# The Treatment of Psychosis in Late Life

Elsa M. Zayas, M.D., and George T. Grossberg, M.D.

The authors emphasize the need for careful differential diagnosis when symptoms of psychosis arise in patients over the age of 65 years. Prevalence of psychotic disorders in the elderly ranges from 0.2%–4.7% in community-based samples to 10% in a nursing home population and as high as 63% in a study of Alzheimer's patients. Risk factors associated with the development of psychotic symptoms and common causes of delirium are reviewed. Because age-related changes affect the pharmacokinetics of neuroleptics, the authors' treatment recommendations, which include the use of traditional and novel antipsychotics, take into account the higher risk of side effects in the elderly.

*(J Clin Psychiatry 1998;59[suppl 1]:5–10)*



Psychotic symptoms can be found throughout the life cycle. Psychosis as defined by DSM-IV is restricted to "delusions or prominent hallucinations, with the hallucinations occurring in the absence of insight into their pathological nature."[1] In this paper, we attempt to look at psychotic symptoms that arise in persons over the age of 65 years, how these symptoms are diagnosed and treated, and the side effects that arise from said treatments.

Kraepelin first coined the term *paraphrenia* to describe patients with a schizophrenic-like illness that developed after the age of 40.[2] Roth in 1955 modified the term to describe patients admitted to the hospital over the age of 65 who were diagnosed with delusions with or without auditory hallucinations.[3] The following diagnoses are found in the literature to refer to psychotic symptoms that arise for the first time in patients over 65: late onset schizophrenia, late onset psychotic disorder, delusional disorders, dementia with psychotic symptoms, and psychotic disorders not otherwise specified.

## EPIDEMIOLOGY

Geriatric data from the Epidemiologic Catchment Area study showed a 6-month prevalence for schizophrenia and schizophreniform disorders ranging from 0.2% to 0.9% at three sites; cognitive impairment including organic psychoses ranged from 16.8% to 23%.[4] Grief and Eastwood[5] found that 12% of all the cases reviewed of patients in different hospital settings diagnosed with psychotic symptoms met ICD-9 criteria for a paranoid diagnosis. Junginger et al.[6] reported the prevalence of psychotic disorders to be 10% in a nursing home population diagnosed using the Structural Clinical Interview for DSM-III-R (SCID). In a community-based sample in Sweden, Skoog et al.[7] found the prevalence of psychotic disorders to be 4.7%. Leuchter and Spar[8] reported a prevalence of 8% in a retrospective study of patients admitted to a geropsychiatry unit. A study done by Ballard et al.[9] found that, of 124 patients previously diagnosed with dementia, 67% had at least one psychotic symptom. In a study of 57 patients with Alzheimer's disease, Kotrla[10] found that 63% developed psychotic symptoms.

## RISK FACTORS

The risk factors that are described as being associated with the development of psychotic symptoms include the following: being cognitively impaired,[4,11,12] having hearing or visual impairment, early life trauma or abuse,[13] being female, single or never married, bedfast status,[11] and having a premorbid personality of paranoid or schizoid traits (Table 1).[14,15] Furthermore, Roth[16] in a review of the literature found that late-onset schizophrenia was frequently associated with long-standing severe bilateral deafness, most often caused by middle ear disease and cognitive impairment.

## NEUROBIOLOGY OF LATE-LIFE PSYCHOSES

Brain structure abnormalities have been reported to be associated with psychotic symptoms in the elderly. Brown, in a review of the literature,[17] reports that structural changes have included white matter hyperintensities,

*From the Department of Psychiatry and Human Behavior, Division of Geriatric Psychiatry, Saint Louis University School of Medicine, St. Louis, Mo.*

*Presented at the closed symposium "Clinical Outcomes in the Treatment of Schizophrenia," April 12, 1996, held in New Orleans, Louisiana, and sponsored by an unrestricted educational grant from Janssen Pharmaceutica, Inc.*

*Reprint requests to: George T. Grossberg, M.D., Professor and Chairman, Department of Psychiatry and Human Behavior, St. Louis University Health Science Center, 1221 S. Grand Blvd., St. Louis, MO 63104.*

