.4 and 9.1 ± 4.9, respectively, $p < .002$). Fewer episodes per day of patient-ventilator asynchrony were noted in the co-sedation group compared with midazolam-only (0.4 ± 0.1 and 1.0 ± 0.2, respectively, $p < .05$). Co-sedation also showed nonsignificant trends toward a shorter time to achieve sedation, a need for fewer dose titrations per day, and a lower total sedative drug cost. There was a trend toward more episodes of ileus with co-sedation compared with midazolam-only (2 vs. 0).

Conclusions: In mechanically ventilated patients, co-sedation with midazolam and fentanyl by constant infusion provides more reliable sedation and is easier to titrate than midazolam alone, without significant difference in the rate of adverse events. (Crit Care Med 2006; 34:1395–1401)

KEY WORDS: sedation; mechanical ventilation; midazolam; fentanyl; benzodiazepine; opiate

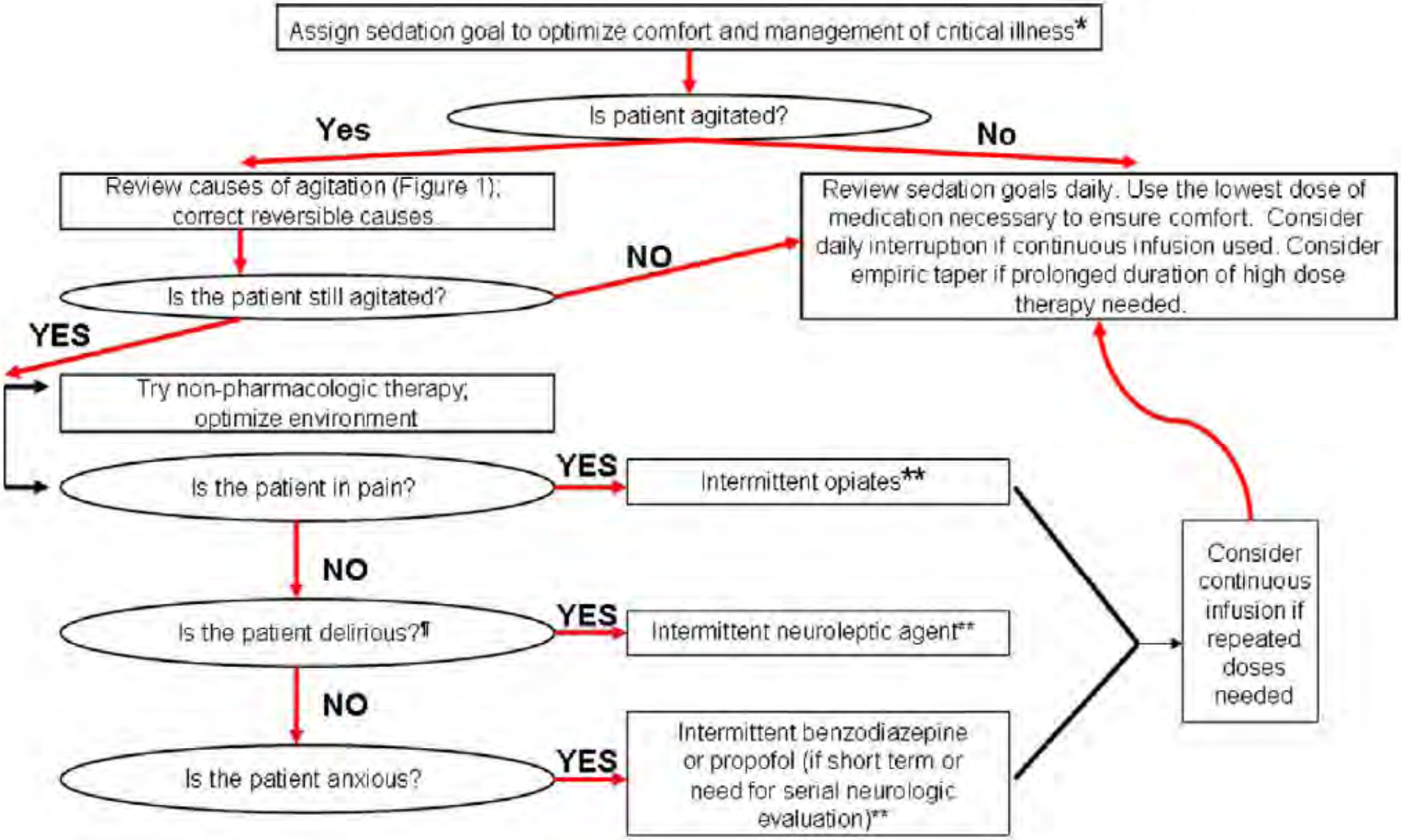
Delirium



Critical Care 2007, **11**:214

Haloperidol

- Starting doses are 2-10 mg (5 mg) bolus over 5-10 minutes. Repeat every 20 minutes till end-point achieved
- 25% of the cumulative dose q6 hourly for maintenance
- Block 60% of the D2 receptor while avoiding side-effects associated with complete D2 blockade
- Once calm, smaller doses can be used
- Adverse events
  - Extrapyramidal symptoms
  - Malignant hyperthermia
  - Torsade de pointe



