THE COURSE AND CLINICAL FEATURES OF OBSESSIVE-COMPULSIVE DISORDER

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Twenty years have passed since the landmark National Epidemiology Catchment Area Survey first demonstrated the prevalence of obsessive-compulsive disorder (OCD) in the general population to be 50 to 100 times greater than had been previously believed (1). This unexpected finding was instrumental in the renewed interest in and rapid growth of our understanding of the clinical features, pathophysiology, and treatment of OCD. Epidemiologic studies in different cultures have confirmed the findings that up to 1% to 2% of the general population worldwide suffer from the disorder at any given time (2). Widespread attention in the media, in addition to growing recognition of the disorder among health care professionals, has resulted in improvements in the diagnosis and treatment of large numbers of patients with OCD who would not even have presented for treatment before 1980.

Knowledge of the clinical features of the disorder has also expanded significantly in the last 10 years. Treatment centers specializing in OCD have succeeded in enrolling large cohorts of patients, so that a more sophisticated analysis of the heterogeneity and comorbidity of OCD and the relationship of these variables to treatment outcome has been possible. Prospective observational studies of the longitudinal course of OCD have contributed further insights into the clinical characteristics and prognosis of the illness (3). Improvements in methodology, including the development of structured interviews with proven reliability and validity, the application of survival analysis and other statistical techniques to assess longitudinal variables, and more sophisticated database management systems, have been instrumental in these advances.

Epidemiologic studies have consistently shown that 2% to 3% of the general population in the United States meet lifetime DSM criteria for OCD (4). In a World Health Organization study that determined the leading causes of mortality and morbidity in developed countries, OCD was found to be the eighth leading cause of disability for any medical or psychiatric condition for ages 15 through 44 (5). Total costs of the disorder in the United States have been estimated at $8 billion in 1990, including $2.1 billion in direct costs and $5.9 billion in indirect costs related to lost productivity (6).

However, despite the increased recognition of the public health significance of OCD during the last decade, surprisingly little is known about the long-term course and prognosis of the disorder. Most studies conducted thus far suggest that OCD is chronic and lifelong. For several reasons, however, questions have been raised about the validity of these findings. Previous studies have been hampered by a number of methodologic limitations, including a lack of standardized assessments, small numbers of subjects, and a sample bias toward more severely ill patients. The introduction of effective treatments for OCD in the last 10 years also raises the question of the relevance of course studies conducted in a pretreatment era.

Obsessive-compulsive disorder spans the life cycle. It has been described in children as young as age 2 (7) and also in the very elderly (8). Evidence supports the hypothesis that OCD is a heterogeneous disorder with multiple causes (9). Neurobiologic studies have demonstrated abnormalities in frontostriatal–basal ganglia circuitry (10). Like any organ system, these neural circuits are susceptible to a variety of pathologic processes, including those associated with autoimmune, infectious, developmental/genetic, and aging processes. Identifying homogeneous subgroups of patients with OCD should help in unraveling its neurobiologic pathogenesis and developing more specific and effective treatment strategies.

This chapter reviews data related to the clinical features

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and course of OCD during the lifespan. It focuses on the heterogeneity and comorbidity of the disorder in relation to its course, and points to a new wave of studies that should complement neurobiologic and genetic studies of the pathogenesis of OCD, lead to fuller recognition of its impact on society, and help to measure the effectiveness of behavioral and pharmacologic treatment strategies that have been developed during the past two decades.

SUBTHRESHOLD SYMPTOMS

It is generally agreed that it is the frequency of obsessions and compulsions, in addition to the degree with which they interfere with function, that distinguishes normal from abnormal. A patient must have had an hour of obsessive-compulsive symptoms daily for a period of 6 months that interfere with social or occupational function to meet DSM-IV criteria for the disorder (11). This requirement has traditionally been thought to translate to a score of 16 or higher on the Yale–Brown Obsessive-Compulsive Scale (Y-BOCS). Like symptoms of anxiety, obsessive-compulsive symptoms are present to some degree in most people. Rachman and Hodgson (12) found that a high percentage of the normal population report some obsessions and compulsions. Similarly, after screening 861 Israeli military recruits at 16 years of age, Apter et al. (13) concluded that obsessive-compulsive phenomena appear on a continuum, with few symptoms and minimal severity at one end and many symptoms and severe impairment on the other. The receiver operating characteristics that would best distinguish the clinical from the subthreshold syndrome of OCD have yet to be delineated. Using Angst's longitudinal follow-up sample, Degonda et al. (14) found a weighted lifetime prevalence for subthreshold obsessive-compulsive symptoms at age 30 of 5.5%. Goodman (15) screened 958 college students and identified 23 subjects with subclinical OCD. At follow-up 1 year later, 87% continued to have significant symptoms. It has been recognized for many years that most normal children go through developmental stages characterized by obsessive-compulsive or superstitious behavior (16). Determining where the clinical syndrome begins and ends is important for pharmacologic and genetic studies. For example, the multicenter collaborative studies of the selective serotonin reuptake inhibitors (SSRIs) in OCD noted a higher rate of response to placebo in patients with Y-BOCS scores between 16 and 20, a finding that prompting some investigators to suggest that patients with Y-BOCS scores below 20 be excluded from controlled trials (17). Family genetic studies have shown a higher risk for both subthreshold and clinical OCD in OCD probands (18).

Most adult patients who meet DSM criteria for OCD remember subthreshold symptoms in childhood. The clinical significance of subthreshold symptoms in childhood continues to be poorly understood. The risk carried by children of parents with OCD for subsequent development of the disorder is poorly defined. No data are available that would make it possible to predict this transition. Similarly, almost no data are available relating the effect of continuing subthreshold symptoms during a period of remission to the likelihood of relapse in adults. Prospective quantitative longitudinal assessment of probands with subthreshold symptoms is needed in child and adult populations.

DEVELOPMENTAL PSYCHOPATHOLOGY

Little systematic study of the developmental antecedents of OCD has been carried out since Janet. In his *Obsessions and Psychasthenia,* Janet (19) postulated that obsessions and compulsions are the most severe stage of an underlying prodromal state that he called *psychasthenia,* a syndrome characterized by feelings of incompleteness and imperfection. He hypothesized that all patients in whom obsessions and compulsions develop pass through a prodromal stage of psychasthenia. His clinical descriptions of the temperamental features of psychasthenics coincide remarkably well with our preliminary findings of the prodromal symptoms of patients with OCD. His description of the patient who "finds on the stairway the word that needed to be said in the parlor" is an astute clinical description and close analogue of the independent variable chosen by Kagan et al. (20) to measure behavioral inhibition (i.e., speech latency in a novel social situation). It is worth noting that Janet included three of the five elements of DSM-III compulsive personality disorder in his description of the psychasthenic state: perfectionism, restricted emotional expression, and indecisiveness. Previous studies have shown that a considerable portion if not the majority of patients with OCD do not meet the DSM-III-R criteria for compulsive personality disorder. The European diagnostic schema for anacastic personality is more directly related to Janet's original definition of psychasthenia and is consistent with the idea of an obsessive spectrum that ranges from normal obsessional behavior through obsessional personality to OCD.

