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# Current Knowledge in Geriatric Syndromes

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Among many characteristics of geriatric medicine that differentiate it from other medical specialties is the prominence of certain clinical problems. Older patients, with or without acute illnesses, commonly present themselves with functional disability - *i*mmobility, *i*nstability (falls), *i*ncontinence and *i*ntellectual impairment. These are the Giants of Geriatrics or geriatric syndromes. Not one of these syndromes is caused by old age. The giants are the result of pathology. These conditions must be very carefully sought and, as far as possible, remedied. Their effects can be ameliorated thus restoring functional capacity to the patient and restoring independence. This article reviews the current knowledge in geriatric syndromes, focusing on intellectual or cognitive impairment (dementia and delirium), falls, and urinary incontinence.

## Dementia

Dementia is one of the most common causes of institutionalization, morbidity, and mortality among the elderly. Dementia is typically preceded by a state of mild cognitive impairment which may last for several years. The essential feature of dementia is a progressive decline of multiple cognitive capacities, such as short- and long-term memory, abstract thinking, judgment, higher cortical functions or personality. The disturbance is severe enough to interfere significantly with work or social activities and later with daily activities.[1]

Dementia is a clinical diagnosis whose evaluation involves assessment of the presenting problem, history about the patient that is provided by an informant (someone who knows the patient well, usually a family member), complete physical and neurological examination and evaluation of activities (or functional status), behavioral, and cognitive status. If dementia is diagnosed, the cause of the dementia is identified, and potentially reversible contributing factors are sought. There are several clearly reversible causes of dementia, for examples, any psychoactive agents or drugs with anticholinergic activity, depression, hypothyroidism, and structural abnormalities (e.g., normal pressure hydrocephalus, chronic subdural hematoma). Major syndromes with progressive dementia include Alzheimer's disease (AD), vascular dementia (VaD), and dementia with Lewy bodies (DLB).[1]

Cholinesterase inhibitors (ChEIs), such as donepezil, rivastigmine and galantamine, have been recommended for the treatment of mild-to-moderate AD. Modest global and cognitive improvement in patients who had mild to moderate AD were demonstrated for the ChEIs in several large, double-blind, randomized, placebo-controlled clinical trials.[1] Also, the efficacy of ChEIs has been reported in DLB, and VaD alone or coexisting with AD. The challenge for ChEI therapy rests on whether it is cost effective. The AD2000 trial, published in 2004, showed no benefit of donepezil versus placebo for institutionalization, progression of disability, costs for health and social services, or caregiver measures of distress. Although the study confirmed that donepezil is well tolerated and associated with small improvements in cognition and activities of daily living. These benefits did not reduce costs of caring for study patients with AD.[2]

Memantine, which may decrease neuronal toxicity resulting from excitatory neurotransmitter glutamate at NMDA receptor, was approved by the USFDA in 2003 for the symptomatic treatment of moderate-to-severe AD[1]. For moderately advanced AD, memantine appears to be beneficial alone or in combination of donepezil. It is unknown whether memantine therapy is cost effective.

Since 2001, the American Academy of Neurology (AAN) recommended vitamin E (1000 IU twice daily) to slow progression of AD based on a large double-blind, randomized, placebo-controlled trial. The challenge for this recommendation is the possibility of an unanticipated serious adverse event. An increased risk for all-cause mortality was demonstrated with high dose vitamin E supplementation in a meta-analysis of Cochrane Clinical Trials Database, published in 2005.[3] Based on current data, it would be prudent to avoid very high dose vitamin E (e.g., >400 IU a day) in the management of AD.

There is insufficient evidence to support the use of other antioxidants, anti-inflammatory, estrogen, or other putative disease-modifying agents specifically to treat AD because of the risk of significant side effects in the absence of demonstrated benefits.

Antipsychotics are commonly used to treat agitation, aggression, or psychosis in patients with dementia. Atypical agents (e.g., risperidone, olanzepine, and quetiapine) may be better tolerated compared with traditional agents (e.g., haloperidol). Systemic reviews of a few randomized trials of atypical antipsychotic drugs for neuropsychiatric symptoms of dementia find modest efficacy and frequent adverse effects, including somnolence, parkinsonism, and gait disturbances. Recent evidence suggests that atypical antipsychotic drug use may be linked to increased mortality. A public health advisory was issued by the USFDA on April 11, 2005, for more deaths associated with use

of atypical antipsychotic drugs in older individuals with dementia[4].

Preliminary, observational evidence suggests that risk of AD can be decreased by continuing to do challenging mental activities (e.g., learning new skills, doing crossword puzzles) and social activities well into old age and by exercising, controlling hypertension, lowering cholesterol levels, following a diet rich in omega-3 fatty acids and low in saturated fats, and drinking alcohol in modest amounts.

