A Geriatrician's Approach to the Elderly with Cognitive Impairment

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Disclosure; Financial Conflicts of Interest

- I do not have any actual, potential or perceived financial conflict of interests with respect to this topic.
  - I believe my opinion and behavior (acts of commission or omission) can be influenced by contributions or gifts from the pharmaceutical industry.
  - I decline support (honoraria) and gifts (trips, meals, entertainment) from the pharmaceutical industry.

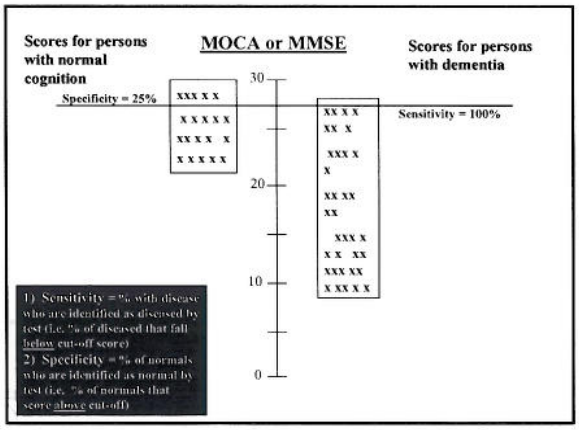
STEP 1: Screening

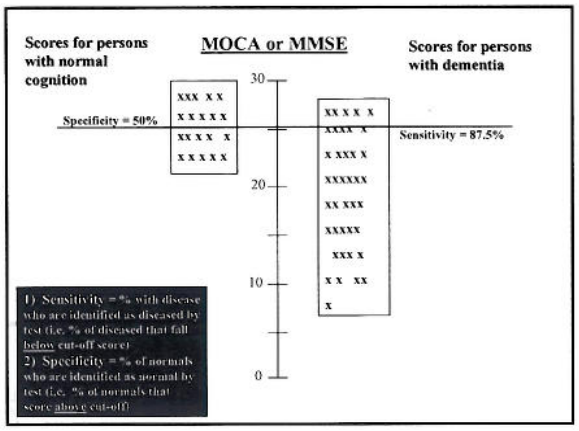
- In order to truly understand the results of the studies to be reviewed we need to understand:
  - The definitions of sensitivity and specificity
  - How sensitivity and specificity are affected by:
    - Cut-off values employed
    - Overlap of cognitive scores
    - Choice of test
  - The above principle are relevant to many other areas of medicine

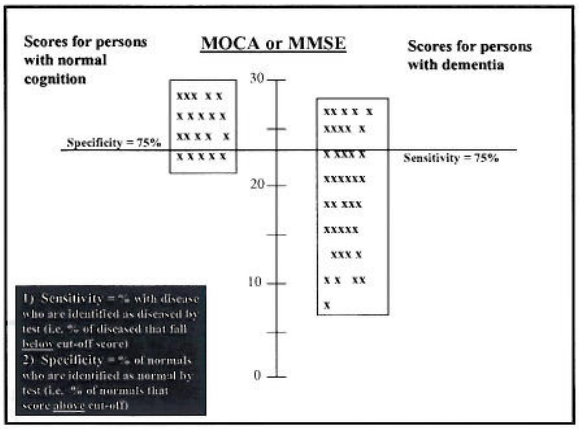
Definitions

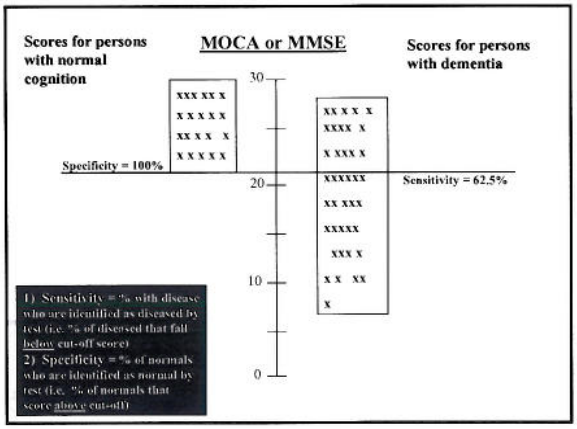
- Sensitivity
  - % of diseased persons identified as diseased (score below cut-off)
- Specificity
  - % of normal persons identified as normal (score above cut-off)

