
1. DEFINITION OF THE DISORDER
Anorexia nervosa is defined as the refusal to maintain body weight at or above a minimally normal weight for age and height (e.g., weight loss leading to maintenance of body weight less than 85% of that expected; or failure to make expected weight gain during period of growth, leading to body weight less than 85% of that expected). In addition, the individual must present an intense fear of gaining weight or becoming fat, even though underweight; a disturbance in the way in which one's body weight or shape is experienced, undue influence of body weight or shape on self-evaluation, or denial of the seriousness of the current low body weight; in postmenarcheal females, amenorrhea, i.e., the absence of at least three consecutive menstrual cycles. (A woman is considered to have amenorrhea if her periods occur only following hormone, e.g., estrogen, administration.). There are two specific types of anorexia nervosa: Restricting Type: during the current episode of anorexia nervosa, the person has not regularly engaged in binge-eating or purging behavior (i.e., self-induced vomiting or the misuse of laxatives, diuretics, or enemas). Binge-Eating/Purging Type: during the current episode of anorexia nervosa, the person has regularly engaged in binge-eating or purging behavior (i.e., self-induced vomiting or the misuse of laxatives, diuretics, or enemas) (American Psychiatric Association, 2000).

Changes in diagnostic categories for eating disorders are present in DSM-IV-TR (American Psychiatric Association, 2000). Anorexia nervosa, along with bulimia nervosa, has been moved to a separate section of the DSM-IV-TR, called Eating Disorders. For both disorders, body image disturbance may now be expressed in different ways, either as a distortion of the experience itself or as the denial of the seriousness of weight loss. The sub-typing of anorexia nervosa now indicates the presence of binge-eating/purging behaviors versus restricting behaviors. A patient who presents with both binge eating and purging behaviors occurring exclusively in the context of anorexia nervosa is now diagnosed as a subtype of anorexia nervosa. Some recent research suggests current diagnostic criteria are too restrictive. For example, the criterion used in some research studies is defined as at least ten percent below ideal weight.
This definition does not meet the criteria for the International Classification of Diseases (ICD) 10th revision (World Health Organization, 1992) or for the Diagnostic and Statistical Manual-IV (DSM-IV), which is defined as weight loss leading to maintenance of body weight less than 85% of that expected; or failure to make expected weight gain during period of growth, leading to body weight less than 85% of that expected. The implications of the degree of weight loss, per se is unclear, as the psychological aspects of the illness often proceed weight loss and failure to address them incipiently may result in more severe cases. Further, weight loss criteria are problematic for those patients who begin dieting at above average weights, and so are required to persist in weight losing behaviors for longer before meeting these criteria. In either case, the specific weight threshold is not based on clear scientific evidence as a diagnostic cut-point, but rather as one that is seen as clinically significant.

2. PREVALENCE AND EPIDEMIOLOGY

A classic eating disorder, anorexia nervosa represents a relatively common and significant disturbance that requires a carefully coordinated and comprehensive intervention. Anorexia nervosa is the third most frequent (approximately 14.6 per 100,000 females) condition in adolescent females between the ages of 15 through 24 years (Lucas et al., 1991). This illness often becomes a chronic where multiple hospitalizations and prolonged treatment are common. There is evidence that treatment can be successful, but even with successful treatment, it is unclear if there is ever complete resolution of significant risks and vulnerabilities for recurrence.

There is significant progress in our epidemiologic database. More recent studies are population based, specifically target juveniles, and employ state of the art two-phase screening designs. From these studies, it appears that the prevalence of eating disorders in adolescence has increased over the past 50 years (e.g. Lucas et al., 1991). While anorexia nervosa continues to be more prevalent in the western industrialized nations of white ethnicity, and in middle and upper-class females, there is an increasing diversity of ethnic and SES groups, including African, Asian, and Indian groups.
In anorexia nervosa, Lucas et al. (1991) performed a population-based incidence study in Rochester, Minnesota over a 50 year span (1935-1984). The incidence rate for anorexia nervosa in females decreased from 16.6 per 100,000 person-years from 1935-1939 to seven in 1950-1954, but then increased to 26.3 in 1980-1984. The incidence rate for women over 20 years of age remains constant, but there is a significant increase for females 15-24. The overall age-adjusted incidence rate for females is 14.6 and for males, 1.8. Lucas and colleagues suggest that the increase in the 15-24 year old group mirrors times in history in which the media portray thinner models, actors, and celebrities. The more severe and unremitting form of anorexia nervosa has remained constant, but teenagers may be more vulnerable to cultural pressures, and thus develop a milder form of the illness in response to such pressures.