A retrospective study of 90 of our OC probands in which a semistructured format was used was designed to elicit prodromal personality traits or temperamental factors commonly found in OCD (22). During this study, we identified 10 factors commonly found in our adult OC probands as children (Table 111.1). These traits tended to vary minimally during the childhood and adolescent years.

The developmental antecedents of OCD overlap significantly with the behavioral inhibition syndrome in children that Kagan et al. (20) described. Four of the developmental traits appear to be shared by patients with OCD and those with other major anxiety disorders: separation anxiety, resistance to change or novelty, risk aversion, and submissiveness. Four of the traits are more specific to OCD: perfectionism, ambivalence, excess devotion to work, and

TABLE 111.1. BEHAVIORAL INHIBITION

Separation anxiety
Resistance to change or novelty
Risk aversion
Submissiveness (compliance)
Sensitivity
Anacastic
Perfectionism
Hypermorality
Ambivalence
Excess devotion to work

excessive morality. The overlap of the developmental antecedents of panic disorder, social phobia, and OCD is consistent with Janet's original conception of the psychasthenic syndrome and adds credibility to the hypothesis that an element of genetic vulnerability is shared among the anxiety disorders. The relationship of adult personality characteristics and clinical subtypes to developmental antecedents awaits further analysis. It appears that some traits are more commonly seen in particular phenomenologic presentations (e.g., incompleteness in perfectionism and the need for symmetry and precision; abnormal risk assessment in high levels of anxiety). It is probable that temperamental factors such as behavioral inhibition increase the risk for the development of a number of psychiatric syndromes. It would be informative to determine the relative risk for development of each of the major anxiety syndromes by following a group of children with behavioral inhibition longitudinally. The environmental and genetic factors that predispose a given individual to the development of a specific anxiety disorder are unknown. It is also worth noting that a significant minority of patients with OCD do not manifest risk-aversive tendencies as children. Further prospective study of the developmental antecedents of OCD and prospective longitudinal evaluation of children at risk should be an important area for future research.

AGE AT ONSET

In most studies of the course of illness, *age at onset* refers to the time that symptoms become severe enough that they meet full DSM criteria for the disorder. The reliability of retrospective recall is an inescapable problem. It is safe to assume that reliability decreases as the years between ascertainment and onset increase. In the Brown cohort drawn from an adult OCD clinic, the mean age at onset of significant OCD symptoms was 20.9 ± 9.6 years, with males having a significantly earlier onset of illness, 19.5 ± 9.2 years, than females, 22.0 ± 9.8 years ($p < .003$) (212). The illness developed before the age of 25 years in 65% of cases, sometimes as early as 2 years. It developed after age 35

Brown OC Study

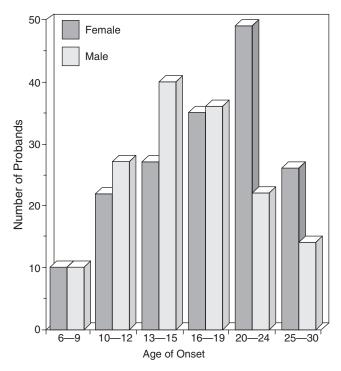Age of onset in Obsessive Compulsive Disorder

FIGURE 111.1. Age at onset in obsessive-compulsive disorder in the Brown study. (From Jenike MA, Baer L, Minichiello WE. An overview of obsessive-compulsive disorder. In: Jenike MA, Baer L, Minichiello WE, eds. *Obsessive-compulsive disorders practical management,* third ed. St. Louis: Mosby, 1998;3–11, with permission.)

in fewer than 15% of obsessional patients (Fig. 111.1). A significant increase in incidence appeared at puberty. Most adult patients remembered having minor obsessive-compulsive symptoms that did not significantly interfere with their ability to function and that did not cause significant distress before the onset of symptoms meeting DSM-III-R criteria for the disorder. Although male patients noticed minor symptoms earlier than female patients, the difference did not reach statistical significance. Most of the patients described a gradual or insidious onset of illness. Emerging data suggest that a considerable percentage of patients with an early, prepubertal onset have an acute attack followed by an episodic course (22). These patients frequently suffer at the same time from multiple tics and other movement disorders, including choreiform movements and behavioral dysregulation. Swedo et al. (23) systematically characterized 50 children with this cluster of symptoms, which they call *pediatric autoimmune neuropsychiatric disorder* (PANDAS). A diagnosis of PANDAS is made if the following criteria are met: (a) the presence of OCD, a tic disorder, or both; (b) prepubertal onset of symptoms; (c) episodic course with

varying symptom severity; (d) dramatic exacerbation of symptoms following a group A β-hemolytic streptococcal infection; and (e) association with neurologic abnormalities. In these children, the average age at onset was 6.3 years for tics and 7.4 years for obsessive-compulsive symptoms. The longitudinal course of children with PANDAS and how they differ from patients in whom OCD develops but who do not meet the criteria for PANDAS is unclear.

NATURAL HISTORY AND COURSE OF ILLNESS

DSM-IV describes the course of OCD as typically chronic with some fluctuation in the severity of symptoms over time. The numerous retrospective and prospective follow-up studies of patients with OCD support this description. However, many of the earlier phenomenologic and follow-up studies of OCD suffered from a number of methodologic limitations, including the following: retrospective study design, small sample size, lack of standardized criteria to determine diagnosis, hospital-based samples not representative of the spectrum of the disorder found in the general population, biases in inclusion and exclusion criteria, chart review rather than personal interview, absence of structured interviews, and lack of consensus regarding the definition of relapse, remission, and recovery. Because of these flaws in design, the earlier studies of OCD may have included subjects who would not meet today's criteria for the diagnosis. In particular, clear distinctions between OCD and compulsive personality disorder were often not made, and obsessions and compulsions occurring in the context of other disorders (e.g., psychosis, eating disorders) may have been included as OCD.

Despite these methodologic shortcomings, several more recent prospective follow-up studies, in which a prospective design, standardized criteria to assess diagnosis, and structured interviews with direct patient contact were used, have also shown that most patients continue to meet either all or some of the criteria for the disorder at follow-up. Relatively few patients experience complete remission. Retrospective and prospective follow-up studies of the course are reviewed in detail below.

