

The image shows the cover of a spiral-bound notebook. The cover has a textured, light-colored fabric-like surface and a dark brown border. A silver metal spiral binding is visible on the left side. The text is centered on the cover in a bold, black, serif font.

Addressing Treatment Issues in Geriatric Depression

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A graphic of a spiral-bound notebook with a brown cover and a light beige page. The spiral binding is on the left side. The word "OBJECTIVES" is centered at the top of the page in a large, black, serif font. Below it is a horizontal line. A list of five objectives follows. The number "2" is in the bottom right corner of the page.

OBJECTIVES

- 1) Identify pertinent medical issues
- 2) Understand dementia-depression interaction
- 3) Encompass differential diagnosis
- 4) Summarize screening options
- 5) Review evidence based treatment

Depression?



Depression in Late Life: NIH Consensus Statement

- Major public health problem
- **NOT** a normal consequence of aging

Lebowitz BD, et al. JAMA 1997;278:1186-1190

Depression in the Elderly: Under-recognition and under-treatment

Nursing Homes: 10.9% prevalence

55% on ADs; 32% at inadequate dose

Brown MN et al. J Am Geriatr Soc 2002;50:69-76

Home Care: 13% prevalence

22% on ADs; 0% in therapy

Bruce ML et al. Am J Psychiatry 2002;159:1367-74

Correct identification by NPs in 37%

Brown EL, et al. J Am Geriatr Soc 2004;52:995-999

Primary care: 42% on ADs;
32% at inadequate dose;
8% in therapy

Unutzer J, et al. J Am Geriatr Soc 51:505-514, 2003

Depression in Elderly: Diagnostic Strategy

- 1) Search for Possible Medical Causes:
 - sub-acute delirium
 - post-stroke depression
 - vascular depression
- 2) Review past psychiatric history:
 - Recurrent major depression/ bipolar
 - Dysthymia; personality factors
- 3) Assess life stresses:
 - Grief; bereavement; adjustment; pain; sensory or social isolation; functional limitation; perceived inadequacy of care
- 4) Assess dementia:
 - Depression prodrome; apathy; executive dysfunction; affect dysregulation
- 5) First episode of major depression



Examples of Medical Disorders which can cause “Depressive” Symptoms

Anemia	Hypoxia
B-12 deficiency	M.I.
Cancer	Pain
CNS metastases	Parkinson’s
Diabetes	Sleep apnea
Hepatitis	Stroke
Hypercalcemia	Thyroid abn.
Hyponatremia	Uremia

Adapted from Rouchell AM, et al
Chap. 17 in Textbook of CL
Psychiatry, APA Press, 2002

Examples of Medications Causing “Depressive” Symptoms

Alcohol

Benzodiazepines

Beta-blockers

Clonidine

Estrogen

Interferon

Isoretinoin

Methyldopa

Metronidazole

Narcotics

Ranitidine

Reserpine

Steroids

Stimulant

(withdrawal)

Topiramate

Vincristine

Post-Stroke Depression: 20-50% within 1 year

Neuroanatomic?

- 1) 7-10 days: left hemisphere > right
- 2) 3-6 months: no hemisphere difference in incidence, but severity inversely correlated with distance from frontal pole
- 3) > 1year: Right > left

Shimoda K, et al. Biol Psychiatry 1999;45:187-192

Non-specific reaction?

Significantly more likely than in other illnesses with comparable disability

Folstein MF, et al. J Neurol Neurosurg Psychiatry 1977;40:1018-1020

Incidence equivalent to post-MI depression.

Ibern I, et al. J Neurol Neurosurg Psychiatr 2003;74:581-585

Vascular Depression: Microvascular etiology

Depressive symptoms in elderly related to:

Severity of deep white matter ischemic hyperintensities in pre-frontal cortex

Thomas AJ, et al. Arch Gen Psychiatry 2002;59:785-792

Hippocampal, anterior cingulate and orbitofrontal volume reductions

Ballmaier M, et al. Am J Psychiatry 2004;161:99-108

Frequency of depression correlates with cerebrovascular risk factors: HTN, DM, A-fib, carotid disease, high cholesterol.

Mast BT, et al. Am J Geriatr Psychiatry 2004;12:84-92.

