AGS HENDERSON LECTURE

DELIRIUM:
APPLYING RESEARCH TO TRANSFORM CARE AT THE BEDSIDE

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Hebrew SeniorLife
Edward Henderson, M.D.
“Hendy”
1806-1973

• Served the American Geriatrics Society for over 20 years

• President, Executive Director, Trustee of the AGS Research Fund

• Credited with bringing AGS from relative obscurity to international prominence
Delirium as an example

Approach to a common geriatric syndrome:

• Identify and measure condition
• Elucidate multifactorial risk factors
• Develop and test interventions
• Create system change to incorporate interventions and improve quality of care
• Disseminate model of care
CASE

Mrs. S is a 78 yo woman (living independently) with diabetes mellitus, arthritis and cataracts, who presents with unstable angina. She is treated with intravenous nitroglycerine, morphine, lidocaine, lorazepam, and ranitidine. A bladder catheter is placed.

Day 2: Cardiac catheterization with angioplasty for continued angina. In evening, pt develops delirium, managed with restraints, lorazepam and haloperidol.

Day 3: Pt develops urinary tract infection with fever and increased confusion. Bladder catheter discontinued; pt incontinent. Sacral skin breakdown noted.

Day 9: Pt remains incontinent, with large sacral pressure sore, and unable to walk or care for herself. Social Work consult for placement.
WHAT IS DELIRIUM?
(Acute Confusional State)

Definition:
• acute decline in attention and cognition

_Pearl:_ Delirium is an important epidemiologic syndrome
• common problem
• serious complications
• often unrecognized
• may be preventable
DSM-IV-TR CRITERIA FOR DELIRIUM

- Disturbance in consciousness with reduced attention
- A change in cognition (e.g., memory deficit, disorientation, language deficit) or perceptual disturbance
- Acute onset and fluctuating course
- Evidence of an underlying medical etiology

Ref: APA; DSM-IV, Text Revision. 2000
**EPIDEMIOLOGY OF DELIRIUM**

**Delirium Rates**

Hospital:
- Prevalence (on admission) 14-24%
- Incidence (in hospital) 6-56%

Postoperative: 15-53%

Intensive care unit: 70-87%

Nursing home/post-acute care: 20-60%

Palliative care up to 80%

**Mortality**

Hospital mortality: 22-76%

One-year mortality: 35-40%

Ref: Inouye SK, NEJM 2006;354:1157-65
IMPACT OF DELIRIUM

Hospital costs (> $8 billion/year)
Post-hospital costs (> $100 billion/year)
  • Institutionalization
  • Rehabilitation
  • Home care
  • Caregiver burden

Aging of U.S. population

COSTS OF DELIRIUM

• In 841 patients, determined total one-year health care costs associated with delirium
• Adjusted average annual costs were 2.5 times higher for patients with delirium
• Total annual costs attributable to delirium were $16,000-$64,000 per patient
• National burden of delirium:

  $40 to 150 billion per year.

RECOGNITION OF DELIRIUM

Previous studies: 32-66% cases unrecognized by physicians

Pearl: We cannot manage delirium or decrease its complications unless we recognize it
NURSES’ RECOGNITION OF DELIRIUM

• Compared nurse recognition of delirium with interviewer ratings (N=797)
• Nurses recognized delirium in only 31% of patients and 19% of observations
• Nearly all disagreements in ratings were due to under-recognition by nurses
• Risk factors for under-recognition: hypoactive delirium; advanced age, vision impairment, dementia

Ref: Inouye SK, Arch Intern Med. 2001;161:2467-2473
DEVELOPMENT
OF A
DELIRIUM INSTRUMENT

CONFUSION ASSESSMENT METHOD (CAM)

- Developed to provide a quick, accurate method for detection of delirium
- For non-psychiatrically trained clinicians
- Both clinical and research settings
- Prospective validation study using criterion standard

SIMPLIFIED DIAGNOSTIC CRITERIA

• Uses 4 criteria assessed by CAM:
  (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), (2) and (3) or (4)
## VALIDATION OF CAM

