# Prospective Study of Tardive Dyskinesia in the Elderly[1]

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## Introduction

Many studies on the prevalence of tardive dyskinesia (TD) have shown increasing age to be the most consistently associated risk factor for its development (Barnes et al. 1983; Bourgeois et al. 1980; Brandon et al. 1971; Casey 1985; Chacko et al. 1985; Crane & Smeets 1974; Delwaide & Desseilles 1974; Jones & Hunter 1969; Kane & Smith 1982; Kane et al. 1982; Owens et al. 1982; Smith & Baldessarini 1980; Toennissen et al. 1985). However, interpretation of research findings has been restricted by methodological variability in such dimensions as population samples, patient setting, diagnosis, and interrater reliability.

Two studies conducted previously at our institution (Kane et al. 1982; Woerner et al. unpublished, 1989) have demonstrated this association between TD and increasing age. In a prevalence survey, 2,250 individuals at 5 sites were evaluated for TD. The rate of idiopathic ("spontaneous") dyskinesia was 0 percent in the chronic state hospital sample and 4.8 percent in the geriatric medical sample, with an overall prevalence of 2.6 percent. The rate of neuroleptic-associated dyskinesia varied from 13.3 percent in the acute psychiatric hospital sample to 36.1 percent in the chronic state hospital sample. The latter prevalence rate in the state facility, when only individuals whose age is greater than 55 were considered, jumped from 36.1 to 67 percent. Both sexes showed a steady rise in the prevalence with age. The prevalence increased with treatment duration for the entire sample, which had a mean duration of neuroleptic exposure of 72 months.

In the separate prospective investigation of more than 600 neuroleptic-treated individuals, Kane and colleagues (1986) found a 40 percent cumulative incidence of TD after 8 years of neuroleptic exposure. For any given length of exposure, the incidence was higher among older patients. After only 2 years of neuroleptic exposure, the likelihood of developing TD for a 50-year-old individual was already 18 percent, and this number jumped to 30 percent after 4 years of exposure.

In order for the relationship of age as a risk factor to be fully understood, sufficiently large cohorts must be followed for long periods and separate incidence curves must be generated for individuals in their 20s, 30s, 60s, 70s, etc. This will allow confidence intervals to be sufficiently narrow and thereby allow for comparisons of hazard rates at different time points, or durations, of neuroleptic exposure. This will help to determine, for example, if older people have a different period of greater vulnerability that may appear earlier or later in treatment than younger people, whether or not the cumulative incidence is greater.

This is a report on the preliminary findings of a prospective study of TD in the elderly, designed to further examine this risk factor and related issues.

## Methods

Patients are evaluated at five sites, including two psychiatric facilities (Hillside Hospital Inpatient Service and the geropsychiatric units at the Beth Israel Medical Center in Manhattan). In addition, there are three geriatric medical facilities, including the Jewish Institute for Geriatric Care (a medical geriatric facility affiliated with Long Island Jewish-Hillside Medical Center) and two skilled nursing/health-related facilities in Brooklyn (affiliated with Beth Israel Medical Center). Eligible subjects are individuals over the age of 55 who are about to be

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treated with antipsychotic drugs for the first time for a duration of 2 weeks or longer and who will be available for subsequent followup. Baseline assessment includes a modified version of the Simpson Dyskinesia Scale (Simpson et al. 1979), which incorporates the Abnormal Involuntary Movement Scale (AIMS) in its global items, and the Simpson-Angus Extrapyramidal Side Effects Scale (Simpson & Angus 1970), which focuses on acute side effects. Other measures include the Mini-Mental State Examination (Folstein et al. 1975) and the Brief Psychiatric Rating Scale (Overall & Gorham 1988). Also at the time of initial evaluation, a chart review is performed, and medication updates are done quarterly throughout the length of the study. A Nurses Observation Scale for Inpatient Evaluation (NOSIE; Guy 1976) is also completed whenever possible. These measures are repeated at regular intervals throughout the study. Patients who exhibit abnormal involuntary movements are seen monthly for 3 months and then quarterly thereafter. Whenever possible, this subgroup also undergoes neurological and laboratory testing designed to identify other neuromedical disorders that may be associated with abnormal involuntary motor activity.

Data on the first subjects were analyzed using survival analysis, which measures the time to occurrence of an outcome—in this case, TD. Neuroleptic dose varies over the period during which an individual is at risk of developing TD. Neuroleptic dose was thus coded as a time-dependent covariate when dose was entered in the survival analysis.