Retrospective Follow-up Studies

In retrospective studies, fluctuations in the severity of psychiatric symptoms and impact on functioning over time are ascertained primarily on the basis of subjects' recall. Results of these studies are summarized in Table 111.2. In most of them, patients were selected based on chart review and were subsequently assessed at the time of the study, either in person or through questionnaire. In the earliest longitudinal study of OCD, a relatively good outcome was observed by Lewis (24), who followed 50 patients with OCD (most of whom received some psychotherapy) at least 5 years after initial assessment; 37% were "quite well," 14% were "much improved," but 46% were minimally improved, unchanged, or worse. Only 10% had had an episodic course marked by later recurrence after remission. Pollitt (25) followed 67

TABLE 111.2. RESTROSPECTIVE FOLLOW-UP STUDIES OF OBSESSIVE-COMPULSIVE DISORDER

Study (Ref.)	No. Patients	Mean Years of Follow-up	Well (%)	Minimally Improved, Unchanged or Much Improved (%)	Worse (%)	Comments
Lewis, 1936 (24)	50	>5	32	14	44	Episodic course in 10%
Pollitt, 1957 (25)	67	3.4	24	36	37	Mostly outpatients
Ingram, 1961 (26)	29	5.9	7	21[a]	72	Inpatients
Kringlen, 1965 (27)	80	13–20	0	24	76	Inpatients
Grimshaw, 1965	100	5	40	24	35	Inpatients
Coryell, 1981 (31)	44	.5+	8	20	8	Inpatients
Thomsen, 1993 (36)	47	6–22	28	26	46	Childhood OCD
Lo, 1967 (28)	88	3.9	23	50	27	Inpatients and outpatients diagnostic heterogeneity

[a]One patient not leucotomized; five patients leucotomized.
OCD, obsessive-compulsive disorder.

nonleucotomized patients for a mean of 3.4 years; 24% were symptom-free (similar to the results with psychotherapy), 36% had mild symptoms and were functioning well, and 12% were improved but with impaired functioning. Only 25% had symptoms that were unchanged or more severe than at baseline. This study was somewhat unusual because most of the patients were selected from an outpatient practice. The results of this study illustrate how outcome is influenced by the baseline severity of the obsessive-compulsive symptoms of the cohort selected. A longer duration of illness at initial evaluation was associated a with poorer outcome with respect to severity of symptoms at follow-up, as might be expected. Duration of illness was also a predictor of course of illness in a study of 29 inpatients with obsessional symptoms followed for 6 years by Ingram (26). In this study, 72% were minimally improved but functioning poorly, unchanged, or worse, and 21% of the patients were much improved. One conclusion that can be drawn is that chronicity at entry appears to predict chronicity at follow-up.

In a study characterized by a long follow-up period, Kringlen (27) found that at 13 to 20 years after initial contact, 42% of patients were unimproved or had worsened symptoms, only 24% were much improved, and 34% described slight improvement in OC symptoms. The patients included in this study were all hospitalized for their first contact, which may contribute to the poorer outcome in this study.

Lo (28) interviewed 88 patients in whom OCD had been diagnosed with a mean follow-up of 3.9 years and found that 23% were symptom-free and 50% had symptoms that were much improved. More than half the patients had distinct obsessions and compulsions. However, 10% had prominent affective symptoms, and 31% were described as having "phobic and ruminative symptoms," with minimal compulsions. Therefore, some of the patients described as being in remission at follow-up may have had major depression with obsessional or ruminative thinking during their index episode. In reviewing these early follow-up studies, Goodwin et al. (29) concluded that the course of OCD is usually chronic, but variable, with fluctuations in the severity of symptoms.

In follow-up studies conducted since 1980, the course of illness has been evaluated according to criteria different from those used in the earlier studies described above. Patients have been retrospectively assigned to categories of "continuous," "waxing and waning," "deteriorative," and "episodic with full remissions between episodes." Rasmussen and Tsuang (30) conducted a study in 1986 in which patients were selected based on current enrollment in an outpatient OCD clinic. The course of OCD was described by most patients as chronic or "continuous" (84% of 44 patients); six subjects (14%) had a deteriorating course, and only one (2%) had an episodic course. The average duration of illness at the time of assessment was more than 15 years,

which again suggests that the chronicity of the disorder may have been influenced by the sample. Because these subjects were acquired through the process of clinic referral and prospective follow-up was not conducted, no former OCD patients who had already recovered and remained well were included.

Coryell (31) observed some improvement at follow-up in 55.6% of a hospitalized cohort of patients with OCD. However, this cohort was significantly less likely to experience remission after discharge (22%) than the comparison cohort of depressed patients (64%).

Synthesizing methodologically varied studies, some of which present an optimistic picture, others a pessimistic one, may require more careful examination of reported outcomes. It is particularly important to separate the best possible outcome ("full remission" or "symptom-free") from what is described as "much improved" or "improved," which may indicate persistent symptoms in the abatement phase of a chronic illness that waxes and wanes. The episodic pattern of full remission (and sometimes later occurrence), when it is clearly identified as such, appears to occur in about 10% to 15% of patients with OCD, although this proportion may increase somewhat as follow-up is extended for several years and may also be greater in childhood OCD (12), in which improvement can be rapid even without treatment (32). In most studies, a smaller proportion of patients (6% to 14%) seem to follow a deteriorating course. Most follow a course marked by chronicity, with some fluctuation of symptoms over time but without clear remissions or deterioration.

Prospective Longitudinal Studies of Course

During the past decade, several prospective longitudinal studies of the course of OCD have been carried out; these are summarized in Table 111.3. Although studies of adults have supported the hypothesis that OCD is a chronic, lifelong disorder, child and adolescent studies have found a surprisingly high percentage of patients with an episodic course. Flament et al. (33) completed a 2-year follow-up study of 59 adolescents in whom OCD, subclinical OCD, or compulsive personality disorder had been identified in an epidemiologic study of high school students, most of whom had not sought clinical treatment. Of 12 patients who had met the criteria at baseline for OCD, only five still met the full criteria at follow-up. Four patients with subclinical manifestations of OCD at baseline did meet the full criteria for OCD at follow-up. In another 5-year prospective follow-up study, of an OC adolescent cohort seeking treatment at a tertiary clinic, Flament et al. (34) concluded that patterns of course are not easily predicted from baseline variables (34). Some patients with subthreshold symptoms at baseline were severely ill at follow-up, whereas others classified at baseline as severely ill no longer had

TABLE 111.3. PROSPECTIVE FOLLOW-UP STUDIES OF OBSESSIVE-COMPULSIVE DISORDER

Study (Ref.)	Treatments	No. Patients	Mean Follow-up (ys)	Remained in Episode (%)	Partial Remission (%)	Full Remission (%)	Comment
Children and adolescents							
Berg et al., 1989 (37)		12	2	42	17[a]	8	17% had compulsive personality traits
Leonard et al., 1993 (43)	SSRIs, BT, psychotherapy, family therapy	54	3.4	43	46	11[b]	70% on medication at follow-up
Adults							
Orloff et al., 1994 (44)	SSRIs, BT	85	2.1			33	
Eisen et al., 1995	SSRIs, BT	51	2	57	31	12	
Stekette et al., 1996	SSRIs, BT	107	0.5–5	47	31	22	mainly outpatients

