CLINICAL ASPECTS OF DYSKINESIA

J. ANANTH, M.D.

Associate Professor, McGill University, Associate Psychiatrist, Allan Memorial Institute and Director, Continuing Medical Education, Douglas Hospital.

Tardive dyskinesia (TD) is a syndrome manifesting in abnormal involuntary movements following prolonged exposure to neuroleptic treatment and the syndrome may be irreversible. This syndrome was initially described by Hall et al. (1956), Schonecker et al. (1957) and Sigwald et al. (1959).

Clinically, this syndrome includes a variety of hyperkinetic involuntary movements primarily of the tongue, mouth and face even though other parts can be affected. These movements are choreiform, coordinated, involuntary, stereotyped and rhythmic. They continue as long as there are no internal or external events to disturb them. Generally, onset of these symptoms is gradual as in the unfolding of a flower and not dramatic as in dystonia. TD is greatly increased by anxiety or heightened vigilance and completely disappears during sleep. Any behavior that increases associated movements will enhance TD. Thus, an asymptomatic patient may manifest dyskinesia of his hands and fingers when his arms swing while walking. The abnormal movements disappear in areas directly involved in a voluntary activity as noticed by the cessation of buccal movements while talking and of the finger movements while writing. On the other hand, dyskinesia is enhanced in areas other than those of voluntary activity. Involuntary movements are more pronounced in a standing than in a sitting or supine position. Generally, it has been noted that patients are unaware of and not disturbed by these movements (Ayd, 1970) but this is far from universal (Uhrbrand and Faurbye, 1960). While this is true in older chronically institutionalized patients, younger patients do feel embarrassed and uncomfortable. It is also stated that respiration, mastication or speech are not affected which is generally true. However, grunting vocalizations, jerky respirations and oral ulcerations are noted in some. Alertness and intelligence are not affected.

Oral facial dyskinesia is the characteristic feature of this syndrome. Initial symptoms include mild forward backward or lateral movements of the tongue (Ayd, 1967). Later, more obvious twisting and protruding movements of the tongue, pouting and sucking movements of the lips, and various chewing movements of the mouth develop. Even though the upper portion of the face is generally spared (Degkwitz, 1969), frequent blinking, blepharospasm and arching of the eyebrows may occur. While orofacial dyskinesia is common and is the first to appear in older patients, abnormal movements of the extremities and trunk are more common in young individuals (Ayd, 1970; Degkwitz, 1969). In addition, in advanced cases, choreiform movements and distal athetosis of limbs and tapping motions of the feet are noted. Postural and gait disturbances include exaggerated lordosis, rocking and swaying, shoulder shrugging and rotary pelvic movements. Lipper (1973) noted impaired or absent optokinetic nystagmus more frequently among the TD patients than among nondyskinetic control group. However, in parkinsonian patients as well, optokinetic nystagmus is decreased.

Presented at the Canadian Psychiatric Association Annual Meeting in Saskatoon, Saskatchewan from September 26—September 30, 1977. The author wishes to thank Jeanne Gould for her secretarial help.
Most often, the insidious development of dyskinesia is noted by the relatives or the physician of the patient while the patient is still on antipsychotic drugs (Degkwitz, 1969). It may also manifest after a reduction in dosage or discontinuation of neuroleptic medication (Degwitz and Wenzel 1967). This indicates that parkinsonian symptoms may mask the signs and even delay the recognition of the TD. In some cases, transient dyskinesias occur which last for only a few days (McAndrew et al., 1972). Even after discontinuation of antipsychotic drugs, the irreversibility of some of the late drug-induced dyskinesia is well established (Crane, 1973) in spite of occasional reports to the contrary (Kline, 1968). Prognostic indicators for recovery are not currently available. Long-term studies suggest that once dyskinesia occurs, it is either static or gradually improves.

