

## Guidelines for antipsychotic drug treatment — The American Psychiatric Association Task Force report on TD

The Task Force made the following recommendations:

- Long-term use of antipsychotic drugs in neurosis, depression, anxiety, personality disorder, and chronic pain states should be discouraged.
- Even in schizophrenia or related chronic psychosis, efforts should be made to maintain patients on the lowest effective dose of antipsychotic drugs while reexamining the need for continued treatment at least every six months. After remission of a first acute psychotic episode, the dose of antipsychotic drug should at least be decreased, and probably best discontinued, within 6 to 12 months. Plans to continue treatment beyond six months require discussion with the patient and family regarding the indication for prolonged antipsychotic drug treatment and the risks of TD. (See "Pharmacotherapy for schizophrenia: Side effect management".)
- Particular care is indicated for patients age 50 and older, patients with affective disorder, patients with treatment-resistant schizophrenia and negative symptoms, and possibly women.
- Since acute antipsychotic drug-induced parkinsonism and akathisia are an indicator of the extent of D2 receptor blockade, these adverse effects should be avoided by dose reduction or by use of a less potent agent. Drug-induced parkinsonism may also mask signs of dyskinesia. It is prudent to use the smallest effective dose required to control an individual patient's symptoms.
- Except for prevention of acute dystonic reactions, chronic use of prophylactic anticholinergic drugs should be discouraged since they do not prevent TD and can aggravate the involuntary movements once they emerge.
- Early antipsychotic drug withdrawal results in a better prognosis for recovery. Thus, patients on antipsychotic drugs should be carefully monitored for signs of TD at regular intervals with use of a standard dyskinesia rating scale such as the Abnormal Involuntary Movement Scale (form 1), which is useful to heighten awareness of mild manifestations of TD [4].
- Where possible, antipsychotic drugs should be tapered and discontinued as soon as the diagnosis of TD is made, although control of the patient's psychosis may ultimately be the most critical factor in the use of the offending drug.

For patients who are developing signs of TD while receiving first generation (conventional) antipsychotic drugs, but still require treatment for psychosis, it is now considered prudent to switch to second generation (atypical) antipsychotic drugs that may be associated with a lower risk for TD. However, there is no convincing evidence that altering the medication regimen ameliorates the course of TD once symptoms have developed. (See 'Second generation antipsychotic drugs' below.)

**Discontinuation of metoclopramide treatment** — Metoclopramide is used primarily as an antiemetic agent and/or as a prokinetic agent for the treatment of gastroparesis. It should be stopped immediately if the diagnosis of TD is made, and alternative treatments of the gastrointestinal symptoms should be used. As a preventive measure, metoclopramide should not be used continuously for longer than 12 weeks.

**PHARMACOLOGIC TREATMENT** — Numerous studies have evaluated various pharmacologic treatments of TD, but few therapies have produced more than slight to moderate benefit in clinical practice [5]. Thus, prevention, early detection, and management of potentially reversible cases are the cornerstones of modern treatment.

When clinically appropriate, pharmacologic interventions may be considered for patients who are developing signs of TD. The two main strategies are:

- Discontinuation of the offending drug
- Switching from a first to a second generation antipsychotic drug

For patients with a diagnosis of TD, additional pharmacologic interventions include the following:

- Use of benzodiazepines, botulinum toxin injections, valbenazine, or tetrabenazine to control symptoms of TD
- Paradoxically, resuming treatment with antipsychotic drugs in order to suppress TD (see 'Resumption of antipsychotic drugs' below)

The need for drugs to control symptoms of TD should be carefully assessed, since symptoms are often mild and not sufficiently bothersome to require treatment. In some cases, family members are more

disturbed by the involuntary movements than the patient, who may be relatively unaware of their clinical manifestations. However, this is more common among chronic or institutionalized patients than in ambulatory patients, many of whom are in psychiatric remission when TD appears.