<table>
<thead>
<tr>
<th></th>
<th>Site I (n=30)</th>
<th>Site II (n=26)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sensitivity</strong></td>
<td>10/10 (100%)</td>
<td>15/16 (94%)</td>
</tr>
<tr>
<td><strong>Specificity</strong></td>
<td>19/20 (95%)</td>
<td>9/10 (90%)</td>
</tr>
<tr>
<td><strong>Positive predictive accuracy</strong></td>
<td>10/11 (91%)</td>
<td>15/16 (94%)</td>
</tr>
<tr>
<td><strong>Negative predictive accuracy</strong></td>
<td>19/19 (100%)</td>
<td>9/10 (90%)</td>
</tr>
<tr>
<td><strong>Likelihood ratio (positive test)</strong></td>
<td>20.0</td>
<td>9.4</td>
</tr>
</tbody>
</table>
SUPPORTING FEATURES OF DELIRIUM

• Disorientation
• Memory impairment
• Perceptual disturbances (hallucinations, illusions, misperceptions)
• Delusions
• Psychomotor agitation or retardation
• Sleep cycle disturbances
• Inappropriate behavior
CAM SIGNIFICANCE

- Helped to improve recognition of delirium
- Widely used standard tool for clinical and research purposes nationally and internationally
- Validated in over 1000 patients with sensitivity 94% and specificity of 89%
- Translated into at least 12 languages
- Used in over 250 original published studies to date

Ref: Wei LA et al. JAGS 2008;56:823-30
MODIFIED MINI-COG TEST

ORIENTATION
1. Time: Day of Week, Year, Day/Night, Last Meal, Days in Hospital
2. Place: City/State, Hospital, Floor

REGISTRATION
3. Name 3 objects: (apple) (table) (penny)
   Ask the patient all 3 after you have said them.
   Repeat until all 3 are learned.

CLOCK-DRAWING
4. Draw circle, draw numbers, and place hands at “ten past eleven”

RECALL
5. Ask for 3 objects in Q3.

ASSESSMENT FOR INATTENTION

*If time to do only one cognitive task, assess attention*

- Digit span test (normal: 5F, 3B)
- Days of week backwards
- Months of year backwards
SPECTRUM OF DELIRIUM

Ranging from:

Hypoactive delirium (lethargy, excess somnolence) -- often missed
to:

Hyperactive delirium (agitated, hallucinating, inappropriate)

**Pearl:** Hypoactive form is more common in older persons (75%) and associated with higher mortality.
<table>
<thead>
<tr>
<th>Feature</th>
<th>Delirium</th>
<th>Dementia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Onset</td>
<td>Abrupt</td>
<td>Insidious</td>
</tr>
<tr>
<td>Duration</td>
<td>Hours to days</td>
<td>Months to years</td>
</tr>
<tr>
<td>Attention</td>
<td>Impaired</td>
<td>Normal unless severe</td>
</tr>
<tr>
<td>Consciousness</td>
<td>Fluctuating, reduced</td>
<td>Clear</td>
</tr>
<tr>
<td>Speech</td>
<td>Incoherent, disorganized</td>
<td>Ordered, anomic/aphasic</td>
</tr>
</tbody>
</table>
PATHOPHYSIOLOGY OF DELIRIUM

• Poorly understood
• Functional rather than structural lesion
• Characteristic EEG findings (generalized slowing)
• Hypothesis: final common pathway of many pathogenic mechanisms:
  a. Dysfunction of neurotransmitter systems
  b. Inflammation/cytokines
  c. Impaired cerebral oxidative metabolism
MULTIFACTORIAL MODEL OF DELIRIUM IN OLDER PERSONS

Ref: Inouye SK et al. JAMA 1996; 275:852-857
ETIOLOGY

Dementia
Electrolytes
Lungs, liver, heart, kidney, brain
Infection
Rx—Treatment and withdrawal (ETOH, benzos)
Injury, pain, stress
Unfamiliar environment
Metabolic

Pearl: Addressing the multifactorial etiology is key to managing delirium.