10

Depression and Alzheimer's Disease: Depression as a Risk Factor

Comprehensive review of literature:

20 studies with 102,172 subjects in 8 countries.

1. Persons with a history of depression are more likely to be diagnosed as having AD later in life.
2. Risk for AD increased with multiple episodes of depression.

Ownby RL, et al. Arch Gen Psychiatry 2006;63:530-538

“Neurotoxicity” of Depression May Contribute to the Development of Dementia

- Untreated time depressed and total hippocampal volume inversely related (N=38)

Sheline YI, et al. Am J Psychiatry 2003;160:1516-1518

- Excess glucocorticoids reduce neurogenesis.

Davidson RJ et al. Annu Rev Psychol 2002;53:545-574

- Larger orbitofrontal cortex volumes in elderly depressed who were treated (N=41) .

Lavretsky H, et al. J Clin Psychiatry 2005;66:964-967

- Antidepressants increase neurogenesis.

Santarelli L, e al. Science 2003;301:805-809

NIMH Consensus Panel on Diagnosis of Depression of AD

More likely to present as dysphoria and loss of interest without neurovegetative signs.

Proposed criteria would require depressed mood or anhedonia

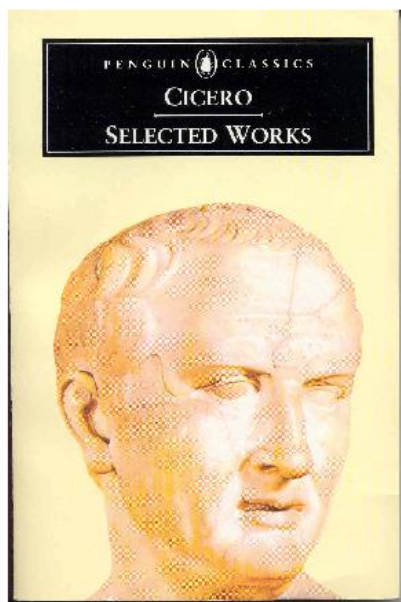
- total of 3 rather than 5 symptoms

Appetite/weight	Sleep	Fatigue
Concentration	Death thoughts	Worthless/guilt
Agitation/retardation		

- irritability and social isolation count
- sx need not be present every day

Olin JT, et al. Am J Geriatr Psychiatry 2002;10:129-141¹³

Cato the Elder: On Old Age



“Old people who are... morose, petulant, ill-tempered, and hard to please - these are faults of character not of age.” 43 BC

Screening for Geriatric Depression

Mandatory screening in nursing homes
(Cornell scale cutoff ≥ 5) led to more use of
antidepressants and more symptom
improvement

Cohen CI, et al. Am J Psychiatry 2003;160:2012-2017

Screening for Geriatric Depression

Psychometric issues: age, site, cognitive status

Hamilton Depression Rating Scale (HDRS):

- most frequently used for outcome studies
- total score on 21, 17 and 6 item versions
- interviewer administered

Geriatric Depression Scale (GDS):

- 15 or 30 item
- self-report
- eliminates somatic and vegetative symptoms
- validity decreases with cognitive impairment

Screening for Geriatric Depression

Cornell Scale for Depression in Dementia (CSDD):

- 19 items
- interviewer administered

Single question: Do you often feel sad or depressed?

Visual Analog Mood Scale

Minimum Data Set (MDS):

- 16 mood indicators over prior 30 days
- incorporates daily staff observations

A graphic of a spiral-bound notebook with a brown cover and a light beige page. The spiral binding is on the left side. The page has a horizontal line near the top. The title "Treatment of Geriatric Depression" is centered on the page.

Treatment of Geriatric Depression

Antidepressants for Elderly Major Depression

- Citalopram (Celexa)
- Escitalopram (Lexapro)
- Fluoxetine (Prozac)
- Paroxetine (Paxil)
- Sertraline (Zoloft)
- Venlafaxine (Effexor)
- Relatively small numbers of randomized controlled trials using :
 - Diagnostic criteria
 - Adequate dose and time

Antidepressants for Elderly Major Depression

About half the studies do not separate from placebo.

