

Developmental and Behavioral Disorders Grown Up: Tourette's Disorder

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CASE VIGNETTES

On assassination of the delusional and perverse Caligula in 41 CE, his uncle, Claudius I, ascended as the emperor of ancient Rome. Claudius was an unlikely heir, marked as a twitching and stammering buffoon, absent-minded with embarrassing “habits,” and an odd and socially indecent laugh, symptoms that only worsened in times of anger or stress. However, ultimately, he proved a respected, although controversial, politician.

Peter the Great became the Russian Emperor in 1721, and he brought the Russian Empire to its status as a leading eastern European state. He was impulsive and exhibited face and arm twitches, often given to severe and sudden fits of rage. A visitor to Peter's court observed the emperor as having his head “tug to the right by convulsions.”

Samuel Johnson (1709–1784) is second only to William Shakespeare as the most quoted of English writers. He opined “'tis better to remain silent and be thought a fool than to open one's mouth and remove all doubt,” but his tics and noises did not oblige his advice, and they rendered him an object of great ridicule. Given to significant anxiety and depression so severe that he “at one time strongly entertained thoughts of Suicide,” Johnson was seen “shaking his head and rolling himself about in a ridiculous manner,” and making sounds like “a half whistle” or “as if clucking like a hen,” performing compulsive rituals when entering doorways, described thus as an “ideot,” and later astonishing observers with his “power of eloquence.”

Encompassing the great and the unsung alike, Tourette's disorder today also captures our attention for its place among the most common—and commonly misconceived—neurodevelopmental disorders.

DIAGNOSTIC CRITERIA AND APPROACHES IN CHILDREN VERSUS ADULTS

Diagnosticians and patients have trod a meandering path since Tourette's disorder was first clinically defined

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in 1885. Clinical definitions and reiterations have emerged and evolved, as have behavioral associations, notions of origin, and manifestations across life stages. One thing, however, has been abiding: diagnosis is exclusively made by history in clinical symptomatology of tics.¹

Whether in children or adults, tics are defined as sudden, rapid, recurrent, nonrhythmic stereotyped movements or vocalizations, often occurring in bouts. Tics first emerge before the age of 18 years, although many patients with Tourette's disorder are often initially evaluated and diagnosed as adults. The DSM-IV-TR classifies tic disorders based on duration (“transient” versus “chronic,” the latter lasting >1 year) and type (“motor” and “vocal”). Another dimension described in the DSM is complexity: “simple” (involving one muscle group or sound) versus “complex” (slower, more purposeful coordinated movements or vocal productions including words or phrases). DSM-IV-TR diagnostic criteria for Tourette's disorder is as follows: both multiple motor and one or more vocal tics have been present at some time during the illness, although not necessarily concurrently. The tics occur many times a day (usually in bouts) nearly every day or intermittently throughout a period of >1 year, and during this period, there was never a tic-free episode of >3 consecutive months. The onset is before the age of 18 years, and the disturbance is not due to the direct physiological effects of a substance (e.g., stimulants) or a general medical condition (e.g., Huntington disease or postviral encephalitis). Importantly, in clinical practice and physiologic origin, the distinctions among the tic disorder classifications can blur.

Tic disorders are highly, but not exclusively, heritable,² so that obtaining comprehensive psychiatric and neurological patient and family history is essential. However, precise genetic mechanisms are unknown at the present time and are most likely to be polygenic with variable penetrance. Tic symptoms range in number, intensity, frequency, complexity, and functional interference. These variables, along with subjectivity and environmental influences, can contribute to impairment. There are several conditions that commonly co-occur in clinically referred patients with Tourette's disorder, and these often have the most impact on psychosocial, academic, and vocational performance. Tics typically reduce or remit in later adolescence or young adulthood, but the associated conditions may often rise or remain front and center among adults in their symptomatic influence and interferences. For this reason, this review

explores the development of tics as well as associated psychiatric comorbid conditions across life stages.

EPIDEMIOLOGY IN CHILDREN VERSUS ADULTS

Tourette's disorder (TD) is much more common than many clinicians are aware, with prevalence estimates ranging from 3 to 8 per 1000.³ Chronic motor tic disorders are even more common. The natural history of TD varies widely among affected individuals, but tics customarily become apparent in the first decade of life, increase before puberty, diminish during adolescence, and essentially remit or stabilize during adulthood. Epidemiologic studies suggest that the prevalence rate of TD is much lower in adults; however, accumulated evidence indicates that TD may persist into adulthood.⁴ Thus, it is imperative to regard TD as a life-cycle disorder that can persist into adulthood.

Historically, TD was regarded as a very rare disorder, and the scope of its potential phenotypes much more narrow than we understand today. These now obsolete epidemiologic perspectives undoubtedly contributed to its underidentification and to the many misconceptions about the origins and complications. Still, a legacy of historical misconceptions that suggested a neurotic conflict basis to tics, or a diagnostic requirement for uttering obscenities, or an inauspicious outcome, even today interferes with timely diagnosis, prevention, and management while also threatening to underestimate TD prevalence. Additional factors that limit current epidemiologic understanding include a paucity of longitudinal research, problems in recruitment of specialized clinical samples or "ascertainment" bias, delineation of the margins of TD phenotypes, and lack of evidence-based endophenotypes.

CHANGE/PERSISTENCE OF SYMPTOM DISEASE CHARACTERISTICS WITH AGE

Tics are generally first observed in children at approximately 6 or 7 years, although more subtle tics that escape detection can appear earlier. Surprisingly, even parents with tic disorders frequently fail to perceive their child's tics.² Transient tics, the most common tics observed in children, typically present as "simple" motor tics (i.e., brief and rapid, and isolated to one muscle group in the face, head, or neck) and resolve within a year. Tics that persist beyond 1 year are termed "chronic," and may become more "complex" sequences of stereotyped or fragments of seemingly purposeful behaviors, such as tapping, grooming, or touching. Some children will subsequently develop phonic tics. These, too, usually first emerge as "simple," characterized by single sounds such as throat clearing, sniffing, coughing, or grunting; in TD, these vocal tics may evolve to "complex" tics including vocalization of syllables, words, or phrases. Both motor and phonic tics sometimes include echo- (imitative of others) or pali- (repeating of oneself) traits, and, less often, copro- (socially inappropriate) traits.

