The Schizophrenias: Medical Diagnosis and Treatment by the Family Physician

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About one percent of the population will develop schizophrenic symptoms sometime during their life. Etiologies are poorly understood and the course is highly variable. The differential diagnosis and medical treatment of the schizophrenias are discussed. Neuroleptic drugs are the most effective single treatment, for they allow most patients to be treated on an ambulatory basis, under the care of community physicians. Adverse effects of neuroleptic agents are common and often subjectively annoying. They may be prevented or minimized by agent selection, dosage schedules, or contra-active treatment.

The prevalence of schizophrenia has probably remained unchanged over the past 100 years and is still approximately one percent of the adult population.[1] Although the incidence of the illness remains unaltered, the treatment of schizophrenia has changed dramatically. Until the middle 1950s the treatment was primarily supportive and custodial, but with the introduction of neuroleptics, ambulatory treatment became possible. Neuroleptics, though not curative, greatly reduce the signs and symptoms and modify the course of schizophrenia, allowing for most patients to function on an ambulatory basis. Some patients may recover completely and may not require continued care, but most patients require close monitoring for years. The following review offers the primary physician practical guidelines for the differential diagnosis and medical management of the schizophrenic patient.

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Diagnosis

The schizophrenias represent a clinical syndrome of poorly understood etiologies. Schizophrenics are a seemingly heterogeneous population, all having a relatively similar endstate. No pathognomonic biologic signs have been identified, and the thought disorder remains the unique diagnostic sign. Thus, the schizophrenias remain classified as "functional psychosis."

Early Signs

Nevertheless, there are some vague signs of a predisposition toward schizophrenia. A schizophrenic person often has a family history of schizophrenia and chronic family communication disturbances. As children, many preschizophrenic individuals have asocial development, poor peer

relationships, and emotional eccentricity leading to scapegoating.[2] Neurologic soft signs and ill health are frequently present. As adolescents, unsocialized aggressiveness among males and overinhibited hyperconformity among females may prevail.[3]

Psychotic Decompensation

Although psychosis may present at any age, the age of highest risk is with young adults. Emotional and biological events may antecede psychotic decompensation in the vulnerable individual. Frequently, a personal or family emotional crisis will precede the onset of symptoms, although a direct causal relationship between emotional stress and psychosis remains unclear.[4] Often the stress represents an actual or fantasized loss (death, separation, etc),[5] or a failure in reaching an important goal or mastering a developmental stage.[6] Medical procedures, such as childbirth and surgery, may immediately predate decompensation; drug abuse or administration (sympathomimetics, hallucinogenics) may also precipitate schizophrenia in those who are biologically predisposed.

Unfortunately, it remains impossible to predict which individuals will ultimately develop schizophrenia.No valid biologic marker or clinical profile has yet been identified. Thus the premorbid characteristics are usually documented retrospectively and treatment is predominantly *ipso facto* rather than preventative.

The signs and symptoms of schizophrenic decompensation may present insidiously or acutely. Although acute symptoms may appear within hours, a careful history usually reveals that psychotic symptoms had been developing for days or weeks. Some of the symptoms are: cognitive and perceptual changes, anxiety and depression, somatic preoccupation, emotional and behavioral changes, physiologic responses to stress, and social withdrawal. The somatic complaints may be vague or may represent developing psychophysiologic symptoms, and are often diagnosed as neurasthenia, neurosis, or malingering.

With the transition to the overt psychotic phase, reality testing breaks down and thinking processes become uncontrollable, leading to the cognitive and perceptual disorganization typically found in schizophrenia.[7] Because this process is subjectively distressing, it often is associated with autonomic signs of mydriasis, tachycardia, increased systolic blood pressure, and sweating. Notably, once the illness has fully developed, the schizophrenic individual is less likely than the nonschizophrenic individual to have psychosomatic illness.[8] Somatic delusions and preoccupations, nonetheless, may remain and make diagnosis of developing medical problems more difficult. For example, it may be difficult to consider the diagnosis of peptic ulcer or gall bladder disease in a chronic delusional patient who fantasizes an electronic device transmitting radio messages from his abdomen.

