# **REVIEW ARTICLE**

# **Failure to Thrive in Childhood**

Walter Nützenadel

# **SUMMARY**

<u>Background</u>: Failure to thrive impairs children's weight gain and growth, their defenses against infection, and their psychomotor and intellectual development.

Methods: This paper is a review of pertinent articles that were published from 1995 to October 2010 and contained the terms "failure to thrive", "underweight", "malnutrition", "malabsorption", "maldigestion" and "refeeding syndrome". The articles were retrieved by a search in the PubMed and Cochrane Library databases.

Results: In developed countries, failure to thrive is usually due to an underlying disease. The degree of malnutrition is assessed with anthropometric techniques. For each patient, the underlying disease must be identified and the mechanism of failure to thrive understood, so that proper medical and nutritional treatment can be provided. Nutritional treatment involves either giving more food, or else raising the caloric density of the patient's food. Liquid formulas can be given as a supplement to normal meals or as balanced or unbalanced tube feeds; they can be given orally, through a nasogastric tube, or through a gastrostomy tube. Severely malnourished children with poor oral intake should be treated with parenteral nutrition. To avoid refeeding syndrome in severely malnourished children, food intake should be increased slowly at first, and phosphate, magnesium, and potassium supplements should be aiven.

<u>Conclusion:</u> The proper treatment of failure to thrive in childhood consists of treatment of the underlying illness, combined with nutritional treatment that addresses the mechanism of the accompanying failure to thrive.

#### ► Cite this as:

Nützenadel W: Failure to thrive in childhood. Dtsch Arztebl Int 2011; 108. Dtsch Arztebl Int 2011; 108(38): 642–9. DOI: 10.3238/arztebl.2011.0642 ailure to thrive is a descriptive term, not a diagnosis. Its definition includes being underweight, loss of weight, and/or insufficient increase in weight and length during childhood. Failure to thrive is caused by a lack of nutrients. Childhood malnutrition is common in developing countries. However, this article focuses less on the clinical symptoms and treatment of this than on the diagnosis and treatment of failure to thrive in childhood in developed countries. As sufficient nourishment is usually available, failure to thrive in today's developed world is usually a symptom of an underlying disease, often a gastrointestinal or neurological disease or childhood cerebral palsy (1–3).

Failure to thrive is not uncommon in developed countries. Depending on the criteria used to define insufficient weight and on the frequency of underlying diseases, 2% to 24% of patients receiving inpatient treatment have indications of symptoms of failure to thrive (4, 5). This affects not only somatic development but also psychosocial and motor maturation, subsequent cognitive performance, immune function, and defenses against infection. Because of the multiple ways in which childhood development is impaired, early correction is needed (6–14).

# **Materials and methods**

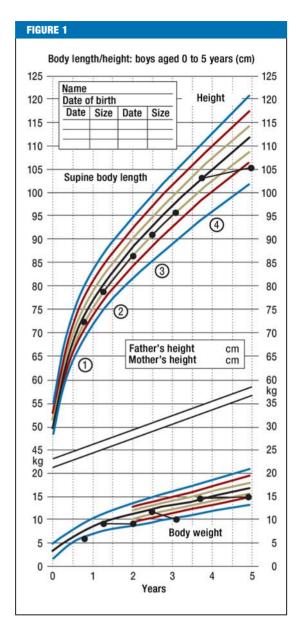
This article aims to provide an overview of the diagnosis and treatment of failure to thrive in childhood in developed countries. This includes a description of the ways in which the severity of malnutrition can be determined. The diagnostic procedure of underlying diseases is also described. A search of the literature was performed in the databases PubMed and Cochrane Library. Publications issued between 1995 and October 2010 were retrieved, using the search terms "failure to thrive," "malnutrition," "underweight," "malabsorption," and "maldigestion" as criteria for the clinical symptoms of failure to thrive, and "refeeding syndrome" as the criterion for potential harm resulting from nutritional treatment.