Varieties of tardive dyskinesia: Apart from the dyskinetic syndromes resulting from various neurological disorders including Huntington’s chorea and psychiatric syndromes including motility disorders of schizophrenia, spontaneous dyskinesias occur in elderly patients. Clinically, while adults generally manifest orofacial dyskinesia children manifest dyskinesia of the extremities. Villeneuve (1972) has described a clinical syndrome with rapid, chewing-like movements of a rabbit’s mouth which he labelled as “Rabbits Syndrome”. In this syndrome, he noted that the tongue was not involved. On the basis of pharmacological response, Casey (1976) speculates that physostigmine responsive group who improve with deanol may be different from hyperdopaminergic group. However, the existence of subgroups and their significance need to be proven.

Predisposing Factors

Older patients have been noted to be more susceptible (Crane and Smeets, 1974; Just et al., 1976). In one study, it was reported that while only two percent of the geriatric patients not receiving the drugs had signs of TD, there was a twenty times greater prevalence (40 percent) among drug-treated patients (Greenblatt et al., 1968). However, some epidemiological studies Kennedy et al., 1971) do not implicate age while others report that advanced age is related to TD (Faurbye et al., 1964; Brandon et al., 1971). These contradictory findings can be explained by the complex characteristics of the chronically treated patient population. The relationship of age and TD may be linked closely with the duration of drug intake whereby the elderly may receive drugs for a longer duration. The earlier reports of an association between brain damage and TD (Druckman et al., 1964; Faurbye et al. 1964) have been contradicted by the more recent workers (Degkwitz and Wenzel 1967; Brandon et al., 1971; Gelenberg 1976). These findings are in conformity with the clinical observation that TD may occur in patients without any detectable organicity. Even though organicity may enhance susceptibility, it is not a prerequisite for the development of TD. Similarly, association between female sex and TD have been claimed by some (Hunter et al., 1964, And 1967, Kennedy et al., 1971) and not by others (Degkwite and Weneel, 1967; Fann, et al., 1972; Crane, 1970). Some have noted no correlation between earlier dystonia and later TD (Klawans, 1973). The relationship between severe early onset of parkinsonian symptoms and TD is interesting. Crane (1972) has suggested that patients exhibiting significant drug-induced parkinsonism are predisposed to TD. Further evidence for this is provided by our own study (Pandurangi et al., 1977) which revealed that the TD group had received anticholinergic drugs more often and in higher doses than the matched control group. Early initiation of antiparkinsonian therapy
may be related to early onset of drug-induced extra-pyramidal symptoms. At present, there is no evidence that the underlying psychiatric illness plays any role in predisposition. The majority of reports indicate that TD occurs in all patients who are on prolonged neuroleptic therapy including schizophrenia, prolonged affective illness and chronic organic brain syndrome (Jus et al. 1976; Brandon et al., 1971; Crane and Smeets, 1974). However, Simpson (1973) reported manic depressive patients developed TD more often than schizophrenic patients indicating that schizophrenics were less susceptible. But this conclusion was based on clinical observation only. TD is also reported to occur in various neurotic as well as medically ill patients who receive neuroleptic treatment (Faurbye et al. 1964; Evans 1965; Klawans et al. 1974). Kunin (1976) has reported a deficiency of manganese in TD and its improvement with this mineral supplement. Thus, it appears that neuroleptics can induce TD in susceptible patients the nature of which is unknown.

