

Diagnosis and Management of Tourette Syndrome: Tourette Syndrome: A Source of Confusion

Authors and Disclosures

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Introduction

Tourette syndrome (TS), or Tourette's disorder, has been defined in the Diagnostic and Statistical Manual of Mental Disorders (DSM-III-R)^[1] and by the TS Classification Study Group^[2] as a condition satisfying criteria for multiple tics, including more than 1 motor tic and at least 1 vocal tic (not necessarily at the same time), with a waxing and waning course of more than 12 months and an age of onset under 21 years. More recently, the criteria were changed in DSM-IV,^[3] but for reasons discussed, these modified criteria are contentious.[†]

Whereas TS was once thought to be rare and exotic, it is now considered relatively common (although estimates of its prevalence vary widely).^[5] The increased awareness of this disorder has led to the inclusion of TS in the mainstream of developmental neuropsychiatric disorders, and it has become a focus of intense research interest.^[6,7]

In reality, there are few agreed-upon "facts" about TS. This is not surprising, in light of the following ambiguities:

- The causative mechanisms and the variety of manifestations tied to those mechanisms are unknown;
- The definition is arbitrary;
- It is unknown whether TS is a unitary or heterogeneous condition;
- There is no test for its presence and, if it is indeed genetic, none for carrier status;
- No epidemiologic study has been completed to determine the number of undiagnosed cases, which are believed to comprise the majority of TS cases^[5]; and
- In the absence of such a study, clinicians are dependent on findings from clinical samples whose differentiating characteristics from cases in the community are largely unknown ("referral bias").

These considerations should prompt caution against making any generalizations about TS. However, greater awareness of the disorder is resulting in the identification of simpler and milder cases.

The symptoms and manifestations of TS are easily misunderstood or distorted by the media and many medical textbooks, and thus cause a great deal of confusion in parents of newly diagnosed children. The diagnosis of a typical case is usually simple for those familiar with the syndrome, but can easily be missed by others. The tics may be attributed to "habits," "stress," or "emotional disorder," and sometimes to attention-seeking behavior or even the consequence of sexual abuse. Confusion can cause anxiety and sometimes serious psychologic problems for TS patients and their families.

Until fairly recently, tics were thought to be of psychogenic origin.^[7] It is now generally accepted that TS is a neurodevelopmental disorder of largely neurogenetic origin, and current thinking about the likely mechanism has changed (although this change is not yet reflected in most published material, as will be discussed in greater detail).

Persons with tic-related problems are increasingly engaging in self-diagnosis, or they and their parents hold on to the hope that a diagnostic label will explain all of their difficulties. Thus, there is pressure on professionals to respond to this felt need. A balanced, basic understanding of what is currently known about TS is therefore important to clinicians.

The most important point to keep in mind is that most persons with TS are not diagnosed.^[5] Individuals with tics may have had worse or more complex symptoms earlier in life that were never recognized (but led to misunderstanding and/or stigmatization), were misdiagnosed, or were not diagnosed as part of a comprehensive assessment. These factors could have influenced the person's development.

We review the current understanding of TS. Only a few of the thousands of references on the subject are cited here. Statements that are based on personal experience are indicated as such.

Problems With the DSM-IV Definition

The diagnostic criteria previously outlined are based on the DSM-III-R^[1] and Tourette Syndrome Association (TSA) Classification Study Group Criteria^[2] (which are an elaboration of DSM-III-R). The latest DSM-IV criteria have not been widely accepted by experts in the field for the following reasons. For example, the DSM-IV criterion that individuals with TS must exhibit distress or impairment is inappropriate for a neurologic condition in young children, who often are unaware of their symptoms (even though the parents may be distressed), or in situations where comorbid disorder makes it impossible to separate out the portion of distress caused by tics alone.^[4] The criterion that 3 months' absence of symptoms disqualifies an individual from a diagnosis of TS is not in keeping with the waxing-and-waning course of this condition. Another problem with the definition is that the traditional requirement of more than 1 motor tic and at least 1 vocal (or phonic) tic makes no sense, since vocal tics *are* motor tics, and phonic tics need not be vocal (eg, sniffing, hissing, spitting). Furthermore, the description of tics as rapid and purposeless is problematic. Some tics are slow or held in position (tonic), and in most instances, the tic movement is performed in response to an uncomfortable premonitory sensation, and therefore is not "purposeless."^[8]

