### "What Happened To Grandma?"

### Understanding Geriatric Cognitive and Functional Decline **Delirium**

Daniel R. Hoefer, MD CMO Outpatient Palliative Care Sharp HospiceCare



425 hospital admissions: = or > age 70; generally more frail patients

106 developed

\_\_\_ (24.9%)

1 year mortality 34.9% with 21.6% without (p<0.006)

2 year mortality (p<0.005) 58.5% with \_\_\_\_\_ 42.6% without \_\_\_\_

Institutionalization of Patients at 2 years 54.4% with \_\_\_\_\_ 27.9% without \_\_\_\_\_



At 2 years, 90% of \_\_\_\_\_ patients are either dead or institutionalized.

Number of hospital bed days for patients with\_\_\_\_ increased from 29.5 to 36.3 (First year of study)

3 year mortality rate is 79% if this event occurs (Rockwood, K, et al)

Rockwood, K, et al, *The Risk of Dementia and Death after\_\_\_\_*, Age Ageing, 1999;28:551-56



Putting it into Perspective:

Stage III a non small cell lung cancer has a 5 year mortality of 86%

Stage IV CHF has a 30-50% mortality at 1 year



#### Answer:

#### Delirium

## "Abrupt declines in cognitive function in the elderly are associated with early death"



## "Clinicians... have underestimated the impact of brain dysfunction"

Timothy, Girard, et al, *Review: Delirium in the Intensive Care Unit,* Critical Care 2008; 12(3): 53: 1-9



The 1 year mortality for hospital induced delirium is 30-40%. That is the same mortality as Myocardial infarction or Sepsis in the elderly.



Because Delirium can be iatrogenic it is a clinical Quality Indicator:

National Quality Measures Clearinghouse of the Healthcare Research and Quality has determined the incidence of delirium to be a marker of quality of care and patient safety.



NIH recognizes delirium as the most common side effect of hospitalization for the elderly.

The IOM (Institute of Medicine) considers early detection of dementia 1 of 6 goals to improve Quality of Care in the health care system.



1 -year health-care costs:

Delirium - \$38 - \$152 Billion

- Hip Fracture \$7 billion
- Non-fatal falls \$19 billion
- Diabetes Mellitus \$91.8 billion
- Cardiovascular Disease \$257.6 billion

Fong, T et al, "Delirium In Elderly Adults: Diagnosis, Prevention and Treatment", 2009Nta Rev Neuro 5(4): 210-20



#### Acute Brain Failure = Delirium

#### Other terms:

- Altered mental status
- Acute confusional state
- Acute brain syndrome
- Toxic metabolic encephalopathy
- Confusion



Terri R Fried MD, et al, *Understanding the Treatment Preferences of Seriously III Patients,* NEJM 2002; 346: 1061-66

For advanced illness patients, 74.4% and 88.8%, of patients would forgo treatment if the treatment burden was low but the probability of severe functional impairment or cognitive impairment was high.

This compares to 98.7% of patients who would want treatment in the treatment burden was low and they were more likely to return to their previous level of function.

Mortality was not the major determinant in patient choice.

n=279 Patients' had no cognitive or functional deficits in this study.



"Up to Date: Physiology and Goals of Care for the Pre-terminal Populations are Not the Same as a Younger and Healthier Geriatric Patient."

Daniel Hoefer, M. D.



#### **Prevalence:**

Hospice: 83% ICU: 80% Nursing Home: 63% Hospital: 5.1% -52.2% Surgery: hip fx 16.0-65.0%, cardiovascular 6.0-52.2%, cataract 4% Non-surgical: 15-30% Prevalence\*: 10-31% Incident\*: 3-29% Occurrence:\*: 11-42%

\*Siddiqi, Najma, et al Occurrence and Outcomes of Delirium in Medical Inpatients: A systematic Literature Review, Age and Aging 2006; 34:350-64

Point of information: cognitive change in the first 8 post-op hours excludes the diagnosis of delirium



#### Changing the Paradigm:

Old: Acute hospital delirium is a medical emergency with significant short term but not long term consequences. You cannot tell who might develop delirium.

New: Acute hospital or outpatient delirium needs emergent evaluation and is associated with both significant short term and long term consequences. We can predict who is likely to develop delirium.



Inouye, Sharon, MD, *Risk Factors for Delirium at Discharge,* Arch Intern Med 2007; 167(13)

Incident delirium

**Risk Factors:** 

- 1. Dementia
- 2. Vision worse than 20/70
- 3. Functional Impairment
- 4. High comorbidities
- 5. Any Restraint

0-1 Low2-3 Intermediate4-5 High



	Delirium	Death or NH Placement
Low risk	4%	15%
Intermediate	18%	39%
High	63%	64%



### **Delirium – Predisposing Factors**



Fig. 1. Age and the probability of transitioning to delirium. The most notable finding related to age was that probability of transitioning to delirium increased dramatically for each year of life after 65 years. Adjusted OR 1.01 (1.00, 1.02) (P = .03). Y-axis = Probability; X-axis = Age in years. (*From* Pandharipande P, Shintani A, Peterson J, et al. Lorazepam is an independent risk factor for transitioning to delirium in intensive care unit patients. Anesthesiology 2006;104(1):23; with permission.)

