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Delusions, hallucinations, and other psychotic symptoms in late life may be more common than previously thought. A Swedish investigation (Ostling et al. 2007) found that the prevalence of any psychotic symptom in a nondemented population-based sample of 95-year-old individuals was 7.1%, with 6.7% experiencing hallucinations, 10.4% having delusions, and 0.6% experiencing paranoid ideation. In this chapter, we review the epidemiology, presentation, diagnosis, and treatment of chronic late-life psychotic disorders not secondary to a mood disorder or a general medical condition other than dementia. Thus, we discuss early-onset schizophrenia, late-onset schizophrenia, and very-late-onset schizophrenia-like psychosis (onset after age 60); delusional disorder; psychosis of Alzheimer's disease (AD); and psychosis associated with other dementias.

AUTHOR: Above paragraph, sentence "In this chapter": Note addition of "diagnosis" to include new section (which was called a "box" and mentions only suspiciousness and paranoia). OK?

Psychotic Disorders in Late Life

Schizophrenia

Early-Onset Schizophrenia

The prevalence of schizophrenia among adults ages 45–64 is approximately 0.6%, and prevalence estimates for schizophrenia among elderly individuals range from 0.1% to 0.5%. Typically, individuals with schizophrenia develop the disease in the second or third decade of life (American Psychiatric Association 2000). Although mortality rates in general, and suicide and homicide rates in particular, are higher among individuals with schizophrenia than in the general population, many of these patients with early-onset schizophrenia are now living into older adulthood. Thus, most older adults with schizophrenia typically have had an early onset of the disease and have a chronic course of illness spanning several decades.

Longitudinal follow-up of schizophrenia patients indicates considerable heterogeneity of outcome. A minority of patients experience remission of both positive and negative symptoms. Auslander and Jeste (2004) reported that in approximately 10% of patients, the criteria for remission may be met, and although the course of illness over time is unchanged in the majority of patients, there is generally an improvement in positive symptoms.

Cognition in older schizophrenia patients. Among community-dwelling older outpatients with schizophrenia, cognitive functioning seems to remain relatively stable other than the changes expected from normal aging (Harvey et al. 1999; Heaton et al. 2001). In general, cognitive functioning is better in persons with later ages at onset (Rajji et al. 2009).

Depression in older schizophrenia patients. Studies have shown depressive symptoms to be distinct from negative symptoms. Depression is also a major predictor of suicidality in older patients with schizophrenia. Recent studies of depression in the this population highlight the role of subsyndromal depression in increasing morbidity (Zisook et al. 2007).

Functional capacity. The level of functional impairment varies considerably among older adults with schizophrenia (Palmer et al. 2003). In general, worse neuropsychological test performance, lower educational level, and neg-

ative symptoms, but not positive symptoms, are associated with poorer functional capacity in older outpatients with schizophrenia.

Late-Onset Schizophrenia

A literature review found that approximately 23% of patients with schizophrenia reportedly had onset of the disorder after age 40, with 3% being older than 60 (Harris and Jeste 1988). One investigation of first-contact patients reported that 29% of the patients had onset after age 44, with 12% reporting onset after age 64 (Jeste et al. 1997). The consensus statement by the International Late-Onset Schizophrenia Group (Howard et al. 2000) suggested that schizophrenia with an onset after age 40 should be called "late-onset schizophrenia" and considered a subtype of schizophrenia rather than a related disorder.

Risk factors and clinical presentation are similar between individuals with early- and late-onset schizophrenia. The self-reported proportion of individuals with positive family history of schizophrenia (10%–15%), genetic risk, and levels of childhood maladjustment is similar in earlier- and late-onset patients (Sachdev et al. 1999). A long-term neuropsychological follow-up of a group of late-onset schizophrenia patients found no evidence of cognitive decline, suggesting a neurodevelopmental rather than a neurodegenerative process (Palmer et al. 2003).

Women predominate among individuals with onset of schizophrenia in middle to late life. It has been speculated that estrogen may serve as an endogenous antipsychotic, masking schizophrenic symptoms in vulnerable women until after menopause, but treatments targeting estrogen have not been found effective (Seeman 1996).

