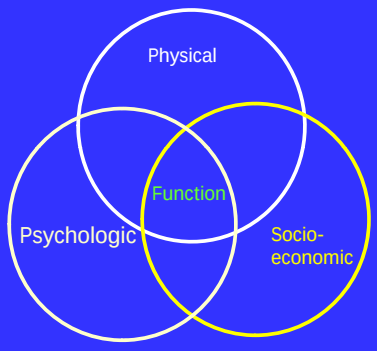
Common Conditions in the Elderly Adult

Vanessa Sepúlveda Rivera, MD FACP
Associate Professor
Internal Medicine and Geriatrics
UPR, School of Medicine

Outline

- Comprehensive Geriatrics Assesment
- Normal Aging
- Geriatrics I"s
- Dementia
- Falls
- Questions

Comprehensive Geriatric Evaluation



Practicing Primary Care Geriatrics

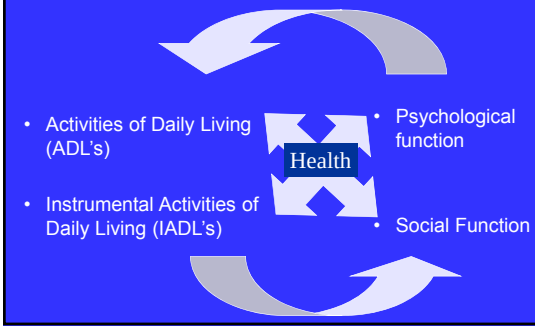
- Geriatrics emphasizes assessment of:
  - Syndromes (confusion,falls, dizziness, dysmobility, incontinence..) which are more common in older people
  - Maintains a rehabilitative focus
  - Concern for iatrogenesis
  - Underlying multiple problems with multiple causes for each problem

Functional status change

- **The probability of institutionalization or death increases as the functional state worsens and is higher for those who are 85 years old at all initial functional states.**

N Engl J Med 2003;349:1048-55.

Functional Assessment



- Activities of Daily Living (ADL's)
- Instrumental Activities of Daily Living (IADL's)
- Psychological function
- Social Function

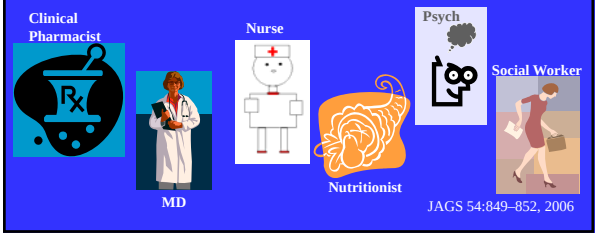
Activities of daily living

- **ADL's**
  - Eating
  - Dressing
  - Bathing
  - Transferring
  - Toileting
  - Continence
- **IADL's**
  - Prepare meals
  - Housework
  - Laundry
  - Medications
  - Transportation
  - Shopping
  - Manage money
  - Telephone

1- Kat's Activities of Daily Living, Geriatrics at Your Fingertips
2- Lawton's Instrumental Activities of Daily Living, Geriatrics at Your Fingertips

Interdisciplinary team

- Philosophy of collaboration
- Integration of specialized knowledge of multiple disciplines



JAGS 54:849–852, 2006

Normal Aging

AGE-RELATED PHYSIOLOGIC CHANGES

- Normal aging versus disease:
  - Aging is a biologic process characterized by a progressive, predictable, inevitable evolution and maturation of an organism until death occurs.
  - Aging is independent of disease, although advancing age is associated to increase susceptibility and prevalence of certain diseases

AGE-RELATED PHYSIOLOGIC CHANGES

- In the same organism, cells and organs age at different rates
- These rates depend not only on genetics or age, but on environment and other factors
- As we age, the variability of these changes increases between individuals

GENERAL CHANGES DUE TO AGING

- Reduction in circadian amplitude in the following processes:
  - Body temperature
  - Plasma cortisol
  - Sleep
- 24-hour body temperature trough and sleep onset occur 1-2 h earlier
- Attenuation of pulsatile secretions of gonadotropins, GH, thyrotropin, melatonin, and ACTH
- The functional significance of these changes is not known

THERMOREGULATION

- Produce less heat per kg of weight
- Have reduced muscle activity and less efficient shivering
- Have difficulty in discriminating temperature differences and problems conserving heat due to impaired vasoconstriction of skin arterioles
- These make them to be at risk for hypothermia
- Also at risk of hyperthermia due to impaired skin vasodilatation and decreased sweat production

VOLUME REGULATION

- Increased basal ADH
- Decreased reserves of body water
- Decreased thirst drive (even after 12-24 h of water deprivation)
- Maximum urine osmolality is decreased so that the amount of urine excreted is higher
- Is also more difficult for them to excrete a water load predisposing them to hyponatremia

AGING AND HOST DEFENSES

- Barrier Defenses:
  - Reduction in skin surface acidity and increase dryness due to decrease eccrine gland secretion
  - Skin is thinner
  - Mucous membranes of genitourinary tract and respiratory tree become colonized with gram - organisms
  - There is also alteration of the ciliary function

AGING AND HOST DEFENSES

- Physical and mechanical defenses:
  - Swallowing impairments (frequent small aspirations)
  - Cough is impaired (decreased force)
  - Urine is less acidic, less concentrated, has less concentration of bacterial adherence-blocking proteins (Tamm Horsfall)
  - Less prostatic fluid which has less antibacterial activity
  - Less complete emptying of bladder

