Respiratory Dyskinesia*
An Underrecognized Phenomenon

Michael W. Rich, M.D.; and Steven M. Radway, M.D.

(Arch 1994: 105:1826-32)

Antipsychotic medications were introduced in the
1950s and proved to be invaluable in the ame-
lioration of schizophrenic symptoms. These agents
 gained widespread acceptance in the treatment of
psychoneurologic disorders, including schizophrenia,
Tourette’s syndrome, effective disorders, and demen-
tia. Antipsychotics are also called neuroleptics be-
cause of their ability to induce a variety of neurologi-
cal side-effects. These include acute dystonia, parkin-
sonism, akathisia, and tardive dyskinesia.

Of these sequelae, tardive dyskinesia is perhaps
the most feared, due to its often dramatic and disab-
ing presentation as well as its frequent irreversibility.
The hyperkinetic movements in tardive dyskinesia
most commonly consist of stereotypy or dystonia and
usually affect the face, tongue, and neck.1 The limbs
and trunk are less commonly involved. Chronic
blockade of dopamine receptors by antipsychotics is
thought to result in supersensitivity of the dopamine
receptors in the nigrostriatal pathway that modulates
voluntary movement. Involuntary dyskinesias there-
by occur. The phenomenon typically requires at least
3 months of neuroleptic use and may occur up to 1
year after withdrawal of the medicine.2 Best esti-
mates place the prevalence of tardive dyskinesia at 20
percent of patients using long-term neuroleptics.3

One family of neuroleptics is the phenothiazines.
Included in this family of drugs are the antiemetics,
such as promethazine (Phenergan; Wyeth) and
prochlorperazine (Compazine; Smith Kline &
French). Another antiemetic, metaclopramide (Reg-
lan; Robins), is also used in the treatment of
gastroesophageal reflux disease and diabetic gastro-
paresis. Long-term use of all of these agents has been
associated with development of tardive dyskinesia.4,5

Treatment with levodopa (contained in Sinemet;
Merck Sharp & Dohme), a dopamine precursor used
in the treatment of parkinsonism, has been found to
induce movement disorders in 30 to 80 percent of
these patients.6

Though tardive dyskinesia generally confines itself
to the head, neck, and limbs, some patients suffer
from a variant referred to as respiratory dyskinesia.
Respiratory dyskinesia is an irregular, tachypneic
pattern of breathing due to involvement of the respi-
atory muscles by tardive dyskinesia. Very few
primary care physicians or subspecialists recognize
and understand respiratory dyskinesia. When re-
viewing tardive dyskinesia, textbooks and articles
either fail to discuss this respiratory variant or dismiss
it as rare. Unfortunately for those afflicted, respi-
atory dyskinesia is not rare. It may mimic other
respiratory or cardiac disorders and is often over-
looked or misdiagnosed. Consequently, potentially
beneficial interventions are not initiated in these pa-
tients. In some patients, unnecessary and potentially
hazardous investigations are undertaken.

The case studies presented below exemplify neu-
roleptic-induced and levodopa-induced respiratory
dyskinesia. A review of the literature pertaining to
respiratory dyskinesia follows. Clues to the diagnosis,
differentiation, and treatment of this disorder are
then offered.

CASE REPORTS

Case 1

The patient was a 62-year-old mentally retarded black man
with a history of hypertension and adult-onset diabetes. He had
a long history of psychosis and received trifluoperazine (Stelazine;
Smith Kline & French) regularly since the mid-1960s. In
November 1990, the patient was receiving trifluoperazine, 5 mg
twice daily, when his primary care physician began to taper the
medication over 1½ months. Ten weeks following his last dose, the
staff at the extended care facility where he resided noted the pa-
tient to be restless, mumbling, and rolling his eyes. He soon
began to issue loud signs and grunts and would hold food in his
mouth as if unable to swallow. Three days later, he developed an
oral temperature of 38.5°C and was brought to the emergency
room. The patient was unable to provide a detailed history, but
he complained of dyspnea. His family denied that he had any
history of cardiac or pulmonary diseases. He had never smoked,
and there was no family history of movement disorders. On ex-
amination, the heart rate was 106 beats per minute and respira-
tions were very irregular at a rate of 28 per minute. The patient
demonstrated prominent stereotypic movements of his face,
mouth, tongue, neck, and upper extremities. Loud grunts and
gasps with inspiration and expiration were heard. During exami-
nation of the oral cavity, his palate and pharynx were observed
to move spontaneously and in an incoordinate manner. Significant