#### **Diagnosis and treatment**

The following steps should be taken in cases of malnutrition or failure to thrive in childhood:

- Diagnosis of failure to thrive and identification of its severity
- Identification of the pathogenesis of failure to thrive
- Diagnosis and differential diagnoses of possible underlying diseases

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#### Changes in somatic parameters in cases of failure to thrive,

based on percentiles for body length in cm (above) and weight in kg (below). The percentile curves shown correspond, from top to bottom, to the 97th, 90th, 75th, 50th, 25th, 10th, and 3rd percentiles.

- ①: Weight <3rd percentile, length normal: insufficient weight-for-length
- ②: Unaffected growth, weight changes from 50th to 3rd percentile = >2 main percentiles: insufficient weight-for-length
- ③: Normal growth, weight falls to <3rd percentile: insufficient weight-for-length</p>
- Trailed evelopment of growth and weight percentiles decreasing from 50th to 10th percentile: retarded somatic development with normal weight-for-length
  - Specific and non-specific treatment for failure to thrive
  - Monitoring of the symptoms of refeeding syndrome resulting from nutritional treatment.

# Diagnosis of failure to thrive and identification of its severity

Body weight, body length, and weight-to-length ratio are objective parameters for establishing nutritional status. Shortfalls can be revealed by comparing these values with normal values. Head growth is less affected by insufficient nutrition. Insufficient weight with microcephaly can indicate a disease that is genetic or acquired prenatally/postnatally with abnormally low somatic parameters.

When carrying out assessment it is important to remember that deviation from a statistical value can also be caused by biological variability, family history, and/ or genetics. It should also be borne in mind that edema or ascites with protein deficiency leads to misleading weight measurements, and that the weight-to-length ratio can remain normal in cases of chronic malnutrition if both weight and length fail to increase. A classification of "normal" or "worrying" therefore always requires interpretation of the data, even when values for parents and siblings are taken into account (15).

Measurements should be taken using calibrated scales suitable for the child, and with appropriate devices to measure body height (stadiometers). Measurements must be assessed by comparing them with normal values for the child's age. The following deviations from the norm are typical of failure to thrive:

- Abnormal weight-to-length ratio with weight-forlength <70% to 79% or body mass index (BMI)</li>
   3rd percentile
- Weight <3rd percentile
- Lack of increase in length and/or weight with percentile deviations >2 main percentiles (3rd, 10th, 25th, 50th, 75th, 90th, 97th) (Figure 1)

Weight-for-length is the ideal weight for a particular body length. It is the weight for the length percentile into which the child falls according to his/her age. (Actual weight  $\div$  weight-for-length)  $\times$  100 is the formula used to calculate deviation (stated as a percentage).

TABLE 1	
Assessment of severity of malnutrition: the Wellcome classification (3)	

	Weight (percentage of age- appropriate weight-for-length)	Length (percentage of ideal value)
Normal	90–110	95–105
Underweight	80–89	90–94
Malnourished	70–79	85–89
Severely malnourished	<70 or edema	<85

This approach assesses the extent to which a child is underweight (*Table 1*). When BMI is used during childhood development, it must be standardized by age so that BMI percentiles for various ages can be determined (16).

The assessment of somatic development using percentile curves over time is most suited to representing the dynamic process of growth and determining biological variability and/or genetic factors as the cause of deviations in anthropometric data (Figure 1). Percentages are based on the percentage distribution of measurements for a particular age, with the 50th percentile corresponding to the median value and the 3rd and 97th percentiles representing approximately ±2 standard deviations. Figure 1 shows the various effects of malnutrition on anthropometric data.

Population-specific and time-related data are important when using percentiles (17, 18). Percentiles must therefore be used cautiously with children from immigrant families or different ethnic groups and require careful interpretation.

Bioelectric impedance measurements to determine body fat percentage cannot be used to ascertain children's nutritional status because of the effects of fluid and electrolyte balance on measurements. Measuring skinfold thickness using calipers, e.g. subscapular or triceps skinfolds, can give an indirect assessment of subcutaneous fat. These measurements are not used as a matter of routine, however, as they are only moderately reproducible.