Clinically referred youth with TD are often diagnosed

with comorbid psychiatric disorders, which typically emerge during childhood, although their timing and expression can be highly variable. In general, childhood neurodevelopment is more unpredictable than that in adults,⁵ whose symptom profiles tend to be more stable. Half or more clinically referred children with TD also meet criteria for attention-deficit hyperactivity disorder (ADHD), with symptom onset usually preceding tic onset. Obsessive-compulsive disorder (OCD) is diagnosed in approximately 20% to 40% of children who come to a clinic for TD; however, up to 90% may meet criteria for subthreshold OCD by having some symptoms. Mood and non-OCD anxiety disorders are also frequently described in clinically referred youth with TD. The role and impact of the comorbid disorders are complex but will be examined separately in this section.

Pathophysiology of Tics and Comorbid Conditions

To best understand the evolution of symptoms as a patient matures, one needs an appreciation of the shared brain-based mechanisms in TD, which are believed fundamental to tics and to many of the comorbid conditions. One crucial mechanism, although incompletely understood, involves disinhibition of several circuits in the brain in the cortico-striatal-thalamic areas. These circuits include regions of the neocortex (particularly prefrontal), the basal ganglia, and the thalamus.⁶ The result of this dysfunction is that neurological information that ordinarily would be inhibited, or "gated," from reaching other areas of the brain instead is unfiltered.

The cluster of symptoms commonly observed in patients with TD including tics, anxiety, obsessions and compulsions, explosiveness, hyperactivity, and impulsivity may share this underlying pathophysiology reflecting a core disorder of disinhibition in the cortico-striatal-thalamic pathways.

Investigation of brain mechanisms using human and animal models sheds light on possible maturational patterns in TD that may contribute to progressive age-related changes in phenotype. A majority of functional and anatomical imaging studies are limited to adults. Available comparisons across age groups describe differences and possible compensatory changes⁷ over time in brain regional size,⁸ shape, and function,⁹ but results across studies are inconsistent and sometimes contradictory.¹⁰ It is unclear whether these differences represent causes, consequences, and/or epiphenomena.¹¹ Findings and interpretations center on the basal ganglia and its projections, as well as limbic and other brain systems,¹² in keeping with theories of flawed gating¹³ along a circuit linking the prefrontal cortex and other neocortical regions with the striatum, globus pallidus, and thalamus.

Research in TD and the comorbid conditions have gained tremendous momentum in recent years revealing clues to its origins and maturational patterns. Substantial further work will be needed to elucidate maturational mechanisms. We will explore what is known of these lifetime patterns and outcomes in this discussion and

emphasize clinical management and prevention strategies through partnerships with families and individuals affected with TD at all life stages.

Genetics of TD and Comorbid Conditions

There is no question that TD is highly heritable, and understanding the patterns in genetic vulnerability may facilitate anticipatory guidance and permit more accurate predictors of adult outcomes. However, the inheritance mode is complex, heterogeneous, and poorly understood. Limitations that likely impede this understanding include the wide range in symptom expression,¹⁴ existence of more than one responsible single-gene major locus, additive polygenic interactions, environmental mediators of gene expression, and others.¹⁵ Multiple candidate-gene studies have implicated a variety of regions but are limited by small power or failed replication of results. The first identified candidate gene (*SLITRK1*) was discovered on Chromosome 13q,¹⁶ but the finding has not been replicated by subsequent investigators, and if related to TD, the gene accounts for only a small minority of cases. Still, *SLITRK1* is suspected to contribute to the development and maintenance of neurologic circuits involved in TD¹⁷ and may provide clues to future genetic and pathophysiological discovery. Genome-wide linkage and association studies offer growing promise in identifying susceptibility genes for complex behavioral traits like TD. The largest whole-genome screen to date of affected sibling pairs and large family pedigrees provides a strong evidence of linkage on Chromosome 2p.¹⁸

Tics: Phenomenology and Course

The patient's subjective experience of tics is often unpleasant and can involve a build up of physical or sensorimotor sensations (premonitory urges) in various parts of the body, anxiety or tenseness, mental images or cognitions, and other perceptions, which can be at least partially suppressed for varying periods of time. In this context, execution of the tic can reduce the unpleasant sensations and produce, at least temporarily, some relief to the patient. Only a minority of young children with TD may report these sensory events, but by the age of 10 years most youth distinctly identify the experience, and by adulthood, >90% of individuals with TD do so. Patients describe these sensations as an unpleasant urge, impulse, tension, or pressure located in discrete body regions in which their tics occur¹; commission of one's stereotyped tic behaviors diminishes the sensations temporarily.

As a child with TD matures, tics typically progress in a rostral to caudal sequence and from simple to complex.¹⁰ Interestingly, repetitive, stereotyped behaviors may be fragments of normal learned and/or hard-wired adaptive motor sequences or linguistic communications. But in tics, these fragments represent leaked, nonfunctional "super-stereotypies," which are performed semi-automatically to alleviate the unpleasant perceptions. Consistent with learning theory, the repetitious performance of tics and non-tic stereotyped behaviors may be

negatively reinforced, i.e., "urge - tic - relief," whereby an unpleasant involuntary urge reinforces the performance of a highly stereotyped behavior to achieve relief.¹⁹

The natural history of tics in TD is a waxing and waning of tic symptoms in which one tic is replaced by another. Children and adolescents with TD may develop new and/or more complex stereotyped behaviors, whereas earlier behaviors, often including tics, abate or remit. Adults can also show changes in clinical symptoms, although at this life stage, symptoms tend to be more stable.⁵ The precise patterns of symptom evolution and outcomes are not predictable for any individual with TD, although both neurodevelopmental and environmental forces certainly contribute. In addition, the implications of tics and of the comorbid conditions, and exacerbating and protective mediating variables, are quite different in the young child with TD from those of an adolescent and/or adult, impacting social, academic, vocational, organizational, and other arenas of function and quality of life.

