# PediatricsinReview

### **Failure to Thrive: Current Clinical Concepts**

Arthur C. Jaffe Pediatr. Rev. 2011;32;100-108 DOI: 10.1542/pir.32-3-100

The online version of this article, along with updated information and services, is located on the World Wide Web at: http://pedsinreview.aappublications.org/cgi/content/full/32/3/100

Pediatrics in Review is the official journal of the American Academy of Pediatrics. A monthly publication, it has been published continuously since 1979. Pediatrics in Review is owned, published, and trademarked by the American Academy of Pediatrics, 141 Northwest Point Boulevard, Elk Grove Village, Illinois, 60007. Copyright © 2011 by the American Academy of Pediatrics. All rights reserved. Print ISSN: 0191-9601. Online ISSN: 1526-3347.



### Failure to Thrive: Current Clinical Concepts

Arthur C. Jaffe, MD\*

Author Disclosure
Dr Jaffe has disclosed
no financial
relationships relevant
to this article. This
commentary does not
contain a discussion
of an unapproved/
investigative use of a
commercial
product/device.

Objectives After completing this article, readers should be able to:

- 1. Characterize the limitations of the classic dichotomy of "nonorganic" versus "organic" failure to thrive (FIT).
- 2. Recognize that FTT is not a diagnosis but rather a physical sign of inadequate nutrition to support growth.
- 3. Know potential sequelae of FTT.
- 4. Understand how the diagnostic process must account for the multifactorial nature of FTT.
- 5. Describe a systems-based, multidisciplinary approach to treatment of FTT.
- 6. Discuss potential adverse effects of nutritional repletion of children who fail to thrive.

#### Introduction

Failure to thrive (FTT) or growth failure has long been a major focus of attention and critical thought for pediatricians. Over many years, consensus has evolved about its cause, outcome, diagnosis, and management. By the last half of the 20th century, mainstream thinking held that FTT developed by one of two alternative mechanisms. On rare occasions, an underlying medical condition could lead to a failure of growth, which would present as "organic" FTT. In such cases, correct management of this underlying disorder would allow the patient to resume his or her normal growth. However, in most FTT cases, as many as 90% in some series, it was believed that no underlying medical diagnosis could be made. Affected children were said to have "nonorganic" FTT (NOFTT). This term and its synonym, "psychosocial" FTT, were often used as euphemisms to imply that the child was intrinsically normal and healthy and that the observed growth failure was due to environmental issues, most commonly family factors such as neglect, indifference, or other failures of parenting. This construct led to children receiving extensive medical evaluations to rule out diagnosable conditions and to prolonged hospitalizations that were designed primarily to document parenting difficulties and demonstrate vigorous and consistent weight gain under the care of hospital personnel. There was concern that, in addition to being at risk for acute complications of severe malnutrition from neglectful or disturbed parenting, children would inexorably suffer long-term adverse neurodevelopmental outcomes.

This view of FTT is now outmoded. According to a large body of newer thinking, FTT is not a syndrome. It is, rather, a physical sign that a child is receiving inadequate nutrition for optimal growth and development. The work of the pediatrician is to determine, in an ordered and logical process, what may be leading to the inadequate nutrition and, when

possible, to treat the underlying pathophysiologic issues, which often are multifactorial. Although this newer construct has now become the current mainstream view of clinicians and researchers working in the field of FTT, readers should be aware that the older, dichotomous view of "organic" versus "nonorganic" FTT may still color the thinking of some health professionals. Specifically, some medical licensure and certification examinations still may ask questions about FTT that reflect this dichotomous approach.

Zenel in 1997 (1) and Gahagan in 2006 (2) wrote thoughtful reviews in this journal that lucidly outline the rationale for reconceptualizing FTT. Rather than repeating their extensive commentaries, this article seeks to

### **Abbreviations**

BMI: body mass index
FTT: failure to thrive
IQ: intelligence quotient
IUGR: intrauterine growth restriction
NOFTT: nonorganic failure to thrive

<sup>\*</sup>Associate Professor, Division of General Pediatrics, Oregon Health & Science University, Doernbecher Children's Hospital, Portland, OR.

complement their work by asking specific questions that highlight salient features of the new model and point out areas of concern or uncertainty that call for further research.

