Arch Argent Pediatr. 2025;e202410422

Failure to thrive: A proposed diagnostic approach

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ABSTRACT

Failure to thrive is a general term describing infants who do not reach weight, length, or body mass index expected for their age. It can be related often to malnutrition due to inadequate caloric and protein intake, but also to excessive loss of nutrients, inadequate metabolism, inadequate absorption, or excessive caloric and energy expenditure. It may be either organic or inorganic in origin, and in most cases, does not require investigation through complementary examinations. It is associated with social and health detrimental outcomes. Most cases of failure to thrive are of non-organic etiology, thus clinical history evaluation and physical examination are of utmost importance in the management of these patients. Therapeutics includes behavioral or nutritional interventions, as well as treatment of possible underlying diseases. The treatment approach is more effective in improving clinical outcomes if applied as early as possible.

Keywords: *failure to thrive; growth disorders; disease management; child.*

doi: http://dx.doi.org/10.5546/aap.2024-10422.eng

To cite: Ferreira DN, Granado KACS, Hortencio TDR, Nogueira RJN. Failure to thrive: A proposed diagnostic approach. *Arch Argent Pediatr.* 2025;e202410422. Online ahead of print 23-JAN-2025.

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Funding: *None.*

Conflicts of interest: *None.*

Received: *4-29-2024*
Accepted*: 11-13-2024*

INTRODUCTION

Failure to thrive is a frequent reason for hospital consultation in pediatrics.[1] The term has recently been replaced by the term "faltering growth" (FG). In fact, "failure to thrive" may have a pejorative connotation.[2,3] In any case, both terms represent a sign of inadequate nutrition and do not define a diagnosis.[3,4]

There is no consensus on which anthropometric criteria should be used for the diagnosis of FG in childhood.

Prevalence depends mainly on the definition used and demographics of the studied population. The highest rates of FG occurs in economically disadvantaged rural and urban areas, with approximately 80% of children with stunted growth showing changes in anthropometric measurements before 18 months of age.[4] The condition is linked to lower intelligence quotient (IQ), heightened neurocognitive or behavioral issues like attention-deficit hyperactivity disorder (ADHD), reduced communication abilities and learning difficulties.[5]

This article presents a narrative review of the current literature on FG in pediatrics. It covers the definition criteria, etiology, and diagnostic methods, and proposes flowcharts on how to manage this clinical finding in daily practice.

DEFINITION

Faltering growth is a state of malnutrition secondary to inadequate caloric-protein intake, inadequate absorption, excessive loss, inadequate metabolism, or excessive energy-protein expenditure. This term describes inadequate growth or inability to maintain growth, which is more common in children <18 months.[4]

There is no consensus on the anthropometric data to be used for the practical definition of this clinical finding; however, the following criteria are commonly used: body mass index (BMI) for age below the 5th percentile, height for age below the 5th percentile, weight deceleration crossing two lines of percentiles, weight for age below the 5th percentile, weight <75% of the average weight for age, weight <75–80% of the average weight for height, and weight gain speed less than the 5th percentile.[3-5]

A combination of anthropometric criteria is recommended to identify with greater precision, children at risk for poor weight and height.

Weight-to-length/height ratio is a noteworthy indicator of acute malnutrition and is useful for identifying children who require immediate nutritional treatment. A weight <70% of the 50th percentile on the weight-to-length/height curve is an indicator of severe malnutrition and may require hospital treatment.[4]

According to the World Health Organization (WHO), children whose weight-to-length/height indicator is below −3 standard deviations or <70% of the median of the National Center for Health Statistics/WHO reference values or who have symmetrical edema involving at least the feet are classified as severely malnourished.[6]

There is criticism regarding the use of graphs with percentiles because the Z scores are standard deviations and they allow greater precision in describing deficient growth, especially near the far ends of the growth curve. The 50th percentile is equivalent to a Z score of 0, and the 3rd percentile is equivalent to a Z score of −1.89.[7] The Z score curves and percentiles are available on the WHO website.[8]