3. CLINICAL DESCRIPTION

In anorexia nervosa, we observe the co-occurrence of pathological thoughts and emotions concerning appearance, eating and food, as well as, eating behavior that is deviant leading to alterations in body composition and functioning that are the direct result of these symptoms. Such an eating disorder is a classical "psycho-somatic" syndrome, in the sense that psychological and somatic functioning are inextricably intertwined. Depression and anxiety disorders often co-occur with anorexia nervosa. Anorexia nervosa is often conceptualized as a developmental disorder. However, few prospective studies examine normative and pathological phenomena in populations at risk to establish the developmental psychopathology. There are only a few studies employing longitudinal designs that begin in prepuberty (e.g., Attie and Brooks-Gunn, 1989; Marchi and Cohen, 1990; Killen et al., 1994).

4. ETIOLOGY AND PATHOGENESIS

While the causes of anorexia nervosa remain unknown, most research suggests multiple determinants for the development of this illness. A review of the many studies of risk factors for anorexia nervosa is structured here in terms of the major developmental phases of childhood and adolescence. Fairburn et al. (1999) structured their analysis of risk factors for anorexia nervosa in terms of those that increase the risk of psychiatric disturbance in general, and those that increase the risk for dieting behavior. Regarding
personal vulnerability factors, those with anorexia nervosa showed greater levels of exposure than healthy controls on negative self-evaluation, perfectionism, a lack of close friendships, major depression, drug abuse, deliberate self-harm and parental depression. Regarding dieting behavior, girls with anorexia nervosa showed an increased exposure when compared to healthy controls to a family member dieting for any reason, critical comments about weight, shape, or eating, and repeated comments by others about weight or shape (Fairburn et al., 1999).

The study of the neurobiology of eating disorders has demonstrated impressive hormonal and neurohormonal system differences in adult and late adolescent patients who are actively ill (e.g., Ferguson & Pike, 2000). Levels of Histidyl-Diketo-Piperazine, a hormone that is involved in the induction of satiety, are shown to increase as those with anorexia nervosa gain weight. This hormonal change may be responsible for premature feelings of satiation. The 20% of those with diabetes mellitus who develop an eating disorder provides evidence that insulin-glucagon systems may be involved in the predisposition of anorexia. In addition, because caloric requirements for weight rehabilitation and maintenance have been shown to differ in patients with anorexia nervosa, bulimia nervosa, and control populations, this may suggest premorbid metabolic abnormalities that act as risk factors for anorexia (Steinhausen, 1995). It is not clear whether any of these changes can be generalized to non-chronic adolescent populations, whether they represent specific risk factors, or are brought on by starvation and perpetuate illness; or, are simply the result of bodily changes due to starvation and semi-starvation. Most of these observed biological differences appear to normalize after refeeding.

Personality differences have been repeatedly found by multiple methods and from a variety of theoretical backgrounds (temperament, personality, ego psychology), showing anorexic girls to be anxious, inhibited and controlled, while bulimic patients tend to be more affectively labile, under-controlled and active (e.g, Shaw and Steiner, 1997). Fairburn et al. (1999) found that negative self-evaluation and perfectionism were common psychological traits in those with anorexia nervosa as compared those with other psychiatric disturbances. These results are consistent with other findings that show not only that
perfectionism and obsessive-compulsive personality traits being more common in those with anorexia nervosa, but also that these traits promote dieting behavior.

