DEPRESSION IN THE ELDERLY - DIAGNOSIS AND PSYCHOPHARMACOLOGIC CONSIDERATIONS

I. Diagnostic Considerations

- A. DSM III criteria for depression
- B. Factors complicating diagnosis of depression in the elderly
- C. Drugs associated with depression
- D. Medical disorders associated with depression
- E. Somatic complaints that mask depression
- F. Characteristics of elderly depressives

II. Pseudodementia

- A. Symptoms of pseudodementia

III. Differentiating pseudodementia from delerium and dementia

- A. Delerium
  1. diagnostic criteria for delerium
  2. medical causes of delerium
  3. drugs that cause delerium

IV. Incidence of depression vs. dementia

V. Dementia

- A. Types of dementia
- B. Criteria for diagnosis of dementia
- C. Reversible or arrestable dementias

DEPRESSION IN THE ELDERLY - DIAGNOSIS AND PSYCHOPHARMACOLOGIC CONSIDERATIONS (cont'd)

VI. Differences between dementia and pseudodementia

VII. Pseudodementia workup

VIII. Treatment considerations in the elderly

A. Psychotherapeutic considerations

B. Antidepressant drugs

1. Types of first generation antidepressants
2. General principles of antidepressant drug usage
3. Specificity of tricyclic antidepressants
4. Predictors of tricyclic response
5. Factors complicating antidepressant drug therapy in the elderly
6. Principles of antidepressant drug therapy in the elderly
7. Tricyclic dosages in the elderly
8. Side effect of antidepressant drugs
   a. anticholinergic effects
      1) relative anticholinergic effects between drugs
   b. cardiovascular effects
      1) hypotension
      2) cardiac effects, EKG effects
9. Newer antidepressants and the elderly
   a. trazodone

b. maprotiline

c. Trimipramine

d. amoxapine

e. normifensine

10. Combination therapy

11. MAOI's

a. efficacy-compaired to tricyclic antidepressants

b. cardiotoxic effects

c. drug-drug interactions

IX. Benzodiazepines, sedative hypnotics

X. Lithium

XI. Psychostimulants

XII. Antipsychotic drugs

PSYCHOPHARMACOLOGY AND THE AGING PATIENT

Background: As an individual ages, changes occur in both the pharmacokinetics (i.e., absorption, distribution, metabolism, elimination) and the pharmacodynamics (i.e., the effects) of a wide variety of drugs. Although still understudied and incompletely understood, both phenomena can be important in determining the response of the aged patient to psychotropic medications (i.e., antidepressants, benzodiazepines, neuroleptics). In addition to age-related changes, the elderly are also susceptible to excessive or undesired drug effects because of concomitant diseases and because they are frequently taking more than one prescribed or nonprescribed drugs. The latter puts them at increased risk for drug-drug interactions.

Objective: This talk will present basic concepts about the pharmacokinetics and pharmacodynamics of psychotropic drugs pertinent to their clinical use in the aged and other special populations. Specifically covered will be changes in these parameters due to:

(a) age-related changes

Principal example: benzodiazepines

(b) disease-related changes

Examples: all three classes

(c) drug-drug interactions: both prescription and non-prescription

(i) pharmacokinetic

Principle example: tricyclic antidepressants

(ii) pharmacodynamic

Principle examples: tricyclic antidepressants and neuroleptics

Guidelines for the Use of Psychotropic Agents in the Elderly

I. Epidemiology

In 1981, 24 million Americans (10% of the population) were over age 65. It is estimated that 56 million Americans will be over 65 in 2035. Today's ten percent use 25% of all prescription drugs or approximately 200 million prescriptions (8 prescriptions per patient per year). About 80% of those prescriptions are for psychotropic drugs. Only 5% of the elderly are in nursing homes so that 95% are taking these drugs largely unsupervised. Significant psychiatric symptoms are present in 20-40% of those in the community. For those in nursing homes, the prevalence of psychiatric symptoms is 60% and upward (Secretary, HEW, 1975). Of all nursing home patients, 75% receive at least one psychotropic agent (Nursing Home Care in U.S., 1974).