In a study conducted at our center, we used a comprehensive battery of measurements of psychopathology, cognition, and functioning to compare 110 subjects with late-onset schizophrenia with 744 early-onset schizophrenia patients. In our study, we noted that persons with late-onset schizophrenia were more likely to be women and to have less severe positive symptoms and lower scores on measures of general psychopathology. We also noted that patients with late-onset schizophrenia did better on cognitive tasks measuring abstraction, cognitive flexibility, and verbal memory. Patients with late-onset schizophrenia had better physical and emotional functioning and were receiving lower average dosages of antipsychotic medications (Vahia et al. 2010). A

meta-analysis also noted that cognitive deficits in late-onset schizophrenia are specific rather than just a function of age (Rajji et al. 2009).

Very-Late-Onset Schizophrenia-Like Psychosis

The consensus statement by the International Late-Onset Schizophrenia Group proposed the diagnostic term *very-late-onset schizophrenia-like psychosis* (VLOSLP) for patients in whom onset of psychosis is after age 60. Table 6–1 compares risk factors for and clinical features of early-onset schizophrenia, late-onset schizophrenia, and VLOSLP. VLOSLP may be difficult to diagnose clinically because its clinical picture can be confused with other conditions such as delirium or psychosis due to underlying medical illness. Nevertheless, new-onset primary psychotic symptoms have been described in adults as old as 100 (Cervantes et al. 2006).

Factors distinguishing VLOSLP patients from "true" schizophrenia patients include a lower genetic load, less evidence of early childhood maladjustment, a relative lack of thought disorder and negative symptoms (including blunted affect), greater risk of tardive dyskinesia (TD), and evidence of a neurodegenerative rather than a neurodevelopmental process (Moore et al. 2006; Palmer et al. 2003).

Clinical vigilance must be exercised when the clinician is treating apparent primary-onset psychotic symptoms in older patients, and "organic" causes should be meticulously ruled out.

AUTHOR: Above paragraph: "In summary" has been deleted; however, please consider whether sentence should be moved to "Diagnostic Approach" or "Treatment" section below. Thanks.

Delusional Disorder

The essential feature of a delusional disorder is a nonbizarre delusion (e.g., persecutory, somatic, erotomanic, grandiose, or jealous) without prominent auditory or visual hallucinations. Symptoms must be present for at least 1 month. When delusional disorder arises in late life, basic personality features, intellectual performance, and occupational function are preserved, but social functioning is compromised. To diagnose delusional disorder, the clinician must rule out other organic causes (Evans et al. 1996).

Table 6–1. Comparison of early-onset schizophrenia, late-onset schizophrenia, and very-late-onset schizophrenia-like psychosis (VLOSLP)

	Early-onset schizophrenia	Late-onset schizophrenia	VLOSLP
Age at onset	Before 40	Middle age (~40–60)	Late life (>60)
Female preponderance	−	+	++
Negative symptoms	++	+	−
Minor physical anomalies	+	+	−
Neuropsychological impairment			
Learning	++	+	?++
Retention	−	−	?++
Progressive cognitive deterioration	−	−	++
Brain structure abnormalities (e.g., strokes, tumors)	−	−	++
Family history of schizophrenia	+	+	−
Early childhood maladjustment	+	+	−
Daily antipsychotic dose	++	+	+
Risk of tardive dyskinesia	+	+	++

Note. + = mildly present; ++ = strongly present; ?++ = probably strongly present, but limited data exist; − = absent.
Source. Adapted from Palmer et al. 2001.

The prevalence of delusional disorder according to DSM-IV-TR (American Psychiatric Association 2000) is 0.03% and is slightly higher among women than among men. It typically first appears in middle to late adulthood, with an average age at onset of 40–49 for men and 60–69 for women (Copeland et al. 1998).

AUTHOR: Paragraph above: DSM-5 lists about 0.2% as prevalence of delusional disorder. Update to that source?

Risk factors for delusional disorder include a family history of schizophrenia and avoidant, paranoid, or schizoid personality disorder (Kendler and Davis 1981). Evans et al. (1996) compared middle-aged and older patients with schizophrenia and delusional disorder and found no differences in neuropsychological impairment but more severe psychopathology associated with delusional disorder.