The retardation of somatic development associated with chronic malnutrition also leads to delayed biological maturation. This can be identified on the basis of delayed development of the skeleton of the hand. Determining skeletal age using X-rays can be useful in differentiating between small size resulting from malnutrition and small size for other reasons, particularly in cases of constitutional developmental delay or familial microsomia. Substantially delayed skeletal age is typical of constitutional developmental delay with delayed somatic development, whereas failure to thrive usually results in only slight retardation of skeletal maturation (Figure 1, point 4).

In addition to anthropometric measurements, clinical symptoms can indicate malnutrition. These are also frequently used to guide diagnosis of underlying diseases (Box 1, Table 2) (19, 20).

There is no standard laboratory value that defines malnutrition. Some fairly useful indicators are low values of albumin, prealbumin, insulin-like growth factor (IGF), insulin-like growth factor-binding protein 3 (IGFBP-3), hemoglobin, iron, and trace elements such as zinc and others.

#### Identification of the pathogenesis of failure to thrive

Failure to thrive is not a disease in its own right but a symptom that accompanies an underlying disease with the pathogeneses of malnutrition described below. This can be useful for differential diagnosis of underlying diseases and the choice of nutritional treatment.

**Insufficient food intake:** This is common with many chronic diseases (*Table 2, Box 2*) and is usually associated with the following symptoms:

- Lack of appetite
- Chronic vomiting
- Swallowing and chewing disorders
- Esophageal dysmotility
- Shortness of breath with heart and lung diseases.

Targeted questions on the patient's medical history, or, even better, a food diary kept for several days, helps reveal low intake. It is also possible to quantify the approximate amounts ingested by weighing food and leftovers. In infants, inadequate fluid intake is easy to determine. In breastfed infants, inadequate fluid intake can only be determined by weighing before and after feeding. When infants are fed on demand, as is often the case today, this is difficult and only reliable if defecation and urination are taken into account.

The number of calories ingested can be compared with national or international recommendations. However, it is important to remember that these ideal values give only a poor reflection of individual needs (*Table 3*) (19, 20).

**Increased energy requirements:** There are no simple methods of determining daily energy requirements. Measurements of individual resting metabolic rate cannot be used to give a reliable indication of increased energy requirements due to increased respiratory effort or increased motor restlessness in neurological or psychiatric diseases, for example. Increased energy requirements must therefore be estimated.

**Malabsorption:** Malabsorption during childhood is a common cause of malnutrition: it is characterized by chronic diarrhea (>4 stools/day for more than 4 weeks) and/or steatorrhea. The fat content of stools collected over 72 hours can be used to quantify malabsorption, the standard value being <4 g/day for infants and <6–8 g/day for older children. If fat intake is simultaneously recorded in a food diary, the resorption quotient can be calculated (normal value for infants >90%, older children >94%). As it is complex, this method is less practicable; the fat content of a single stool sample is not highly representative.

# BOX 1

# Symptoms of failure to thrive

# Clinical

# Main symptom:

- Weight <3rd percentile and/or loss of weight falling</li>
  2 main percentiles
- Growth retardation >2 main percentiles, weight <89% of age-appropriate weight-for-length</li>

# Other indications:

- Pallid skin
- Dry, cracked skin
- Sparse hair growth
- Poorly developed musculature
- Lack of subcutaneous fat
- Swollen abdomen with malabsorption
- Clinical indications of vitamin deficiency, e.g. rickets

# Laboratory tests

- Anemia
- Iron deficiency
- Low vitamin B12
- Abnormal electrolytes
- Low albumin
- Low insulin-like growth factor (IGF) and insulin-like growth factor-binding protein 3 (IGFBP-3)