### How Reliable Are Growth Charts for Diagnosing FTT?

Plotting a child's weight, length, and head circumference on standardized growth charts remains a critically important, essential step in providing an objective description of a child's growth and describing how far off the statistical norm he or she is. Frequently quoted chart-based definitions of FTT in children younger than 2 years of age include: a child whose weight is below the 3rd or 5th percentile for age on more than one consecutive occasion, a child whose weight drops down two major percentile lines, a child whose weight is less than 80% of the ideal weight for age, and a child who is below the 3rd or 5th percentile on the weight-for-length curve.

As widely accepted as these definitions are, they are fraught with confusion. For example, the first two definitions require serial measurements over time. How is the clinician to respond when he or she notices a child who is "below the curves" on the first visit? The last two definitions facilitate diagnosis on one visit, but what about a child who does not meet the 80% criterion precisely or is not quite below the 3rd percentile but looks malnourished? These definitions do not provide standards for assessment of the body mass index (BMI) in children older than age 2 years. There is, in fact, some debate about the clinical utility of BMI measurement in very young children. How may the pediatrician most reliably identify FTT in an older child? Unfortunately, no standard uniform approach exists to identify reliably each child who has FTT solely by use of growth curves.

There are other issues. First, the previously cited definitions do not clearly point out the need to evaluate whether a symmetric fall-off in the growth curves is present. They do not explicitly remind the clinician that when the FTT is due to poor food intake, weight tends to fall first, sparing the length and head circumference; that a symmetric fall in weight and height suggests a chronic medical condition; that short stature below the 50th percentile, with relative sparing of weight, suggests an underlying endocrine disorder; or that an early drop-off in head circumference suggests a lack of brain growth. The pediatrician still must exercise clinical judgment in interpreting seemingly objective data.

Also, the widely accepted growth curve-based definitions refer to children who are believed to be generally healthy and free of underlying conditions that are known to affect growth. Children born with certain genetic conditions may appear to have FTT when they are evaluated using normal growth curves, but their perceived growth problems disappear when they are compared graphically to other children who have the same condition. Growth charts are readily available for such genetic conditions as Down, Turner, and Williams syndrome, among others, and it is essential to plot a child's growth on the appropriate curves to determine if FTT truly is present.

Others who require special consideration include children who are chronically immobilized, such as those who have severe neuromotor disabilities. Often, such children have major oromotor dysfunction, are at risk for pulmonary aspiration syndrome, or have other issues that lead to inability to eat by mouth or maintain adequate growth. They often receive feeding gastrostomies to optimize nutrition. However, because they are immobile, they frequently have minimal caloric needs compared with other children and, thus, are at risk for excessive weight gain, even obesity. Such children may be difficult to weigh and measure correctly because of their neurologic status and immobility, making it difficult to assess their status using the standard growth curves. Other anthropometric techniques, such as measuring arm span or the ratio of upper body to lower extremity length, may be more appropriate.

Another concern with the use of growth charts is that clinicians intuitively expect that a child is biologically destined to move along his or her predetermined growth channels inexorably and that any deviation from the original channel indicates a growth aberration. However, Mei and associates (3) described shifts in growth curves during the first 60 months of age in a cohort of 10,844 children. Between birth and 6 months of age, 39% of healthy children crossed two major percentile lines (up or down) on the weight-for-age curve, as did 6% to 15% of children between 6 and 24 months of age. Similar shifts occurred with the length-for-age curve. Strikingly, on the weight-for-height curve, 62% of children between birth and 6 months and 20% to 27% of children between 6 and 24 months crossed two major percentile lines. The authors concluded that pediatricians should consider the prevalence of growth rate shifts during infancy and early childhood before initiating evaluations of growth concerns.

This caveat is humbling, for it is in precisely this age range that the question of FTT often is raised. Careful measurement of weight and length and thoughtful evaluation of the child's growth curves remain essential for diagnosis and management of growth concerns, but the pediatrician must still use clinical judgment and not be overly reliant on arbitrary mathematical definitions of FTT.