Table 1. Risk Factors Associated with Late-Onset Psychosis

| |
|---|
| Cognitive impairment |
| Hearing impairment |
| Visual impairment |
| Early life trauma or abuse |
| Female gender |
| Single or never married |
| Bedfast status |
| Premorbid paranoid personality |
| Premorbid schizoid personality |

as assessed by magnetic resonance imaging of the brain, and focal brain disease of vascular origin. Flint et al.,[18] in a study of 21 subjects with paraphrenia, found that 5 subjects showed evidence of clinically unsuspected cerebral infarctions. Most of the lesions were subcortical or in the frontal lobes. This was felt to be consistent with lesions affecting limbic and subcortical pathways in the genesis of psychosis. Lesser et al.[19] found that two thirds of the subjects with late-onset psychotic disorders had abnormal brain imaging studies, and 50% of the subjects had white matter lesions greater than 5 $cm^2$ and/or lacunar infarctions. Miller et al.[20] found that when compared to healthy elderly subjects patients who developed their psychotic symptoms after the age of 45 were more likely to have cortical and subcortical white matter lesions and performed more poorly on neuropsychological tests, particularly on frontal lobe and memory abilities. Others report that functional studies show frontal and medial temporal lobe dysfunction.[17] Almeida et al.[21] found that late-life paraphrenics were more likely than controls to exhibit soft signs on neurologic examination.

## DIFFERENTIAL DIAGNOSIS (FIGURE 1)

When older patients present with new onset psychotic disorders, it is essential that the patient be evaluated for possible reversible causes of their symptoms. A thorough psychiatric history should be obtained to determine if this is truly a new onset psychotic disorder. One should assess the patients for the presence of any other psychiatric illness currently or in the past, for example, the presence of a mood disorder or cognitive disorder.[22] Patients should be evaluated for the presence of organic causes of their symptoms.

Delirium presents with acute mental status changes, which can be accompanied by psychotic symptoms. These may consist of hallucinations often of the visual type, and frequently with paranoid delusions. Common causes of delirium in the elderly include infections, especially urinary tract and upper respiratory; drugs, especially anticholinergics; electrolyte imbalance; arrhythmias and myocardial infarctions.[22] One should also evaluate for the presence of transient ischemic attacks, cerebral vascular accidents, and structural brain lesions such as tumors or subdural hematomas. Critically important in delirium is to evaluate the patient's medications as well as to look for the presence of withdrawal symptoms both from prescribed medications such as benzodiazepines and substances of potential abuse such as alcohol.

## TREATMENT OF PSYCHOSIS

The Omnibus Budget Reconciliation Act (OBRA 1987)[23] regulates the prescribing of neuroleptics in the nursing home. Prescribing recommendations include: (1) patients should be free of unnecessary drugs; (2) they should not be prescribed an antipsychotic unless a specific condition is documented; (3) attempts at dose reductions should be made every 6 months; (4) there should be drug holidays when possible; (5) behavioral programming should exist as an alternative. Prior to the implementation of OBRA, about 50% of nursing home residents were receiving neuroleptics.[24] Harrington[25] in a review of the literature found that, prior to the implementation of OBRA, the percentage of nursing home residents on antipsychotic therapy ranged from 22% to 86%. Currently, studies have shown that approximately 25% of patients on antipsychotic therapy in the nursing home can have their antipsychotics safely discontinued.[26] When nursing home staff are educated about neuroleptics and their appropriate use, Ray[27] found that the use of neuroleptics decreased by 72% in the study home compared to the control home.