These problems are mentioned here to illustrate some of the difficulties facing workers in the field and those attempting to understand the growing literature on the subject.^[9]

Description

The onset of TS typically occurs between 5 and 7 years of age. Most patients describe premonitory sensations and act out the tics to relieve an irresistibly unpleasant sensation such as tightness, tension, or increased sensitivity in a particular area of the body. This conscious effort differentiates tics from many other "involuntary" hyperkinesias.^[8,10-14] In my experience, this awareness is usually easy to elicit by the time the patient is 10 years old (if the right questions are asked), but may be elicited much earlier in some intelligent, mature children. Adults may describe odd, unpleasant feelings using words like "itch" or "pain," although neither quite fits.

The range of tic symptoms is vast. Tics are usually described as sudden, rapid, stereotyped, and purposeless movements of coordinated muscle groups that tend to occur in bouts.^[9] The most common tics involve excessive eye blinking (often combined with a brief blepharospasm), throat clearing, head shaking, and facial grimacing. Thus, there is a greater centering of tics in the upper body, with trunk and lower extremity involvement being less common; however, movement can occur in any area of the body. Typically, the tics start as simple ones in the upper body and may then spread, to varying degrees, to other parts of the body. (It should be realized that the commonly experienced twitching of muscles around the eye, or sometimes in the face, is a "fasciculation" of a bundle of muscle fibers and is not a tic.) Coprolalia (obscene or socially inappropriate speech), although dramatic, is an infrequent manifestation, contrary to impressions created by the media.^[9] Increases in tic frequency or severity when the person is excited, tense, or bored may create confusion as to causation.

What stands in the way of diagnosis?

In my experience, there are several obstacles to diagnosis, as well as to a broader understanding of TS.

1. **Lack of knowledge.** The physician may not have familiarity with the disorder.
2. **Difficulty of defining tics.** Tics are not always easy to define. Some of them may be confused with speech dysfluencies, mannerisms (as in autism), stereotypies of mental handicap, and the effects of allergies. The distinction between complex tics (supposedly without a cognitive component) and compulsions is often blurred.
3. **Denial.** The patient or physician may attribute symptoms to something else, such as nervousness, stress, habits, or allergies.
4. **Fallacy.** Some believe that coprolalia or emotional disturbance must be present to define the disorder. In fact, few patients with TS have coprolalia, and, even in those who do, it may be only temporary or intermittent.
5. **Being "kind" to the patient.** Physicians may be reluctant to tell patients the truth about their disorder, because the diagnosis of TS is assumed to be very bad news.

Differential Diagnosis

No tests can rule TS out or in. There are other rare causes of tics, such as Wilson's disease or neuroacanthocytosis, which typically have a different course.^[15] Depending on the extent to which "defensive medicine" must be practiced, some physicians obtain serum copper and ceruloplasmin to rule out Wilson's disease. EEGs and CT scans have no value in the absence of other indications of brain pathology. When in doubt, a neurologic consultation and appropriate tests should be obtained.

