The Eating Disorders
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Chapter 31

The Relationship of the Eating and Affective Disorders

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INTRODUCTION

At the turn of the century, Freud [1] speculated about the relationship between anorexia nervosa and melancholia. Abraham, in writing of a patient suffering from excessive hunger and binge eating, was impressed with the addictive intoxicating aspect of the behavior, which he interpreted as substitute libidinal gratification [2]. Over the ensuing years, much of the psychoanalytic focus in anorexia nervosa in adolescent females revolved around fear of oral impregnation, denial of genitality, and the concept of organ neurosis in which the ego is fixated at the oral phase and produces secondary hormonal changes. Fenichel, in his psychoanalytic compendium, points out that anorexia nervosa can be the result of a variety of dynamic processes and may be an affective equivalent of a depression that antedates other signs of depression [3]. He also mentions cyclic food addiction in woman and its relationship to manic depressive illness as well as the relationship of bulimia to mourning. Working from an existential framework, Binswanger detailed the case history of his anorexic patient, Ellen West, and described her overwhelming sense of despair and alienation [4]. Bruch, also in moving beyond the standard psychoanalytic conflict formulations, emphasized the self-despair and pervasive sense of personal ineffectiveness in patients with anorexia nervosa [5]. From a phenomenologic orientation, these depictions may equate with a depressive illness.

In recent years, growing theoretical and clinical interest in the eating disorders has led to increased precision in diagnosis. As the eating disorders have been more carefully studied, more distinct subtypes have been defined [6-9]. Now it is perhaps more correct to talk of primary restrictive anorexia nervosa, bulimia nervosa, and normal-weight bulimia. It is also important to recognize that these syndromes are not completely static, and the clinical course for any particular patient may cross diagnostic boundaries. However, with this fractionation of the eating disorders and the emergence of bulimia as a diagnostic entity, the relationship to the affective disorders has become more visible.

At the same time, the boundaries of the affective disorders have come under new scrutiny and revision. What was previously passed off as personality and character, and ergo not susceptible to biological intervention, is being reexamined—albeit with a high-resolution clinical microscope. Akiskal, in his study of subaffective disorders, has uncovered many treatable conditions that formerly were ascribed to personality [10]. Keller and Shapiro's work on "double depression" has also been enlightening by recognizing the coexistence of a depressive personality core with a superimposed affective episode [11]. The borderline quality of many patients with eating disorders has been frequently observed and may rivet the clinician's attention. Carroll et al caution that the presence of dramatic psychopathology may mask the more traditional signs and symptoms of major depressive disorders [12].

As in all diagnostic schema, how hard one looks and where one draws the line determines the yield. It is extremely important to take a careful and detailed history from the patient and, when possible, obtain corroborative history from family members, as the compelling nature of the eating disorder symptoms may indeed obscure other pathology. If one insists on full DSM-III criteria for a major affective disorder in eating disorder patients before considering a codiagnosis and pharmacologic intervention, a number of treatable patients may be missed.

In this chapter, I will briefly review the current lines of inquiry and data concerning an affective disorder-eating disorder linkage without attempting a thorough critique of research strategies.

STUDIES OF PSYCHOPATHOLOGY

In an often-cited study, Cantwell followed 26 patients who had been hospitalized as adolescents for anorexia nervosa [13]. The distinction was not made between pure restricters and bulimics. Almost 50% of the patients, by parent and self-report, were diagnosed as having an affective disorder at follow-up. In a retrospective evaluation of premorbid psychiatric symptomatology, 61% of the patients reported dysphoric mood, and 71% reported being fearful. These findings agree with three earlier studies by Dally [14], Theander [15], and Morgan and Russell [16], who reported significant psychiatric morbidity at initial presentation and follow-up.

Stonehill and Crisp found that anorexia nervosa patients scored significantly higher than healthy female students on the anxiety, obsessional somatic, and depression scales of a standardized instrument [17]. When patients who vomited were separated out, the depression scores were even higher. However, the anorexic group scored significantly lower on the anxiety, somatic, phobic, and depression scales than a matched group of depressed outpatients. Stonehill and Crisp felt that this lent support to the view that anorexia nervosa is not a simple variant of depression. They ascribed the high level of scores on the depression scale to the overrepresentation of early morning awakening, which is quite prominent in anorexia nervosa supposedly apart from any affective disorder.