[a] Subjects had subclinical OCD at follow-up (i.e., obsessions compulsions were present but not at full criteria).
[b] Three of the six subjects in remission (i.e., symptom-free) were receiving medication.
BT, behavioral therapy; OCD, obsessive-compulsive disorder; SSRIs, selective serotonin reuptake inhibitors; Y-BOCS, Yale–Brown Obsessive-Compulsive Scale.

clinical levels of symptomatology at follow-up. This finding was substantiated in a recent study by Valleni-Basile et al. (35). When they screened a community sample of 3,283 adolescents with a self-report instrument followed by the Schedule for Affective Disorders and Schizophrenia (SADS), they found 1-year incidence rates of OCD and subthreshold OCD of 0.7% and 8.4%, respectively. Interestingly, transition probabilities demonstrated a pattern of moving from more severe to less severe categories in subsequent years. Of the patients with OCD at baseline, 17% had OCD at follow-up. Only 1.5% of those with subclinical OCD had progressed to OCD that met syndromal criteria. In contrast, in a Danish follow-up study of 23 adolescents presenting with OCD to a community clinic, half of the subjects retained an OCD diagnosis at follow-up. One-third of the subjects had had an episodic course, and two-thirds had had a chronic course (36). Berg et al. (37) reported a 2-year follow-up of 59 high school students with DSM criteria for OCD who were identified as part of an epidemiologic survey. Most of the subjects had never sought treatment. The course of illness was much more variable than had originally been predicted. Some patients with subthreshold symptoms at baseline were severely ill at follow-up, whereas others classified as severely ill at baseline no longer had clinical levels of symptomatology at follow-up. Although these studies have given us our first prospective glimpse of the early course of OCD, they also suffer from significant methodologic limitations. Follow-up was at a single point, an average of 4.8 years from baseline. Interim data about remissions and relapses during the study period were not obtained. However, the evidence suggests that the course of illness may be much more variable and episodic in child and adolescent samples than was previously believed.

In a three-site prospective longitudinal study of adult patients with OCD conducted by Eisen et al. (38), data were collected on the course of illness in 78 subjects for 2 years. Two instruments with proven reliability and validity were used to evaluate severity of symptoms: the Y-BOCS (39) and the Psychiatric Rating Scale for OCD (PSR-OC) (40). On the PSR-OC, scores ranged from 6 for patients who were severely symptomatic and unable to function at work or socially to 0 for patients who had no obsessive-compulsive symptoms and used no avoidance. Follow-up measures were obtained at 3, 6, 12, and 24 months after baseline assessment.

The probability of achieving at least partial remission during the 2-year study period was 47%. However, if more stringent criteria were used to define remission, in which patients had only occasional or no obsessions and compulsions for 8 consecutive weeks (PSR-OC score ≤ 2, which is equivalent to a Y-BOCS score ≤ 8), the probability of achieving remission was only 12%. Once a patient was in remission, the probability of subsequent relapse (defined as returning to a Y-BOCS score ≥ 16 and a PSR-OC score >4 for any length of time) was 48%. Of the 22 patients who achieved partial remission, 10 relapsed and 12 remained in partial remission throughout the study.

In another prospective study, 107 clinic patients with OCD were followed for up to 5 years after intake (41). The probability of full remission for at least a 2-month period was 22% at 5 years, and the probability of partial remission was 53%. Although outcome in this study was assessed with

a 3-point rating scale, the results are comparable with those in the study of Eisen et al. (38), in which a 6-point PSR-OC and the Y-BOCS were used.

Skoog and Skoog (42) recently described a 40-year follow-up study of 144 patients with OCD who were identified as inpatients in the late 1940s and early 1950s. Two-thirds were improved within a decade after the onset of OCD, and most of the patients reported an intermittent course, with at least two remissions during that time period. However, a chronic course was more common in the later follow-up period, and 20% showed either no improvement or a deteriorative course during the 40 years. Although the length of follow-up in this study was remarkable, methodologic flaws limit the conclusions that can be drawn. First, the sample consisted of psychiatric inpatients hospitalized in the 1940s. The baseline severity of obsessive-compulsive symptoms was unclear because of the lack of scales with proven reliability and validity. It seems likely that patients with a primary diagnosis of major depression were included. Finally, the study was conducted before the widespread availability of the SSRIs and behavioral treatments.

In summary, only a handful of prospective studies of the course of illness in OCD are available. A significantly greater degree of episodic illness is seen in child and adolescent samples than in the adult population. A number of methodologic considerations may account for some of these inconsistencies. The earlier retrospective studies were completed before the introduction of standardized diagnostic criteria, standardized ratings of symptom severity, and effective pharmacologic and behavioral treatment strategies. In addition, because until recently patients with OCD were reluctant to seek treatment, patients with more debilitating symptoms may have been overrepresented in these earlier studies, so that the results are biased toward a worse prognosis. In our pilot study, patients were followed who were already enrolled in our clinic, a factor that potentially contributed to the chronic course noted in many of the subjects. A prospective longitudinal study of the course of 400 patients with OCD is currently in progress.

Effect of Treatment on Course of Illness

Effective pharmacologic and behavioral treatments for OCD became available in the late 1980s in the United States. A follow-up study of children with OCD was conducted by Leonard et al. (43) to determine outcome after standardized short-term treatment with clomipramine (a medication known to be effective in OCD). Fifty-four children and adolescents were re-interviewed 2 to 7 years after participation in a controlled trial of clomipramine and a variety of interim interventions. Obsessive-compulsive symptoms were more severe in only 10 of the subjects at reassessment, so that as a whole, the cohort had improved at follow-up. However, only three subjects (6%) were considered to be in true remission (defined as no obsessions or

compulsions and no medication), and 23 subjects (43%) still met full criteria for OCD. Most of the patients were taking medication at follow-up. It is worth noting that the patients who made up this sample were referred to a tertiary research center and were severely ill with a more chronic course than is seen in most childhood samples of OCD.

The results of a 1994 study conducted by Orloff et al. (44) are a greater cause for optimism than those of the studies described above. Most of the 85 subjects assessed 1 to 3 years after baseline evaluations were much improved at follow-up based on chart review. The mean follow-up Y-BOCS score of 9.3 was in the range of mild to minimal obsessions and compulsions that do not interfere with functioning. This improvement in obsessive-compulsive symptoms in comparison with baseline symptomatology was attributed to the current availability of effective behavioral and pharmacologic treatments for OCD (techniques of exposure–response prevention and SSRIs). In fact, 99% of subjects had received at least a 10-week trial of an SSRI and 45% had received some behavior therapy. Most patients were still taking medication at the time of follow-up. Relapses were common in those patients who discontinued medication, which suggests that continued treatment may be required to maintain an improvement in OC symptoms over time.