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1826
laboratory values included a negative toxicology screen for salicylates. Arterial blood gases on room air showed a pH of 7.60, Pco2 of 14, Po2 of 128, and bicarbonate value of 14 consistent with an acute respiratory alkalosis. Blood count, chest x-ray film, and electrocardiogram were all unremarkable. The patient was admitted with the presumptive diagnosis of sepsis. During his hospitalization, it was noticed that the patient’s movement disorder was worse with anxiety and disappeared completely during sleep. The gasping, grunting, and abnormal breathing pattern did the same. A neurology consultant diagnosed the patient as having tardive dyskinesia with a respiratory component. Lorazepam (Ativan; Tardive, 1 mg three times daily, was initiated and within 2 days the dyskinesia had improved as had the dyspnea. Repeat blood gases on room air showed a pH of 7.47, PaCO2 of 33, PaO2 of 89, and bicarbonate of 24. Although examinations and cultures failed to determine the source of infection, a 10-day course of ticarcillin/clavulanate (Timentin; Smith Kline Beecham) was given for presumed aspiration pneumonia. Intravenous fluids were administered to treat dehydration secondary to decreased oral intake. To evaluate the patient’s oropharyngeal dysphagia due to the dyskinesia, contrast radiographic swallowing studies were done. These revealed ineffectual oral preparation of food, delayed swallowing, and normal esophageal motility. Diaphragmatic fluoroscopy to assess possible diaphragmatic dyskinesia showed a delay in contraction of the left hemidiaphragm relative to the right hemidiaphragm. The patient was discharged but returned 2 weeks later because of inadequate oral intake. A percutaneous gastrostomy tube was placed. During endoscopic placement, the epiglottis was noted to be moving abnormally.

CASE 2

The patient was an 86-year-old white man with a history of coronary artery disease, hypertension, and congestive heart failure. He presented with the chief complaint of persistent dyspnea at rest over the 3 days prior to admission. He also suffered from Parkinson’s disease for which he had been receiving carbidopa/levodopa 10/100 (Sinemet; Merck Sharp & Dohme), three times daily for several years. One month prior to presentation, the family noticed the insidious onset of abnormal orofacial movements. The patient had a 40 pack-year history of smoking but had not smoked in over 40 years. There was no family history of movement disorders. On presentation he demonstrated stereotypy of the mouth, face, tongue, neck, and upper trunk. His breathing was irregular both in depth and frequency with a respiratory rate of 28 per minute. Pulmonary and cardiac examinations were normal. Significant laboratory studies included an electrocardiogram with normal sinus rhythm and without any changes suggestive of myocardial ischemia or infarction. The chest x-ray film showed moderate cardiomegaly without parenchymal infiltrates. Renal panel and blood count were unremarkable. An arterial blood gas determination during hospitalization showed a pH of 7.48, PaCO2 of 31, PaO2 of 78, and bicarbonate of 23 on room air. The patient was admitted to the coronary care unit with the diagnosis of unstable angina. During his hospital course, it was noticed that the orofacial and respiratory dyskinesia worsened with anxiety and pain, but disappeared during sleep. Fluoroscopic evaluation of the diaphragm revealed normal movement. The patient was seen by a neurologist, who recognized the tardive dyskinesia and its respiratory component. Consequently, the patient was discharged with a scheduled taper of his carbidopa/levodopa to be completed over a 1-month period. Following completion of the taper, he was found to be free of all evidence of orofacial or respiratory dyskinesias.