## Mild cognitive impairment (MCI)

Mild cognitive impairment is an impairment in one or more cognitive domains (typically memory) that is greater than would be expected for age or educational level, but that is insufficient to interfere with social and occupational functioning, as is required for a dementia syndrome.[5-7] Up to 50% of patients with mild cognitive impairment that affects memory develop dementia within 3 years. Risk factors that predict the progression of MCI to dementia include the presence of cognitive impairment, extrapyramidal signs, vascular risk factors, MRI-based hippocampal atrophy, or APOE genotyping.[7] No drug is so far approved for the treatment of MCI. In a recent randomized controlled trial using donepezil, no treatment benefit was found.[8] Another 3-year study that compared donepezil and vitamin E with placebo for the rate of progression of MCI to dementia showed no benefit of vitamin E.[9] The participants using donepezil showed a slower rate of progression during the first year of treatment, but this effect disappeared by the second year.

## Delirium

Delirium is a clinical syndrome characterized by an acute, fluctuating change in mental status, with inattention and altered levels of consciousness It is very common among the elderly, especially those who are hospitalized.[10] A recent systematic review confirmed that hospitalized patients with delirium have higher risk of medical complications (including death), longer hospitalization, higher hospital costs, and increased risk of functional decline and death after discharge.

The hallmark of delirium is acute cognitive dysfunction with impaired attentiveness, and altered levels of consciousness which develops suddenly or over a short time (usually hours to days). In some frail elderly patients, delirium precedes the appearance of another illness and is the only early manifestation of that illness. Delirium can be classified on the basis of psychomotor activity (i.e., level of arousal) to hyperactive, hypoactive, and mixed delirium.[10] The hypoactive form of delirium is more common among older patients and often goes unrecognized.

Predisposing risk factors of delirium include advanced old age, underlying dementia, functional impairment, and medical comorbidity and its treatments. Factors that can precipitate delirium are drugs (especially psychoactive and anticholinergic agents), electrolyte and metabolic abnormalities, and infection.

Management of delirium includes treatment of underlying disorders, removal of contributing factors, behavioral control, avoidance of iatrogenic complications, and support of the patient and family. Psychoactive drug treatment may be required to treat severe agitation that would threaten the patients' own safety or would result in the interruption of essential therapy. For most patients, low doses of high-potency antipsychotics (e.g., haloperidol) are preferred.[10] Atypical neuroleptics have recently been suggested to treat the agitation of hyperactive delirium. However, there is, as yet, no convincing evidence of their efficacy, with the exception of some lower-level evidence of risperidone.

Given the negative prognostic implications of delirium, the attention is shifting from treatment to prevention. Successful preventive strategies include multicomponent approaches to reduce risk factors. In 1999, The Yale Delirium Prevention Trial demonstrated the effectiveness of intervention protocols to reduce delirium in medical older patients, targeted toward six risk factors: orientation and therapeutic activities for cognitive impairment, early mobilization, nonpharmacologic approaches to minimize the use of psychoactive drugs, interventions to prevent sleep deprivation, equipments for vision and hearing impairment, and intervention for volume depletion.[11] In 2001, a randomized clinical trial involving patients who had had hip fracture also demonstrated the effectiveness of proactive geriatric consultation to reduce the incidence postoperative delirium.[12] In a recent controlled study involving elderly hip-fracture patients, the incidence of postoperative delirium was not reduced by prophylactic administration of haloperidol, although duration and severity of delirium were decreased.[13]

## Falls

Falls are a common and complex geriatric syndrome that cause considerable mortality, morbidity, and reduced functioning. However, physicians are often unaware of falls because a routine history and physical examination typically does not include a specific evaluation for falls and because many people who fall do not have an obvious injury. For these reasons, elderly patients should be asked about falls at least once per year.[14]

A fall is usually caused by a complex interaction among intrinsic factors (age-related decline in function, disorders, and adverse drug effects), extrinsic factors (environmental hazards), and situational factors (related to the activity being done). Age-related changes can impair systems involved in maintaining stability (e.g., visual acuity, proprioceptive sensation, and vestibular system). Chronic and acute disorders and use of drugs are major risk factors for falls. The risk of falls increases with the number of drugs taken. Psychoactive drugs are the drugs most commonly reported as increasing the risk of falls and fall-related injuries. Environmental factors can increase the risk of falls, or by interacting with intrinsic factors. Certain activities may increase the risk of falls and fall-related injuries.