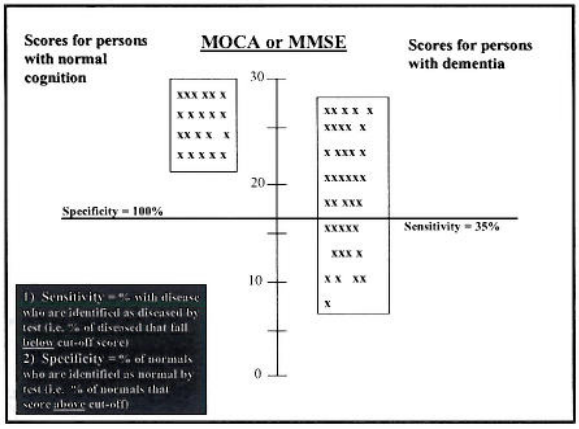
Sensitivity and specificity are affected by the cut-off score employed







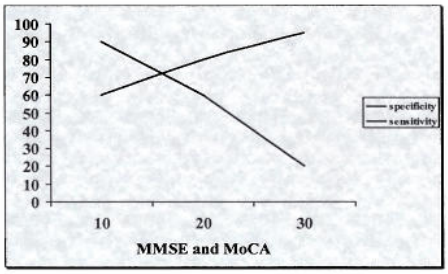




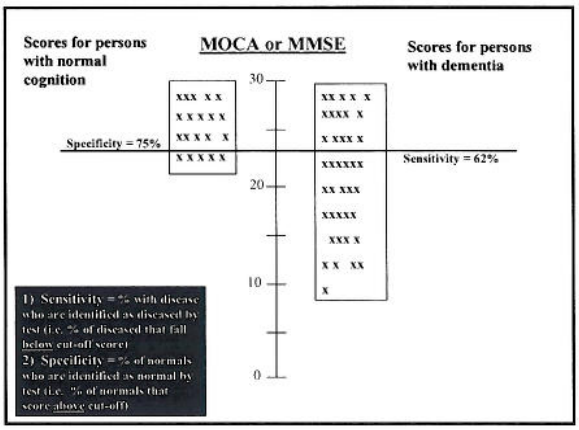
Take Home Message #1

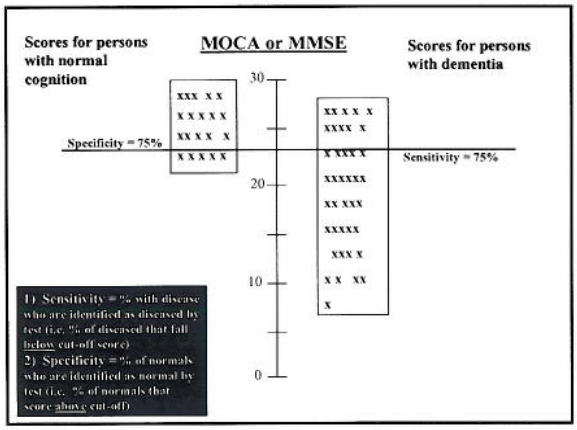
- **Sensitivity and Specificity for any given test are dependent on cut-off score studied**
- For scales where high scores are good and low scores are bad (MMSE, MOCA)
  - When cut-off is lowered
    - Sensitivity decreases
    - Specificity increases
  - When cut-off is raise
    - Sensitivity increases
    - Specificity decreases

