Stunting of Growth as a Major Feature of Anorexia Nervosa in Male Adolescents

Dalit Modan-Moses, Amit Yaroslavsky, Ilia Novikov, Sharon Segev, Anat Toledano, Edith Miterany and Daniel Stein

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Stunting of Growth as a Major Feature of Anorexia Nervosa in Male Adolescents

Dalit Modan-Moses, MD; Amit Yaroslavsky, MD; Ilia Novikov, PhD; Sharon Segev, BSc; Anat Toledano, BSc; Edith Miterany, MD; and Daniel Stein, MD

ABSTRACT. Objective. To assess growth retardation in male adolescent patients who have a diagnosis of anorexia nervosa (AN) and the effect of weight restoration on catch-up growth.

Methods. Medical charts of all male adolescent AN patients (n = 12) who were admitted to the Pediatric Psychosomatic Department at the Sheba Medical Center from January 1, 1994, to December 31, 1998, were reviewed. Height and weight measurements were obtained before the onset of AN, at admission, and thereafter routinely during hospitalization and follow-up.

Results. Eleven patients exhibited growth retardation during the course of their illness, as evident in a decrease in their height standard deviation score (SDS). The mean height SDS at the time of admission (−0.81 ± 0.93) was significantly lower than the premorbid SDS (−0.21 ± 0.91). Weight restoration resulted in accelerated linear growth (up to 2 cm/mo) in all patients. Positive weight gain (weight gain rate >1 kg/y) was associated with a mean height gain of 6.97 ± 6.48 cm/y, whereas weight loss or failure to gain weight (weight gain rate ≤1 kg/y) was associated with a mean height rate of 2.7 ± 3.9 cm/y. This between-group difference was highly significant. Complete catch-up growth was not achieved in 9 of 12 patients. There was a trend for the mean adult final height SDS (−0.52 ± 0.84) to be higher than the admission height SDS but lower than both the premorbid height SDS and the midparental target height SDS (−0.21 ± 0.79).

Conclusions. Linear growth retardation was a prominent feature of AN in our sample of male adolescent patients, preceding, in some cases, the reported detection of the eating disorder. Weight restoration, particularly when target weight is based on the premorbid height percentile, may be associated with significant catch-up growth, but complete catch-up growth may not be achieved. Pediatrics 2003;111:270–276; anorexia nervosa, growth failure, final height, malnutrition, male.

ABBREVIATIONS. AN, anorexia nervosa; DSM-IV, Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition; SDS, standard deviation scores; IBW, ideal body weight.

The need for adequate caloric intake, weight gain, and body fat for the progression of growth and puberty is well documented. In children, starvation or illness is associated with a decreased growth rate, whereas recovery or refeeding results in accelerated linear growth, often referred to as “catch-up” growth.1–3 However, to the best of our knowledge, there are no recent systematized studies concerning the effect of undernutrition during puberty on growth rate and final adult height.

Animal experiments have shown that if growth is slowed for prolonged periods or into puberty, then complete catch-up (ie, attainment of expected final height) is not achieved.1 Findings in humans are less consistent, however. Acheson4 claimed that complete catch-up growth is not achieved because during starvation, skeletal maturation is not slowed down as much as linear growth. By contrast, Prader and Tanner1 and Lacey et al5 found that the rate of bone-age progression during the recovery phase may be lower than the rate of linear growth catch-up, so the final relation of height to bone age may return to normal.

Anorexia nervosa (AN), characterized by a significant reduction in current or expected weight; refusal to gain weight; amenorrhea; and a disturbance in body image, overvalued importance of weight for self-esteem, or denial of the severity of weight reduction,6 represents a ready group for studying the effect of caloric restriction during adolescence on growth. There have been several reports of AN7,8 or other forms of voluntary caloric restriction9,10 presenting as growth failure or short stature. Reports regarding catch-up growth range from failure to gain any height7 to complete catch-up growth.2,7,9 This apparent discrepancy reflects small patient series, heterogeneous patient populations, variable duration of follow-up, and absence of premorbid growth data.

