# Delirium Diagnosis & Management in the ICU & other Places

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# Cognitive Impairment in the ICU

- Over 25 different terms have been used to describe
  - ICU psychosis
  - ICU syndrome
  - Acute confusional state
  - Septic encephalopathy
  - Acute brain failure
  - Delirium

# Delirium?

- “acute organ dysfunction” of the brain
- Anything that hurts the brain or impairs its proper functioning can provoke a delirium!

# Delirium

- Delirium is a form of organ dysfunction
  - Much like low-grade shock for the cardiovascular
  - Hypoxemia for pulmonary
  - Inattention for brain
- Inattention is the hallmark and pivotal feature of delirium

# What is delirium?

- Acute confusion, Transient cognitive impairment, Clouded state, Encephalopathy, ICU psychosis
  = acute form of brain failure; medical emergency
  - ATTENTION, mood, arousal, self-awareness
  - Fluctuating global cognitive impairment
  - Hallucinations-visual, tactile-organic
  - Often reversible
  - Usually improves if patient does not die

# What are the criteria for delirium?

- Criteria for dx of delirium (DSM IV):
  - Disturbance of consciousness
  - Change in cognition or development of perceptual disturbance not accounted for by a dementia
  - Development over short period of time - usually hours to days; tends to fluctuate during course of day.
  - Evidence on hx, PE or lab findings that disturbance caused by direct physiological consequences of a general medical condition

# What are the S & S of delirium?

- Main defect:  attention -->
  - Less aware of surroundings
  - Easily distractible
  - Trouble with concentration & commands
- Main aspects of cog. disordered: thinking, perception, memory
  - +  sleep-wake cycle, disorientation, ↓ LOC
  - + ↑ or ↓ psychomotor activity
  - +/- emotional  &  irritability

# Delirium
## subtypes

- Hyperactive 25 %
  - Demand attention
- Hypoactive 50 %
  - Often missed
- Mixed 25 %

# Who becomes delirious?

- Elderly:
  - 10-38% at hospital admission;  higher in nursing homes
  - up to 80% hospitalized for acute physical illness
- Surgery:
  - 10-15% general
  - 30% open heart surgery
  - > 50% hip fractures

# What predisposes the elderly to delirium?

- Aging processes in the brain
- Structural brain disease
- ↓ capacity for homeostatic regulation/resistance to stress/disease
- Impaired vision & hearing
- Chronic diseases
- Age-related  response to drugs.

# Delirium Risk Factors

- Age
- Cognitive impairment
  - 25% delirious are demented
  - 40% demented in hospital delirious
- Severe illness
- Hip fracture
- Fever or hypothermia
- Hypotension
- Malnutrition
- High number of meds
- Sensory impairment
- Psychoactive medications
- Use of lines and restraints
- Metabolic disorders:
  - Azotemia
  - Hypo- or hyperglycemia
  - Hypo- or hypernatremia
- Depression
- Alcoholism
- Pain

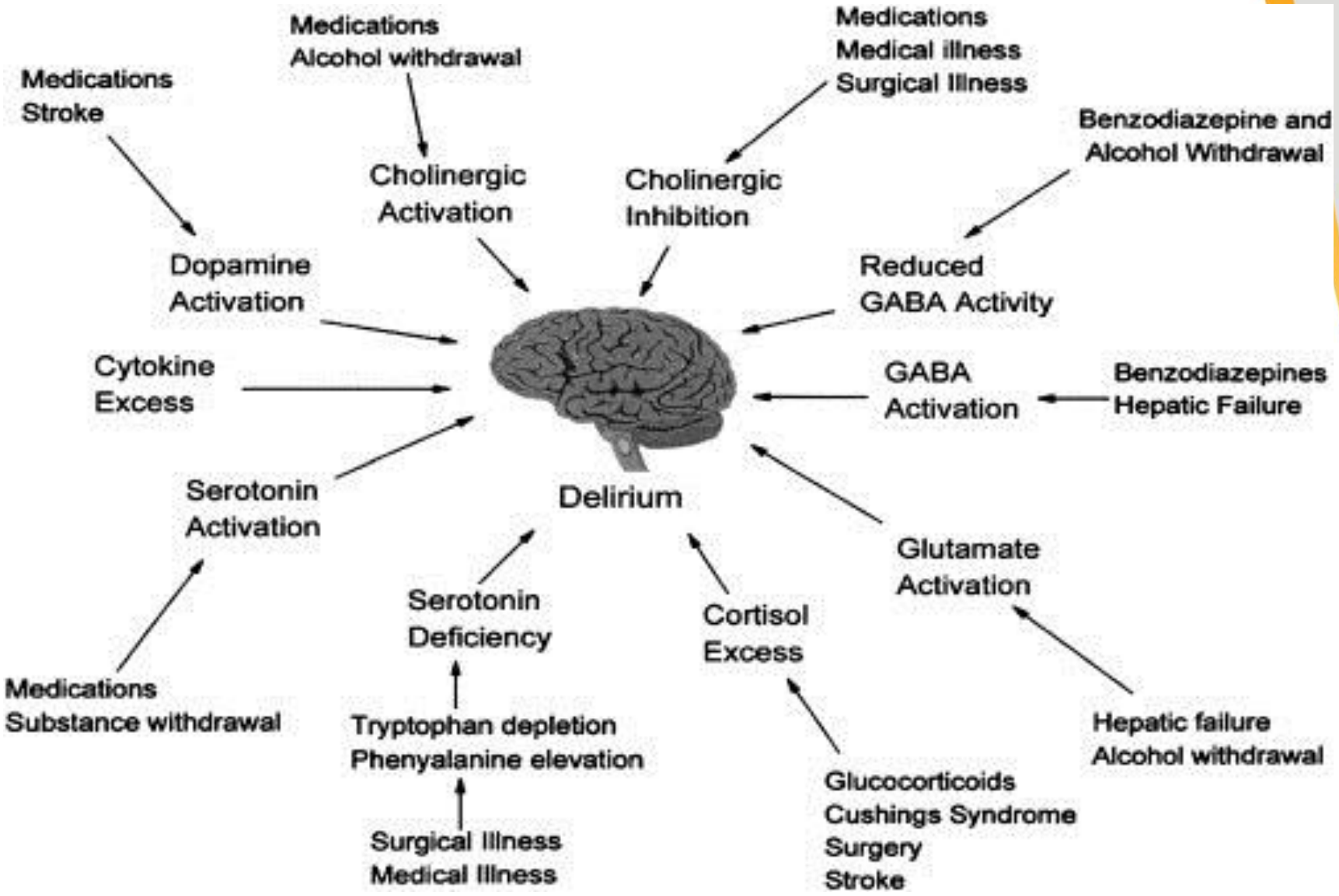
# Delirium can be prevented !