BASELINE VULNERABILITY

Development and Validation of a Predictive Model for Delirium based on Admission Characteristics

### INDEPENDENT RISK FACTORS FOR DELIRIUM (N=107)

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Adjusted Relative Risk (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vision Impairment</td>
<td>3.5 (1.2, 10.7)</td>
</tr>
<tr>
<td>Severe Illness</td>
<td>3.5 (1.5, 8.2)</td>
</tr>
<tr>
<td>Cognitive Impairment</td>
<td>2.8 (1.2, 6.7)</td>
</tr>
<tr>
<td>BUN/Cr Ratio ≥ 18</td>
<td>2.0 (0.9, 4.6)</td>
</tr>
</tbody>
</table>

PRECIPITATING FACTORS

Development and Validation of a Predictive Model for Delirium based on Hospitalization – Related Factors

### INDEPENDENT PRECIPITATING FACTORS FOR DELIRIUM

(N = 196)

<table>
<thead>
<tr>
<th>Precipitating Factor</th>
<th>Adjusted Relative Risk (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Use of physical restraints</td>
<td>4.4 (2.5 - 7.9)</td>
</tr>
<tr>
<td>Malnutrition</td>
<td>4.0 (2.2 - 7.4)</td>
</tr>
<tr>
<td>&gt; 3 medications added</td>
<td>2.9 (1.6 - 5.4)</td>
</tr>
<tr>
<td>Use of bladder catheter</td>
<td>2.4 (1.2 - 4.7)</td>
</tr>
<tr>
<td>Any iatrogenic event</td>
<td>1.9 (1.1 - 3.2)</td>
</tr>
</tbody>
</table>
MEDICATIONS ASSOCIATED WITH DELIRIUM

* Sedative-hypnotics
  Benzodiazepines (Dalmane, Valium)
  Barbiturates
  "Sleepers" (Chloral hydrate)

* Narcotics

* Anticholinergics
  Antihistamines (Benadryl, Atarax)
  Antispasmodics (Belladonna, Lomotil)
  Tricyclic antidepressants
  Antiparkinsonian agents (Cogentin, Artane)
  Antiarrhythmics (Quinidine, Norpace)

Cardiac (Digitalis, Lidocaine)
Antihypertensives (Beta-blockers, Aldomet)

Miscellaneous
  H2-blockers
  Steroids
  Metoclopramide

Lithium
Anticonvulsants
NSAID’s
MINIMIZE PSYCHOACTIVE MEDICATIONS

Pearl: Evaluating drug usage is a high-yield intervention for delirium in the hospital

1) Frequently review medication list
2) Minimize psychoactive medications
   • Avoid PRN’s
   • Use nonpharmacological approaches
   • Substitute less toxic alternatives
     (e.g. antacid or Carafate for H₂ blocker/PPI
     Metamucil/Kaopectate for Lomotil/Imodium)
   • Reduce dosage
3) Re-evaluate chronic medication usage
   • Hospital ideal time to make changes
   • Substrate is not the same
NONPHARMACOLOGICAL SLEEP PROTOCOL

1. Give a 5 minute back rub
2. Give a warm drink (patient’s choice of warm milk or herbal tea)
3. Put on relaxation tapes
4. Allow one hour to assess effectiveness

EFFECTIVENESS OF SLEEP PROTOCOL
(N = 111)

• Feasible, with adherence rate of 74%
• Effective with dose-response relationship
  --quality of sleep correlated with number of parts of protocol received
  --reduced use of sleep medications from 54% to 31% (p<0.002)
• Nontoxic, acceptable to patients
SLEEP

• Schedule medications, vital signs, procedures to allow uninterrupted sleep
• Lights off and decreased noise-level at night
• No naps during the day
EVALUATION AND MANAGEMENT OF DELIRIUM

1. Cognitive Evaluation:
   
   Mini-Cog and Confusion Assessment Method
   
   **Pearl:** You may need to use detective work to determine if acute change (e.g., family member, previous nurse)

2. Search for underlying etiology:
   
   Physical examination (including neurological exam) and vital signs
   Review medication list (current and preadmission), alcohol history
   Targeted metabolic work-up: CBC, lyes, BUN/Cr, Glucose, LFT’s, Calcium, p02, EKG
   Search for occult infection
   Neuroimaging or LP in < 5% cases
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