AGING AND HOST DEFENSES

- Immune response and non-specific host defense:
  - Less febrile response to infection
  - Humoral antibody-mediated response is decreased (vaccines…)
  - Alteration in helper T-cell function
  - Increased autoidiotype antibody
  - Involution of thymus

AGING AND HOST DEFENSES

- Immune response and non-specific host defense:
  - Decreased production of naïve lymphocytes
  - Impaired T-cell mediated response (decreased response to PPD, booster)

CHANGES IN LABORATORY VALUES

- Hematologic data:
  - No normal age-related change
- Arterial blood gases:
  - pH and pCO2 do not change with age
  - Decrease in pO2 (~3 mm Hg per decade)
  - 100 - (age/3)
  - Due to ventilation perfusion mismatch

CHANGES IN LABORATORY VALUES

- Chemistries:
  - Electrolytes and serum creatinine are unchanged
  - Due to decrease in muscle mass serum creatinine level is unreliable
  - Uric acid and alkaline phosphatase increase slightly

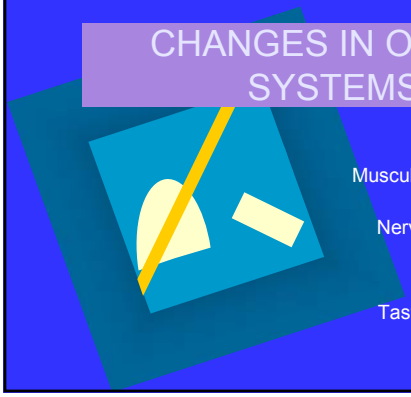
ANATOMY

- Maximum height occurs at age 30-40
- Decrease of ~5 cm by age 75
- This loss is greater in women
- Secondary to:
  - Postural changes (increased hip and knee flexion)
  - Decreased vertebral body height
  - Vertebral disk compaction
  - Flattening of the foot arch

ANATOMY

- Men increase weight up to age 50 and then decreases
- In women the change is less dramatic
- Fat compartment expands from 15% - 30% at age 75
- Wider hips, longer noses, bigger ears
- Hair where you do not want it-a form of metaplasia

CHANGES IN ORGAN SYSTEMS



Skin
Muscular and skeletal systems
Nervous system
Vision
Hearing
Taste and smell

SKIN

- Normal aging of skin is different from *photoaging* (changes caused by exposure to sunlight)
- Increase in time required for cellular renewal and decrease moisture (eccrine and apocrine glands function decrease), causing thinner dryer skin
- Functioning melanocytes decrease 10-20% each dec
- Langerhans cells reduced by 50% (skin immune defenses)=less sensitivity to allergic stimuli and neoplasia
- Dermis loses ~20% of its thickness due to loss of proteoglycan and some collagen. Elastic fibers thicken and fragment

SKIN

- Dermis capillary network reduces and fibroblasts number decreases (senile purpura)
- Thinning of subcutaneous fat
- Androgenetic alopecia (genetics) and involutional alopecia (aging)-decrease hair shaft diameter and less active follicles
- Graying of hair due to loss of # and function of melanocytes

Hyperpigmented skin lentigines (brown macules)

Solar, or senile purpura, actinic purpura (nonpalpable ecchymotic areas). Also shown depigmented stellate pseudoscars.

MUSCULO-SKELETAL SYSTEM

- Vary from one person to another and different muscle groups in the same person age differently
- From 30-80 y/o muscle mass decreases in relation to body weight by 30-40%
- Strength also decreases, (hand grip 60%) but depends on physical activity
- Type II, fast twitching muscle decreases in # or size
- Size and number of myofibrils decreases
- Contraction of muscle is also altered:
  - Slower time to peak tension and relaxation
- Tendons and ligaments stiffer; decrease water cont

Musculoskeletal system

- Degeneration of cartilaginous tissues
- Fibrosis
- ↓Elasticity
- Bone changes:
  - Osteoarthritis
  - Osteopenia

NERVOUS SYSTEM

- Weight of the brain decreases as does the blood flow to the brain (20%)
- Age-related loss of neurons which is not generalized (apoptosis):
  - Most prominent losses occur in the largest cells
  - Eg in the cerebellum Purkinge's cells die
  - In subcortical regions locus ceruleus and substantia nigra have the greatest losses

NERVOUS SYSTEM

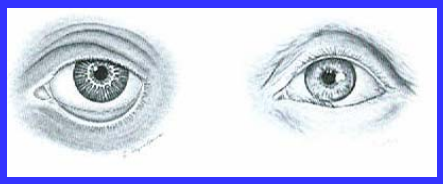
- Density of dendritic connections is decreased, although in some areas may increase
- Lipofuscin accumulates (hippocampus and frontal cortex)
- Myelin decrease in white matter
- There are changes in neurotransmitters, but no change in electrophysiology, thinking or behavior
- Loss of anterior horn spinal motor neurons after 60 (decrease in finger and toe vibratory and tactile threshold)

Visual System

- Periorbital tissues atrophy; upper eyelid is droopy and the lower eyelid is loose (ectropion or entropion)
- Lachrymal gland function decrease
- Watery eyes due to displacement of punctum
- Conjunctiva atrophies and yellows
- Iris is more rigid=smaller and sluggish response pupil