METHODS

A computer-assisted search (Medline) of the literature, years 1966 through May 1993, was run under the subjects of “respiratory dyskinesias,” “dyskinesias, drug-induced,” “tardive dyskinesia,” and then a combination of “dyskinesias, drug-induced” with “breathing disorders.” Cross references from bibliographies were also used. A total of 37 cases was found by this method. The following criteria had to be met in order to classify a case as respiratory dyskinesia: (1) have a breathing pattern described as tachypneic and irregular; (2) if associated with neuroleptic use, the breathing disorder must have been first noted after at least 3 months of neuroleptic exposure or within 1 year after discontinuation of the neuroleptic; and (3) if associated with levodopa use, the breathing disorder must have been first noted after initiation of levodopa therapy. Four cases failed to meet these requirements and are therefore excluded from the data in Table 1. Table 2 summarizes the clinical findings gleaned from the 33 remaining cases that met this definition of respiratory dyskinesia.

**DISCUSSION**

**Prevalence**

Though textbooks and articles that review tardive dyskinesia describe the respiratory component as rare, the few studies that attempt to define its prevalence suggest otherwise.

Six studies have addressed the prevalence of respiratory dyskinesia among patients with tardive dyskinesia (Table 2). Compilation of these data places the prevalence of respiratory dyskinesia among patients with tardive dyskinesia at 16 percent, though individual studies report from 3 to 45 percent.

**Table 1—Summary of Clinical Findings Reported in the Literature for Respiratory Dyskinesia**

<table>
<thead>
<tr>
<th>Description</th>
<th>No. of cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Presence of orofacial dyskinesia</td>
<td>27 of 32 (84)%</td>
</tr>
<tr>
<td>Female: male ratio</td>
<td>17:15 (1.1 to 1)</td>
</tr>
<tr>
<td>Age &gt;60: age &lt;80 ratio</td>
<td>20:12 (1.7 to 1)</td>
</tr>
<tr>
<td>Presence of underlying CNS disorder other than Parkinson's</td>
<td>10 of 32 (31)%</td>
</tr>
<tr>
<td>Dyspnea</td>
<td>12 of 19 (63)%</td>
</tr>
<tr>
<td>Respiratory alkalosis</td>
<td>8 of 11 (73)%</td>
</tr>
<tr>
<td>Dysphonia (eg, grunting, gasping)</td>
<td>15 of 32 (47)%</td>
</tr>
<tr>
<td>Complications</td>
<td>7 of 33 (21)%</td>
</tr>
<tr>
<td>Initial misdiagnosis</td>
<td>12 of 33 (36)%</td>
</tr>
</tbody>
</table>

*Note that the presence or absence of specific findings were not always noted in the reported cases. Simple ratios and percentages (parentheses) were thus reported from the data available."

**Table 2—Prevalence of Respiratory Dyskinesia (RD) Among Patients With Tardive Dyskinesia (TD)**

<table>
<thead>
<tr>
<th>Study</th>
<th>Patients With TD, n</th>
<th>Patients With RD, n (and as % of TD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Miller and Jankovic5</td>
<td>79</td>
<td>11 (14)%</td>
</tr>
<tr>
<td>Yassa and Lai14</td>
<td>108</td>
<td>8 (7)%</td>
</tr>
<tr>
<td>Inada et al20</td>
<td>71</td>
<td>2 (3)%</td>
</tr>
<tr>
<td>Chiu et al23</td>
<td>85</td>
<td>11 (15)%</td>
</tr>
<tr>
<td>Hunter et al24</td>
<td>13</td>
<td>2 (15)%</td>
</tr>
<tr>
<td>Youssef and Waddington25</td>
<td>76</td>
<td>34 (45)%</td>
</tr>
<tr>
<td>Totals</td>
<td>432</td>
<td>68 (15.7)%</td>
</tr>
</tbody>
</table>

CHEST / 105 / 6 / JUNE, 1994 1827
This wide range in results reflects variations in the populations studied as well as the height of suspicion and diagnostic criteria used by each reporting group. Standardized diagnostic criteria have yet to be developed and the interpretation of signs (such as irregularity of breathing) depends upon clinicians’ skill and judgment.