Psychosis of Alzheimer's Disease

Ropacki and Jeste (2005) estimated the median prevalence of psychosis in AD to be about 41% (range = 12.2%–74.1%) in their review of 55 studies. Psychosis is associated with more rapid cognitive decline. Some studies have reported a significant association between psychosis and age, age at onset of AD, and illness duration. Paulsen et al. (2000) found a cumulative incidence of psychotic symptoms of 20% at 1 year, 36% at 2 years, 50% at 3 years, and 51% at 4 years in a large sample of patients with probable AD. Active suicidal ideation and history of psychosis are rare. Because psychotic symptoms in dementia patients tend to remit in the late stages of the disease, very-long-term maintenance therapy with antipsychotics is typically unnecessary.

AD patients with and without psychosis differ in several important ways. Neuropsychologically, AD patients with psychosis show greater impairment in executive functioning, more rapid cognitive decline, and a greater prevalence of extrapyramidal symptoms (EPS) than do AD patients without psychosis. Neuropathologically, dementia patients with psychosis showed increased neurodegenerative changes in the cortex, increased norepinephrine in subcortical regions, and reduced serotonin levels in both cortical and subcortical areas.

Jeste and Finkel (2000) recommended specific diagnostic criteria for psychosis of AD: presence of visual or auditory hallucinations or delusions, a primary diagnosis of AD, and duration (at least 1 month) and time of onset (symptoms of AD preceding those of psychosis) criteria. Alternative causes of

psychosis must be excluded, and sufficient functional impairment should be present for this diagnosis to be made.

Psychosis in Other Dementias

Psychosis is also common in other dementias. Visual hallucinations and secondary delusions are common in Lewy body disease, and vascular dementia also may be accompanied by delusions or hallucinations (Schneider et al. 2006). Naimark et al. (1996) found psychotic symptoms in approximately one-third of a sample of patients with Parkinson's disease, with hallucinations being more common than delusions. Psychosis in frontotemporal dementias is poorly characterized but may be as common as that in AD.

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2) Please verify that approach applies only to "suspiciousness and paranoia."

Diagnostic Approach to Patients With New Onset of Suspiciousness and Paranoia[1]

A careful psychiatric evaluation and history are key components of the initial approach to the suspicious or paranoid patient. Interviews of family members may be necessary for establishing a diagnosis, particularly if delusions and agitation are present. Part of the task of the clinician is to determine whether the suspicious behavior is warranted. Older adults are occasionally abused or neglected; therefore, confronting family members about a patient's accusations of harm or neglect is often part of the assessment. If, after such a confrontation, the clinician is not convinced that the accusations are totally explained by the delusion, a social services agency or department should be requested to investigate further.

[1]We wish to thank Lisa Gwyther, M.S.W., and Harold Goforth, M.D., for providing this section on diagnostic approach to patients with new onset of suspiciousness and paranoia.

Challenging the delusional patient usually is not recommended. It is important to seek an understanding of the patient's thought processes, so providing an atmosphere of acceptance (although not necessarily agreement) will allow the patient to express his or her beliefs and feelings. Reassurance should be provided in a manner conveying that although the clinician may not fully understand the whole situation, the goal is for the patient to feel better and more secure.

A laboratory workup is usually needed in new cases of paranoia to rule out an organic delusional syndrome. Blood chemistry, a complete blood count, and a thyroid profile should be obtained. If respiratory symptoms are present, a chest X ray may be needed. A computed tomography or magnetic resonance imaging brain scan may be indicated, especially if cognitive impairment or focal neurological findings are present. Because suspiciousness is often associated with sensory impairment, particularly visual and auditory deficits, audiometric and visual testing may identify potential areas for further intervention.

Treatment

Although conventional agents substantially improved the positive symptoms of schizophrenia (e.g., hallucinations and delusions), several treatment liabilities, such as movement disorders, sedation, orthostatic hypotension, elevated prolactin concentrations, and most notably TD, have been recognized over the years. Atypical antipsychotics have been linked to increased risk of metabolic dysfunction, including diabetes, dyslipidemia, and obesity, leading to a worsened cardiovascular risk profile. In elderly patients with dementia, atypical antipsychotics have been associated with increased risk of cerebrovascular adverse events and mortality compared with placebo, leading pharmaceutical regulatory agencies to issue warnings about their use. However, lack of evidence-based alternatives restricts clinicians to off-label treatments, which must be used with caution and close monitoring. Psychosocial treatments for older adults with psychosis show promise as adjunctive treatments.