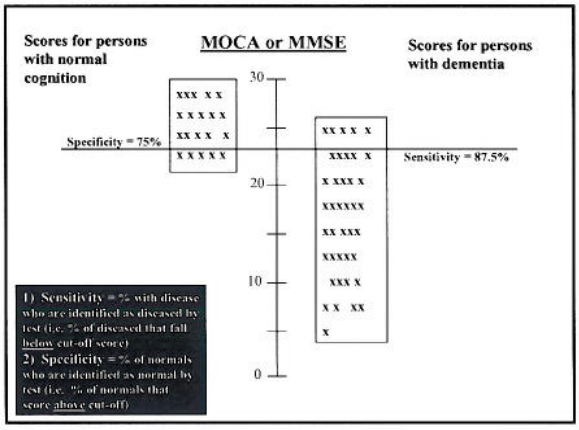
Sensitivity vs. Specificity

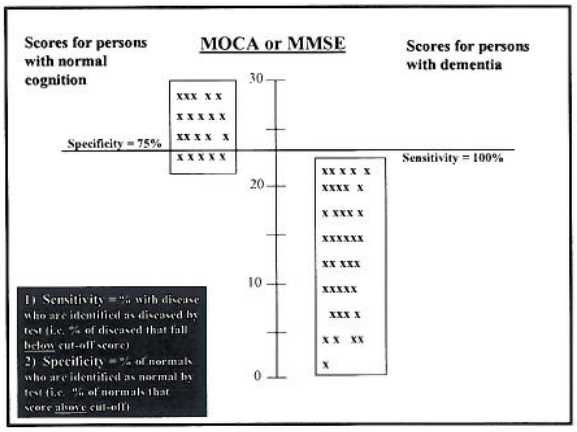


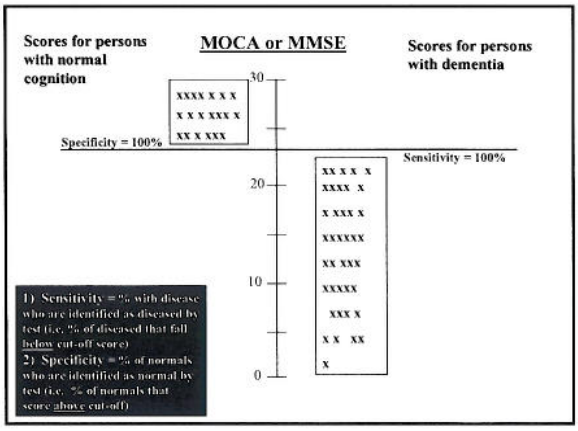
Sensitivity and specificity are affected by the population in which the test is being used
- Overlap of cognitive scores spectrum of disease)

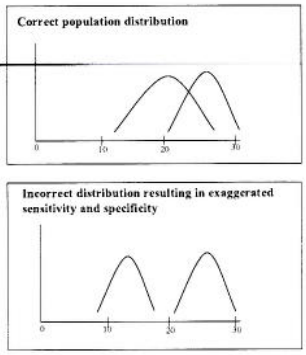












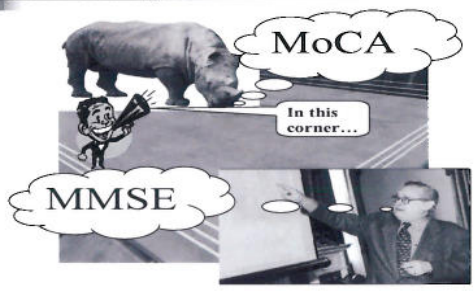
Take Home Message #2

- The sensitivity and specificity depend on the **amount of test score overlap** between normal and diseased
  - Sensitivity and specificity **depend on sample / population**
- Since the populations we take care of are clinically different from those in studies
  - The Sensitivity and Specificity of a test in clinical practice will likely not match that in studies (we cannot know if it does)
  - We can still compare the tests within 1 study

3 Take Home Messages

1. Sensitivity and Specificity for any given test are dependent on **cut-off score**
2. Sensitivity and Specificity depend on **sample / population**
   - Since the populations we take care of clinically are different from those in studies the Sensitivity and Specificity of a test in clinical practice will likely not match that in studies
3. Sensitivity and Specificity are dependent on the **test** employed

THE MAIN EVENT



MOCA validation process

- Developed based on clinical intuition of main author (ZN)
- Iterative modification based on 5 years of clinical use
- Tested on 46 MCI / AD with MMSE > 24 vs. 46 normal
  - 5 items replaced & weighting adjusted
- **We are now in the stage of clinical distribution and concurrent validation**
  - **Ongoing process (www.mocatest.org)**

3 MOCA Validation Studies in area of Dementia

1. **Nasreddine et al. The Montreal Cognitive Assessment, MOCA: A brief Screening Tool For Mild Cognitive Impairment. Journal of the American Geriatrics Society 2005; 53: 695-699**
   1. Limited analysis – did not vary cut-offs
2. Smith et al. The Montreal Cognitive Assessment: validity and Utility in a Memory Clinic Setting. The Canadian Journal of psychiatry 2007; 52; 329-332
   1. Unusual definition of abnormal
3. Luis et al. Cross validation of the Montreal Cognitive Assessment in community dwelling older adults residing in the Southern US. International Journal of Geriatric Psychiatry 2008
   1. Problem with spectrum of disease