**Prevalence**

The prevalence of TD is difficult to estimate. The reported occurrence of TD in chronic institutionalized patients varies from 0.5 to 56 percent with an average of about 15 percent. This wide discrepancy may be related to the type of patient population, the diagnostic criteria, and the assessment procedures. Hoff and Hoffman (1967) reported the incidence of dyskinesia to be 0.5 percent, Villeneuve et al. (1969) and Roxburgh (1970) two percent, Eckman (1968) three percent and many others six to 56 percent. Some studies show a low incidence as inclusion was limited to oral dyskineties only (Dynes 1970; Lehmann et al. 1970; Turuner and Achte 1967) and others included only the most severe cases (Roxburgh, 1970) while Villeneuve et al. (1969) collected data on the basis of hospital records and questionnaires completed by the ward physicians. Among studies reporting a high incidence of dyskinesia, Greenblatt et al. (1968) included exclusively geriatric patients and Kennedy et al. (1971) included patients on a high dose of trifluoperazine for a number of years. Similarly Crane’s (1968; 1970) subjects were on large doses of chlorpromazine or trifluoperazine. Hippius and Lange (1970) and Brandon et al. (1971) may have included patients with motor disorders unrelated to drugs, thereby contributing to the reported high incidence. The same may be true of Fann’s (1972) study. In the study by Jus et al. (1976) the 56 percent incidence may be related to the older age of the population and employment of polygraphic diagnosis. Of great concern is the recent report of a 41 percent prevalence among out-patients (Asnis et al. 1977) as it suggests that high incidence of TD is not restricted to institutionalized regressed patients. These indicate that perhaps only some are susceptible and others are relatively immune to the syndrome. More important is the fact that none of the above mentioned figures represent either the incidence or prevalence among a given number of stable population but only give the number of TD in a residual population without indicating the total number in the denominator. Thus these are not very accurate epidemiological figures. The incidence and prevalence of TD among all patients receiving neuroleptics may perhaps be as low as not to cause alarm. In one such study, six of 90 patients had dyskinesia. A clear uniform definition, good assessment and prospective study in a sample population receiving neuroleptic medication are urgently needed. The impression that TD is very frequent does not seem to have a very convincing foundation at present.

**Precipitating Factors**

**Role of medication:** Dyskinesia is not a syndrome occurring exclusively in patients
receiving neuroleptic drugs. It occurs spontaneously (Pakkenberg and Fog, 1974) as well in untreated schizophrenic patients (Stevens, 1974) and in those with organic brain syndromes (Appenzeller and Biehl, 1968). However, it has been confirmed that the incidence of TD in patients with a history of drug treatment is higher than in similar patients not exposed to neuroleptic treatment (Greenblatt et al. 1968; Heinrich et al. 1969; Hippius and Lange 1970; and Seide and Muller 1967) while only Demers (1966) and Brandon et al. (1971) could not find any significant difference in TD between the two groups. These findings indicate that neuroleptics are only precipitating factors in the occurrence of TD.

However TD is reported to occur predominantly in patients who have been on neuroleptic medication for prolonged periods and in high doses. However, small doses for shorter duration do not offer any immunity against the occurrence of TD (Klawans et al., 1974). Some studies indicate that even though TD can occur spontaneously, drug treatment increases the susceptibility for this syndrome. Curran (1973) and Turek (1975) have with some justification argued that a direct relationship between neuroleptic drugs and TD is not proven with sufficient evidence on the basis that lowering of phenothiazines would enhance rather than decrease TD and that no knowledge of predisposing factors is available. However, both these objections do not hold validity as a direct relation can exist even when the drug is only a precipitating factor in predisposed individuals and that the underlying mechanism of withdrawal dyskinesia is at least partially elucidated. At present, we do not know whether any particular drug is more likely to induce TD than other and we do not know whether the total amount of medication given over time or the total amount given in any one day has any effect whatever on the likelihood that the patient would develop TD. All neuroleptic preparations including phenothiazines (Crane, 1973), butyrophenones (Jacobson et al., 1974), reserpine (Degkwitz, 1969; Wolf, 1973) and thioxanthines (Ananth and Costin, 1977) have been implicated. Thoridazine, a drug which is reported to cause fewer extrapyramidal symptoms than other neuroleptics, does produce TD (Crane, 1973). Thus all drugs which can produce extrapyramidal signs can produce TD. However, the only neuroleptic which is reported not to produce parkinsonism and has the capacity of suppressing TD (Ayd, 1974) is Clozapine. Further confirmation of this claim is awaited. Animal experiments indicate that even the newer neuroleptic loxitane has the potential of producing TD (Sayers et al., 1975). Even though some studies indicate a correlation between the duration of drug treatment and the dosage and TD (Crane and Smeets 1974; Pryce and Edwards 1966; Crane, 1970) there are occasional reports of the occurrence of TD following exposure to small doses of phenothiazines for relatively short periods of time (Evans, 1965; Simpson, 1973; Moline, 1975; Thorton and Thorton, 1973). In most patients TD makes an insidious appearance while patients are still taking antipsychotic drugs (Degkwitz, 1969). However, it is frequently seen during the first four weeks of dosage reduction or withdrawal (Crane and Smeets, 1974).