Response Rates:

Drug: 35-72%

Placebo: 30-52%

Remission Rates:

Drug: 28-44%

Placebo: 18-38%

Issues:

1. High placebo response rates
2. Differences from placebo more significant in severely depressed
3. Generalization to real world
4. Limited data in medically frail, \geq age 75
5. No differences in response rates among agents
6. More drop-outs for TCAs

Antidepressants in Late-Life Major Depression

Some clinical issues in the elderly:

- Fluoxetine: Weight loss
- Paroxetine: Anticholinergic memory impairment
- Escitalopram/Citalopram/Sertraline: low P-450

- Larger facilities with fewer private pay patients have lower use of antidepressants
- Little information on dosing and response

Drugs Metabolized by P-450 2D6

Analgesics:

Codeine
Methadone
Tramadol

Alzheimer's drugs:

Donepezil
Galantamine

Antipsychotics:

Clozapine
Haloperidol
Quetiapine
Risperidone
Thioridazine

Benztropine

Cardiovascular drugs:

Diltiazem
Encainide
Metoprolol
Mexilitine
Nifedipine
Propranolol
Timolol

Dextromethorphan

Ondansetron

Tamoxifen

Tricyclic Antidepressants

SSRIs: Common and Infrequent Adverse Effects

Common

- GI: Nausea, anorexia, diarrhea
- Insomnia or somnolence
- Tremor
- Sexual

Infrequent

- SIADH: hyponatremia
- EPS and Hypofrontal syndrome
- Bleeding
- Bradycardia
- Serotonin syndrome (confusion, GI hyperactivity, myoclonus)
- Increased risk for hip fracture

DeAbajo FJ. BMJ 1999;319:1106-1109
Dalton SO, et al Arch Int Med 2003;163:59-64

Goldberg RJ. Arch Fam Med 1998;7:78-84

Schneeweiss S, et al. J Clin Psychopharmacol 2004;24:632-638

Stimulants for Elderly Depression

One double blind, placebo control study

N=13

Methylphenidate 10-20 mg/d

Significant HAM-D reductions
within 8 days.

Wallace AE, et al. Am J Psychiatry 1995;152:929-931

MAOIs for Elderly Depression

N=37, outpatients, 7 weeks, phenelzine

Georgotas A, et al. Am J Psychiatry **1987**;144:798

Selegiline transdermal patch:

Pooled data for N=198 \geq 65 years:

6-12 mg/24 hrs

No overall differences in effectiveness with
younger patients

AEs: rash, insomnia, postural hypotension

Tyramine-restriction not needed at 6 mgs

Amsterdam JD. J Clin Psychiatry 2003;64:208-214.

Bodkin JA, et al. Am J Psychiatry 2002;159:1869-1875

25

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Atypical Antipsychotics as Antidepressant Augmenters in Elderly

At this time, insufficient published
double blind data in the elderly

Combined Treatment

187 patients with recurrent episodes of major depression; average age 67

Recovered after Nortriptyline (NPT)
+ Interpersonal Psychotherapy (IPT)

Randomized and followed 3 years for relapse:

NPT + IPT: 20%

NPT + med clinic visits: 43%

Placebo + med clinic visits: 90%

Combined Treatment

116 patients > age 70.
Recovered after paroxetine (10-40 mg/d)
plus weekly interpersonal psychotherapy
(IPT) over 8 weeks.
Stabilized for 16 weeks, then randomized

Recurrence in 2 years

drug + visits	37%
drug + IPT	35%
placebo + visits	58%
placebo + IPT	68%

Pharmacogenomics emerging

The serotonin transporter gene has S or L alleles.

N=246, MDD, age ≥ 65

LL 32%, SS 22%, SL 45%

SS or SL did not respond to paroxetine.

No effect on response to mirtazapine, but L allele associated with higher mirtazapine discontinuation.

Murphy GM, et al. Arch Gen Psychiatry 2004;61:1163-9

ECT for Elderly Major Depression

Prospective, multi-site comparison of 268 pts.
Analysis by age groups: ≤ 59 , 60-74, ≥ 75

Response rates by age:

≤ 59 :	54%
60-74:	73%
≥ 75 :	67%

No differences in tolerance even though older pts
had more baseline cognitive impairment
and medical problems.