Several hormonal changes may contribute to growth retardation in AN. These include low thyroxine (T4) and triiodothyronine (T3), elevated cortisol, and low sex hormone levels.11–13 Growth hormone resistance—characterized by growth hormone hypersecretion and low serum levels of growth hormone-binding protein, insulin-like growth factor I, and insulin-like growth factor-binding protein 3—has also been related to growth failure in patients with AN.14,15

Although AN affects mainly the female gender,
obtained to the nearest 0.1 kg, with the patient wearing a hospital gown and without any footwear.

Premorbid height and weight measurements were obtained for each case from the primary care physician and/or the school nurse. Height and weight measurements were obtained at admission. Thereafter, during hospitalization, weight was obtained weekly and height was obtained monthly. During the outpatient follow-up period, height and weight were obtained at every visit, according to a schedule outlined below. For the purpose of analysis, only height measurements taken at least 3 months apart were considered.

Standard deviation scores (SDS), or z scores, for height and weight were calculated on the basis of data on growth in a reference population from the National Center for Health Statistics (Centers for Disease Control and Prevention, Atlanta, GA). The use of SDS for growth allows for comparison of data obtained at different ages. A z score of 0 corresponds to the 50th percentile, and a z score of −1.0 indicates 1 SD below the mean, which corresponds to approximately the 15th percentile of the reference population.

Percent of height-appropriate body weight was calculated as measured weight/ideal body weight (IBW) × 100, where IBW was defined as the 50th percentile weight corresponding to the age at which the child’s height was the 50th percentile height. The midparental target height was calculated from the average of the parents’ heights, plus 6.55 cm.

Management

After assessment of the nutritional status, a nutritional rehabilitation program is constructed. This program is geared toward a weight gain of 0.5 to 1.0 kg/wk. Target weight is established according to age and the estimated potential height, which is based on the premorbid height SDS.

Patients are discharged on reaching their target weight and maintaining it for at least 2 weeks. After discharge, patients are followed every 2 weeks during the first 2 months, once a month during the next 4 months, and every 3 months thereafter until they have reached the age of 18. In patients who have not finished growing, target weight is readjusted every 3 months during the follow-up period and is increased gradually to allow for the expected height gain, based on the potential height. Patients who terminate their regular follow-up before the age of 18 are invited for a final evaluation around that age.

Data Analysis

Height and weight parameters at admission and at last follow-up were compared using the paired Wilcoxon test. Patients who had growth deceleration before admission were evaluated against the other patients by comparing the distributions in the 2 groups with the Wilcoxon test for independent samples.

To examine the relation of height gain to weight gain, we analyzed the growth data of patients with evidence of growth failure either before hospitalization or during follow-up. Linear-growth rate (cm/y) and weight-gain rate (kg/y) were calculated for each time fragment between 2 serial measurements for each of these patients. We divided the resulting 36 time fragments available into 2 subgroups according to the weight gain being >1 kg/y or ≤1 kg/y. According to the National Center for Health Statistics growth curves, a weight gain of <2 kg/y is below the third percentile for all growing children. The 1 kg/y cutoff point, therefore, represents a particularly strict criterion for failure to gain weight. The relationship between linear growth and weight changes was estimated using Spearman’s nonparametric correlation coefficients in each group. The Wilcoxon test for independent samples was used to compare the average changes in the 2 groups. Results were considered as significant when the 2-sided P value was < .05. Calculations were performed using the SAS 6.12 for Windows software (SAS, Inc, Cary, NC).

RESULTS

Patient Characteristics

The pertinent admission and follow-up data of the 12 patients are summarized in Table 1. The mean age at admission was 14.3 ± 1.6 years (range: 11.7–16.6 years). The mean reported duration of symptoms
before hospitalization was 12.4 ± 11.1 months (range: 3–42 months). Mean duration of follow-up was 38.8 ± 19.4 months (range: 9–78 months). All patients who terminated their regular follow-up before the age of 18 were invited for a final evaluation around that age. Three patients were hospitalized in other institutions before their admission to our department, and 5 patients had recurrent admissions to our facility during the follow-up period because of relapse of their eating disorder. The mothers of 2 of the patients had a history of AN.