Schizophrenia Diagnosis

The diagnosis of schizophrenia should be made only when psychosis presents. There is no exact diagnostic scheme, and the diagnosis rests on the clinical evaluation of the course and symptomatology. The diagnostic systems of Bleuler[9] and Schnieder[10] are listed in Table 1. According to Bleuler, the four A's are characteristic of schizophrenia and are present under no other conditions. Schnieder concludes the same about his First Rank Symptoms. The secondary symptoms of Bleuler are frequently seen with other psychotic disorders but may be absent in schizophrenia. Although the primary care physician will find these schemes useful, recent study has documented that neither of them are unique to schizophrenia and neither has prognostic value.[3]

Schizophrenic Types

Schizophrenia is divided into various clinical types (Table 2). These types are distinguished by presenting form, course, and age of onset. Such

typing is of limited value to the physician because many patients present with mixed symptoms, and the form may change with subsequent exacerbations. Nevertheless, correctly diagnosing a type facilitates treatment and helps to insure as quick a remission as possible.

All 11 types involve a pathology of the total personality, manifested as disorganized and illogical thinking, inadequate or inappropriate emotional responses to people or events, heightened emotional sensitivity, impaired volition and judgment, idiosyncratic belief systems (eg, delusions), and perceptual distortions (illusions and hallucinations).

The simple type is characterized chiefly by a slow and insidious onset plus emotional detachment and apathy. The hebephrenic type is associated with the fragmentation of thinking processes, silliness, and regressive mannerisms in behavior. The catatonic type consists of two subtypes: excited and withdrawn. The excited subtype is associated with excessive and sometimes violent motor behavior and emotions; the withdrawn subtype with stupor, mutism, negativism, and waxy flexibility. The paranoid type is characterized primarily by the presence of grandiose and persecutory delusions, often associated with hallucinations. Excessive religiosity, blaming, aggressiveness, and hostile behavior are also common. However, personality disorganization is less common with this type than with the hebephrenic and catatonic schizophrenias.

Besides the simple, hebephrenic, catatonic, and paranoid, there are seven additional types. The acute schizophrenic type is associated with excitement, dysphoria, confusion, perplexity, and emotional turmoil. The latent type includes patients with nonpsychotic schizophrenic symptoms, and the residual type describes the postpsychotic period when psychotic symptoms are no longer present. The schizo-affective type is a mixture of schizophrenic symptoms and elation or depression. In the childhood type, symptoms appear before puberty and include atypical behavior, inability to distinguish self from the environment, and delayed or uneven personality development. The chronic undifferentiated type is a mixture of schizophrenic symptoms that cannot be classified under other types. The other and unspecified type includes any type of schizophrenia not previously described.

Table 1. Diagnostic Criteria

1. Bleuler's Primary and Secondary Symptoms*

A. Primary Symptoms: Bleuler's four A's, which may not be evident early in the disorder:

1) Disturbances in *affect,* either inappropriate or flattened.
2) Loose *associations,* wandering from topic to topic with little relevancy.
3) *Autistic* thinking, or involvement in fantasy material, often completely absorbed in ideas of reference to self.
4) *Ambivalence,* often not quickly apparent but characterized by conflicting and simultaneously positive and negative feelings toward another person.

B. Secondary Symptoms:

1) Erratic behavior, often day-night reversal.
2) Anhedonia, or inability to experience gratification or immersion in life experiences.
3) Anger and frustration, often in reaction to inability to function.
4) Dependence, a part of the boundary problem and the reality problem of being unable to handle the exigencies of life.
5) Depression, with occasional suicide attempts.
6) Pathologic coping devices, or attempts to "explain" what is happening (eg, delusions, hallucinations, preoccupations, and depersonalizations).
7) "Boundary" problems, or inability to differentiate oneself (both self and body) as distinct from others.
8) Feelings of markedly enhanced or muted sensory awareness.
9) Reports of "racing thoughts."
10) Mental exhaustion.
11) Deficits in focusing attention and concentration.
12) Disturbances in speech perception and word meanings.