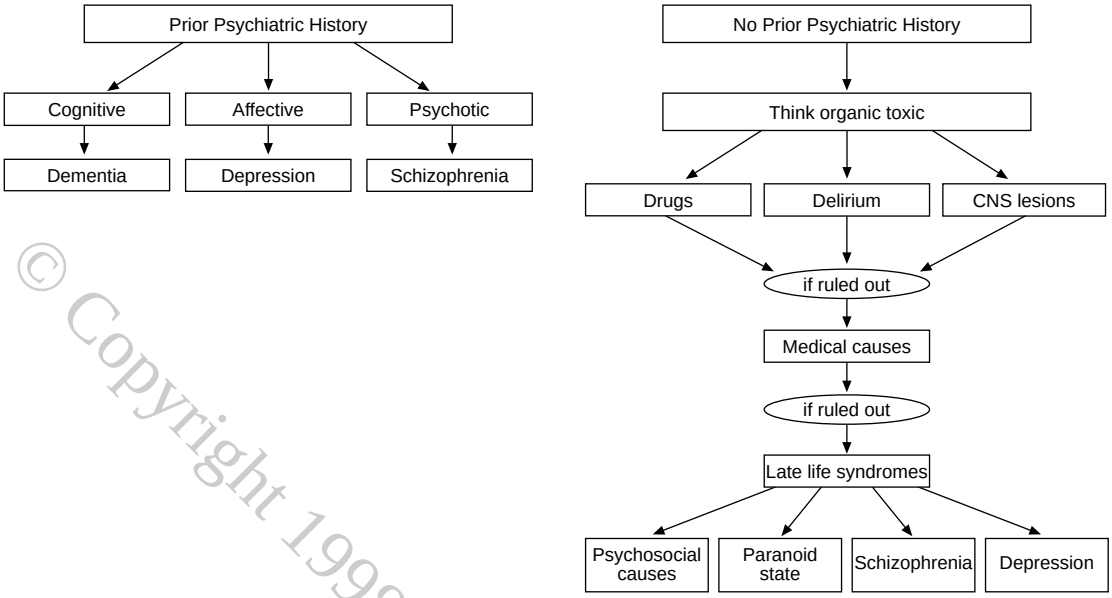
## PHARMACOKINETICS

Age-related changes can affect the pharmacokinetics of neuroleptics. Absorption can be altered by changes in gastric acidity, gastric emptying, splanchnic blood flow, and changes in absorption rate.[28] Antacids, and some compounds with huge absorbing surfaces like Metamucil, may delay absorption and delay the onset of action of some drugs.[24,29] Body composition changes in the elderly include a decrease in lean body mass and a decrease in total body water accompanied by an increase in total body fat.[28,29] There are decreases in liver mass, liver blood flow, and renal blood flow and function. The hepatic cytochrome p450 does not appear to undergo age-associated decline.[30]

Phenothiazines are lipophilic, well absorbed, and have extensive first-pass metabolism in the liver.[28] Lipid soluble substances are distributed in body fat. In the elderly, the volume of distribution is increased, because of the increase in total body fat. This results in an increase in the half-life of lipophilic substances.

The half-life of a drug is directly proportional to the volume of distribution divided by the clearance of said drug;[24] for this reason elderly patients should be given lower doses of lipophilic drugs. The antidopaminergic effects of estrogen may contribute to the need for lower doses of neuroleptics in women.[31]

Figure 1. Late-Life Psychosis: Diagnostic Tree*




*Adapted from reference 22.



Rabin et al.[32] reported that the response rate of patients with late-onset schizophrenia treated with neuroleptics was 57%. Pearlson et al.[33] reported a response rate of 75% in a similar group. Jeste and colleagues[14] found that treatment is more effective on positive than negative symptoms in both early- and late-onset schizophrenia. Rockwell and associates[34] found that patients with schizophrenia responded better to treatment than patients with somatic delusional disorders. In contrast, Flint and colleagues[35] reported that patients with somatic delusions and schizophrenia responded better to treatment with neuroleptics.

The most frequently prescribed medications for the treatment of psychosis are neuroleptics. Neuroleptics can be classified as high, intermediate, and low potency. High-potency neuroleptics are, for example, haloperidol, fluphenazine, and thiothixene; intermediate-potency neuroleptics are perphenazine, loxapine, and molindone; and low-potency agents are chlorpromazine and thioridazine. Newer antipsychotics include risperidone and clozapine.[24]

High-potency neuroleptics have higher affinity for the dopamine receptors and less affinity for the alpha and muscarinic receptors. The high-potency neuroleptics tend to cause extrapyramidal or parkinsonian symptoms, akathisia, acute dyskinesia, and acute dystonic reactions. Akathisia can be misdiagnosed as anxiety or agitation in the elderly.

The lower potency neuroleptics have greater affinity for the histaminic, $\alpha_1$-adrenergic, and muscarinic receptors. Their muscarinic activity may cause urinary retention, dry mouth, and constipation. They should be used with precaution in patients with closed-angle glaucoma. Their activity on histaminic receptors can cause sedation and hypotension. Their affinity for the $\alpha$-adrenergic receptors causes orthostatic hypotension. Elderly patients are very sensitive to all of the above-mentioned side effects. This must be considered prior to the administration of a neuroleptic. Pollack and Mulsant[24] recommend the use of intermediate-potency neuroleptics in the elderly, for example, perphenazine, loxapine, or molindone. In a review, he also reports a prescribed average dose of 200 mg/day of chlorpromazine equivalents. Mulsant et al.[36] in their review of the literature recommend the use of intermediate-potency neuroleptics and advocate starting at half the initial neuroleptic dose used in younger patients. Titration should be based on response and monitoring for side effects.

