Drug-Induced Movement Disorders: Emergencies and Management

Bradley J. Robottom, MD[a], Lisa M. Shulman, MD[b], William J. Weiner, MD[b,*]

KEYWORDS

• Movement disorders • Emergency • Dystonia
• Parkinsonism • Drug-induced • Tremor

Movement disorders often have an insidious onset and slow progression, and are not often associated with emergency situations. However, neurologists may be called on to diagnose and treat evolving movement disorders or acute complications of existing diseases in the emergency room or intensive care unit. Such situations meet the working definition of an "emergency," a rapidly evolving disorder (hours to days) in which the failure to diagnose and treat may lead to significant morbidity or mortality.[1] Because the key to diagnosis in movement disorders is recognition, key features that help to distinguish each movement disorder are presented in **Table 1**. This article discusses rapidly evolving situations that may require emergency intervention. Several of the disorders discussed are rare, so treatment guidelines are often not based on randomized, double-blind, placebo-controlled trials.

NEUROLEPTIC MALIGNANT SYNDROME

Neuroleptic malignant syndrome (NMS), first described in 1960,[2] is an iatrogenic disorder resulting from exposure to drugs that block dopamine receptors. Although most cases are caused by neuroleptics (both typical and atypical, even clozapine),[3–6] other medications such as prochlorperazine, metoclopramide, amoxapine, tetrabenazine, droperidal, lithium, and promethazine are also implicated.[7–11] Diagnostic criteria

The authors do not have any financial conflicts of interest in regards to the content of this article.
[a] Durham Office, 4111 Ben Franklin Boulevard, Durham, NC 27704, USA
[b] Department of Neurology, University of Maryland School of Medicine, 110 South Paca Street, Third Floor, Baltimore, MD 21201, USA
* Corresponding author.
E-mail address: Wweiner@som.umaryland.edu

Neurol Clin 30 (2012) 309–320
doi:10.1016/j.ncl.2011.09.007 **neurologic.theclinics.com**
0733-8619/12/$ – see front matter

Table 1
Clinical definitions of movement disorders

Myoclonus	• Sudden, brief, shocklike movements • May be due to muscle contraction (positive myoclonus) or loss of muscle tone (negative myoclonus or asterixis)
Dystonia	• Involuntary sustained muscle contractions that produce twisting or squeezing movements • Often accompanied by abnormal posture
Parkinsonism	• Cardinal features include bradykinesia, rigidity, tremor, and postural instability • All features need not be present • Drug-induced parkinsonism is often symmetric and may lack tremor
Tremor	• Rhythmic, oscillatory movement produced by alternating or synchronous contractions of antagonist muscles
Tics	• Brief, paroxysmal movements or vocalizations sometimes accompanied by premonitory urge • May be stereotyped • Unlike other hyperkinetic movements, may be voluntarily suppressed for a short period of time
Chorea	• Involuntary, irregular, purposeless movements that "flow" into one another in a random fashion • Rapid, large-amplitude proximal movements that are sometimes described as "flinging," are referred to as ballism, and represent an extreme end of the spectrum of chorea

integrating clinical and laboratory features (**Table 2**) have been developed.[12] Newer consensus guidelines that include expert opinion from psychiatrists, neurologists, anesthesiologists, and emergency medicine specialists are in development.[13] Because the incidence of NMS is low (0.2%),[14] a high index of suspicion is necessary to make the appropriate diagnosis. NMS is important to consider in any patient with acute-onset parkinsonism and fever because it is life threatening (mortality rate 5%–20%). Young and middle-aged men appear to be at higher risk.[15] Postpartum women may also have an elevated risk.[16] Case reports of identical twins with NMS suggest that there may be genetic susceptibility as well.[17]

NMS is a clinical syndrome comprising fever, rigidity, mental status change, autonomic dysfunction, and other movement disorders (tremor, dystonia, and myoclonus). Key laboratory abnormalities include leukocytosis and elevated creatine phosphokinase. In addition, acute-phase reactants including albumin and serum iron are decreased.[18] Symptoms often begin after initiation or an increase in neuroleptic dose.[3] NMS increases in severity over 48 to 72 hours and lasts 2 to 14 days.[19] Medical

Table 2
Diagnostic criteria for NMS

Criteria	Feature
Major	Fever, rigidity, elevated creatine phosphokinase level
Minor	Tachycardia, abnormal blood pressure, tachypnea, altered consciousness, diaphoresis, leukocytosis

The presence of all 3 major, or 2 major and 4 minor criteria, indicates a high likelihood of NMS in the appropriate clinical context.

complications can be chronic and irreversible and include renal failure from rhabdomyolysis, respiratory failure from decreased chest wall compliance, aspiration pneumonia, and other complications of immobility such as deep venous thrombosis and pressure ulcers. Pulmonary embolism, pneumonia, or renal failure may result in death.