2. Schneider's First-Rank Symptoms

1) Hears voices speaking his thoughts aloud.
2) Experiences himself as the subject of hallucinatory voices, arguments, or discussions.
3) Hears hallucinatory voices describing his activity as it takes place.
4) Experiences delusional percept.
5) Experiences somatic passivity.
6) Experiences thought insertion.
7) Experiences thought withdrawal.
8) Experiences thought broadcast.
9) Experiences externally controlled or imposed affect.
10) Experiences externally controlled or imposed impulses.
11) Experiences externally controlled or imposed motor activity.

*Brophy, JM: The Schizophrenias. In Krupp MA, Chatton MS (eds): Current Medical Diagnosis and Treatment. Lange Medical Publications, Los Altos, California, 1976, p 620

Table 2. Types of Schizophrenia*

295.0	Simple type
295.1	Hebephrenic type
295.2	Catatonic type
295.23	Excited
295.24	Withdrawn
295.3	Paranoid type
295.4	Acute schizophrenic type
295.5	Latent type
295.6	Residual type
295.7	Schizo-affective type
295.73	Excited
295.74	Depressed
295.8	Childhood type
295.90	Chronic undifferentiated type
295.99	Other (and unspecified) types

*American Psychiatric Association: DSM-II: Diagnostic and Statistical Manual of Mental Disorders, ed 2. American Psychiatric Association, Washington, DC, 1968

The catatonic and hebephrenic types are seen less often now than a half century ago in contrast to the paranoid form which is more frequently diagnosed. Furthermore, the acute and chronic undifferentiated types are commonly diagnosed today because the symptom picture is often mixed.

Differential Diagnosis

The differential diagnosis between schizophrenia and other disorders which may mask schizophrenia is listed in Table 3. The diagnosis, however, may be difficult to establish in the acute psychotic patient. The most common differential diagnosis is affective disorders (withdrawn depressive, agitated manics) or drug toxicity (amphetamines, hallucinogens, corticosteroids). The physician should obtain a complete longitudinal history and observe the patient for some period before making the diagnosis. A physical examination and indicated laboratory tests (chemistries, drug screens, etc) should be obtained prior to initiating treatment. Unless the patient is experiencing catastrophic symptoms where rapid symptom relief is necessary, drug treatment should be withheld pending adequate documentation of the diagnosis.

Prognosis

Prognosis varies widely. Langfeldt proposed a reactive vs process classification to separate more precisely the schizophrenic-like illnesses from true schizophrenia.[11] As the name implies, a "reactive" patient's illness is an acute reaction against

an identifiable stress. Reactive patients have a better prognosis, tending to have a family history unlike most schizophrenics and a better premorbid social and occupational adjustment. Indeed, many of these patients will recover completely without medical intervention, although neuroleptics normally hasten the recovery. In contrast, the process group, with its guarded prognosis, has a seemingly greater biologic predisposition, more premorbid cognitive and affectual impairment, and an insidious onset. Without medication, many of this group will deteriorate so drastically that they will require custodial care. Their response to neuroleptics may range from marked improvement to a marginal-functioning, stable, chronic state. The risk of personality deterioration increases with each schizophrenic relapse. Although the distinction between these two classes is not clear cut, it provides the physician with some sense of the course of the illness.

Treatment

General Considerations

A relationship based on trust is important for the development of any long-term, physician-patient relationship but especially with patients who exhibit schizophrenic symptoms because they have heightened emotional sensitivity and rely more greatly on the physician's guidance. To establish the diagnosis and monitor the response to treatment, the physician must encourage the patient to discuss fears and anxieties openly. Such a relationship will help the physician prevent a patient in remission from decompensating. Physical findings and laboratory tests are of limited value. Careful clinical observation is essential.