### What Are the Sequelae of FTT?

For many years, there has been recognition that the undernutrition seen in FTT in first-world environments is typically not severe enough to lead to clinical conditions such as marasmus or kwashiorkor, although serious nutritional or vitamin deficiency diseases still may occur in very rare cases. However, a rich body of evidence, reviewed by Corbett and Drewett (4) in a 2004 metaanalysis, continues to suggest that poor nutrition in young children, especially infants, may result in longterm problems in cognitive development. On the other hand, Rudolf and Logan (5) reached opposite conclusions in another meta-analysis in 2005. They found that FTT was associated with an intelligence quotient (IQ) 3 points lower than expected, but the difference was of questionable clinical significance. They also reported that early-onset FTT was associated with some persistent reduction in weight and height later in childhood. However, they concluded that there was little evidence that FTT was predictive of damaging consequences for growth and intellectual development. In individual studies, a number of researchers have followed infants or toddlers who had FTT for periods as long as 8 years and reported measurable deficits in IQ, learning difficulties, and behavioral difficulties. (6)(7)(8) Some commentators argue that interpreting these findings is difficult because the study participants tended to have very severe FTT and significantly disordered family environments at the time of diagnosis, including problems such as overt parental mental illness and substance abuse.

Although many children who experience FTT in early life eventually seem to have normal function, the overall trend is worrisome. A meaningful number of children have persistent intellectual or behavioral deficits, and it is currently impossible to predict which children will do well and which will have later difficulties. It is unclear whether energy or protein inadequacy alone is associated with the adverse long-term outcomes or whether deficiencies of vitamins, minerals, or other micronutrients might be responsible. For example, Lozoff and associates (9) showed that infants who experience iron deficiency anemia in infancy have measurably poorer developmental and behavioral outcomes 10 years later, despite having received appropriate treatment at the time of diagnosis.

More recently, attention has started to turn to other, noncognitive developmental outcomes of early FTT. Drewett and colleagues (10) studied a group of 89

12-year-old children who had had FTT as infants. Compared with a control group, they were shorter, lighter, and had lower BMIs, and they reported having lesser appetites. They were satisfied with their body shapes and did not differ from the controls on measures related to anxiety, depression, or low self-esteem. The authors concluded that FTT in infancy is not associated with adverse emotional development in childhood. On the other hand, Raikkonen and coworkers (11) measured scores on a standardized assessment of adult hostility in a large cohort of adults who had a mean age of 63.4 years. The participants' growth histories were obtained by review of their birth, child welfare clinic, and school records. Men and women who had higher levels of hostility in adulthood were born lighter and thinner, showed slower weight gain from birth to 6 months, were lighter throughout childhood, and were heavier in adulthood than were individuals who had lower levels of hostility. There is no current consensus about long-term noncognitive, emotional sequelae of FTT in early childhood.

Although methodologic difficulties continue to present problems in gathering data and analyzing long-term outcomes in children who have FTT, the general trend of the research is to express concern about long-term adverse effects on cognition, learning, and behavior. This line of evidence strongly supports the common current practice of instituting early and vigorous nutritional therapy for children who fail to thrive.

### What is the Diagnostic Approach to FTT?

Recognition that FTT is a physical sign of undernutrition allows a framework for classifying its causes. When considering the differential diagnosis, it is important to remember that FTT often is a multifactorial condition. Because a given patient may have more than one contributing factor to his or her poor growth, diagnostic evaluation should not automatically end as soon as one potential cause is identified. In addition to primary contributing factors, the pediatrician should pay heed to possible secondary exacerbating factors. Family stresses associated with the struggle to get an undernourished child to gain weight or stresses occurring after hearing that the physician is concerned about FTT may add yet another layer of psychosocial factors that potentiate the condition.

Because FTT is a sign of undernutrition, the diagnostic approach must focus on that problem. Undernutrition, broadly speaking, may occur because of one of three mechanisms. The child may have inadequate intake, ingesting insufficient nutrients for growth. Even if taking in adequate nutrients, he or she may have malabsorption

that prevents foodstuffs from being available for growth. Finally, although a child may have both appropriate intake of food and normal absorption across the gut wall, he or she may have increased metabolic demand due to chronic disease or genetic or metabolic disorders. As seen in the Table, this classification scheme allows the clinician to approach the diagnosis of a child methodically and rationally.

As always in medicine, careful and thoughtful consideration must be given to the clinical history. The assessment of whether adequate nutrition is being presented to the child requires in-depth questioning to determine what kinds of milk, formula, foods, and vitamins are being offered. Does the family know what an appropriate diet is for their child's age and developmental level? Are there adequate financial resources for the family to obtain these foods? Is breastfeeding proceeding well, both from the mother's and the child's perspective? Is formula being prepared correctly or is it too dilute? Is the child getting an excessive amount of juice, which may lead to satiety without supplying adequate calories? Is there evidence of neglect? Does the child have intrinsic conditions that interfere with food intake, such as oromotor dysfunction, developmental delay, or feeding aversions due to behavior problems or in learned response to pain? Is there recurrent emesis, suggestive of conditions such as gastroesophageal reflux disease, malrotation with intermittent volvulus, or increased intracranial pressure? Often, obtaining an accurate history of nutritional intake requires the use of a 3-day food diary, with consultation by a nutritionist to calculate actual intake of energy, protein, vitamins, and minerals.