Schizophrenia and Delusional Disorder

Pharmacological Treatment

Pharmacotherapy for schizophrenia and delusional disorder in older adults is restricted by a paucity of randomized placebo-controlled, double-blinded clinical trials in this population. Maintenance pharmacotherapy is usually required for older patients with schizophrenia because of risk of relapse. Older patients are at higher risk for adverse antipsychotic effects as a result of age-related pharmacokinetic and pharmacodynamic factors, coexisting medical illnesses, and concomitant medications. Therefore, the recommended starting and maintenance doses of antipsychotics in older individuals are 50% and 25%–30% lower than the usual younger adult doses, respectively (American Psychiatric Association 1997).

AUTHOR: Paragraph above: last sentence: Please confirm in newer APA practice guideline 2004, with guideline watch from 2009 (http://psychiatryonline.org/guidelines.aspx) and update reference as needed.

Few efficacy comparisons between conventional and atypical antipsychotics have been done in patients with schizophrenia older than 65 (Jeste et al. 1999). The National Institute of Mental Health's Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) study, which included adults ages 18–65 years, found no significant differences in effectiveness between the conventional antipsychotic perphenazine and the atypical antipsychotics risperidone, olanzapine, quetiapine, or ziprasidone, but it is unknown how these findings would translate to patients older than 65 (Lieberman et al. 2005).

Use of conventional or typical antipsychotics in this population is problematic given the higher incidence of TD in older patients. Aging appears to be the most important risk factor for the development of TD (American Psychiatric Association 2000; Yassa and Nair 1992). Atypical antipsychotics have a less favorable side-effect profile in terms of metabolic function. Common metabolic side effects include excessive weight gain and obesity, glucose intolerance, new-onset type 2 diabetes mellitus, diabetic ketoacidosis, and dyslipidemia (Jin et al. 2004). Although no guidelines are available for management of these side effects specifically in older patients with schizophrenia, monitor-

ing recommendations of the American Diabetes Association et al. (2004) are potentially applicable. Because elderly patients tend to be at higher risk for cardiovascular disease than are younger patients, closer monitoring would be necessary for older adults.

The only large-scale randomized, double-blind, controlled trial comparing two atypical antipsychotics in adults older than 60 was Jeste et al.'s (2003) multisite international study of risperidone and olanzapine. In that trial, 175 patients with schizophrenia or schizoaffective disorder ages 60 years and older were randomly assigned to receive risperidone (1–3 mg/day; median, 2 mg/day) or olanzapine (5–20 mg/day; median, 10 mg/day). Both groups had significant improvement in symptoms and reduction in EPS rating scale scores. Clinically relevant weight gain was significantly less frequent in patients taking risperidone.

Given the dearth of randomized controlled data, Alexopoulos et al. (2004) conducted a consensus survey of 48 American experts on antipsychotic treatment in older adults. The experts' first-line recommendation for late-life schizophrenia was risperidone (1.25–3.5 mg/day). The second-line recommendations included quetiapine (100–300 mg/day), olanzapine (7.5–15 mg/day), and aripiprazole (15–30 mg/day). Support for the use of clozapine, ziprasidone, and high-potency conventional antipsychotics was limited. In a more recent trial (Scott et al. 2010), atypical antipsychotics at geriatric doses were effective in treating VLOSLP as well.

Given the data on the increased risk of strokes and mortality in elderly patients with dementia treated with atypical antipsychotics (Gill et al. 2005) and the consequent U.S. Food and Drug Administration (FDA) black box warnings (discussed in the subsection "Psychosis of Alzheimer's Disease and Other Dementias" later in this chapter), clinicians should exercise caution when using these drugs in older patients with schizophrenia.

Few data are available specifically on the pharmacological treatment of delusional disorder in late life. Alexopoulos et al.'s (2004) survey of 48 experts in geriatric care concluded that antipsychotics are the only recommended treatment, and their first-line recommendation for older adults with delusional disorder was risperidone (0.75–2.5 mg/day), followed by olanzapine (5–10 mg/day) and quetiapine (50–200 mg/day).