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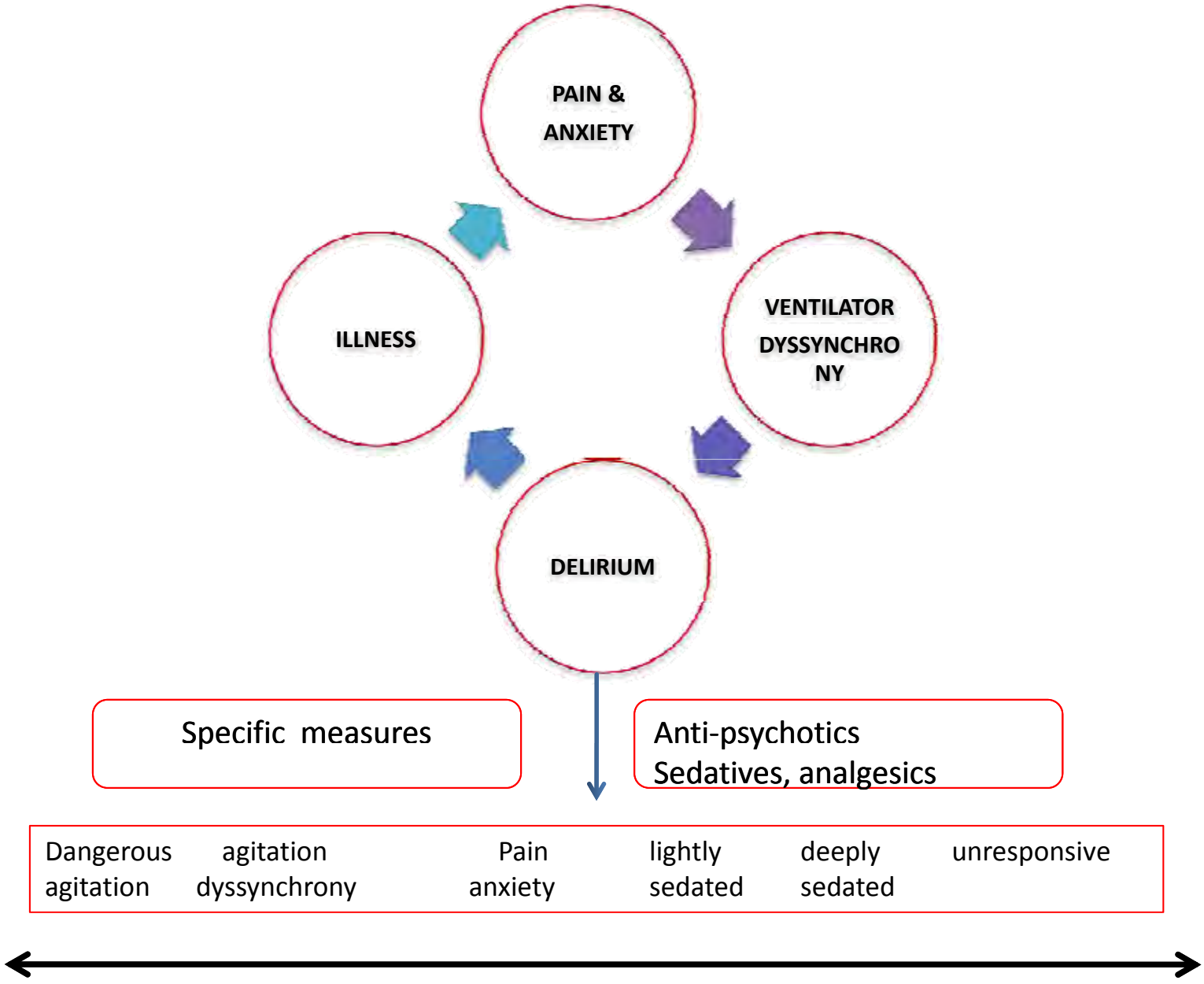
AGITATION in the ICU



- Agitation is a distressing issue in ICU
- “Look around” before reaching for syringe
- Patient focused & target based sedation
- Reassess on a daily basis for pain & delirium
- “Wake up & breathe”