Nasreddine et al - Design

- 94 MCI & 93 AD (90 MMSE ≥17),90 NC at 2 Quebec MDCs
  - Clinical diagnoses
- French and English MMSEs / MOCAs
  - Note; language-based (verbal) tests must be separately validated in each language
    - I am not certain this was done

Nasreddine et al - Results

SENS = % with MCI or dementia below cut-off

- MOCA (cut-off 25/26)
  - 90% SENS to detect MCI
  - 100% SENS to detect AD
- MMSE (cut-off 25/26)
  - 18% SENS to detect MCI
  - 78% SENS to detect AD
- MOCA seems to win on SENS (particularly for MCI) at **these** cut-off scores
  - Did not examine effect of varying cut-offs

Nasreddine et al - Results

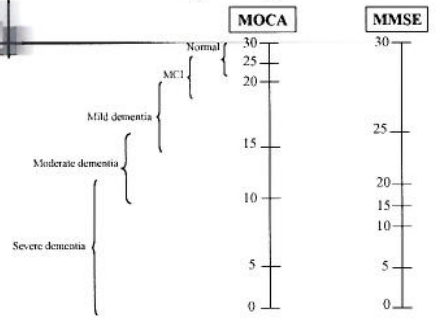
SPEC = % Normals ≥ 26 (correctly identified as normal

- MOCA (cut-off 25/26)
  - 87% SPEC to normals
    - Mislabelled 13% as impaired
- MMSE (cut-off 25/26)
  - 100% SPEC to normals
- MMSE seems to win on SPECS at **these** cut-off scores
  - Did not examine effect of varying cut-offs

MY SUMMARY of MOCA studies

- In all tests, when sensitivity increases, specificity decreases (the reverse is also true). This trade-off of sensitivity vs. specificity means that **the increased sensitivity of the MOCA comes with the expected price – lower specificity resulting in more normal people being labelled as impaired (higher false positives).**
- At a cut-off of 25/26 MOCA better at picking up AD than MMSE (with cut-off of 25/26)
  - This may not be true if MMSE cut-offs are altered
    Despite the limitations with these studies, I believe the MOCA better than MMSE at detecting MCI / early dementia
  - Likely a ceiling effect of the MMSE that increasing cut-off will probably not compensate for.

Tests may have differential sensitivity in different ranges of cognitive decline



Nasreddine et al – recommendations

- If patients have cognitive complaints and functional impairment then likely have a dementia
  - MMSE first
  - MOCA if MMSE ≥ 26 (MCI, Mild dementia)
- If patients have cognitive complaints but no functional impairment then likely normal or MCI
  - MOCA first

Step 2: Diagnosis

- Those who have screened positive for cognitive impairment then need a diagnostic evaluation to determine the cause(s) of the cognitive impairment

Diagnosis – my approach

- Is the patient cognitively changing?
  - May decide not to investigate stable longstanding cognitive deficits
- Determine if the patient is depressed or delirious.
  - If history suggests an underlying dementia would inform family of the possibility and link them to the Alzheimer Society so they can learn about dementia but would defer the final diagnosis for 2 – 3 months until the patient has recovered from the depression / delirium
- Use DSM criteria as a common language in assessing Dementia, delirium, depression

2a: Rule DEPRESSION in/out

- DSM criteria – M SIG E CAPS
  - Derived from a younger population without medical comorbidities
  - Given that physical illness can mimic many of these features (i.e. confounding variables), would employ the criteria more flexibly than suggested by DSM
    - Physical illness can interfere with sleep and interests, can lead to worries / negative ruminations, can decrease energy and appetite, can effect concentration (via delirium)
    - Look for persistent low mood or anhedonia > 2 weeks + other features not explained by physical illness

Persistent low mood or anhedonia > 2 weeks

- Differentiate from labile mood, resolving grief reaction
- Differentiate from apathy of dementia
  - Older person living alone who seems withdrawn
    - If enjoys family visits (can be 'drawn out') and eats well when food is presented then suspect dementia
    - If cannot be 'drawn out' (does not respond positively to family or food) then suspect depression

