Schizophrenia is a chronic neuropsychiatric disorder that produces psychotic, negative and disorganized symptoms. Psychotic and disorganized symptoms are grouped together as positive symptoms. Negative symptoms include apathy, affective blunting, and ambivalence. Schizophrenia appears in the late teens or early twenties when the brain undergoes the final phase of development. Elderly patients with chronic schizophrenia now survive into the seventh or eighth decade of life presenting special diagnostic and therapeutic challenges to clinicians. Although schizophrenia rarely begins after age 45, some schizophrenic patients do not require hospitalization until age 50 to 60 (13%) or later (10%).

The “new” onset psychotic symptoms in an elderly patient are more frequently a manifestation of dementia, delirium psychotic mood disorder, or substance abuse. Delusional disorders are also uncommon in the elderly. A very small number of patients develop schizophrenia after age 50 (i.e., paraphrenia).

Classic concepts of schizophrenia describe a relentless downhill course referred to as dementia praecox. Recent studies indicate that negative symptoms plateau at age 40 to 60 in many schizophrenics (Table 1). Positive symptoms persist into later life and require sustained therapy.

Patients continue to manifest Schneiderian symptoms including auditory hallucinations (90-100%), thought insertion or deletion (30-40%), thought disorder (50-60%), paranoid ideation and delusions (90-100%). Older patients frequently conceal the presence of positive symptoms due to concern over medications and hospitalization. Negative symptoms e.g., social isolation, and anhedonia, are poorly studied in elderly schizophrenics,
and may diminish slightly as the patients age. In general, the schizophrenic symptoms in older patients resemble younger individuals. Elderly schizophrenics have four times higher rates of tardive dyskinesia from chronic neuroleptic usage than younger patients. Most elderly schizophrenic patients remain in the community where they live independently, receive care from family, or reside in group homes, and other community-based institutional settings. Clinical differences between elderly male and female schizophrenics are unknown. Active symptoms persist beyond age 85; however, clinical descriptions are rare for very old schizophrenics. Elderly schizophrenic patients rarely begin to manifest new deficit or negative symptoms in late life, (e.g., incontinence or refusal to eat) unless new medical or neurological problems occur. A biomedical-psychosocial approach is necessary to maintain elderly patients in the community.

Elderly chronic schizophrenic patients with major relapses or new hospitalization need careful evaluation to determine the cause. Schizophrenic symptoms tend to remain stable although relapse on medication occurs in the elderly (Table 2).

Medication non-compliance is a common reason that explains why older schizophrenics manifest symptoms. Elderly patients can cheek medications and a past history of non-compliance or paranoia about medication should alert the treatment team to perform mouth-cheeks. Patients can be switched to liquid or given depot preparations. Non-compliant patients may refuse to take medication, change physicians, or undergo programmed dose reductions as part of OBRA compliance in nursing homes. Some patients have drug discontinuation as a result of medical problems or perceived medication side effects. Patients receiving lower doses of antipsychotic medications may exhibit old symptoms, new psychiatric symptoms, or evidence of break-through dyskinesia. The clinician can restart the antipsychotic medication at previous or slightly higher dosages. Clinicians should restart previous effective medications at comparable dosages and wait several months to determine efficacy. Patients who fail to respond to one or two months of the previous antipsychotic can have medications changed. Most patients improve with consistent therapy and attention to contributing factor such as medical problems. Blood levels will confirm compliance but serum neuroleptic levels do not predict response.

Caregiver death is a second common cause of schizophrenic relapse and hospitalizations. Elderly family members who care for elderly schizophrenic’s can become incapacitated by medical problems or die. These patients may require several months of active intervention, e.g.,
partial hospital programs, to assure stability in a new placement, like a group home.
Bereavement is poorly described in elderly schizophrenics who will mourn the loss of a spouse or family member.

Assessment and management of medical problems pose a serious obstacle to adequate care of the patient with schizophrenia. Studies show that primary care doctors miss about one third of health problems in patients with schizophrenia and psychiatrists miss about one half of medical diagnosis’s despite their medical training. Elderly schizophrenia patients under-report physical symptoms from medical problems and probably comply less than other elders. The chronically mentally ill patient has high rates of substance abuse and cigarettes smoking. Chronic lung disease is common in the elderly schizophrenics because 60% percent of patients have smoked. Psychogenic water drinking persists into old age and may produce edema or abnormalities of electrolytes that primary care doctors will misinterpret as congestive heart failure or renal disease. Typical neuroleptic medication may increases blood glucose levels, although there is no clear association between diabetes and schizophrenia. Patients with schizophrenia fail to recognize internal bodily sensations producing anisoagnosia. This syndrome may contribute to underreporting of physical symptoms. The caregiver for the elderly schizophrenic individual should accompany the patient to the physician’s office to assist with reporting of symptoms and medication compliance. Physicians should simplify dosing schedules and minimize injectable medications. Caregivers must carefully report all psychoactive medications to primary care doctors because many psychotropic drugs have significant cardiovascular toxicities.