A document published in 2014 suggested that pediatric malnutrition can be classified as mild, moderate, or severe in two ways: using point data or comparing two data.[9,10]

When only punctual data are available, the classification is as follows:

a) Mild malnutrition: Z score for weight/height, BMI/age, and arm circumference measurement ranging between −1 and −1.9;
b) Moderate malnutrition: Z score for weight/height, BMI/age, and arm circumference measurement ranging between −2 and −2.9;
c) Severe malnutrition: Z score for weight/height, BMI/age, height/age, and the measurement of arm circumference equal ≤−3.

When data comparison is possible, the classification should be made as follows:

a) Mild malnutrition: speed of weight gain (in children aged <2 years) <75% of the expected weight; weight loss (2–20 years old) of 5% of the usual weight; deceleration of 1 Z score on the weight/height curve; 51–75% intake of estimated energy and protein requirements.
b) Moderate malnutrition: speed of weight gain (in children aged <2 years) <50% of the expected weight; weight loss (2–20 years old) of 7.5% of the usual weight; deceleration of 2 Z scores on the weight/height curve; intake of 26–50% of the estimated energy and protein requirements.
c) Severe malnutrition: speed of weight gain (in children aged <2 years) <25% of the expected weight; weight loss (2–20 years old) of 10% of the usual weight; deceleration of

3 Z-scores on the weight/height curve; and intake ≤25% of the estimated energy and protein requirements.

The verification of changes in a single indicator defines the diagnosis of undernutrition in pediatric patients. In the presence of indicators corresponding to different classifications, case severity must be determined using the most serious indicator to identify malnutrition in a timely manner and prioritize the most compromised indicator.[10]

ETIOLOGY

Traditionally, the etiology has been classified into two groups: organic and non-organic. However, this classification has been questioned because both situations can occur concurrently.[6]

Thus, it is preferable that the etiologies be categorized as inadequate caloric-protein intake, inadequate absorption or metabolism, increased loss, and increased energy-protein expenditure (*Table 1*).[3,6,11]

SPECIAL ASPECTS OF ANAMNESIS AND PHYSICAL EXAMINATION

As recommended in clinical practice, a complete anamnesis and physical examination should be performed. However, it is important to highlight some notable aspects, as described below. *Figure 1* presents a flowchart of the initial assessment of cases with FG.[4,6,11-16]

ANAMNESIS

It must contain a detailed assessment of the child's and family's eating habits, duration and frequency of meals, caloric and protein intake, fluid intake (juices, soft drinks, and milk), child's relationship with parents, environment during meals, who feeds the patient, and eating habits outside the home.[6,12]

Breastfed children should be observed during breastfeeding to identify possible inadequacies of the technique. For infants using infant formula, ask the caregiver to explain the step-by-step preparation of the formula, paying special attention to the dilution.[4] A three-day food diary or 24-h recall can facilitate the measurement of caloric intake.[6,11]