Is dyskinesia reversible? The terms persistent dyskinesia and T. D. are used interchangeably thus creating semantic difficulty. If T. D. by definition is persistent, it has to be irreversible. However, such a statement is only partially true. MacAndrews et al. (1972) found that drug-induced dyskinesia in children improved following drug withdrawal. Begkwitz (1969) reported that about 50 per cent of his TD patients became asymptomatic after several months of drug free period. However, all of them
were under 50 years of age. Recovery rate seems to increase with the duration of follow up. Thus approximately 90 percent of the patients in a six to 24 month follow up study (Crane, 1971) and almost all the patients in a 36 month follow up study (Haddenbrock, 1966) showed improvement of their dyskinetic symptoms. Thus irreversibility is not absolute and many improve over time and only in some dyskinesia persists. In some, however, TD persists while in all patients after discontinuation of medication, the symptoms do not become worse. Some reports indicate that TD disappears in 19 to 40 percent of patients even on continued treatment (Marsden, et al., 1975 ; Kobayashi 1976). Based on this, Kline (1968) questioned whether the irreversibility of this syndrome had been adequately documented. Quikin (1977) reported that when medication is withheld upon the observation of early symptoms of TD, the syndrome is always reversible. Therefore it is clear that many cases are reversible and some are probably treatment-resistant. It is presumed that TD is irreversible based on the unproven assumption of underlying irreversible brain damage or by conforming to the definition that TD is irreversible and excluding anything that is reversible from the TD group. Instead of irreversible it is preferable to use the term treatment-resistant which will provide some optimism for searching new forms of therapy.

CONCLUSIONS

Tardive dyskinesia is a clinically distinct syndrome with characteristic involuntary movements, associated most often with the administration of neuroleptic drugs. As it can occur spontaneously as well as with the administration of other drugs, it is not a syndrome exclusive to neuroleptic therapy.

The involuntary movements by the nature of their manifestations and by being iatrogenic and not disease related evoke attention of all the relatives as well as physicians. At one time considered irreversible, the same notion is still repeated by many recent workers perhaps by following the definition that irreversibility is a characteristic of the syndrome and reversibility is a criterion of exclusion. However, contrary to this notion, earlier cases are frequently reversible and even advanced cases may completely recover—unfortunately it is not possible to predict who would improve and who would not. The presumed organicity as an underlying pathogenic mechanism is not borne out, thus providing optimism. With our current knowledge, to think in terms of irreversibility is definitely unwarranted and perhaps one can call them treatment-resistant. With new developments they may all be reversible.

TD does not seem to be as prevalent as the reported studies seem to indicate. These figures do not reflect either the new cases or all the cases of TD in a defined population over a fixed period of time. Thus they merely reflect the cumulative number of TD cases among the residual population of mental hospitals. These figures therefore may be higher than the actual prevalence or incidence. The figure of 3 to 6 percent suggested by the American College of Neuropsychopharmacology (1973) refers to those who would exhibit some aspects of TD at “one time or another”. This seems to refer to “morbidity risk” which is many times higher than incidence.

However, the symptoms are overt enough to be recognized easily and at the same time severe and incapacitating. However rare it is, as these are iatrogenic and treatment-resistant, certain clinical and legal implications need be considered. Should one be treating a patient with neuroleptics which can produce TD? The answer is an unequivocal yes. The advantages of neuroleptics in treating acute as well
as long term psychotic patients far out weigh the risk. However, a minimal effective dose should be administered for minimum length of time. Regarding maintenance therapy as Gardos and Cole (1976) have suggested, minimum dosage needed to prevent relapses be administered; asymptomatic patient who is fully functional should be allowed to discontinue medication if he so desires and be observed closely; and in a dyskinetic patient medication should be completely withdrawn if the clinical state is compatible with such an action. Legally one could ask whether it is advisable to tell the patient of the possibility of the occurrence of TD. Or is it wise to withhold neuroleptics?