Tics typically follow a waxing and waning course over time and often occur in bouts, ranging from seconds to minutes to hours to days or weeks; this pattern may reflect an underlying brain oscillatory mechanism not yet discovered but which may hold a key to understanding the pathophysiology, course, and outcome.²⁰ The ebb and flow of tics occur within an overarching lifetime history of peak intensity in pre- or early adolescence (age, 9–12 years)²¹ or a "worst ever" crest.²² Available evidence suggests that most individuals with TD will have persistent tics, but with a sharp decline in adolescence²³ followed by a sustained improvement in tic-associated impairment.²⁴ In contrast to children, adults with TD seldom if ever have progressively severe tics.²⁵

Adulthood tic outcome is unpredictable and highly variable across individuals, but a "rule of thirds" applies; one third of individuals with TD experience virtual or entire remission, another third of individuals show significant improvement, and the final third of individuals have persistent tic severity,²⁶ for which many will remain moderate or severe. Importantly, preadult peak tic severity likely predicts maximum potential adulthood tic severity among those for whom tics do persist.²⁷ However, even in adults with persistent tics, only a minority experience "catastrophic" tics,²² e.g., self-injurious or highly disruptive. Among adults with persistent mild-moderate tics, many are fully unaware their tics continue,²⁸ perhaps a testament to clinical insignificance in this group. Still, reliable adult outcome data are limited and findings inconsistent.²⁹

A minority of individuals with TD will also have coprolalia (uttering obscenities) and/or copropraxia (vulgar gestures). These oft-dreaded symptoms are nearly pathognomonic for TD, are widely recognized but poorly studied, and available data may not generalize. Although most tics will emerge in childhood, coprophenomena, particularly coprolalia, may not emerge until adulthood.³⁰ However, coprophenomena most often emerge

initially in childhood, and in one third of such children, these symptoms remit by adulthood.³⁰ Moreover, their presence in childhood does not appear to predict tic severity in adulthood.²⁷ This pattern may contrast with outcomes of other tic types for which severity shows modest predictability, at least on reaching young adulthood.²⁵ For example, self-injurious tics may become quite damaging and recalcitrant in adulthood.³¹

In 1998, Swedo et al³² described the clinical characteristics of 50 children with OCD and/or tic disorders in which the onset or exacerbation of symptoms was precipitated by Group A beta-hemolytic *Streptococcus* infection; the term pediatric autoimmune neuropsychiatric disorders associated with *Streptococcus* was first created to describe this theoretical subgroup of children with OCD and/or tic disorders. Five working criteria for the diagnosis of pediatric autoimmune neuropsychiatric disorders associated with *Streptococcus* were proposed: (i) presence of lifetime diagnostic criteria for DSM-IV OCD and/or tic disorder; (ii) onset between the age of 3 years and the beginning of puberty; (iii) episodic course of symptom severity; (iv) temporal association between symptom onset and/or exacerbation and Group A beta-hemolytic *Streptococcus* infection, as documented by positive throat culture and/or elevated anti-Group A beta-hemolytic *Streptococcus* antibody titers; and (v) association with neurological abnormalities during symptom exacerbation, such as tics or choreiform movements but not chorea per se. Swedo et al speculated that an autoimmune process similar to Sydenham chorea and rheumatic fever may play a role in the development of pediatric autoimmune neuropsychiatric disorders associated with *Streptococcus*. The hypothesis of a subgroup of children with pediatric autoimmune neuropsychiatric disorders associated with *Streptococcus* has generated a host of clinical and basic research. To date, there is still controversy regarding the existence of such a diagnostic entity and its hypothesized pathophysiology and additional studies are needed.

Comorbid Psychiatric Conditions

Semi-independent of tic outcomes are psychiatric comorbid disorders outcomes. Many of these disorders, such as ADHD and OCD, are more likely than tics to persist into adulthood, imposing qualitative and functional impairment.³³ These disorders may precede tic onset, or they may appear concomitantly or even emerge later in development, including in adulthood. Given the frequency with which comorbid conditions occur and the potential-associated impairment, they must be anticipated, identified, and optimally treated.

Some comorbid conditions may affect children and adults similarly, such as sleep disturbances, but the presence of comorbid conditions often differs in children and adults, including ADHD and learning disorders. Anxiety and aggression have not been adequately compared between children and adults with TD. Among children with TD, learning disability, oppositional and defiant

behaviors, and motor coordination problems are more likely to be identified than in adults with TD³⁰; nevertheless, these behavioral and developmental impairments are central to pediatric screening and subspecialty referral and may be under-recognized in adult populations. In contrast, adults with TD are more likely than children to present with obsessions and compulsions, mood disorders, and self-injurious behaviors.³⁰ In addition, some comorbid conditions are virtually unique to the adolescent or adult populations, including personality disorders and substance abuse or dependence.

ADHD, Learning Disabilities, and Executive Functions

ADHD, learning disabilities, and executive dysfunctions share frontal-striatal correlates and frequently occur in TD. These problems interfere with life functioning to some degree in most adults with TD.³¹ ADHD is the most common co-occurring condition in TD, and symptom onset frequently, if not usually, precedes tic onset. Among children with comorbid ADHD, it is this condition that is most likely to impose disability burden, as is the case with adult ADHD.²³ Further, comorbid ADHD tends to be more chronic than tics, and the tics have little impact on subsequent adult ADHD outcome.²³

Also common in children and adults with TD are nonverbal learning disabilities. Related executive functions challenges, such as working memory and organizational skills, have been less consistently demonstrated in children with TD, and adults with TD may have fully intact executive functions.³⁴ However, these and other specific cognitive deficits in children and adults with TD are highly variable across studies. Performance on tasks of executive functions, for example, is rather susceptible to influences of comorbid ADHD or OCD³⁴ and muddy the clarity of test results and interpretations of maturational distinctions in adults with TD; this is an important point to clarify because executive functions difficulty appears likely to be a correlate of ADHD across the life span.³⁵

Visual-motor integration function, including skills in handwriting, sports performance, video games, and musical instrument playing, is impaired in many children with TD and may predict future tic severity and poorer psychosocial functioning in adulthood.³⁶ Investigations of fine-motor skills among adults with TD are limited, but such impairment has been identified,³⁷ including in the original TD literature of the late 1800s, although the evidence is not robust or known to be correlated with tic severity. Fine-motor impairment may imply a deficit in complex coordination mediated by circuits involving the basal ganglia.³⁶

Neurodevelopmental processes and their correlating neurocognitive manifestations have not been well characterized in TD; there is little extant evidence regarding neurocognitive performance in adults with TD. Future studies of maturational changes will require longitudinal designs.³⁸

Obsessions and Compulsions

Obsessions are intrusive, repetitive, thoughts, images, or ideas; compulsions are repetitive behaviors or rituals as attempts to ward off or reduce the unwanted thoughts or images. Patients with TD often describe a need or feeling to get things “just right,” and behaviors are repeated to achieve a feeling of symmetry or exactness in touch or appearance.³⁹ In patients with OCD without TD, contamination concerns or violent images tend to be more common. The distinctions may imply a different cause (i.e., TD versus non-TD OCD), lifetime course, and management strategy.⁴⁰

Between 20% and 60% of clinically referred children with TD may have obsessions and compulsive behaviors (OCB), but OCD that meets diagnostic threshold (i.e., causing distress or functional interference) is somewhat less common.¹ Although OCB/OCD may first emerge at any point during childhood through young adulthood, symptoms usually peak roughly 2 years after tic symptoms peak,²⁵ or may emerge after tics subside or disappear.²⁶ Among children with TD, OCB/OCD is associated with anxiety, depression, and externalizing behaviors.