**Weight**

Premorbidly, patients tended to be slightly overweight, their weight being 108 ± 8% of their IBW. Three patients (patients 2, 5, and 7) were overweight (weight >120% of IBW). At the time of admission, the mean body mass index was 15.7 ± 1.3 kg/m² (range: 13.5–18 kg/m²). The weight of 4 of the patients (patients 3, 5, 11, and 12) was below 85% of IBW at the time of admission. All patients with growth retardation. In some patients, the apparent “adequate” weight-for-height at the time of admission actually reflects stunting of growth (see also Fig 1B).

### Linear Growth

The mean premorbid height SDS was −0.21 ± 0.91. At the time of admission, the mean height SDS was significantly lower, −0.81 ± 0.93 (P = .008).

Ten of the 12 patients exhibited growth retardation at the time of admission, as evident in a decrease in height SDS at admission, compared with the premorbid height SDS. One patient (patient 2) had evidence of stunted growth 3.5 years before admission, and 3 other patients (patients 4, 7, and 12) exhibited growth retardation at least 1.5 years before hospitalization (Fig 1). In 1 of the 2 patients (patient 3) who did not show growth failure at admission (the other one being patient 6), a markedly decreased linear growth was observed during the follow-up period, before weight restoration. Weight restoration resulted in accelerated linear growth (up to a rate of 16 cm/y) in all patients with growth retardation. In some patients, a “staircase” pattern of growth was observed, ie, rapid weight restoration during hospitalization resulting in accelerated height gain, alternating with growth arrest during periods of weight loss or failure to attain or maintain target weight (Fig 1A).

To define further the relationship between height gain and weight gain, we correlated the changes in height to changes in weight during the intervals between serial height and weight measurements. Only measurements taken at least 3 months apart were considered for this analysis. Thirty-six time fragments were found for the patients with growth retardation. Positive weight gain (weight gain rate >1 kg/y) was associated with a mean height gain of 6.97 ± 6.48 cm/y, whereas weight loss or failure to