In 1980, Jackson et al. evaluated the respiratory patterns of patients with tardive dyskinesia. Their average respiratory rate and standard deviation were calculated and were then compared with those for subjects without tardive dyskinesia. The tardive dyskinesia subjects averaged 21.7 respirations per minute compared with 17.8 for the control subjects. The standard deviation for the respiratory period was much greater for the tardive dyskinesia patients correlating to greater irregularity in breathing pattern. This suggests that a broad spectrum of ventilatory abnormalities may exist in patients with tardive dyskinesia, only some of which become clinically apparent as respiratory dyskinesia.

It has been estimated that greater than 350,000 persons in the United States have or will have tardive dyskinesia due to neuroleptics, and then add to this figure the substantial number of patients affected by levodopa.6,27 If approximately 16 percent of these patients exhibit some degree of respiratory dyskinesia, the number potentially affected could be greater than 100,000. Perhaps 50,000 of these patients will have clinically significant respiratory dyskinesia with gasping, grunting, dyspnea, significant alkalosis, and even aspiration.

Risk Factors for Acquiring Respiratory Dyskinesia

The apparent close relationship between tardive dyskinesia and respiratory dyskinesia allows one to extrapolate from tardive dyskinesia those risk factors which may predispose to respiratory dyskinesia. Studies consistently implicate advanced age as a risk for acquiring tardive dyskinesia.3,31,32 Three fifths of the subjects in this review were patients age 60 years or older.

Less consistently implicated as risk factors for tardive dyskinesia are length of drug exposure, cumulative drug dosage, maximum drug dosage, female sex, and organic mental disorders.3,32 In this review, a 17 to 15 female to male ratio exists. Ten of the patients suffered from an underlying central nervous system disorder other than parkinsonism. Drug dosages and length of administration cannot be commented upon since these were not included in most of the case reports.

None of these specific risk factors proved to be statistically significant predictors of respiratory dyskinesia due to the small number of subjects thus far reported.

Neurologic Control of Ventilation

Both voluntary and involuntary neurologic pathways govern the muscles of respiration (Fig 1). Respiratory centers in the brainstem control the automaticity of breathing and are not under conscious control. Voluntary control of the muscles of respiration initiates in the classic motor strip and premotor areas of the frontal cortex. These neurons then descend with the pyramidal tract that controls other somatic muscles.33 They receive modification via a circuit involving the basal ganglia, thalamus, and cortex.34-36 The role of basal ganglia in coordination of ventilation has been demonstrated in parkinsonian patients. In these patients, respirations have been described as rapid and shallow with hindered voluntary respiration.37

The respiratory centers also exert some control on upper airway musculature in coordination with respiratory muscles.37 By this mechanism, respiratory dyskinesia often includes manifestations of pharyngeal dyskinesia (such as dysphagia and aerophagia) and laryngeal dyskinesia (such as grunts, gasps, and interrupted speech).

Clinical Picture

Patients with respiratory dyskinesia have an irreg-
ular breathing pattern accompanied by tachypnea (Table 1). This tachypnea and irregularity was objectively documented by Nakamura et al\textsuperscript{18} who measured respiratory airflow and abdominal movement and by DeKeyser and Vincken\textsuperscript{26} who performed spirometry. Our case review demonstrates that patients usually complain of dyspnea, as in 12 of the 19 patients who were specifically asked.

Antipsychotics cause tardive dyskinesia after long-term use, either during therapy or upon withdrawal. The tardive dyskinesia that results is often irreversible. In contrast, levodopa may cause dyskinesia early in therapy which tends to disappear upon withdrawal of levodopa. This dyskinesia usually occurs near “peak-dose” (when serum levels are highest) but may also occur at the “end-of-dose” (when the clinical effect of levodopa on parkinsonism begins to wear off) or in a “biphasic” fashion (at the beginning and the end of clinical effectiveness).\textsuperscript{38,39} In three of the cases of respiratory dyskinesia, levodopa clearly acted in a “peak-dose” fashion. This effect was objectively demonstrated via clinical observation and spirometry that found abnormal respirations 1 to 2 h after levodopa ingestion and resolution prior to the next dose.\textsuperscript{27,29}

As explained previously, pharyngeal and laryngeal dysmotility may be a part of respiratory dyskinesia. Respiations in more severe cases are often punctuated by gasps, grunts, and other noises which may represent dysphonia from involvement of the vocal cords and pharynx in tardive dyskinesia. Speech may also be affected. Some patients are interrupted in midsentence by grunts or gasps. Oropharyngeal dyskinesia may present as dysphagia or aerophagia and can result in aspiration. Our first patient demonstrated dysphagia. By examination and endoscopy, he also had obvious upper airway dyskinesia. The contrast swallowing study reported in the same patient revealed no evidence of esophageal dysmotility. Esophageal motility, after all, is an involuntary motor function that has no known cortical or basal ganglia input.