| Cognitive impairment | Orientation protocol |
|---|---|
| Sleep deprivation | Non-pharmacological<br>• Sleep protocol<br>• Noise reduction |
| Immobility | Early mobilization<br>Reduce immobilizing<br>Aides/Adaptations |
| Visual impairment | Visual aids |
| Hearing impairment | Wax removal<br>Amplification |
| Dehydration | Volume repletion |

(Inouye SK et al. N Engl J Med. 1999; 340: 669)

# What causes delirium?

- Widespread decline in cerebral metabolism & derangement of neurotransmitters
- Several mechanisms likely:
  - Failure of cerebral oxidative mechanisms
  - Failure of cholinergic neurotransmission
  - CNS effects of lymphokines
- Functional rather than structural


Medications
Stroke
Medications
Alcohol withdrawal
Medications
Medical illness
Surgical Illness
Benzodiazepine and
Alcohol Withdrawal
Cholinergic
Activation
Cholinergic
Inhibition
Dopamine
Activation
Reduced
GABA Activity
Cytokine
Excess
GABA
Activation
Benzodiazepines
Hepatic Failure
Serotonin
Activation
Delirium
Glutamate
Activation
Serotonin
Deficiency
Cortisol
Excess
Medications
Substance withdrawal
Tryptophan depletion
Phenyalanine elevation
Hepatic failure
Alcohol withdrawal
Glucocorticoids
Cushings Syndrome
Surgery
Stroke
Surgical Illness
Medical Illness

# Causes of delirium

- Primary intracranial pathology
- Systemic disease secondarily affecting the brain
- Exogenous toxic agents, eg drugs
- Withdrawal from substances of abuse, sedatives

# General Causes of Delirium

- Usually multifactorial
- Predisposing causes
  - AGE, poor vision/hearing, recent relocation, premorbid cognitive problems, multiple chronic disease and use of multiple medications
- Precipitating causes
  - fluid/electrolyte disturbance, drug toxicity/withdrawal, infections, metabolic disturbances, hypoxia and hypotension

# Is there an easy way to remember the causes of delirium?

- ***I*** Infection

- ***W*** Withdrawal
- ***A*** Acute metabolic
- ***T*** Trauma
- ***C*** CNS pathology
- ***H*** Hypoxia

- ***D*** Deficiencies
- ***E*** Endocrine
- ***A*** Acute vascular/MI
- ***T*** Toxins-drugs
- ***H*** Heavy metals

# Medications Associated with Delirium

- Sedatives- hypnotics; Benzodiazepines - toxicity or withdrawal
- Narcotics- especially Pethidine
- Anticholinergics
  - Tricyclic Antidepressants
    e.g. Amitriptyline, Doxepin, Imipramine
  - Dimenhydrinate (Benadryl)
  - Oxybutynin
  - Anti-Parkinsonian Drugs
    e.g. Pacitane,

# Differential Diagnosis of Delirium

- Communication Problem (patient or staff!)
- Mood disorder (depression and severe anxiety)
- Psychosis
- CVA
- Post-ictal
- Dementia

# Delirium vs Dementia

| Characteristic | Delirium | Dementia |
|---|---|---|
| Onset | Sudden | Insidious |
| Course over 24 hours | Fluctuating | Stable |
| Consciousness | Reduced | Clear |
| Attention Span | Globally disordered | Relatively normal |
| Cognition | Globally disordered | Global impairment |
| Hallucinations | Common | Usually absent |
| Psychomotor activity | Increased, reduced or shifting unpredictably | Often normal |
| Speech | Often incoherent | Reduced vocabulary |
| Involuntary movements | Asterixis or course tremor common | Often absent |

# Clinician's approach to delirium Diagnostic

- Keep high index of suspicion
- Repeated assessments
- Clarify pre-morbid status and sequence of events
- Exclude important differential diagnosis
- Identify all predisposing and precipitating factors