Personality traits such as being concerned about the opinions of others creates a greater vulnerability to respond to social pressures. Likewise, a desire to avoid conflict predisposes the anorexic to focus on the easily controllable domain of the body and weight rather than focusing on interpersonal conflicts. Being a perfectionist and self-disciplined makes it relatively easier to hold to a strict diet and exercise regimen necessary for the maintenance of the disorder. Halmi et al. (2000) showed that the scores of patients with anorexia nervosa exceeded those of non-clinical controls on the Multidimensional Perfectionism Scale (MPS) and on the Eating Disorder Inventory (EDI) perfectionism subscale. Both the MPS and the EDI were highly correlated with each other for those with anorexia nervosa. This data suggests that perfectionism is a strong and informative characteristic of anorexia nervosa. In conclusion, each of the above-mentioned characteristics, in the presence of a stressor, adds to the cumulative risk for the development of anorexia nervosa.

A variety of non-specific factors have been associated with anorexia nervosa. Being of female gender, having a high parental social class, familial focus on food, health, fitness and appearance, being acculturated into Western culture, having a pear shaped body and a body mass index high in fat are identified as constituting risks. Women diagnosed with an eating disorder in some studies have reported a high incidence of sexual abuse. Male university students who reported physical and sexual abuse in childhood were also at a greater risk for eating disorders (Kinzl et al., 1997). However, in females, the rates of abuse seem higher in bulimia nervosa than anorexia nervosa. The nature of this relationship is difficult to assess because of differences in diagnostic criteria for abuse, a high base rate of sexual abuse in the general female population, and a high rate of abuse associated with other psychiatric diagnoses. The issue is insufficiently explored in juveniles.

The relationship between the age of onset and outcome in anorexia nervosa is still unclear, mostly because
of methodological problems. In addition, one must be careful in assessing pathology in different age
groups because we are not certain what anorexia might look like in different age cohorts. Expressing a
drive for thinness at age eight may not result in any significant weight changes, but this same behavior in
adolescence can be tied to reduced caloric intake (Steinahusen, 1995). Anorexia nervosa does seem to
develop at a precise time in adolescent development and some suggest that this may be explained by a
patient’s inability to manage the developmental demands of adolescence (Bruch, 1978). Adolescence is
also a time marked by an increase in adipose tissue for females and an unease and unhappiness with
bodily appearance. A recent study investigated the risks for weight concerns in a community sample of
adolescent girls, between 12 to 14 years of age using as self-report version of the EDE (EDE-Q). In a
sample of 808 non-clinical schoolgirls, 34% stated they had a strong desire to lose weight, of these, 34%
had a BMI less than 20 (Carter et al., 1997). Twenty-four percent restricted food to influence their
weight and shape, and 5% fasted for eight hours for more than half the days. Thirty-eight percent
reported vigorous exercise to control their weight.

There continues to be evidence for the familial clustering of eating disorders and eating attitudes
suggesting a role for heritable causation, but there are no adequate longitudinal studies controlling shared
and non-shared environments. There is a three to ten percent prevalence for eating disorders with siblings,
27% with mothers, 16% with fathers, and 29% with first-degree relatives (Steinhausen, 1995). While
these numbers do not clear up the relative contributions of environment versus genetics, in families of
those with anorexia nervosa, there is evidence of increased parental eating disorders, family dieting, and
adverse comments from family members about eating, weight, or appearance (Faiburn et al., 1999).
Studies of families find distinct characteristics by both self-report and observational methods. Families of
anorexic patients appear more controlled and organized. These trends are also apparent in observer rated
transactions (Humphrey, 1989). However, the addition of other psychopathological contrast groups and
non-clinical families sometimes obscures these differences.

**Preschool:** It is debated if there is continuity between eating problems in early childhood and those of
adolescence. Demographics of early feeding problems suggest discontinuity, because boys are at greater risk of eating disorders in early childhood while in adolescence, girls become at greater risk. However, Agras et al. (1999) showed that infant feeding behavior and body mass during the 1st month of life predicted the emergence of childhood disordered eating. These results suggest that eating disturbances may begin in childhood and be a function of both parental and child characteristics. Marchi and Cohen (1990), using a lagged design, studied two different overlapping (ages 0-10 and 9-18) cohorts and followed them prospectively for 2.5 years. They studied six eating behaviors at three time points by maternal interview and found that maladaptive early eating patterns increased the likelihood of later problems. Picky eating and digestive problems predict pre-anorexic behavior. The number of subjects followed were too small to capture the onset of anorexia nervosa, so presyndromal definitions of the illness were accepted. Other salient features of eating disorders were not studied.