### Table 1: Patient Characteristics and Growth Data

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age at Admission (Years)</th>
<th>Reported Duration of Symptoms (Months)</th>
<th>Length of Follow-up (Months)</th>
<th>Premorbid (SDS)</th>
<th>Admission (SDS)</th>
<th>Final (SDS)</th>
<th>Midparental (SDS)</th>
<th>% of IBW</th>
<th>Admission Last Follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>12.4</td>
<td>18</td>
<td>43</td>
<td>0.54</td>
<td>154 (0.32)</td>
<td>180 (0.90)</td>
<td>173.5 (−0.47)</td>
<td>74.4</td>
<td>91</td>
</tr>
<tr>
<td>2</td>
<td>14</td>
<td>18</td>
<td>48</td>
<td>−0.52</td>
<td>150 (−1.70)</td>
<td>166 (−1.36)</td>
<td>181.5 (0.65)</td>
<td>80.3</td>
<td>106.9</td>
</tr>
<tr>
<td>3</td>
<td>11.7</td>
<td>3</td>
<td>78</td>
<td>−0.83</td>
<td>144 (−0.45)</td>
<td>167.5 (−1.19)</td>
<td>167.5 (−1.30)</td>
<td>85.9*</td>
<td>101.5</td>
</tr>
<tr>
<td>4</td>
<td>16.6</td>
<td>6</td>
<td>17</td>
<td>1.39</td>
<td>171.5 (−0.42)</td>
<td>173.5 (−0.37)</td>
<td>178.5 (0.23)</td>
<td>81.3</td>
<td>100.6</td>
</tr>
<tr>
<td>5</td>
<td>15.3</td>
<td>24</td>
<td>9</td>
<td>0.54</td>
<td>173 (0.41)</td>
<td>176 (0.35)</td>
<td>NA</td>
<td>88.1*</td>
<td>90.6</td>
</tr>
<tr>
<td>6</td>
<td>16.2</td>
<td>9</td>
<td>17</td>
<td>−0.35</td>
<td>173 (−0.12)</td>
<td>174 (−0.25)</td>
<td>167.5 (−1.30)</td>
<td>85.3</td>
<td>94.7</td>
</tr>
<tr>
<td>7</td>
<td>16.1</td>
<td>12</td>
<td>32</td>
<td>−1.89</td>
<td>153.5 (−2.50)</td>
<td>173 (−0.54)</td>
<td>180.5 (0.51)</td>
<td>72.7</td>
<td>118.1</td>
</tr>
<tr>
<td>8</td>
<td>15.6</td>
<td>3</td>
<td>50</td>
<td>−0.98</td>
<td>160 (−1.50)</td>
<td>162 (−1.75)</td>
<td>165.5 (−1.60)</td>
<td>82.2</td>
<td>113.7</td>
</tr>
<tr>
<td>9</td>
<td>15.3</td>
<td>2</td>
<td>30</td>
<td>−0.87</td>
<td>158 (−1.60)</td>
<td>161.5 (−1.98)</td>
<td>177 (0.02)</td>
<td>84.8</td>
<td>103.7</td>
</tr>
<tr>
<td>10</td>
<td>12.4</td>
<td>6</td>
<td>42</td>
<td>0.43</td>
<td>152 (0.07)</td>
<td>177 (0.02)</td>
<td>176.5 (−0.04)</td>
<td>81.5</td>
<td>101.1</td>
</tr>
<tr>
<td>11</td>
<td>12.3</td>
<td>6</td>
<td>66</td>
<td>−0.02</td>
<td>148 (−0.39)</td>
<td>173 (−0.26)</td>
<td>181.5 (0.65)</td>
<td>92.7*</td>
<td>92.8</td>
</tr>
<tr>
<td>12</td>
<td>15.2</td>
<td>42</td>
<td>34</td>
<td>0.90</td>
<td>156 (−1.82)</td>
<td>178 (0.16)</td>
<td>179 (0.30)</td>
<td>92.8*</td>
<td>110.1</td>
</tr>
<tr>
<td>Mean</td>
<td>14.3</td>
<td>12.4</td>
<td>38.8</td>
<td>−0.21</td>
<td>157.8 (−0.81)</td>
<td>172 (−0.52)</td>
<td>175.3 (−0.21)</td>
<td>83.5</td>
<td>102.1</td>
</tr>
<tr>
<td>SD</td>
<td>1.6</td>
<td>1.1</td>
<td>19.36</td>
<td>0.91</td>
<td>9.5 (0.93)</td>
<td>5.9 (0.84)</td>
<td>5.7 (0.79)</td>
<td>5.9</td>
<td>8.6</td>
</tr>
</tbody>
</table>

NA indicates not applicable.

* The “admission” data in the table reflect (for reasons of standardization) the height and weight measurements at the time of the first admission to our department, which does not necessarily coincide with the lowest weight-for-height in the course of the disease. Because of this, the weights of patients 3, 5, 11, and 12 seem not to fulfill the DSM-IV diagnostic criteria for AN of refusal to maintain body weight at or above 85% of that expected. Patient 3 met the formal weight criteria for AN later in the course of his illness (worst height-for-weight: age 16.5 years; height: 160 cm; weight: 40 kg; weight-for-height: 82.5% of IBW). Patient 5 was premorbidly obese and had lost 25% of his body weight during the 2 years preceding his admission. At the time of hospitalization, his weight was at 88% of his IBW, but later during his follow-up he met the formal criteria for AN (worst height-for-weight: age 15 10/12 years; height: 176 cm; weight: 56.2 kg; weight-for-height: 84.5% of IBW). Patient 11 was treated in another institution before his admission to our department and thus met the formal criteria for the diagnosis of AN before he presented to our institution (at age 11 8/12 years; height: 145 cm; weight: 31 kg; weight-for-height: 83.8%). Patient 12 had virtually no linear growth during the 2 years preceding his admission, with his height decreasing from the 95th percentile to the third percentile. Thus, his apparent “adequate” weight-for-height at the time of admission actually reflects stunting of growth (see also Fig 1B).
gain weight (weight gain rate ≤ 1 kg/y) was associated with minimal height gain—only 2.7 ± 3.86 cm/y (P < .015; Fig 2). Correlation analysis revealed a significant positive correlation between weight gain and height gain in the positive weight gain group (weight gain rate > 1 kg/y; r = 0.44, P < .04) but not in the negative weight gain group.