#### References:

[https://www.uptodate.com/contents/tardive-dyskinesia-prevention-and-treatment?search=tardive%20dyskinesia%20treatment&source=search\\_result&selectedTitle=1~150&usage\\_type=default&display\\_rank=1](https://www.uptodate.com/contents/tardive-dyskinesia-prevention-and-treatment?search=tardive%20dyskinesia%20treatment&source=search_result&selectedTitle=1~150&usage_type=default&display_rank=1)

[https://www.uptodate.com/contents/tardive-dyskinesia-clinical-features-and-diagnosis?search=tardive%20dyskinesia&source=search\\_result&selectedTitle=1~150&usage\\_type=default&display\\_rank=1](https://www.uptodate.com/contents/tardive-dyskinesia-clinical-features-and-diagnosis?search=tardive%20dyskinesia&source=search_result&selectedTitle=1~150&usage_type=default&display_rank=1)

[https://www.uptodate.com/contents/second-generation-antipsychotic-medications-pharmacology-administration-and-side-effects?topicRef=4908&source=see\\_link](https://www.uptodate.com/contents/second-generation-antipsychotic-medications-pharmacology-administration-and-side-effects?topicRef=4908&source=see_link)

Tancredi LR. Malpractice and tardive dyskinesia: a conceptual dilemma. J Clin Psychopharmacol 1988; 8:71S.

Tardive dyskinesia: summary of a Task Force Report of the American Psychiatric Association. By the Task Force on Late Neurological Effects of Antipsychotic Drugs. Am J Psychiatry 1980; 137:1163.

Tardive dyskinesia: a Task Force Report of the American Psychiatric Association. American Psychiatric Association Press, Washington, DC 1992.

Guy W. ECDEU Assessment Manual for Psychopharmacology: Publication ADM 76-358. US Department of Public Health, Education, and Welfare, Washington, DC 1976.

Tarsy D. Tardive Dyskinesia. Curr Treat Options Neurol 2000; 2:205.

Soares-Weiser K, Rathbone J. Neuroleptic reduction and/or cessation and neuroleptics as specific treatments for tardive dyskinesia. Cochrane Database Syst Rev 2006; :CD000459.

Soares-Weiser K, Fernandez HH. Tardive dyskinesia. Semin Neurol 2007; 27:159.

Bhidayasiri R, Fahn S, Weiner WJ, et al. Evidence-based guideline: treatment of tardive syndromes: report of the Guideline Development Subcommittee of the American Academy of Neurology. Neurology 2013; 81:463.

Lieberman JA, Saltz BL, Johns CA, et al. The effects of clozapine on tardive dyskinesia. Br J Psychiatry 1991; 158:503.

Tamminga CA, Thaker GK, Moran M, et al. Clozapine in tardive dyskinesia: observations from human and animal model studies. *J Clin Psychiatry* 1994; 55 Suppl B:102.

Factor SA, Friedman JH. The emerging role of clozapine in the treatment of movement disorders. *Mov Disord* 1997; 12:483.

Spivak B, Mester R, Abesgaus J, et al. Clozapine treatment for neuroleptic-induced tardive dyskinesia, parkinsonism, and chronic akathisia in schizophrenic patients. *J Clin Psychiatry* 1997; 58:318.

Emsley R, Turner HJ, Schronen J, et al. A single-blind, randomized trial comparing quetiapine and haloperidol in the treatment of tardive dyskinesia. *J Clin Psychiatry* 2004; 65:696.

Sasaki Y, Kusumi I, Koyama T. A case of tardive dystonia successfully managed with quetiapine. *J Clin Psychiatry* 2004; 65:583.

Bouckaert F, Herman G, Peuskens J. Rapid remission of severe tardive dyskinesia and tardive dystonia with quetiapine. *Int J Geriatr Psychiatry* 2005; 20:287.

Tarsy D, Baldessarini RJ, Tarazi FI. Effects of newer antipsychotics on extrapyramidal function. *CNS Drugs* 2002; 16:23.

Caroff SN, Mann SC, Campbell EC, Sullivan KA. Movement disorders associated with atypical antipsychotic drugs. *J Clin Psychiatry* 2002; 63 Suppl 4:12.

Gunne LM, Häggström JE, Sjöquist B. Association with persistent neuroleptic-induced dyskinesia of regional changes in brain GABA synthesis. *Nature* 1984; 309:347.