Visual System

- Ectropion – inflamation
- Entropion with trichiasis



Visual System

- Lens yellows causing decreased transparency of blue light
- *Presbyopia* due to the changes in iris and lens
  - Starts after the 4th decade
  - Distance needed to focus an object increases due to loss of elasticity and atrophy of ciliary muscle
- Slower adaptation to light
- Lens opacities cause more sensitivity to glare (cataract removal)
- Less contrast sensitivity

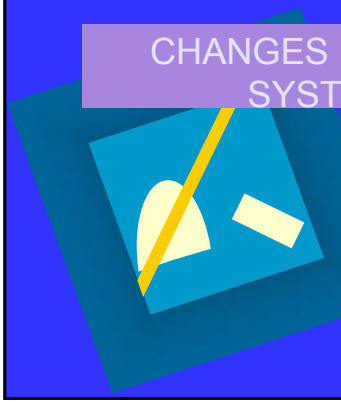
HEARING

- Cerumen is dryer and more tenacious increasing probability of impaction
- TM is thicker and looks duller
- Degenerative changes at ossicular joints, however sound transmission is preserved
- Loss of high and low frequency audition
- Presbycussis:
  - Loss of high tones (above 2000 Hz)
  - Bilaterally symmetrical
  - Slowly progressive

TASTE AND SMELL

- Number of lingual papillae diminish
- Number of taste buds and neurophysiologic response are unaltered
- Acuity of olfaction declines

CHANGES IN ORGAN SYSTEMS



Cardiovascular system
Respiratory system
Gastrointestinal system
Renal system
Hematopoietic function
Endocrine system
Reproductive system

CARDIOVASCULAR SYSTEM

- Maximum heart rate declines with age
  - 220 - age = men
  - 220 - (0.6 x age) = women
- Same cardiac output
- Recovery after exertion is more prolonged
- Heart rate response to a stimulatory maneuver (hand grip) is decreased

CARDIOVASCULAR SYSTEM

- The reason is decreased beta-adrenergic responsiveness. Arterial vasodilation impair
- Both systolic and diastolic (plateaus at age 60) BP increase with age.
- Hearts are stiffer (diastolic dysfunction)
- Increased rate of premature contractions
- Increased risk for orthostatic hypotension

RESPIRATORY SYSTEM

- Age-related changes contribute to:
  - increased frequency of infections
  - Increased likelihood of hypoxia
  - Decreased maximum oxygen utilization
- These changes are usually mild and not clinically significant
- Enlargement of alveolar ducts due to loss in elastic lung parenchyma results in decreased surface area for gas exchange

RESPIRATORY SYSTEM

- Lung elasticity and elastic recoil are decreased, as a result thorax expands causing increased work of breathing (expiration)
- Endurance of respiratory muscles in stress situations decreases
- Mucociliary clearance is slower and less effective

RESPIRATORY SYSTEM

- Cough is less vigorous and due to greater closing volumes, it is not able to clear all portions of the lungs
- Decreased response to hypoxemia, hypercapnia and mechanical loading
- With exercise many of these changes normalize (deconditioning)

GASTROINTESTINAL SYSTEM

- Gums recede, exposing tooth cementum
- Enamel and dentin wear out, but teeth maintain their integrity well in the absence of caries
- Subtle decreases in salivary production
- Chew food less effectively
  - Keeping wet and dry food in mouth longer
  - Swallow larger pieces of food

GASTROINTESTINAL SYSTEM

- Swallowing is less coordinated (aspiration)
- Decrease parietal cells, gastric acid production, and intrinsic factor
- Absorption of calcium, iron, lactose, xylose, and vitamin D are decreased in the small intestine
- Lactase levels decline (intolerance)

GASTROINTESTINAL SYSTEM

- Large intestine shows slowed transit, altered coordination of contraction, increase in opioid receptors (drug-induced constipation)
- No change in liver function
- Bile has higher lithogenic index
- No change in pancreas exocrine function

RENAL SYSTEM

- Despite the major changes that occur with aging, electrolyte homeostasis is well preserved unless is challenged
- Renal mass decreases by 25-30%
- Loss of renal cortex and nephrons with the longest loops is most prominent
- Linear decreases in creatinine clearance (7.5-10ml/decade), although wide variability

RENAL SYSTEM

- Serum creatinine does not change with age because there is decreased creatinine production due to decreased muscle mass
- Reduction of acidification
- Hydroxylation of vitamin D is impaired
- Metabolism of parathyroid hormone, calcitonin, an glucagon are also impaired

HEMATOPOIETIC FUNCTION

- Bone marrow mass decreases and fat increases
- At high demand, functional reserve may be limited
- Under normal conditions, will maintain normal counts of WBC, RBC, and PLT

ENDOCRINE SYSTEM

- GLUCOSE AND INSULIN
  - Slight increases in FBG, 1%/decade after age 20 is not significant
  - Post-pandrial glucose increase 9-10 mg/dl/decade at 1 h, this results in minor changes in glycosilated hemoglobin
  - Plasma insulin levels are increased with age possibly due to decreased clearance
  - Peripheral tissues are less responsive to insulin

ENDOCRINE SYSTEM

- ANTIDIURETIC HORMONE
  - Increased vasopressin response to osmotic stimuli
  - Decreased vasopressin response to volume change
  - May be compensatory for vasopressin renal resistance
- THYROID
  - Thyrotropin is unchanged with age
  - No changes in circulating levels of thyroid hormone

ENDOCRINE SYSTEM

- GROWTH HORMONE
  - GH levels decrease linearly in men, but not in women until after menopause
  - In both, men and women nocturnal peaks decrease
  - Baseline GH does not change, nor does clearance
  - Pituitary response to GHRH is also decreased