Poor SLEEP

- 3 phases: initiation, maintenance, terminal insomnia (early AM wakening)
- Look for a change in usual pattern
- Rule out **6 Ps**
  - **P**ain, **P**ND (orthopnea), **P**ee (BPH, UTI, diuretic), **P**artner (bed mate, roommate, pet), **P**harmaceuticals (diuretics or stimulants such as caffeine or cholinesterase inhibitors), **P**hysical environment (temperature, noise)
- Ask what is going through their minds when they cannot sleep (worries, regrets, negative ruminations)

Decreased Interests

- Determine whether patient has dropped interests due to physical reasons (pain, mobility, incontinence, acute illness ...), depression or dementia
- In depression patients "operate below their abilities"
- In dementia patients try to "operate above their abilities" and reluctantly withdraw due to social embarrassment

GUILT

- A dangerous word to use as some patients can become offended
- If the patient uses the word then explore further as they are showing a great deal of trust
- Use the word 'REGRETS' and judge if their regrets are reasonable given their experience or if they are exaggerated and represent negative ruminations

Decreased ENERGY

- Determine if the person can differentiate their physical strength from their mental / emotional energy
  - Some can if they do not have significant cognitive issues
- Determine if changes in energy occurred at a time not explained by physical illness

Decreased CONCENTRATION

- Measured by DLROW or serial 7s
- Noted when patient is not focussed on the assessment (drifting off)
- Think of concentration, attention and level of consciousness as a spectrum
  - All are normal in pure dementia
  - May be impaired in depression or delirium
  - Level of consciousness (head bobbing sign) indicates delirium

Change in APPETITE

- Rarely encounter hyperphagic patients
  - tend to be those with longstanding waxing and waning depression. Call their psychiatrist if they are becoming hyperphagic
- More commonly see loss of appetite. Ask:
  - Have you lost your appetite?
  - Have you lost weight?
  - Do you still enjoy food?
  - Do you desire food and look forward to meals?
- Patients can lose their appetite when they are ill or on appetite suppressing drugs (narcotics, Cholinesterase inhibitors, sulphas and other antibiotics, digoxin ...)

Physical Complaints

- Depression commonly presents with somatic complaints in older patients
- If patient has multiple complaints that constantly shift over time, think of depression.
  - Often encounter unexplained GI symptoms or pain vs. magnification of symptoms (objective vs. subjective mismatch)
  - Negotiation strategy - some patients may take antidepressants only if they believe the meds will help with pain control

Psychomotor change

- Positive vs. negative symptoms
  - Agitated vs. withdrawn
  - If agitated would ensure you are not dealing with a delirium
  - Would tend to get psychiatry involved in agitated depression

SUICIDAL ideation

- Passive suicidal ideation
  - Do you ever wish you would not wake up in the morning?
  - Do you ever wish you were dead?
- Active suicidal ideation
  - Patient has a plan they are willing to act on
  - 'Form' patient and send to a psychiatric facility (any hospital with a psychiatric ward) for further evaluation
  - Call ER and give story to psychiatrist
  - Ask for psychiatrist's name so you can note the phone discussion in chart

2b: Rule Delirium in/out

	Delirium	Dementia
Onset	Abrupt	Gradual
Course	Short	Long
Fluctuation	Present	Absent
Hallucinations	Present	Absent
Attention	Impaired	Normal
LOC	Altered	Normal
Psychomotor	Altered	Normal

It is common for Delirium to be superimposed on Dementia!

This table oversimplifies so let us look at exceptions to the rules as well as the most reliable signs of Delirium

Onset & Duration (exceptions)

- Delirium
  - May have prolonged low grade delirium with chronic ETOH, BDZ, Narcotic, Anticholinergic (e.g. TCA, Ditropan) use
- Dementia
  - Can have rapid onset with strokes or CJD (see Health Canada CJD website)

Fluctuation

- Delirium
  - **New onset unpredictable fluctuation** (hour by hour not day by day)
- Depression
  - Predictable diurnal variation (worse in morning)
- Dementia
  - Predictable diurnal variation (worse in afternoon or evening)

Hallucinations

- Delirium
  - Especially if family describe **new onset hallucinations**
- Dementia / Psychiatric Disorders
  - Long-standing hallucinations
  - E.g. Lewy Body disease, Psychotic Depression, Bipolar disease