Blood gases in respiratory dyskinesia usually reveal an uncompensated respiratory alkalosis. In 11 of the cases reviewed, arterial blood gases were obtained. Eight of these blood gases represented an acute primary respiratory alkalosis that improved or resolved following treatment. Weiner et al\textsuperscript{17} hypothesized that the alkalosis is not compensated due to the intermittent nature of the respiratory dyskinesia. For example, respiratory dyskinesia improves when the patient is relaxed and disappears altogether with sleep. Complete compensation by the kidneys requires 2 to 4 days of chronic respiratory alkalosis.\textsuperscript{40}

In only 5 of the 32 cases reviewed was respiratory dyskinesia unaccompanied by tardive dyskinesia.\textsuperscript{12,18,27,28} Respiratory dyskinesia likely occurs independently of or preceding other features of tardive dyskinesia with greater frequency than reported. Since only five such instances have been reported thus far, this may simply reflect misdiagnosis of respiratory dyskinesia when unaccompanied by orofacial dyskinesias. Chiang et al\textsuperscript{19} offer another explanation for the underdiagnosis of respiratory dyskinesia. They note that of the four standardized rating scales for tardive dyskinesia, only one scale considers the respiratory facets.

Several pieces of evidence found in these 33 cases support the conclusion that respiratory dyskinesia is a subset of tardive dyskinesia. First, respiratory dyskinesia was usually accompanied by the classic movements of tardive dyskinesia. Like tardive dyskinesia, respiratory dyskinesia is exacerbated by anxiety and pain but disappears with sleep. Respiratory dyskinesia is also a consequence of neuroleptic, antinemic, or levodopa use. Most cases of orofacial and respiratory dyskinesia follow neuroleptic or levodopa use. However, as many as one out of four patients with orofacial dyskinesia have no history of neuroleptic or levodopa use.\textsuperscript{3} Spontaneous orofacial dyskinesias have been well described and are indistinguishable from drug-induced tardive dyskinesia.\textsuperscript{41-43} This syndrome may be a form of adult-onset focal dystonia. Chiu and Chan\textsuperscript{17} described a 71-year-old woman with spontaneous orofacial dyskinesia. She also manifested evidence of respiratory dyskinesia such as tachyypnea, irregular breathing causing a respiratory alkalosis. The patient's spontaneous orofacial and respiratory dyskinesia disappeared with sleep.

The respiratory dyskinesia induced by neuroleptics may be more severe than that induced by levodopa. For example, of the seven cases in which respiratory dyskinesia resulted in complications (see the next section), all were associated with neuroleptics\textsuperscript{6,12,14-16,19} (and our first case). More than half of the cases of respiratory dyskinesia induced by neuroleptics were accompanied by dysphonia, whereas dysphonia did not occur in any of the cases related to levodopa therapy. Lastly, the vast majority of neuroleptic-related cases were accompanied by orofacial dyskinesia, in comparison to only two of five cases related to levodopa. Nonetheless, due to the small number of cases of respiratory dyskinesia described in the literature, in particular those due to levodopa, no conclusions can be drawn presently in regard to possible clinical differences between the neuroleptic and levodopa-induced breathing disorders.

Complications

Though most cases of respiratory dyskinesia appear to be mild, authors have reported severe mor-
bidity and even near-mortality resulting from the disorder. A patient of Goswami and Channabasavana\textsuperscript{14} developed such severe respiratory compromise that cyanosis occurred, a diazepam (Valium; Roche) drip was administered, and transfer to an intensive care unit was contemplated. Yassa and Lal\textsuperscript{16} reported a patient with severe respiratory dyskinesia who suffered dysphagia and recurrent aspiration pneumonia. Sakamoto and Hayasaka\textsuperscript{18} described a patient whose respiratory function became so compromised as to require mechanical ventilation and sedation.

