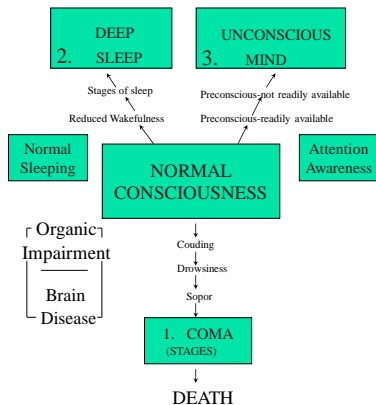


## 譫妄症

黃宗正  
臺大醫院 精神部  
2009.10.25



## Epidemiology

- the most common complication of hospital admission for older people
  - \* About 30% of elderly hospitalized medical patients
  - \* Community: 1-14% (related to age)
  - \* Hospital mortality: 10-65%
- 1/3 to 2/3 unrecognized by primary treating clinicians

Young & Inouye, 2007

## Outline

- What is “consciousness”?
- Definition and epidemiology
- Causes and risk factors
- Clinical features
- Evaluation and diagnosis
- Pathophysiology
- Treatment
- Prevention
- Case vignette

## DELIRIUM (Acute Confusional State)

- Definition:
  - acute decline in attention and cognition
- DSM-IV criteria:
  - \* A. disturbance of consciousness
    - Attentional deficits: focus, maintain, shift
  - \* B. change in cognition
    - Orientation, memory, language,...
  - \* C. develop over a short period, fluctuation in a day
  - \* D. organic etiology

## Causes and risk factors

- Causes
  - \* VINDICATE
    - MID: metabolic, infection, drug
- Risk factors
  - Aging
  - Cognitive decline
  - Psychactive medications
  - Polypharmacy
  - Concurrent severe medical diseases
  - Sensory deprivation/overload
  - Sleep deprivation
  - ...

## 臨床表現 (1)

- Hyperactive and hyperalert
  - \* frequently diagnosed
  - \* Often increased sympathetic activity
    - Typical: alcohol or BZD withdrawal
    - High risk of fall (then fracture and difficult to care)
  - \* EEG: low voltage fast wave
- Hypoactive and hypoalert
  - \* EEG: slowing, increased latency of evoked potential
- Mixed
  - \* Alternating irregularly

### Subtypes of Delirium: frequency depends on definition

	Liptzin 1993	Kobayashi 1992	Liu* 1997	Camus 2000	Marcantonio 2002
Hyperactive type	15%	78%	68.8%	46.5%*	29%
Hypoactive type	19%	7%	13.5%	26.2%	71%
Mixed type	52%	15%	17.7%	-	-
Neither	14%	-	-	27.3@	-

\* Liu CY, et al: *International Medical Journal* 1997;4:181-185

(Courtesy of Dr. Liu CY)

### Subtypes of Delirium

- Larger studies did not find any difference in causative factors between various presentation forms of delirium

de Rooij, et al., *Int J Geriatr Psychiatry* 2005

(Courtesy of Dr. Liu CY)

## 臨床表現 (2)

- Hallucinations and delusions
  - \* More common in hyperactive/hyperalert variant
  - \* VH > AH
  - \* Delusions: fragmented, persecutory
  - \* "ICU psychosis"--- delirium!
- Sleep cycle disturbance
- Sundowning

## Differential diagnosis

- Delirium vs.Dementia
  - \* D/D by acute onset
    - Exception: dementia with Lewy body
  - \* More frequent delusions and hallucinations
    - Exception: dementia with Lewy body

## Hypoactive delirium vs. depression

- Personal hygiene
- Engagement in interview
- Fluctuation of mood
- Fluctuation of cognition
- Onset

## EVALUATION AND DIAGNOSIS OF DELIRIUM

- **CAM**
  - MMSE, Delirium Rating Scale
- Search for underlying etiology
  - PE, NE
  - Review medication list
  - Metabolic work-up: CBC, electrolytes, biochemistry, pO<sub>2</sub>, EKG
  - Search for possible occult infection
  - Others

- 1.急性發病：與病人的原先狀態比較，是否有急性的精神狀態改變？
- 2.注意力障礙：A. 病人是否很難集中注意力，容易分神？或是很難注意別人說些甚麼？ B. (若A有任何異常) 這種行為變化是否在會談中起伏或改變？ C. 描述此異常行為
- 3.思考解構 (disorganized thinking)：病人的思考是否混亂？語無倫次或答非所問？思緒不清楚或不合邏輯？或談話主題間常有難預期的跳躍思考？
- 4.意識狀態改變：你評估病人的意識障礙程度：清醒、過度警覺、嗜睡、難喚醒 (stupor)、昏迷或不確定？

### SHORTENED MMSE

#### ORIENTATION

1. What is the: (year) (season) (date) (day) (month)?
2. Where are we: (state) (county) (town) (hospital) (floor)?

#### REGISTRATION

3. Name 3 objects (Repeat until all 3 are learned)

#### ATTENTION

4. Spell "WORLD" backwards.

#### RECALL

5. Ask for 3 objects in Q3.

\*1,2,3,4 rely on good attention

\*tests for attention: A test

## Confusion Assessment Method

- (1) acute onset and fluctuating course
- (2) inattention
- (3) disorganized thinking
- (4) altered level of consciousness