Occasionally, nonpsychotic young adults will present with developing psychopathology. If the symptom picture includes cognitive disorganization, obsessive rumination, depression and anxiety, and reduced or inappropriate socio-occupational functioning, schizophrenia must be considered, especially if there is no history of drug abuse or clinical or laboratory evidence of or-

Table 3. Differential Diagnosis of Idiopathic Schizophrenia

I. Schizophreniform (secondary) psychosis associated with:

1. Central nervous system disorders
   a) Huntington chorea
   b) Temporal lobe disorders
   c) Multiple sclerosis
   d) Systemic lupus erythematosus
   e) Neoplasm
   f) Luetic disease
2. Metabolic, endocrine, nutritional disorders
   a) Porphyria
   b) Thyrotoxicosis
   c) Myxedema
   d) Addison disease
   e) Cushing syndrome
   f) Hypoparathyroidism
   g) Pituitary dysfunction
   h) Pernicious anemia
   i) Folic acid deficiency
   j) Pellagra
   k) Folate deficiency
   l) Alcoholic hallucinosis and paranoia
   m) Hypoglycemia
3. Drug toxicity
   a) Sympathomimetics, eg, amphetamines, methylphenidate, levodopa, diethylpropion
   b) Anti-inflammatory agents, eg, steroids, phenylbutazone, indomethacin
   c) Disulfiram
   d) Chronic bromism
   e) Hallucinogenic agents (psychedelics, ketamine, phencyclidine)
   f) Tricyclic and MAOI (monamine-oxidase inhibitors) antidepressants
   g) Anticholinergic agents, eg, antiparkinsonian drugs, belladonna and atropine-like agents
4. Other organic psychotic disorders

II. Other Functional Disorders

1. Affective disorders
2. Hysterical reactions
3. Borderline syndromes
4. Severe characterologic disturbances
5. Ganser syndrome
6. Nonspecific psychosis

III. Malingerers

Table 4. Major Tranquilizers (Neuroleptics)

Generic Name	Trade Name	Chlorpromazine Dose Ratio	Expert* Dose Range
Phenothiazines			
A. Aliphatic			
Chlorpromazine	Thorazine	1:1	15-1500
B. Piperidine			
Mesoridazine	Serentil	1:2	75-400
Piperacetazine	Quide	1:3	20-160
Thioridazine	Mellaril	1:1	150-800
C. Piperizine			
Butaperazine	Repoise	1:8	25-110
Fluphenazine	Prolixin Permitil	1:50	3-45
Perphenazine	Trilafon	1:10	12-60
Prochlorperazine	Compazine	1:6	25-150
Trifluoperazine	Stelazine	1:20	10-40
Thioxanthenes			
Chlorprothixene	Taractan	1:1	40-600
Thiothixene	Navane	1:20	10-60
Butyrophenones			
Haloperidol	Haldol	1:50	2-16
Dihydroindolones			
Molindone	Moban	1:15	50-225
Dibenzoxazepines			
Loxapine	Loxitane	1:10	50-250

*Davis JM, Cole JO: Anti-psychotic Drugs. In Freedman AM, Kaplan HI, Sadock BJ (eds): Comprehensive Textbook of Psychiatry, vol 2, ed 2. Baltimore, Williams and Wilkins, 1975, p 1927

ganicity. In most cases the illness will not progress to overt psychosis if the family physician administers neuroleptics and directive and supportive care promptly. Hospitalization is seldom required but the patient will benefit from a few days of medical leave from work.

Patients who suffer acute decompensation often are escorted to the physician's office or hospital by friends or occasionally by law enforcement officials. Patients typically have difficulty presenting a valid history so this information should be gathered from others. The patient requires a regular medical work-up to establish the differential diagnosis. Psychological testing, especially the Rorschach and Thematic Apperception Tests, is helpful in establishing the diagnosis. Psychiatric consultation or patient referral may be indicated for patients who present with complex diagnostic or treatment problems. When made, the reasons for the referral should be openly discussed with the patient prior to making the referral appointment. Working with family members early and engaging them in the treatment and rehabilitation programs is helpful. The family's guilt feelings must be dealt with early. There is little evidence which suggests that faulty parenting causes schizophrenia. It is helpful to explain to the patient and family the nature of the illness and the need

for immediate treatment.