In discussing what he termed "bulimia nervosa" as an ominous variant of anorexia nervosa, Russell reported on 30 patients (28 females and 2 males), 24 of whom suffered at least moderate depression [8]. Russell doubted that there were primary depressives, because the eating disorder did not appear to improve with the relief of depressive symptoms, and the depressive symptoms did not seem to be of an endogenous variety.

Ben-Tovin et al used the Present State Examination to evaluate the mental status of 21 anorexics and found that they did not closely resemble any other published group [18]. The predominant affect was depressive, which differentiated them from patients with anxiety states. There was some similarity to an inpatient sample of depressives in terms of the mixture of symptoms, but the anorexic group could be separated by the absence of depressive delusions, ideas of reference, and retardation. Out of this anorexic group, which included 12 abstainers and nine vomiters, a case for a clinical depression using operational criteria could be made for certain in only three patients, with seven patients seen as probable cases of depression. In a depressive sample of 23 patients, 16 definites and three probable cases were identified. The spread and diagnostic frequency between these two groups was significant and lead the authors to conclude that the findings they uncovered were possibly related to starvation states and their secondary effects, the ongoing existential struggles of the anorexic, a reflection of underlying personality, or a coincidental finding. Despite the differences in depressive symptoms reported by anorexics and depressives, Ben-Tovin et al were impressed by the qualitative depressive feelings identified by their patients and suggested that the measures of depression used were not able to tap the existential despair and guilt of the anorexic with its focus on the loathing of the body and fear of losing control over eating and resultant weight gain.

In their comprehensive study of 105 female inpatient anorexics, Casper et al gave further support to the notion that bulimics constitute a subgroup of anorexia highly impacted by depression, obsessionalism, and somatization [6]. They make the point that bulimia is not simply a disorder of appetite but a highly complex symptom with depression, anxiety, and guilt interwoven within its matrix. To some degree, their conclusions are at variance with Russell [8] and Stonehill and Crisp [17], who tended to minimize the affective linkage of the illness.

Using the same 105 patient sample, Eckert et al concluded that anorexia nervosa patients manifest a clinically significant level of depression as measured by symptoms and mood [19]. The severity of the depression correlated with other features of the illness felt to be indicative of greater severity, such as more bulimic vomiting, greater disturbance in body image, greater denial, more impairment in relationship with their fathers, and sexual disturbance. Depression was observed to be reduced but not eliminated over time, and patients who gained more weight were observed to experience a greater reduction in depression. While

clearly recognizing that weight loss and depression exist together, the authors did not feel that their data allowed them to draw any etiological conclusions.

Using DSM-III criteria, Strober was able to assign a diagnosis of major depression to 41% of his bulimic patients but to only 9% of the restricters [20]. Premorbid personality characteristics differed between the two groups, with the bulimic patients often described as unhappy, fearful, clinging, and quarrelsome during childhood. Strober saw these qualities as implying affective instability.

Pyle et al studied 34 bulimic patients of whom most reported feelings of depression and problems with interpersonal relationships and self concept [21]. Mean MMPI scores on the D, Pd, Pt, and Sc scales were at least two standard deviations above the norm. There also appeared to be a high rate of substance abuse in these patients. Over 75% of them reported a decrease in sexual interest since the start of their illness, and 90% identified some traumatic event being associated with the onset of the bulimia, with the most frequent event being a loss or separation. This latter finding may be retrospective elaboration or could truly represent the beginning of a depressive episode.

Hendren reviewed the case records of all patients diagnosed as having anorexia nervosa at the Mayo Clinic over a seven-year period [22]. From the 230 cases with an anorexia nervosa diagnosis, 84 women were eventually evaluated on the basis of research diagnostic criteria (RDC) for major depressive disorder and endogenous major depressive disorder. Fifty-six percent met the RDC criteria for a major depressive disorder and 35% met RDC criteria for an endogenous depression. MMPI data was also reviewed and agreed in large part with the results reported above.

The trend of the above studies is in the direction of a significant relationship between eating disorders—particularly bulimia and affective illness. The lack of consistency in defining depression from study to study makes the drawing of general conclusions difficult.

FAMILY STUDIES

The idea that affective disorders run in families has received greater credence over the last 20 years. Recently, the Yale-NIMH collaborative family study of depression reported on a study of psychiatric disorders in 2,003 first-degree relatives of 335 probands and found considerable support for a familial relationship with differential rates and types of illness observed depending on the diagnosis of the proband [23]. Of additional possible significance for our discussion was the finding of Leckman and his colleagues that appetite disturbance and excessive guilt in depressed probands was associated with increased rates of major depression among family members with a 2.5 times greater risk for the same subtype [24]!