In adults, OCB/OCD are more highly associated with ADHD and self-injurious behavior¹; OCB/OCD is more likely to be associated with distress and/or impairment than are other comorbid disorders. When severe, OCD may play a central role in poorer outcomes in adult TD such as emergency department visits or hospitalization.³³

Anxiety

Non-OCD anxiety disorders are also quite common in both children⁴¹ and adults with TD. These disorders include a wide range of conditions, such as generalized anxiety disorder, social, and other phobias. Among children with TD, comorbidity with almost any of the anxiety disorders, especially separation anxiety, is correlated with more severe tics, and anxiety may, in fact, mediate tic severity.⁴² In adults, coprophenomena correlate highly with generalized anxiety,⁴³ whereas correlation with other severe tic manifestations has not been well studied. In children and adults, it is a well-known phenomenon that stressful experiences increase tics, but there are few systematic studies. Anxiety in both children⁴⁴ and adults⁴⁵ with TD may be a function of heightened reactivity in physiologic stress-related hormone release.

Affective Disorders

Both children and adults with TD are at risk for mood disorders, and, similar to the population at large, etiology is multifactorial. However, it is not entirely clear whether patients with TD are at greater risk for mood disorders than other patients with chronic illness. Tic severity may or may not correlate with depression, but adults with TD with coprolalia report higher depressive symptoms than those without coprolalia.⁴⁶ Comorbid ADHD and OCD also independently increase the risk for depression; in addition, many of the medications pre-

scribed to children and adults for tic reduction can increase the risk.⁴⁶

Bipolar disorder has been reported as frequent in children and adults with TD. A recent longitudinal study, after children diagnosed with bipolar disorder through young adulthood, found persistent psychosocial impairments, but symptoms were not specific for bipolar disorder⁴⁷; neither hypothesized clinical descriptions of bipolar disorder in childhood TD nor their adulthood outcomes can be inferred at this time.⁴⁶

Explosive Outbursts (Rage Attacks)

Explosive, angry outbursts are not uncommon in both clinically referred children and adults with TD. Some studies suggest that the outbursts are positively correlated with the triad of TD,⁴⁸ ADHD, and OCD.⁴⁹ Similar to tics, many patients with outbursts report premonitory feelings of tension, followed by relief, and subsequent remorse; these episodes may represent a similar disorder of disinhibition. Psychosocial variables such as parenting style or family function may also be explanatory. There is some speculation that bipolar disorder may be associated with explosive outbursts in clinically referred patients with TD, but this theory has not been systematically examined.

Autism

Although diagnostic criteria for TD do not include the core social or language impairments of autism spectrum disorders (ASD), the two disorders share several features, and the growing awareness and investigation of both disorders have revealed frequent co-occurrence, particularly with Asperger syndrome.⁵⁰ In addition to stereotyped movements that are aggravated by emotional states (tics in TD and stereotypies in ASD), shared features include impulsivity, repetitive behaviors, echolalia, anxiety, explosive outbursts, and male preponderance. Features suggest overlap with diagnostic criteria for ADHD, OCD, and learning disorder.⁵¹ Both disorders share similar putative pathophysiologic mechanisms that implicate dopamine and serotonin dysfunction. A large international database of more than 7000 patients with TD, representing evaluations by expert clinicians from six continents, found 4.6%, or 1 in 22, with comorbid ASD.⁵² Conversely, among patients with autism as a primary diagnosis, an Italian tertiary care autism referral center identified 22% of 105 individuals with ASD also had chronic tic disorders (only one had Asperger syndrome and three had pervasive developmental disorder—not otherwise specified).⁵³ In a Swedish community-based sample of more than 4000 children, nearly 2% were found to have a chronic tic disorder; of these, 8.4% had a comorbid ASD.⁵⁴

Personality Disorders

Enduring, maladaptive behavior patterns emerge in adolescence or young adulthood and result in distress or impairment.⁵⁵ “Cluster A” personality traits and disor-

ders, particularly schizotypal, characterized by odd or eccentric behaviors,⁵⁶ have been found to be more prevalent in TD adult clinical populations than among controls and are especially associated with anxiety and OCB/OCD.⁵⁷ These “schizophrenia-like” symptoms include paranoia and feelings of persecution, and, as seen in the presumably related schizophrenia⁵⁸ may share a common frontal-striatal physiological pathway with TD. Despite the appreciable comorbidity with OCB/OCD, “Cluster C” obsessive-compulsive personality disorder has not been reported in association with TD.

Substance Use/Abuse

Substance abuse and dependence occur more commonly in many psychiatric disorders among affected adolescents and adults, as is the case for TD.⁵⁹ Some theorists suggest that patients with TD may have a neural predisposition to specific chemical substances that serve to reduce unpleasant symptoms, perhaps by “correcting” central disinhibition mechanisms or by regulating reward mechanisms common to TD and substance abuse among susceptible individuals with a specific allele.⁶⁰

Cigarette smoking and alcohol abuse are common among adults with TD. Alcohol abuse is common among adults with TD,⁶¹ reported in 30%. TD sufferers often report a marked reduction in premonitory urges and tics with alcohol consumption.⁶² Those who use tobacco often report its beneficial effect in tic reduction, although it is unclear if the true benefit comes as tic reduction (perhaps through a nicotinic cholinergic agonist mechanism⁶³) or emotional enhancement.⁶⁴ Medicinal transdermal nicotine may help reduce tics.⁶⁵

Similar theories suggest a central “endocannabinoid” receptor system may be at play, implicating a high density of such receptors in the basal ganglia and a close functional relationship with dopamine in regulating motor activity.⁶⁶ Indeed, studies reveal that delta-9-tetrahydrocannabinol (a major psychoactive ingredient in marijuana) reduces tics in some patients and may serve as a useful alternative to conventional psychotropic options for recalcitrant severe tics.⁶⁷

Sleep

Sleep is problematic for children and adults with TD, although with some distinctions. Up to 50% of children and adults with TD have markedly disturbed sleep, and limited available polysomnogram data reveal prolonged sleep latency, more wakefulness after sleep onset, increased non-tic motor activity in non-rapid eye movement sleep,⁶⁸ and persistent tic motor activity in children⁶⁹ and adults.⁷⁰ In contrast to children with TD, adults also have less total slow-wave sleep than control adults.⁷⁰

The causes and consequences of these disturbances are unknown; sleep regulation may share neural pathways that generate tics, but sleep disturbances are also likely exacerbated by comorbid disorders. Sleep loss is known to impair frontal cortex and executive function.⁶⁸ Medications that are used to treat tics and several

comorbid conditions, including stimulants, neuroleptics, and selective serotonin reuptake inhibitors, also have impact on sleep, although not necessarily deleterious and perhaps helpful. It is also possible that insufficient and nonrestorative sleep, with potential impact on stress and anxiety, arousal and mood, can also increase tics.