Past familiarity with the patient is useful in outlining and implementing a treatment program, including establishing medication dosage schedules. The new patient can be safely started on low doses of any neuroleptic, and the dosage can be adjusted depending on clinical response. If the patient is to be followed as an outpatient, family members or friends must provide supportive care, and the patient should be seen regularly by his/her physician until the symptoms subside.

The decision to hospitalize should be carefully weighed and depends on the nature and severity of symptoms, the availability of a social support system (interested family and friends), the past familiarity with the patient, and the risk of the patient harming himself or others. Most patients who lack catastrophic developing symptoms or who have partially recovered can be treated on an ambulatory basis. In contrast, acute schizophrenia is a medical emergency and the patient must therefore receive vigorous and immediate treatment.[12] Hospitalization can be avoided in many patients if a social support system is available to provide the necessary care. Other patients, perhaps equally ill, require hospitalization because basic care is not otherwise available. If a patient has responded dramatically to readministration of neuroleptics previously, ambulatory treatment may be attempted. However, with patients experiencing their first psychotic symptoms, patients with poor prior responses to neuroleptics, and patients with unknown responses to treatment, hospitalization is normally indicated. Patients with serious threats or histories of violence or self-harm require hospitalization.

The decision to discharge from the hospital is based both on a significant reduction of symptoms which allows outpatient management and on the development of sufficient rapport with the patient and his family to insure continuity of care.

Most patients will require long-term management and maintenance neuroleptics. Once symptoms have remitted the patient should be encouraged to resume prepsychotic occupational and social responsibilities, but on a gradual basis. Patients with limited premorbid adaptability and those with significant postpsychotic residuals require referral to various community agencies and a vocational rehabilitation center for rehabilitative care.

The rehabilitation plan should be realistic for the patient, and positive behavioral and rehabilitative goals should be outlined with a tentative time schedule for completion. A "push program" may be realistic for some patients but just the opposite of what is required for others. The overall treatment emphasis should be toward producing symptom remission and improving the patient's socially adaptive functioning.

Neuroleptic Agents

Neuroleptics are a group of antipsychotic drugs which currently include the phenothiazines, thioxanthenes, butyrophenones, dihydroindolones, and dibenzoxazepines (Table 4). They vary greatly in potency, and in general, the more potent agents are the least sedating. Like neuroleptics, the rauwolfia alkaloids (reserpines) also have antipsychotic effects, but they are seldom used today because of their delayed onset of action, reduced efficacy, and greater adverse liability. Most neuroleptics (except thioridazine) are available in both parenteral and oral dosage forms, and fluphenazine has a long-acting injectable form. The basic guidelines for administering these drugs are listed in Table 5; more specific guidelines are given below.

Acute Schizophrenic Decompensation

Neuroleptics and supportive care are the treatments of choice for acute schizophrenic decompensation. Brief hospitalization is often indicated. The dosage requirements for neuroleptics, however, vary greatly and should be individualized and dependent on response to previous neuroleptic trials, body weight, age, and severity of symptoms. In general, an agent like chlorpromazine 50 to 100 mg or fluphenazine 5 mg

Table 5. Basic Guidelines for Administering Neuroleptic Drugs

1. Are neuroleptics indicated? If so, are there any contraindications, such as comatosed states, presence of large amounts of central nervous system depressants (alcohol, barbiturates, narcotics, etc), bone marrow depression, or perhaps first trimester pregnancy?
2. Comprehensive drug and medical history is essential for best selecting neuroleptic agent and initial dosage.
3. Injectable neuroleptics are highly effective for rapidly reducing agitation and catastrophic psychotic symptoms.
4. Identifying target symptoms is helpful for monitoring response to therapy.
5. Avoid combination and psychotropic polypharmacy whenever possible.
6. Give the drug a chance to work in therapeutic dosages before switching to or adding another.
7. Dosages can normally be consolidated to single daily bedtime dose.
8. Adverse effects may be multiple and subjectively annoying. They may be minimized or prevented through agent selection and dosage schedule, thus increasing comfort and drug compliance.
9. Avoid underdosing. Higher dosages may be indicated initially for treating acute or severe symptoms.
10. Do not overdose either. Maintenance dosage should be minimal dosage required to maintain symptom relief and minimize side effects. Consider discontinuing drug treatment if symptoms come on acutely and are now absent. Maintenance therapy not always indicated.
11. The relapse rate in patients is nonetheless high following neuroleptic discontinuation. Patients should be followed closely and neuroleptics readministered if psychotic symptoms reappear.
12. Consider long-acting depot neuroleptics for patients who take medication irregularly. They greatly reduce the relapse rate.
13. Most patients on maintenance neuroleptics do not require antiparkinsonian drugs.
14. The treatment program must be highly individualized. Most patients require long-term neuroleptic and rehabilitative care and a trusting, supportive, physician-patient relationship.