ENDOCRINE SYSTEM

- Administration of GH can reverse some changes of aging (decline in muscle mass, reduced body fat)
- Side effects:
  - impair glucose tolerance
  - induce nerve compression syndromes
- GHRH does the same without the side effects
- Calcitonin decrease total but not in bioactive

REPRODUCTIVE SYSTEM

- WOMEN
  - Ovary decreases in size (20g-2.5g), becomes fibrotic and involuted
  - Responsiveness of the ovary to follicle stimulating hormone (FSH) and luteinizing hormone (LH) decreases
  - Estrogen and progesterone production is markedly decreased

REPRODUCTIVE SYSTEM

- WOMEN
  - Testosterone and androstenedione production are decreased
  - Reduced conversion of adrenal androgens to estrone and testosterone
  - Uterus and vagina atrophy
  - Vaginal secretions are diminished
  - Vaginal pH increases

REPRODUCTIVE SYSTEM

- WOMEN
  - Breasts
    - Show involution of glands
    - Fat tissue increases
    - Ligamentous support relaxes
    - Loss of muscular tone

REPRODUCTIVE SYSTEM

- MEN
  - Gradual decline in male reproductive ability
  - Do not have total loss of reproductive ability as seen in women
  - Decrease in daily sperm production and eyaculate
  - Sperm have increased frequency of chromosomal abnormalities
  - Total, free, and bioavailable testosterone decreases

REPRODUCTIVE SYSTEM

- MEN
  - Sex hormone binding globulin increases with age, so there is a decrease in free testosterone
  - Total testosterone is stable until age 80
  - Free testosterone decreases linearly (partial testicular failure)
  - Benign prostatic hypertrophy is present in 90% of men aged 85 (not clear if disease or age-related)

Geriatrics I's

Geriatric I's

- Immobility
- Instability
- Incontinence
- Intellectual impairment
- Infection
- Iatrogenesis
- Impaired eyes/ears

Geriatric I's

- Irritable bowel
- Isolation (depression)
- Inanition (malnutrition)
- Impecunity
- Insomnia
- Immune deficiency
- Impotence (sexual dysfunction)

Immobility

- Broken hip
- Severe angina
- Arthritis
- Fear (falling or bad neighborhood, neurologic diseases, anxiety disorders)
- Depression

Immobility

- Delirium
- Sedentary lifestyle = Deconditioning = musculo-skeletal and cardiovascular
- Functional limitations created when caregivers do things to help persons with disabilities

Instability

- Changes in postural control
  - Decreased proprioception
  - Slower righting reflexes
  - Decreased muscle tone
  - Increased postural sway
  - Orthostatic hypotension

Instability

- Changes in gait
  - Feet not picked up as high
  - Men: flexed posture and wide-base, short-stepped gait
  - Women: narrow-based,waddling gait
- Increased prevalence of conditions causing nocturia (CHF, diuretics, venous insufficiency…)

Instability

- Pathologic conditions
  - Degenerative joint disease
  - Fractures
  - Stroke
  - Disuse and deconditioning
  - Peripheral neuropathy
  - Impaired vision and hearing
  - Dementia

Incontinence

- Bladder capacity declines
- Involuntary bladder contractions are more common (Urge)
- Decline in bladder outlet and urethral resistance; estrogen deficiency, childbirth, surgeries (Stress)
- Prostatic enlargement (Overflow)

Incontinence

- Abnormal arginine vasopressin (AVP)
  - Lack of diurnal rhythm of AVP may precipitate nocturnal polyuria
- Urine is less acidic and becomes colonized by gram – organisms
- Do not forget transient/reversible factors
  - D Delirium
  - R Restricted mobility, retention
  - I Infection, Inflammation, Impaction
  - P Polyuria, pharmaceutical

Intellectual Impairment

- Thought slowness
- Prevalence of dementia increases with aging (47% in those over 85 years old- Evans et al. 1989, Bachman et al. 1992)
- Delirium
- Depression

Infection

- Alterations in immune defenses
- Longer hospital stays (nosocomial infections)
- Physiologic changes (lung, bladder, skin..)
- Chronic diseases (diabetes mellitus, malignancy..)
- Prostatic hypertrophy

Impairment of Eyes and Ears

- Eyes
  - Presbyopia
  - Cataracts
  - Glaucoma
  - Macular degeneration
  - Diabetic retinopathy

Cataract

- Causes
  - Aging
  - Trauma
  - UV light exposure
  - Drugs-steroids
  - DM
  - Hypoparathyroidism
  - Hypothyroidism
  - Hypervitaminosis
- Treatment
  - Laser Surgery
  - Vitamin E - reduce risk

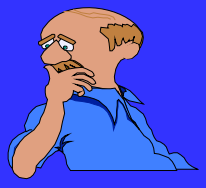
Macular degeneration

Impairment of Eyes and Ears

- Ears
  - Most common in highly industrialized societies
  - Usually sensorineural type
    - Damage to hearing organ, peripheral nervous system, and/or central nervous system
  - Tinnitus
  - Cerumen plugs
  - Tympanosclerosis - scarring of tympanic membrane

Impairment of Eyes and Ears

- Ears
  - Otosclerosis - fixation of ossicular chain lead to conduction hearing loss
  - Ototoxic medications
    - Aminoglycosides
    - Furosemide
    - Aspirin in high doses
  - Sound trauma