Prepuberty and Adolescence: Unlike school age children, dieting is found to be for the purpose of weight lose in 40%-60% of high school girls (Steinhausen, 1995). In a short-term prospective study, Attie and Brooks-Gunn (1989) tested the hypothesis that the development of eating problems represents an accommodation to puberty, following 193 girls from seventh through 10th grade for two years. Multiple regressions confirmed that eating problems emerged in response to pubertal change, especially fat accumulation. Girls who felt most negatively about their bodies at puberty were at highest risk for the development of eating difficulties, after initial eating problem scores were taken into account. Several cross-sectional studies identify problems that associate with disturbed eating and with body dissatisfaction in prepuberty.

Contextual risk factors in this developmental phase are described and include: teasing by peers, discomfort in discussing problems with parents, maternal preoccupation with restricting dietary intake, and acculturation to the Western values in immigrants. First generation immigrants, for example, are less likely to develop anorexia nervosa then the second and later generations. Interestingly, French et al. (1996) report that of the adolescence from a population based sample of 7-12 graders, homosexual males
reported far greater disordered eating and weight concerns than heterosexual males.

RISK FACTORS FOR ANOREXIA NERVOSA: THE DEVELOPMENTAL VIEW

Social Context

- Temperament
- Eating regulation
- Attachment
- Self-Regulation

Sequela

- Eating regulation
- Temperament

Birth

Adul
5. DIFFERENTIAL DIAGNOSIS

After insuring that the patient’s weight loss is not due to a medical condition, the major problems for the diagnostician is to make certain that the patient who is presenting with severe weight loss and weight preoccupation is indeed suffering from anorexia nervosa. The major alternative considerations are: major depression that is accompanied by weight loss due to appetite suppression and decreased mood, a psychotic disorder that involves a paranoid or delusional belief about eating or weight, and an obsessive compulsive disorder that involves rituals about food and weight but is characterized as undesired or ego-dystonic. Careful interviews with patients, family members, and other clinicians are required to clarify diagnostic questions of this type.

Aside from making sure the patient has anorexia nervosa, it is important to consider the possibility of co-morbid psychiatric illnesses. Much research has investigated the co-occurrence of eating disorders with other psychiatric syndromes. Most eating disorder patients who are included in research projects come from specialized eating disorder clinics and there may be an overrepresentation of more seriously compromised individuals. Herzog et al., (1996) studied a large clinic sample of mixed adults and adolescents and found that about 63% of all eating disorder patients had a lifetime affective disorder. This comorbidity was especially high in patients with mixed anorexic and bulimic features. Depression and anorexia nervosa show independent familial transmission. Others suggest high level of anxiety disorders in anorexia nervosa on 6 year follow up, occurring separately from and together with persistent eating disorders. Rastam (1992) found 35% of anorexic patients also suffer from co-morbid obsessive-compulsive disorder. Substance abuse is commonly diagnosed in patients with eating disorders (e.g., Corcos et al., 2001). A moderate degree of overlap between avoidant personality and anorexia nervosa has been shown in adult patients, but it remains debatable whether such findings are applicable to adolescents or children.

6. CLINICAL INSTRUMENTS AND METHODS FOR DIAGNOSIS
The assessment of eating disorders remains a complex area of clinical activity, because the disorders present with a mix of disturbances in multiple domains with overlapping symptoms. Specific structured interviews (e.g., the EDE - Cooper and Fairburn, 1987) are available in both adult and child forms. The Eating Disorder Examination is applicable to patients less than 14 years of age (e.g., Bryant-Waugh et al., 1988). Clinical self-reports are also available: the Eating Disorder Inventory (EDI) has normative data down to age 14 years (Shore and Porter, 1990). The Eating Attitudes Test (EAT-26) has a version applicable to school-age children (Maloney et al., 1988), the KEDS to middle school children.