No prospective, randomized trials exist for NMS. Key steps in treatment include withdrawal of the causative agent and treatment with dopaminergic agents. Bromocriptine has been used most often and is considered the drug of choice[20]; however, other dopaminergic agents including carbidopa/levodopa, ropinirole, and pramipexole are likely effective. Dantrolene, a nonspecific muscle relaxant, reduces muscular rigidity and minimizes rhabdomyolysis if the dopaminergic agent does not reverse the symptoms.[21] Combination therapy has been found to be safe and effective,[20] and treatment should continue for 7 to 10 days depending on the half-life of the causative agent. One-third of patients may relapse if neuroleptics are restarted too early, so waiting at least 2 weeks after NMS has cleared is good practice.[22] In patients who require acute treatment of psychosis, electroconvulsive therapy has been successful.[23]

PARKINSONISM-HYPERPYREXIA SYNDROME

Parkinsonism-hyperpyrexia syndrome (PHS) may be indistinguishable from NMS except that it occurs in patients with preexisting parkinsonism. PHS occurs in patients with Parkinson disease (PD) who abruptly withdraw or reduce dopaminergic medications. It was first reported in the context of abrupt discontinuation of antiparkinsonian medications during "levodopa holidays" in the 1980s.[24–26] Although levodopa holidays are no longer recommended, patient noncompliance or abrupt changes in medication replicate that scenario. Aggressive medication adjustments are not uncommon, particularly after deep brain stimulation surgery (DBS) in PD. Clinicians must realize that PHS is a potential complication and that DBS does not protect the patient from PHS.[27] Although abrupt withdrawal of first-line antiparkinsonian medication (carbidopa/levodopa and dopamine agonists) is the typical scenario for PHS, discontinuation of amantadine or tolcapone has also been reported as causative.[28,29] Rapidly switching between dopamine agonists may also lead to PHS.[30] Dehydration and metabolic disturbances may also precipitate it.[31] Treatment involves supportive measures and reinstituting dopaminergic therapy. Bromocriptine and dantrolene may be added as additional therapy. High-dose intravenous methylprednisolone has been proposed as adjunctive therapy, and appears to be effective based on one small, randomized trial.[32] Despite treatment, permanent worsening of PD and fatalities have been reported.[33]

SEROTONIN SYNDROME

Any drug that enhances serotonergic transmission can precipitate serotonin syndrome (SS), which has the core clinical features of fever, myoclonus, and altered mental status.[34] SS was first described in 1960 in patients receiving monoamine oxidase inhibitor (MAO-I) monotherapy,[35] but is now encountered in patients taking 2 or more drugs with serotonergic actions (tricyclic antidepressants or selective serotonin reuptake inhibitors [SSRI] in combination with nonselective MAO-I) (**Box 1**).[36] Although selective MAO-B inhibitors (rasagiline, selegiline) do carry a warning regarding their use in combination with SSRIs, the agents are routinely used together in PD patients with only rare reports of SS occurring.[37] An underrecognized causative agent of SS is fentanyl, a widely used anesthetic that is a direct serotonin agonist. When used in patients taking SSRIs, it has the potential to cause SS.[38,39] Many of