Irritable Bowel

- Constipation
  - Poor fluid intake
  - Medications (opioids, calcium channel blockers, anticholinergics...)
  - Immobility
  - Endocrine or metabolic disorders (hypothyroidism, hypercalcemia…)
  - Diabetic autonomic neuropathy
  - Depression

Irritable Bowel

- Fecal incontinence
  - Fecal impaction
  - Laxative overuse
  - Neurologic disorders (stroke,dementia, spinal cord disease)
  - Diarrheal illness
  - Diabetic autonomic neuropathy
  - Rectal sphincter damage

Isolation (depression)

- Increased monoamine oxidase activity
- Decreased neurotransmitter concentrations
- Genetic predisposition
- Chronic medical conditions (pain or loss of function)
- Drugs

Isolation (depression)

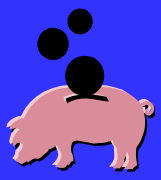
- Sensory deprivation (vision or hearing problems)
- Dementia
- Loss of job and/or income
- Loss of social support

Inanition (malnutrition)

- Decreased taste and smell
- Depression and Isolation
- Physical weakness
- Dental and periodontal disease
- Drugs (digoxin, antitumor agents, reserpine..)
- Chronic diseases
- Low socioeconomic level

Impecunity

- Loss of income
- 60 % of Puerto Rican elderly persons are classified as poor



Iatrogenesis

- Oversights and omissions
- Lack of expertise managing older persons
- Inevitable problems in titrating therapy in an environment which is very labile
- Therapeutic window narrows with age and patient may present toxic reactions to drugs with normal doses

Iatrogenesis

- Polypharmacy
- Overzealous labeling (overdiagnosis)
  - Dementia
  - Incontinence
- Underdiagnosis
- Bedrest (pressure sores, deconditioning, postural hypotension, contractures, depression, DVT, constipation…)

Iatrogenesis

- Enforced dependency
- Environmental hazards
  - bedrails
- Transfer trauma

"All substances are poisons; there is none which is not a poison. The right dose differentiates a poison from a remedy."

Paracelcus

Insomnia

- Delayed sleep onset
- Frequent awakenings (decreased deep phase sleep)
- Early morning awakenings
- Pain
- Orthopnea or paroxysmal nocturnal dyspnea
- Nocturia
- Gastro-esophageal reflux disease

Insomnia

- Nocturnal myoclonus- periodic leg movements
- Sleep apnea
- Daytime naps
- Earlier bedtime
- Medications
  - hypnotics
  - alcohol-sleep fragmentation
  - Anticholinergics-disorientation

Immune Deficiency

Impotence

- Sexual dysfunction
  - Decreased libido
  - Dyspareunia
  - Anorgasmia
  - Erectile dysfunction

Erectile Dysfunction

- Vascular Compromise
  - Most common cause
  - Low penile-brachial pressure index
- Neurogenic Disorder
  - Second common cause
    - DM, Parkinson disease, CVA
- Medications: 25%
  - Beta blockers
  - Thiazide
  - Diuretics
  - Clonidine
  - Alcohol
  - Spironolactone
  - Finasteride
  - Antihistamines
  - H2 receptor antagonists
  - Digoxin
  - Marijuana
  - Metoclopramide
  - Sedative
  - Antidepressants

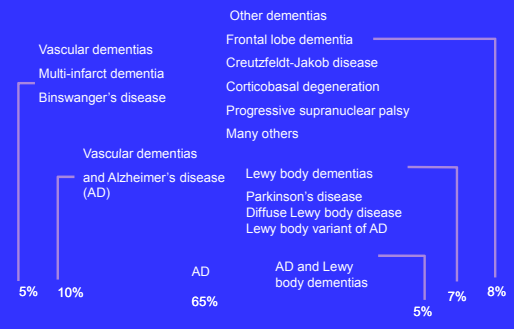
What makes older people special?

- Shorter life expectancy
- Decreased reserves (homeostenosis)
- Physiologic changes
- Increased stress (depression is common)
- Multiple chronic diseases
- Atypical presentation of common illnessess
- Multiple causes of malnutrition
- Multiple causes for disability
- Multiples sources of pain and discomfort
- Special pharmacologic considerations

In summary, all of these cause extraordinary complexity

Dementia

Differential Diagnosis of Dementia



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What Is Alzheimer's Disease?

- Progressive, neurodegenerative disease
- Most common form of dementia
  - Approximately 4.5 million Americans affected
- Unknown etiology
- Impairment in activities of daily living, behavior, and cognition
- Average life span following diagnosis is 7 to 10 years

Barriers to Early Detection of Alzheimer's Disease

- Misidentification by the family of early signs of Alzheimer's disease (AD) as normal aging process
- Social skills often maintained in early AD
- Denial and lack of insight by patient
- Reluctance to report symptoms (patient and caregiver)—stigma
- Lack of definitive screening tools

Risk Factors for Alzheimer's Disease

- Known risk factors
  - Aging: ≥65 (up to 12%)
    ≥75 (up to 23%)
    ≥85 (up to 47%)
  - Genetics: -mutations in the APP (cs21), presenilin-1 (cs14), presenilin-2(cs1)
    * Polymorphism ApoE(cs19)
  - Female gender
- Possible risk factors
  - Head trauma
  - Depression
  - Hypothyroidism
  - Diet and lifestyle
  - Education "brain battering hypothesis"
  - B12 deficiency