The history also should address the possibility of malabsorption syndromes, with detailed questions about stool frequency and consistency. Many states now require newborn screening for cystic fibrosis, and those results should be obtained, although such screening does not have 100% sensitivity or specificity. A family history of respiratory and gastrointestinal disorders should be elicited. Most children older than 6 months of age have been exposed to baby foods that contain gluten, so celiac disease is a frequent diagnostic consideration. Questioning should probe for a family history suggestive of celiac disease or endocrine conditions that may be associated with that diagnosis. In addition, if the child is having abnormal stools, the physician should ask about a family history suggestive of milk protein intolerance or sensitivity.

If concerns about a specific chronic disease that could increase metabolic demand are not raised during the initial clinical history, a detailed review of systems should

## Table. Diagnostic Classification of Causes and Selected Examples of Failure to Thrive

#### Inadequate Nutritional Intake

- · Not enough food offered
  - -Food insecurity
  - Poor knowledge of child's needs
     Poor transition to table food
     Avoidance of high-calorie foods
  - -Formula dilution
  - -Excessive juice
  - -Breastfeeding difficulties
  - -Neglect
- · Child not taking enough food
  - -Oromotor dysfunction
  - -Developmental delay
  - -Behavioral feeding problem
    Altered oromotor sensitivity
    Pain and conditioned aversion
- Emesis
- -Gastroesophageal reflux
- -Malrotation with intermittent volvulus
- -Increased intracranial pressure

### Malabsorption

- · Cystic fibrosis
- Celiac disease
- Food protein insensitivity or intolerance

#### Increased Metabolic Demand

- Insulin resistance (eg, intrauterine growth restriction)
- Congenital infections (eg, human immunodeficiency virus, TORCH)
- Syndromes (eg, Russell-Silver, Turner, Down)
- Chronic disease (eg, cardiac, renal, endocrine)

be undertaken to search for subtle suggestions of issues such as congestive heart failure, chronic renal disease, or endocrine disorders that may be associated with FTT. Importantly, the physician should ask about the perinatal history, with attention to possible intrauterine growth restriction (IUGR). Evidence now strongly suggests that IUGR from any cause may be associated with insulin resistance, which has long-term implications for growth potential and adverse metabolic sequelae if excessive weight gain is induced.

The complete physical examination should focus on any clinical questions that have been raised during the history. It is appropriate to look carefully for subtle signs of dysmorphology, such as minimal discrepancies in limb length that may be found in Russell-Silver syndrome. If initial growth measurements have not included the head circumference and weight-length ratio or BMI, they should be obtained. If readily available, caliper measurement of skinfold thickness and mid-arm muscle circumference can provide valuable information about a child's nutritional status.

### What is Involved in the Laboratory Evaluation of FTT?

According to the classic view of FTT, in which it was essential to identify any "organic" causes, extensive screening was undertaken to eliminate any and all possibilities before making the diagnosis, by exclusion, of "nonorganic" or "psychosocial" FTT, with its implication of faulty parenting. However, as far back as 1978, Sills (12) clearly showed that laboratory studies had very little, if any, clinical utility in the evaluation of FTT. In his retrospective review of 185 children hospitalized for FTT, he found that 34 (18%) had proven organic causes. In all 34 patients, the specific diagnosis was strongly suggested by the history and physical examination findings. A total of 2,607 laboratory tests were undertaken for the entire group of 185 patients. Only 36 tests (1.4%) were of positive diagnostic assistance, and all of them were in the 34 patients whose diagnosis was strongly suggested by history and examination. No unsuspected diagnoses were uncovered by the results of any of the 2,607 laboratory tests.

Today, there still is no evidence to support the extensive, systematic use of screening laboratory evaluations in diagnosing FTT. Consideration of diagnostic possibilities according to the modern construct portrayed in the Table should lead to a rational, cost-efficient, case-based approach to evaluation. However, this more narrow approach has potential difficulties. Often, when the physician identifies FTT and tells the family that their child is not growing normally, the family fails to see a problem. They may look at growth curves and even understand them, but they see a child who appears to be healthy, active, and meeting developmental milestones.