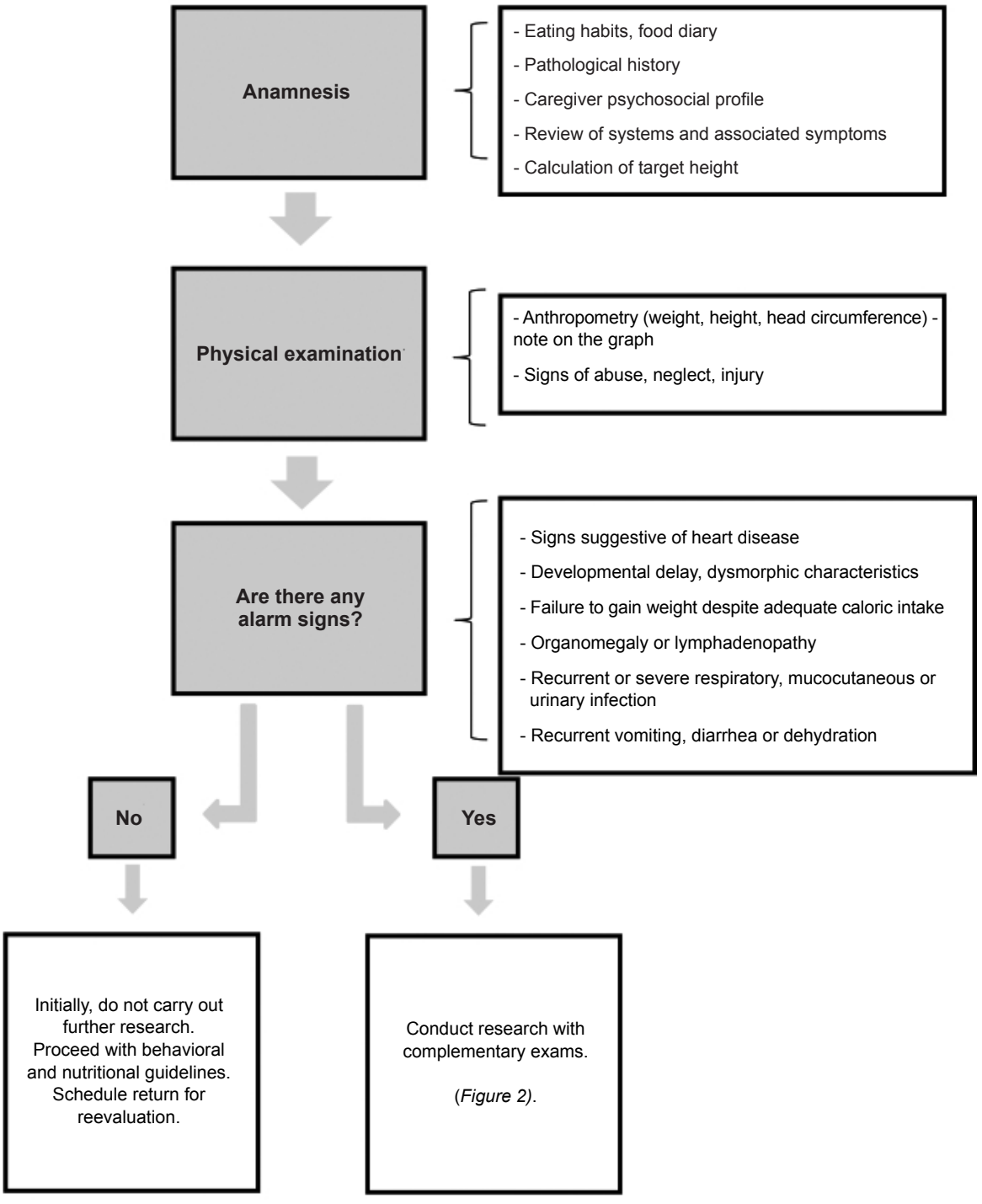
It is important to calculate the child's parental target based on the parents' stature, according to the following formula:[13]

Girls = height of mother (cm) + (height of father [cm] − 13)/2

Table 1. Causes of failure to thrive[10,11,15,28,29]

Improper ingestion
- Inadequate breastfeeding/infant formula
- Gastroesophageal reflux disease
- Negligence
- Lack of food
- Cleft lip/palate
- Eating disorder
- Irritable bowel syndrome
Improper absorption / metabolization / increased loss
- Food allergy
- Celiac disease
- Pylorus stenosis
- Intestinal malformation
- Inborn errors of metabolism
- Nephropathy
- Hepatopathy
- Inflammatory bowel disease
Excessive protein energy expense
- Thyroid disease
- Immunodeficiency
- Infection
- Chronic lung disease
- Heart disease
- Nephropathy
- Malignancy