Maldonado, JR, Delirium in the Acute Care Setting: Characteristic, Diagnosis and Treatment, Critical Care Clinic 24 (2008); 657-722



40% of elderly who develop hospital delirium never return to their previous cognitive function\*

\* Based on studies from 3months to 5 years in length.



"To test the hypothesis that hospitalization in the elderly is associated with subsequent cognitive decline."

N = 1870 Followed for 12 years Evaluated every 3 years

Wilson, R.S. PhD, et al, *Cognitive Decline After Hospitalization in a Community Population of Older Persons,* Neurology, 2012 On Line Pub



Global Hospital Cognitive Decline:

- 1. Pre-hospital : 0.031 units per year
- 2. Post-hospital: 0.075 units per year

Overall decline increases by 240% Memory decline increase by 330% Executive function decreases by 170%

Worse if older, longer hospital stay, or more severe illness.





Predicted 10-year paths of change in composite measure of global cognition for typical participants hospitalized in year 4 (red line) or not hospitalized (black line) from a mixed-effects model adjusted for age, sex, race, and education.



Patients with dementia are 500% more likely to develop hospital induced delirium.

(66%-89% of demented patients)

Cole, Martin G, MD, FRCP, *Delirium in Elderly Patients,* 2004, J Ger Psychiatry, vol.12(1), pp.7-21





Delirium accelerates cognitive decline in Alzheimer disease T. G. Fong, R. N. Jones, P. Shi, E. R. Marcantonio, L. Yap, J. L. Rudolph, F. M. Yang, D. K. Kiely, S. K. Inouye Neurology May 2009, 72 (18) 1570-1575; DOI: 10.1212/WNL.0b013e3181a4129a



Forms of Delirium:

- Hyperactive rare
- Mixed
- Hypoactive most common



#### SCALING OUTCOME SEVERITY











status, adjusted by age and sex.

Melanie Dani, et al, Delirium, Frailty and Mortality, J Gerontol A Biol Sci Med Sci, 2018, Vol. 73, No. 3, 415–418





time to death (months)

Black solid line = no delirium; black dotted line = hyperactive Grey solid line = mixed; grey dotted line = hyperactive

SHAR

Hospice Care Bellelli, Giuseppe, et al; *Delirium subtypes and 1-year mortality among elderly patients discharged from a post-acute rehabilitation* facility; J Gerontol A Biol Sci Med Sci (2007)62 (10): 1182-1183



Hospice Care

SHARP.

*Figure 2.* Kaplan-Meier survival curve for 1year mortality post–intensive care unit (ICU) admission (ICU delirium days predictor). Log-rank chi-square statistic = 28.3; degrees of freedom = 3; P < 001.

Pisani, Kong, Kasl, et al; *Delirium and Mortality in Older ICU Patients*; American Journal of Respiratory and Critical Care Medicine, Vol 180, No 11 (2009), 1092-1097



Estimated survival curves of the time to death for five delirium resolution patterns. Estimated survival obtained from discrete time survival models fitted with general baseline hazard and a constant risk of death due to delirium. Parameters were estimated with logistic regression. Y = Delirium Present; N = Delirium Not Present. PAC = post-acute care.

Kiely, Dan, MPH, MA, et al; *Persistent Delirium Predicts Increased Mortality*; J Am Geriatr Soc. 2009 January; 57(1): 55–61.



Worst case scenario:

Hypoactive delirium which persists with no resolution of any symptoms





Pathophysiology:

- 1. Direct Brain Insults
  - a. Hypoxia
  - b. Hypoglycemia
  - c. Stoke (however, only 3% of stoke patients develop delirium)
  - d. Metabolic abnormalities
  - e. Drugs

MacLullich, Alasdair MJ, et al, *Unraveling the Pathophysiology of Delirium; A focus on the role of Aberrant Stress Responses,* Journal of Psychosomatic Research, 2008; 65: 229-38



#### Pathophysiology (cont.)

- 2. Aberrant stress response
  - a. Inflammation (baseline increase with age, infections)
    - i. Increase in pro-inflammatory cytokines and altered prostaglandins (IL1, IL2, IL6, TNF, Interferon)
  - b. Sickness behavior response
    - i. Limbic-hypothalamic-pituitary-adrenal response