Final Height Data
Final height (defined as height at age 17 or older and no linear growth for at least 1 year) was measured by us in 8 of the patients. For the other 4 patients, who terminated their follow-up before the age of 18 and refused to be reevaluated in our facility, final height was measured using a wall-mounted stadiometer in the primary care clinic and reported to us by the patients and parents. Table 1 indicates that despite the growth acceleration after weight restoration, only 2 of the 11 patients with growth retardation (patients 1 and 7) achieved complete catch-up growth (ie, a final height SDS equal to or greater than their premorbid height SDS). The mean final height SDS was −0.52 ± 0.84, whereas the mean midparental target height SDS was −0.21 ± 0.79. Thus, final height SDS tended to be lower than both the premorbid SDS (−0.21 ± 0.91) and the target height and higher than the admission SDS (−0.81 ± 0.93), although the differences did not reach statistical significance (see Fig 3 for the differences between final height and target height). When the patients who were not measured in our facility were excluded, the mean final height SDS for the other 8 patients was −0.71 ± 0.96.

DISCUSSION
The aim of the present study was to assess growth retardation and its correction after weight restoration in male patients with AN. The mean premorbid height SDS of the 12 patients was −0.21 ± 0.91, similar to the expected height SDS in a normal population. The mean premorbid weight, however, was 108 ± 8% of the IBW. Furthermore, some of our patients were overweight (weight > 120% of IBW), consistent with previous reports of male patients with AN.24,25

The results of the present study support both of our hypotheses. Growth failure was a prominent feature in our group of male adolescent inpatients with AN, appearing in 11 of 12 patients. In 10 of these patients, it was already evident at the time of hospitalization, and 1 other patient exhibited growth retardation in the early stages of treatment, before weight gain. Moreover, decreased linear growth preceded the reported onset of symptoms by 1.5 to 3.5 years before the time when symptoms were first noted.
years in a third of our sample. These findings propose that early signs of AN may not be detected in a significant number of male patients with AN, delaying the diagnosis of the disorder.

Weight restoration resulted in accelerated linear growth (up to 2 cm/mo) in all patients with growth retardation. Despite this robust correction of growth failure, complete catch-up growth was not achieved: mean final height SDS of our patients tended to be lower than both the premorbid height SDS and the target height SDS, and only 2 of the 11 patients with growth failure achieved complete catch-up growth (ie, a final height SDS equal to or greater than their premorbid height SDS).

Our results emphasize the utmost importance of a relentless effort to pursue and maintain the target weight of male patients with AN for the restoration of height to the premorbid percentile for age. This is evident in the significant association in our sample of positive weight gain with positive mean height gain and of weight loss or failure to gain weight with minimal height gain. The existence of a significant correlation of weight gain and height gain only in the positive weight gain group lends additional support to this requirement. In a healthy growing child or adolescent or during catch-up growth, a strong correlation between height gain and weight gain is the rule. However, because negative height gain is not possible, different degrees of weight loss all may result in a similar degree of growth failure (ie, lack of linear growth) as evident in the lack of correlation between weight gain and height gain in the negative weight gain group.

The inability to achieve complete catch-up growth in most of our patients further indicates that a weight restoration program geared at restitution of height to the premorbid percentile for age should be initiated as early as possible in the treatment of male adolescents with AN.26 Acceptance of weight as appropriate for height as measured at admission, with no consideration of the premorbid or potential height, may result in perpetuation of growth retardation, leading eventually to short stature.