Certain conditions affecting the brain may result in TS-like symptoms, either in childhood or later in life. These may be termed "secondary Tourettism." Examples include damage from drugs, Huntington's disease, head injury, and encephalitis.^[16] Sudden withdrawal from neuroleptic drugs can result in "emergent" tics. These varying paths to a similar Tourette picture suggest that TS may represent a multifactorial pattern of CNS response, including variations occurring in normal development, rather than a unique disorder.^[17]

Recent research has suggested that a proportion of abrupt-onset or exacerbation cases of TS and/or obsessive-compulsive disorder (OCD) may be the result of cross-reactivity to the M-protein in the cell walls of group A beta-hemolytic streptococci,^[18-21] a condition referred to as pediatric autoimmune neuropsychiatric disorder associated with streptococcal infections (PANDAS). This theory is difficult to prove, however, given the ubiquity of streptococcal infections and the naturally fluctuating course of the disorder. It would be premature to base treatment recommendations on these possibilities. Vocal tics are common in Sydenham's chorea, which may share a similar etiology.^[22]

Misleading Information

It is my impression that the psychiatric texts tend to have the best information, but textbooks (whether old or recent) are generally very misleading, and even dangerous. The kind of misinformation that may be accessed by the public and professionals includes the following statements of "fact": TS is caused by a gene on chromosome 18^[23]; tics will become progressively worse if the patient pays attention to them^[24]; and many persons with TS are sexual exhibitionists.^[25]

The news media mostly pay attention to extreme or unique cases of TS, showing little or no interest in more typical situations. In 2 instances, deaths have been attributed directly to TS. In 1 case, a person died trying to climb down a chimney to kill his brother. The other case involved a teenager who died driving through a police roadblock in a stolen vehicle. In neither case was TS a sufficient cause.

Prevalence

The remainder of this review utilizes a shorthand device of referring to individuals with tics only (TS group), and those who have significant psychiatric comorbidity (TS+ group). This distinction originated with Leslie Packer, PhD, a psychologist with the Long Island Chapter of the TSA.

In all studies, there is a marked male predominance.^[5] In females, OCD may be an alternate phenotypic expression.^[9]

Depending on the definition used, the prevalence of TS has been reported as anywhere from 0.05% (1/2000) to 75%. The generally accepted prevalence of 0.05% is often used,^[5] especially if chronic multiple tics are included.^[9] It has been very difficult to make a practical determination of the actual community or epidemiologic prevalence, even with an accurate definition of TS. The automatic suppression of tics in the presence of strangers, the tendency to attribute mild symptoms to other factors or to ignore them, and the waning of the disorder with increasing age, all make such a study problematic. However, one study is under way in the UK,^[26] and a screening study of recruits to the Israeli Defense Forces was conducted and formed a prevalence of 0.04%.^[27] Studies also have been done in communities, attempting to ascertain cases through canvassing via the media's or physicians' practices.^[28-31]

A total population study by Zeitlin and Robertson^[26] in Essex, UK, is currently under way (Robertson, personal communication, 1997), using the DSM-III-R definition. The study's first phase has had some surprising results: The prevalence of TS for children aged 13-14 years in a randomly selected school was 3%, with little comorbidity. In contrast, the rate was only 0.05% in the regional psychiatric services. This finding suggests that roughly 1 in 60 children meeting criteria for TS were evaluated in clinics. In addition, this study suggests that TS is 1 of the most common childhood neuropsychiatric disorders.

What is the Prognosis of TS?

There are few studies of clinical outcome that encompass the life span of individuals with TS.^[32-35] Clinical impressions from referral clinics that have followed large numbers of patients suggest that the severity and the waxing-and-waning course often diminish with each passing decade of adult life.^[36] Existing tic patterns become more stable and easier to work around. Tics are usually most severe in childhood, but adolescence may be a time of increased symptomatology. However, this is by no means true for all patients with TS. Severity in childhood is not predictive of adult success or impairment. In TS+ cases, the overall outcome may be most closely related to the course of the comorbid disorder(s).^[9]

Is TS Genetic?