A "case" is defined as a rating by two experienced raters of two or greater on at least two body area globals, or of three or greater in one body area global.

## Results

As of the time of this preliminary analysis, 129 individuals were enrolled in the study. We intend to evaluate a total of 400 persons by the time the study is completed (Table 1).

Table 2 demonstrates the characteristics of the 84 subjects who were included in the analysis. They ranged in age from 57 to 96 years (mean age 76.6), and they were in the study for periods varying from 4 to 72 weeks (mean 23 weeks). Duration of cumulative neuroleptic exposure ranged from 2 to 70 weeks (mean 16.7). The sample was 72.6 percent female and was primarily Caucasian (89.3%). Participants were primarily acute inpatients (78.6%); the balance were mostly chronic inpatients. Psychiatric diagnoses and organic mental syndrome diagnoses tended not to overlap in individuals.

**TABLE 1.** Characteristics of 129 Individuals Examined at Baseline and Excluded From or Included In the Life Table Analysis.

| Characteristic | Number | Subtotal |
|---|---|---|
| *Excluded from analysis (n = 45)* | | |
| Abnormal movements at baseline | | 10 |
| With prior neuroleptic exposure | 3 | |
| Without prior neuroleptic exposure | 7 | |
| Never treated or treated 2 wk | | 14 |
| Followed for 1 mo because | | 17 |
| Refused | 5 | |
| Deceased | 5 | |
| Moved/untraceable | 3 | |
| Recent entry to study | 4 | |
| Long history of prior treatment without abnormal movements at baseline | | 4 |
| *Included in analysis (n = 84)* | | |
| Developed abnormal movements during study | | 13 |

**TABLE 2.** Characteristics of Study Subjects ($n$ = 84).

| Characteristic | Mean | SD | Range |
|---|---|---|---|
| Age | 76.6 | 8.9 | 57–96 |
| Weeks in study | 23.0 | 18.5 | 4–72 |
| Cumulative weeks on neuroleptics | 16.7 | 12.3 | 2–70 |

| Characteristics | Percent |
|---|---|
| Gender (female) | 72.6 |
| Ethnicity | |
| White | 89.3 |
| Black | 6.0 |
| Hispanic | 4.8 |
| Status | |
| Chronic inpatient | 20.2 |
| Acute inpatient | 78.6 |
| Outpatient | 1.2 |
| Psychiatric diagnosis | |
| None | 61.9 |
| Schizoaffective | 1.2 |
| Major affective | 27.4 |
| Personality disorder | 1.2 |
| Other | 8.3 |
| Organic diagnosis | |
| None | 33.3 |
| Primary degenerative | 11.9 |
| Multi-infarct dementia | 15.5 |
| Organic affective/delusional | 16.7 |
| Other | 22.6 |

The central finding of this preliminary analysis is shown in Figure 1. The cumulative incidence of abnormal involuntary movements was 48.9 percent after 40 weeks of cumulative neuroleptic exposure. Symptoms primarily occurred in the lip, jaw, and tongue regions. There was a paucity of movements in the face, neck, trunk, and upper and lower extremities (Figure 2). Age did not have any significant effect on the prevalence of TD within the age spectrum of 57 to 96. No significant male/female differences were found. A significantly greater rate of TD development was found in patients with psychiatric diagnoses (Figure 3). Patients with organic diagnoses, who tended to be nonpsychiatric, had significantly lower risk of developing TD.

Since the effect of diagnosis could be due to higher neuroleptic dosage in the psychiatric group, we ran a survival analysis wherein dose was a time-dependent covariate. Dose had no significant effect on the instantaneous risk of developing TD.

## Discussion

A TD incidence rate of 48.9 percent after 40 weeks of cumulative neuroleptic exposure suggests that elderly individuals over the age of 55 may be especially vulnerable to the neurologic side effects of antipsychotic medication. These results must be