-- The diagnosis of delirium requires the presence of criteria:

**[(1) and (2)] + either (3) or (4)**

(Inouye SK, 1990)

#### The Confusion Assessment Method Instrument:

1. **[Acute Onset]** Is there evidence of an acute change in mental status from the patient's baseline?
- 2A. **[Inattention]** Did the patient have difficulty focusing attention, for example, being easily distractible, or having difficulty keeping track of what was being said?
- 2B. **[If present or abnormal]** Did this behavior fluctuate during the interview, that is, tend to come and go or increase and decrease in severity?
3. **[Disorganized thinking]** Was the patient's thinking disorganized or incoherent, such as rambling or irrelevant conversation, unclear or illogical flow of ideas, or unpredictable switching from subject to subject?
4. **[Altered level of consciousness]** Overall, how would you rate this patient's level of consciousness? (Alert [normal]; Vigilant [hyperalert, overly sensitive to environmental stimuli, startled very easily]; Lethargic [drowsy, easily aroused]; Stupor [difficult to arouse]; Coma; [unarousable]; Uncertain)
5. **[Disorientation]** Was the patient disoriented at any time during the interview, such as thinking that he or she was somewhere other than the hospital, using the wrong bed, or misjudging the time of day?
6. **[Memory impairment]** Did the patient demonstrate any memory problems during the interview, such as inability to remember events in the hospital or difficulty remembering instructions?
7. **[Perceptual disturbances]** Did the patient have any evidence of perceptual disturbances, for example, hallucinations, illusions or misinterpretations (such as thinking something was moving when it was not)?
- 8A. **[Psychomotor agitation]** At any time during the interview did the patient have an unusually increased level of motor activity such as restlessness, picking at bedclothes, tapping fingers or making frequent sudden changes of position?
- 8B. **[Psychomotor retardation]** At any time during the interview did the patient have an unusually decreased level of motor activity such as sluggishness, staring into space, staying in one position for a long time or moving very slowly?
9. **[Altered sleep-wake cycle]** Did the patient have evidence of disturbance of the sleep-wake cycle, such as excessive daytime sleepiness with insomnia at night?

## CAM

- Scored based on observations made during formal cognitive assessment
  - \* E.g. MMSE or Short Portable Mental Status Questionnaire
- For research purposes, use of the full nine-item CAM instrument is recommended to maximize sensitivity

## EEG

- EEG slowing, **increased latency** of evoked potential
- Sometimes can be useful
  - \* Ono-convulsive seizure
  - \* Toxicity or metabolic derangement: **triphasic wave**
  - \* Creutzfeldt-Jakob disease
- **Not** all cases have EEG changes
- May not be practical
  - \* Pt transfer
  - \* Examination itself is disturbing to the pt

## Metabolic encephalopathy

- Hepatic (Portosystemic) encephalopathy
  - \* Chronic confusion state, tremor, asterixis
- Hepatocerebral degeneration (Wilson disease)

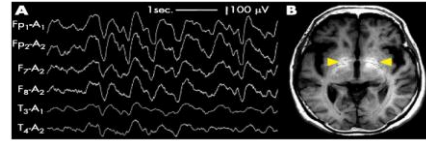


Figure 1 EEG showing triphasic waves (A). T1 axial scan (B) showing signal change in the globus pallidus (arrowheads).

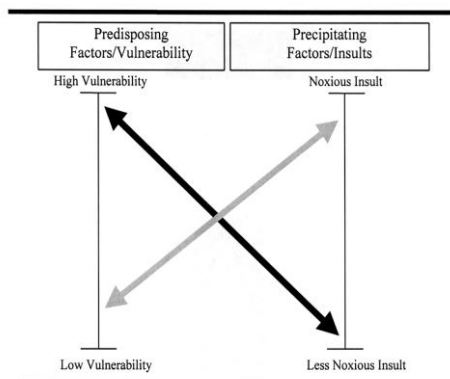
Fukushima et.al. *J Neurol Neurosurg Psychiatry*. 2008 Jan;79(1):96.

## CRITERIA FOR NEUROIMAGING

1. History of recent falls or head trauma
2. Signs of head trauma
3. Focal neurologic changes
4. Fever/acute mental status changes, suspicion of encephalitis
5. No identifiable etiology of acute mental status change

## PATHOPHYSIOLOGY

- Usually functional rather than structural lesion
- Characteristic EEG findings (usually generalized slowing)
- multiple pathogenic mechanisms → final common pathway:
  - \* Failure of **cholinergic transmission**
  - \* Widespread reduction of **cerebral oxidative metabolism**
  - \* HPA: cortisol excess
  - \* Cytokine excess



## UTI or systemic inflammation

- \* Modulator such as cytokine involved
- \* Disrupt the BBB

## TREATMENT

- Treat possible underlying causes
- Good supportive care
- Do no harm
- Symptomatic Tx