Since TS was first characterized, it has been known to have a strong genetic component.^[37] A major effort to identify the putative gene has been under way for several years, but with most of the genome excluded, this approach appears to have failed.^[38] It was formerly asserted that the genetic pattern was most likely a major dominant gene with variable expressivity and incomplete penetrance.^[39] This view, the basis for genetic counseling, has now been questioned in favor of an additive polygenic model that involves multiple genetic and environmental factors, including the possible role of prenatal sex hormones, genomic imprinting, and early infections.^[40] Bilineal inheritance (ie, inheriting from both sides of the family, surprisingly common, due to assortative mating) is thought to be conducive to greater severity and complexity.^[37-39,41-44]

In family studies, assumptions of homogeneity and the belief that chronic tics are part of the Tourette spectrum may not always be valid. A sib-pair approach is now being used^[9]: Where 2 children are affected in the same family, there are technical advantages of analyzing a large number of pairs over a small number of large pedigrees. Even in monozygotic twins, the clinical picture is not identical. Exposure of the developing brain to steroid hormones, as well as other early influences, may be involved.^[9]

Treatment Approaches in Patients With Comorbid Illness

Treatment is often dictated by comorbid conditions. Before undertaking any intervention, it is essential to complete a thorough evaluation of associated problems in the child, family, and school, and to assess their relative importance. Based on the experience at our clinic, automatic treatment of tics is not indicated (at present, only 15% of our patients are on medication).

Attention-Deficit/Hyperactivity Disorder

ADHD seems to co-occur in a high proportion of cases; however, the range of comorbidity varies considerably among studies.^[27,45] Preliminary data from a multisite study demonstrated a 16% to 89% range of comorbidity at different sites.^[46] Pauls and coworkers^[37] have indicated the possibility of a subtype of TS associated with ADHD, but the nature of the relationship remains controversial. Earlier reports suggested that stimulant drugs used to treat ADHD might actually cause TS,^[47] and the US package insert for methylphenidate, Physician's Desk Reference,^[48] and its equivalent Canadian Compendium of Pharmaceuticals and Specialties,^[49] emphasize this possibility in the contraindications sections.

The most common viewpoint is that stimulants may provoke an exacerbation in a minority of TS patients; in others there is no effect or even an apparent improvement.^[50-53] Drug alternatives are generally less effective,^[54] but include guanfacine,^[55] clonidine,^[56-58] desipramine,^[58,59] and nortriptyline.^[60] In practice, stimulants are used with caution, since long-term effects are not known.

Obsessive-Compulsive Disorder

OCD is generally thought to be more common in TS, although Shapiro and Shapiro disagree.^[61] Obsessive-compulsive behaviors (OCB) refer to symptoms whose severity does not reach the threshold for a diagnosis of OCD. In females, OCD and OCB may be alternative expressions of the putative TS genes.^[35,62-64] "Just right" feelings refer to the strong need to reach a specific end point in order to feel comfortable, and are typical of both TS and OCD, especially when they are comorbid.^[14] OCD patients without tics report more premonitory feelings of anxiety. Some follow-up reports have been published describing OCD children who develop tics or TS.^[32,65] Treatment, if necessary, usually involves selective serotonin reuptake inhibitors,^[66] clomipramine (a tricyclic antidepressant), and/or behavioral therapy.^[9]

Other Comorbid Problems

In persons with learning disorders and TS, there may be cognitive problems involving output and organizational skills.^[67] These may require modifications of school learning and testing.^[68] Sleep disorders are thought to be more common in patients with TS, but this finding can probably be explained by coexisting ADHD or OCD,^[69] except during times of major tic upsurge. The usual methods of management apply here as well, but adjustment of medication timing may be necessary. Aggressive thoughts and impulses may be more common in persons with tics,^[70] but whether these are acted out is not known. Peer socialization problems have been reported as more frequent in patients with TS than in controls.^[71] Recommendations for management have been provided by Packer.^[68]

A TS-like picture has been described in many disorders affecting the CNS, including mental retardation,^[72] encephalitis,^[16] and autism,^[73] as well as in a mixed special-education population.^[28]

Treatment for Tics

Education of the patient and significant others is always needed and often is the only required intervention. Medication for tics is symptomatic, not curative, and typically necessary only in a minority of cases, sometimes for only brief periods. Individual and group sensitivity to the social and personal impact of tics varies widely. It is reasonable and ethical to try whenever possible to modify individual and group tolerance of tics before medicating the patient.