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Double Blind Studies of Depression Sub-types in The Elderly

Psychotic depression

Post-stroke depression

Depression with Parkinson's disease

Depression with Alzheimer's disease

Late-life Psychotic Depression

(One double blind study)

Nortriptyline (NTP) vs. NTP+perphenazine

10 weeks

N=36

Mean age 72

Conclusions:

No difference in resolution of depression or psychosis (44% response rate)

ECT proposed as Rx of choice

Post-stroke Depression

Literature review: 6 treatment and 3 prevention randomized, controlled trials between 1970-2004.

Treatment N= 314 (TCAs: NTP, IMI, DMI
SSRIs: CIT, FLU)

Prevention N=285 (NTP, FLU, SER)

Conclusion: Data suggests benefit for treatment (more TCA dropouts). Data inadequate re prevention.

Bhogal SK, et al. JAGS, 2005;53:1051-1057.
Almeida OP, et al. J Clin Psychiatry 2006;67:1104-09

Depression in Parkinson's Disease

Depressive symptoms account for 40% of observed variation in quality of life in PD.

3 randomized control trials (total N=106)
Nortriptyline (1980)
Citalopram (1998)
Sertraline (2003)

Conclusion: Insufficient evidence of effectiveness

Chabnam GN e al. Cochrane Database Syst Rev 2003;3:CD003465
Leentjens, AFG. J Geriatr Psychiatry Neurol 2004;17:120-126.

Depression with Alzheimer's Disease

9 placebo controlled trials (SSRIs and TCAs)
HAM-D outcomes

4/9 Positive:

Cognitive benefit: 0/9

ADL benefit: mixed

Lykestos CG and Olin J. Biol Psychiatry 2002;52:243-252

Issues: Definition, sample size

Behavioral Treatment of Depression in Dementia Patients

N=88; Randomized study

Nine 60 minute sessions with 6 month outcome follow-up

- 1) Increasing pleasant events and positive interactions
- 2) Helping care-giver problem-solving

Vs.

- 3) Non-specific information
- 4) Wait list control

Outcome: Groups 1 and 2 showed significant improvements in depression scores for both pts. and care-givers.

Teri L, et al. J Gerontol B Psychol Sci Soc Sci 1997;52:159-166

36

Collaborative Care Models Improve Outcome

IMPACT Study:

N=1801 \geq age 60 with major depression and/or dysthymia

Randomized to usual care or “depression care manager” with psychiatrist supervisor, plus education, med management support or brief psychotherapy.

12 months:

- response: 45% vs. 19%
- remission: 25% vs. 8%

Unutzer J, et al. JAMA
2002;288:2836-2845

PROSPECT Study:

N= 215 primary care pts. \geq age 60 with major depression

Randomized to usual care +/- care managers trained in IPT.

8 months:

- remission: 43% vs. 28%
- remission rates differed by site (IPT therapist effect?)
- Pts. with physical, emotional, or functional limitations or high anxiety did less well and should be referred

Bruce ML, et al. JAMA 2004;291:1081-109137

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Emergence of Collaborative Care Models

“Usual care” for major depression in the elderly in primary care is no longer acceptable.

Some Concluding Observations

- 1) Despite increasing antidepressant use, many elderly depressed patients have residual symptoms.
- 2) There may be also be overuse of antidepressants used to treat isolated symptoms such as fatigue, insomnia, or weight which are often secondary to medical illness.

Carlson WL, et al Harvard Review Psychiatry 2007:15:128-132

- 3) Psychotherapeutic needs are poorly studied and poorly understood.
- 4) Case management treatment model should be considered.

Some Concluding Observations

5) Though research evidence standards are difficult to meet, the following interventions may be important:

- Activity
- Exercise
- Simulated presence
- Socialization
- Video use
- Pets
- Music
- Massage
- Bright lights
- Aromatherapy

Snowden M, et al. J Am Geriatr Soc 2003;51:1305-1317.

40

Some Concluding Observations

- 6) The cardinal symptoms of depression may differ in the elderly and may show predominance of executive dysfunction (e.g., psychomotor retardation, reduced interest, lack of spontaneity, difficulties in shifting sets).
- 7) Geriatric depression: An interplay of vascular, dementing, and depressive illness.