We recommend the use of high-potency neuroleptics at low doses, for example, haloperidol at a starting dose of 0.25 mg a.m. and h.s., and titrating to a maximum dose of 2 mg/day (Table 2). For an intermediate-potency neuroleptic, we recommend starting perphenazine at a dose of 2 mg/day, and titrating to a maximum dose of 12 mg/day. We tend not to recommend the use of low-potency neuroleptics as these can cause both peripheral as well as central anticholinergic side effects. They may produce confusion as well as increase the risk of falls in the elderly secondary to their side effects of sedation and orthostasis.

## CLOZAPINE

Clozapine is an atypical antipsychotic. Compared with the typical neuroleptics, it has a greater affinity for $D_2$ receptors and is more selective for mesolimbic and mesocortical pathways. Clozapine is reported to have the

following side effects: drowsiness, salivation, tachycardia, dizziness, constipation, nausea/vomiting, hypotension, sweating, dry mouth, tremor, seizure, and agranulocytosis. It is required that patients prescribed clozapine have their cellular blood count monitored weekly, and physicians must monitor total white count as well as neutrophil counts. Clozapine should be used after patients have been treated and have failed two trials of conventional neuroleptics. Failure can be defined as a lack of symptom response on a therapeutic dose and/or the emergence of side effects such as parkinsonism or tardive dyskinesia.

Pitner et al.[37] reported their experience with clozapine in four elderly patients with psychotic symptoms. Two of the patients did have relief of their psychotic symptoms. Falls, symptomatic bradycardia, and delirium were reported, and the patients with moderate-to-severe dementia experienced these symptoms after the first dose. The authors recommended a starting dose of 6.25 mg/day, with weekly titration. Oberholzer et al.,[38] in their study of 18 psychogeriatric patients with dementia, reported that four patients had to discontinue the drug because of side effects. They found no leukopenia, and the mean daily dose was 53.2 mg. In a study done by Chengappa et al.[39] looking at the use of clozapine in elderly women, the side effects more frequently seen were postural hypotension, excessive salivation, and sedation. One patient developed agranulocytosis. They reported that two patients had a better response to clozapine than to conventional neuroleptics. In a prospective open-label trial, Factor and colleagues[40] treated 17 patients with Parkinson's disease complicated by psychosis with doses of clozapine ranging from 6.25 to 150 mg/day and reported improvement in psychotic and motor symptoms.

## RISPERIDONE

Risperidone, a benzisoxazole, is a novel antipsychotic. It is a potent antagonist of the 5-HT receptor as well as having $D_2$ blocking action. It is thought to cause fewer extrapyramidal symptoms than older high-potency antipsychotics.[41] It is also reported to have efficacy for both the positive and negative symptoms of schizophrenia. Side effects include orthostatic hypotension, sedation, fatigue, and palpitations. We often recommend starting at 0.25 mg a.m. and h.s. and titrating the dose slowly to a ceiling of 2 mg/day in two divided doses.[42] Elderly psychotic patients who are naive to neuroleptics will do best with low doses of risperidone (2 mg/day or less). Those who have been taking neuroleptics may require higher dosing.

Raheja and colleagues[43] reported on two elderly subjects treated with a dose of 3 mg/day of risperidone who had no side effects and no changes in their ECG or laboratory findings. Jeanblanc and Davis[44] reported using risperidone in five elderly patients at a starting dose of 0.5 mg b.i.d. and noticing antipsychotic effects in 10 days.

Table 2. Geriatric Dosing of Representative Neuroleptics*

| Generic Name | Dosage (mg/d) |
|---|---|
| Haloperidol | 0.25–2 |
| Thiothixene | 1–5 |
| Loxapine | 2.5–15 |
| Clozapine | 6.5–150 |
| Risperidone | 0.5–2 |

*Adapted from reference 42.

Madhusoodanan et al.[45] reported having used risperidone to treat 11 geriatric patients with psychotic symptoms; 8 patients responded, 1 did not, and 2 had to discontinue treatment because of hypotension and dizziness. Of the 8 patients who responded, 7 had improvement in both positive and negative symptoms. Four of the patients had decreases in their extrapyramidal symptoms and symptoms of tardive dyskinesia.