should be given initially and repeated every four to six hours as indicated. Older patients and those at risk for adverse effects should be given lower dosages. Sedation may be a welcomed adverse effect because it provides for needed rest and sleep.

For the patient requiring medication yet refusing oral medication, parenteral medication is indicated. Injectable neuroleptics (eg, haloperidol 2.5 to 5 mg) are highly effective for rapidly reducing psychotic excitement and cognitive disorganization when given on an hourly basis until the desired response occurs. By adjusting the dosage to maximize efficacy, the oral daily dose can be established after a few days of treatment. Prophylactic antiparkinsonian agents (benztropine mesylate, trihexyphenidyl) will reduce the risk of extrapyramidal symptoms but they will also reduce absorption of oral medication and reduce, therefore, the efficacy of neuroleptics.

Maintenance Therapy for the Chronic Patient

When symptoms have subsided the dosage can be reduced slowly to a maintenance level, which is often one half to one third the daily dosage for acute symptoms. Depot fluphenazines (fluphenazine enanthate and decanoate) should be considered for patients who take medications irregularly, a practice which places them at a high risk for psychotic decompensation. These injec-

Table 6. Neuroleptic Drugs—Adverse Effects

Type	Comment
1. Anticholinergic	Dose related. Tolerance develops.
A. Dry mouth, blurred vision, nasal congestion, constipation, urinary retention, may aggravate glaucoma, paralytic ilius	
B. Tachycardia	
C. Inhibition of ejaculation and impotence	Mostly with thioridazine.
2. Central Nervous System	
A. Extrapyramidal	
i. Reversible	
a. Pseudoparkinsonism	Reduce dose, use antiparkinsonian drugs.
b. Akathisia (leg restlessness)	Reduce dose, use antiparkinsonian drugs.
c. Dystonic reactions	Use parenteral antiparkinsonian drugs.
ii. Possibly irreversible	
a. Tardive dyskinesia	Late onset. Agent-dose related?
B. Seizures (rare)	Dose related.
C. Sedation	Dose related. Tolerance develops.
D. Hypothermia	
E. Behavioral toxicity	Reduce dose.
F. Toxic delirium	Dose related. Mostly with aged.
3. Cardiovascular	
A. Orthostatic hypotension	Mostly with chlorpromazine and thioridazine.
B. ECG changes	Mostly with thioridazine and mesoridazine.
4. Allergic	
A. Cholestatic jaundice (rare)	Occurs first month of treatment. Flu-like prodrome.
B. Agranulocytosis (rare)	Occurs first three months of treatment.
C. Eosinophilia	Benign. Occurs early in treatment.
D. Contact dermatitis	
E. Photosensitivity	Occurs mostly with chlorpromazine.
5. Endocrine and Metabolic	
A. Weight gain	
B. Edema	
C. Gynecomastia, galactorrhea	
D. Menstrual irregularities.	
6. Skin and Eyes	
A. Pigmentary retinopathy	May occur with high dose thioridazine.
B. Skin pigmentation and eye opacities (cornea, lens, retina)	May occur with high dose, long-term chlorpromazine.
7. Death	
A. "Sudden death"	Not proven.
B. Neuroleptic overdose (rare)	May occur mostly with thioridazine and mesoridazine.