### Good supportive care

- Physical
  - Adequate O2 supply
  - Good sleep, diet and fluid
  - Mobility
  - Sensory aids
  - Appropriate light level
  - Decrease noises
- Cognitive: Frequent reorientation
  - Clock and calendar
- Psychosocial
  - Encourage familiar persons to visit and care
  - Familiar objects for rehab
  - Other visitors are briefed

### Symptomatic drug tx

- Junior resident syndrome
- Drug of choice: low dose haloperidol
  - 較少之抗膽鹼，心血管，呼吸系統副作用
  - 0.5 mg q2h; max < 5mg/d
  - EPS; QTc prolongation
- Benzodiazepine
  - 酒精或是鎮靜劑之戒斷性譫妄症
  - 抗精神病藥物反應不佳時合併使用
  - In PD, DLB pts
  - lorazepam: 0.5-1 mg q2h; max < 3mg/d
- Atypical antipsychotics
  - Risperidone, Olanzapine, Quetiapine--- **watch out CV side effects!**
  - Sulpiride, amisulpride

## Barrough (1583)

- Treatment of delirium
  - Treatment had to involve attention to the **patient's needs**; if he was troubled by the light, he had to be placed in a dark room. Moreover, **let his dearest friends come to him**, and let them **sometime speak gently and softly** unto him, and sometimes rebuke him sharply' His diet had to be light. The patient had to be **left undisturbed**, since 'perturbations of the mind do hurt frenetick ( delirious ) persons exceedingly. **Sleep needed to be ensured by the use of appropriate medications** such as **opium** or henband, taking care **not to oversedate** the patient, as this could turn the 'frenesie ( hyperactive form of delirium ) into a lethargie ( hypocative form of delirium ) whereby **you may cause him to sleepe so that you can awake him no more**'.

### Do no harm

- Avoid
  - Ward transfer
  - Physical restraint
  - Catheter
  - Constipation
  - Anticholinergic drugs and unnecessary drugs

### Haldol

- Mild delirium--- 0.5 mg
- Moderate--- 1 mg
- Severe--- 2 mg
- May repeat every 30-120 mins, until pt calm down
- If haldol> 5-10mg, may combine with ativan im. (other drugs not absorbed well by I.m.) 0.5-2 mg
- The total dose of haldol is calculated--- cut half the next day, in divided dose--- taper off in 3-5 days.

## ACEI in delirium

- Up to 2008, no evidence supports the efficacy of ACEI in delirium
- Documented evidence for rivastigmine in DLB (frequently associated with delirium)
  - \* DLB: prominent dopaminergic, cholinergic deficits may be related with attentional deficits?

## YALE DELIRIUM PREVENTION PROGRAM

- Designed to counteract iatrogenic influences leading to delirium in the hospital
- Multicomponent intervention strategy targeted at 6 delirium risk factors
- RISK REDUCTION: from 15% to 10% for those without delirium at baseline

Risk Factor	Intervention
Cognitive Impairment.....	Reality orientation Therapeutic activities protocol
Sleep Deprivation.....	Nonpharmacological sleep protocol Sleep enhancement protocol
Immobilization.....	Early mobilization protocol Minimizing immobilizing equipment
Vision Impairment.....	Vision aids Adaptive equipment
Hearing Impairment.....	Amplifying devices Adaptive equipment and techniques
Dehydration.....	Early recognition and volume repletion

(Inouye SK. NEJM, 1999)

## YALE DELIRIUM PREVENTION TRIAL RESULTS

Outcome	Intervention Group (N=426)	Usual Care Group (N=426)	Matched OR (CI) or p-value
Incident delirium, n (%)	42 (9.9%)	64 (15.0 %)	.60 (.39-.92) p=.02
Total delirium days	105	161	p=.02
No. delirium episodes	62	90	p=.03
Delirium severity score	3.9	3.5	p=.25
Recurrence rate	13 (31.0%)	17 (26.6%)	p=.62

(Inouye SK. NEJM, 1999)

## Consequence of Delirium

- Prolong hospital stay
- Not entirely reversible
- Post-delirious amnesia or PTSD !!
- Predict posthospitalization cognitive decline and loss of community independent life
- Vicious cycle
  - \* Delirium --- secondary dehydration--- physical derangement, emotional turmoil --- physical restraint ---aggravated delirium

## Communications with pt and family

- Initially
  - \* Clarify history, including cognitive function
- How to explain his delirious behaviors to the pt?
  - \* PTSD
- How to explain the outcome of delirium?
  - \* Transient and can be recovered completely?
    - Independent predictor for poor outcome
    - Mortality, complications (fall, incontinence...), functional decline

## A 55 y/o female patient at ER

- Mutism with eye open
- Restricted affect, suspected to be depressed
- Bedside NP testing

## 60 y/O woman

- Lung ca with brain meta. s/p R/T
  - \* Apparent VH, reverse sleep pattern
  - \* Internist ever gave remeron, ativan, haldol, but ineffective
  - \* Seroquel (12.5-25 mg hs) used for 2 weeks, still in vain

## Conclusions

- Common problem
- Serious complications
- Often unrecognized
- Can be preventable
  - **multicomponent intervention**

謝謝您的聆聽