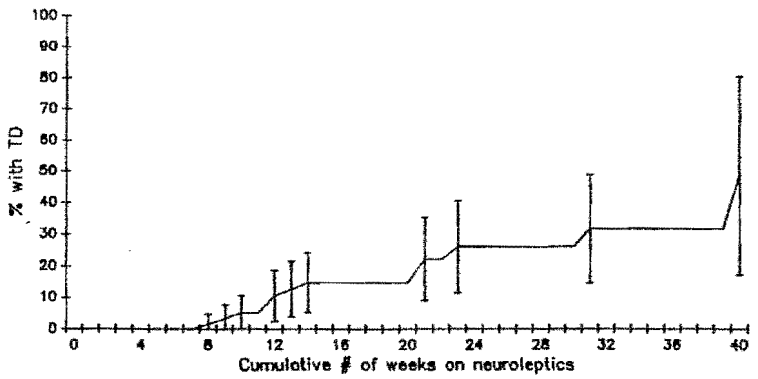


**FIGURE 1.** Incidence (%) of abnormal involuntary movements by cumulative neuroleptic exposure. The cumulative incidence after 40 weeks of cumulative treatment is 48.9%.

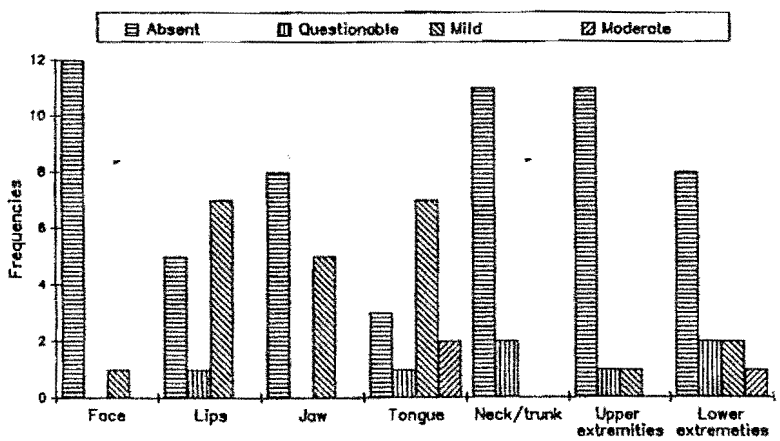


**FIGURE 2.** Distribution of Abnormal Involuntary Movement Scale scores in the 13 neuroleptic-associated cases. Note that movements were primarily seen in the oral region.

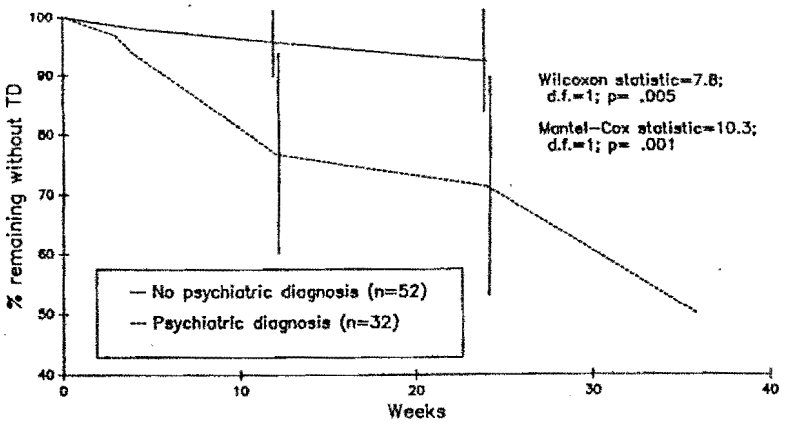


**FIGURE 3.** Life Table Analysis of new onset cases of tardive dyskinesia (TD) by psychiatric diagnosis. Note that the majority of cases have primarily psychiatric diagnoses that are not also considered organic mental syndromes.

considered as preliminary in view of the early stage of this investigation and relatively small sample size. Our finding of seven "spontaneous" dyskinesia cases at baseline prior to drug treatment is consistent with previously reported rates of idiopathic dyskinesia from our center and in the literature, and suggests that the base rate of this condition is not excessively high. The term "spontaneous" is a little misleading because so-called spontaneous cases of dyskinesia may be associated with one of many neuromedical conditions, either as the primary manifestation or as an incidental finding. The finding that elderly individuals with psychiatric diagnoses had a higher risk of developing TD is interesting since the majority of psychiatric diagnoses in the study were some sort of affective disorder. This is consistent with prior reports of affective disorder's being a risk factor for TD development.

Alternatively, there could be a systematic bias against the identification of abnormal motor activity in the elderly who already have one or more neuromedical illnesses, such as hemiparesis, that make the evaluation of these kinds of abnormalities more difficult. Clearly, evaluation of all 400 patients must be completed before these more subtle dimensions can be examined.

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