Migraine

Limited studies report that migraine is more prevalent in children with TD (range, 16–27%)⁷¹ than in controls, and even more prevalent in adults with TD (39%).⁷² Theories implicate serotonergic or other neurohumoral basal ganglia dysfunction or its related systems.

FUNCTIONAL/ADAPTIVE OUTCOMES IN ADULTHOOD

Most available data regarding Tourette’s disorder (TD) adulthood functional outcome have been cross-sectional and acquired retrospectively, but longitudinal investigations are under way and are necessary to elucidate risks and resilience.³⁹ Early longitudinal data suggested adults cope well despite comorbidity.³¹ More recent data using a variety of investigative designs challenge such outcomes. Importantly, increasing awareness of the prevalence and range in expression of TD has resulted in greater identification and a shift to management strategies that de-emphasize tics and focus on dimensional functions to understand global outcome.²⁶ Adult outcomes for youth with TD today will be different than for youth of 1960s through early 1980s, an era when treatment of tics, regardless of severity, with long-term typical neuroleptics was de rigueur, with the potential for significant adverse effects.

Quality of Life

There is surprisingly little data available regarding the impact of tics on quality of life (QOL), whether health related or perceived, either in children or in adults with TD. Several studies recently published or currently under way mostly focused on health-related impact. Past assumptions that correlated the mere presence of tics with disability are invalid. A clear understanding of TD-specific QOL risk factors, moderators, and mediators will be necessary so as to personalize treatment to ensure most favorable outcomes.

In studying QOL in children and adolescents with TD, correlation between child self-report and parent report is mostly high, but this correlation diminishes for adolescents. Children with tics generally have lower QOL than their unaffected peers in most areas of function, including psychosocial distress from tics.⁷³ Interestingly, parents of adolescents rate tics as having more impact on their child’s QOL than the adolescents themselves report; tic impact on QOL may diminish for many adolescents with TD, perhaps in parallel with the common waning of tic severity at this life stage. Parent perceptions of psychosocial stress in their children or adolescents highly predict later childhood depressive and obsessions and com-

pulsive behaviors (OCB) symptom severity,²¹ although children without psychosocial dysfunction may still develop these symptoms in adulthood.²⁸ Psychosocial adjustment in youth with TD is understood most fully in the context of the family,⁷⁴ as the family may model appropriate social interaction and coping.

Among adults with TD, health-related QOL is impaired in those for whom tics are associated with limitations, such as physical injury or disruption of daily activities, as well as interference with employment or studies. Increased vocal, but not motor, tic severity is correlated with poorer psychosocial outcomes, including mood swings, anxiety, depression, and temper outbursts, as well as greater financial dependence on others.⁷⁵ Psychosocial impact centers on embarrassment and feeling rejected, difficulty in making friendships, or in developing relationships.⁷⁶ However, because only a minority of adults with TD continue to have severe tics, these findings may not generalize.

Tics

Today, many adults with TD find their tics inconsequential or even remitted, despite frequent evidence of persistence of tics,²⁷ with interference absent or only mild in degree.³¹ Adults may be less aware than children of their tics, perhaps due to diminished severity or accommodation.²⁸ Tics typically continue to wax and wane in most adults, but their magnitude in frequency and intensity often decreases. Adults often develop effective coping strategies as a result of years of experience managing their tics.

Comorbid Psychiatric Conditions

Although the impact of tics usually diminishes in adolescence, OCB/obsessive-compulsive disorder often emerges or worsens. In children, OCB may serve a protective function by enhancing attention to detail, though perhaps at a cost of quality in social relations.⁷⁴ Qualitative adult outcome of those with persistent OCB/obsessive-compulsive disorder may be associated with social anxiety and poor self-esteem.⁷⁷ Generalized anxiety and mood disorders also persist, perhaps even in most adults with TD,⁷⁶ and may impose a significant toll on functional outcome. Similarly, attention-deficit hyperactivity disorder symptoms are usually persistent, although past or current tics appear to have little impact on attention-deficit hyperactivity disorder outcome.²³ Learning disabilities and executive dysfunctions are generally lifelong, and outcomes variable and complicated, with limited available data in TD.

Other Outcomes

Important indices of adult TD functional outcome not yet well studied include employment history and satisfaction, higher education achievement, social relationships, and family constructs. Limited employment outcome data find high unemployment rates in adults with TD, with employment status not correlated with greater

tic severity, depression, anxiety, or OCB when compared with employed adults with TD.

MANAGEMENT/TREATMENT/SUPPORT IN CHILDREN VERSUS ADULTS (MEDICAL AND PSYCHOSOCIAL)

A busy general pediatrician cares for about 1500 patients,⁷⁸ and 10 to 15 have or will develop Tourette's disorder (TD), given current epidemiologic estimates. Clinicians who care for children with special needs will encounter a higher proportion of children with TD.⁷⁹ Currently, many or most of these children go undiagnosed; long-term consequences of failed or delayed identification may vary from negligible to potentially devastating psychosocial, academic, vocational, and health-related outcomes. Preventive strategies and anticipatory guidance may help obviate later challenges to "undoing" maladaptive self-concepts and/or underachievement and may facilitate the development of strategies in compensation, self-advocacy, and temperance.

Early Identification of TD

Delays in diagnosis of TD persist; a recent Danish study reported the median delay between presenting symptom (i.e., tic or a comorbid symptom) and TD diagnosis to be >5 years, and between tic onset and TD diagnosis nearly 3 years.⁸⁰ Although US data are not available, Denmark child neurologists rather than pediatricians are most apt to make this diagnosis; similar patterns are likely in the US as general pediatricians may be unsure in making the diagnosis and/or poorly informed about TD, and often find themselves challenged for time or support in conducting routine developmental surveillance and screening, even of higher-risk children. With the difficulty in access to subspecialist care, skilled primary care diagnosis offers a reasonable approach to timely diagnosis and early intervention.