Box 1 Drugs reported to cause serotonin syndrome
Monoamine oxidase inhibitors
Selective serotonin reuptake inhibitors
Serotonin and norepinephrine reuptake inhibitors
Tricyclic antidepressants
L-Tryptophan
Buspirone
Opiates (except morphine)
Lithium
Triptans
3,4-Methylenedioxymethamphetamine (ecstasy)
Lysergic acid diethylamide (LSD)
Amphetamines
Cocaine

the clinical features overlap with NMS; however, SS may have additional clinical features such as myoclonus, hyperreflexia, seizures, and mood alteration (restlessness, elevated mood).[40] This overlap may relate to the impact that elevated serotonin levels have on lowering dopamine levels. Treatment consists of discontinuation of the causative agent, supportive therapy, and cyproheptadine for severe cases. Cyproheptadine, an antihistamine and serotonin antagonist, is given in divided doses up to a maximum dose of 32 mg/d.[41] SS may resolve quickly[42] or can be fatal. Two case reports have been published detailing the use of electroconvulsive therapy for the treatment of refractory SS.[43] As with NMS and PHS, the rarity and seriousness of SS precludes large, randomized trials.

ACUTE DYSTONIC REACTION

Acute dystonic reaction is most commonly seen after exposure to dopamine receptor blockers, both neuroleptics and antiemetics. Dystonia begins within 24 hours of exposure, and 90% of reactions occur within 5 days.[44] Acute dystonic reactions are less common than tardive dyskinesia or drug-induced parkinsonism, affecting approximately 6% of patients exposed to "typical" neuroleptics and 1% to 2% of those exposed to "atypical" neuroleptics.[45] Clinical manifestations are diverse, usually affecting the head and neck. Laryngeal dystonia, blepharospasm, cervical dystonia, oculogyric crisis, and focal limb dystonia have all been reported. Acute dystonic reactions are more common in young men,[46] whereas tardive dyskinesia and drug-induced parkinsonism are more common in the elderly.[45] Concomitant alcohol abuse may increase the risk of developing acute dystonic reactions and akathisia.[47,48] Treatment with an intravenous anticholinergic agent such as benztropine (1–2 mg) or with diphenhydramine (25–50 mg) is very effective (**Table 3**). Because of the possibility of a reoccurrence, a short oral course of an anticholinergic (4–7 days) may be necessary.[45] After an acute dystonic reaction, patients are at higher risk for future dystonic reactions when exposed to other dopamine receptor blockers.[49]

Table 3
Treatment of hyperkinetic movement disorders

Movement Disorder	Medication Class	Medication	Initial Daily Dose (mg)	Recommended Maximum Daily Dose (mg)
Chorea	Neuroleptic	Haloperidol	0.5	8
		Risperidone	0.5	6
	Dopamine-depleting agent[a]	Tetrabenazine	12.5	75
	Benzodiazepine	Clonazepam	0.5	6
Myoclonus	Anticonvulsant	Valproic acid	750	Titrate to serum level
		Levetiracetam	500	3000
		Primidone[a]	12.5	750
	Benzodiazepine	Clonazepam	0.5	6
Tics	Neuroleptic	Haloperidol	0.5	8
		Risperidone	0.5	6
	Dopamine-depleting agent[a]	Tetrabenazine	12.5	75
	Antihypertensive[a]	Clonidine	0.1	0.6
		Guanfacine	1	3
Acute dystonic reaction	Anticholinergic	Benztropine	1	6
		Diphenhydramine	25	400

[a] These agents are generally not helpful in acute treatment but can be given with a neuroleptic that could eventually be discontinued.

COCAINE AND AMPHETAMINES

Cocaine and amphetamines both enhance neurotransmission of monoamines (dopamine, norepinephrine, and serotonin). Cocaine blocks neurotransmitter reuptake at the synaptic nerve endings[50] while amphetamines increase release of neurotransmitters from synaptic nerve endings.[51] Chronic use of these psychostimulants can lead to stereotypic motor behaviors, tics, dystonia, chorea, and myoclonus.[52–54] Amphetamine use is highly associated with punding behaviors (complex prolonged, purposeless, and stereotyped behavior),[55] while chorea is well described in cocaine users ("crack dancing").[56] While abnormal movements usually appear during intoxication, they may persist for days or weeks, and have been described during withdrawal.[57–60] In patients with tic disorders, psychostimulants have the potential to lead to an acute worsening[61–63]; this has not been proved in a randomized treatment trial of methylphenidate in children with attention-deficit/hyperactivity disorder and tic disorders.[64] No specific treatment is available for neurologic complications of psychostimulant toxicity.