The effect of treatment on the course of illness in OCD was also evaluated in the prospective study conducted by Eisen et al. (38), described above, in which 77 adults meeting DSM criteria for OCD were followed with frequent interim assessments for more than 2 years. Pharmacologic data gathered included doses of medications and duration of treatment. Patients had to have received a maximum dose of at least one SSRI for a minimum of 12 weeks to be considered to have received adequate pharmacotherapy for OCD. Information obtained on behavior therapy included amount of time spent in sessions, time spent doing homework, whether the patient practiced exposure–response prevention, and imagined homework. Patients were considered to have received adequate behavior therapy if they reported undergoing behavior therapy with a therapist who used exposure–response prevention and if they spent at least 20 hours practicing exposure–response prevention homework assignments. Fifty-five subjects (84% of the total sample) received an adequate trial of at least one SSRI during the study period, and 12 patients (18%) received adequate behavior therapy. The probability of partial remission for those patients who received an adequate trial of at least one SSRI was 51% during the 2-year study period.

The mean Global Assessment of Function (GAF) and Y-BOCS scores at intake and at 2 years were similar for those subjects who received an adequate trial of an SSRI and those who did not receive adequate pharmacotherapy. However, the mean GAF scores at intake of patients who subsequently underwent adequate behavior therapy during the course of the study were lower than the mean GAF

scores of patients who did not undergo behavior therapy. The change in GAF score at 2 years was significantly greater in the group of patients who received behavior therapy, so that these patients in effect "caught up"; their final GAF scores were similar to the scores of the patients who did not undergo behavior therapy.

Although this study was conducted at a time when current behavioral and pharmacotherapies were available, the results again support the findings that for the majority of patients, the course of illness in OCD is continuous with fluctuations in severity rather than episodic with clear periods of remission between periods of exacerbation of symptoms.

QUALITY OF LIFE

No longitudinal follow-up study of OCD has systematically measured psychosocial functioning and quality of life over time. Most treatment outcome studies have primarily focused on symptomatic relief. Also, no attempt has been made to examine the relationship between symptom severity and psychosocial functioning over time. For a significant percentage of OCD patients, impairment in function and quality of life is severe (45). It is the only major psychiatric disorder for which neurosurgery continues to be a treatment option. It will be important in future studies to gather prospective information on levels of psychosocial impairment during periods of remission when subjects no longer meet full criteria for a diagnosis of OCD. In the National Collaborative Study of Depression, even subsyndromal symptoms were associated with significant dysfunction in multiple areas (46). Similarly, preliminary data from Eisen et al. (38) suggest that psychosocial functioning continues to be impaired during partial remission despite symptomatic improvement; for example, after 1 year of follow-up, 29% of subjects in partial remission continued to miss work much of the time or were virtually incapable of carrying out activities at their jobs (38).

PREDICTORS OF LONG-TERM COURSE OF ILLNESS

Although a number of studies have examined predictors of outcome in OCD, the results have been inconsistent. Most have focused on identifying predictors of short-term outcome following pharmacologic or behavioral treatment. None of the existing studies has examined predictors of remission or relapse rates. These studies have been methodologically compromised by small sample size, inclusion or exclusion criteria that led to sample bias, and inadequate duration of follow-up. Characteristics such as age at onset of OCD, duration of illness, severity of illness at baseline, and phenomenologic subtype have not been associated with

outcome in a consistent way. More recently, emerging data have clarified that OCD is a heterogeneous disorder and have begun to point to the existence of discrete subtypes of illness. It will be important to determine whether these "subtypes" influence the likelihood of remission or relapse. The most likely prediction variables are reviewed below.

One subtype of OCD is associated with a family or lifetime history of tic disorders. Although variation between studies is considerable, it is generally accepted that approximately 20% of patients with OCD have a lifetime history of tics, and that 5% to 10% have a lifetime history of Tourette disorder (47,48). Family and genetic studies have demonstrated that OCD patients with a family or lifetime history of multiple tics are more likely to have first-degree family members affected by OCD or Tourette syndrome than are OCD probands without tics (49,50) They are also significantly more likely to have onset of illness at an early age. OCD patients with tics appear to be less likely to respond to SSRIs, and their OCD symptoms respond differentially to augmentation of an SSRI with a neuroleptic (51). Certain OCD symptoms have been shown to develop more commonly in this subgroup, including the need for symmetry, ordering, arranging, and hoarding (52). The presence of a tic disorder predicted more severe symptoms of OCD at follow-up in children (47). The predictive power of a personal or family history of multiple tics in regard to remission and relapse rates should be investigated.

The role of personality disorder in outcome also has not been explored prospectively, although the relationship has been investigated in a number of acute treatment studies with inconsistent findings. In the study of Jenike et al. (53), schizotypy was a negative predictor for outcome after pharmacologic and behavioral treatment. In a study by Baer et al. (54), the presence of any single personality disorder was not related to improvement on any outcome measure in a 12-week placebo-controlled trial of clomipramine in OCD. However, a larger number of personality disorders was consistently related to poorer outcome, as was the presence of a DSM-III cluster, a personality diagnosis. A subsequent single-site study of the effect of a personality disorder on the response to fluoxetine failed to confirm that a cluster A diagnosis is a negative predictor of outcome (55).

The DSM-IV field trial of OCD established that a significant percentage of patients with OCD have poor insight (56). The validity of this new diagnostic category is still in question. Data pertaining to the effect of poor insight or overvalued ideation on behavioral treatment response have been inconsistent (57,58). Eisen and Rasmussen (59) retrospectively assessed the course of illness in four subgroups of OCD: OCD and schizophrenia, OCD and schizotypal personality disorder, OCD with poor insight, and OCD without psychotic features. A deteriorative course was noted in 82% of the patients with coexisting schizophrenia, 69% of those with coexisting schizotypal personality disorder, 17% of those with poor insight, and only 8% of those with-

out psychotic features. This study was hampered by the lack of a valid and reliable scale to measure poor insight and by the retrospective assessment of the course. We have recently published data on the reliability and validity of a new scale, the Brown Assessment of Beliefs Scale (BABS), that has demonstrated excellent sensitivity to change with short-term treatment (60). Eisen et al. (61) assessed change in BABS scores in patients with OCD who participated in the first phase of a double-blinded relapse study of sertraline in OCD. They found no significant correlation between degree of insight as measured by the BABS and outcome after 16 weeks of sertraline. The role of insight in remission and relapse deserves further scrutiny.

Obsessive-compulsive disorder has been linked to alterations in neurologic function involving the basal ganglia after head trauma, encephalitis, and birth events (62). Hollander et al. (63) described a subset of patients with OCD who had an increased number of neurologic soft signs and neuropsychological abnormalities in comparison with a control group matched for age, sex, and handedness. The examination of soft signs involved fine motor coordination, involuntary movements, sensory function, and visuospatial tasks. Soft signs were correlated with severity of obsessions. Receiver operating characteristic analysis found that a cutoff of three or more signs yielded the minimum number of combined errors of sensitivity and specificity in blindly distinguishing OCD subjects from controls. When these criteria were used, 25 of 40 subjects were considered to have soft neurologic signs. A second study of OCD adolescents found a high frequency of age-inappropriate synkinesias and lateralization of deficits to the left side of the body (64). In a nonblinded study in which a clinical neurologic examination was performed in childhood and adolescent OCD subjects, most of the patients had abnormal neurologic findings, including choreiform movements, nonspecific neurodevelopmental signs, and left hemisyndrome (65). Significantly more signs of central nervous system dysfunction were observed in the OCD group, manifested by abnormalities in fine motor coordination, involuntary movements, and abnormal sensory and visuospatial function. Some evidence was found of an increased number of left-sided signs that were suggestive of right-sided dysfunction. The hypothesis that this subgroup is etiologically distinct requires further validation in a study of predictive outcome.