Jeste DV, Wyatt RJ. Therapeutic strategies against tardive dyskinesia. Two decades of experience. *Arch Gen Psychiatry* 1982; 39:803.

Thaker GK, Nguyen JA, Strauss ME, et al. Clonazepam treatment of tardive dyskinesia: a practical GABA-mimetic strategy. *Am J Psychiatry* 1990; 147:445.

Bobruff A, Gardos G, Tarsy D, et al. Clonazepam and phenobarbital in tardive dyskinesia. *Am J Psychiatry* 1981; 138:189.

Bergman H, Bhoopathi PS, Soares-Weiser K. Benzodiazepines for antipsychotic-induced tardive dyskinesia. *Cochrane Database Syst Rev* 2018; 1:CD000205.

Bhoopathi PS, Soares-Weiser K. Benzodiazepines for neuroleptic-induced tardive dyskinesia. *Cochrane Database Syst Rev* 2006; :CD000205.

Tarsy D, Kaufman D, Sethi KD, et al. An open-label study of botulinum toxin A for treatment of tardive dystonia. *Clin Neuropharmacol* 1997; 20:90.

Brashear A, Ambrosius WT, Eckert GJ, Siemers ER. Comparison of treatment of tardive dystonia and idiopathic cervical dystonia with botulinum toxin type A. *Mov Disord* 1998; 13:158.

Hauser RA, Factor SA, Marder SR, et al. KINECT 3: A Phase 3 Randomized, Double-Blind, Placebo-Controlled Trial of Valbenazine for Tardive Dyskinesia. *Am J Psychiatry* 2017; 174:476.

FDA approves first drug to treat tardive dyskinesia.

<https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm552418.htm> (Accessed on April 24, 2017).

Godwin-Austen RB, Clark T. Persistent phenothiazine dyskinesia treated with tetrabenazine. *Br Med J* 1971; 4:25.

Kazamatsuri H, Chien C, Cole JO. Treatment of tardive dyskinesia. I. Clinical efficacy of a dopamine-depleting agent, tetrabenazine. *Arch Gen Psychiatry* 1972; 27:95.

Kazamatsuri H, Chien CP, Cole JO. Long-term treatment of tardive dyskinesia with haloperidol and tetrabenazine. *Am J Psychiatry* 1973; 130:479.

Kang UJ, Burke RE, Fahn S. Natural history and treatment of tardive dystonia. *Mov Disord* 1986; 1:193.

Lang AE, Marsden CD. Alpha methylparatyrosine and tetrabenazine in movement disorders. *Clin Neuropharmacol* 1982; 5:375.

Fernandez HH, Factor SA, Hauser RA, et al. Randomized controlled trial of deutetabenazine for tardive dyskinesia: The ARM-TD study. *Neurology* 2017; 88:2003.

Suzuki T, Hori T, Baba A, et al. Effectiveness of anticholinergics and neuroleptic dose reduction on neuroleptic-induced pleurothotonus (the Pisa syndrome). *J Clin Psychopharmacol* 1999; 19:277.

Zhang WF, Tan YL, Zhang XY, et al. Extract of Ginkgo biloba treatment for tardive dyskinesia in schizophrenia: a randomized, double-blind, placebo-controlled trial. *J Clin Psychiatry* 2011; 72:615.

Jeste DV, Lohr JB, Clark K, Wyatt RJ. Pharmacological treatments of tardive dyskinesia in the 1980s. *J Clin Psychopharmacol* 1988; 8:385.

Gardos G, Casey DE, Cole JO, et al. Ten-year outcome of tardive dyskinesia. *Am J Psychiatry* 1994; 151:836.

Fernandez HH, Krupp B, Friedman JH. The course of tardive dyskinesia and parkinsonism in psychiatric inpatients: 14-year follow-up. *Neurology* 2001; 56:805.

Tammenmaa IA, Sailas E, McGrath JJ, et al. Systematic review of cholinergic drugs for neuroleptic-induced tardive dyskinesia: a meta-analysis of randomized controlled trials. *Prog Neuropsychopharmacol Biol Psychiatry* 2004; 28:1099.