Before the physician can investigate possible psychosocial barriers to adequate nutritional intake, he or she must make a therapeutic alliance with the family. Achieving this goal may require convincing the family that due attention is being given to the possibility of occult organic disease, necessitating the ordering of some laboratory tests to foster the relationship with the family. Obtaining laboratory studies also allows the pediatrician to explain to the family that early investigation of environmental, psychosocial, or behavioral causes of FTT is a coequal part of the overall comprehensive evaluation of

their child's clinical status. Developmental, oromotor, social work, or mental health consultations are part of the routine diagnostic armamentarium and are not deferred until an occult organic disease has been proven not to exist.

When the physician feels that laboratory studies are warranted, even when there are no specific clinical indications, a reasonable selection might include a complete blood count with red cell indices (to evaluate for anemia and iron deficiency), a complete chemistry panel (including tests for renal and hepatic function), celiac screening, stool examination for fats and reducing substances, and a sweat chloride test for cystic fibrosis. Screening for hypothyroidism or growth hormone deficiency should be considered only if the child's length has decelerated and is below the 50th percentile on the length-for-age chart. Of note, a length above the 50th percentile is strong evidence that no endocrine disorder is present.

### How Much of the Evaluation May Occur in the Pediatrician's Office and When is Hospitalization Indicated?

The chronicity and the multifactorial nature of FTT mean that a major investment of time and energy is necessary for optimal evaluation and management. The professional expertise of the pediatrician caring for a child who has FTT is best demonstrated by use of a systems-based approach. In addition to the pediatrician's skills in medical diagnosis and management, there is a need for evaluation of the child's temperament and development, oromotor functioning, nutritional needs and deficits, and family and social support systems. The pediatrician is served best by working closely with other professionals, such as nurses, occupational or physical therapists, speech and language pathologists, nutritionists, social workers, psychiatrists, and psychologists. If the physician can access and use a team comprising some or all of these disciplines in his or her medical home, it may be reasonable to manage the child in that setting. However, if it is difficult or impractical to provide this necessary range of services, the child, family, and physician are all better served by referring the patient to an interdisciplinary team of experts who have that capability.

The role of hospitalization in FTT has evolved. In the dichotomous "organic" versus "nonorganic" FTT construct, there were several indications for admission. One was to expedite the efficient and complete performance of a vast panoply of laboratory studies, including blood tests, stool and urine assays, and radiologic examinations, and to have the child seen by a range of consultants to ensure that occult organic disease was not being overlooked. Another reason for admission was to present an

appropriate type and amount of food to the child, document that the child was ingesting that food, and observe subsequent consistent weight gain. This approach was believed to serve the dual purposes of confirming the diagnosis of NOFTT, with its assumption that faulty parenting was the mechanism of disease, and returning the child to health because exogenously caused poor nutrition was the sole problem. It was assumed that this process could take 2 weeks or more.

For a variety of reasons, this approach is no longer advisable or feasible. Cost constraints plus the recognition that children and their families are best served by staying out of the hospital, if at all possible, have combined to limit the use of hospital admissions in evaluating children who have FTT. Most diagnostic and consultative evaluations can be performed on an ambulatory basis. The argument can be made that, in appropriate circumstances, there is value in having repetitive, objective assessments of a child's feeding behaviors while he or she interacts with all usual caretakers. Such serial evaluations may be undertaken in a hospital setting if experts are readily available and can attend each feeding session to evaluate the behaviors and coach the family members to improve the child's food intake. Routine 2-week admissions for FTT are not practical today. Children occasionally may be admitted for several days to document weight gain with measured food intake, but even this practice is problematic. It is very difficult to evaluate weight changes over 2 or 3 days. Acute gains or losses may be explained by edema or diuresis or by whether food or liquid intake, urination, or defecation occur before or after the child is weighed. Confirmation of real weight gain requires tracking growth measurements over several weeks, which can and should be performed in an ambulatory environment.

The current approach to FTT, emphasizing undernutrition, leads naturally to efforts to maximize nutritional repletion by supplemental means. Such efforts may include nasogastric tube feeding or gastrostomy feeding if a lengthy period of repletion is predicted. There may be a role for a brief admission (ie, several days) to teach the family how to place and manage a nasogastric tube. Typically, the general pediatrician or team of experts in a specialized care setting institutes nasogastric tube feeding in the home environment because of limitations on hospitalization coverage.

