02 - 29.2 Medication Induced Movement Disorders

29.2 Medication-Induced Movement Disorders

Silva S, Swanson JM, van Zwieten-Boot B, Vitiello B, Wagner KD, Mangum B. Child and adolescent psychopharmacology in the new millennium: A workshop for academia, industry, and government. J Am Acad Child Adolesc Psychiatry. 2006;45(3):261–270. Fava GA, Tomba E, Tossani E. Innovative trends in the design of therapeutic trials in psychopharmacology and psychotherapy. Prog Neuropsychopharmacol Biol Psychiatry. 2013;40:306–311. Kosky N. A possible association between high normal and high dose olanzapine and prolongation of the PR interval. J Psychopharmacol. 2002;16:181. Lam RW, Wan DDC, Cohen NL, Kennedy SH. Combining antidepressants for treatment-resistant depression: A review. J Clin Psychiatry. 2002;63:685. Lieberman JA, Stroup TS, McEvoy JP, Swartz MS, Rosenheck RA. Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) investigators. N Engl J Med. 2005;353:1209. Liguori A. Psychopharmacology of attention: The impact of drugs in an age of increased distractions. Exp Clin Psychopharmacol. 2013;21(5):343–344. Malizia AL. The role of emission tomography in pharmacokinetic and pharmacodynamic studies in clinical psychopharmacology. J Psychopharmacol. 2006;20(Suppl 4):100–107. McGrath PJ, Stewart JW, Quitkin FM, Chen Y, Alpert JE. Predictors of relapse in a prospective study of fluoxetine treatment of major depression. Am J Psychiatry. 2006;163(9):1542. Meyer JH, Ginovart N, Boovariwala A, Sagrati S, Hussey D. Elevated monoamine oxidase a levels in the brain: An explanation for the monoamine imbalance of major depression. Arch Gen Psychiatry. 2006;63:1209. Moncrieff J. Magic bullets for mental disorders: The emergence of the concept of an “antipsychotic” drug. J Hist Neurosci. 2013;22(1):30–46. Preskorn SH. Pharmacogenomics, informatics, and individual drug therapy in psychiatry: Past, present and future. J Psychopharmacol. 2006;20(Suppl 4): 85–94. Sussman N. General principles of psychopharmacology. In: Sadock BJ, Sadock VA, Ruiz P, eds. Kaplan & Sadock’s Comprehensive Textbook of Psychiatry. 9th ed. Vol. 2. Philadelphia: Lippincott Williams & Wilkins; 2009:2965. Wadsworth EJK, Moss SC, Simpson SA, Smith AP. Psychotropic medication use and accidents, injuries, and cognitive failures. Hum Psychopharmacol. 2005;20(6):391–400. Zajecka J, Goldstein C. Combining and augmenting: Choosing the right therapies for treatment-resistant depression. Psychiatr Ann. 2005;35(12):994–1000. 29.2 Medication-Induced Movement Disorders Medication-induced movement disorders are commonly associated with the use of psychotropic drugs. Although most

frequently associated with drugs that block dopamine type 2 (D2) receptors, abnormal motor activity may occur with other types of medications as well. Sometimes it can be difficult to determine if abnormal motor movements are an adverse event or a symptom of an underlying disorder. For example, anxiety can resemble akathisia, and alcohol or benzodiazepine withdrawal can cause tremor. The American Psychiatric Association has decided to retain the term neuroleptic when discussing side effects associated with drugs used to treat psychosis—the dopamine receptor antagonists (DRAs) and second-generation antipsychotics (SGAs). The rationale for continued use of the term is that it was originally used to describe the tendency of

these drugs to cause abnormal movements. The most common neuroleptic-related movement disorders are parkinsonism, acute dystonia, and acute akathisia. Neuroleptic malignant syndrome is a life-threatening and often misdiagnosed condition. Neuroleptic-induced tardive dyskinesia is a lateappearing adverse effect of neuroleptic drugs and can be irreversible; recent data, however, indicate that the syndrome, although still serious and potentially disabling, is less pernicious than was previously thought in patients taking DRAs. The newer antipsychotics, the serotonin-dopamine antagonists (SDAs), block binding to dopamine receptors to a much lesser degree and thereby are presumed to be less likely to produce such movement disorders. Nevertheless, this risk remains and vigilance is still required when these drugs are prescribed. Table 29.2-1 lists the selected medications associated with movement disorders and their impact on relevant neuroreceptors. Table 29.2-1 Selected Medications Associated with Movement Disorders: Impact on Relevant Neuroreceptors NEUROLEPTIC-INDUCED PARKINSONISM AND OTHER MEDICATIONINDUCED PARKINSONISM Diagnosis, Signs, and Symptoms