Attention, Concentration, LOC

- Delirium
  - Attention, Concentration and **altered Level of Consciousness (i.e. drowsy, somnolent)**
- Depression
  - Can alter Attention, Concentration but not LOC
- Dementia
  - Normal Attention, Concentration, LOC

Patterns of Psychomotor Change in delirium

- **Hyperactive** ("wild man!"); 25%
- **Hypoactive** ("out of it!", "snowed", "pleasantly confused"); 50%
- **Mixed delirium** (features of both), with reversal of normal day-night cycle ("sundowning"); 25%

Confusion Assessment Method (CAM)

1. History of acute onset of change in patient's normal mental status & fluctuating course?

AND

2. Lack of attention?

Sensitivity: 94-100%
Specificity: 90-95%
Kappa: 0.81

AND EITHER

3. Disorganized thinking?
4. Altered Level of Consciousness?

Inouye SK: Ann Intern Med 1990;113(12):941-8
Arch Intern Med. 1995; 155:301

Treatment / Management

Once you identify Delirium, now what?

- Identify the acute medical problem(s) that could be either triggering the delirium, or prolonging it!
- Clarify pre-morbid functional status and sequence of events
- Identify all predisposing and precipitating factors, and consider the differential

Causes of Delirium?

mnemonic

I WATCH DEATH

I WATCH DEATH

- I Infection: Most common are pneumonias & UTI in elderly, but sepsis, cellulitis, SBE and meningitis can also occur

I WATCH DEATH

- I Infection
- W Withdrawal: benzodiazapines, ETOH, typical neuroleptics, anticholinergics

I WATCH DEATH

- I Infection
- W Withdrawal
- A Acute metabolic: electrolytes, renal failure, acid-base disorders, abnormal glycemic control, pancreatitis ...

I WATCH DEATH

- I Infection
- W Withdrawal
- A Acute metabolic
- T Trauma: head injury (SDH, SAH), pain, vertebral or hip fracture, concealed bleed, urinary retention, fecal impaction

I WATCH DEATH

- I Infection
- W Withdrawal
- A Acute metabolic
- T Trauma
- C CNS pathology: tumor, AVM, encephalitis, meningitis, abscess

I WATCH DEATH

- I Infection
- W Withdrawal
- A Acute metabolic
- T Trauma
- C CNS pathology
- H Hypoxia (or increased CO_2) from COPD exacerbation, CHF

I WATCH DEATH

- I Infection
- W Withdrawal
- A Acute metabolic
- T Trauma
- C CNS pathology
- H Hypoxia
- D Deficiencies: B-12, folate, protein, calories, water

I WATCH DEATH

- I Infection
- W Withdrawal
- A Acute metabolic
- T Trauma
- C CNS pathology
- H Hypoxia
- D Deficiencies
- E Endocrine
  thyroid, cortisol, cancer cytokines

I WATCH DEATH

- I Infection
- W Withdrawal
- A Acute metabolic
- T Trauma
- C CNS pathology
- H Hypoxia
- D Deficiencies
- E Endocrine
- A Acute vascular/MI : stroke, intracerebral bleed

I WATCH DEATH

- 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
  Really anything; anti-cholinergics (TCA, Ditropan), benzos (especially long-acting), narcotics, seizure meds and other psychotropics are common culprits

I WATCH DEATH

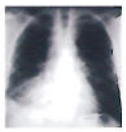
- I Infection
- W Withdrawal
- A Acute metabolic
- T Trauma
- C CNS pathology
- H Hypoxia
- D Deficiencies
- E Endocrine
- A Acute vascular/MI
- T Toxins-drugs:
- H Heavy metals
  - lead, manganese, bismuth, mercury, solvents, arsenic, thallium

How to find out more? One of the most useful and underused medical tools:

Physical Exam

- **Vitals**: normal range of BP, HR (**unexplained sinus tachycardia**), Spo2, Temperature (**some older patients do not become febrile with infections**)?
- **Good physical exam:** particular emphasis on cardiac, pulmonary and neurologic systems
- **Hydration status**
- **Also rule out**
  - fecal impaction (DRE)
  - urinary retention (bladder U/S, in-and-out catheter)
  - Infected decubitus ulcer