Risperidone appears to be a safe and effective treatment for psychotic symptoms in the elderly. It may be particularly suited for those who have not responded to traditional neuroleptics, those who could not tolerate older agents secondary to side effects, and older patients with preexisting parkinsonism with psychosis. Risperidone is currently being studied in the behavioral disturbances of dementia, namely psychosis as well as agitation.

## SIDE EFFECTS OF NEUROLEPTICS (TABLE 3)

Parkinsonism is a frequent neuroleptic side effect that has a triad of symptoms: resting tremor, rigidity, and bradykinesia. The elderly are particularly vulnerable to developing parkinsonism.[46] As well, patients with Lewy body dementia are also exquisitely sensitive to the side effects of neuroleptics.[47] Geriatric patients, while being treated with neuroleptics, were 5.4 times more likely to begin on an antiparkinsonian medication for the above side effects.[48] This side effect may be treated by reducing the neuroleptic dosage, and/or using anticholinergics such as benztropine at a dose of 0.5 mg to 1 mg/day. One should be careful when using antiparkinsonian agents as they can cause confusion and delirium in the elderly as well as a variety of annoying peripheral anticholinergic side effects.

Akathisia is characterized by increased restlessness, psychomotor activity, and agitation and an inability to sit still.[28] This is a frequent side effect that can be mistaken for increasing agitation and or worsening agitation especially in the demented elderly.[29] Akathisia can be treated with β-blockers, benzodiazepines, and anticholinergics.[28] Perhaps the most efficacious are the β-blockers, with a recommended dose of propranolol being 30–80 mg/day.[49]

Tardive dyskinesia consists of abnormal involuntary choreiform movements. This movement disorder is more frequently observed in the peribuccal, periocular areas, but

Table 3. Side Effects of Neoroleptics

| Receptors | Side Effects |
|---|---|
| Dopaminergic | Parkinsonism<br>Akathisia<br>Dystonias<br>Tardive dyskinesia |
| Histaminic | Sedation<br>Weight gain |
| Alpha-Adrenergic | Orthostatic hypotension |
| Muscarinic | Sedation<br>Delirium<br>Falls<br>Constipation<br>Urinary retention |
| Quinidine-like | Arrhythmias<br>Torsades de pointes |

can be seen in the hands, legs, torso, and feet. A significant risk factor is advanced age. Other associated risk factors are previous history of drug-induced parkinsonism, organic brain disease, and female sex. Jeste et al. in a prospective longitudinal study of 266 patients who were over the age of 45 found the cumulative incidence of tardive dyskinesia to be 26%, 52%, and 60% after 1, 2, and 3 years, respectively.[50] The principal risk factors for the development of tardive dyskinesia were the duration of prior neuroleptic use at baseline, cumulative amount of high-potency neuroleptics, history of alcohol abuse/dependence, and the presence of borderline or minimal dyskinesia on initial assessment.

Other side effects may be secondary to the muscarinic or quinidine-like effects of neuroleptics. These include sedation, delirium, falls, and cardiac conduction abnormalities. Sedation can lead to confusion and falls. Orthostasis can also cause falls, placing the elderly patient at a higher risk for hip fractures. Falls that lead to hip fractures are a leading cause of hospitalization and death in the elderly[51]; 14% of hip fractures in the elderly have been attributed to the use of psychotropics.[25] Neuroleptics can cause the emergence of cardiac arrhythmias. Haloperidol is reported to cause QTc prolongation and torsades de pointes. Recent cases in the literature have reported on the association between high-dose intravenous haloperidol and the occurrence of QTc prolongation and torsades de pointes.[52,53]

## CONCLUSION

This article has attempted to review psychotic disorders that occur in older patients. Psychosis is a symptom that is sometimes difficult to diagnose and treat. We have reviewed current treatment strategies, which include the use of traditional and novel antipsychotics, and have given some dosing guidelines. One must keep in mind the differential diagnosis, treatment strategies, and potential side effects that these drugs can cause in the elderly, so as to maximize benefits of treatment while minimizing side effects.

*Drug names:* benztropine (Cogentin and others), chlorpromazine (Thorazine and others), clozapine (Clozaril), fluphenazine (Prolixin and others), haloperidol (Haldol and others), loxapine (Loxitane), molindone (Moban), perphenazine (Trilafon), propranolol (Inderal and others), risperidone (Risperdal), thioridazine (mellaril and others), thiothixene (Navane).