At the same time, care must be taken to provide appropriate and ongoing education to families as needed; labels including "Tourette syndrome" can frighten or be stigmatizing to children and families who anticipate the gamut of socially devastating symptoms. For adults, real consequences of a TD diagnosis can include denial to insurance policies, regardless of clinical status.

It is important to expect a high frequency of psychiatric comorbid disorders in clinically referred youth, as only a minority of patients with TD will have no other psychiatric conditions, often overlooked and predating tic onset.⁸¹ Routine screening for comorbid conditions in children and adolescents with TD, as well as those at increased risk to developing TD (e.g., family history of tics, TD or obsessive-compulsive disorder [OCD], or child's comorbid disorder) should be a central tenet of comprehensive diagnostic evaluation and preparation for an optimal outcome. These conditions include attention-deficit hyperactivity disorder (ADHD), obsessions and compulsive behaviors/OCD, anxiety or depression, substance use or abuse, academic or employment problems, difficulties with sleep, family conflicts, or interpersonal challenges, among others. As up to 1

in 5 school-age children will meet criteria for a transient tic disorder,⁷⁹ caution should be taken not to overdiagnose or raise unnecessary alarm, but monitoring and appropriate screening are indicated.

Enhancing Quality of Life

Although broadly interpreted, QOL as a process and endpoint should be a primary focus in management and support of children identified with TD. Importantly, the development of a TD-specific QOL scale in a mostly adult TD sample found health-related QOL perceptions affected mainly by psychological and cognitive problems.⁸² Emphasis on adaptive development that promotes and cultivates natural strengths and interests and explores the ethics, values, resources, and interpersonal dynamics of the child's family are key management strategies. It is important for the clinician to develop an in-depth understanding of both parent and child perspectives; these have been shown in other chronic conditions to differ from each other and from those of managing pediatricians.⁸³ Parent perspectives about functional impairment⁸⁴ and QOL will often appropriately focus on behaviors other than tics, including learning difficulty, ADHD or explosive outbursts,⁸⁵ and QOL may be more positively impacted by effective management of externalizing behaviors than tics.⁷³

Parenting

Parenting awareness and understanding of the child's subjective experience are of central importance, as the family environment can serve as both protective and exacerbating influences. As family-based stress is associated with social and emotional adjustment in children with TD⁷⁴ and may be exacerbated in families of children affected with ADHD or multiple coexisting conditions,²¹ monitoring, and guidance of family functioning may facilitate more favorable developmental outcomes. Parents may be unnerved by a child's disruptive behavior or tics or show impatient or inconsistent parenting. Although sources of explosive outbursts are not well understood, it is conceivable that parents can inadvertently reinforce undesirable behavior through increased attention or acquiescence. As TD is highly heritable, parents of children with TD are often further challenged by their own symptoms or disorders. Parenting styles that are accepting and autonomy promoting rather than rejecting or controlling, building the child's locus of control, are protective against anxiety and depression in children with TD.⁸⁶ Investigators have reported that internal locus of control serves as a mediator between symptom severity and well-being in both children and adults; indeed, adults with TD report that personal acceptance is their most useful strategy in coping with TD.⁷⁵ Thus, education of parents and facilitation in the development of appropriate parenting skills are essential.

Tic Management and Treatment

Because the natural history of TD is of fluctuations with eventual diminution by adolescence for most children, treatment may not be necessary at all. It is often sufficient

to provide active monitoring, support, and facilitation of access to educational resources for children, their families, teachers, and peers. The national Tourette Syndrome Association⁸⁷ has developed resources to build awareness and develop skills in self-advocacy. Among adults, preventive disclosure of TD may reduce social rejection and stigma⁸⁸; this strategy may also prove beneficial to youth.

It is important to keep in mind that while >90% of adults with TD are aware of premonitory urges or sensations, far fewer children and adolescents are aware,⁸⁹ and the urges usually diminish in intensity or frequency in adolescence and adulthood. Behavioral strategies that depend on awareness of premonitory urge may not be available to young children or developmentally challenged youth. The experimental behavioral tic intervention habit reversal training may produce improved life satisfaction and psychosocial function in adults⁹⁰; a multicenter trial in children is completed and an adult trial is under way. Simplified habit reversal training is cost effective and has recently been manualized⁹¹; it can be taught to children and adults in approximately eight 1-hour sessions or fewer.⁹² Exposure and response prevention may be a useful adjunct to habit reversal training in adolescents and adults who have comorbid OCD; exposure and response prevention may also be useful in secondary reduction of tic severity.¹⁹

Medication is an effective treatment for TD but should not be considered as necessary for every patient with tic symptoms; supportive measures, education, and active monitoring may be sufficient for patients with mild tics. Pharmacological treatment of tics is recommended if the tics are causing significant distress or functional impairment to the child. Results of medication treatments are highly variable, and adverse effects can be problematic and must be weighed against potential for effectiveness. Most adverse effects of the medications used to treat tics, such as fatigue, headaches, stomachaches, and dizziness are mild and tend to improve over time. Motor effects, such as dyskinesias, are less common but do occur with the use of neuroleptics, particularly the conventional (typical) agents.⁹³ Tardive dyskinesia, a later onset and permanent movement disorder,⁹⁴ is more likely to occur in adults than youth but has only rarely been reported among patients treated for TD. Review of most likely and less common adverse effects and drug-drug interactions is always indicated at the beginning of treatment, so that parents and adult patients can make informed decisions about the use of medications.⁹⁵ It is sometimes challenging, even for experienced physicians, to accurately assess medication effects, and improvements or exacerbations may be inaccurately attributed to medication when the symptoms are more likely due to the natural history of fluctuations in tics over time.