3,4-METHYLENEDIOXYMETHAMPHETAMINE

3,4-Methylenedioxymethamphetamine, or ecstasy, is a "designer drug" that has effects similar to those of psychostimulants and hallucinogens.[51] Side effects can include a variety of neurologic symptoms including anxiety, tremor, ataxia, rigidity, myoclonus, and nystagmus.[65,66] Of importance, ecstasy may also cause seizures and malignant hyperthermia.[67] It should be considered in the differential diagnosis of both NMS and SS. The mechanism of hyperthermia in ecstasy overdose may be attributable to massive serotonin release, and there are many similarities to the

symptoms seen in classic SS as well as NMS.[68] Treatment is generally supportive, though aggressive measures should be taken to prevent extreme hyperthermia. In case reports, dantrolene has been effective in the treatment of ecstasy overdose complicated by hyperthermia (>40°C).[69]

OPIOIDS

Opioids are prescribed commonly for the treatment of pain, but are also frequently abused. When used at typical doses, opioids may cause myoclonus and reduce the seizure threshold.[70] One prescription opioid, meperidine, has a much higher likelihood of adverse neurologic effects and is of particular interest. Meperidine may cause a variety of neuropsychiatric adverse effects including agitation, delirium, hallucinations, seizure, tremor, and myoclonus.[71,72] In addition, meperidine may contribute to the development of SS in patients taking tricyclic antidepressants, SSRIs, or serotonin and norepinephrine reuptake inhibitors.[73–75]

MOTOR FLUCTUATIONS AND DYSKINESIA IN PARKINSON DISEASE

Motor fluctuations are common in advanced PD, seen in 40% of patients by 4 to 6 years with an increasing frequency of 10% per year.[76] Generally not dangerous, motor fluctuations are one of the more common disease-specific reasons for which patients seek emergency treatment. During "off" periods, prominent rigidity, bradykinesia, and postural instability may develop, making it impossible for the patients to care for themselves or to walk. Psychiatric features may become pronounced, including depressed mood, anxiety, and, panic. Dysautonomia including tachycardia, diaphoresis, and variations in blood pressure may occur.[77] While "off" periods do not usually result in a visit to the emergency department, some situations lead to emergency evaluation. Patients with suddenly worsening "off" periods associated with new symptoms (eg, freezing, unpredictable, or prolonged "off" periods) are more likely to seek urgent evaluation.[77] In these situations investigation should search for a potential cause of the abrupt change. A careful compilation of medication history is necessary to ensure that no changes have been made to the antiparkinsonian regimen. Patients should also be questioned about the addition of medications to their regimen, particularly dopamine receptor blockers (antipsychotics and antiemetics), as exposure to dopamine receptor antagonists may lead to abrupt deterioration in PD. Concurrent infection (urinary tract infection, pneumonia) or metabolic derangement should be considered. In a patient with falls and abruptly worsening PD, subdural hematoma should be considered.[78]

Levodopa-induced dyskinesia (LID) is usually not dangerous and is most often managed in the outpatient setting. However, severe LID may lead to rhabdomyolysis and dehydration.[77] Generalized LID may be complicated by involvement of respiratory muscles, with patients reporting symptoms of dyspnea, tachypnea, chest wall discomfort, and involuntary grunting.[79] Failure to recognize respiratory dyskinesia may lead to unnecessary testing. Greater emphasis on medical and medication history may improve the diagnosis of respiratory dyskinesia in the emergency setting. Treatment of dyskinesia should include lowering (or holding) levodopa dosage. Benzodiazepines may be useful to treat concomitant anxiety. Neuroleptics should not be used. Long-term management for chronic dyskinesia may involve the addition of amantadine or DBS.[80]

PSYCHOSIS IN PARKINSON DISEASE

Psychosis in PD is a common reason for inpatient admission and is a strong predictor of nursing home placement.[81] It is more commonly encountered in PD with dementia

(PDD), occurring in 45% to 64% of patients.[82,83] Visual hallucinations are more common than auditory hallucinations, and usually consist of complex, formed visual images, often of unknown but nonthreatening people.[84] Paranoid delusions may accompany hallucinations, and constitute a greater problem. Hallucinations and mild delusions may be treated at home, but paranoia may become extreme and require hospitalization. PD psychosis may be precipitated by metabolic derangements, infections (urinary tract infection, pneumonia), and changes in drug therapy, including addition of any dopaminergics or anticholinergics.