# Clinician's approach to delirium Diagnostic

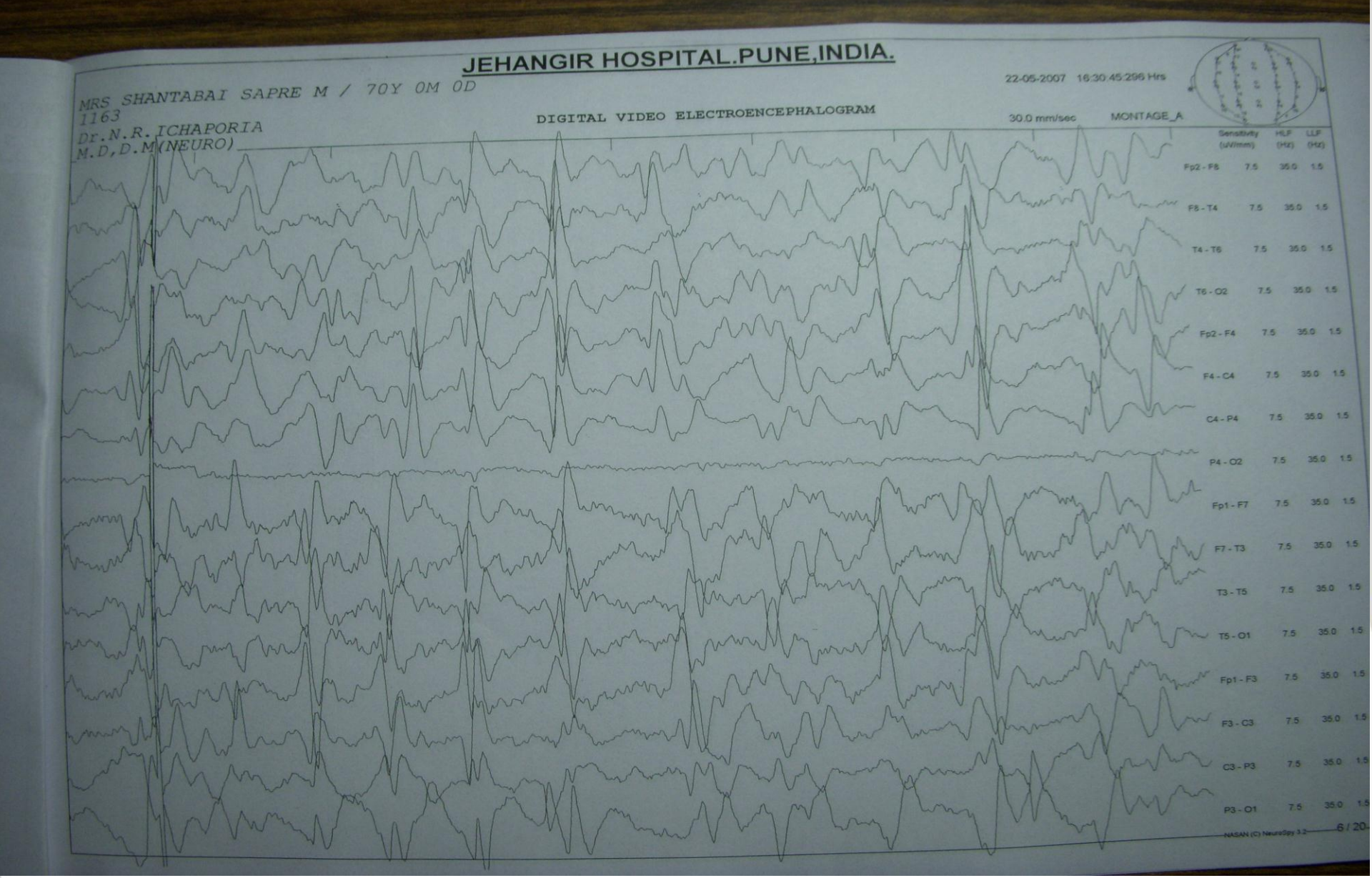
- Good Physical Exam:
  - Assess Hydration Status
  - ? New Localizing Neurological Findings
  - ? CHF/Pneumonia
  - Rectal Exam to R/O Impaction
  - ? Distended Bladder
  - ? Infected Ulcer

# Clinician's approach to delirium Diagnostic

- Review medication list
- Serum levels e.g. Digoxin/phenytoin…
- Metabolic work up
  - CBC
  - Lytes/BUN/creat/glucose
  - Ca, albumin
  - Liver function tests
- 02 saturation/ABG's to R/O  pCO2

# Clinician's approach to delirium Diagnostic

- ECG to R/O silent MI
- CXR to R/O pneumonia as physical exam often difficult/inaccurate
- CNS work-up (if indicated):  i.e. Imaging if localizing signs or history of head injury.
- Never forget EEG-Non-convulsive status, normal in Psy illness, triphasic waves, Beta activity, Alpha coma.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Dr.N.R.ICHAPORIA
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30.0 mm/sec
MONTAGE_A
Sensitivity (uV/mm)
HLF (Hz)
LLF (Hz)
Fp2 - F8
F8 - T4
T4 - T6
T6 - O2
Fp2 - F4
F4 - C4
C4 - P4
P4 - O2
Fp1 - F7
F7 - T3
T3 - T5
T5 - O1
Fp1 - F3
F3 - C3
C3 - P3
P3 - O1
NASAN (C) NeuroSpy 3.2
6 / 20

# Delirium Treatment

- Early recognition → the most important step
  - Undiagnosed, no efforts made to reverse it
- Once detected
  - Focus on identifying the etiology
- Both prevention and treatment focus on
  - Minimize and/or eliminate predisposing and precipitating factors

# Treatment

- General measures
  - Ensure sleep
  - Maintain fluid and nutritional state
  - Provide support and nursing care
  - Rest in a quiet, well-lit room
  - Maintain orientation
  - Avoid noise (ICU, General wards)
  - Only familiar family members/close friends to visit
  - Sedate the agitated, fearful patient/relieve pain
  - Minimise medications
  - Avoid restraints, if possible

# Clinician's approach to delirium Pharmacological Principles

- SINGLE medication preferable to multiple
- Start low and go slow
- Choose a drug with low anticholinergic activity
- Stop the drug ASAP and correct underlying cause
- Continue to use Non-Pharmacological Interventions

# Possible Pharmacotherapy for Symtomatic Management

- Benzodiazepines (lorazepam, Diazepam, Midazolam)
- Neuroleptics (haloperidol, risperidone, olanzapine, qutiapine)
- Anticonvulsants (carbamazipine, valproate)
- Serotinergic agents (5 HT uptake blockers)
- Lithium
- B-blockers

# Clinician's approach to delirium Pharmacological Principles

## Haloperidol

- Try to only use for SEVERE agitation
- Lowest anticholinergic activity of all major neuroleptics
- High potency
- Can use used IM/IV
- Start with 0.5 - 1 mg initial dose, gradually titrating to a maximum of 4 mg/day
- Once initial dose is given, wait approximately 2-4 hours before repeating the dose
- Taper the dose as soon as possible
- Avoid in individuals with Parkinson's Disease

# Clinician's approach to delirium Pharmacological Principles

## Benzodiazepines

- Avoid use in combination with antipsychotics unless severe agitation and safety concern - SINGLE drug is better
- Best reserved for Delirium 2° to Alcohol or Benzodiazepine withdrawal.
- Relatively contraindicated in Delirium from Hepatic Encephalopathy.