Symptoms of neuroleptic-induced parkinsonism and other medication-induced parkinsonism include muscle stiffness (lead pipe rigidity), cogwheel rigidity, shuffling gait, stooped posture, and drooling. The pill-rolling tremor of idiopathic parkinsonism is rare, but a regular, coarse tremor similar to essential tremor may be present. The socalled rabbit syndrome, a tremor affecting the lips and perioral muscles, is another parkinsonian effect seen with antipsychotics, although perioral tremor is more likely than other tremors to occur late in the course of treatment. Epidemiology Parkinsonian adverse effects typically occur within 5 to 90 days of the initiation of treatment. Patients who are elderly and female are at the highest risk for neurolepticinduced parkinsonism, although the disorder can occur at all ages. Etiology Neuroleptic-induced parkinsonism is caused by the blockade of D2 receptors in the caudate at the termination of the nigrostriatal dopamine neurons. All antipsychotics can cause the symptoms, especially high-potency drugs with low levels of anticholinergic activity, most notably haloperidol (Haldol). Differential Diagnosis Included in the differential diagnosis are idiopathic parkinsonism, other organic causes of parkinsonism, and depression, which can also be associated with parkinsonian symptoms. Decreased psychomotor activity and blunted facial expression are symptoms of depression and idiopathic parkinsonism. Treatment Parkinsonism can be treated with anticholinergic agents, benztropine (Cogentin), amantadine (Symmetrel), or diphenhydramine (Benadryl) (Table 29.2-2). Anticholinergics should be withdrawn after 4 to 6 weeks to assess whether tolerance to the parkinsonian effects has developed; about half of patients with neuroleptic-induced parkinsonism require continued treatment. Even after the antipsychotics are withdrawn, parkinsonian symptoms can last up to 2 weeks and even up to 3 months in elderly patients. With such patients, the clinician may continue the anticholinergic drug after the antipsychotic has been stopped until the parkinsonian symptoms resolve completely. Table 29.2-2 Drug Treatment of Extrapyramidal Disorders

NEUROLEPTIC MALIGNANT SYNDROME Diagnosis, Signs, and Symptoms Neuroleptic malignant syndrome is a life-threatening complication that can occur anytime during the course of antipsychotic treatment. The motor and behavioral symptoms include muscular rigidity and dystonia, akinesia, mutism, obtundation, and agitation. The autonomic symptoms include hyperthermia, diaphoresis, and increased pulse and blood pressure. Laboratory findings include an increased white blood cell count and increased levels of creatinine phosphokinase, liver enzymes, plasma myoglobin, and myoglobinuria, occasionally associated with renal failure. Epidemiology About 0.01 to 0.02 percent of patients treated with antipsychotics develop neuroleptic malignant syndrome. Men are affected more frequently than women, and young patients are affected more commonly than elderly patients. The mortality rate can reach 10 to 20 percent or even higher when depot antipsychotic medications are involved. Course and Prognosis The symptoms usually evolve over 24 to 72 hours, and the untreated syndrome lasts 10 to 14 days. The diagnosis is often missed in the early stages, and the withdrawal or agitation may mistakenly be considered to reflect an exacerbation of the psychosis. Treatment In addition to supportive medical treatment, the most commonly used medications for

the condition are dantrolene (Dantrium) and bromocriptine (Parlodel), although amantadine (Symmetrel) is sometimes used (Table 29.2-3). Bromocriptine and amantadine pose direct DRA effects and may serve to overcome the antipsychoticinduced dopamine receptor blockade. The lowest effective dosage of the antipsychotic drug should be used to reduce the chance of neuroleptic malignant syndrome. Highpotency drugs, such as haloperidol, pose the greatest risk. Antipsychotic drugs with anticholinergic effects seem less likely to cause neuroleptic malignant syndrome. Electroconvulsive therapy (ECT) has been used. Table 29.2-3 Treatment of Neuroleptic Malignant Syndrome MEDICATION-INDUCED ACUTE DYSTONIA Diagnosis, Signs, and Symptoms Dystonias are brief or prolonged contractions of muscles that result in obviously abnormal movements or postures, including oculogyric crises, tongue protrusion, trismus, torticollis, laryngeal–pharyngeal dystonias, and dystonic postures of the limbs and trunk. Other dystonias include blepharospasm and glossopharyngeal dystonia; the latter results in dysarthria, dysphagia, and even difficulty in breathing, which can cause cyanosis. Children are particularly likely to evidence opisthotonos, scoliosis, lordosis, and writhing movements. Dystonia can be painful and frightening and often results in noncompliance with future drug treatment regimens. Epidemiology The development of acute dystonic symptoms is characterized by their early onset during the course of treatment with neuroleptics. There is a higher incidence of acute dystonia in men, in patients younger than age 30 years, and in patients given high dosages of high-potency medications.