The focus is on preventing or reducing the number of future falls and fall-related injuries and complications, while maintaining as much of patients' function and independence as possible. In general, fall prevention interventions can be categorized into multidimensional fall risk assessment coupled with risk reduction, exercise programs of various types, and environment assessment and modification.[14] The objectives of the multidimensional fall risk assessment are to identify risk factors for future falls and to implement appropriate interventions to reduce fall risk. Comprehensive multidimensional fall risk assessment is most appropriate for high-risk individuals (e.g., those who have just fallen or have multiple risk factors for falls). Clinical guidelines recommended that a comprehensive multidimensional fall risk assessment should include the following: a history of fall circumstances and medical problems; review of medications; mobility assessment; an examination of vision, gait and balance, and lower

extremity joint function; a basic neurological examination, including muscle strength and mental status; and assessment of cardiovascular status. Other components of fall risk assessment include functional performance tests and an environmental assessment.[14] Focused multidimensional fall risk assessment is used to screen older populations to identify risk for falls in independent community-living elderly populations. Typically, this model includes simple performance-based tests of gait, balance, mobility, or strength, such as the Timed Get-Up-and-Go Test.[14]

A meta-analysis of randomized controlled trials of fall prevention interventions, published in 2004, indicated that the most effective strategy used individualized multidimentional risk assessment combined with interventions that were directed toward reducing these risks.[15] The next most effective single intervention in this meta-analysis was exercise that was intended to improve ba-lance, strength, flexibility, or endurance. Other recent randomized trials proved to be effective in reducing fall rates have involved multifactorial intervention programs, which is consistent with the concept that falls usually are the result of interactions between multiple intrinsic and extrinsic risk factors. The most effective interventions generally have included risk assessment; tailored exercise or physical therapy to improve gait, balance, and strength; medication management; and other elements, such as education about fall risk factors, referrals to healthcare providers for treatment of chronic conditions that may contribute to fall risk, and having vision assessed and corrected.

## Urinary incontinence

Eight to 34% of community-dwelling elderly persons suffer from urinary incontinence; rates are higher in women than in men, and urinary incontinence affects > 50% of elderly patients in hospitals and in nursing homes. Yet, urinary incontinence is abnormal regardless of age, mobility, mental status, or frailty. Moreover, incontinence often causes the affected person to feel embarrassed, isolated, and depressed. Incontinence remains a neglected problem despite the fact that it is highly treatable and often curable.

Incontinence can be classified to those that are transient (reversible) and those that reflect intrinsic urinary tract dysfunction (resulting in established urinary incontinence). The reversible causes can be recalled using the mnemonic DIAPPERS: Delirium, Infection (symptomatic urinary tract infection), Atrophic urethritis and vaginitis, Pharmaceuticals (alcohol and drug use), Psychiatric disorders (especially depression), Excessive urine output (e.g., from hyperglycemia), Restricted mobility, and Stool impaction. Untreated transient incontinence may become persistent but should not be considered established merely because it is long-standing. If leakage persists after transient causes of incontinence have been addressed, established incontinence due to lower urinary tract causes must be considered. Detrusor over-activity or overactive bladder (OAB) is the leading urinary tract cause of incontinence in elderly persons regardless of their mental status.[16] Stress incontinence is the second most common cause of urinary incontinence in elderly women. Outlet obstruction is the second most common cause of incontinence in men, but most men with obstruction are not incontinent. Detrusor under-activity sufficient to cause urinary retention and overflow incontinence occurs in about 5% of incontinent persons. Functional problems in elderly persons (e.g., environment, cognitive function, mobility, manual dexterity, medical factors, motivation) are often superimposed on lower urinary tract dysfunction. These factors may contribute to established incontinence but rarely cause it.

Non-pharmacologic management should be the first line of therapy in all cases of urinary incontinence. In the subset of patients who fail to respond, the addition of pharmacologic agents is a viable option. The cornerstone of treatment of OAB is behavior therapy, such as bladder retraining, and prompted voiding regimens.[16] Pelvic muscle exercises (e.g., Kegel's exercises) are often effective for stress incontinence. Detrusor under-activity is managed by reducing residual volume, eliminating potential contributors to impaired detrusor function (e.g., fecal impaction, drug adverse effects).

Oxybutynin and tolterodine are the two most commonly used antimuscarinic agents in the treatment of OAB.[16] Although oxybutynin has been shown to reduce urinary incontinence effectively, there is high incidence of anticholinergic side effects. The efficacy of tolterodine is comparable to oxybutynin, but the incidence of anticholinergic side effects is much lower. Available data favor use of the extended-release formulations of tolterodine over the immediate release because of greater efficacy, higher tolerability, and higher adherence rates. Outlet obstruction in men is treated with oral -adrenergic blockers, which relieve symptoms and may improve postvoiding residual volume, outlet resistance, and urinary flow rate. Patients who fail to respond to noninvasive treatment or those in whom surgery may be appropriate should be referred to urologists for evaluation and further management.[16]

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