# Clinician's approach to delirium Pharmacological Principles

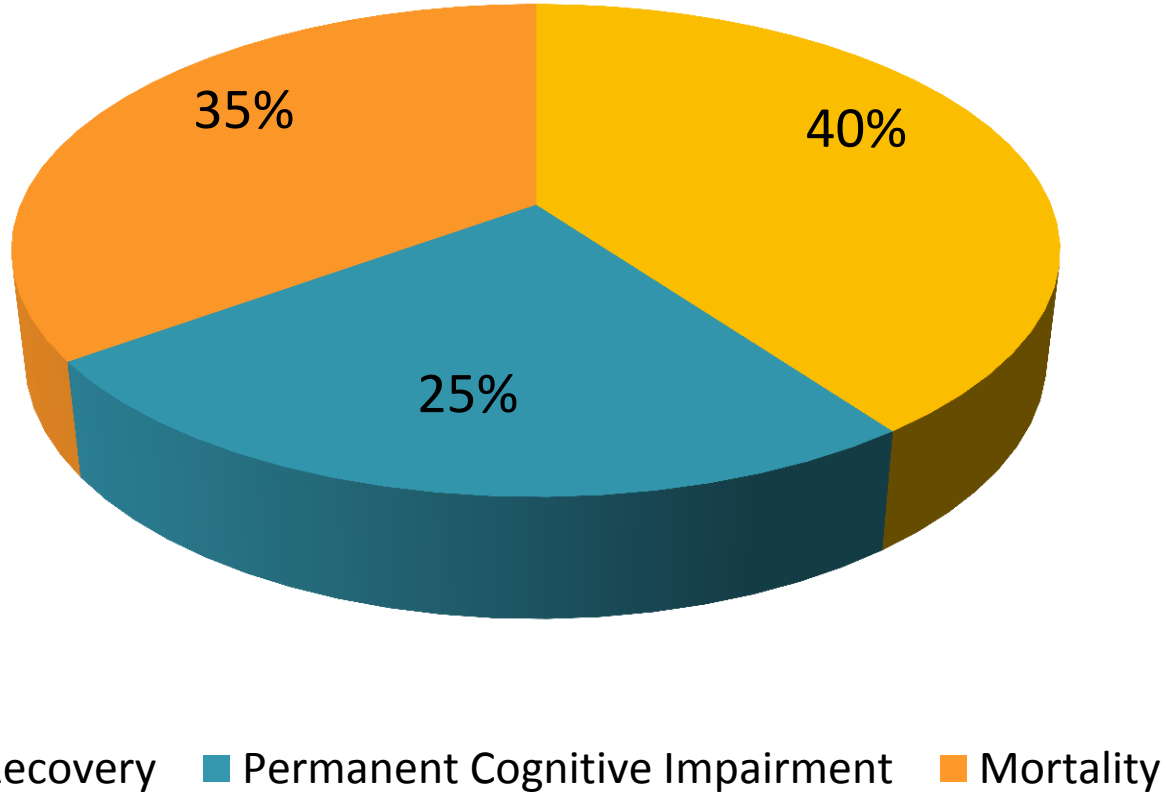
Atypical Antipsychotics (Risperidone, Olanzepine, Quetiapine)

- No controlled studies at present of their use in delirium (just case reports)
- MAY TRY:
  - Low dose Risperidone starting at .25 mg BID
  - Olanzapine - 2.5 mg/d as starting dose
  - Quetiapine - 12.5 mg/d starting dose

# What's the prognosis in delirium?

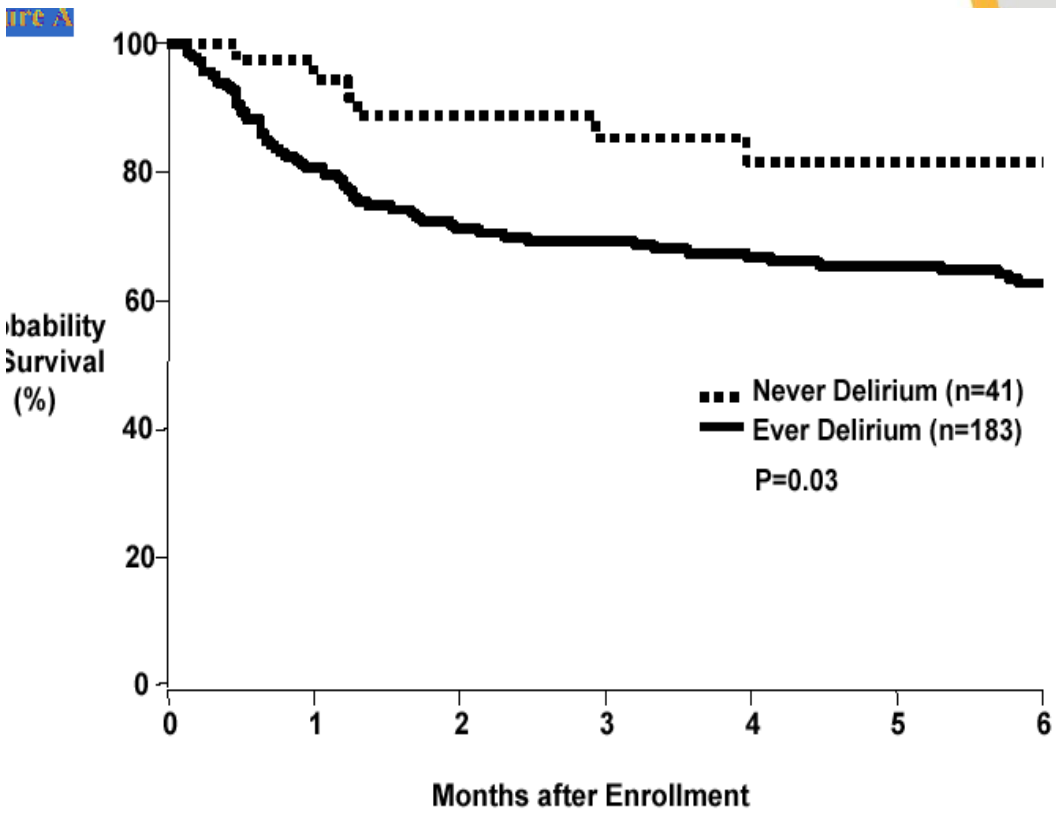
- 6-35% die in hospital
- Generally full recovery but 1/4 → long term cognitive impairment
- ↑ hospitalization
- ↑ institutionalization
- ↑ complications
  - UTI, ulcers, caregiver stress