Ref: Inouye SK, NEJM 2006;354:1157-65
DELIRIUM MANAGEMENT
PHARMACOLOGIC APPROACHES

Pearl: Reserve for patients with severe agitation which will:

1. cause interruption of essential medical therapies
   (e.g., intubation)
2. pose safety hazard to patient or staff

Treatment:

• Haloperidol 0.25-0.50 mg po or IM (IV short acting, risk of torsades)
• Repeat dose Q 30 minutes until sedation achieved
  (maximum haloperidol dose 3-5 mg/24 hours)
• Maintenance: 50% loading dose in divided doses over next 24 hours
• Taper dose over next few days
THE YALE DELIRIUM PREVENTION TRIAL

# YALE DELIRIUM PREVENTION PROGRAM

Multicomponent intervention strategy targeted at 6 delirium risk factors

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cognitive Impairment</td>
<td>Reality orientation</td>
</tr>
<tr>
<td></td>
<td>Therapeutic activities protocol</td>
</tr>
<tr>
<td>Sleep Deprivation</td>
<td>Nonpharmacological sleep protocol</td>
</tr>
<tr>
<td></td>
<td>Sleep enhancement protocol</td>
</tr>
<tr>
<td>Immobilization</td>
<td>Early mobilization protocol</td>
</tr>
<tr>
<td></td>
<td>Minimizing immobilizing equipment</td>
</tr>
<tr>
<td>Vision Impairment</td>
<td>Vision aids</td>
</tr>
<tr>
<td></td>
<td>Adaptive equipment</td>
</tr>
<tr>
<td>Hearing Impairment</td>
<td>Amplifying devices</td>
</tr>
<tr>
<td></td>
<td>Adaptive equipment and techniques</td>
</tr>
<tr>
<td>Dehydration</td>
<td>Early recognition and volume repletion</td>
</tr>
</tbody>
</table>

## Yale Delirium Prevention Trial

### Results

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Intervention Group (N=426)</th>
<th>Usual Care Group (N=426)</th>
<th>Matched OR (CI) or p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incident delirium, n (%)</td>
<td>42 (9.9%)</td>
<td>64 (15.0%)</td>
<td>.60 (.39-.92) p= .02</td>
</tr>
<tr>
<td>Total delirium days</td>
<td>105</td>
<td>161</td>
<td>p=.02</td>
</tr>
<tr>
<td>No. delirium episodes</td>
<td>62</td>
<td>90</td>
<td>p=.03</td>
</tr>
<tr>
<td>Delirium severity score</td>
<td>3.9</td>
<td>3.5</td>
<td>p=.25</td>
</tr>
<tr>
<td>Recurrence rate</td>
<td>13 (31.0%)</td>
<td>17 (26.6%)</td>
<td>p=.62</td>
</tr>
</tbody>
</table>
DELIRIUM PREVENTION TRIAL: SIGNIFICANCE

• Practical, real-world intervention strategy targeted towards evidence-based risk factors
• Targeted, multicomponent strategy works
• Significant reduction in risk of delirium and total delirium days, without significant effect on delirium severity or recurrence

Pearl: Primary prevention of delirium likely to be the most effective treatment strategy
THE HOSPITAL ELDER LIFE PROGRAM (HELP)

A model of care to prevent delirium and functional decline in hospitalized older patients

HELP EFFECTIVENESS: PREVIOUS STUDIES

• Prevented decline in cognitive and physical function at hospital discharge\textsuperscript{1}
• Reduced incident delirium, total delirium days and delirium episodes\textsuperscript{2}

Refs: \textsuperscript{1} Inouye SK et al, JAGS 2000;48:1697-706;
\textsuperscript{2} Inouye SK et al, NEJM 1999;340:669-76
HOSPITAL COST-EFFECTIVENESS RESULTS
(N = 852)

• Intermediate risk patients (72% of sample), HELP resulted in lower overall hospital costs, averaging $831 per patient (range $415-1,689)

• Savings offset intervention costs, thus, HELP is cost-effective for intermediate risk patients

• Savings occur across every cost category (e.g., nursing, room, diagnostic procedures, ICU)