Previous studies have claimed growth retardation to be an important feature of AN,7,8 with weight restoration resulting in catch-up growth in many patients.2,7,8 However, it has not been established yet whether the growth retardation seen in AN affects final adult height. In the single study that previously addressed this issue,2 final adult heights of 71 patients with AN (13 male and 58 female) were reported. These authors alleged that most patients reached their expected heights. However, the final height percentile was compared with the height percentile at diagnosis, and no reference was made to premorbid height percentiles. Moreover, because only limited information was given regarding the age distribution of this group, it is possible that at least some of the patients had already completed most of their growth before the onset of their illness. Siegel et al27 reported a higher-than-expected incidence of short stature among 10 male patients with AN, but no reference to growth rate or patterns was made. By contrast, our data suggest that the stunted stature of the patients at the end of follow-up (ie, final height SDS \(-0.52 \pm 0.84\)) is the result of pro-

[Fig. 2. Linear growth during periods of positive weight gain—at least 1 kg/y (●)—is evidently much greater than linear growth during periods of weight loss or failure to gain weight (○). Note that in 13 of 16 points corresponding to periods with poor weight gain, the growth rate is subnormal (ie, <2 cm/y).]
longed malnutrition and not related to premorbid short stature (premorbid height SDS: \(-0.21 \pm 0.91\)).

It is important to consider why some of our patients apparently sought medical attention relatively late in the course of their eating disturbance. Lack of awareness of AN in male individuals may be 1 factor that leads to a delay in diagnosis. We further propose that because of the baseline high caloric requirements of male adolescents, decreased caloric intake may go unnoticed for a significant period of time. In addition, weight loss in our patients may have been masked by their reduced height, present already before admission. Finally, growth failure may not be recognized in adolescents whose heights are in the upper percentiles. For instance, 1 patient (patient 12) shifted from the 95th to the 50th height percentile before AN was noticed, perhaps because he was still perceived as normal relative to his peers (Fig 1B).

Whatever the reason, a delay in the diagnosis of AN in male adolescents may result in severe malnutrition and compromised height. Therefore, the diagnosis of AN should be considered in short, underweight adolescents, as well as in youths who demonstrate growth deceleration with hitherto normal height progression. Obtaining a detailed history of caloric intake, attitude to food, body image, and sports participation in such patients may facilitate earlier diagnosis of AN. As the incidence of AN is increasing and the age of onset is decreasing,\(^{11,16}\) the need for prompt evaluation and treatment becomes even more important.

Our series includes 12 patients, which makes it 1 of the largest series describing growth in male patients with AN, and it provides important premorbid and follow-up data as well as final-height data not provided by other series. One possible limitation of our study concerns the reliability of premorbid height, measured by the school nurse. It should nevertheless be noted that in Israel, school nurses are certified public health nurses trained in obtaining anthropometric measurements, and inspection of the growth curves revealed good consistency between different measurements of each patient.

Another limitation of our study is that Tanner stages of sexual development and results of endocrine function tests were not recorded in most of the charts. Therefore, we were unable to investigate the relationships among pubertal stages, onset of AN,
and adult height or to calculate the premorbid predicted adult height. Some may argue that the growth deceleration and subsequent catch-up growth observed in our patients represent the effects of delayed puberty per se. However, close inspection of the growth data precludes this possibility. First, the severity of growth failure observed in some of our patients far exceeds the prepubertal growth deceleration observed in children with delayed puberty, which is in the range of 4.0 to 4.5 cm/y.28,29 For instance, patient 12 had virtually no linear growth for the 2 years preceding his hospitalization (Fig 1B). Indeed, as depicted in Fig 2, linear growth rate was 2 cm/y or less during 13 of 16 time frames that represent the periods of failure to gain weight of all patients investigated. Second, the “staircase” pattern of growth exhibited by some of our patients, ie, periods of accelerated height gain intersected by periods of growth arrest during weight loss or failure to attain or maintain target weight (Fig 1A), is not consistent with a normal pubertal growth spurt. Finally, although patients with delayed puberty may not reach their parental target height,30,31 they typically regain or even exceed their own childhood growth percentile.32 In contrast, in our patients, catch-up growth was incomplete, and their premorbid height percentile was not reached.

CONCLUSION
Our findings support the importance of growth retardation in male adolescent patients with AN. For achieving maximal catch-up growth, premorbid growth data should be obtained, and target weight should be based on the expected rather than the measured height percentile at the time of diagnosis. Larger scale prospective linear studies, which will include sexual maturation evaluation as well as endocrine studies, are required to verify our observations and to define further the factors that influence the final height and the optimal therapeutic approach for optimizing catch-up growth in male adolescents with AN.

REFERENCES
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