While not directly addressing the relationship of eating disorders to affective illness, Crisp et al studied the relationship of parental psychoneurotic characteristics to the prognosis of patients with anorexia nervosa [25]. They found that after the patient's weight restoration, maternal anxiety and paternal depression increased if the marital relationship was judged to be poor. Also, in patients who demonstrated bulimic symptoms, the fathers were seen as having an undue preoccupation with discipline and self-control and having a propensity for developing affective illness. Increased levels of anxiety and depression emerged with the daughter's recovery. Poor outcome was associated with high levels of parental psychiatric morbidity particularly in respect to depression. This study, while seeming to make a strong statement about anorexia nervosa in adolescents and its dynamic relationship to parental psychopathology, could also be interpreted as supporting the idea that affective loading and a particularly severe form of eating disorder may be related.

Cantwell et al reported a high degree of affective illness in the families of the anorexic patients he studied [13]. Out of 26 patients studied, 2 fathers, 15 mothers, 6 siblings, and 3 maternal grandparents were given a diagnosis of affective disorder. Four of the mothers had made suicide attempts. After affective disorders, alcohol abuse was diagnosed most frequently, appearing in 16 relatives.

Winokur et al studied the presence of primary affective disorders in the relatives of 25 patients with anorexia nervosa and 25 normal controls according to RDC criteria [26]. Affective disorders were present in 22% of the relatives of the anorexic patients and in only 10% of controls. Of the 43 relatives of anorexics who had an affective disorder, 34 were given a diagnosis of unipolar depression, and 9 were given a bipolar diagnosis. In both groups, more female than male relatives had a history of affective disorder, but the rate was significantly higher in female relatives of anorexic patients. Seventy-six percent of the anorexic families had at least one relative with affective disorder compared to 48% in the control group.

In an attempt to further validate the bulimia-restriction distinction in anorexia nervosa, Strober et al analyzed MMPI scores of parents of bulimics and restricters [27]. Their data suggested that the severity of bulimia in anorexia nervosa is associated with more pronounced affective disturbance in both parents along with greater impulsivity in fathers. The morbid risk of affective disorder in first- and second-degree relatives of the combined group was computed to be 15% which is more

than two times the average expected lifetime risk for affective disorder in the general population. Seventy-one percent of the bulimic group versus 40% of the restricter group had positive family histories. Affective disorder was almost four times greater in the mothers of the bulimic group and was more prevalent in the fathers of the bulimics, but not at a statistically significant level. Alcoholism was shown to be present in 83% of the families of bulimics and 49% of the restricters, which may also point to a linkage with affective disorders.

Hudson and his group evaluated ten normal-weight nonanorexic bulimic patients for familial affective disorder [28]. Their results were similar to other investigators and revealed a risk factor for major depression of about 22% in first-degree relatives of the bulimic patients. In another study, Hudson et al evaluated 420 first-degree relatives of 14 patients with anorexia nervosa, 55 patients with bulimia, and 20 patients with both disorders [29]. The found the prevalence of familial affective disorder to be significantly greater in patients with anorexia nervosa and/or bulimia than in patients with bipolar disorder. The morbid risk of affective disorders in relatives of the total eating disorder group was 27%.

In a prospective study of 40 anorexic patients, Rivinus et al [30] found significantly more depression in the relatives of the patient group compared with a control group. When substance abuse diagnoses were added to depression, the familial impact of impairment was even greater. An increase in multigenerational impairment and increased frequency of affected relatives within families was also observed in the patient group.

Gershon et al [31] attempted to ascertain the presence of an identifiable subgroup of anorexic patients with a higher risk of affective illness in their relatives as a way of further evaluating the data that suggest anorexia nervosa and major affective disorder may share etiological factors. The presence of affective disorder, self-induced vomiting, or bulimia in the patient did not predict affective illness in the relatives, which suggested the absence of clinically observable genetic heterogeneity with anorexia nervosa defined by these features. The data seemed to support the idea of a shared genetic vulnerability between anorexia nervosa and affective disorders.