## REFERENCES


1. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition. Washington, DC: American Psychiatric Association; 1994
2. Kreapelin E; Barclay EM, trans. Dementia Preacox and Paraphrenia (1919). New York, NY: Robert E. Kreiger; 1971
3. Roth M. The natural history of mental disorders in old age. J Ment Sci 1955;101:281–301
4. Myers JK, Weissman MM, Tischler G. Six month prevalence of psychiatric disorders in three communities. Arch Gen Psychiatry 1984;41:959–970
5. Grief C, Eastwood RM. Paranoid disorders in the elderly. J Geriatric Psychiatry 1993;8:681–684
6. Junginger J, Phelan E, Cherry K, et al. Prevalence of psychopathology in elderly persons in nursing homes and in the community. Hosp Community Psychiatry 1993;44:381–383
7. Skoog I, Nilsson L, Landahl S, et al. Mental disorders and the use of psychotropic drugs in an 85-year-old urban population. Int Psychogeriatr 1993;5:33–48
8. Leuchter AF, Spar JE. The late-onset psychoses: clinical and diagnostic features. Journal Nerv Ment Dis 1985;173:488–494
9. Ballard CG, Bannister CL, Patel A, et al. Classification of psychotic symptoms in demented sufferers. Acta Psychiatr Scand 1995;92:63–68
10. Kotrla KJ, Chacko RC, Harper RG, et al. Clinical variables associated with psychosis in Alzheimer's disease. Am J Psychiatry 1995;152:1377–1379
11. Ohi G, Kai I, Ichikawa S, et al. Psychotic manifestation in the bed-fast elderly. Human Ergol 1989;18:237–240
12. Varner RV, Gaitz CM. Schizophrenia and paranoid disorders in the aged. Psychiatr Clin North Am 1982;5:107–118
13. Gurian BS, Wexler D, Baker EH. Late-life paranoia: possible association with early trauma and infertility. Int J Geriatric Psychiatry 1992;7:277–284
14. Jeste DV, Harris MJ, Krull A, et al. Clinical and neuropsychological characteristics of patients with late-onset schizophrenia. Am J Psychiatry 1995; 152:722–730
15. Eastwood MR, Corbin SL, Reed M, et al. Acquired hearing loss and psychiatric illness: an estimate of prevalence and co-morbidity in a geriatric setting. Br J Psychiatry 1985;147:552–556
16. Roth M. The psychiatric disorders of late life. Psychiatr Ann 1976;9: 417–445
17. Brown FW. The neurobiology of late-life psychosis. Crit Rev Neurobiol 1993;7:275–289
18. Flint AJ, Rifat SL, Eastwood MR. Late-onset paranoia: distinct from paraphrenia? Int J Geriatric Psychiatry 1991;6:103–109
19. Lesser IM, Jeste DV, Boone KB, et al. Late-onset psychotic disorder, not otherwise specified: clinical and neuroimaging findings. Biol Psychiatry 1992;31:419–423
20. Miller BL, Lesser AM, Boone KB, et al. Brain lesions and cognitive function in late-life psychosis. Br J Psychiatry 1991;158:76–82
21. Almeida OP, Howard RJ, Levy R, et al. Psychotic states arising in late-life (late paraphrenia); the role of risk factors. Br J Psychiatry 1995;166: 215–228
22. Grossberg GT, Manepalli J. The older patient with psychotic symptoms. Psychiatric Services 1995;46:55–59
23. Burke WJ. Neuroleptic drug use in the nursing home: the impact of OBRA. Am Fam Physician 1991;43:2125–2130
24. Pollock B, Mulsant BH. Antipsychotics in older patients: a safety perspective. Drugs Aging 1995;6:3312–3323
25. Harrington C, Tompkin C, Curtis M, et al. Psychotropic drug-use in long term care facilities: a review of the literature. Gerontologist 1992;32; 822–833
26. Courtney DL. Effects of antipsychotic withdrawal in elderly nursing home residents. Kans Med 1994;95 246–247
27. Ray WA, Taylor JA, Meador KG, et al. Reducing antipsychotic drug use in nursing homes: a controlled trial of provider education. Arch Intern Med 1993;153:713–721