# Delirium: Prognosis



# Delirium and mortality

- 275 ventilated patients
- delirium was an independent predictor of higher 6-month mortality
- even after adjusting for relevant covariates




Ely, et al JAMA. 291(14): 1753-1762, 2004

# ICU Delirium and Cost

39% higher ICU costs

31% higher hospital costs

Milbrandt et al Crit. Care Med. 32 (4):955-962, 2004

# Prevalence

- Critically ill patients great risk of delirium
  - Eg more than 8 out of 10 ventilated patients
  - One of the most frequent forms of organ dysfunction
  - Unrecognized in 66% to 84%
  - Especially the hypoactive type

# Cognitive Impairment
## Following ICU Hospitalization

- 1 in 3 survivors of ICU
- Like mild to moderate dementia
- In ARDS as high as 80%
- Various cognitive deficits
  - Difficulties in areas of attention/concentration
  - Executive functioning (planning/organizing)
  - Memory (short-term, verbal, and visual)
  - Processing speed
  - Visuo-spatial construction

# Cognitive Impairment
## Following ICU Hospitalization

- Significant “real world” consequences
  - Problems returning to work
  - Balancing a cheque book
  - Finding a parked car
  - Preparing a simple meal

# Delirium
## Detecting and Monitoring

- The Confusion Assessment Method for the ICU (CAM-ICU)
  - A valid and reliable serial assessment tool
  - Both ventilated and non-ventilated ICU patients
  - Easy to use
  - Less than 2 minutes to complete

# Delirium - Conclusions

- A medical emergency!!
- Common but under-recognized
- Treatment: Address the underlying cause. Non-Pharmacological approaches are essential. Pharmacological treatments are largely symptoms based.

# Delirium and the ICU

# Delirium in the ICU

- A survey of 912 healthcare professionals
  - 68 % thought that >25% of ventilated patients experience delirium
  - 92 % felt ..significant or very serious problem in ICU
  - 78 % acknowledged under diagnosis
  - Only 40% reported routine screening
  - Only 16% used a specific tool for delirium assessment

Ely et al Crit Care Med. 2004 Jan;32(1):106-12

# Why Delirium in ICU

- Number of causal factors apart from age
  - Reduction in cerebral metabolism
  - Primary intracranial disease
  - Systemic diseases
  - Secondary infection of the brain
  - Exogenous toxic agents
  - Withdrawal from substances of abuse
  - Hypoxemia and metabolic disturbances
  - Administration of psychoactive medications
- On average ICU patients have greater than 10 risk factors for delirium which places them at a very high risk for this complication

# Delirium and Clinical Outcomes
## "so what?"

- Is there evidence that delirium is associated with poor outcome in ICU patients independent of severity of illness, age, coma, drugs, and other covariates?

  **YES**

- 4 areas of evidence
  - ICU Delirium and Mortality
  - ICU Delirium and Hospital Length of stay
  - ICU Delirium and Cost
  - ICU Delirium and Dementia Interaction

# Delirium as a Predictor of Mortality in Mechanically Ventilated Patients in the Intensive Care Unit

- 275 consecutive ventilated patients admitted to adult ICUs → 224 survivors
  - 81.7 % developed delirium at some point
  - Higher 6-month mortality
  - Longer hospital stay

E. Wesley Ely et al JAMA. 2004;291:1753-1762.

# Diminished QOL in ICU survivors

- Psychiatric disorders
  - Clinically significant depression 30 %
  - Post-traumatic stress disorder 15 to 40 %
- Especially when combined with cognitive impairment, these lead to significantly diminished quality of life

# Two Step Approach to Assessing Consciousness

- Step 1 Levelo:
  - Sedation Assessment (RASS, SAS, MAAS)
- Step 2 Content:
  - Delirium Assessment (CAM-ICU)

# Step 1: Sedation Assessment

- Richmond Agitation – Sedation Scale (RASS)

+4 Combative
+3 Very agitated
+2 Agitated
+1 Restless

0 Alert / calm

| | | |
|---|---|---|
| -1 Drowsy | eye contact >10 sec | Verbal |
| -2 Light sedation | eye contact <10 sec | |
| -3 Moderate | No eye contact | |
| -4 Deep | Physical stimulation required | Physical |
| -5 Unarousable | No response even with physical stimulation | |

Sessler, et al AJRCCM 2002
Elv. E.W., et al. JAMA 2003

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# Step 2: Confusion Assessment Method for the ICU (CAM-ICU) Assessment