II. Approach to the Patient

A. History

Always consider dementia in anyone over 40 years of age and in certain selected younger patients. One of the most vital concerns is to talk with family members

Common Concerns: Headaches

Nausea or vomiting

Dystaxia

Seizures

Incontinence

Personality changes

Episodes--of agitation and/or confusion

Alcohol - sedative hypnotic abuse

Medication history

B. Carefully evaluate the chart in hospitalized consultations. One third to 50% of time should be spent here. Nursing notes may be most revealing. Interview nurses.

C. Mental Status and Neurological Examination

1. Mental Status Exam

-Disorientation

-Recent memory and new learning ability impairment

-Deficits in attention and concentration

-Lack of abstracting ability (concrete)

-Inability to do rudimentary calculations

-Constructional dyspraxia

-Aphasia or apraxia

-Perservation

2. Neurologic Exam

-Gait and Posture: Flexion Attitude, Paratonic rid-igity (gegenhalten), Pelvicrural flexion contracture

-Reflexes: Grasp, Tonic foot response, Snout, Suck-Palmomental reflex, Corneomandibular, Glabellar tap

-Motor Impersistence: (Don't confuse with being uncooperative)
Keeping tongue out
Maintain lateral fixed gaze
"Ah" or "ee"
Grip

-Perservation, Post Hyperventilation, apnea, Pseudobular Palsy

D. Differential Diagnosis

-Affective syndrome, depressed

-Endocrine Disorders

-Chronic CV, lung, liver or kidney disease

-Normal Pressure Hydrocephalus

-B_{12} - Folate deficiency

-Drug Intoxication

-Alcoholism

-CNS Infection (e.g., cryptococcus, syphilis)

-Intracranial mass

-Parkinson's disease

-Wilson's disease

-Huntington's disease

-Alzheimer's, Jakob-Creutzfeldt

E. Workup

When no clues from history, PE, MSE or neurologic exam, the following ancillary procedures are recommended:

Basic: CBC, Syphilis serology, SMA-12 or other screening

test with electrolytes, serum albumin, Thyroid function, Chest x-ray, Urinalysis

Elective: Skull x-ray, Brain scan, EEG, Isotope cisternography, Cerebral angiography, CAT scan

F. Treatment

1. Restitution of lost function

-Correct patients medical and physical limitations

-Intensive medical treatment, feeding and physical therapy may need to be done before other approaches are begun.

-Eyeglasses, hearing aids

2. Reduction of dependence on lost functions

-Primarily done thru environmental manipulation

-The less the environment varies, the better the patient will function

-The ability to adjust to change is invariable affected: easily visible clocks, calendars, pictures of family, personal items

-If the patient is moved, take as many personal items as possible for orientating signals

3. Utilization of residual functions

-Aim here is to treat target symptoms with centrally active pharmacologic agents

III. Pathophysiologic Concerns

A. Pharmacokinetic Alterations (ADME)

1. Absorption: often impaired

-Decreased total gastric acidity

-Atony from atrophy and deterioration of smooth muscle

-Decreased GI arterial supply from atherosclerosis or decreased cardiac output (C.O.)

2. Distribution

-Lean body mass replaced by fat which traps lipophilic psychotropic agents

-Distribution slowed by decreased C.O. and increased circulation time commonly due to myocardial pathology

-Transport altered by decreased serum albumin, increased free fraction of drug

3. Metabolism

-Even with normal LFT's, hepatic metabolizing systems are less efficient with advance age leading to longer elimination times: especially important for drugs with multiple active metabolites

4. Excretion

-Renal blood flow decreases

-Clearance and renal absorptive ability diminishes 6% per decade past age 30

-GFR may diminish 30%-50% from age 45 to 90

B. Pharmacodynamic Alterations

-Neuronal loss and cytoarchitectural changes can alter both sensitivity and reactivity to psychotropic agents: alterations in receptors (e.g., tardive dyskinesia) and feedback systems (e.g., spontaneous buccolinguofacial dyskinesia)

IV. Antianxiety Agents (Anxiety neurosis does not begin in senescence!)

A. Barbiturates, Ethchlorvynol, Glutethimide, Meprobamate

-Avoid. Can cause paradoxical excitement and also induce hepatic drug metabolizing enzymes which alter other concomitant drugs.

-Dystaxia more likely with possible falling and fractures.

B. Antihistamines (diphenhydramine, hydroxyzine)

-Highly anticholinergic. May be additive with other drugs or increase constipation, urinary retention, and glaucoma.