Figure 1. Initial assessment of the patient with failure to thrive[4,7,11-16,28]



Boys = height of mother (cm) + (height of father [cm] + 13)/2

Family channel can be established by adding 10 cm above and below the value found if the patient is a male. If the patient is a female, 9 cm must be added and subtracted from the value found to establish the margin of growth variation. These data should be noted on the child's stature chart.[13]

PHYSICAL EXAMINATION

Accurate anthropometry (weight, height, and head circumference) must be performed, and register on a specific graph. The presence of associated symptoms, such as vomiting, diarrhea, choking, and respiratory symptoms, can orientate to organic etiologies.[4,6]

Beware of alarm signs, such as cardiac findings suggestive of congenital heart disease or heart failure (for example, murmur, edema, and distention of the jugular vein), developmental delay, dysmorphic characteristics, failure to gain weight despite adequate caloric intake, organomegaly or lymphadenopathy, recurrent or severe respiratory, mucocutaneous, or urinary infection, recurrent vomiting, diarrhea, or dehydration.[4,12]

A study showed that 92%-96% of children with non-organic symptoms and without obvious organic symptoms were diagnosed with behavioral etiology. The absence of non-organic symptoms does not completely exclude non-organic cause.[14]

Family factors can also contribute to inadequate caloric intake. These include mental health disorders, inadequate nutritional knowledge, and financial difficulties. It is important to trace the psychosocial history of the child's caregivers, paying attention to signs of abuse or physical neglect, such as poor hygiene and nutrition, chronic illness without treatment, recurrent or unexplained injuries, extensive or dispersed bruises, bilateral fractures, or burns.[4,15,16]

COMPLEMENTARY EVALUATION

Complementary tests identify the cause of FG in <1% of children, and their use is generally not recommended unless anamnesis and physical examination suggest the need for additional testing.[4] Failure to respond to nutritional and behavioral treatment may also lead to further examinations. A traditional assessment guided by anamnesis and physical examination findings shows a good predictive value.[1] Recently a South Korean study evaluated serum micronutrient levels in children with non-organic growth failure. The results showed no significant differences between the parameters observed in children without growth impairment.[17]

In cases where tests are necessary, an initial investigation with a complete blood count, blood gas analysis (with dosages of sodium, potassium, ionic calcium, chloride, and lactate), total calcium, magnesium, phosphorus, urea, creatinine, urinalysis, urine culture, albumin, and C-reactive protein is advised.[3,4,6,12,18]

Hypoalbuminemia is associated with several comorbidities, which may represent a decrease in the synthesis of albumin by the liver, increased catabolism, inadequate protein intake, and increased losses (renal or mainly through the gastrointestinal tract).[19-21] Therefore, in cases where there is severe hypoalbuminemia, i.e., serum albumin level <2.5 g/dL, the investigation should be complemented with the request for 24 h proteinuria (in order to assess the presence of nephrotic syndrome),[22,23] alpha 1 fecal antitrypsin (to evaluate protein-losing enteropathy),[24] a complete liver profile (aspartate aminotransferase, alanine aminotransferase, alkaline phosphatase, gamma glutamyl transferase, clotting parameters, and abdominal ultrasound), and protein electrophoresis.[19]

In cases with evidence of inflammatory activity with values above the reference limit (elevated C-reactive protein level), the investigation of inflammatory and/or infectious diseases should be considered.[25]

In certain situations, the investigation should also include thyroid function, iron profile, and vitamin B12 dosing, in addition to serology for the main congenital infections, such as syphilis, toxoplasmosis, rubella, cytomegalovirus, and herpes simplex virus (STORCH).[1,3,4,18]

Children who present with clinical signs of intestinal malabsorption, such as diarrhea and steatorrhea, should undergo fecal fat analysis by a semi quantitative test or preferably, using the Van de Kamer method. Additionally, studies for celiac disease, with serum immunoglobulin A (IgA) and anti-transglutaminase IgA levels must be performed. Consider a sweat test with chloride measurements to rule out cystic fibrosis.[1,3,4,6,8,18,26,27]