1. Acute onset of mental status changes or a fluctuating course

and

2. Inattention

and

3. Disorganized Thinking

or

4. Altered level of consciousness

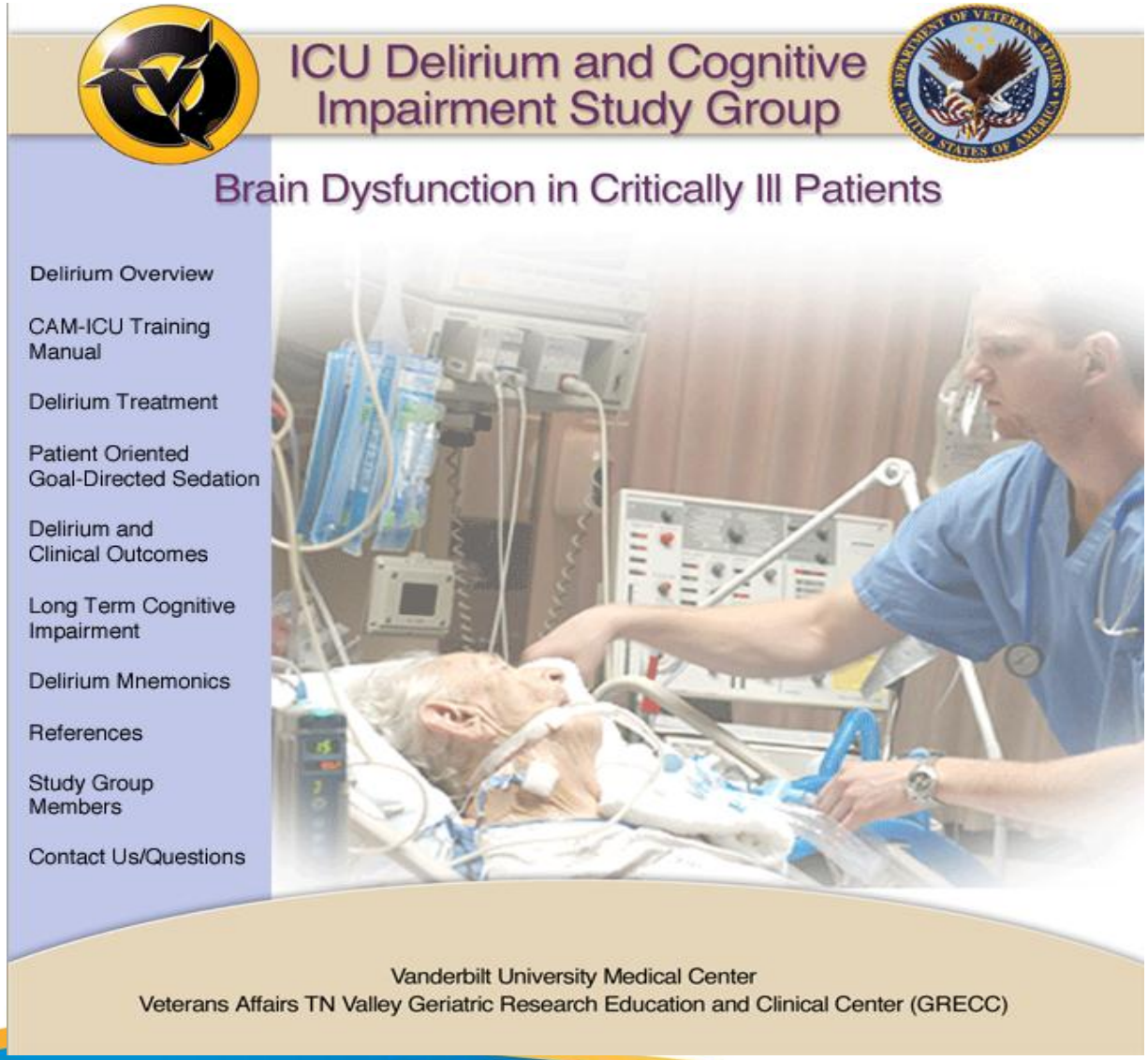
= Delirium

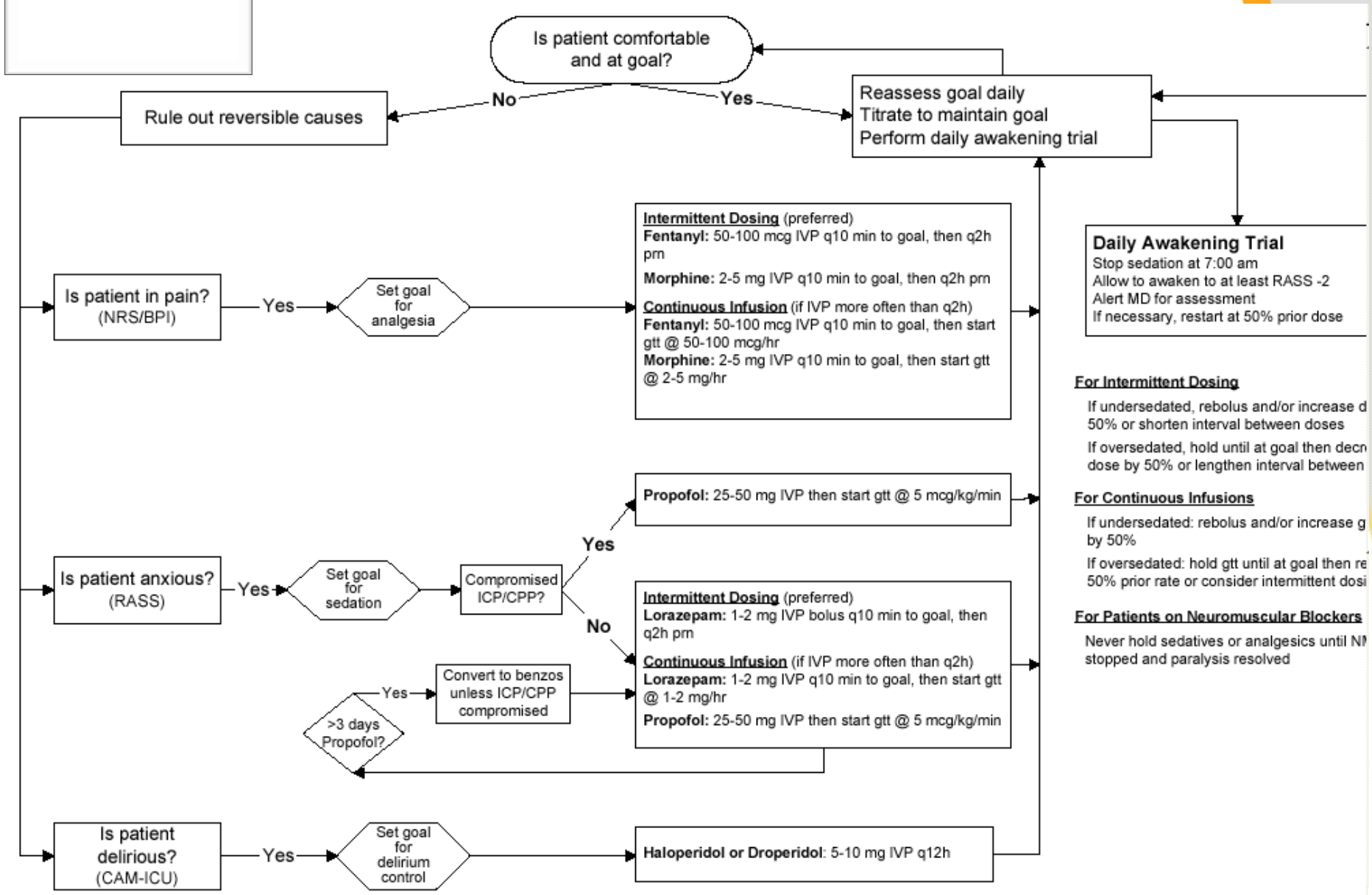
Ely et al. Crit Care Med 2001;29:1370-79  Ely, E.W., et al. JAMA 2001;286:2703-2710

# Prevention is the Best Medicine

- It is easier to PREVENT than to TREAT
- Prevention difficult in the ICU
- Treatment of delirium in the intensive care unit is particularly challenging and most likely to require medications,  and/or physical restraints

# www.icudelirium.org




Is patient comfortable and at goal?
No
Yes
Rule out reversible causes
Reassess goal daily
Titrate to maintain goal
Perform daily awakening trial
Daily Awakening Trial
Stop sedation at 7:00 am
Allow to awaken to at least RASS -2
Alert MD for assessment
If necessary, restart at 50% prior dose
Is patient in pain? (NRS/BPI)
Yes
Set goal for analgesia
Intermittent Dosing (preferred)
Fentanyl: 50-100 mcg IVP q10 min to goal, then q2h prn
Morphine: 2-5 mg IVP q10 min to goal, then q2h prn
Continuous Infusion (if IVP more often than q2h)
Fentanyl: 50-100 mcg IVP q10 min to goal, then start gtt @ 50-100 mcg/hr
Morphine: 2-5 mg IVP q10 min to goal, then start gtt @ 2-5 mg/hr