7. TREATMENT

Treatment of anorexia nervosa requires that individual, familial, medical, and nutritional aspects of the disease be addressed using a comprehensive and multidisciplinary approach. Guidelines for the psychiatric and medical treatment of anorexia nervosa are published (Yager et al., 1993; Society of Adolescent Medicine, 1995), though the focus is more on adult populations. With adolescent patients, most clinicians base their interventions on one of three approaches: individual psychodynamic therapy (e.g., Bruch, 1978); family therapy (e.g., Minuchin et al., 1978); or family-based treatment (e.g., Dare & Eisler, 1997).

In the United States, the role of hospitalization for anorexia nervosa has changed dramatically over the past ten years. Currently hospitalization in America is limited to brief, acute weight restoration and refeeding. A low discharge weight may create the unnecessary risk for relapse and poor prognosis. Studies report up to 40% of hospitalized patients with anorexia nervosa are readmitted at least once, and with each successive hospitalization the length of stay was longer in duration than any other nonorganic disorder. The Society of Adolescent Medicine’s publication of medical treatment guidelines suggests a more consistent pattern of acute hospitalization for patients with anorexia nervosa. (Society of Adolescent Medicine, 1995) Inpatient treatment studies of young adults suggest a continued role for this modality for severe cases. However, because of inpatient treatments high cost and its disruption of
an adolescence normal life, outpatient treatments are of great importance. Studies of intensive day
treatment programs also are suggestive, but specific studies of children and adolescents in such settings
are lacking.

A large variety of outpatient approaches to individual, family, and group therapy are employed in the
treatment of anorexia nervosa. Specific research in adolescent anorexia nervosa has found the most
promising results in the treatment effectiveness of family therapy. Russell et al. (1987) treated
adolescent patients (less than or equal to 18 years of age, with an illness duration of less than three
years) with family therapy for one year. In his model, the parents are is encouraged to take charge of the
patient's eating under weight is restored and normal eating is resumed. This therapy was compared to
individual therapy that emphasized support, education, and problem solving. Outcomes at a one-year
follow-up were decidedly superior for the younger patients (under 19 years of age) who received family
therapy and superior for the older patients who received individual therapy. Other therapies that may be
helpful for adult patients and may help adolescents include Cognitive-Behavioral Therapy (Agras, 2000),
Interpersonal Therapy (IPT) (Agras, 2000) and Dialectical Behavioral Therapy (DBT) (Safer et al.,
2001). Nonetheless, in a study of four psychotherapies for adults with anorexia nervosa, none appeared
be promising (Dare et al., 2001).

Psychopharmacological interventions for anorexia nervosa have been examined in adult samples, but the
use of these agents in adolescents is relatively unexplored. During periods of acute medical compromise,
psychopharmacologic agents appear to be of limited use. Among adult patients, medications that have
been most frequently used include antidepressants and low-dose neuroleptics. Low dose neuroleptics
are used to address severe obsessional thinking, anxiety, and psychotic-like thinking, but pose problems
with binge induction and little evidence of other benefits compared to controls. Several older studies,
although small in sample size, demonstrated few significant improvements in patients using
psychopharmacologic intervention. Studies that are more recent have explored the role of serotonin
reuptake inhibitors in the treatment of anorexia nervosa in terms of relapse prevention, but systematic
studies are not yet available. New agents, such as the atypical psychotics, are also used, but evidence for their effectiveness is sketchy.

8. COURSE AND PROGNOSIS

The course of anorexia nervosa is variable with some patients recovering completely after the index episode. Other patients develop a fluctuating course of weight gains and losses while some remain in a chronically deteriorating course. Some authors suggest a starvation dependence model likening it to alcohol dependence. Under such a hypothesis, patients are both psychologically and physiologically addicted to the effects of starvation, and that persistent weight loss may reflect a tolerance for starvation. More than a third have recurrent affective illnesses and suicide has been reported in up to 5% of patients with chronic anorexia nervosa. Although vocational and academic functioning may be good, psychological and social impairment persists even after weight restoration.