Making the Diagnosis of Alzheimer's Disease

- History
- Physical
- Neurologic exam including Mini–Mental State Examination (MMSE)
- Blood and urine screen
- Imaging test (CT, MRI, etc), if indicated
- Standardized clinical diagnostic criteria (eg, DSM-IV)

Symptoms of Alzheimer's Disease

1. Memory loss affecting job skills or other activities
2. Difficulty performing familiar tasks
3. Problems with language
4. Disorientation regarding time or place
5. Impaired judgment
6. Problems with abstract thinking
7. Misplacing objects
8. Changes in mood or behavior
9. Changes in personality
10. Loss of initiative

Mini Mental State Exam (MMSE)

- 30 point test
- Adjusted for age and level of education
- Can be administered by anyone but takes several minutes
- A decline of 4 or more pts in the MMSE over 1-4 years = significant

MMSE (1)

- Orientación
  - Tiempo (5pts)
  a) Año
  b) Época
  c) Día
  d) Fecha
  e) Mes
  - Lugar (5pts)
  a) Piso
  b) Edificio
  c) Ciudad
  d) País
  e) Nación
- Registro (3pts)
  a) Tres palabras: piña, mesa, peso
- Atención y cálculo (5pts)
  a) Resta en serie de múltiplos de 7
  b) O, deletrear MUNDO al revés
- Repetición de tres palabras (3pts)
- Nombrar dos objetos (2pts)
  a) Reloj
  b) Lápiz o bolígrafo
- Repetición (1pt)
  a) Pancha plancha con cuatro planchas

MMSE (2)

- Comprensión (3pts)
  a)Comando de tres pasos: Coger papel con mano derecha, doblarlo por la mitad y devolver a la mesa
- Comprensión de Lectura (1pt)
  a)Cierra los ojos
- Escritura (1pt)
  a)Escribir oración completa
- Dibujo (1pt)

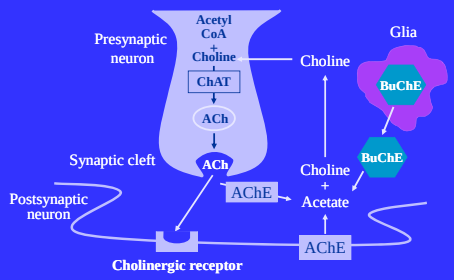
MMSE Adjustment by Age and Level of Education

Education	65-69	70-74	75-79	80-84	>84
0-4th grade	22	22	21	20	19
25th	19	19	18	16	15
5-8th grade	26	25	25	25	23
25th	24	24	22	22	21
9-High School	28	27	27	25	26
25th	27	26	25	23	23
College	29	28	28	27	27
25th	28	27	27	26	25

Patient Functioning in 3 Key Domains as Disease Progresses

	Stages of Alzheimer's Disease		
	Mild	Moderate	Severe
Activities of daily living (ADLs)	Problems with routine tasks	Needs help with basic ADLs (eg, feeding, dressing, bathing)	Progresses to total dependence on caregiver (eg, feeding, toileting)
Behavior	Changes in personality	Anxiety, suspicion, pacing, insomnia	Agitation, wandering
Cognition	- Confusion, memory loss, – Misplacing objects – Forgetting names – Disorientation	Difficulty recognizing family and friends Chronic loss of recent memory	Loss of speech Misidentifies or is unable to recognize familiar people

Normal Cholinergic Function



ACh = acetylcholine; AChE = acetylcholinesterase; BuChE = butyrylcholinesterase; ChAT = choline acetyltransferase; CoA = coenzyme A.
Adapted from Mycek M et al. In: Harvey RA, Champe PC, eds. *Pharmacology: Lippincott's Illustrated Reviews*. Philadelphia, Pa: JB Lippincott Co; 1992:35-44.

Acetylcholinesterase Inhibitors

- Drugs used to treat Alzheimer's disease act by inhibiting acetylcholinesterase activity
- These drugs block the esterase-mediated metabolism of acetylcholine to choline and acetate. This results in:
  - Increased acetylcholine in the synaptic cleft
  - Increased availability of acetylcholine for postsynaptic and presynaptic nicotinic (and muscarinic) acetylcholine receptors

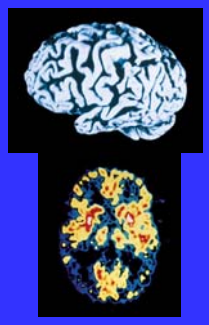
Nordberg A, Svensson A-L. *Drug Safety*. 1998;19:465-480.

Functional Deficits From Decrease in Acetylcholine

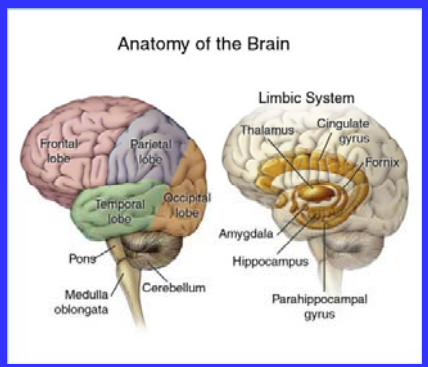
- Majority of functional deficits in Alzheimer's disease are related to a decrease in acetylcholine (ACh)—up to 90%
  - ACh decrease results from loss of cholinergic neurons
  - ACh is associated with sleep cycles, mood, attention, memory, and cognition
  - ACh is broken down by cholinesterases