Another important area of investigation is symptom subtype in OCD. Thus far, specific obsessions and compulsions have not predicted outcome in the vast majority of follow-up studies. In a preliminary analysis of 544 patients from a multicenter trial of acute clomipramine, the authors failed to find any significant correlation between symptom subtype, identified by the Y-BOC Symptom Checklist, and outcome (66). Recent work in which factor analysis was used to cluster groups of obsessions and compulsions suggests that certain symptom clusters may identify subtypes of OCD (67,68). Data obtained with positron emission tomography (PET) have shown that regional activation of the prefrontal cortex varies according to factor (69), and emerging genetic data suggest that familial loading varies according to factor (70). Symmetry and certain obsessions, such as aggressive and sexual obsessions, are more frequent in patients with OCD and chronic tics (71). One family study suggests that the rate of OCD is higher in first-degree relatives of probands with aggressive obsessions (49). The analytic technique used to identify factors from the Y-BOC Symptom Checklist may be fruitful in predicting the course of OCD. Evidence is increasing that patients in whom hoarding is a primary obsessive-compulsive symptom are resistant to traditional behavioral and pharmacologic interventions (72–74). In addition, hoarding was the only compulsion associated with a lower probability of remission in our pilot study.

The data regarding early onset and outcome of OCD are quite inconsistent. In a number of studies, an earlier age at onset of OCD was associated with a worse prognosis. In the study of Ravizza et al. (75), the age at onset of patients who failed to respond to a trial of an SSRI was earlier than that of responders. Thomsen (36) reported that attainment of puberty by the time of referral predicted a better prognosis than a prepubertal onset. In a reanalysis of the multicenter efficacy and safety data for clomipramine, Ackerman et al. (76), using stratification and logistic regression techniques to identify multiple prognostic factors and control for confounds, found a later age at onset to be a strong predictor of response. Skoog and Skoog (42) reported that onset of OCD before age 20 was related to a poorer outcome, especially in men. In other studies, age at onset did not predict severity of illness at follow-up. Adolescents in the study of Berg et al. (37) had an extremely variable course. In our sample, the onset of major obsessive-compulsive symptoms before age 14 predicted a higher likelihood of remission.

The severity of OCD symptoms at baseline was not predictive of long-term outcome in most studies (77–81), although the truncated pretreatment range of severity makes such a relationship difficult to demonstrate. It seems likely that more severe symptoms are associated with a greater degree of functional impairment and a greater number of comorbid conditions, although this hypothesis remains to be tested. However, in the only study we could locate that examined level of functioning in OCD, pretreatment functioning did not predict follow-up outcome (73). Duration of symptoms was not predictive in any study (78,79,81, 82), although it is possible that chronicity accompanied by comorbidity may worsen prognosis. Type of ritual (washing vs. checking) was not predictive in two studies (11,79) and predicted erratically in others (77,83), a finding that argues against any consistent relationship of symptom type to outcome.

PHENOMENOLOGIC SUBTYPES AND THEIR STABILITY OVER TIME

The beginning clinician is often struck by the diversity of the clinical presentations of OCD. However, this initial impression is soon replaced by the realization that the obsessions and compulsions are remarkably limited in number and stereotypic. During the last 15 years, we have characterized the phenomenologic and clinical features of more than 1,000 patients with OCD. The basic types and frequencies of obsessive-compulsive symptoms have been found to be consistent across cultures and time (84). Why particular symptom patterns develop in given persons remains unknown. The most common obsessions include contamination, pathologic doubt, aggressive and sexual thoughts, somatic concerns, and the need for symmetry and precision. The most common rituals are checking, cleaning, and counting.

Aside from a relatively gross analysis of the course in terms of variation in overall intensity of symptoms, finer analyses of variations in symptom focus or symptom mix have not been attempted. Nevertheless, in their study of childhood OCD, Swedo and Leonard (22) reported that 90% of patients experienced some change in symptom pattern over time, often starting with a solitary ritual without associated obsessive thoughts (notably uncommon in adults), then later adding new symptoms that sometimes became predominant over earlier ones. More work is needed to delineate the frequency and magnitude of the cyclic variations in intensity and focus of obsessive-compulsive symptoms.

COMORBIDITY

Biological markers and neuropharmacologic challenge studies depend on the selection of homogeneous clinical populations that reduce the variance. In studying a disorder like OCD, the presence of other axis I disorders is a serious obstacle for researchers wishing to obtain homogeneous subgroups. The majority (57%) of OCD patients presenting to our clinic have at least one other DSM-III-R diagnosis. To complicate matters further, OCD is a chronic illness, and an even higher percentage of our patients have a lifetime history of another axis I disorder. Distinguishing primary from secondary diagnoses can often be difficult, if not impossible.

Studies examining the coexistence of OCD and other psychiatric disorders can be divided into two groups: (a) those examining the coexistence of other psychiatric disorders in a clinically defined population of patients with OCD and (b) those primarily focused on recording the incidence of obsessive-compulsive symptoms in other diagnostic groups. The coexistence of other anxiety states, depression, and psychotic symptoms with obsessive-compulsive symptoms was well documented in the early literature. However, few systematic clinical psychopathologic studies had been completed before 1985. Earlier studies were retrospective and failed to utilize standardized diagnostic criteria or reliable structured instruments.

The dispute about the relationship between OCD and schizophrenia has been of central interest. Controversy centers on whether a psychopathologic continuum exists for the two disorders. Some investigators have suggested that obsessions are a preliminary sign of schizophrenia, whereas others have claimed that obsessional thoughts are a neurotic defense against psychotic decompensation. Most current researchers feel that the two disorders are different entities without any true relationship. If OCD was closely related to schizophrenia, one would expect that schizophrenia would develop in a significant percentage of OCD patients. However, follow-up studies have shown that the incidence of progression to schizophrenia in primary OCD probands is low, between 1.0% and 3.3%. Rosen (85), in a retrospective chart review of 850 inpatients with schizophrenia, found that approximately 10% exhibited prominent obsessive-compulsive symptoms. This finding was replicated by Fenton and McGlashan (86), who found that 10% of schizophrenics in a Chestnut Lodge (Rockville, Maryland) follow-up study exhibited prominent obsessive-compulsive symptoms. These obsessive-compulsive schizophrenic patients tended to have a more chronic course and a greater frequency of social or occupational impairment in comparison with a matched sample of schizophrenics without obsessive-compulsive features. Recently, Eisen et al. (87) interviewed 77 patients who met SADS criteria for schizophrenia and found that 7.8% met DSM-III-R criteria for OCD. The average Y-BOCS score for those meeting the criteria for OCD was 22.3 ± 5.2.