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Disease	Typical symptoms of failure to thrive
Intestinal	
Celiac disease	Diarrhea, anemia, mental abnormalities, lack of appetite, age >8 months, positive gliadin in and/or transglutaminase antibodies
Cystic fibrosis	Steatorrhea, chronic coughing, loss of salt, increased NaCl in sweat
Crohnls disease	Diarrhea (possibly bloody diarrhea), abdominal pain, lack of appetite, school age
Gastroesophageal reflux	No diarrhea, vomiting, infancy, positive pH-metry
Congenital defects	Secretory/osmotic diarrhea, newborn/infant
Intestinal cow's milk allergy	Diarrhea, often bloody stools, colitis, mainly infants
Psychosocial	
	No diarrhea, reduced availability of nutrition, neglect, deprivation, any age
Psychiatric	
Anorexia nervosa	Puberty/prepuberty, more often affects girls than boys, no diarrhea, obstipation, psychiatric symptoms
Neurological, cardiac, nephrological, rheumatological, oncological, pulmonary, immunological disease, chronic infections	Many organ-specific symptoms, any age

#### BOX 2

# Common underlying diseases associated with failure to thrive

#### Newborns:

- Short bowel following necrotizing enterocolitis
- Volvulus and intestinal resections
- Congenital resorption defects and structural defects of the small intestine
- Insufficient food intake

#### Infants (2 to 8 months):

- Insufficient food intake
- Neglect
- Intestinal allergy to cow's milk protein
- Esophagitis with gastroesophageal reflux
- Cystic fibrosis
- Eating disorders and/or increased energy requirements in cases of underlying cardiac, neurological, oncological, or renal disease
- Celiac disease
- Chronic diarrhea in cases of immune-system defects
- Autoimmune enteropathy
- Postenteritis syndrome and malabsorption syndromes
- Munchausen syndrome by proxy

#### Small children (9 to 36 months):

- Insufficient food intake
- Neglect
- Celiac disease
- Cystic fibrosis
- Eating disorders and/or increased energy requirements in cases of underlying cardiac, neurological, oncological, or renal disease
- Chronic diarrhea in cases of immune-system defects
- Munchausen syndrome by proxy

#### Children (3 to 16 years):

- Insufficient food intake
- Neglect
- Psychiatric disorders, particularly anorexia nervosa
- Chronic inflammatory intestinal diseases
- Celiac disease
- Cystic fibrosis
- Eating disorders and/or increased energy requirements in cases of underlying cardiac, neurological, oncological, or renal disease
- Chronic diarrhea in cases of immune-system defects
- Lambliasis and other chronic intestinal infections

# Diagnosis and differential diagnoses of possible underlying diseases

The many possible causes of malnutrition require a targeted diagnostic approach that takes into account common clinical pictures and their main symptoms (*Table 2, Box 2*). This requires comprehensive clinical examination. Some information that can be gathered in cases of malnutrition is stated below.

**Medical history:** Questions on medical history must cover the following subjects:

- Parents' occupations and income
- Employment status
- Marital status
- Birth order
- Kindergarten or school attendance
- Friends and other social contacts

The answers to these questions provide important information on the following:

- Possible neglect
- Abuse and deprivation
- Availability of food
- Psychological or psychiatric diseases in the patient or parents.

Family medical history also provides indications of any familial or genetic causes of small size.

How daily nourishment is obtained is extremely important in cases of malnutrition and must be inquired after closely. Anorexia should not be immediately attributed to a psychiatric eating disorder, as a marked

lack of appetite with abnormal behavior can also occur with physical diseases.

When a medical history is taken, it should be oriented towards the symptoms of possible underlying diseases (*Table 2, Box 2*). Information on stool-related symptoms (consistency, frequency of defecation, quantity of stool, fat content, blood or mucus in the stools) indicates malabsorption or a chronic inflammatory intestinal disease. Abdominal symptoms are important, particularly their time of onset and association with the type of food ingested.

**Physical information:** Box 1 lists clinical symptoms of malnutrition. Examination for additional symptoms of an underlying disease should include the frequency of symptoms and the age at which they begin (Table 2, Box 2).

**Laboratory and other diagnostics:** Laboratory tests and other diagnostic procedures should be based on a suspected diagnosis derived from the child's age, medical history, and clinical information. Manifestations of underlying diseases are stated in *Figure 2*, *Table 2*, and *Box 2*.