Table 7. Neuroleptic-Induced Extrapyramidal Symptoms (EPS)

1. Pseudoparkinsonism

A. *Akinesia (hypokinesia, bradykinesia)*
Muscle fatigue and weakness
Reduction in physical activity
Joint and muscle pain in advanced form

B. *Rigidity*
Stiffness and slowness of voluntary movements
Gait and posture disturbances
Masklike immobility of facies
Cogwheel movements
Shuffling, festinating gait
Slow monotonous speech
Stooped posture
Dysarthria

C. *Tremor*
Rhythmic 4 to 8 / second oscillating resting tremor
Pill-rolling tremor of hands and fingers
Frequently begins unilaterally in upper extremities and gradually spreads bilaterally. May involve head, perioral ("rabbit syndrome"), trunk, or lower extremities

D. *Autonomic nervous system*
Drooling
Hyperhidrosis and heat intolerance
Sialorrhea and seborrhea

2. Akathisia

Subjective desire to be in constant motion
Poorly tolerated subjectively
Inability to sit or stand still
Rocking and shifting of weight while standing
Initial insomnia

3. Acute Dystonic Reactions

A. *Dystonias*—Prolonged tonic contractions of muscle groups, especially about the head and neck with bizarre posturing: torticollis, retrocollis, tongue protrusion or curling, facial grimacing, dysphagia, dysphasia, and oculogyric crisis
Less frequently: Hyperextension of neck and trunk with opisthotonos, scoliosis, lordosis, and impaired gait

B. *Dyskinesias*—Clonic musculature contractions, such as tics, spasms, and involuntary muscle movements

4. Tardive Dyskinesia

May be transient or persistent

A. *Adults*—Most common form is repetitive, involuntary stereotypical movement of tongue, lips, mouth, and facial musculature.
Less frequently are choreiform or hyperkinetic movements of trunk or extremities.

B. *Children*—Most frequently, involuntary choreiform bodily movements
Less frequently, involuntary muscular movements of face

tions are normally well tolerated and can be given on an every-one-to-four-weeks basis.

Neuroleptic withdrawal should be considered for patients who have recovered well on low dosage treatment. Nonetheless, these patients must be closely monitored because approximately 40 percent of them will decompensate within six months.[13,14] Therefore, it is important that the clinician be familiar with the early signs and symptoms of decompensation so that treatment can be reinitiated. This list includes cognitive disorganization, perceptual distortions, disturbed sleep and dreams, panic, and depression. Normally, treatment includes readministering neuroleptic medication or increasing the dosage as well as evaluating the environmental stresses. The patient should also be closely watched for the development of neuroleptic adverse effects (Table 6).

Schizophrenic people may also have periods of depression. Normally, they are reactive in origin, mild, and transient. A more severe and sustained depression may occur especially during the immediate postpsychotic period. The depression may be "masked" by the flattened affect, the general reduction in social activity in the schizophrenic person, and the reduction in insomnia due to the sedating effects of neuroleptics. Nonetheless, depression can be identified through the patient's reports and evidence of pessimism, low self-esteem, helplessness, and hopelessness. The severity of the depression is a good general guide to the risk of suicide. However, occasionally suicide may unpredictably occur and not be associated with a depressed mood. This is especially true of patients responding to auditory hallucinations and delusions. Depressed schizophrenic patients should be followed more closely. It is helpful to discuss treatment plans and observation with those who are close to the patient and to discuss openly with the patient his troubled concerns. Brief hospitalization may be required but this is normally not necessary if rapport and a social support system are available. Antidepressant drugs are often helpful, but they should be initially prescribed in low dose because the patient may be highly sensitive to low dosages and may even experience psychotic decompensation on higher dosages. Stimulants, such as amphetamines and methylphenidate, are not recommended for the latter reason.

Adverse Effects of Neuroleptics

None of the neuroleptic agents produce true physical dependency, although withdrawal symptoms may develop with rapid discontinuation (headache, insomnia, nausea, vomiting).[15] Though neuroleptics have a wide range of safety, adverse effects are multiple and often annoying. Most of the adverse effects are dose related and represent a pharmacologic extension of the drug actions. Tolerance to neuroleptic adverse effects often develops with continued administration. The elderly and those in ill health or with central nervous system impairment are at a higher risk and should be monitored when on low-dose neuroleptic medication before the dosage is increased.