The relationship between obsessions, compulsions, and depression was the subject of several early studies. These were primarily retrospective and failed to use diagnostic criteria or structured interviewing. Thus, many aspects of the association between depression and OCD remain unclear. One aspect that deserves further study is whether the affective episodes in OCD are primary or secondary. Dividing depressed obsessional patients into these two categories (i.e., primary and secondary) was originally advocated by Lewis (24). No systematic study of the frequency of obsessions and compulsions in a sample of depressed patients existed until recently. Although a great deal of interest has been shown in the question of whether compulsive personality increases the risk for development of a major depression, the results remain inconclusive, with wide variations in percentages across studies possibly caused by the lack of standardized diagnostic criteria.

The phenomenologic and biological evidence relating OCD to affective disorder has been reviewed by Insel (88). It has been noted that obsessive-compulsive features are rarely, if ever, seen in mania. We reported a case of OCD

in a patient with bipolar disorder whose obsessions and compulsions worsened in direct proportion to the severity of his depression and totally disappeared when he became manic (89). Although preliminary evidence suggests that OCD is rarely seen in mania, no systematic data on the frequency of obsessive-compulsive symptoms in a bipolar population were available until recently. Kruger et al. (90) and Chen and Dilsaver (91) reported on the frequency of OCD in bipolar and unipolar populations. Chen et al. found that 21% of patients with bipolar disorder, 12.2% of patients with unipolar depression, and 5.9% of patients with other disorders had OCD in the National Epidemiology Catchment Area Survey sample. Kruger et al. found that 35% of patients with both bipolar and unipolar depression had an obsessive-compulsive syndrome. Many of these depressed patients suffer from obsessions, which are at times difficult to differentiate from ruminations.

In our subsample of 250 patients who met DSM-III criteria for OCD, only 25% denied depression on admission (72). The majority admitted to feelings of inadequacy and hopelessness, and only one patient gave a history of euphoria. During the course of their illness, most reported that depression developed after the obsessive-compulsive symptoms; therefore, the patients were classified as having secondary depression. A minority (8%) of patients had a simultaneous onset of obsessive-compulsive symptoms and depressive episodes.

Kringlen (27) reported that more than 50% of 91 obsessional patients in his series had phobic symptoms. Among the 104 depressed obsessional patients of Videbach (92), 42 (40%) described phobic symptoms. In contrast, Welner et al. (93) found associated phobias in only 7 (5%) of 150 patients with severe OCD. Additional evidence supporting a shared vulnerability to OCD and other anxiety disorders is the high incidence of childhood phobias reported by obsessional patients. Lo (28) reported that 21 (35%) of his 59 obsessional patients had had significant phobias during childhood. Videbach (92) observed the same in 52 (50%) of his 104 depressed, ruminative patients. Similarly, Ingram (26) reported that 22 (25%) of 89 OCD patients had had significant phobias in childhood. During the last 5 years, several studies have examined the association of OCD with other anxiety disorders. In a study of 60 patients with panic disorder in which the SADS-LA and personal interviews were used, Breier et al. (94) found that 17% met the DSM-III criteria for OCD. Subsequent studies by Mellman and Uhde (95) and Barlow (96) confirmed these initial findings of the overlap between panic and OCD. Insel (88) pointed out the importance of the distinction between primary and secondary anxiety disorders. For example, it is often difficult to distinguish a primary social phobia with obsessive features from primary OCD that is centered on obsessing about having to complete a ritual in public. The finding of a high frequency of current and lifetime anxiety disorders suggests that OCD patients are vulnerable to virtually all types of anxiety. The high prevalence of anxiety states in these patients may be a consequence of common developmental/temperamental traits whose phenotypic expression is secondary to shared genotypic and psychosocial factors. Of particular interest in this regard is the high lifetime prevalence (12%) of separation anxiety in this group of patients (97), a finding that has also been well documented in panic disorder (20).

Table 111.4 summarizes the common axis I disorders associated with OCD in the Brown cohort. Two-thirds of obsessive-compulsive patients have a lifetime history of a major depression, and one-third have a major depression at the time of first evaluation. The majority (85%) have a mood disorder secondary to their OCD, and 15% appear to have a concurrent unipolar recurrent depression. A significant overlap is also seen with the other axis I anxiety disorders, including panic disorder, panic disorder with agoraphobia, social phobia, generalized anxiety disorder, and separation anxiety disorder. Other comorbid conditions

TABLE 111.4. COEXISTING AXIS I DIAGNOSES IN PRIMARY OBSESSIVE-COMPULSIVE DISORDER

Diagnosis	Current Semistructured (*n* = 100) (%)	Lifetime Semistructured (*n* = 100) (%)	From SADS (*n* = 60) (%)
Major depressive disorder	31	67	78
Simple phobia	7	22	28
Separation anxiety disorder	—	2	17
Social phobia	11	18	26
Eating disorder	8	17	8
Alcohol abuse (dependence)	8	14	16
Panic disorder	6	12	15
Tourette syndrome	5	7	6

SADS, Schedule for Affective Disorders and Schizophrenia.
Adapted from Jenike et al., with permission.

that appear more frequently than one would expect include eating disorders, Tourette syndrome, and schizophrenia. Comorbid axis I conditions can influence the course of illness and affect choice and order of treatment.

Special attention has been focused recently on patients with tics and OCD. Approximately 20% of patients with OCD have a lifetime history of multiple tics, and 5% to 10% have a lifetime history of Tourette syndrome (82). The age at onset in this subgroup is earlier, and they have family pedigrees loaded for both Tourette syndrome and OCD (49). Miguel et al. (98) studied similarities and differences in the clinical symptoms of 15 outpatients with OCD but not tics and 12 adult patients with Tourette syndrome but not OCD. All patients with OCD reported that some cognition preceded their compulsions, whereas only 2 of 12 patients with Tourette syndrome reported any cognition. In contrast, all patients with Tourette syndrome reported that sensory phenomena preceded their repetitive behaviors; no OCD patients reported such sensations (97).

Considerable interest has been shown in the overlap of OCD with eating disorders, particularly anorexia nervosa. In the study of Thiel et al. (99), 37% of 93 women who met criteria for anorexia or bulimia nervosa also met DSM-III-R criteria for OCD and had a score of 16 or higher on the Y-BOCS. Rastam et al. (100) also reported a high rate of OCD in a sample of 16-year-old girls in whom anorexia nervosa had been diagnosed.

Axis II conditions in OCD are covered extensively elsewhere in this volume. The most commonly encountered diagnoses are dependent, avoidant, passive–aggressive, and compulsive. Schizotypal, paranoid, and borderline personalities are found less commonly in OCD but appear to be associated with a poor outcome.