### What is the Treatment of FTT?

Because FTT is a sign of undernutrition, nutritional repletion is the *sine qua non* of successful therapy. Even in cases in which a malabsorption syndrome is present or in which a chronic medical condition is diagnosed, suc-

cessful medical or surgical interventions may not, by themselves, be sufficient to restore the child's nutritional status to normal. Anorexia, nausea, emesis, pain, or malaise due to the condition or its treatment may potentiate a child's disinterest in eating or inadvertently positively reinforce undesirable or aversive feeding behaviors. Family members may respond to illness-associated anxieties and fears by understandably but inappropriately communicating their stress to the child during mealtimes or feeding situations.

In such cases, as well as in the more common situation in which the FTT is due, in large measure, to poor intake of nutrients, the first step in successful treatment is the careful, structured observation of the child's eating or feeding behavior and of how he or she interacts with family members during meals. Does the child exhibit hunger? Can the child attend to eating at mealtimes for a developmentally appropriate length of time and tolerate sitting in a highchair or at a table? Does the child have difficulty chewing or swallowing food of certain consistencies or temperatures? Does the child have aversive eating or feeding behaviors, such as screaming, crying, gagging, hitting, or biting himself or herself or others during the meal? Does the child turn his or her head away from food, induce emesis, or pocket food in the mouth for long periods of time? Based on the results of these observations, it may be important to have a detailed evaluation performed by an expert in oromotor function in young children, such as an occupational therapist or speech and language pathologist.

Depending on the results of such evaluation, initial treatment may include procedures such as decreasing oromotor hypersensitivity; altering food textures, colors, or temperatures in a stepwise fashion; spacing meal times optimally to drive hunger; and working with the family to develop child-specific behavioral interventions, such as positive reinforcement for desired eating behaviors and extinction procedures to eliminate undesired behaviors. Punishment of undesired behaviors should be explicitly avoided. Only in the most unusual circumstances, in controlled settings with rigorous safeguards, have some behavioral experts reported success in using carefully designed punishment paradigms to improve eating behaviors.

Behavioral interventions, even with successful dietary manipulations to maximize nutritional intake, might take weeks or months to demonstrate appropriate catch-up weight gain and, in fact, may fail to produce the desired improvement. Because of the concerns about potential long-term intellectual, emotional, or behavioral sequelae of FTT, it may be desirable to maximize nutritional intake by supplemental enteral feeding.

In recent years, many pediatricians caring for patients who have FTT have turned to early and vigorous use of nasogastric tube feeding to accelerate weight gain and a return to statistical normalcy on the growth curves. This maneuver often is successful but may still take a number of months to achieve the desired results. During that time, there will almost always be loss of whatever appetite the child does have, an increase in aversive behaviors, possible problems maintaining proper placement of the tube, and nasal irritation and pulmonary aspiration of formula. These issues raise concerns for families and for the professionals caring for the child. Thus, a number of children receive a long-term feeding gastrostomy with or without an initial trial of nasogastric tube feeding. Clearly, decisions about supplemental feeding are complex, and advising families about their benefits and risks is best left, whenever possible, to teams that have expertise in this arena.

### Are There Long-term Risks to Vigorous Nutritional Repletion?

Reports on the long-term growth of young children who have FTT are widely discrepant. Some individuals appear to continue to be small and thin throughout life, others appear to be normal, and some even appear to become overweight. Consideration is being given to the possibility that certain individuals may be biologically programmed to be at weights or heights that are below the standards that are generally accepted as appropriate, based on population-based growth curves. In other words, what is statistically normal may not be biologically normal. According to this view, aggressively increasing nutritional intake to produce weight gain may not be beneficial to all patients.

Insulin resistance has been suggested as one cause for concern. In 1999, Cianfarani and associates (13) proposed that children who experienced IUGR might eventually develop insulin resistance as a defense mechanism to protect against postnatal hypoglycemia. In 2000, Jaquet and colleagues (14) showed that young adults who had been born with IUGR did, in fact, demonstrate such insulin resistance. Steward (15) summarized growing evidence that a subpopulation of term infants whose birthweights were above the traditional cut-off value of 2,500 g may actually have unrecognized IUGR. Infants who have clear-cut IUGR are known to be at risk for subsequent FTT, and this additional group of unrecognized infants may bear a similar risk. According to this line of thought, vigorous nutritional intervention in such infants or young children who have FTT might exacerbate their insulin resistance and eventually drive them

into frank metabolic syndrome. Although an individual's weight or BMI might be statistically within the normal range, that person might be functionally obese. Recent endocrinologic research has suggested other evidence to support this possibility, including perturbations of hormones such as leptin, ghrelin, and adiponectin. There is no straightforward method of identifying such a child because body habitus, truncal obesity, or skinfold measurements may not meet current standards for obesity. No evidence refutes the essential hypothesis that some individuals may be programmed to be smaller and slighter than typically is considered normal and that well-intended nutritional interventions may produce unexpected, deleterious outcomes.