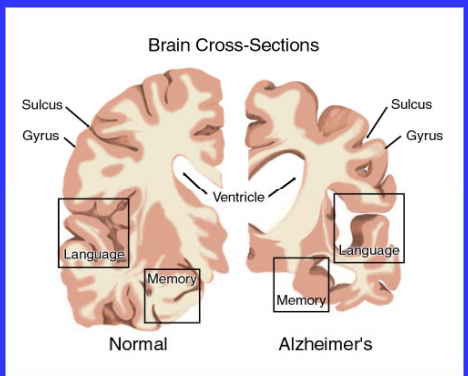
The Effect of Alzheimer's Disease on the Brain

- Structural changes are associated with dysfunctional cholinergic activity resulting in functional decline
  - Changes in brain weight, volume, ventricular size, and gyral atrophy that occur with normal aging are intensified with Alzheimer's disease
  - Specific brain regions are affected
    - Frontal and temporal cortex more involved than other regions
    - Hippocampal atrophy

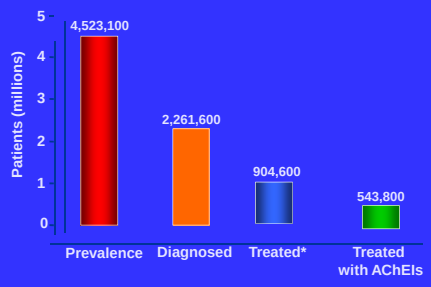


Courtesy of Albert Enz, PhD, Novartis Pharmaceuticals Corporation; the National Institute on Aging (NIH), Bethesda, Md.





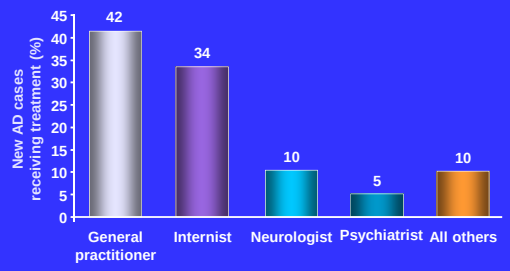
Treatment of Alzheimer's Disease



* Any drug treatment, not limited to acetylcholinesterase inhibitors.

Source: Decision Resources, March 2000.

Primary Care Physician Usually the First to Treat



Source: NDTI (Diagnosis codes: 3310, 2900, 2901, 2902, 2903, 2904, 3109, 2912 first visit, non-referred), Moving Annual Total (MAT). November 2002.

Management Strategies

- Share diagnosis of Alzheimer's disease (AD) with patient, family, and caregiver
- Provide education about
  - AD and its clinical course
  - Management of daily activities and behavioral disturbances
  - Reduction of caregiver's burden (respite care, social support, Alzheimer's Association)
  - Prevention of excess disability

Management Strategies

- Treatment of AD symptoms
  - Pharmacologic
    - Cholinesterase inhibitors
      - » Exelon®* (rivastigmine tartrate)
      - » Reminyl®* (galantamine)
      - » Aricept®* (donepezil)
      - » Cognex®* (tacrine)
    - N-methyl-D aspartate receptor antagonist (NMDA)
      - » Namenda (memantine): inhibit glutamate transmission. AD associated with abnormal high levels of this excitatory NT associated with accelerated cell death.

*Exelon is a registered trademark of Novartis Pharmaceutical Corp.; *Reminyl is a registered trademark of Janssen Pharmaceutica Products, L.P.; *Aricept is a registered trademark of Eisai Co, Ltd; *Cognex is a registered trademark of Firs Horizon Pharmaceutical Corp.

Management Strategies

- Others: Vitamin E, Selegiline, Ginkobiloba
- Nonpharmacologic
  - Compensatory technique (ie, memory book)
  - Environmental adaptations (ie, well-lit, quiet atmosphere)
  - Safety considerations

Medications for Alzheimer's Disease: Pharmacokinetic Parameters

Medication	Eliminaton Half-life, h	Bioavailability, %	Protein Binding, %	Route of Metabolism
Cholinesterase inhibitors				
Donezepil hydrochloride	70	100	96	CYP 450 (2D6 and 3A4)
Galantamine hydrobromide	5-7	90	18	CYP 450 (2D6 and 3A4)
Rivastigmine tartrate	1.5	40	40	Cholinesterase-mediated hydrolysis.
NMDA-receptor antagonists				
Memantine hydrochloride	60-80	100	45	57-82% excreted unchanged in urine.

The Glutamate Hypothesis of Cognitive Deficit

Abnormal glutaminergic activity leads to sustained low-level activation of NMDA receptors

Cognitive deficit ← **Neuronal damage/loss following chronic insult**

Medications for AD: Specific Drug-Drug Interactions

Donepezil

Effect on metabolism of other medications

Cisapride, terfenadine: In vitro studies show little likelihood of interaction

Cimetidine, digoxin, furosemide, ketoconazole, theophylline, warfarin: No effect on pharmacokynetics of these drugs observed

Effect of other drugs on metabolism of medication

Ketoconazole, quinidine: In vitro inhibition has been observed, ketoconazole increased donezepil AUC_{0-24} and C_{max} by 36% in 18 healthy subjects

Carbamazepine, dexamethasone, phenobarbital, phenytoin, rifampin: These CYP2D6 and CYP3A4 inducers could increase elimination.

Digoxin, cimetidine: Donepezil not significantly affected.