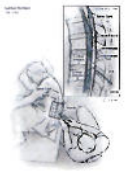
Delirium workup: Lab testing



- Basic labs most helpful!
  - CBC, electrolytes, BUN/Cr, glucose
  - TSH, B-12, LFTs Calcium, & albumen
- Infection workup (Urinalysis, CXR) +/- blood cultures

Other Investigations

- selected additional testing; drug levels, toxic screen, ABG
- EKG
- CT Head if focal signs
- ? EEG (if suspect seizure)
- ? role for LP (do last, and only if history suggests)



Dementia vs. Mild Cognitive Impairment (MCI)

- Avoid making a definitive diagnosis of dementia if the patient has a significant depression or delirium that could be mimicking a dementia.
- Avoid cholinesterase inhibitors while patient is recovering from a delirium
- Advise families that the history suggests an underlying dementia and link them to the Alzheimer Society so they can learn about the signs of dementia and can observe for these while they are awaiting 2 – 3 month follow-up for a dementia assessment

3. Dementia

- Once again employ the DSM criteria – look for a deficit in each of the following categories (**5 As** + function + progression) base on history, physical examination, cognitive testing:
  1. **A**mnesia
  2. **A**phasia, **A**praxia, **A**gnosia, **A**nd Executive dysfunction
  3. Progressive
  4. Impacts on social and / or occupational functioning

Amnesia

- If family look at you quizzically when you are asking questions about memory ("mom remembers things from 20 years ago so I do not see why you are asking about memory"), stop and inform them that you interested in short-term memory for things that happened an hour or day ago. Inform them that with memory problems that progress, the initial problem is "putting new memories in" (encoding – more true of Alzheimer's) while old memories are stable and retained.

Amnesia

- Look for changes from baseline
  - Repeating questions or stories
  - Losing items (keys, purse ...)
  - Forgetting details of important events
  - Trouble recalling names
  - Mixing up relatives and friends
  - Increased use of compensatory strategies (lists, calendars, memory cues)

Aphasia (expressive)

- Ask if patient has word finding problems ('words on the tip of their tongue')
  - Word searching
  - Mixing up languages
  - Losing last language learned first
  - Patterns
    - Sudden loss then stable or improving suggests stroke, bleed
    - Progressive word –finding problems (more frequent and more severe / noticeable) suggests Alzheimer's
    - Severe and more pronounced than memory problems suggests stroke, bleed, Semantic Dementia, Primary Progressive Aphasia
- Later develop reading and writing difficulty

Apraxia

- Difficulty executing a motor task despite intact motor and sensory function
  - May notice during dressing post examination
  - On exam can ask patient to show how to:
    - Comb hair
    - Brush teeth
    - Cut paper with a scissor
  - Sometimes difficult to differentiate from executive dysfunction (use of stove, TV, remote...)

Agnosia

- Difficulty identifying objects despite an intact sensory function
  - Difficulty recognizing family members or close friends
    - Differentiate this from difficulty recalling names. In agnosias they cannot recall the person's role in their life.

And Executive Dysfunction

- Instrumental Activities of daily Living (IADLs) – change from baseline due to cognition
  - S Shopping
  - H Housekeeping / Hobbies
  - A Accounting / finances
  - F Food preparation
  - T Telephone / Tool use
    Transportation (Driving)

And Executive Dysfunction

- ADLs (lose after IADLs)
  - D Dressing
  - E Eating
  - A Ambulation
  - T Transfers
  - H Hygiene

Psychotic Symptoms (delusions, hallucinations)

- First rule out delirium.
- If due to the dementia then only treat if extremely upsetting to patient, leading to significant social disruption
- Do not treat for comfort of caregivers – teach them how to cope.
- If forced to use antipsychotics keep in mind that symptoms can wax and wane so should periodically try to wean off (every 6 months)
  - Warn family (and patient if can comprehend) of the low risk of stroke, MI, death and DOCUMENT the discussions / informed consent in chart (with date and names of participants)

Delusions

- > 50% of persons with AD experience simplistic persecutory delusions
  - People stealing from them (may be reinforced by hiding money and not recalling where hid money)
  - Spousal infidelity (may be reinforced by visits from CCAC, Psychogeriatrics)
- If delusions are complex then consider a psychiatric disorder (bipolar disease, psychotic depression ..)