No medication that is used to treat tics has been developed specifically for this purpose. Rather, their tic-reducing effects have been secondarily discovered and therefore published information and trials for TD are limited, particularly for children. A detailed discussion of medication selection and management is beyond the scope of this

article. (For more detailed discussions of medication management of tics, see Refs. 96 and 97). The following medication options represent standard of care (Table 1).⁹⁸

Alpha-adrenergic agonists (clonidine and guanfacine) show modest efficacy in reducing tics in about one third of patients. In addition, these agents may be useful in

Table 1. Medications Used in the Treatment of Tics

Medication	Usual starting dose	Usual daily treatment dose	Comments
Alpha-adrenergic agonists			
Clonidine	0.025 to 0.05 mg (in divided doses b.i.d. to t.i.d.)	0.1 to 0.3 mg	First non-neuroleptic used for tic suppression. Not consistently as effective as neuroleptics. Also helpful for ADHD
Clonidine transdermal	0.1 mg/day	0.1 mg/day to 0.3 mg/day	Same as clonidine tablets, localized skin rash
Guanfacine	0.25 to 0.5 mg (in divided doses b.i.d.)	1 to 3 mg	Longer acting and perhaps less sedating than clonidine. May be a good first choice for tic suppression in children with ADHD
Neuroleptics (typical)			
Haloperidol	0.25 to 0.5 mg	1 to 5 mg	The standard treatment for many years for tics. Generally not recommended as first line medication for tic suppression due to side effects
Pimozide	0.5 to 1 mg	1 to 6 mg	Risk for drug interactions and cardiac side effects make this a second choice for tic suppression
Fluphenazine	0.5 to 1 mg	1.5 to 10 mg	Similar to haloperidol, but may have milder side effect profile. A good alternative first choice typical neuroleptic for tic suppression
Neuroleptics (atypical)			
Risperidone	0.125 to 0.5 mg	1 to 3 mg	Generally the recommended first-line atypical neuroleptic for tic suppression. May have less risk for motor side effects than haloperidol and fluphenazine. May also benefit impulse control and aggression. Weight gain can be a significant problem
Ziprasidone	20 mg	20 to 100 mg	Atypical neuroleptic with less associated weight gain but may be sedating
Olanzapine	2.5 to 5 mg	5 to 20 mg	Not well studied in TD; registered weight gain is greater than for risperidone. Risk for diabetes and metabolic changes
Aripiprazole	1 to 2.5 mg	5 to 20 mg	Unique mechanism of action. Appears promising as a tic suppressing medication. Dosing not well established. Less often associated with weight gain
Tetrabenazine	25 mg	37.5 to 150 mg	Recently available in the United States
Benzodiazepines			
Clonazepam	0.025 to 0.5 mg	0.5 to 6 mg	Some potential for developing tolerance. Slow tapering is required for discontinuation

Adapted from Guide to the Diagnosis and Treatment of Tourette Syndrome—Tourette Syndrome Association Medical Advisory Board, 2008. TTS, Transdermal Therapeutic System; TD, Tourette's Disorder.

treating comorbid symptoms of ADHD such as hyperactivity and impulsivity and can also facilitate sleep initiation. Their side effect profiles, including sedation and irritability, are milder than for neuroleptics and for these reasons are reasonable initial agents in treating TD.

Neuroleptics, both typical and atypical, are the most effective agents in tic reduction, presumed largely due to impact on systems of dopamine neurotransmission. The only formally approved medications labeled for treatment of TD are haloperidol and pimozide, both typical neuroleptics. Use of these older “typical” agents has generally given way to use of newer “atypical” agents. The shift to preferential selection of atypical neuroleptics is due to their presumed lower risk for tardive dyskinesia and restlessness than for the typical agents, as well as their additional impact on serotonin systems, of potential benefit in treating some comorbid disorders. Their common side-effect profiles include increased appetite, excessive weight gain, insulin resistance, and hyperprolactinemia. Among atypical agents, risperidone shows greatest evidence for efficacy, but recent trials suggest that aripiprazole may be promising. Because none of the atypical agents has been FDA-approved for treating TD, their use is “off-label.”

Other agents with less available evidence in tic treatment may also be considered as second- or third-line agents and may be selected in considering side effects, medical conditions, or concurrent treatment of comorbid conditions. Effective reduction of anxiety with benzodiazepines or with selective serotonin reuptake inhibitors may secondarily reduce tics. Other classes of agents with variable reported effect include nicotine as a transdermal patch or chewing gum, muscle relaxants (Baclofen), and antiepileptic agents (topiramate and levetiracetam). Botulinum toxin injection into select muscle groups may be used when tics are self-injuring or quite severe.

Deep brain stimulation is a highly experimental surgical procedure for TD that shows some promise among adults with severe and recalcitrant tics. Standards in methods and brain targets have not been established, but case reports and small series suggest potential benefit for motor tics and some comorbid conditions,³³ though less so for phonic tics or non-tic behavioral symptoms.⁹⁹

TD has recently been qualified within the individuals with disabilities education improvement act under “other health impaired,” and pediatricians can assist families and schools by planning for transitions between grade levels, schools, and developmental levels using medical home transition resources.¹⁰⁰ Teachers can assist in transitions by sharing their experiences of effective strategies, and such communications can be applied toward higher education settings or employment.

Comorbid Psychiatric Conditions

Comorbid disruptive behavioral, anxiety, and mood disorders can make coping with tics more difficult for children and adults with TD regardless of tic severity⁵; thus, comprehensive screening and assessment of these disor-

ders are essential. Treatment of the psychiatric comorbid disorders is essential if symptoms are causing significant distress or impairment to the child. Some prioritization in the initial assessment of which symptoms or disorders are causing the most distress or impairment to the child is necessary. It is important to remember that as tics wane in children, for adolescents and adults, the presence and influence of the comorbid conditions may increase. Families and pediatricians should anticipate this trend and monitor for these changes by communicating routinely regarding social, behavioral, health, and academic progress.

OCD often poses particular challenges to function and QOL in both youth and adults with TD. If symptoms are causing significant distress or impairment, OCD/obsessions and compulsive behaviors should be targeted for treatment. First-line therapy includes cognitive behavioral treatment such as exposure and response prevention and may include the addition of selective serotonin reuptake inhibitors if symptoms are in the moderate to severe range. Treatment of tics can follow stabilization of the OCD symptoms.⁴⁰ Family members must be part of OCD treatment to avoid enabling of the patient’s rituals. Tic-related OCD symptoms may be unresponsive to medications ordinarily effective in treatment of non-tic OCD; augmentation and other medication strategies can be helpful.⁴⁰

Special mention must be made of treatment of comorbid ADHD, which usually entails the use of psychostimulant medication. Although the Physicians’ Desk Reference (2009) lists tics or TD as a contraindication to use of methylphenidate preparations and as a precaution regarding the use of amphetamine preparations, in fact most children and adults with TD tolerate these medications well. There has been no scientific evidence, at least in group data, that tics are significantly induced or increased by the use of stimulants in youth with ADHD and tics.^{23,101,102} Long-term outcomes of untreated ADHD suggest youth are at increased risk for substance abuse, antisocial personality disorder, divorce, and other psychiatric disorders in adulthood.¹⁰³⁻¹⁰⁵ If a stimulant is indicated, starting with a low dose of a methylphenidate-based preparation with a slow titration upward generally mitigates the likelihood of significant increase in tics.