Lohr JB, Kuczenski R, Niculescu AB. Oxidative mechanisms and tardive dyskinesia. *CNS Drugs* 2003; 17:47.

Adler LA, Peselow E, Rotrosen J, et al. Vitamin E treatment of tardive dyskinesia. *Am J Psychiatry* 1993; 150:1405.

Dabiri LM, Pasta D, Darby JK, Mosbacher D. Effectiveness of vitamin E for treatment of long-term tardive dyskinesia. *Am J Psychiatry* 1994; 151:925.

Lohr JB, Cadet JL, Lohr MA, et al. Alpha-tocopherol in tardive dyskinesia. *Lancet* 1987; 1:913.

Egan MF, Hyde TM, Albers GW, et al. Treatment of tardive dyskinesia with vitamin E. *Am J Psychiatry* 1992; 149:773.

Shriqui CL, Bradwejn J, Annable L, Jones BD. Vitamin E in the treatment of tardive dyskinesia: a double-blind placebo-controlled study. *Am J Psychiatry* 1992; 149:391.

Dorevitch A, Kalian M, Shlafman M, Lerner V. Treatment of long-term tardive dyskinesia with vitamin E. *Biol Psychiatry* 1997; 41:114.

Soares-Weiser K, Maayan N, Bergman H. Vitamin E for antipsychotic-induced tardive dyskinesia. *Cochrane Database Syst Rev* 2018; 1:CD000209.

Angus S, Sugars J, Boltezar R, et al. A controlled trial of amantadine hydrochloride and neuroleptics in the treatment of tardive dyskinesia. *J Clin Psychopharmacol* 1997; 17:88.

Soares-Weiser KV, Joy C. Miscellaneous treatments for neuroleptic-induced tardive dyskinesia. *Cochrane Database Syst Rev* 2003; :CD000208.

Adelufosi AO, Abayomi O, Ojo TM. Pyridoxal 5 phosphate for neuroleptic-induced tardive dyskinesia. *Cochrane Database Syst Rev* 2015; :CD010501.

Bona JR. Treatment of neuroleptic-induced tardive dyskinesia with levetiracetam: a case series. *J Clin Psychopharmacol* 2006; 26:215.

Konitsiotis S, Pappa S, Mantas C, Mavreas V. Levetiracetam in tardive dyskinesia: an open label study. *Mov Disord* 2006; 21:1219.

Woods SW, Saksa JR, Baker CB, et al. Effects of levetiracetam on tardive dyskinesia: a randomized, double-blind, placebo-controlled study. *J Clin Psychiatry* 2008; 69:546.

Soares K, Rathbone J, Deeks J. Gamma-aminobutyric acid agonists for neuroleptic-induced tardive dyskinesia. *Cochrane Database Syst Rev* 2004; :CD000203.

Pouclet-Courtemanche H, Rouaud T, Thobois S, et al. Long-term efficacy and tolerability of bilateral pallidal stimulation to treat tardive dyskinesia. *Neurology* 2016; 86:651.

Trottenberg T, Paul G, Meissner W, et al. Pallidal and thalamic neurostimulation in severe tardive dystonia. *J Neurol Neurosurg Psychiatry* 2001; 70:557.

Eltahawy HA, Feinstein A, Khan F, et al. Bilateral globus pallidus internus deep brain stimulation in tardive dyskinesia: a case report. *Mov Disord* 2004; 19:969.

Franzini A, Marras C, Ferroli P, et al. Long-term high-frequency bilateral pallidal stimulation for neuroleptic-induced tardive dystonia. Report of two cases. *J Neurosurg* 2005; 102:721.

Trottenberg T, Volkmann J, Deuschl G, et al. Treatment of severe tardive dystonia with pallidal deep brain stimulation. *Neurology* 2005; 64:344.

Tai CH, Tseng SH, Liu HM, Wu RM. Bilateral deep brain stimulation of subthalamic nucleus alleviates tardive dystonia. *Neurology* 2006; 66:1778.

Gruber D, Trottenberg T, Kivi A, et al. Long-term effects of pallidal deep brain stimulation in tardive dystonia. *Neurology* 2009; 73:53.