C. Beta-Blockers (propranolol, metoprolol)

-Used to block sympathetic signs of anxiety.

-May compromise cardiac reserve by blocking needed adrenergic stimuli.

-May mask sympathetic signs of hypoglycemia in diabetics.

D. Benzodiazepines

1. Chlordiazepoxide, diazepam, flurazepam

-All produce pharmacologically active metabolites: desmethyldiazepam and oxazepam.

- Increases in half-life and in elderly, the half-life of these agents may approach 2-3 days and easily accumulate

after one or two weeks of therapy. Flurazepam plus its major metabolite has longest half-life of all these agents. (50-100 hrs in middle age, up to one week in elderly).

-Can accumulate and diminish cerebral function in elderly patients in usual dosages.

2. Chlorazepate and prazepam

-These agents are prodrugs for production of desmethyldiazepam. Chlorazepate and related agents require acid hydrolysis in stomach to be active. Any cause of increased gastric pH will diminish available active agent (e.g., age, post-gastrectomy, PA, antacids). Prazepam requires N-deaylkalation via passage through the liver. Portocaval shunting, impaired hepatic microsomal enzyme systems, and reduced hepatic blood flow will diminish available active agent.

3. Lorazepam, oxazepam, and temazepam

-Metabolized by simple glucaronide conjugation and have no active metabolites

-Probably drugs of choice in the elderly where a benzo-diazepine is wanted.

4. Intramuscular use

-For chlordiazepoxide and diazepam, the intramuscular absorption is inferior to oral absorption. Can produce erratic and unpredictable results for pre-op or procedures

(e.g., endoscopy). Can cause late onset delirium.

V. Tricyclic Antidepressants

A. Predictors of positive response

Does the patient have an affective syndrome (e.g.,

-Insidious onset, psychomotor disturbance, anorexia, weight loss, middle and terminal insomnia, decline in sexual drive)?

Not for use in treating patients with mood complaint only--i.e., symptomatic diagnosis.

B. Predictors of poor response

-Absences of vegetative symptoms, absence of familial history of affective illness, presences of neurotic and hysterical traits, previous poor response.

-Presence of psychotic symptoms in addition to the affective syndrome is an indication for ECT or the short term addition of an antipsychotic drug plus the antidepressant.

C. Usage

-Start with lower doses, do not initially give all of dose at bedtime in elderly patients. Typically, a secondary amine tricyclic antidepressant (e.g., nortriptyline) is better tolerated than a tertiary by the elderly from multiple standpoints: less risk of cardiotoxicity, orthostatic hypotension, memory impairment, and anticholinergic peripheral side-effects.

Drug	Type	Effective Dose in Middle Age	Effective Dose in Elderly	Therapeutic Plasma Conc.
Imipramine	tertiary	150-300 mg.	75-200 mg.	150-300 ng/ml
Amitriptyline	tertiary	150-300	75-200	150-250
Doxepin	tertiary	150-300	75-200	uncertain
Desipramine	secondary	150-250	75-200	uncertain
Nortriptyline	secondary	50-100	25- 75	50-100
*Protriptyline	secondary	20-60	10- 40	uncertain

*Typically not well tolerated by elderly

D. Actions ranked from highest to lowest:

Anticholinergic	Sedation	Cardiac	Orthostatic
AMI	DOX	DOX, AMI	IMI
DOX, IMI	AMI	IMI	DES
NOR	IMI	NOR	AMI
DES	NOR	DES	NOR
	DES		

E. Toxicity

-Cardiac: Dysrhythmias or block, orthostatic hypotension, impaired myocardial contractility QRS of 0.10 or greater bodes danger

-Mental: Central anticholinergic syndrome of confusion, loss of recent memory and agitation. Usually but not always have peripheral atropinic effects: Dry mucous membranes, decreased sweating, mydriasis, blurred vision, tachycardia,

elevated temperature, decreased bowel sounds and urinary outflow difficulty.

VI. Lithium Carbonate

A. Usage

-Primary value is for prophylaxis of manic-depressive illness.

-Used by some physicians as a panacea for other disorders with little scientific basis.

-Comes in 300 mg. tablets, capsules, and sustained release.

-Therapeutic level in young adults 0.6-1.2 mEq/L.

-Effective prophylactic level probably above 0.8 mEq/L.

-In elderly patients, 0.4-0.7 mEq/L can be sufficient.