Children with comorbid ADHD appear particularly vulnerable to multiple sleep-related disturbances¹⁰⁶ and may be apt to continue having related difficulties into adulthood. TD-specific sleep intervention outcomes have not been closely investigated, but it is reasonable to recommend good “sleep hygiene” as a lifestyle and to consult a sleep specialist when indicated.

Abuse

Parenting children with TD can be very stressful,¹⁰⁷ and these parents themselves are at greater risk for their own dysregulated behaviors.¹⁰⁸ Children with disabilities are, in general, particularly vulnerable to abuse,¹⁰⁹ but those with TD have not been specifically methodically studied. Some adult personality disorders are asso-

ciated with abuse victimization during childhood,¹¹⁰ although causality should not be assumed. Physicians underidentify and underreport child abuse¹¹¹ and potential adulthood outcomes for all domains of health and well-being are jeopardized. Pediatricians must be mindful of their critical role in screening and management of potential physical, sexual, and emotional abuse.

Substance Use and Abuse

Youth with TD are at increased risk to later develop substance abuse and dependence. Older individuals with TD are also likely susceptible to tobacco use; nicotine may be therapeutic for tics and ADHD symptoms and assist in alertness. Screening and assessment of child and family drug and tobacco use is indicated; education and nonjudgmental support may reduce later risk behaviors.

Relationships, Employment, and Family planning

Adolescents and young adults with TD may require guidance in the facilitation and maintenance of healthy interpersonal relationships, accessing housing and insurance, and information regarding college, military service, and employment. Some may have questions or concerns regarding risks to offspring; although TD is strongly heritable, patterns of genetic transmission are unknown but fertile areas of investigation. The Tourette Syndrome Association, Inc. provides peer and professional opinion and general legal information on a variety of adult-oriented topics.⁸⁷

PREDICTORS/MEDIATORS OF ADULT OUTCOMES

Many adults with Tourette's disorder (TD) are never diagnosed, and perhaps lead lives much the same as unaffected adults. Outcomes data are susceptible to sampling bias, variables in definition of "outcome," and other methodological limitations. No longer do we see tics fully, or even fundamentally, as defining TD outcome; increasingly our evidence base regarding psychiatric comorbidity and symptoms act both as outcomes, as well as predictors and mediators of outcomes. Investigators now explore behaviors, developmental skills, environmental factors, including stress, imaging, and biomarkers, which may provide clues to facilitate the discovery of endophenotypes that are needed to elucidate outcomes and personalized treatment. With this in mind, several useful findings have emerged.

Early childhood tic severity does not reliably predict adulthood tic severity,²² but a positive correlation is found when comparing tic severity in late childhood with adolescence/early adulthood.²⁵ Distinctions regarding individual "resiliency" versus "vulnerability"²⁶ may predict tic outcome more meaningfully than do objective tic severity measures. Still, social perceptions of TD are similarly negative between children and adult observers, and adults view males with tics more negatively than they view females with tics.¹¹² Depression predicts modest increases in tic severity.²¹

Genetic and Environmental Correlates

Transmission of TD or obsessive-compulsive disorder/obsessions and compulsive behaviors to a child with 2 affected parents (i.e., both parents with tics and/or obsessions and compulsive behaviors) is significantly associated with severity of that child's later behavioral dysfunction, particularly obsessions and compulsive behaviors severity and self-injurious behavior, but not tic severity, when compared with TD children who have zero or one affected parent.¹¹³

Maternal smoking during pregnancy may be associated with later tic severity among TD-diagnosed offspring as children and adults, and in their risk for developing comorbid OCD,¹¹⁴ but association should not be confused with causality. Brain imaging methods shed light; sensorimotor cortical thinning among adults, but not children, with persistent tics, maps body regions where tics frequently occur and correlates with adult tic severity, suggesting a possible marker for tic persistence in adulthood.¹¹⁵ In children, caudate volumes inversely predict adulthood tic and obsessions and compulsive behaviors severity.¹¹⁶

Academic and Psychometric Predictors and Mediators of Adult Outcomes

Adult self-reports of TD-related academic difficulties have been found to predict lower job prestige, whereas social and behavioral school problems (which can include mood swings, poor self-regulation, anger, or aggression) predict their perceived impact on job selection.¹¹⁷ A longitudinal study found early social or educational dysfunction correlates with later adult dysfunction in employment, alcohol abuse, or criminal activity, unrelated to tic severity.²⁸ The investigator proposes that early assertive intervention in childhood may mediate a more propitious adult outcome.

In one longitudinal study, high intelligence quotient in children with TD may predict development of OCD in adulthood, on the order of 2.8-fold per 10-point intelligence quotient increase; the risk of developing clinically significant OCD symptoms by early adulthood was 8 times higher in a child with an intelligence quotient of 120 than a child scoring 100. The authors suggest that education of such higher-risk patients and their parents about this possibility may be useful,²⁵ especially as comorbid OCD likely is a more severe and impairing disorder than OCD not associated with TD.¹¹⁸

Fine motor skills deficits in children with TD may predict adult tic severity and poor psychosocial function. This deficit may reflect a neurologic endophenotype, as fine motor coordination is mediated by circuits involving the basal ganglia. Children with fine motor deficits may be discouraged from participation in sports, musical, or other social activities, which would otherwise build self-esteem.³⁶

Summary and Implications for Current Practice

Adult outcomes in TD are highly variable, but these variations depend largely on contemporary and evolving definitions of the disorder. Historical accounts dating as far as 2 millennia ago and encompassing our more recent past highlight the more extraordinary tic and related phenotypes that capture some, but not most, adults with TD. The presence of chronic motor and phonic tics remain central to the diagnosis, but these symptoms often diminish or disappear as youth approach adulthood, whereas comorbid conditions emerge or intensify in expression or functional impairment. Recent and developing epidemiologic, phenomenological, and technological advances are revealing a very diverse outcome landscape. Emphases in early identification, prevention and intervention, anticipatory guidance, and psychosocial family-centered support persist as core medical home tenets in serving children, youth, and adults with TD.

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