Serious new medical problems can destabilize the older schizophrenic patient. Elderly schizophrenic patients may have alteration of their psychotropic drug regimen while hospitalized for medical illnesses. Neuroleptic levels may fluctuate from alteration in drug metabolism induced by new non-psychotrophic medications. The stress of hospitalization or surgery can sometimes precipitate psychotic episodes and delirium. Previously stable patients may require weeks or months of active therapy to regain baseline stability through interventions, such as, acute psychiatric hospitalization or long term partial hospital care.

Schizophrenic patients can become delirious from medical problems or medications. Delirium may increase positive symptoms and produce behavioral problems, e.g. fighting, wandering,
incontinence. Management of the underlying medical problems, e.g., UTI or pneumonia improves patient’s symptoms.

Elderly chronic schizophrenic patients can develop symptoms of depression. The biology and natural history of late-life onset depression in schizophrenia is unknown. Patients can manifest more negative symptoms and antidepressants may be effective. The decision to treat depression in elderly schizophrenics is based on consideration of the efficacy of antidepressant therapy verses antidepressant side effects. Clinicians should make individual determinations on the appropriate use of antidepressants therapy in elderly schizophrenics based on quantifiable somatic symptoms, e.g., weight loss, sleep disturbance, observed energy level.

Elderly schizophrenic patients may have episodes of psychogenic water drinking as part of a long history of excessive water ingestion. Water intoxication can resemble increased psychosis, confusion, or delirium. Fluid intake and electrolytes are worth monitoring in elderly schizophrenic patients who demonstrate wide variation of behavior and symptoms. New onset psychogenic water drinking is suspicious for unrecognized medical problems or medication side effects, e.g., dry mouth.

Some elderly schizophrenic patients begin to deteriorate as a result of dementia (Table 3). The incidence of dementia in elderly schizophrenics is unclear, however; at least 10% will develop cognitive decline with aging. The neuropsychological symptoms of dementia in schizophrenia resemble those in Alzheimer’s disease or vascular dementia. There are severe cognitive impairment, intense negative symptoms, active positive symptoms, and significant functional impairment. The Mental-Mini Status Examination can be used to assess cognitive decline in elderly schizophrenics. The cut-off scores for dementia are identical to those for the normal population. Older patients lose 1.2 to 4.6 points per decade of life that is not related to treatment history or pre-morbid features.

The cause of dementia in elderly schizophrenics is unknown. Post-mortem studies of elderly demented schizophrenic patients show minimal Alzheimer type pathology or vascular injury.
Chronic, long term neuroleptic use does not cause demonstrable neuropathology, and there is no evidence of neuroleptic induced damage to the brain. Elderly schizophrenic patients do not have increased risk of idiopathic Parkinson’s Disease or diffuse Lewy body disease. Management strategies for elderly patients with dementia and schizophrenia are identical to those for patients with Alzheimer’s disease. Many demented schizophrenic patients have increased hallucinations and abnormal behavior that are frequently unresponsive to increased dose of antipsychotic medications. Management includes documentation of cognitive deficits, behavioral management, and structured daily activities that correspond to cognitive competence.

### The Anatomy and Therapy of Schizophrenic Symptoms

<table>
<thead>
<tr>
<th>CLUSTER</th>
<th>SYMPTOM</th>
<th>IMPLICATED BRAIN REGION</th>
<th>THERAPY</th>
<th>RESPONSE TO MEDICATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Psychotic</td>
<td>Hallucinations</td>
<td>Temporal lobe</td>
<td>Typical /atypical neuroleptic</td>
<td>Good</td>
</tr>
<tr>
<td>Negative</td>
<td>Social withdrawal anhedonia</td>
<td>Frontal lobe</td>
<td>Atypical neuroleptic</td>
<td>Poor</td>
</tr>
<tr>
<td>Disorganized</td>
<td>Thought disorder inappropriate affect</td>
<td>Temporal lobe</td>
<td>Typical /atypical neuroleptic</td>
<td>Fair</td>
</tr>
</tbody>
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The treatment of an elderly schizophrenic patient with increased positive or negative symptoms begins with an assessment of possible causes for worsening of symptoms. When evaluation fails to show new problems, e.g., delirium, dementia, medical instability, or caregiver loss, patients should be tried on a different class of high potency antipsychotic. Low potency antipsychotics are frequently ineffective because side effects, e.g., orthostatic hypertension, sedation, limit the maximum tolerated dose. Neuroleptic levels can also be used to determine absorption of medication and compliance. The typical or old antipsychotics remain effective for some schizophrenic patients. Tardive dyskinesia is a major complication, i.e., involuntary movement of the lips, tongue, hands head or other muscle groups. Most TD occurs after 6 or 7 years of therapy with neuroleptics although dosage changes may produce symptoms. The risk for TD continues in patients over the age of 65, and competent patients should provide informed consent.