For Intermittent Dosing
If undersedated, rebolus and/or increase d
50% or shorten interval between doses
If oversedated, hold until at goal then decr
dose by 50% or lengthen interval between
For Continuous Infusions
If undersedated: rebolus and/or increase g
by 50%
If oversedated: hold gtt until at goal then re
50% prior rate or consider intermittent dosi
For Patients on Neuromuscular Blockers
Never hold sedatives or analgesics until NM
stopped and paralysis resolved
Is patient anxious? (RASS)
Yes
Set goal for sedation
Compromised ICP/CPP?
Yes
Propofol: 25-50 mg IVP then start gtt @ 5 mcg/kg/min
No
Intermittent Dosing (preferred)
Lorazepam: 1-2 mg IVP bolus q10 min to goal, then q2h prn
Continuous Infusion (if IVP more often than q2h)
Lorazepam: 1-2 mg IVP q10 min to goal, then start gtt @ 1-2 mg/hr
Propofol: 25-50 mg IVP then start gtt @ 5 mcg/kg/min
Yes
Convert to benzos unless ICP/CPP compromised
>3 days Propofol?
Is patient delirious? (CAM-ICU)
Yes
Set goal for delirium control
Haloperidol or Droperidol: 5-10 mg IVP q12h

# General clues to distinguish dementia and delirium

- Relatively abrupt decline in cognition, function and behaviour
- Change in level of consciousness
- Presence of hallucinations
- Presence of potential causal agent(s)
- Neurological deficits other than above