MacLulllich, Alasdair MJ, et al, *Unraveling the Pathophysiology of Delirium; A focus on the role of Aberrant Stress Responses,* Journal of Psychosomatic Research, 2008; 65: 229-38



### **DSM IIIR Criteria:**

- 1. Acute Onset
- 2. Fluctuating Coarse
- 3. Inattention
- 4. Disorganized thinking
- 5. ALOC
- 6. Disorientation
- 7. Memory Impairment
- 8. Perceptual disturbance
- 9. Psychomotor agitation or retardation
- 10. Sleep/wake disturbance

DSM V - provided these changes cannot be better explained by another cause



#### Delirium: Inouye, SK, et al Ann Intern Med, 1990 113:94 Confusion Assessment Model: a standardized screening tool

1 and 2 are mandatory. Plus Either 3 or 4

- 1. Sudden onset mental status change. Fluctuating in nature.
- 2. Inattention
  - a. Difficulty focusing, keeping track of what is said or is easily distracted
- 3. Disorganized Thinking
  - a. Incoherent, rambling, unclear or illogical flow of ideas, unpredictable switching from subject to subject
- 4. Altered Level of Consciousness
  - a. Vigilant (Hyper-alert, overly sensitive to stimuli, easy to startle)
  - b. Lethargic (drowsy but arousable)
  - c. Stuporous (drowsy and difficult to arouse)
  - d. Comatose (unarousable)



**Pearl** Delirium is missed up to 68% of the time in hospitalized patients.

**Pearl:** delirium is frequently misdiagnoses as depression, dementia or "normal old age"

**Pearl:** present at discharge 32-60% of patients



Preventing Delirium is the most useful strategy for reducing its frequency and complications.

Once present, management of delirium has not been shown to improve long term mortality or institutionalization.

Pitkala, KH et al, *Multicomponent Geriatric Intervention for Elderly Patients with Delirium,* J Gernotol A Biol Sci Med Sci 2006; 61(2): 176-81







Most common causes:

- Meds 31%
- Infections 23%
- CHF 21%
- Metabolic abnormalities 19%

(Rockwood, Kenneth, J of Geront, 1993)



#### **Delirium is latrogenic**

- 1. Dehydration
- 2. Immobilization
- 3. Restraints: chemical or physical
- 4. Psychoactive medications
- 5. Indwelling catheters
- 6. Metabolic derangements
- 7. Malnutrition
- 8. Sleep deprivation
- 9. Complications of diagnostic or therapeutic procedures

(Inouye, 1992, 94, 96)(Lazarus 1991)(Creditor 1993)(Koponen 1989)



#### Reminder:

 $\bullet$ 

- Delirium is directly related to the number of medicines prescribed and the number of drug-drug interactions.
  - Anticholinergic medicines are the most concerning

Farrell, Kathleen DO, et al, "Misdiagnosing Delirium as Depression in Medically III Elderly Patients", Arch Intern Med 1995, 155



#### "Polypharmacy of the Elderly is an latrogenic Disease"

#### Daniel Hoefer, MD



## Physiologic Changes in the Elderly Geriatric Patient:

- 1. 40% decrease in hepatic blood flow
- 2. Decreased creatinine clearance
- 3. Decreased protein binding
- 4. Altered body composition/volumes of distribution
  - a. Increased fat to water ratio
- 5. Increased cognitive sensitivity
  - a. Increased blood brain barrier permeability
  - b. Loss of cholinergic neurons
- 6. Increased physiologic sensitivity
- 7. MMSE is lower in delirium



### Normal brain for age!

Beware!



#### **Delirium is associated with:**

- 1. Increased hospital medical complications\*
- 2. Increased ICU use
- 3. Increased Hospital and Skilled Care LOS
- 4. Increased Rates of institutionalization
- 5. Increased Readmissions
- 6. Increased Cost
- 7. Increased mortality
- 8. Permanent functional loss
- 9. Permanent cognitive decline from baseline

Cause and effect – eg. An iatrogenic infection from a foley may cause delirium. Delirium increases the risk of falls by 400%.



Levkoff, Sue E, et al, *Progression and Resolution of Delirium in Elderly Patients Hospitalized for Acute Care,* Am J Ger Psych, 1994: 2(3); 230-38

Does delirium go away? Harvard Delirium Project

325 = n

31.3% developed delirium96% had delirium symptoms at discharge

Only 20.8% of the 31.3% and 17.7% of the 96% showed complete resolution of symptoms at 3 and 6 mo.



McCusker, Jane MD, DrPH, et al, *The Coarse of Delirium in Older Medical Inpatients, a Prospective Study,* J Gen Intern Med 2003; 18: 696-704

Standardized face-to-face evaluations at 1, 2, 6 and 12 months

n = 135 34 prevalent delirium 91 incident delirium

Symptoms at Diagnosis

Dementia4.5No Dementia3.4

Symptoms at 12 mo

3.5 2.2





FIGURE 1. Mean number of delirium symptoms at baseline and follow-up in demented and non-demented patients.