# Specific and non-specific treatment for failure to thrive

Treatment of the underlying disease is the top priority in cases of symptomatic malnutrition. Nutritional treatment, however, may also be required if the underlying disease cannot be treated satisfactorily or if malnutrition is not caused by organic factors (1–3, 21, 22).

Ideally, the choice of nutritional treatment would be based on the results of randomized, comparative studies into efficacy and evidence. Comparative studies are hindered by differing underlying diseases, the impossibility of blinding nutritional treatment, and the problem of informing children and obtaining their informed consent. There are studies comparing different treatments in malnourished children in industrially underdeveloped countries and addressing specific questions, but none on how to treat symptomatic malnutrition resulting from various underlying diseases.

The treatment options available are described below. The following are important requirements:

- Good relations with parents and care providers
- Assessment of what is possible in the child's home
- Consideration of what is or is not feasible
- Realistic assessment of success.

Simpler procedures are less invasive but also less likely to succeed. The choices made should take into account the parents' opinions and the pathogenesis of malnutrition. Food intake should be approximately 110% to 120% of recommended intake (*Table 3*). Changes and adaptations of intake should be made at intervals of 1 to 2 weeks according to changes in weight.

Increased food intake: This simple, physiological method achieves positive results in cases of insufficient availability of food, a suboptimum range of food, malnutrition for psychosocial reasons, and deprivation. Restoring normal body weight confirms the approach to treatment and the accuracy of the suspected pathogenesis. The probability of success is lower in cases of marked lack of appetite and malabsorption.

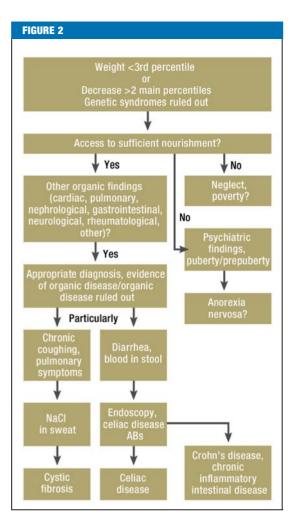
**Enrichment of food:** The aim of this is to increase energy intake by increasing calorie content, mostly by adding carbohydrates and/or fats. However, increased calorie content also leads to an altered, suboptimum ratio of calorie, protein, water, and micronutrient intake.

For infants, the concentration of powdered formula by volume can simply be increased (e.g. from 13% to 15%, representing an increase in energy intake of approximately 15%). Other options are the addition of complex carbohydrates (1 to 3 g/100 mL) and/or oil (rapeseed or sunflower oil, 0.5 to 1.0 mL/100 mL). For malabsorption, particularly fat assimilation disorders, adding medium-chain triglycerides (MCTs) can also be beneficial. There are many available supplements based on complex carbohydrates and fats.

In small children and school-age children, energy intake can also be increased by adding cream to sauces, puddings, yoghurts, and potato or vegetable dishes, and with fat-rich pastries. Frequent snacks between meals, including milkshakes, ice cream, nuts, potato chips, chocolate bars, and muesli bars, are also effective.

It is generally easy to find energy-rich meals that also appeal to children. However, an early feeling of fullness often hinders increased calorie intake.

**Drinks and tube feeding:** Nutritional drinks are available as supplements in Tetrapaks or small bottles.



Diagnosis of failure to thrive ABs: antibodies

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Recommendations for additional nutrition for healthy children, according to the German Nutrition Society (Deutsche Gesellschaft für Ernährung, DGE) (3, 24)

Age	ko	:al/d	g protein/kg/d*			
	Female	Male				
0-1 months	450	500	2.7			
1–2 months	450	500	2.0			
2–4 months	450	500	1.5			
4–6 months	700	700	2.0			
6-12 months	700	700	1.1			
1–4 years	1000	1100	1.0			
4–7 years	1400	1500	0.9			
7–10 years	1700	1900	0.9			
10-13 years	2000	2300	0.9		0.9	
13–15 years	2200	2700	0.9		0.9	
15–19 years	2500	3100	0.8 female	0.9 male		