Psychosocial Treatments

Recent years have seen the development and testing of psychosocial interventions for older adults with chronic psychotic disorders. In a randomized controlled trial, Granholm et al. (2005) noted that cognitive-behavioral social skills training (CBSST), which combined cognitive and behavioral coping techniques, training in social functioning and problem solving, and compensatory aids for neurocognitive impairments, led to significantly increased frequency of social functioning activities, greater cognitive insight (more objectivity in reappraising psychotic symptoms), and greater skill mastery. An increase in cognitive insight was significantly correlated with greater reduction in positive symptoms. At 12-month follow-up (Granholm et al. 2007), the CBSST group had maintained their greater skill acquisition and performance of everyday living skills.

Patterson et al. (2006) conducted a randomized controlled trial of a behavioral group intervention called Functional Adaptation Skills Training (FAST), a manualized behavioral intervention designed to improve everyday living skills such as medication management, social skills, communication skills, organization and planning, transportation, and financial management. The researchers noted that the FAST group showed significant improvement in daily living skills and social skills but not medication management.

In an examination of employment outcomes among middle-aged and older adults with schizophrenia, Twamley et al. (2005) reported that the highest rates of volunteer or paid work (81%) and competitive or paid work (69%) occurred for the patients who were placed in a job chosen with a vocational counselor and then received individualized on-site support.

Psychosis of Alzheimer's Disease and Other Dementias

Since their introduction in the 1990s, the atypical antipsychotics have for the most part replaced conventional antipsychotics in treating psychosis, aggression, and agitation in patients with dementia because of greater tolerability, lower risk for acute EPS, and comparatively lower risk of TD (Kindermann et al. 2002). Most antipsychotic prescriptions in older adults are for behavioral disturbances associated with dementia, despite their lacking this FDA-approved indication (Ballard and Waite 2006). Only a few randomized con-

trolled trials have compared typical and atypical classes of antipsychotics for dementia, and results have been inconclusive (De Deyn et al. 1999).

AUTHOR: Above paragraph: 1) first sentence: Note change from "over the past decade" to "in the 1990s." OK?
2) Last sentence has been moved from single-sentence paragraph below next one. Note change from "the two classes" to "typical and atypical classes." OK?

In the CATIE-AD trial (Schneider et al. 2006), which was the largest (N=421) non-industry-sponsored trial of atypical antipsychotics for psychosis or agitation/aggression in people with dementia, olanzapine, quetiapine, and risperidone were no better than placebo for the primary outcome (time to discontinuation for any reason). Time to discontinuation due to lack of efficacy favored olanzapine and risperidone, whereas time to discontinuation due to adverse events favored placebo.

In addition to the liabilities described earlier, use of atypical antipsychotics in elderly dementia patients has been associated with cerebrovascular adverse events and death, leading to black box warnings by the FDA. Retrospective database reviews did not find any difference in incidence of cerebrovascular adverse events for typical versus atypical antipsychotic use, although none of these studies were originally designed to examine cerebrovascular adverse event risk.

AUTHOR: AUTHOR: Above paragraph: 1) Is black box warning mentioned above different from one mentioned in next paragraph? If different, please consider adding date above to clarify. If same, please consider combining text. Thanks!
2) First sentence: Please indicate in which section the liabilities were described.
3) Last sentence: Please consider adding citations and references for reviews.

In May 2004, the FDA also issued a black box warning that elderly patients with dementia taking atypical antipsychotic drugs are at an increased risk for death compared with those taking placebo. The data on risk of mor-

tality associated with typical versus atypical antipsychotics have been mixed (Jeste et al. 2008).

Unfortunately, data are also insufficient to support systematic use of any of the alternatives to antipsychotics, and few well-designed randomized controlled trials of behavioral and psychosocial interventions have been done in patients with dementia, but there are promising possibilities (e.g., behavioral management techniques, caregiver education) (Ayalon et al. 2006; Cohen-Mansfield 2001; Livingston et al. 2005). However, when strict inclusion criteria are used, such as those of the American Psychological Association (____), very few of these can be considered evidenced-based because the results are often inconclusive.

AUTHOR: Above paragraph, last sentence: Please add citation and reference for American Psychological Association. Thanks.

Patients with Lewy body dementia and parkinsonian dementia are especially sensitive to side effects such as EPS and anticholinergic effects, so very low doses and slow titration schedules should be used to avoid worsening of motor symptoms (Chou et al. 2007; Masand 2000). Low-dose clozapine has shown efficacy in reducing symptoms of psychosis, and clozapine does not worsen and can even improve the parkinsonian tremor.

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