Hallucinations

- Decide if these are true hallucinations – is anyone ever present when they occur?
- DDX
  - Charles bonnet hallucinations due to decreased vision or hearing
  - Misperceptions (see or hear things at night)
- New onset
  - Consider delirium
- Long-standing
  - Consider psychiatric disorder (bipolar disease, psychotic depression ..) or Lewy Body Disease
    - Avoid neuroleptics in Lewy Body Disease as can precipitate significant parkinsonism with falls & trauma

Working through the DDX of dementia

Common presenting features

Alzheimer disease

- Progressive short-term memory loss
  - Encoding problem so cues do not help
- MAY present with progressively more frequent / noticeable word-finding changes. When present this is highly suggestive of AD
- Limited insight – not fully aware of presence of memory loss and impact on function

Vascular dementia

- 3 levels of evidence
  - Neuroimaging performed in the course of the dementia demonstrating cerebrovascular disease (more than mild microangiopathic ischemia) significant enough and in locations to account for deficits (i.e. not pure motor areas)
  - Established arterial disease (stroke, carotid stenosis, CAD, RAS, PVD) – consider the arterial tree as a single organ. If these are present will treat vascular risk factors
  - Vascular risk factors.

Vascular dementia

- Presentation not suggestive of AD
  - Good insight
  - Early apraxia / agnosia with ischemia in relevant regions
  - Retrieval rather than encoding problem – memory loss responds to cues
  - Step-wise decline?
    - Beware of False Negatives – many cannot recall stepwise decline
    - Beware of False Positives – recurrent deliriums with incomplete recovery can give AD a saw toothed pattern that looks like a step-wise decline. **Search for neurological changes suggestive of stroke that occurred during period of decline**
- Do not use the term 'vascular dementia' with patients – they do not know what this means. Call it '**Stroke dementia**'.

Mixed dementia (AD + vascular)

- **Moving ratio concept**.
  - When you first see patient they may be 99% vascular and 1% AD (so look like pure vascular)
  - A few years later the ratio will shift and they will be < 50% vascular and > 50% AD. This does not mean you were wrong when you first saw them. The AD component required more time to 'declare itself' so follow your vascular dementia patients carefully.

Lewy Body dementia

- McKeith et al. neurology 1996; 47: 1113-1124
  - Dementia occurring at the same time as mild parkinsonian features
  - Long-standing Hallucinations (visual, auditory)
  - Long-standing Fluctuation (cognition, attention, alertness)
- Supportive features
  - Vivid nightmares due to changes in REM sleep (lack of muscle paralysis – kick, punch and run in sleep)
  - Neuroleptic sensitivity
  - Cognitive profile (memory responds to cuing, early executive dysfunction, early visuospatial dysfunction – driving skills)

Parkinson's Dementia

- Common in patients who have passed through the 5 – 10 year 'honeymoon period' (motor symptoms only) of Parkinson's disease
- Similar cognitive profile to Lewy body Disease
  - memory responds to cuing, early executive dysfunction, early visuospatial dysfunction (driving skills)
- Emre et al. Clinical diagnostic criteria for dementia associated with Parkinson's disease.
  - Movement Disorders 2007; 22(12): 1689-1707

Frontotemporal Lobar Degeneration (FTLD)

- Behavioural type
  - Classic Frontal Lobe dementia with early loss of executive function (relevant to driving)
    - Earlier onset
    - Presenting symptoms can be positive (impulsiveness, anger control problems) or negative (withdrawal – looks depressed). More commonly referred to Psychiatry.
    - Test well (MMSE 30/30) but function more poorly than screens (that do not test executive function well) would suggest
      - Neuropsychology helpful in diagnosis

Frontotemporal Lobar Degeneration

- Language types
  - Semantic dementia
  - PPA: Primary (non-fluent) Progressive Aphasia
- Severe early expressive aphasia with no obvious cause on neuroimaging
  - Test poorly (MMSE 5/30 - because testing is language based) but function much better than test results would predict
    - Neuropsychology and Speech-language Pathology helpful in diagnosis

Normal Pressure Hydrocephalous (NPH)

- AD is a cortical dementia
- NPH can look more like subcortical dementias (e.g. subcortical vascular, LBD, Parkinson's dementia ...)
- **3Bs** – **B**rain (cognition), **B**alance (falls), **B**ladder (incontinence)
- Diagnosis with CSF Flow study or LP drain (Do not accept simple LP with fluid withdrawal as prone to False Negative results)

THE

END