Emergency treatment of psychosis requires a multifaceted approach. The patient's living conditions need to be assessed to determine whether hospitalization is required. A thorough workup for metabolic or infectious disorders is indicated. Nonessential psychoactive medications should be discontinued. Dopaminergic drugs that are least potent with respect to motor function should be reduced (anticholinergics, amantadine, dopamine agonists, MAO-B inhibitors, catechol-*O*-methyltransferase inhibitors).[85] The daily levodopa dose may also need to be lowered. An antipsychotic medication can be started, and is often necessary to resolve psychosis. Useful antipsychotics include clozapine and quetiapine. Clozapine has the most robust evidence base.[86] Despite the lack of compelling evidence for quetiapine,[86] it is often prescribed because of clozapine's risk of agranulocytosis and the need for monitoring the complete blood count on a frequent basis. Other antipsychotics, "typical" and "atypical," may cause unacceptable worsening of motor function and should not be used for treatment of psychosis in PD.[85,86]

ACUTE PARKINSONISM

Acute or subacute onset of parkinsonism has a broad differential diagnosis. Parkinsonism as part of a primary neurodegenerative disease is insidious in onset and slowly progressive. However, when parkinsonism develops over a period of days to weeks, a secondary cause should be considered. In this situation a review of the medication list, investigation for a structural lesion, and examination for pathognomonic findings are most important. In the absence of a structural abnormality, particular attention should be given to potential medication or toxic exposures (**Table 4**).[87]

While neuroleptics (typical and atypical) and dopamine-blocking antiemetics (especially metoclopramide) are widely recognized in causing parkinsonism, other medication classes and occupational toxins have also been implicated.

Table 4
Iatrogenic and toxic causes of acute parkinsonism

Drug-induced	Neuroleptics
	Antiepileptics
	Antidepressants
	Chemotherapeutic agents
	Amiodarone
	Antiemetics
Toxic	1-methyl-1-4-phenyl-4-proprionoxypiperidine (MPTP)
	Carbon monoxide
	Carbon disulfide
	Manganese
	Cyanide
	Methanol

SUMMARY

Although movement disorders are often not regarded as emergencies, there will be situations when the neurologist will be called upon to consult emergently. A common etiology in movement disorders emergencies is that of a toxic exposure, to either prescription or illicit drugs. The workup should always include a careful record of medication and drug history. Because these cases are rare, consulting a neurologist is advisable. This article has reviewed the diagnosis and management of acute-onset movement disorders occurring secondary to drug use, drug withdrawal syndromes, and drug-induced emergencies occurring in patients with movement disorders. These disorders are uncommon and few in any randomized controlled trials that have been conducted. When possible, treatment recommendations are made based on randomized trial data; however, due to the uncommon nature of the disorders, clinical experience and literature reports form the basis for many treatment recommendations.

REFERENCES

1. Frucht SJ, Fahn S, editors. Movement disorder emergencies: diagnosis and treatment. Totowa (NJ): Humana Press; 2005. p. 1.
2. Delay J, Pichot P, Lemperiere T. Un neuroleptique majeur non phenothiazine et non reserpinique l'haloperidal dans le traitement des psychoses. Ann Med Pscyhol 1960;118:145–52 [in French].
3. Shalev A, Munitz H. The neuroleptic malignant syndrome: agent and host interaction. Acta Psychiatr Scand 1986;50:18–25.
4. Caroff SN, Mann SC. Neuroleptic malignant syndrome. Psychopharmacol Bull 1988;24:25–9.
5. Shalev A, Hermesh H, Munitz H. Mortality from neuroleptic malignant syndrome. J Clin Psychiatry 1989;50:18–25.
6. Hasan S, Buckley P. Novel antipsychotics and the neuroleptic malignant syndrome: a review and critique. Am J Psychiatry 1998;115:1113–6.
7. Caroff SN, Mann SC, Campbell EC. Neuroleptic malignant syndrome. Adverse Drug React Bull 2001;209:799–802.
8. Khan FY, Qusad MJ. Neuroleptic malignant syndrome. Neuroscience 2006;11(2): 104–6.
9. Petzinger GM, Bressman SB. A case of tetrabenazine-induced neuroleptic malignant syndrome after prolonged treatment. Mov Disord 1997;12(2):246–8.
10. Washington C, Haines KA, Tam CW. Amoxipine-induced neuroleptic malignant syndrome. DICP 1989;23(9):713.
11. Gill J, Singh H, Nugent K. Acute lithium intoxication and neuroleptic malignant syndrome. Pharmacotherapy 2003;23(6):811–5.
12. Levenson JL. Neuroleptic malignant syndrome. Am J Psychiatry 1985;142(10): 1137–45.
13. Gurrera R, Caroff S, Cohen A. Neuroleptic malignant syndrome diagnosis: an international consensus study using the Delphi technique. Eur Psychiatry 2010; 25(Suppl 1):949.
14. Caroff SN, Mann SC. Neuroleptic malignant syndrome. Med Clin North Am 1993; 77:202.
15. Kipps CM, Fung VSC, Grattan-Smith P, et al. Movement disorder emergencies. Mov Disord 2005;20(3):322–34.
16. Alexander PJ, Thomas RM, Das A. Is risk of neuroleptic malignant syndrome increased in the postpartum period? J Clin Psychiatry 1998;59(5):254–5.