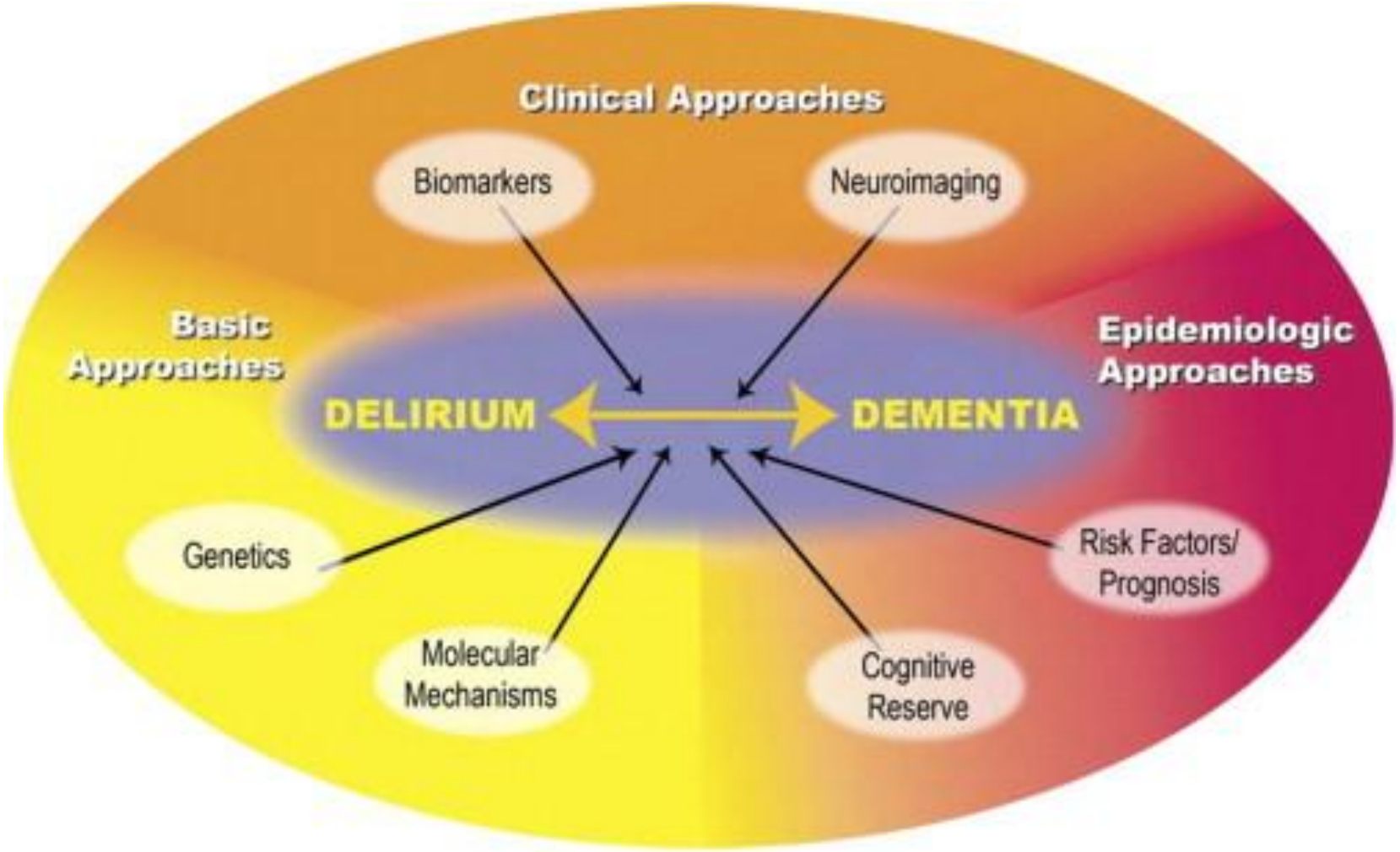
# Delirium - The cost of inattention

- EDITORIAL
- Critical Care Medicine

  Volume 32 • Number 4 • April 2004

# Outline

- What is Cognitive impairment ?
- What is Delirium ? who, what, how, why, etc
- How to prevent, detect and manage delirium.
- Sequelae ?
- What is special about Delirium in the ICU !


Clinical Approaches
Biomarkers
Neuroimaging
Basic Approaches
Epidemiologic Approaches
DELIRIUM
DEMENTIA
Genetics
Risk Factors/ Prognosis
Molecular Mechanisms
Cognitive Reserve

# Cognitive impairment/brain failure

- NOT a normal part of aging
- The diminished ability to think
- Failure of a major organ system-the brain
- Not a diagnosis

- >50% not identified
- Need to use standardized MSE

# Medications Associated With Delirium

- Any drug can potentially cause confusion.
- Take a careful history of any new drug STARTED or any old drug STOPPED recently.

# Medications Associated with Delirium

- Antiparkinsonian agents
- Cardiac e.g. Digitalis, Nicorandil
- Miscellaneous
  - H2 blockers
  - Lithium
  - Steroids
  - Anticonvulsants
  - Antihistamines eg Benadryl
  - Metoclopramide
  - NSAIDs e.g. Indocid

# Delirium subtypes

- In ICU all 3 delirious states
- Often hyperactive delirium → ICU psychosis
- Neurology generally
  - “Delirium” → hyperactive patients
  - “Acute encephalopathy” → hypoactive

# Patient-Oriented Goal-Directed Sedation Delivery

- Appropriate titration of sedatives and analgesics
  - Especially if mechanical ventilation
- Patient comfort a primary goal in ICU
  - Adequate pain control
  - Anxiolysis
  - Prevention and treatment of delirium
  - Appropriate balance is challenging
  - Rational “target levels” of sedation

# Sedation in the ICU

- RCT of 128 inpatients receiving mechanical ventilation and continuous sedation in medical ICU
- Intervention: Interrupt sedation until patient awake on a daily basis versus usual care
- Duration of ventilation 4.9 vs 7.3 (p=0.004) in intervention vs control group
- Median Length of stay 6.4 vs 9.9 days (p=0.02)

Kress et al NEJM May 18, 2000

# Clinician's approach to delirium
# Non-Pharmacological Therapeutic

- Treat all precipitating causes including pain!
- Optimise physiological status (hydration, nutrition etc)
- Inform and educate staff and family
- Minimise predisposing factors (lighting, hearing etc)
- Stabilise environment and re-orientate
- Encourage familiar faces for reassurance e.g. family members
- Low stimulation - avoid excessive noise
- Avoid restraints

# Clinician's approach to delirium Pharmacological Principles

- Avoid physical and chemical restraints if possible
- Minimise medication use
- Use sedation only if severely agitated and restless
- Avoid continuous use of sedation, if possible