Neuroleptics are the most predictably effective medication; dosages are not as high as those used for patients with schizophrenia. As usual, the rule is "start low, go slow." The best-studied drugs are the dopamine-blockers haloperidol and pimozide.^[74,75] Risperidone, a newer drug, targets dopamine D2, serotonin 5-HT₂, and alpha1-adrenergic receptors.^[76] Mechanisms of drug action in interacting systems are not yet well understood.

The effectiveness of clonidine is controversial.^[57,58,77] Clonidine is available as a skin patch in the US only. In Canada, a convenient oral dose formulation of 0.025mg exists. In the US, only 0.1-mg tablets are available and must initially be divided.

Tetrabenazine was approved in Canada in December 1996 but has not yet been approved in the US. Unlike the postsynaptic dopamine blockers, it depletes presynaptic vesicles. It can cause depression of undetermined responsiveness to antidepressants. The largest clinical experience with this drug has been published by Jankovic and Beach.^[78]

Augmenting agents in treatment-resistant cases may include clonazepam^[57] and transdermal nicotine.^[79,80] Neither has proven efficacy from double-blind studies, however.

Other therapies. Behavioral therapy was formerly thought to be inefficacious, but may assist in shifting tic type or location.^[81,82] The effects of a significant disorder on children's developing sense of self and the meanings they and their families give to their symptoms may also need to be a focus of attention for psychotherapy. A useful and sensitive discussion on this has been provided by Cohen and colleagues.^[83]

Conclusions

Providing services for persons with TS and TS+ demands a broad perspective on epidemiology, development, psychopathology, family needs and interactions, psychopharmacology, and education, as well as the collaboration of different disciplines. Treatment of persons with comorbid disease or of those who are very sensitive to medication usually requires management by or consultation with an expert. A broad range of skills will need to be applied very differently in persons with common, simple, mild TS disorder compared with those with more complex, comorbid, or severe TS. While TS+ is common in patients referred to clinics and may challenge clinical skills, those with TS are increasingly being identified and need help in putting their symptoms in perspective. As interest in TS grows, there is much confusing information in the media, on the World Wide Web, and in textbooks. Despite the confusion and misinformation, it is hoped that increased interest will eventually result in a better understanding of the pathophysiology of the condition and its more successful management.

Online Resources

- [Tourette's Syndrome: A Model Neuropsychiatric Disorder-Grand Rounds at the Clinical Center of the National Institutes of Health](#). A comprehensive analysis of the physical manifestations, associated comorbidities, natural history of neuropathologic progression, and possible environmental/genetic etiology of this neuropsychiatric disorder. Also included is a clinical case study emphasizing the critical aspects involved in the neuropsychologic evaluation and diagnosis of suspected Tourette syndrome. Provided by Massachusetts General Hospital Neurology Service.
- [A.D.H.D. and Tourette Syndrome: Child, Adolescent, Adult](#). Brief commentary on the clinical significance of Tourette syndrome and the specific pharmacologic strategies employed for the management of its spectrum of symptoms. Links are provided to additional pages. Provided by A.D.D. Clinic.
- [Guide to the Diagnosis and Treatment of Tourette Syndrome](#). Comprehensive overview addressing aspects involved in the management and diagnosis of Tourette syndrome, including neuropsychiatric and clinical assessment, the significance of differential diagnosis, an

epidemiologic profile, genetic/non-genetic factors contributory to onset, symptomatology, and pharmacologic/psychodynamic therapeutic strategies. Provided by Internet Mental Health.

- [Tourette Syndrome](#). A general overview of diagnostic criteria, clinical progression, associated comorbidities, etiologic factors, prognosis, and therapeutic options for managing the pathophysiology of Tourette syndrome. Provided by National Institute of Neurological Disorder and Stroke.