\*Grams of protein/kilogram of body weight. Individual needs may differ from standard values

#### **KEY MESSAGES**

- In pediatric hospitals in developed countries, 2% to 25% of patients suffer from malnutrition.
- In developed countries, failure to thrive in childhood is usually a symptom of an underlying disease.
- Diagnosis and treatment of the underlying disease are needed for successful treatment of failure to thrive.
- Nutritional rehabilitation for marked malnutrition or unsatisfactory treatment of the underlying disease can involve balanced tube feeds in addition to other food intake, or oral or tube feeding alone.
- Because malnutrition causes somatic and psychological/intellectual developmental delay, early intervention is important.

They can also be used in the form of tube feeds. The most effective way to increase energy intake is to use a tube, either nasogastric or PEG (percutaneous endoscopic gastrostomy). The associated invasiveness and complications must always be considered.

It is useful to be able to state the calculated energy requirement and use foods with specific therapeutic effects but an unpleasant taste.

Industrially-prepared products can be divided into unbalanced foods, which contain mostly macromolecular nutrients, and fully-balanced foods containing micromolecular nutrients based on protein hydrolysates or free amino acids. The available ranges also differ considerably in price, but prescriptions for tube feeds are often paid for by health insurance providers.

Most industrially-prepared tube feeds are based on milk protein, contain some medium-chain fats, are low in cholesterol and lactose, and are gluten- and fructose-free. Some are available with additional dietary fiber (10 to 15 g/1000 kcal). Energy content is usually 1.0 kcal/mL, but tube feeds with a higher calorie content (1.5 kcal/mL) are also available.

Self-prepared tube feeds can be made from puréed meals. However, this can be problematic: Puréed meals usually need to be thinned because of their high viscosity, and this is associated with a risk of insufficient nutrient content and the danger of bacterial contamination. The advantages are the low prices of the foods used, the involvement of the child in preparing meals, and eating as a family.

Several daily tube feeds imitate regular mealtimes, while continuous intake using a feeding pump reduces the risk of vomiting and feeling full. Only polyurethane or silicon tubes should be used as these don't need to be changed.

PEG use avoids the cosmetic disadvantage of a visible nasal tube, foreign bodies affecting the tube in the nasopharyngeal cavity, and inconvenience caused by repeat tube changes. Despite the invasive nature and possible complications of PEGs, such as local inflam-

mation, dislocation, aspiration, faults and obstruction of the tube, parents usually prefer PEGs to nasal tubes for long-term tube feeding (3, 21, 22).

**Parenteral feeding:** Parenteral feeding is often needed initially in cases of severe malnutrition. As this can cause significant complications, the aim should be to switch to oral feeding early on. Long-term parenteral feeding should only be used in patients with intestinal failure caused by chronic diarrhea, congenital defects of the intestinal mucosa, or short bowel syndrome. Full discussion of childhood parenteral feeding lies outside the scope of this review (23).

# Monitoring of refeeding syndrome resulting from nutritional treatment

The invasive procedures involved in nutritional rehabilitation can lead to swift restoration of normal food intake on the one hand, but on the other hand pose a risk of life-threatening refeeding syndrome (e1, e2).

The pathogenesis of refeeding syndrome is not fully understood. It consists essentially of changes in electrolyte levels (low phosphate, magnesium, and potassium levels), disruptions to fluid balance with edema, impaired heart function, and hypoglycemia with abnormal intracellular energy production. Initial rehabilitation for severe malnutrition therefore requires increased potassium, magnesium, phosphate, and a slow increase of calorie intake, which should lead to normal values for the child's age after 10 to 14 days. Blood sugar, serum electrolytes, blood gases, weight, and urination should be carefully monitored.

# Conflict of interest statement

The author declares that no conflict of interest exists.

Manuscript received on 31 March 2010, revised version accepted on 28 December 2010.

Translated from the original German by Caroline Devitt, MA.

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