Etiology Although it is most common with intramuscular doses of high-potency antipsychotics, dystonia can occur with any antipsychotic. The mechanism of action is thought to be dopaminergic hyperactivity in the basal ganglia that occurs when central nervous system (CNS) levels of the antipsychotic drug begin to fall between doses. Differential Diagnosis The differential diagnosis includes seizures and tardive dyskinesia. Course and Prognosis Dystonia can fluctuate spontaneously and respond to reassurance, so the clinician gets the false impression that the movement is hysterical or completely under conscious control. Treatment Prophylaxis with anticholinergics or related drugs (outlined in Table 29.2-2) usually prevents dystonia, although the risks of prophylactic treatment weigh against that benefit. Treatment with intramuscular anticholinergics or intravenous or intramuscular diphenhydramine (Benadryl) (50 mg) almost

always relieves the symptoms. Diazepam (Valium) (10 mg intravenously), amobarbital (Amytal), caffeine sodium benzoate, and hypnosis have also been reported to be effective. Although tolerance for the adverse effects usually develops, it is prudent to change the antipsychotic if the patient is particularly concerned that the reaction may recur. MEDICATION-INDUCED ACUTE AKATHISIA Diagnosis, Signs, and Symptoms Akathisia is subjective feelings of restlessness, objective signs of restlessness, or both. Examples include a sense of anxiety, inability to relax, jitteriness, pacing, rocking motions while sitting, and rapid alternation of sitting and standing. Akathisia has been associated with the use of a wide range of psychiatric drugs, including antipsychotics, antidepressants, and sympathomimetics. Once akathisia is recognized and diagnosed, the antipsychotic dose should be reduced to the minimal effective level. Akathisia may be associated with a poor treatment outcome. Epidemiology Middle-aged women are at increased risk of akathisia, and the time course is similar to that for neuroleptic-induced parkinsonism. Treatment

Three basic steps in the treatment of akathisia are reducing medication dosage, attempting treatment with appropriate drugs, and considering changing the neuroleptic. The most efficacious drugs are β-adrenergic receptor antagonists, although anticholinergic drugs, benzodiazepines, and cyproheptadine (Periactin) may benefit some patients. In some cases of akathisia, no treatment seems to be effective. TARDIVE DYSKINESIA Diagnosis, Signs, and Symptoms Tardive dyskinesia is a delayed effect of antipsychotics; it rarely occurs until after 6 months of treatment. The disorder consists of abnormal, involuntary, irregular choreoathetoid movements of the muscles of the head, limbs, and trunk. The severity of the movements ranges from minimal—often missed by patients and their families—to grossly incapacitating. Perioral movements are the most common and include darting, twisting, and protruding movements of the tongue; chewing and lateral jaw movements; lip puckering; and facial grimacing. Finger movements and hand clenching are also common. Torticollis, retrocollis, trunk twisting, and pelvic thrusting occur in severe cases. In the most serious cases, patients may have breathing and swallowing irregularities that result in aerophagia, belching, and grunting. Respiratory dyskinesia has also been reported. Dyskinesia is exacerbated by stress and disappears during sleep. Epidemiology Tardive dyskinesia develops in about 10 to 20 percent of patients who are treated for more than a year. About 20 to 40 percent of patients who require long-term hospitalization have tardive dyskinesia. Women are more likely to be affected than men. Children, patients who are more than 50 years of age, and patients with brain damage or mood disorders are also at high risk. Course and Prognosis Between 5 and 40 percent of all cases of tardive dyskinesia eventually remit, and between 50 and 90 percent of all mild cases remit. Tardive dyskinesia is less likely to remit in elderly patients than in young patients, however. Treatment The three basic approaches to tardive dyskinesia are prevention, diagnosis, and management. Prevention is best achieved by using antipsychotic medications only when clearly indicated and in the lowest effective doses. The atypical antipsychotics are associated with less tardive dyskinesia than the older antipsychotics. Clozapine (Clozaril) is the only antipsychotic to have minimal risk of tardive dyskinesia and can even help improve preexisting symptoms of tardive dyskinesia. This has been attributed to its low affinity for D2 receptors and high affinity for 5-hydroxytryptamine (5-HT)