17. Otani K, Horiuchi M, Kondo T, et al. Is the predisposition to neuroleptic malignant syndrome genetically transmitted. Br J Psychiatry 1991;158(1):850–3.
18. Rosebush P, Anglin R, Richards C, et al. Neuroleptic malignant syndrome and acute phase response. J Clin Psychopharmacol 2008;28:459–61.
19. Berman BD. Neuroleptic malignant syndrome: a review for neurohospitalists. The Neurohospitalist 2011;1(1):41–7.
20. Rosenberg MR, Green M. Neuroleptic malignant syndrome: review of response to therapy. Arch Intern Med 1989;149:1927–31.
21. Adnet P, Lestavel P, Krivosic-Horber R. Neuroleptic malignant syndrome. Br J Anaesth 2000;85:129–35.
22. Rosebush PI, Stewart TD, Gelenberg AJ. Twenty neuroleptic rechallenges after neuroleptic malignant syndrome in 15 patients. J Clin Psychiatry 1989;50: 295–8.
23. Caroff SN, Mann SC, Keck PE. Specific treatment of the neuroleptic malignant syndrome. Biol Psychiatry 1998;44:378–81.
24. Weiner WJ, Koller WC, Perlik S, et al. Drug holiday and management of Parkinson disease. Neurology 1980;30:1257–61.
25. Sechi G, Tanda F, Mutani R. Fatal hyperpyrexia after withdrawal from levodopa. Neurology 1984;34:249–51.
26. Friedman JH, Feinberg SS, Feldman RG. A neuroleptic malignant-like syndrome due to levodopa therapy withdrawal. JAMA 1985;15:2792–5.
27. Factor SA. Fatal parkinsonism-hyperpyrexia syndrome in a Parkinson's disease patient while actively treated with deep brain stimulation. Mov Disord 2007; 22(1):148–53.
28. Ito T, Shibata K, Watanabe A, et al. Neuroleptic malignant syndrome following withdrawal of amantadine in a patient with influenza a encephalopathy. Eur J Pediatr 2001;160(6):401.
29. Iwuagwu CU, Riley D, Bonomo RA. Neuroleptic malignant-like syndrome in an elderly patient caused by abrupt withdrawal of tolcapone, a catechol-O-methyl transferase inhibitor. Am J Med 2000;108(6):517–8.
30. Reimer J, Kuhlmann A, Muller T. Neuroleptic malignant-like syndrome after rapid switch from bromocriptine to pergolide. Parkinsonism Relat Disord 2002;9(2):115–6.
31. Kuno S, Mizuta E, Yamasaki S. Neuroleptic malignant syndrome in parkinsonian patients: risk factors. Eur Neurol 1997;38:56–9.
32. Sato Y, Asoh T, Metoki N, et al. Efficacy of methylprednisolone pulse therapy on neuroleptic malignant syndrome in Parkinson's disease. J Neurol Neurosurg Psychiatry 2003;74:574–6.
33. Factor SA, Weiner WJ. Movement disorders emergencies: adults and children. American Academy of Neurology, 61st Annual Meeting. Seattle, WA, April 25–May 2, 2009.
34. Sternbach H. The serotonin syndrome. Am J Psychiatry 1991;148:705–13.
35. Oates JA, Sjoerdsma A. Neurologic effects of tryptophan in patients receiving a monoamine oxidase inhibitor. Neurology 1960;10:1076–8.
36. Mason PJ, Morris VA, Balcezak TJ. Serotonin syndrome. Presentation of 2 cases and review of the literature. Medicine 2000;79:201–9.
37. Robottom BJ. Efficacy, safety, and patient preference of monoamine oxidase B inhibitors in the treatment of Parkinson's disease. Patient Prefer Adherence 2011;5:57–64.
38. Alkhatib AA, Peterson KA, Tuteja AK. Serotonin syndrome as a complication of fentanyl sedation during esophagogastroduodenoscopy. Dig Dis Sci 2010;55: 215–6.