The idea that familially mediated variables play a crucial role in the pathogenesis of the eating disorders was further advanced by a recent report by Strober et al [32]. They found a five-fold increased risk of eating disorders in the female relatives of anorexics compared with relatives of controls. Subclinical anorexia nervosa was the most frequent disorder observed in the relatives of anorexics, with a greater total transmission of eating disorders occurring in the families of bulimic anorexics. Interestingly, all diagnoses of severe restrictive anorexia nervosa were made in relatives of restricter probands, whereas the preponderance of bulimic diagnoses were made in the relatives of anorexic/bulimic probands—suggesting familial segregation of the disorders. The authors offered several hypotheses for the familial transmission of which the cotransmission of an affective disorder or other psychopathology may be one. However, they caution that the data do not support any conclusions.

A recent study by Stern et al questions the relationship of familial affective disorder to normal-weight bulimia [33]. Their findings, which used strict diagnostic criteria, direct family interview, and blind raters, were at odds with the above. They only found a 9% prevalence of affective disorder in the relatives of bulimic probands, compared with 10% in the relatives of controls. However, a history of affective disorder was considerably more common among the bulimic patients, but it did not reach statistical significance and their study was limited to normal-weight bulimia.

Again, the differing methodologies may account for the variance in results, ie, patient report, family questionnaire, and direct interview. However, the trend of most of the data is consistently in the same direction except for the last study cited—namely, that there does seem to be some connection between eating disorders and affective illness.

BIOLOGICAL STUDIES

For convenience, under this heading are subsumed the neuroanatomical, neurophysiologic, neuroendocrine, neurochemical, and psychopharmacologic data that have been forthcoming in relating the eating disorders to the affective disorders.

That such relationships should exist biologically should not be very surprising when one considers the overlap of systems involved in the maintenance of eating and mood. The hypothalamus has been implicated as being an important structure in the regulation of both appetite and mood. Opioid peptides, neuropeptides, and monoamines are increasingly being suggested as important neuroregulators of both systems [34,35].

Catecholamine metabolism has been thought to be integral to the understanding of affective illness for some time. Though the limitations of this hypothesis have become more apparent, the monoamines are still thought to be important neuroregulators even if not solely responsible for affective illness [36-38]. Halmi et al studied MHPG during treatment in a group of 25 anorexics with secondary depressive symptoms [39].

MHPG is a major metabolite of brain norephinphrine and may correlate with central noradrenergic activity. An increase in MHPG correlated with a decrease in depression on two of three measures of depression. Gerner and Gwirtsman found that 24-hour urinary MHPG was low for all 11 female anorexic patients tested compared with control subjects [40]. This finding appeared to be independent of depression.

Abraham et al measured urinary MHPG in seven anorexics during a bed rest and refeeding program and found a positive relationship between MHPG and body weight, but no correlation between body weight and depression [41]. They interpreted their findings as reflecting a general metabolic effect. In an attempt to resolve some of the confusing findings concerning the significance of low urinary MHPG levels in anorexia nervosa, Biederman et al studied a group of anorexia nervosa patients before and after five weeks of treatment and a group of matched controls [42]. A subgroup of the patients who met RDC criteria for a concomitant major depressive disorder was found to have lower pre- and posttreatment mean urinary MHPG levels than both normal controls and nondepressed anorexia nervosa patients, both of whom had similar values. The median value of all urinary MHPG samples was used as a cutoff point to assess the distribution of values. They reported that significantly more depressed patients excreted low MHPG compared with nondepressed patients and normal controls.

Kaye et al studied CNS dopamine and serotonin metabolites and norepinephrine in underweight anorectics, recently weight-recovered anorectics, and long-term weight-recovered anorectics [43]. They found that the dopamine metabolite homovanillic acid (HVA) and the serotonin metabolite 5-hydroxyindolacetic acid (5-HIAA) were reduced in underweight anorectics but returned to normal shortly after weight was normalized. Norepinephrine levels, on the other hand, were similar to normals in underweight anorectics and after weight restoration. However, long-term weight-recovered anorectics had a 50% decrease in CSF norepinephrine levels compared with controls. The investigators felt that these changes in neurotransmitter metabolism are an integral part of the neurobiology of anorexia nervosa and may influence the changes in mood, behavior, and neuroendocrine function that have been observed. A longstanding disturbance in CNS norepinephrine may certainly point to a coexisting affective disturbance.