Pearl: In geriatrics, good care is often cost-effective care

Ref: Rizzo JA et al. Medical Care; 2001;39:740-52
LONG-TERM COST EFFECTIVENESS: NURSING HOME COSTS

• One yr follow-up of Delirium Prevention Trial pts
• Intervention did not affect the likelihood of nursing home placement
• Among patients receiving long-term nursing home placement (>100 days), intervention resulted in:
  – Lower total costs ($50,881 vs. $60,327, p=.01)
  – Shorter length of stay (241 vs. 280 days, p<.05)
  – Lower costs per survival day ($148 vs. $175, p<.02)

HELP DISSEMINATION

• HELP National Dissemination Project 1999-2010:
  – over 60 active sites
  – over 25 states and 6 countries

• Potential sites:
  – Contact us, register
  – Receive program materials
  – Ongoing support from dissemination team
HELP DISSEMINATION
(UPMC Shadyside Hospital)

• Found reduced delirium and LOS in 4,763 hospitalized patients over 3.5 years receiving HELP.

• LOS reduced by 0.3 days per patient, for cost savings of $790 per patient on average ($1.3 million/year on one unit).

• Program sustained for over 7 years, and serving >5,000 patients per year

Rubin et al. JAGS 2006;54:969-74
HELP and Fall Prevention

• **ONLY** evidence-based program that can prevent hospital falls (Medicare no-pay condition)
• Altered mental status/delirium is the leading risk factor for falls in the hospital
• At 29 hospitals with HELP, 95% of sites reported a reduction in the rate of falls
• At 3 HELP sites (Maine, Cornell, Moses Taylor), we have received data documenting fall reduction:
  – Site 1: 11.4 to 3.8 per 1000 patient-days
  – Site 2: 4.7 to 1.2 per 1000 patient-days
  – Site 3: 4.2% to 2.4% in 4000 patients/1 yr

Inouye SK. NEJM 2009;360: 2390-3
HELP WEBSITE
http://hospitalelderlifeprogram.org

• Supported by a grant from National Library of Medicine

• Useful components for clinicians:
  – General information on delirium and hospitalization for patients and families
  – Searchable bibliography
  – Information on HELP
  – Links to useful websites on delirium and hospital care
DELIRIUM
HEALTH POLICY IMPLICATIONS

Delirium serves as a marker for quality of hospital care for the elderly

- Often iatrogenic
- Linked to processes of care
- Common, bad outcomes

Delirium serves as a window for identifying quality – improving changes.

NEW DIRECTIONS FOR RESEARCH

• Long-term outcomes: Does delirium lead to dementia?
• Delirium treatment: effective management of delirium once it occurs
• Value of early recognition and treatment
• Cognitive reserve capacity: protective effect of education, diet, activities/exercise
• Pathophysiology: neuroimaging, biomarkers, molecular mechanisms
The Final Pearl

Delirium may provide the unique opportunity for early intervention and prevention of cognitive damage
Unique Aspects of Geriatric Medicine

- Focus on function and quality of life
- Multifactorial etiology/multimorbidity
- Geriatric syndromes
- Unique research approaches
- Translational work from bench to bedside
- Framing healthcare for the next century
“On the Shoulders of Giants”

Acampora, D  Foreman, MD  Metzger, E
Agostini, JV  Givens, JL  Mion, L
Alsop, DC  Gottlieb, G  Morrison, RS
Baker, DI  Holford, TF  Pisani, MA
Bogardus, ST  Horwitz, RI  Rizzo, JA
Bradley, EH  Jones, RN  Rubin, FH
Brown, CJ  Kiely, DK  Rudolph, JL
Charpentier, P  Kuchel, GA  Schlesinger, MJ
Cooney, LM  Leff, B  Siu, AL
Crosby, G  Leslie, DL  Studenski, S
Cuppes, LA  Lipsitz, LA  Tinetti, ME
Culley, DJ  Lydon, TJ  Viscoli, CM
Fick, DM  Marcantonio, ER  Yang, FM
Fong, TG  McAvay, GJ  Zhang, Y
“The wind beneath my wings”

My family: Steve Benjamin and Jordan Helfand
My mother: Lily Ann Inouye
In memory of:
Joshua Helfand, Bradley and Mitsuo Inouye