RELATIONSHIP OF HETEROGENEITY TO COMORBIDITY

We have become increasingly interested in developing a model for subtyping patients with OCD according to what we see as the three core features of the disorder: abnormal risk assessment, pathologic doubt, and incompleteness. These features cut across phenomenologic subtypes, such as checking, washing, or the need for symmetry, although some subtypes are more closely associated with one core feature than another.

Like most phobics, persons with OCD continually worry that if there's a one in a million chance that something terrible will happen, it will happen to them. If there's a one in a million chance that the elevator cable will snap, the phobic patient is certain that it will snap when he is in the elevator. In the same way, many of the thoughts of the patient with OCD are dominated by improbable events that most of us would not think twice about. Many checkers suffer from "what if?" What if I don't unplug the coffee

machine and there's a fire? The patients with sexual or aggressive obsessions also worry. What if I do pick up the knife?

On the opposite side of the spectrum are the patients with OCD who experience little or no anxiety that something terrible will happen. Janet observed that many patients with OCD are tormented by an inner sense of imperfection. Their actions are never completely achieved to their satisfaction. Many of our patients describe an inner drive that is connected with a wish to have things perfect, absolutely certain, or completely under control. When they achieve such perfection, they describe a curious sensation that they can compare to no other feeling. Janet called it the "occasional brief appearance of sublime ecstasy." This absolute feeling of certainty or perfection is rarely attained, and therefore the patients experience a feeling of incompleteness.

Feelings of going exactly through the middle of a door, of having both shoelaces tied to exactly the same tension, of having ones hands perfectly clean, of saying ones prayers exactly right, or of having one's hair parted precisely down the middle are clinical examples. Most of us can relate to the feeling of wanting to have something just so or perfect and the feeling of accomplishment when we finally get it that way, and to feelings of frustration and incompleteness when it's not that way. But for the obsessive, this feeling becomes attached to an action that would hold little significance for most of us, just as most of us do not think about the one in a million chance that something will go wrong. Patients with trichotillomania or Tourette syndrome also describe a feeling of incompleteness with continued tension until they have finished pulling out an entire patch of hair or completed a sequence of tics to their satisfaction. Both say that it is impossible to stop in the middle of a compulsive action despite the consequences.

The core features appear to relate both to the clinical features of OCD and to the comorbid disorders. In patients with abnormal risk assessment, high levels of anxiety are associated with symptoms. They are also likely to have comorbid axis I generalized anxiety disorder or social phobia, avoidant and dependent personality features, and a family history of an anxiety disorder. In contrast, patients with incompleteness are likely to manifest low levels of anxiety, comorbid multiple tics or habit disorders (e.g., trichotillomania, onychophagia), and compulsive personality features. Empiric validation of these subgroups may have important implications for diagnosis and treatment. Some evidence has already been found that patients with treatment-resistant OCD and tic spectrum disorder are particularly responsive to dopaminergic antagonists. These patients are also more likely to exhibit incompleteness.

Baer et al. (67) applied principal component analysis to 107 patients with OCD who completed the Y-BOC Symptom Checklist and examined the correlations between the factor scores and the presence of comorbid tic or personality disorders. Three factors, symmetry/hoarding, contamina-

tion/cleaning, and pure obsessions, best explained the variance. Only the first factor was significantly related to OCPD (obsessive-compulsive personality disorder) or a lifetime history of Tourette syndrome.

COMMENT

During the past 15 years, significant advances have revolutionized the way we conceptualize and treat OCD. Epidemiologic studies have confirmed that OCD is an underrecognized common major psychiatric disorder with a lifetime prevalence of 2% to 3% in the general population, and they have been instrumental in focusing the attention of researchers, clinicians, and the media on OCD. Studies of the clinical features and course of the disorder and associated comorbid conditions have appeared in the literature since the turn of the twentieth century and have been the subject of numerous prospective and retrospective studies of its course, reviewed here.

Finally, future studies will continue to benefit from further refinement of our thinking about the heterogeneity and comorbidity of OCD and the search for homogeneous subtypes. The identification of an OCD–tic subtype has already led to important new genetic and biological studies and has been directly relevant to treatment. The recent effort to characterize pediatric autoimmune neuropsychiatric disorders and their relationship to genetic vulnerability to streptococcal infection offers a promising lead for furthering our understanding of the pathophysiology of OCD. It is possible that we will increase our understanding of predictions of remission and relapse related to possible homogeneous subtypes of illness. A review of these studies suggests that the course of OCD, long thought to be chronic, may be more episodic than previously believed, particularly in children and adolescents. It also appears that in some subjects, pharmacologic and behavioral treatments may alter the natural course of illness. However, a long-term prospective follow-up study of a large number of patients with OCD is needed to confirm these observations. In addition, the effectiveness of these treatments in routine practice are not known.

SUMMARY

The prevailing notion that the course of OCD is chronic and deteriorating has not been consistently borne out by the evidence, particularly in children followed prospectively. Furthermore, the natural course of this disorder appears to have been altered by the availability of effective pharmacologic and behavioral therapy. In their review of follow-up studies, Goodwin et al. (29) found that the course of OCD can be categorized as (a) unremitting and chronic, (b) phasic with periods of complete remission, or (c) episodic with incomplete remission that permits normal social functioning. Although the results of studies varied considerably in regard to the percentage of patients in each category, the majority of patients in each study were always in the last group, and the course of about 10% of patients was marked by progressive deterioration. These figures are consistent with our own study of patients meeting DSM-III criteria for OCD (Table 111.3). Although previous descriptive studies found a chronic waxing and waning course in 85% of patients, no attempt was made in previous studies to subdivide the waxing and waning course into predictable patterns or subtypes. More recent studies in which a prospective design and standardized criteria were used have shown that the episodic form of this disorder (clear periods of remission while the patient is off medication) is uncommon. The periodicity, duration, and severity of episodes in patients with OCD vary considerably. Once established, obsessions and compulsions usually persist, although the content, intensity, and frequency of the symptoms change over time.

The introduction of the SSRIs has led to a significantly improved prognosis for patients with OCD during the last decade. In a follow-up study by Orloff et al. (44) of a cohort of 83 OCD patients assessed 1 to 3 years after initial evaluation, 64% had a decrease of more than 50% in Y-BOCS score, and 33% had a decrease of more than 75% in Y-BOCS score at follow-up. These results are at odds with those of two other prospective longitudinal observational studies of the course of OCD that have recently been initiated at our site. Eisen et al. (38) examined 68 obsessive-compulsive outpatients evaluated at the Yale–Brown clinics and followed them prospectively during a 2-year period. Of the 51 patients who started the study meeting full criteria, 57% still met full criteria after 2 years. Survival analysis revealed a 47% probability of achieving at least partial remission during the 2-year study period. In another prospective study, by Steketee et al., 107 clinic patients with OCD were followed for up to 5 years after intake. The probability of partial remission for at least a 2-month period was 53%, and for full remission (no longer meeting criteria) at 5 years it was 22% (41).

DISCLOSURE

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