Monoamine oxidase (MAO) is an important enzyme in the degradation of many biogenic amines and thus has been the subject of studies attempting to link biochemical disturbances with a variety of psychiatric illness. The data generated from these studies appear inconclusive. Biederman et al studied platelet MAO activity prospectively in a group of young anorexia nervosa patients with and without an RDC major depressive disorder along with a matched control group [44]. They found that the depressed anorexics had lower MAO activity compared with nondepressed anorexics and controls. This finding led them to conclude that MAO activity may be useful in identifying a depressed subtype of anorexia nervosa that may be etiologically related to other low-platelet MAO conditions such as bipolar affective disorder and alcoholism.

Over the last 15 years, there has been great activity in the exploration of the neuroendocrine basis of depression [45,46]. The development of the dexamethasone suppression test (DST) for depression was enthusiastically greeted initially as a long-awaited biological marker of psychiatric illness [47,48]. This neuroendocrine line of inquiry has been naturally extended to the eating disorders as a way of establishing a connection to the affective disorders.

As part of the study cited above, Gerner and Gwirtsman studied 21 female primary anorexics and one male anorexic [40]. The 21 women demonstrated a uniform and marked abnormal DST. Interestingly, the male anorexic had a normal DST. No correlation was observed between depression and abnormal DST leading the investigators to conclude that the abnormality was a product of primary anorexia nervosa but not solely of weight loss, because the patients were not starving. In addition, three drug-free schizophrenic patients who had starved themselves to 75% of their ideal weight had normal DST. The findings of low MHPG and abnormal DST led the authors to the speculation that low hypothalamic norepinephrine, via its tonic inhibition of corticotrophin-releasing factor, might be responsible for the abnormal DST and point to an adrenergic vulnerability in anorexic patients, which might explain the strong familial association of affective illness and high degree of risk for depression in recovered anorexics.

Beside nonsuppression of cortisol by dexamethasone, there are other measures of adrenocortical activity that are disturbed in anorexia nervosa. Walsh et al studied a group of anorexic women and reported an increased absolute cortisol production rate adjusted for body size and weight, increased plasma cortisol concentration, and increased urinary free cortisol [49]. All of these findings were statistically significant when compared with controls matched for age and sex. The above findings, while similar to those observed in malnutrition, are different on several measures of adrenocortical function. Walsh speculated that the increased adrenal activity in anorexia nervosa is out of proportion to the malnutrition and might reflect response to any number of stresses—depressive illness being one.

Given the fact that the malnourished state in anorexia

nervosa confounds much of the data generated, the normal-weight bulimic population became a promising group for study. Hudson et al reported abnormal DST results in five of nine normal-weight bulimics without a history of anorexia nervosa [28]. This percentage compared favorably with the results obtained by Carroll and coworkers on patients with major depression [46]. In an expanded study, Hudson and coworkers reported on a slightly more mixed group of normal weight bulimics, some of whom were on psychotropic medication, and found 47% nonsuppression on the DST [50].

More evidence is provided by Gwirtsman et al, who reported that 67% of 18 normal-weight bulimic patients had abnormal DST [51]. These findings lead the authors to adjust their previous conclusion that neuroendocrine abnormalities previously found in anorexics were solely an artifact of low weight. They now suggested that weight may only be a partial determinant of cortisol nonsuppression. Though the neuroendocrine abnormalities observed were not associated with diagnosable major depressive disorder, a diagnosis of dysthymic disorder could be made in 50% of their patients, with over half of the dysthymic patients also carrying a borderline personality diagnosis. Thus, the neuroendocrine abnormalities observed could be seen as a result of disorders in the affective and borderline spectrum rather than purely as a result of the bulimia itself.

Gadpaille et al studied amenorrheic and menstruating runners and found that the amenorrheic runners had an overwhelming representation of affective disorders, eating disorders and affectively ill relatives when compared to menstruating runners. Their findings raise the possibility of a shared neuroendocrine vulnerability in the eating and affective disorders [82].

In a study of 29 normal-weight bulimic women, Blinder et al found that there was a significantly greater incidence of prior history of anorexia nervosa and current clinical diagnosis of depression among the DST positive subgroup [52]. This data suggested to them that appetite disturbance may be closely linked to affective disturbance in certain patient subgroups and that perhaps the ingestive dysfunction may be a phasic manifestation of an underlying affective disorder.