I cannot imagine myself explaining the side effects to a highly paranoid schizophrenic and obtaining his full consent to treat. Furthermore, it is not even possible to predict who develops TD. Under these circumstances, it is not preferable to explain this side effect at least to acute schizophrenic patients.

This perhaps slightly exaggerated current interest in TD may act as a catalyst to provide further clinical data and assist in treatment.

REFERENCES

American College of Neuropsychopharmacology (1973). Food and Drug Administration task force: Neurologic syndromes associated with antipsychotic drug use. New Eng. J. Med., 289, 20.

Ananth, J. & Costin, A. (1977). Dyskinesia with Thiothixene. Amer. J. Psychiat., 134, 6, 689.

Appenzeller, O., Biehl, J. P. (1968). Mouthing in the elderly. A cerebellar sign. J. Neurol. Sci., 6, 249.

Arns, G. M., Lepold, M., Dvorskin, R. Schwartz, A. (1977). A survey of tardive dyskinesia in outpatients. Paper presented at APA Meeting, Toronto.

Ayd, F. J. Jr. (1967). Persistent Dyskinesia. Med. Sci., 18, 32.

Ayd, F. J. Jr. (1970). Prevention of recurrence in: Clinical Handbook of Psychopharmacology. (Ed.) A. DiMascio and R. I. Shader. Science House. New York.

Ayd, F. J., Jr. (1974). Clozapine: A New neuroleptic. Int. Drug. Therap. Newsletter 9, 5.

Brandon, S., McClelland, H. A. and Protheroe, C. (1971). A study of facial dyskinesia in a mental hospital population. Brit. J. Psychiat. 118, 171.

Casey, D. E. (1976). Tardive dyskinesia: Are there subtypes? New Eng. J. Med., 1078.

Crane, G. E. (1968). Tardive dyskinesia in patients treated with neuroleptics: A review of the literature. Amer. J. Psychiat., 124, (Feb. suppl). 40.

Crane, G. E. (1970). High doses of trifluoperazine and tardive dyskinesia. Arch. Neurol. 22, 176.

Crane, G. E. (1972). Pseudoparkinsonism and tardive dyskinesia. Arch. Neurol. 27, 426.

Crane, G. E. (1971). Persistence of neurological symptoms due to neuroleptic drugs. Amer. J. Psychiat., 127, 1407.

Crane, G. E. (1975). Tardive dyskinesia: A review in Neuropsychopharmacology: proceedings of the 9th Congress of the Collegium Internationale Neuropharmacologicum (Ed.) J. R. Boissier, H. Hippius, and R. Pichot. Amsterdam Excerpta Medica foundation, 346.

Crane, G. E. (1973). Rapid reversal of tardive dyskinesia. Amer. J. Psychiat., 130, 1159.

Crane, G. E. and Smeets, R. A. (1974). Tardive dyskinesia and drug therapy in geriatric patients. Arch. Gen. Psychiat., 30, 341.

Curran, J. P. (1973). Tardive dyskinesia: Side effect or not? Amer. J. Psychiat., 130, 406.

Deckwitz, R. and Wenzel, W. (1967). Persistent extrapyramidal side effects after long term application of neuroleptics in: Neuropsychopharmacology. Proceedings of the Fifth International Congress of the Collegium Internationale Neuropsychopharmacologicum (Ed.) H. Brill. Amsterdam, Excerpta Medica, 698.

Deckwitz, R. (1969). Extrapyramidal motor disorders following long-term treatment with neuroleptic drugs. In: Psychotropic drugs and Dysfunctions of basal ganglia. (Ed.) C. E. Crane and R. Gardner. U. S. Public Health Service Publication 1938, Washington, D. C., 22.

Demers, J. C. A. (1966). Neuromuscular effects of long-term phenothiazine medication, electroconvulsive therapy and leukotomy. J. Nerv. Ment. Dis., 143, 73.