receptor antagonism. Patients who are receiving antipsychotics should be examined regularly for the appearance of abnormal movements, preferably with the use of a standardized rating scale (Table 29.2-4). Patients frequently experience an exacerbation of their symptoms when the DRA is

withheld, whereas substitution of an SDA may limit the abnormal movements without worsening the progression of the dyskinesia. Table 29.2-4 Abnormal Involuntary Movement Scale (AIMS) Examination Procedure Once tardive dyskinesia is recognized, the clinician should consider reducing the dose of the antipsychotic or even stopping the medication altogether. Alternatively, the clinician may switch the patient to clozapine or to one of the new SDAs. In patients who cannot continue taking any antipsychotic medication, lithium (Eskalith), carbamazepine (Tegretol), or benzodiazepines may effectively reduce the symptoms of both the movement disorder and the psychosis. TARDIVE DYSTONIA AND TARDIVE AKATHISIA On occasion, dystonia and akathisia emerge late in the course of treatment. These symptoms may persist for months or years despite drug discontinuation or dose reduction. MEDICATION-INDUCED POSTURAL TREMOR Diagnosis, Signs, and Symptoms Tremor is a rhythmic alteration in movement that is usually faster than one beat per

second. Fine tremor (8 to 12 Hz) is most common. Epidemiology Typically, tremors decrease during periods of relaxation and sleep and increase with stress or anxiety. Etiology Whereas all the above diagnoses specifically include an association with a neuroleptic, a range of psychiatric medications can produce tremor—most notably, lithium, stimulants, antidepressants, caffeine, and valproate (Depakene). Treatment The treatment involves four principles:

1. The lowest possible dose of the psychiatric drug should be taken.
2. Patients should minimize caffeine consumption.
3. The psychiatric drug should be taken at bedtime to minimize the amount of daytime tremor.
4. β-adrenergic receptor antagonists (e.g., propranolol [Inderal]) can be given to treat drug-induced tremors. OTHER MEDICATION-INDUCED MOVEMENT DISORDERS Nocturnal Myoclonus Nocturnal myoclonus consists of highly stereotyped, abrupt contractions of certain leg muscles during sleep. Patients lack any subjective awareness of the leg jerks. The condition may be present in about 40 percent of persons over 65 years of age. The cause is unknown, but it is a rare side effect of selective serotonin reuptake inhibitors (SSRIs). The repetitive leg movements occur every 20 to 60 seconds, with extensions of the large toe and flexion of the ankle, the knee, and the hips. Frequent awakenings, unrefreshing sleep, and daytime sleepiness are major symptoms. No treatment for nocturnal myoclonus is universally effective. Treatments that may be useful include benzodiazepines, levodopa (Larodopa), quinine, and, in rare cases, opioids. Restless Leg Syndrome In restless leg syndrome, persons feel deep sensations of creeping inside the calves whenever sitting or lying down. The dysesthesias are rarely painful but are agonizingly relentless and cause an almost irresistible urge to move the legs; thus, this syndrome interferes with sleep and with falling asleep. It peaks in middle age and occurs in 5 percent of the population. The cause is unknown, but it is a rare side effect of SSRIs.

Symptoms are relieved by movement and by leg massage. The dopamine receptor agonists ropinirole (Requip) and pramipexole (Mirapex) are effective in treating this syndrome. Other treatments include the benzodiazepines, levodopa, quinine, opioids, propranolol, valproate, and carbamazepine. HYPERTHERMIC SYNDROMES All the medication-induced movement disorders may be associated with hyperthermia. Table 29.2-5 lists the various conditions associated with hyperthermia. Table 29.2-5 Drug-Induced Central Hyperthermic Syndromesa REFERENCES Ananth

J, Parameswaran S, Gunatilake S, Burgoyne K, Sidhom T. Neuroleptic malignant syndrome and atypical antipsychotic drugs. J Clin Psychiatry. 2004;65(4):464.