Varieties of studies have looked at the short, intermediate, and long-term outcome of patients with anorexia nervosa after treatment. Most of these studies are of adult populations, although many of the patients in these studies presumably had anorexia nervosa as teenagers. Studies have generally demonstrated that approximately half have good outcome, a quarter have intermediate outcomes and about a quarter do poorly. (e.g., Steinhausen et al., 1993) Recovery in these studies generally has been confined to measures of weight and nutritional rehabilitation, but some studies indicate that other psychiatric and social aspects of the illness may persist. Others report that the bulimic subtype of anorectic patients had a higher short-term recovery rate than restricting anorectics, but this finding is contested. In a study comparing the outcomes of patients with anorexia nervosa and bulimia nervosa, researchers found that more than twice of those with bulimia nervosa achieved full recovery when compared to those with anorexia nervosa, and approximately one third of each group relapsed after full recovery (Herzog et al., 1999).

Treatment compliance and personality variables may be important moderators of improved treatment
outcome, and a poor prognosis for a previous treatment is a strong indicator for a patient’s response to a new treatment. Higher levels of general psychopathology increase the risk of poorer treatment outcomes. Historical studies suggest that outcome was least favorable for subjects who had experienced great initial weight loss followed by repeated inpatient treatments. Complications during pregnancy, premorbid obesity, and a premorbid eating disorder were most important in predicting poor long-term outcome. A cross-cultural study revealed that outcome for an adolescent eating disorder is relatively similar across cultures, and that the later the onset the better the prognosis (Steinhausen et al., 2000).

Anorexia takes a great toll on reproductive functioning as well. Patients may fail to ovulate, experience oligomenorrhea, amenorrhea, reduced sex drive, infertility, and hyperemesis gravidarum. If pregnancy is achieved patients should be monitored and viewed as being high risk. Often there is insufficient weight gain, underweight babies for gestational date, higher frequency of cesarean section births, low birth weight infants, increased congenital anomalies, increased neonatal morbidity, and problems in infant feeding. During motherhood, patients show increased postpartum depression than non-clinical controls. Recent studies continue to document that the most significant medical problems for adolescents differing from adults are the potential for significant growth retardation, pubertal delay or interruption, and peak bone mass reduction.

Risks of death because of complications of anorexia nervosa are estimated at 6-15%, with half the deaths resulting from suicide. In a prospective 21-year follow-up study, 16% of 84 patients with anorexia nervosa had died (mortality rate 9.8) on account of the disorder and its complications and 10% still met full diagnostic criteria (Loewe et al., 2001).

9. PROMISING AREAS FOR FUTURE INVESTIGATION
Anorexia nervosa is a serious and potentially life-threatening condition. This disorder is pervasive in adolescence and is of unknown causes, however, it appears that anorexia nervosa develops out of a particular social, psychological, biological, and familial context. There is an insufficient understanding of how to effectively treat anorexia, but early family therapy treatment appears promising. Treatment in
the first year of onset yields the best outcomes overall. Pharmacological treatment does not appear to alleviate the core symptoms of anorexia nervosa, such as the disordered thought processes prevalent in this eating disorder. Pharmacological interventions may, however, be useful in treating the symptoms of a comorbid disorder, such as depression, anxiety, and obsessive compulsive disorder, accompanying anorexia nervosa.

Any developmental model of eating disorders must account for the normal development of complex factors in multiple domains and their interaction, in order to establish risks and causal models, but as it currently stands, we have many deficiencies in our knowledge base. Available data support a multidimensional model of eating disorders, encompassing cultural, social, psychological and biological variables as important in the pathogenesis and diagnosis and treatment. This is a conservative model that may only reflect our ignorance. More is known about risk, very little about protective factors. Longitudinal studies investigating the relationship between risks and disturbances have not been well documented across all developmental phases. Future studies need to longitudinally investigate developmental pathways which lead to the naturalistic development of anorexia nervosa.

Ten years ago, treatment outcome studies were rare, especially those applying standardized instruments - this clearly has changed. There are some persistent methodological problems: most studies involve mixed samples of adults and juveniles; age of onset of illness and duration of illness is rarely controlled for, and thus may confound treatment results. What is needed are studies to address this issue from a developmental perspective. This may require a tailoring of treatment to developmental stage - something that has been done infrequently to date. Randomized, controlled clinical trials, sophisticated, multi-center comparisons as well as studies investigating the long-term efficacy of psychotherapies of different types as well as psychopharmacological interventions all need to be further pursued.
References


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