Druckman, R., Seelinger, D., & Thulin, B. (1962). Chronic involuntary movements induced by phenothiazines. J. Nerv. Ment. Dis., 133, 69.
CLINICAL ASPECTS OF DYSKINESIA

Dynes, J. B. (1968). Drug induced parkinsonism like syndrome. Virginia Med. Monthly, 95 ; 746.

Eckman, F. (1968). Zur problematik Von dauerchaden nach neuroleptischer langzeitbe handlung. Therapie der Cegenwart ; 107 ; 316.

Evans, J. H. (1955). Persistent oral dyskinesia in treatment with phenothiazine derivatives. Lancet, 1, 458.

Fann, W. E., Davis, J. M., & Janowski, D. S. (1972). The prevalence of tardive dyskinesia in mental hospital patients. Dis. Nerv. Syst. 37, 182.

Farrow, A., Rasch, P. J., Peterson, P. B. Brandborg, P., & Pakkenberg, H. (1964). Neurological symptoms in pharmacotherapy of psychoses. Acta Psychiat. Scand., 40, 10.

Farris, G., & Cole J. O. (1976). Maintenance antipsychotic therapy: Is the cure worse than the disease? Amer. J. Psychiat., 133, 32.

Geenberg, A. J. (1976). Computerized tomography in patients with tardive dyskinesia. Amer. J. Psychiat., 133, 578.

Greenblatt, D. L., Dominick, J. R., Sottsky, B. A., & DiMascio, A. (1968). Phenothiazine induced dyskinesia in nursing home patients. J. Amer. Geriat. Soc., 16, 27.

Haddenbrock, S. (1966). Zur wukungssweise und zur frage zentralorganischer Spatschaden der neuroleptischen daupergehandlung Nervenarzt 20 ; 199.

Hall, R. A., Jackson, R. B., & Swain, J. M. (1956). Neurotoxic reactions resulting from chlorpromazine administration. J.A.M.A., 161 ; 214.

Heinrich, K., Wegener, I. & Bender, H. J. (1968). Spate extrapyramidale hyperkinesen bei neuroleptischer langzeit-therapie. Pharmakopsychiatrie, Neuropsychopharmakologie 1 ; 169.

Hippius, H., & Lange, J. (1970). Zur problematik der spaten extrapyramydalen Hyperkinesen nach langfristiger neuroleptischer therapie. Arzneim Forsch. 20 ; 888.

Hopp, H. and Hoffman, G. (1967). Das Persistierende extrapyramidalen Hyperkinesen nach langfristiger neuroleptischer therapie. Arzneim Forsch. 20 ; 888.

Hunter, R., Earl, C. J. and Thorsnicket, S. (1964). An apparently irreversible syndrome of abnormal movements following phenothiazine medication. Proc. R. Soc. Med., 57 ; 24.

Jacobsen, G., Baldessarini, R. J., and Manschreck, T. (1979). Tardive and withdrawal dyskinesia associated with Haloperidol. Amer. J. Psychiat., 131 ; 910.

Jus, A., Pineau, R., Lachance, R., Jus, K., Pires, P., and Villemeur, R. (1976). Epidemiology of tardive dyskinesia. Dis. Nerv. Syst., 37, 210.

Kennedy, P. F., Hershon, H. I. and McGurk, R. J. (1971). Extrapyramidal disorders after prolonged phenothiazine therapy. Brit. J. psychiat, 118, 509.

Kiloh, L. G., Smith, J. S. and Williams, S. E. Anti-parkinsonian drugs as causal agents in tardive dyskinesia. Med. J. Aust. 391-392, 1973.

Klawans, H. L., Jr. (1973). The pharmacology of extrapyramidal movement disorders. Karger, Basel pp. 7-47, 64.

Klawans, H. L., Berger, D., Bruyn, G. W., & Paulson, G. W. (1974). Neuroleptic induced tardive dyskinesia in nonpsychotic patients. Arch. Neurol, 30, 338.

Kline, N. S. (1968). On the rarity of irreversible oral dyskinesia following phenothiazines. Amer. J. Psychiat., 124 [Suppl.] 48.