B. Target Organs for Evaluation

-Thyroid: Goiter and hypothyroidism can result.

-Renal: Nephrogenic diabetes insipidus syndrome can result.

-Cardiac: Very rarely sinus bradycardia occurs ("sick" sinus syndrome).

-Chronic nephrosclerotic changes with loss of concentrating ability remains a controversial subject but only a consideration after long-term treatment of many years.

C. Toxicity

-Half-life 36-48 hrs in elderly vs. 24 hours in younger adults.

-Similar to bromism but with excessive thirst and polyuria.

-Will prolong depolarizing and non-depolarizing neuromuscular blockers. Has induced latent myasthenia gravis.

-Leukocytosis often a normal finding. Has been used for this effect in patients with leukopenia.

D. Sodium Balance

-Of crucial importance

-Lithium levels vary inversely with sodium.

-Sodium loss (e.g., diuretics, low salt diet, salt losing nephropathy) will elevate serum lithium.

-Sodium load enhances lithium excretion (e.g., country ham, excessive table salt, normal saline IV).

E. Use with Neuroleptics or Antidepressants

-For rapid control of manic excitement, short-term use of neuroleptics in conjunction with lithium. For depressive episodes in patients with manic-depressive illness, short-term use of antidepressants in addition to lithium is sometimes necessary.

-Recent research suggests that phenothiazines increase the passive diffusion of lithium ion across cell membranes.

VII. Neuroleptic Agents

A. Uses

-In patients with OBS, use is usually prn only and then for episodes of definite agitation and excitement. Chronic use to prevent recurrent episodes or to improve cognitive status is of doubtful advantage and may worsen status instead especially such use of the low potency agents.

Heightened risk of tardive dyskinesia in the elderly especially with high potency agents

-In elderly patients with schizophrenia, maintenance use at lowest possible dose appropriate in cases where there is clear evidence of continued usefulness.

Recommended Antipsychotic Dosage in Elderly Persons with Dementia

Drug	Prn Dose*	Anticholinergic Potency	Hypotension
Chlorpromazine (Thorazine)	10-50 mg.	high	high
Thioridazine (Mellaril)	10-50 mg.	high	moderate
Mesoridazine (Serentil)	5-25 mg.	moderate	moderate
Thiothixene (Navane)	1- 2 mg.	low	low
Trifluoperazine (Stelazine)	1- 2 mg.	low	low
Haloperidol (Haldol)	1/2-1.5 mg.	low	low
Fluphenazine HCL (Prolixin HCL)	1/2-1.5 mg.	low	low

*Not to be used more than QID.

Recommended Antipsychotic Dosages* in Elderly Schizophrenics

Drug	Acute Daily Starting Dose	Daily Maintenance Dosage Range	Sedation	Hypotension	EPS**
Chlorpromazine (Thorazine)	50-150 mg.	100-500 mg.	high	high	low
Thioridazine (Mellaril)	50-150 mg.	100-400 mg.	high	high	low
Mesoridazine (Serentil)	25- 75 mg.	50-200 mg.	moderate	moderate	low
Thiothixene (Navene)	2-10 mg.	5- 30 mg.	moderate	low	moderate
Trifluoperazine (Stelazine)	2- 8 mg.	4- 20 mg.	low	low	high
Haloperidol (Haldol)	1- 6 mg.	2- 15 mg.	low	low	high
Fluphenazine	1- 5 mg.	2.5-15 mg.	low	low	high

C. Side Effects

1. GI: Most serious in the elderly is paralytic ileus or megacolon
2. CV: Orthostatic hypotension. Do sitting-standing BP.
3. Neuro: Parkinsonism, tardive dyskinesia.
4. Psychiatric: Anticholinergic confusion.
5. Urologic: Urinary outflow difficulty.

D. Rapid Intramuscular Titration in the Elderly

1. Mesoridazine 5 mg. q 1-2 hrs (25 mg/ml).
   20 units (5/25 ml) in U-100 insulin syringe.
2. Haloperidol 1/2 mg. q 1-2 hrs (5 mg/ml).
   10 units (0.5/5 ml) in U-100 insulin syringe.

VIII. Ergot alkaloids and vasodilators

High dose Hydergine (6mg/day) may be beneficial benefits if given for at least 6 months. Vasodilators appear of no benefit.