Medications for AD: Specific Drug-Drug Interactions

Galantamine

Effect on metabolism of other medications

Digoxin, warfarin: No effect on pharmacokynetics of these agents; does not inhibit metabolic pathways catalyzed by CYP1A2, CYP2A6, CYP3A4, CYP2C, CYP2D6, and CYP2E1.

Effect of other drugs on metabolism of medication

Ketoconazole, paroxetine, erythromycin: Increases in galantamine AUC (30%, 40%, and 12%, respectively) have been observed.

Amitriptyline, fluoxetine, fluvoxamine, quinidine: Galantamine clearance decreased by 25-33%.

Cimetidine, ranitidine: No effect of ranitidine on Galantamine; cimetidine increased AUC by 16%.

Medications for AD: Specific Drug-Drug Interactions

Rivastigmine

Effect on metabolism of other medications

Diazepam, digoxin, fluoxetine, warfarin: No interaction has been observed when administered with these drugs.

Effect of other drugs on metabolism of medication

Antacids, antihypertensives, beta-blockers, calcium channel blockers, antidiabetics, NSAIDs, estrogens, salicylate analgesics, antianginals, antihistamines: Pharmacokynetics were not influenced by addition of these agents.

Medications for AD: Specific Drug-Drug Interactions

Memantine

Effect on metabolism of other medications

Hydrochlorothiazide/triamterene: Coadministration with HCTZ did not affect bioavailability of either memantine or triamterene; bioavailability of HCTZ decreased by 20%.

Effect of other drugs on metabolism of medication

Since memantine is predominantly renally eliminated, drugs that are substrates and/or inhibitors of the cytochrome P450 system are not expected to alter the metabolism of memantine.

Falls

Background and Significance

- 35-40% generally healthy older persons fall annually.
- Incidence rates in nursing homes and hospital: 3x
- Fall related injuries accounts for 6% of all medical expenditures (10 billions)

Background and Significance

- 5% will require hospitalization.
- Responsible for 2/3 of the deaths resulting from unintentional injuries.
- Psychological and social consequences.

Prevalence of falls Among the Elderly

Community based	325/1,000
Hospital based	1,500/1,000
Long Term Care based	1,650/1,000

Source: Rubenstein

Falls are a Health Hazard for the Elderly

- Mortality
- Morbidity
  - Fractures (hip,wrist,vertebrae,skull)
  - Soft tissue injury
  - Subdural hematoma
  - Accidental hipotermia
  - Loss of confidence
  - Patient and family anxiety

Risk Factors for Falling

Muscle weakness	Arthritis
History of falls	Impaired ADL
Gait deficit	Depression
Balance deficit	Cognitive impairment
Use assistive device	Age >80 years
Visual deficit	

ETIOLOGY OF FALLS

• Accident/environment	37%
• Pathologies	
– Weakness,balance/gait	12%
– Drop attack	11%
– Dizziness/vertigo	8%
– Orthostatic hypotension	5%
– CNS lesions	1%
– Syncope	1%
– Unknown	8%
– Other (acute illness, confussion, poor eyesight, drugs)	18%

Source: Rubenstein

Falls Directed Assessment

- Funtional status scales (ADL, IADL)
- Mental status/Depression
- Medication review
- Specific gait and balance (Tinetti)
- Muscle strength testing
- Vision and hearing screening
- Home environmental assessment

Multifactorial Interventions in Community-Dwelling Older Adults

- Gait training
- Advise on the appropriate use of assistive devices
- Review and modification of medication
- Exercise programs
- Treatment of postural hypotension
- Modification of environmental hazards
- Treatment of cardiovascular disorders

Multifactorial Interventions in Long Term Care

- Staff education programs
- Gait training
- Advise on the appropriate use of assistive devices
- Review and modification of medications

Single Interventions

- History
- Environmental modification
- Medications (Benzodiazepines, Neuroleptics, Antidepressants) Four or more medication
- Assistive devices
- Behavioral and educational programs

Guidelines for Proper Medication Prescribing and Medication Reduction

A lternatives
V ague history or symptoms
O TC (over-the-counter) medications have side effects too
I nteractions (drug-drug, drug-disease)
D uration

T herapeutic vs. Preventive
O nce-a-day vs. Twice, thrice, or four times a day
O ther doctors

M oney
A dverse effects of other drugs
N eed
Y es/No (Is the person actually taking the medication?)

Management

- Changes in environment and activity
- Removal of loose rugs
- Use of nightlights
- Stair rails
- Ample lighting without glare
- Avoid multifocal glasses while walking
- Ophtalmologist evaluation

Management

- Review and reduction of medications
- Modification of salt restriction
- Adequate hydration
- Compensatory strategies
- Pressure stockings
- Referral to physical therapist

Postural Blood Pressure

- ≥ 20 mmHg (or ≥ 20%) drop in systolic blood pressure, with or without symptoms
- Readings after ≥5 minutes in supine position

Balance and Gait

- Patient's report or observation of unsteadiness
- Impairment on brief assessment (Get up and Go test)

Strengthening

- Balance (Tai Chi)
- Balance and Strength
- Water Exercises

Falls; Management

- **Targeted Musculoskeletal Exam**:
  - Joints and range of motion
  - Examination of feet
- **Targeted Neurologic Examination:**
  - Impaired proprioception
  - Impaired cognition
  - Decreased muscle strength
- **Targeted Cardiovascular Exam:**
  - Syncope
  - Arrhythmia

Practicing Primary Care Geriatrics

All of these make Geriatrics one of the most difficult and intellectually challenging fields in Medicine