In the presence of warning signs of primary immunodeficiency, immunoglobulin dosing is requested, along with initial examinations. Among the warning signs in childhood, the following stand out: ≥2 pneumonias in the last year; ≥4 new ear infections in the last year; recurrent stomatitis or moniliasis for >2 months; recurrent abscesses; an episode of severe systemic infection (meningitis, osteoarthritis, and septicemia); recurrent intestinal infections, chronic diarrhea, and giardiasis; severe asthma, collagen disease or autoimmune disease; adverse effect on bacillus Calmette–Guérin (BCG) vaccine and/or mycobacterial

infection; clinical phenotype suggesting syndrome associated with immunodeficiency; family history of immunodeficiency.[18,28]

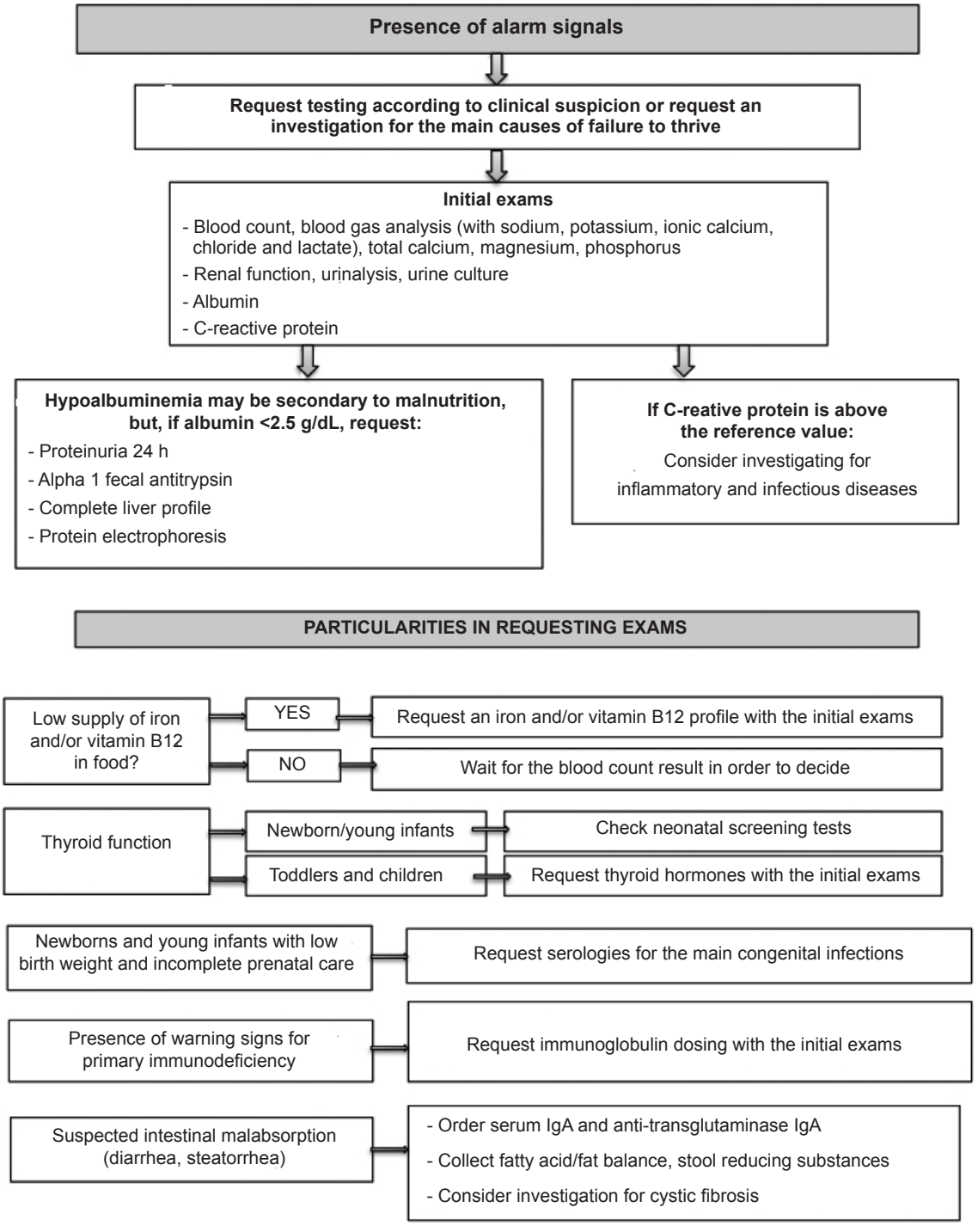
Figure 2 proposes a flow chart for the investigative approach in cases that require complementary exams.[1,3,4,6,12,17-27]