Bai YM, Yu SC, Chen JY, Lin CY, Chou P. Risperidone for pre-existing severe tardive dyskinesia: A 48-week prospective follow-up study. Int Clin Psychopharmacol. 2005;20:79. Bratti IM, Kane JM, Marder SR. Chronic restlessness with antipsychotics. Am J Psychiatry. 2007;164(11):1648. Caroff SN, Mann SC, Campbell EC, Sullivan KA. Movement disorders associated with atypical antipsychotic drugs. J Clin Psychiatry. 2002;63(Suppl 4):12. Damier P, Thobois S, Witjas T, Cuny E, Derost P. Bilateral deep brain stimulation of the globus pallidus to treat tardive dyskinesia. Arch Gen Psychiatry. 2007;64:170. Dayalu P, Chou KL. Antipsychotic-induced extrapyramidal symptoms and their management. Expert Opin Pharmacother. 2008;9:1451. Factor SA, Lang AE, Weiner WJ, eds. Drug Induced Movement Disorders. 2nd ed. Malden, MA: Blackwell Futura; 2005. Gunes A, Dahl ML, Spina E, Scordo MG. Further evidence for the association between 5-HT2C receptor gene polymorphisms and extrapyramidal side effects in male schizophrenic patients. Eur J Clin Pharmacol. 2008;64:477. Gunes A, Scordo MG, Jaanson P, Dahl ML. Serotonin and dopamine receptor gene polymorphisms and the risk of extrapyramidal side effects in perphenazine-treated schizophrenic patients. Psychopharmacology. 2007;190:479. Guzey C, Scordo MG, Spina E, Landsem VM, Spigset O. Antipsychotic-induced extrapyramidal symptoms in patients with schizophrenia: Associations with dopamine and serotonin receptor and transporter polymorphisms. Eur J Clin Pharmacol. 2007; 63:233. Janicak PG, Beedle D. Medication-induced movement disorders. In: Sadock BJ, Sadock VA, Ruiz P, eds. Kaplan & Sadock’s Comprehensive Textbook of Psychiatry. 9th ed. Vol. 2. Philadelphia: Lippincott Williams & Wilkins; 2009:2996. Janno S, Holi M, Tuisku K, Wahlbeck K. Prevalence of neuroleptic-induced movement disorders in chronic schizophrenic inpatients. Am J Psychiatry. 2004;161:160. Koning JP, Tenback DE, van os J, Aleman A, Kahn RS, van Harten PN. Dyskinesia and parkinsonism in antipsychotic-naive patients with schizophrenia, first-degree relatives and healthy controls: A meta-analysis. Schizophr Bull. 2010:36(4):723–731. Lee PE, Sykora K, Gill SS, Mamdani M, Marras C, Anderson G, Shulman KI, Stukel T, Normand SL, Rochon PA. Antipsychotic medications and drug-induced movement disorders other than parkinsonism: A population-based cohort study in older adults. J Am Geriatr Soc. 2005;53(8):1374–1379. Lencer R, Eismann G, Kasten M, Kabakci K, Geithe V. Family history of movement disorders as a predictor for neurolepticinduced extrapyramidal symptoms. Br J Psychiatry. 2004;185:465. Lyons KE, Pahwa R. Efficacy and tolerability of levetiracetam in Parkinson disease patients with levodopa-induced dyskinesia. Clin Neuropharmacol. 2006;29(3):148–153. Meco G, Fabrizio E, Epifanio A, Morgante F, Valente M. Levetiracetam in tardive dyskinesia. Clin Neuropharmacol. 2006;29:265. Miller del D, Caroff SN, Davis SM, Rosenheck RA, McEvoy JP. Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) investigators: Extrapyramidal side-effects of antipsychotics in a randomised trial. Br J Psychiatry. 2008;193:279. Pappa S, Dazzan P. Spontaneous movement disorders in antipsychotic-naive patients with first-episode psychoses: A systematic review. Psychol Med. 2009;39:1065–1076. Poyurovsky M, Pashinian A, Weizman R, Fuchs C, Weizman A. Low-dose mirtazapine: A new option in the treatment of antipsychotic-induced akathisia. A randomized, double-blind, placebo- and propranolol-controlled trial. Biol Psychiatry. 2006;59:1071. Soares-Weiser K, Fernandez HH. Tardive dyskinesia. Semin Neurol. 2007;27:159. Strous RD, Stryjer R, Maayan R, Gal G, Viglin D. Analysis of clinical symptomatology, extrapyramidal symptoms and neurocognitive dysfunction following dehydroepiandrosterone (DHEA) administration in olanzapine treated

Revision #1
Created 2026-01-04 19:51:41 UTC by Omar Ayman
Updated 2026-01-04 19:51:41 UTC by Omar Ayman