The response of thyroid stimulating hormone (TSH) to thyroid releasing hormone (TRH) is thought to be blunted in depression, with generally normal circulating thyroxin (T_4) and triiodothyronine (T_3). In anorexia nervosa, the TSH response to TRH is normal, although the peak response is most often delayed [53]. Gwirtsman et al found eight of ten normal weight bulimic patients to have blunted TRH tests [51]. Unlike the situation in depression, T_3 is significantly decreased in anorexia nervosa, which is probably secondary to a diminished rate of conversion of T_4 to T_3, which also may be partially responsible for the decreased breakdown of cortisol. Also, anorexics have a lower mean T_4 than normals [54,55]. Whybrow and Prange have suggested that thyroid hormones may be important in regulating noradrenergic receptors in the brain and as a result may influence the development of and recovery from affective illness [56].

Activation is a fundamental neurophysiologically determined state of living organisms. In the affective disorders this state can be both underactive and overactive. It has been known for some time that hyperactivity is a clinical feature of anorexia nervosa [57]. This observation has been used to design an operant conditioning paradigm for the treatment of this condition [58]. Winokur et al were impressed by the presence of racing thoughts in their patients and felt that this suggested similarity to bipolar affective disorder, particularly when considered along with a history of distinct episodes of both depression and hypomania [26]. Mills and Medlicott [59] in exploring the theoretical basis of naloxone treatment in anorexia nervosa, make some extremely interesting points relating arousal, perfectionism, compulsivity, and anorexia. The mechanism they posit is that anorexia enhances arousal, which serves perfectionism and compulsivity. In their view, the depression observed in anorexia is related to the exhaustion produced from fighting compulsion.

Crisp and Stonehill pointed out in a rather complicated study that there is a relationship between weight loss, reduced sleep time, sleep discontinuity on one hand and weight gain, longer sleep time, sleep continuity and later waking on the other [60]. These changes appeared to transcend psychiatric diagnosis and to be primarily related to nutritional factors. The findings are similar to those uncovered in relationship to anorexia nervosa and suggest a common hypothalamic disruption in anorexia nervosa and other psychiatric illness. Though the authors did not observe a relationship between early morning awakening and depression, this is still felt to be a cardinal sign of endogenous depression.

Rapid eye movement (REM) latency has been thought to be a psychobiologic marker for primary depression [61]. Katz et al studied a mixed group of eating disorder patients with all-night sleep recordings and found a significantly reduced REM latency in the eating disorders group, which was approximately midway between previously established values for normal controls and primary depressives [62]. When the eating disorders group was divided into short versus long REM latency subgroups, Hamilton scores for depression were significantly higher in the former group; bulimia was a part of the clinical picture in the short latency group and

DSM-III criteria for major depression were met by all the short REM latency patients. Mean urinary cortisol was higher in the short latency REM group, but because of a wide distribution of values, this finding did not reach statistical significance.

The application of psychopharmacology to the eating disorders became a logical step as the affective components of the eating disorders began to be better appreciated. As of this writing, almost every class of psychotropic agent has been used in the eating disorders. Many of the studies of psychotropic agents in the treatment of eating disorders are of an anecdotal or open experimental structure, which mitigates the positive effects reported. However, the experience of the investigators is important from a clinical empirical standpoint.

L-dopa was utilized in a group of six anorexics because of what appeared to be clinical similarity to patients with Parkinson's Disease [63]. Four of the patients were noted to be improved with this medication. Amitriptyline was reported to promote weight gain, decrease weight focus and improve mood in six young anorexics admitted to a pediatric ward [64]. The effects of the amitriptyline were noted between the sixth to twelfth day, and weight change was felt to be preceeded by a brightening of mood and improved sociability. The authors questioned the representative nature of their sample, as it was a young sample with an eight-month average length of illness—all factors which auger well for a good prognosis. The also questioned other treatment factors that might have been operative, because the response to the tricyclic medication was quite rapid.

In one of the few double-blind studies, Pope et al treated 11 chronically bulimic women with imiprimine and assigned a similar group of 11 patients to placebo [65]. Eventually 19 patients completed the six-week study with a 70% decrease in bingeing observed in the imipramine treated group and virtually no change in the placebo group. After the six-week blind study period was completed, patients in the placebo group were offered antidepressant treatment and changes were made in antidepressant medications in treated patients who were not responding. Eventually 20 of 22 patients received a complete course of therapy with at least one antidepressant. On follow-up of one to eight months, 90% of treated patients reported a moderate or marked decrease in binge eating. Also, decrease in Hamilton Depression Scale scores and reduction in binge eating were significantly correlated, suggesting a connection between antibulimic and antidepressant drug effects. Mitchell and Groat in a double-blind controlled study using amitriptyline observed similar results [66].