This line of thinking creates a major dilemma for the pediatrician caring for a child who has FTT. On the one hand, there is substantial evidence, although not definite proof, that some children who have FTT may have adverse neurodevelopmental outcomes. That evidence argues for nutritional intervention. However, some children who have "FTT," according to the usual definitions, are at risk of developing metabolic syndrome later in life if clinicians overcorrect their growth parameters. For these children, nutritional therapy should be assiduously avoided. There is no definite guidance for the physician at this point; each child must be evaluated individually.

### Summary

- Based on consensus, FTT is best considered a physical sign of undernutrition and not a clinical syndrome caused by "organic" or "nonorganic" factors. (1)(2)
- Based on strong research evidence, infants and young children may cross major percentile lines on growth curves during a normal course of growth. Therefore, documentation of weights or lengths falling off of growth channels is not, by itself, proof of FTT. (3)
- Based on conflicting research evidence, it is unclear how many children have adverse neurodevelopmental outcomes from FTT. (4)(5)(6)(7)(8)
- Based on some research evidence, extensive laboratory screening is of little utility in the evaluation of FTT. (12)
- Based on some research evidence, certain children who appear to have FTT may be biologically programmed to be smaller and thinner than most children. Insulin resistance may be a mechanism, and aggressive nutritional intervention may put these children at risk of developing metabolic syndrome. (13)(14)(15)

#### References

- 1. Zenel JA. Failure to thrive: a general pediatrician's perspective. Pediatr Rev. 1997;18:371-378
- 2. Gahagan S. Failure to thrive: a consequence of undernutrition. Pediatr Rev. 2006;27:e1-e11
- 3. Mei Z, Grummer-Strawn LM, Thompson D, Dietz WH. Shifts in percentiles of growth during early childhood: analysis of longitudinal data from the California Child Health and Development Study. Pediatrics. 2004;113:e617-e627
- 4. Corbett SS, Drewett RF. To what extent is failure to thrive in infancy associated with poorer cognitive development? A review and meta-analysis. J Child Psychol Psychiatry. 2004;45:641-654
- 5. Rudolf MCJ, Logan S. What is the long term outcome for children who fail to thrive? A systematic review. Arch Dis Child. 2005;90:925-931
- 6. Drotar D, Sturm L. Prediction of intellectual development in young children with early histories of nonorganic failure to thrive. J Pediatr Psychiatr. 1988;13:281-296
- 7. Black MM, Dubowitz H, Krishnakumar A, Starr RH. Early intervention and recovery among children with failure to thrive: follow-up at age 8. Pediatrics. 2007;120:59-69
- 8. Emond AM, Blair PS, Emmett PM, Drewett RF. Weight falter-

- ing in infancy and IQ levels at 8 years in the Avon Longitudinal Study of Parents and Children. Pediatrics. 2007;120:e1051-e1058 9. Lozoff B, Jimenez E, Hagen J, Mollen E, Wolf A. Poorer behavioral and developmental outcome more than 10 years after treatment for iron deficiency in infancy. Pediatrics. 2000;105:e51
- 10. Drewett RF, Corbett SS, Wright CM. Physical and emotional development, appetite and body image in adolescents who failed to thrive as infants. J Child Psychol Psychiatry. 2006;47:524-531
- 11. Raikkonen K, Pesonen A-K, Heinonen K, Lahti J, et al. Infant growth and hostility in adult life. Psychosomatic Med. 2008;70: 306-313
- 12. Sills RH. Failure to thrive: the role of clinical and laboratory evaluation. Am J Dis Child. 1978;132:967-969
- 13. Cianfarani S, Germani D, Branca F. Low birthweight and adult insulin resistance: the "catch-up growth" hypothesis. Arch Dis Child Fetal Neonatal Ed. 1999;81:F71-F73
- 14. Jaquet D, Gaboriau A, Czernichow P, Levy-Marchal C. Insulin resistance early in adulthood in subjects born with intrauterine growth retardation. J Clin Endocrinol Metab. 2000;85:1401-1406 15. Steward DK. Biological vulnerability in infants with failure to thrive: the association with birthweight. Child Care Health Dev. 2001;27:555-567