Three new atypical anti-psychotic medications play a major role in the treatment of schizophrenia. The positive and negative aspects of these drugs require careful assessment prior to initiation of
therapy. The beneficial aspects of atypical anti-psychotics include lower side effect profile, increased effect on negative symptoms, improvement of symptoms in previous therapy resistance, and less resistance from patients due to drug toxicity. The anti-psychotics also produce less EPS and may benefit some patients with tardive dyskenisia. The negative aspect to atypical anti-psychotic medications includes (1) lack of injectable or depo preparation, (2) significant cost increases, and (3) inflated expectation for efficacy and toxicity.

Patients who are well controlled on regular anti-psychotic medication should continue with these medications as along as the patient is well controlled and lacks significant side effects. Patients receiving anti-psychotic medications for the first time can be started on either typical or an atypical medication. The selection of an atypical agent depends on toxicity and desired efficacy. Respiridone may have a slightly higher level of EPS than olanzapine or seroquel. Seroquel maybe more sedating and otthrostatic than olanzapine or respiridone. The dosing and titration schedule for elderly patients is reduced in all atypical antipsychotics depending on the patient’s health and cognitive status. Hospitalized patients or those residing in nursing homes can be titrated more rapidly than patients who reside at home or in assisted living facilities. In general, respiridone and olanzapine behave like high potency neuroleptics while seroquel functions more like low potency neuroleptics. All atypical psychotics can produce side effects common to typical anti psychotics, however, the frequency and severity of these symptoms is markedly reduced. Patient should not receive prophylactic anti-cholinergic medications (e.g., Cogentin) when placed on atypical anti-psychotic. There are no comprehensive outcome studies on therapy with atypical anti-psychotics for elderly patients. All medications have higher blood levels and longer half-life in elderly patients than in younger patients according to unpublished data. Toxicity levels are lower for elderly individuals and therapeutic blood monitoring may assist with avoiding toxic levels and assuring compliance. Atypical anti-psychotics do not have injectable forms. The use of atypical anti-psychotics in conjunction with typical psychotics, i.e., combination therapy is unproven in the elderly, however the toxicity is cumulative. Patients receiving combination of typical and atypical anti-psychotics must be monitored carefully to avoid falls or other significant complication. There is no evidence that elderly experience higher rates of liver or bone marrow damage from atypical anti-psychotics than in younger patients. Older patients do have higher rates of disease in these organ systems and physicians should routinely check liver function studies and blood counts prior to initiation of anti-psychotic medications.
Schizoaffective disorder is diagnosed in 11% to 19% of younger patients with serious mental illness, however, its frequency in older patients is unknown. This clinical entity combines persistent psychotic symptoms and depressive, or bipolar symptoms. Schizoaffective disorder in younger individuals produces high morbidity; a chronic course similar to schizophrenia and a suicide rate similar to bipolar disorder. The natural history of this disorder in the elderly is unknown.

Clinicians should suspect neurological disease in any new case of schizophrenia that presents over age 65. Deterioration of previously stable, chronic schizophrenics warrants careful evaluation. Causes of decompensation include caregiver death, non-compliance, medical problems, delirium, and dementia. The most important step in treating any elderly schizophrenics is careful evaluation.

CAUSES OF RELAPSE IN ELDERLY SCHIZOPHRENIC PATIENTS

- IS THE PATIENT TRULY SCHIZOPHRENIC?
- IS THE PATIENT TAKING MEDICATION?
- IS THE CAREGIVER SYSTEM INTACT?
- IS THE PATIENT MEDICALLY SICK?
- IS THE PATIENT DEMENTED?
- IS THE PATIENT EXPERIENCING:
  - Substance abuse
  - Psychogenic water intoxication
  - Depression
  - Abuse by Caregiver

SEQential drug trials