Brotman et al reported on an uncontrolled retrospective study of 22 bulimics treated with at least one therapeutic trial of antidepressants [67]. Of 17 depressed bulimics, 10 achieved a remission in depressive symptoms. Only 4 of these 17 depressed bulimics maintained both a decrease in binge eating and remission of depression at follow-up. The patients who decreased their bingeing after the drug trial were less often depressed than those patients whose bingeing did not decrease. This study suggests that antidepressant medication may have independent antibinge and antidepressant effects, which would imply a less direct linkage between bulimia and affective illness. However, the fact that four of five true responders had an underlying depression that was successfully treated argues for a more intimate relationship.

In a recent controlled double-blind crossover study, Hughes et al found desipramine to be of value in the treatment of nondepressed bulimics. Sixty-eight percent of their patients were eventually able to completely eliminate their bulimic behaviors within the ten weeks of treatment. Whether this effect could be sustained over a longer time frame is open to question. The desipramine blood levels did not seem to completely predict response but seemed to indicate a group of patients in which response could be enhanced by more aggressive treatment and more rational management of side-effects and compliance. A prior history of anorexia nervosa did not predict response to desipramine, which led the authors to regard the distinction between anorexia nervosa and bulimia with less certainty. This study, while seeming to make a strong statement concerning the independence of antibulimic antidepressant drug effects and perhaps the independence of bulimia and affective illness, is confounded by the fact that over 50% of the patients had a history consistent with a major affective disorder. In addition, the Zung scores (though not in the depressed range) improved significantly in the desipramine-treated group, pointing to a more general effect [68].

The follow-up report of Pope et al based on the patients cited above sheds some more light on this issue. They reported 95% partial improvement in bulimia and 50% complete remission after two years. The improvement was noted not just on measures of bulimia but in a marked reduction in depressive symptoms as well. This suggested to them that antidepressants provide an overall therapeutic effect for bulimmic patients [69].

A double blind study of pheytoin versus placebo in bulimia produced moderate to marked improvement in only 42% of treated patients [70]. However, this was significant compared with placebo. On follow-up of four phenytoin responders, two were observed to relapse after two months while continuing the medication.

Of related interest is a recent case report of the successful usage of another anticonvulsant, carbamazepine, in bulimia [71]. This agent is finding in-

creased applicability in the treatment of bipolar affective disorder. The one bulimic patient who responded, out of the six treated, had a history of brief dramatic mood swings. The observation of mood instability in the eating disorder population has also led others to employ lithium [72,73]. Hsu recently reported on 14 normal weight bulimics who were treated in an uncontrolled fashion with lithium and a cognitive behavioral psychotherapeutic approach [74]. Twelve of these patients improved markedly or moderately, including four of six patients who relapsed or failed to improve with behavior therapy alone. Hsu raises the possibility that lithium achieved its effectiveness as an antidepressant acting on a variant of affective illness perhaps by dampening the dysphoria that precipitates a binge. Indeed, over 70% of his patients had elevated Beck inventories. Hsu was clinically impressed by the mood swings and emotional instability of his patients and suggests that lithium may have provided a general calming effect in emotionally labile patients.

Atypical depression is a classification that has been offered to describe a group of depressives who have a reactive mood and reversal of some of the typical neurovegetative signs of depression. This group seems to respond more effectively to monoamine oxidase inhibitors (MAOI) [75]. The overeating of bulimics and their mood disturbance suggested to investigators that they might indeed also respond to MAOIs. Walsh and coworkers studied six patients who met both criteria for bulimia and atypical depression [76]. All of the patients were reported to respond dramatically to MAOIs. The usefulness of MAOIs in bulimia was further reinforced by Walsh et al in a double-blind controlled study of phenelzine with significant positive effect reported [77].

Pope et al reported on their extensive experience in treating 65 consecutive bulimics with a variety of antidepressants and found promising results with tricyclics, trazadone, and MAOIs, which produced by far the best response [78]. The structure of this study in using tricyclics as the initial drug probably led to the underestimation of the effectiveness of the nontricyclic antidepressants. The authors felt that they could safely conclude that antidepressant medications have a clear place in the treatment of bulimia.