28. Gregory C, Mckenna P. Pharmacological management of schizophrenia in older patients. Drugs Aging 1994;5:254–262
29. Wise MG, Tierney J. Psychopharmacology in the elderly. J Louisiana State Med Soc 1992;144:471–476
30. Pollock BG, Perel JM, Altieri L. et al. Debrisoquine hydroxylation phenotyping in geriatric psychopharmacology. Psychopharmacol Bull 1992;28:163–168
31. Yonkers KA, Kando JC, Cole JO, et al. Gender differences in pharmacokinetics and pharmacodynamics of psychotropic medication. Am J Psychiatry 1992;149:587–595
32. Rabin P, Pauker S, Thomas J. Can schizophrenia begin after age 44? Compr Psychiatry 1984;25:290–293
33. Pearlson GD, Kreger L, Rabins PV, et al. A chart review study of late onset and early onset schizophrenia. Am J Psychiatry 1989;146:1568–1574
34. Rockwell E, Krull AJ, Dimsdale J, et al. Late-onset psychosis with somatic delusions. Psychosomatics 1994;35:66–72
35. Flint AJ, Rifat SL, Eastwood MR. Late-onset psychosis with somatic delusions [letter]. Psychosomatics 1994;35:66–72
36. Mulsant BH, Gershon S. Neuroleptics in the treatment of psychosis in late-life: a rational approach. Int J Geriatric Psychiatry 1993;8:979–992
37. Pitner JK, Mintzer JE, Pennypacker LC, et al. Efficacy and adverse effects of clozapine in four elderly psychotic patients. J Clin Psychiatry 1995; 56:180–185
38. Oberholzer AF, Hendriksen C, Monsch AU, et al. Safety and effectiveness of low-dose clozapine in psychogeriatric patients: a preliminary study. Int Psychogeriatr 1992;4:187–195
39. Chengappa KNR, Baker RW, Kreinbrook SB, et al. Clozapine use in female geriatric patients with psychoses. J Geriatr Psychiatry Neurol 1995;8: 12–15
40. Factor SA, Brown D, Molho ES, et al. Clozapine: a 2-year open trial in Parkinson's disease with psychosis. Neurology 1994;44:544–546
41. Grossberg G. The older patient with psychotic symptoms. Psychiatr Services 1995;46:55–60
42. Zayas EM, Grossberg GT. Treating the agitated Alzheimer patient. J Clin Psychiatry. 1996;57(suppl 7):46–51
43. Raheja RK, Bharwani I, Penetrante AE. Efficacy of risperidone for behavioral disorders in the elderly: a clinical observation. J Geriatr Psychiatry Neurol 1995:8:159–161
44. Jeanblanc W, Davis YB. Risperidone for treating dementia-associated aggression [letter]. Am J Psychiatry 1995;152:1239
45. Madhusoodanan S, Brenner R, Araujo L, et al. Efficacy of risperidone treatment for psychoses associated with schizophrenia, schizoaffective disorder, bipolar disorder, or senile dementia in 11 geriatric patients: a case series. J Clin Psychiatry 1995;56:514–518
46. Wilson JA, MacLennan WJ. Drug induced Parkinsonism in elderly patients [review]. Age Ageing 1989;18:208–210
47. McKeith I, Fairbain A, Perry R, et al. Neuroleptic sensitivity in patients with senile dementia of Lewy body type. Br Med J 1992;305:673–678
48. Avorn J, Bohn RL, Mogun H, et al. Neuroleptic drug exposure and treatment of Parkinsonism in the elderly; a case-control study. Am J Med 1995; 99:48–54
49. Tonda ME, Guthrie SK. Treatment of acute neuroleptic-induced movement disorders. Pharmacotherapy 1994;14:543–560
50. Jeste DV, Caligiuri MP, Paulsen JS, et al. Risk of tardive dyskinesia in older patients. Arch Gen Psychiatry 1995;52:756–765
51. Ray WA. Psychotropic drugs and injuries among the elderly: a review. J Clin Psychopharmacol 1992;12:386–396
52. Di Salvo TG, O'Gara PT. Torsade de pointes caused by high-dose intravenous haloperidol in cardiac patients. Clin Cardiol 1995;18:285–290
53. Hunt N, Stern TA. The association between intravenous haloperidol and Torsades de Pointes: three cases and a literature review. Psychosomatics 1995;36:541–549