### HealthyChildren.org Parent Resources from AAP

http://www.healthychildren.org/English/health-issues/conditions/chronic/Pages/ Failure-to-Thrive.aspx

### PIR Quiz

### Quiz also available online at http://pedsinreview.aappublications.org

- 6. You are evaluating a 2-year-old child who has been referred to you for poor weight gain. Before seeing the patient, you examine his growth chart, which reveals weight below the 5th percentile (50th percentile for 12 months), height at the 25th percentile, and head circumference at the 50th percentile. Solely considering the growth chart parameters, which of the following is the *most* likely reason for his poor weight gain?
  - A. Cystic fibrosis.
  - B. Growth hormone deficiency.
  - C. Inadequate caloric intake.
  - D. Metabolic disorder.
  - E. Underlying genetic disorder.
- 7. You are seeing an 18-month-old boy who has Down syndrome for a health supervision visit. His mother is concerned that he is not gaining weight well. She reports that he is a picky eater and often spits up after feedings. He has no history of cardiac or intestinal conditions but has been diagnosed with otitis media three times. Of the following, which is the *most* important to do first?
  - A. Initiate ranitidine therapy for reflux.
  - B. Obtain his neonatal records.
  - C. Plot his weight, height, and head circumference on a Down syndrome growth chart.
  - D. Refer him to a dietitian for nutritional counseling.
  - E. Refer him to an otolaryngologist for insertion of tympanostomy tubes.
- 8. You diagnose FTT in a 15-month-old boy at his first visit to the clinic. His development is normal and he has no history of vomiting, diarrhea, or chronic infections. He has had no primary care physician before now. His growth parameters are: weight at the 10th percentile, height less than the 5th percentile (50th percentile for 10 months), and head circumference at the 25th percentile. There are no abnormal findings on physical examination. Which of the following is most likely to reveal a diagnosis in this child?
  - A. Complete blood count with differential count.
  - B. Complete metabolic panel.
  - C. Growth hormone testing.
  - D. Immunologic testing.
  - E. Sweat test.
- 9. A 2-year-old girl in your clinic has FTT, with her weight and height less than the 5th percentile for age. Her physical examination findings are normal. Which of the following additional historical or examination findings would *most* likely lead you to recommend hospitalization at this time?
  - A. Failure to gain weight on several visits despite dietary intervention.
  - B. Head circumference also below the 5th percentile.
  - C. History of gastroesophageal reflux.
  - D. Moderate speech delay.
  - E. Recent divorce of parents.
- 10. You are giving a lecture to a group of medical students about the management of FTT, and one of them asks whether hospitalization is always indicated. Of the following, the *most* likely benefit of hospitalizing children who have FTT is that:
  - A. Laboratory evaluation can be performed more efficiently, leading to a diagnosis more quickly.
  - B. Nurses can educate parents on the proper use of a nasogastric feeding tube.
  - C. Parents finally understand that the child's FTT is a serious problem.
  - D. Therapists and consultants can efficiently and repeatedly evaluate the child's eating behaviors.
  - E. Weight gain in the hospital proves that there is nonorganic FTT.

### **Failure to Thrive: Current Clinical Concepts**

Arthur C. Jaffe Pediatr. Rev. 2011;32;100-108 DOI: 10.1542/pir.32-3-100

Updated Information & Services	including high-resolution figures, can be found at: http://pedsinreview.aappublications.org/cgi/content/full/32/3/100
Subspecialty Collections	This article, along with others on similar topics, appears in the following collection(s):  Nutrition and Nutritional Disorders  http://pedsinreview.aappublications.org/cgi/collection/nutritional_disorders Preventive Pediatrics  http://pedsinreview.aappublications.org/cgi/collection/preventive_pediatrics Growth and Development  http://pedsinreview.aappublications.org/cgi/collection/growth_development
Permissions & Licensing	Information about reproducing this article in parts (figures, tables) or in its entirety can be found online at: http://pedsinreview.aappublications.org/misc/Permissions.shtml
Reprints	Information about ordering reprints can be found online: http://pedsinreview.aappublications.org/misc/reprints.shtml