As a consequence of our first patient's severe dysphagia, a percutaneous gastric feeding tube was placed to avoid dehydration and malnutrition from insufficient oral intake. The coupling of this patient's oropharyngeal dysmotility with his respiratory dyskinesia posed significant aspiration risk. Indeed, the patient's low grade fever was thought to be due to aspiration pneumonia.

Finally, each episode of respiratory alkalosis carries with it the potential adverse effects of uncompensated alkalosis on the heart, brain, and other organs.

**Differential Diagnosis**

Whenever a patient presents with respiratory alkalosis, the possibility of respiratory dyskinesia should be considered. Suspicion should greatly increase if the patient has orofacial dyskinesias or a history of long-term use of neuroleptics, anti-emetics, or levodopa.

The diagnosis of respiratory dyskinesia is one of exclusion. Other potential causes of respiratory alkalosis must be considered (Table 3). In conjunction with a thorough history and physical examination, the following battery of simple diagnostic tests will rule out most of these disorders: arterial blood gases, complete blood count, blood culture, chest x-ray film, electrocardiogram, liver function panel, and toxicology screen. If clinically indicated, more sophisticated tests such as a ventilation-perfusion scan and CT of the head can be performed.

Once the acute causes of respiratory alkalosis have been ruled out, the clinician is left with two disorders that are difficult to distinguish from one another, namely psychogenic hyperventilation and respiratory dyskinesia.

Respiratory dyskinesia and psychogenic hyperventilation each occur in patients with psychiatric histories and either may present with tachypnea and respiratory alkalosis. Respiratory dyskinesia was mistaken for psychogenic hyperventilation in at least four of the cases in this review. Factors which would argue in favor of a diagnosis of respiratory dyskinesia as opposed to psychogenic hyperventilation include the presence of an irregular breathing pattern, dysphonia, orofacial dyskinesia, and interrupted speech.

**Treatment**

Treatment of respiratory dyskinesia is based upon the assumption that it is a component of tardive dyskinesia. Treatment options are therefore similar. When tardive dyskinesia is induced by levodopa, a decrease in the levodopa dose generally eliminates the movement disorder.\textsuperscript{6} Similarly, in the five cases of respiratory dyskinesia caused by levodopa, dose reduction led to resolution of the breathing disorder.

Neuroleptic- or antiemetic-related dyskinesias also merit an attempt at weaning the offending drug. When considering withdrawal of a neuroleptic agent, one must weigh the risk of precipitating a psychotic relapse. Withdrawal of such medications may improve tardive dyskinesia but resolution is rarely complete. In other cases, decreasing neuroleptic doses may even exacerbate the disorder by unblocking the dopamine receptors. In such patients, increasing the neuroleptic doses is often necessary to further block the upregulated receptors. In four of the patients in our review, a taper of phenothiazines resulted in some improvement in respiratory dyskinesia. In contrast, three other cases of respiratory dyskinesia improved only when phenothiazine doses were increased.

Agents such as reserpine and tetrabenazine have been used to ameliorate tardive dyskinesia.\textsuperscript{44-46} These agents act by depleting the presynaptic storage of dopamine. Four of the patients in our review were treated with reserpine at initial doses of 0.4 to 0.8 mg