Wacker, Priscilla, et al, *Post-Operative Delirium is Associated with Poor Cognitive Outcomes and Dementia*, Dement Geriatri Cogn Disord 2006; 21:221-27

#### Is delirium the precursor for dementia?

For this study – no pre-existing cognitive, hearing or visual deficit known Hip or Knee replacement

Fracture – 60% developed delirium Elective Repair – 24.6% developed delirium.

5 year prospective Study

Results: Patients who developed delirium were 1050% (10.5) times more likely to have developed dementia than those who did not.



Hospital induced delirium is associated with at 12.5 greater risk of dementia diagnosis in a 4.1 year window.

JAMA. 2010 Jul 28;304(4):443-51. doi: 10.1001/jama.2010.1013. Delirium in elderly patients and the risk of postdischarge mortality, institutionalization, and dementia: a meta-analysis. Witlox J<sup>1</sup>, Eurelings LS, de Jonghe JF, Kalisvaart KJ, Eikelenboom P, van Gool WA.



Study	N	Population	Study design	Follow-up period	Delirium measure	Cognitive outcome measure	Findings
Koponen and Riekkinen, 1989	70	Geriatric psychiatric hospitalized patients	Prospective	l year	Clinical Rating	D-Test <sup>2</sup>	Cognitive deterioration associated with delirium observed in 36% of patients at 1-year follow-up
Francis and Kapor, 1992	229	General hospitalized medical patients	Descriptive	2 years	Chart review, clinical interview, MMSE	Modified Telephone MMSE	Decline in MMSE scores in patients with delirium compared to controls
Rockwood, 1999	203	General hospitalized medical patients	Prospective	3 years	DRS, <sup>b</sup> MMSE, <sup>c</sup> Clinical Judgment, CIRS <sup>d</sup>	MMSE, Blessed Dementia Rating Scale, Gero-psychiatric Interview	Delirium was associated with increased dementia at follow-up
Dolan et al., 2000	682	Hip replacement surgery	Prospective	2 years	Chart review, proxy interviews using a modified version of the CAM	MMSE	Patients with delirium were more likely to have cognitive impairments at 2-year follow-up
Rahkonen et al., 2000	51	Community-dwelling elderly hospitalized for acute delirium	Prospective	2 years	DSM-Criteria	Neuropsychological battery	Patients had higher than expected dementia incidence rates over 2 years
McCusker et al., 2001	315	Medical patients	Prospective	l year	CAM <sup>e</sup>	MMSE	Patients with delirium had lower MMSE scores at 1-year follow-up compared to controls
Katz et al., 2001	102	Residential care patients	Prospective	l year	Clinical evaluations	MMSE, Buschke Selective Reminding Tests, Stroop Test, Verbal Vigilance	Patients who develop delirium within the context of a medical illness demonstrated greater cognitive decline
Rahkonen et al., 2001	199	Community-dwelling patients	Prospective	3 years	Surrogate interviews, clinical interviews, chart review	MMSE, ADL, <sup>e</sup> IADL, <sup>s</sup> Chart Review	Increased risk for new diagnosis of dementia among "oldest old"
Jackson et al., 2003	34	Medical ICU patients	Prospective	6 months	CAM-ICU <sup>k</sup>	Comprehensive neuropsychological battery	No significant association between delirium duration and cognitive outcomes

#### Table 1. Studies That Assess the Association Between Delirium and Long-Term Cognitive Outcomes

<sup>a</sup>D-Test = D-Test is the full title. elsewhere.
<sup>b</sup>DRS = Delirium Rating Scale.
<sup>c</sup>Mini-Mental State Exam.
<sup>d</sup>Cumulative Illness Rating Scale.
<sup>e</sup>CAM = Confusion Assessment Method.
<sup>f</sup>ADL = Activities of Daily Living.
<sup>g</sup>IADL = Instrumental Activities of Daily Living.
<sup>k</sup>CAM-ICU = Confusion Assessment for the Intensive Care Unit.



Bickel, Hurst et al, *High Risk of Cognitive and Functional Decline After Post-operative Delirium,* Dementia Geriatric Cognitive Disord 2008; 26: 26-31

> 3 year prospective study Pre-op and post-op evaluations at 8 and 38 months = or > 60 years Excluded if pre-existing dementia or pre-op delirium

N=200 41 developed post-operative delirium X =73.8 69.5 women

Fracture 28% Elective 72%



#### 167 survived to 38 mo

	Delirium	No delirium
Death	36.6%	10.8%
Severe Functional Impairment	52%	10.5%
Cognitive Impairment	53.8%	4.4%



Data doesn't lie!

# Hospital induced delirium is telling you the future of your patient.