39. Kirschner R, Donovan JW. Serotonin syndrome precipitated by fentanyl during procedural sedation. J Emerg Med 2010;38(4):477–80.
40. Radomski JW, Dursun SM, Reveley MA, et al. An exploratory approach to the serotonin syndrome: an update of clinical phenomenology and revised diagnostic criteria. Med Hypotheses 2000;55(3):218–24.
41. Hall M, Buckley N. Serotonin syndrome. Aust Prescr 2003;26:62–3.
42. Mills KC. Serotonin syndrome: a clinical update. Crit Care Clin 1997;13(4): 763–83.
43. Okamoto N, Sakamoto K, Nagafusa Y, et al. Electroconvulsive therapy as a potentially effective treatment for severe serotonin syndrome: two case reports. J Clin Psychopharmacol 2010;30(3):350–2.
44. Diederich NJ, Goetz CG. Drug-induced movement disorders. Neurol Clin 1998; 16(1):125–39.
45. Pierre JM. Extrapyramidal symptoms with atypical antipsychotics: incidence, prevention and management. Drug Saf 2005;28(3):191–208.
46. van Harten PN, Hock HW, Kahn RS. Acute dystonia induced by drug treatment. BMJ 1999;319:623–6.
47. Lutz EG. Neuroleptic-induced akathisia and dystonia triggered by alcohol. JAMA 1976;236:2422–3.
48. Freed E. Alcohol-triggered neuroleptic-induced tremor, rigidity, and dystonia. Med J Aust 1981;2:44–5.
49. Campbell D. The management of acute dystonic reactions. Aust Prescriber 2001; 24:19–20.
50. Lange RA, Hillis LD. Cardiovascular complications of cocaine use. N Engl J Med 2001;345:351–8.
51. Brust JCM. Substance abuse and movement disorders. Mov Disord 2010;25: 2010–20.
52. Rylander G. Psychosis and the punding and choreiform syndromes in addictions to central stimulant drugs. Psychiatry Neurol Neurchir 1972;75:203–12.
53. Derlet RW, Alberston TE. Emergency department presentation of cocaine intoxication. Ann Emerg Med 1989;18:182–6.
54. Brody SL, Slovis CM, Wrenn KD. Cocaine-related medical problems: consecutive series of 233 patients. Am J Med 1990;88:325–31.
55. Randrup A, Munkvad J. Stereotyped activities produced by amphetamine in several species and man. Psychopharmacologia 1967;11:300–10.
56. Daras M, Koppel BS, Atos-Radzion E. Cocaine-induced choreoathetoid movements (crack-dancing). Neurology 1994;44:751–2.
57. Choy-Kwong M, Lipton RB. Dystonia related to cocaine withdrawal: a case report and pathogenic hypothesis. Neurology 1989;39:996–7.
58. Kumor K. Cocaine withdrawal dystonia. Neurology 1990;40:863–4.
59. Weiner WJ, Rubinstein A, Lewin B, et al. Cocaine-induced persistent dyskinesias. Neurology 2001;56:964–5.
60. Lundh H, Tunving K. An extrapyramidal choreiform syndrome caused by amphetamine addiction. J Neurol Neurosurg Psychiatry 1981;44:728–30.
61. Pascual-Leone A, Dhuna A. Cocaine-associated multifocal tics. Neurology 1990; 40:999–1000.
62. Factor SA, Sanchez-Ramos JR, Weiner WJ, et al. Cocaine and Tourette's syndrome. Ann Neurol 1988;23:423–4.
63. Golden GS. Gilles de la Tourette's syndrome following amphetamine administration. Dev Med Child Neurol 1976;16:76–7.