**Table 3—Differential Diagnosis of Respiratory Alkalosis**

<table>
<thead>
<tr>
<th>Due to hypoxemia</th>
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<tbody>
<tr>
<td>Pneumonia</td>
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<tr>
<td>Pulmonary embolism</td>
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<tr>
<td>Pulmonary edema</td>
<td></td>
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<tr>
<td>Other ventilation-perfusion mismatches</td>
<td></td>
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<tr>
<td>Hypotension</td>
<td></td>
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<tr>
<td>Central nervous system disorders</td>
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<tr>
<td>Cerebrovascular accident</td>
<td></td>
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<tr>
<td>Encephalitis, meningitis</td>
<td></td>
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<tr>
<td>Trauma</td>
<td></td>
</tr>
<tr>
<td>Tumor</td>
<td></td>
</tr>
<tr>
<td>Respiratory/tardive dyskinesia</td>
<td></td>
</tr>
<tr>
<td>Medications</td>
<td></td>
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<tr>
<td>Salicylates</td>
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<tr>
<td>Theophylline</td>
<td></td>
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<tr>
<td>Progesterone</td>
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</tr>
<tr>
<td>Miscellaneous</td>
<td></td>
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<tr>
<td>Gram-negative bacteremia</td>
<td></td>
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<tr>
<td>Recovery from metabolic acidosis</td>
<td></td>
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<tr>
<td>Anxiety/hyperventilatory syndrome</td>
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<tr>
<td>Liver failure</td>
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<tr>
<td>Mechanical hyperventilation</td>
<td></td>
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<tr>
<td>Fever</td>
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Respiratory Dyskinesia (Rich, Radwany)
daily. Respiratory abnormalities only partially resolved. Reserpine has the potential for severe systemic toxicity due to its anticholinergic properties. Tetrabenazine appears to have a better side-effect profile and is thus preferred over reserpine for dyskinesias though it has not yet been reported as a treatment for respiratory dyskinesia.\textsuperscript{46}

Recently, benzodiazepines have shown benefit in the treatment of tardive dyskinesia.\textsuperscript{47} It has been postulated that benzodiazepines have GABA-minergic properties that suppress nigrostriatal pathways.\textsuperscript{47,48} Four cases of respiratory dyskinesia responded favorably to diazepam, up to 30 mg daily. A fifth case improved with lorazepam, 3 mg daily. Neither tardive dyskinesia nor respiratory dyskinesia completely resolve in response to benzodiazepines.

A number of other pharmacologic agents have been reported in small studies to have some effect in reducing tardive dyskinesia. These include calcium channel blockers,\textsuperscript{49-52} the antioxidant vitamin E,\textsuperscript{53} the dopamine antagonist sulpiride,\textsuperscript{55} bromocriptine,\textsuperscript{56} propranolol,\textsuperscript{57-60} and clonidine.\textsuperscript{61-64} None of these compounds has been reported or advocated specifically as treatment for respiratory dyskinesia.

Just as the treatment of tardive dyskinesia has proven challenging and sometimes impossible, respiratory dyskinesia has resisted many attempted interventions. A reasonable approach would be as follows. When the dyskinesia is due to levodopa, reduction of dosage should suffice. The initial approach to neuroleptic-induced dyskinesias should be dose reduction whenever possible. Unfortunately, in contrast to levodopa, phenothiazine reduction may lead to partial improvement, no change, or even worsening of the movement disorder. When dyskinesias remain disabling or neuroleptics must be continued, increasing the dosage of neuroleptic or using benzodiazepines or tetrabenazine appear to be the next most reliable alternatives.

**Conclusions**

Tardive dyskinesia is a common sequela of phenothiazine and levodopa administration. Nearly one out of six of these patients with tardive dyskinesia will have clinical evidence of respiratory muscle involvement, termed respiratory dyskinesia. Some of these patients will suffer significant morbidity and even near-mortality as a result of their affliction. Abnormal respirations or acute respiratory alkalosis in a patient taking phenothiazines or levodopa should raise the clinician’s suspicion of respiratory dyskinesia. That suspicion should heighten further when orofacial dyskinesia is apparent and when the breathing disorder disappears with sleep, worsens with anxiety or pain, and interferes with normal speech. A simple battery of tests will rule out other mimicking respiratory and cardiac disorders. Treatment options are few and usually of only limited effect. Adherence to directives offered in this review should reduce the number of lengthy, expensive workups and potential mismanagement. Our understanding of respiratory dyskinesia remains poor. Further studies are necessary to create more reliable diagnostic criteria and to more scientifically evaluate treatment modalities.

**Acknowledgments:** The authors would like to thank the following individuals for their assistance in the preparation of this manuscript: Thomas Olbrych, M.D.; Dale P. Murphy, M.D.; Thomas Strachan, M.D.; Beth Long; and Evalyn Lehman.

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Respiratory Dyskinesia (Rich, Radwany)