CONCLUSIONS

Certainly the preponderance of data would allow one to conclude that the eating disorders carry with them, at the minimum, an increased risk for developing an affective disorder. The difference in risk between pure restrictive anorexia and bulimia and the heavy loading for affective illness in the families of bulimics point to the potential importance of biologic endowment in this disorder. Still, the nature of the relationship between the eating disorders and affective disorders remains to be clarified.

Hudson et al feel that their data suggest that bulimia may indeed be a forme fruste of an affective disorder [28]. In more recent work, they studied a group of active and remitted bulimics and found high lifetime rates of major affective disorders as well as anxiety and substance abuse disorders. They interpreted their results as providing further support for the existence of a phenomenologic relationship between bulimia and major affective disorder [83]. Strober, in reviewing his data, speculated that some adolescent cases of bulimia nervosa might represent a "phenotypically unique phase-bound manifestation of the affective disorder spectra" or that bulimia nervosa is the product of and final common pathway for different but overlapping etiologic factors of which affective biologic endowment is but one [20]. Gerner and Gwirtsman leaned toward an adrenergic vulnerability model to explain the strong familial association of affective dysfunction in anorexic patients [40].

The successful treatment of some eating disorders with antidepressant agents have led some to conclude that the eating disorders are manifestations of affective illness, but this view may be somewhat overzealous. Walsh et al observed the close variation of bulimic symptoms and depression but backed away from concluding that they are one and the same [75]. Glassman and Walsh caution against equating bulimia with an affective disorder on the basis of response to antidepressants and make the point that everything that improves with an antidepressant is not necessarily depression [79]. They suggest that both conditions may arise from a unitary biological matrix with environmnental and intrapsychic factors determining the final outcome.

In a recent commentary, Altshuler and Weiner strongly question the relationship between anorexia nervosa and depression and raise some troublesome issues concerning reliability of diagnosis, research methodology, and epidemiology [80]. However, they do not distinguish between restrictive anorexia nervosa, bulimia nervosa, and normal-weight bulimia. Also their diagnostic focus was on major depression rather than a broader notion of affective impairment. Both of these factors could certainly contribute to underestimating the potential for linkage between the eating disorders and affective disorders.

Swift et al have concluded that affective disorders and eating disorders are related but in an unclear way. They have proposed an interactive, multidetermined model for understanding this complex relationship [84].

Hinz and Williamson argue that the data does not yet justify the conclusion that bulimia is a variant of an affective disorder. They view bulimia as a chronic psychiatric disorder which, like other chronic disorders, may be accompanied by depression [85].

Even if eating disorders are not manifestations of affective disorders, the high incidence of affective impairment in eating disorder patients must be explained. The issues are sufficiently complex that a multi-axial biopsychosocial approach is necessary for perspective. Garner et al have studied the question of the continuity of anorexia nervosa and have concluded that there are qualitative differences between true anorexia nervosa and weight preoccupation in supposed normals [81]. Despite a culturally reinforced "drive for thinness," many young women flirt with anorexia nervosa and bulimia without succumbing. This leads one to speculate about predisposing factors. Certainly episodic or chronic affective dysregulation could provide a fertile ground for the growth of maladaptive culturally reinforced coping strategies, as may other factors. The affective dysregulation serves to deprive the individual of the emotional stability necessary to surrender maladaptive behaviors and establish less self-destructive defenses.

That there should be greater representation of affectively disordered individuals among bulimics than restricting anorexics should not be all that surprising when one considers the instability created by mood swings and poor impulse control. The bulimia itself represents the shifting internal environment that may be attempting to cope with pubertal body changes, individuation, and autonomy. In addition, the bulimic behaviors are sufficiently complex that they can become self-perpetuating and addicting, particularly when they are seen as providing mood change. Restrictive anorexia, on the other hand, would seem to require different constitutional factors, parenting experiences, and ego defenses.

The clinical encounter requires continuous reformulation as new information is uncovered and new impressions registered. In the treatment of patients with eating disorders, this process is magnified because of the many problems that present simultaneously. Addressing the biological underpinnings is just one factor in what must be a comprehensive rehabilitative effort. However, it is important to appreciate how disorganizing an affective disorder can be—particularly in a young individual who is attempting to consolidate a sense of self. The successful treatment of the underlying affective disorder allows new learning to proceed.

In conclusion, it would seem reasonable for a prudent clinician to maintain a high index of suspicion for a concurrent affective disorder when evaluating or treating a patient with one of the eating disorders, particularly in the context of mood instability, substance abuse, or a family history of affective dysfunction.

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