TREATMENT

If FG is diagnosed and organic conditions are not suggested, appropriate tools for growth recovery must be provided, with nutritional and behavioral guidelines appropriate for the age.[4,12]

If an organic cause is identified in the history,

Figure 2. Investigation of the patient with alarm signs[1,3,4,6,12,17-27]



physical examination, or additional tests, the approach will depend on the diagnosis.[4,12]

Hospitalization should be considered in some situations as follows:

- The child did not improve with outpatient treatment.
- Suspicion of abuse or neglect (signs of traumatic injury, serious psychosocial impairment of the caregiver, or signs of severe malnutrition).[1,3,18,26]
- Any child who does not show improvement while in the hospital justifies further evaluation through laboratory and imaging tests, as indicated on a case-by-case basis, and can benefit from enteral tube placement. [6]

It is important to notice that a retrospective study with 497 patients has shown that organic causes may require more than admission to hospitalization to be identified and a follow up is mandatory.[28]

CONSEQUENCES

In a severe malnutrition situation, the development of cognitive skills can be impaired in the long term. Childhood severe malnutrition can lead to cognitive impairments, behavioral issues such as attention-deficit hyperactivity disorder, and communication difficulties. Furthermore, FG (FG) can negatively impact academic performance, cognitive achievements, stature, and socioeconomic outcomes. In low- and middle-income countries, FG often coexists with various other health and social challenges, including impaired brain development, delayed cognitive performance, increased susceptibility to infections, and higher childhood mortality. These children also face lower physical work capacity, reduced earnings, and diminished human capital in adulthood.[5,29]

PROGNOSIS

There is consensus that severe and prolonged malnutrition can negatively affect a child's growth and cognitive development.[3,4,26] Preterm infants with low birth weight who develop failure to thrive also demonstrated long-term developmental effects. At eight years of age, these children were shorter, had lower cognitive scores, and presented worse overall academic performance than similar premature neonates who did not develop failure to thrive. A previous study shows that it is unclear whether children with normal birth weight who fail to thrive and then recover have similar long-term consequences. Afterwards, children with a history of failure to thrive have an increased risk of recurrence. Therefore, their growth should be monitored constantly.[4]

Recently, dysbiosis has been implicated in a cause-consequence relationship with growth failure.[30]

CONCLUSION

Despite being a frequent cause of consultation in pediatrics, FG raises doubts about how to approach it in the daily practice. The importance of a detailed clinical evaluation is emphasized, which leads to a diagnosis of a non-organic cause in most cases, avoiding unnecessary expenses and stress for patients and their caregivers. Insufficient intake should be explored in all cases. Most children show good nutritional recovery with adequate behavioral and nutritional interventions, which is the first line treatment for cases without a defined organic cause. However, awareness is needed in relation to the alarm signs of an organic involvement for further investigation and treatment. Early intervention in children who fail to thrive can reduce the long-term consequences of malnutrition and improves quality of life and development. ■

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