Kobayashi, R. M. (1976). Orofacial dyskinesia : Clinical features, mechanisms and drug therapy. West. J. Med. 125 ; 227.

Kunin, R. A. (1976). Manganese in dyskinesia. Amer. J. Psychiat., 133 ; 105.

Lehmann, H. E., Ban, T. A. and Saxena, B. (1970). A survey of extrapyramidal manifestations in the inpatient population of a psychiatric hospital. Laval Medical, 41, 909.

Lipper, J. (1973). Impairment of optokinetic nystagmus in patients with tardive dyskinesia. Arch. Gen. Psychiat., 26 ; 331.

Marsden, C. D., Tarsy, D., Baldessarini, R. J. (1975). Spontaneous and drug induced movement disorders in psychotic patients. In : Psychiatric aspects of neurological disease. (Ed.) D. F. Benson and D. Blumer, New York Grune and Stratton, 219.

McAndrews, J. B., Case, Q. and Trefurt, D. A. (1972). Effects of prolonged phenothiazine intake on psychotic and other hospitalized children. J. Autism Child Schizo. 2, 75.

Moline, R. A (1975). A typical tardive dyskinesia. Amer. J. Psychiat., 132, 534.

Pakkenberg, H. & Foo, R. (1974). Spontaneous oral dyskinesia. Arch. Neurol., 31, 352.

Pandurangi, Channabavanna, H. M., Ananth, J. (1977). Dyskinesia in an Indian Mental Hospital. (in press).

Quitkin, F., Rifkin, A., Gochfeld, L., & Klein, D. F. (1977). Tardive Dyskinesia: Are first signs reversible? Amer. J. Psychiat., 134, 84.

Roxburgh, R. A. (1970). Treatment of phenothiazine induced oral dyskinesia. Brit. J. Psychiat., 116, 277.
Sayers, A. C., Bureki, H. R., Ruch, M. and Asfer, H. (1973). Neuroleptic induced hypersensitivity of striatal dopamine receptors in the rat as a model of tardive dyskinesia. Psychopharmacologia 41, 97.

Schonecker, M. (1957). Ein eigentümlicher syn­drom in oralen Bereich bei Megaphen Applikation. Nervenarzt, 28, 35.

Sillie, H., and Muller, H. F. (1967). Choreiform movements as side effects of phenothiazine medication in geriatric patients. J. Geriat. Soc. 15; 517.

Slowald, J., Bouttier, D., Raymondaud, C. and Pilot, C. (1959). Quatre cases de dyskinesie facio-bucco-maxillo-masticatrice à évolution prolongée secondaire à un traitement par les neuroleptiques. Rev. Neurol., 100, 751.

Simpson, G. M. (1973). Tardive dyskinesia. Brit. J. Psychiat., 122, 618.

Stevens, J. R. (1974). Motor Disorders in Schizophrenia. New Eng. J. Med. 290, 110.

Thornton, W. E. and Thornton, B. P. (1973). Tardive dyskinesia. J. A. M. A. 226; 674.

Turek, I. S. (1975). Drug induced dyskinesia: Reality or myth? Dis. Nerv. Syst., 36, 397.

Turunen, S. and Achte, K. A. (1967). Buccolingual-masticatory syndrome as a side effect of neuroleptic therapy. Psychiat. Quart. 41; 268.

Uhrbrand, L. and Faarbye, A. (1960). Reversible and irreversible dyskinesia after treatment with perphenazine, chlorpromazine, reserpine, and electroconvulsive therapy. Psychopharmacologia, 1, 408.

Villeneuve, A. (1972). The Rabbit Syndrome.* A peculiar extrapyramidal syndrome. Canad. Psychiat. Assoc. J., 17; Sup. 69.

Villeneuve, A., Lavallee, J. C. and Lemieux, L. H. (1969). Dyskinase tardive neurolep­tique. Laval Medical 40; 832.

Wolf, S. M. (1973). Reserpine: cause and treatment of oral-facial dyskinesia. Bull. Los Angeles Neurol. Soc., 38, 80.