Because of their distressing nature and the reduced drug compliance associated with them, adverse effects should be prevented or minimized through agent selection, dosage schedule, and contra-active treatment.

Neuroleptic-induced extrapyramidal symptoms (EPS) are common during neuroleptic administration, and tardive dyskinesia may persist following neuroleptic discontinuation. A description of EPS and the differential diagnosis of them is given in Tables 7 and 8.[16] Pseudoparkinsonism, akathisia, and dystonic reactions are a function of biological sensitivity, molecular structure, dose, age, sex, and duration of administration. They are more commonly associated with the more potent neuroleptics and higher dosages. Dystonic reactions present more commonly in young adult males; akathisia and pseudoparkinsonism, in older females. Approximately 50 percent of the patients started on neuroleptics will require contra-active antiparkinsonian (AP) drugs in contrast to 20 percent on maintenance neuroleptics. Contra-active treatment for these three EPS is AP drugs, reduction in neuroleptic dosage, or substitution of a less potent neuroleptic. Levodopa is not recommended as it may exacerbate the schizophrenic symptoms. Treatment of tardive dyskinesia remains unknown, but it may possibly be prevented through conservative dosages of neuroleptics.

Toxicity may develop. This includes agranulocytosis and cholestatic jaundice, but both are rare and normally occur within the first three months of neuroleptic administration. Thus, neuroleptic toxicity should be considered in the differential diagnosis of patients who develop these disorders during the initial neuroleptic period. Eye and skin changes are dose related with chlorpromazine and thioridazine. ECG changes are associated with thioridazine and mesoridazine administration and are reversible with drug termination. Tardive dyskinesia is associated with long-term neuroleptic administration but may manifest after months of therapy.

An overdose of neuroleptics may be lethal. It is associated with sedation, hypotension, extrapyramidal effects, hypothermia, grand mal seizures, and cardiac conduction disturbances. Gastric lavage, even hours later, can be effective in removing significant amounts of the drug. Hypotension can be reversed with the use of norepinephrine or isoproterenol. Epinephrine should never be used since this agent stimulates beta as well as alpha adrenergic receptors, and since neuroleptics block the alpha receptors, epinephrine may lead to a further reduction of blood pressure.

Comprehensive Care

The primary care physician can and should oversee the comprehensive treatment of his/her schizophrenic patients in all phases of the illness. Besides providing ongoing care the physician must be acquainted with the various available community services (eg, vocational rehabilitation, sheltered workshops, rehabilitation centers) and make the appropriate referrals. As several agencies may be involved in some aspect of the treatment program it is important that the treatment plan be communicated and integrated to reduce redundancy.

The final treatment for schizophrenia remains undiscovered and therefore, despite recent advances, schizophrenia is often associated with some chronic functional limitations. Nonetheless, the schizophrenic patient appreciates the empathy and continued concern of the family physician who assumes the responsibility for his/her long-term management.

Table 8. Extrapyramidal Symptoms (EPS)

Form	Common Clinical Differential Diagnosis	Onset	Age and Sex Predominance		Dose Related	Antiparkinsonian* Drug Contra-active Treatment Efficacy
Reversible						
1. Pseudoparkinsonism	Parkinson syndrome, apathy, retarded depressions, tremors of other origins	Days to Weeks	Geriatric	FM 3:1	Yes	0 to 4
2. Akathisia	Psychotic agitation, restless leg syndrome	Days Weeks	Middle	FM 3:2	Yes	0 to 3
3. Acute dystonic reactions	Psychotic posturing, hysteria, tetany, meningitis, tetanus	First 72 hours	Youths	MF 2:1	Yes	4
Potentially Irreversible						
1. Tardive dyskinesia	Huntington chorea, levodopa treatment, other involuntary movement disorders, transient neuroleptic withdrawal dyskinesias	Long-term neuroleptic administration	Geriatric	FM 2:1	Unknown	-2 to 0

*Treatment Response 4 - marked improvement 2 - moderate improvement 0 - no improvement -2 - worse

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