64. Kurlan R. Treatment of ADHD in children with tics: a randomized controlled trial. Neurology 2001;58:527–36.
65. Brown C, Osterloh J. Multiple severe complications from recreational ingestion of MDMA (ecstasy). JAMA 1987;258:780–1.
66. Hinkelbein J, Gabel A, Volz M, et al. Suicide attempt with high dose ecstasy. Anesthetist 2003;52:51–4.
67. Regenthal R, Kruger M, Rudolf K, et al. Survival after massive "ecstasy" (MDMA) ingestion. Intensive Care Med 1999;25:640–1.
68. Ames D, Wirshing WC. Ecstasy, the serotonin syndrome, and neuroleptic malignant syndrome—a possible link? JAMA 1993;269:869–70.
69. Grunau BE, Wiens MO, Brubacher JR. Dantrolene in the treatment of MDMA-related hyperpyrexia: a systematic review. CJEM 2010;12:435–42.
70. Lauterbach EC. Hiccup and apparent myoclonus after hydrocodone: a review of the opiate-related hiccup and myoclonus literature. Clin Neuropharmacol 1999; 22:87–92.
71. Hershey LA. Meperidine and central neurotoxicity. Ann Intern Med 1983;98: 548–9.
72. Kaiko RF, Folwy KM, Grabinski PY, et al. Central nervous system excitatory effects of meperidine in cancer patients. Ann Neurol 1983;13:180–5.
73. Dougherty JA, Young H, Shafi T. Serotonin syndrome induced by amitriptyline, meperidine, and venlafaxine. Ann Pharmacol 2002;36:1647–8.
74. Tissot TA. Probable meperidine-induced serotonin syndrome in a patient with a history of fluoxetine use. Anesthesiology 2003;98:1511–2.
75. Latta KS, Ginsberg B, Barkin RL. Meperidine: a critical review. Am J Ther 2002;9: 53–68.
76. Ahlskog JE, Muenter MD. Frequency of levodopa-related dyskinesias and motor fluctuations as estimated from the cumulative literature. Mov Disord 2001;16(3): 448–58.
77. Factor SA, Molho ES. Emergency department presentations of patients with Parkinson's disease. Am J Emerg Med 2000;18(2):209–15.
78. Chou SM, Gutmann L. Deteriorating parkinsonism and subdural hematomas. Neurology 2001;57:1295.
79. Weiner WJ, Goetz CG, Nausieda PA, et al. Respiratory dyskinesias: extrapyramidal dysfunction and dyspnea. Ann Intern Med 1978;88:327–31.
80. Pahwa R, Factor SA, Lyons KE, et al. Practice parameter: treatment of Parkinson disease motor fluctuations and dyskinesia (an evidence-based review): report of the Quality Standards Subcommittee of the American Academy of Neurology. Neurology 2006;66:983–95.
81. Aarsland D, Larsen JP, Tandberg E, et al. Predictors of nursing home placement in Parkinson's disease: a population-based, prospective study. J Am Geriatr Soc 2000;48:938–42.
82. Robottom BJ, Weiner WJ. Parkinson's disease dementia. Curr Psychiatry Rev 2009;5(3):218–25.
83. Giladi N, Treves TA, Paleacu D, et al. Risk factors for dementia, depression and psychosis in long-standing Parkinson's disease. J Neural Transm 2000;107(1):59–71.
84. Mosimann UP, Rowan EN, Partington CE, et al. Characteristics of visual hallucinations in Parkinson disease dementia and dementia with Lewy bodies. Am J Geriatr Psychiatry 2006;14:153–60.
85. Friedman JH, Factor SA. Atypical antipsychotics in the treatment of drug-induced psychosis in Parkinson's disease. Mov Disord 2000;15:201–11.

86. Miyasaki JM, Shannon K, Voon V, et al. Practice parameter: evaluation and treatment of depression, psychosis, and dementia in Parkinson disease (an evidence-based review). Neurology 2006;66:996–1002.
87. Robottom BJ, Weiner WJ, Factor SA. Movement disorders emergencies part 1: hypokinetic disorders. Arch Neurol 2011;68:567–72.