Investigation of the child with failure to thrive

Each month we present authoritative advice on the investigation of a common clinical problem, specially written for family doctors by the Board of Continuing Medical Education of the Royal Australasian College of Physicians.

RALF G. HEINE
MD, FRACP

Dr Heine is Consultant Paediatrician and Gastroenterologist, Royal Children's Hospital, and Associate Senior Lecturer, Department of Paediatrics, The University of Melbourne, Melbourne, Vic.

Series Editor
CHRISTOPHER S. POKORNY
MB BS, FRACP

Dr Pokorny is Honorary Secretary, Board of Continuing Education, Royal Australasian College of Physicians, and a gastroenterologist in private practice, Sydney, NSW.

Monitoring weight and height

Poor weight gain is a common complaint in paediatric practice. Weight and height should ideally be measured as part of every paediatric consultation. In general, as long as weight and height are progressing along a certain percentile it can be assumed that the child is healthy.

Failure to thrive is a term used to describe inadequate weight gain in children under 2 years of age. Young infants are prone to develop it because of their high energy requirements. Persistent failure to thrive indicates protein–energy malnutrition due to chronic illness or insufficient energy intake. Linear growth is affected if poor weight gain persists for several weeks, and head growth is usually preserved unless malnutrition is severe.

Parents are often unduly concerned about the growth of their children, particularly in the second year of life when the growth velocity slows down. When assessing a child with presumed growth failure, it is crucial to confirm on a percentile chart that the weight gain has been abnormal. The crossing of two major percentile lines or a fall below the third percentile is considered abnormal.

Causes of failure to thrive

Nonorganic causes

In a significant proportion of cases, failure to thrive is due to nonorganic causes, such as disturbed mother–infant interaction, poor feeding technique, errors in formula preparation, emotional neglect or even child abuse.[1] Iron deficiency anaemia is common in this setting. Some parents commence their young children on nutritionally inappropriate low-fat diets because of concerns about heart disease and obesity.[2]

A detailed medical and dietary history usually provides a clue as to why the child is not gaining weight. If a nonorganic cause is suspected, then

IN SUMMARY

- **When assessing a child with presumed growth failure, confirm on a percentile chart that the weight gain has been abnormal. The crossing of two major percentile lines or a fall below the third percentile is considered abnormal.**
- **Consider poor feeding technique, errors in formula preparation, emotional neglect or even child abuse. If one of these nonorganic causes is suspected, assess growth pattern after education and dietary interventions, and defer extensive investigations.**
- **The organic causes of failure to thrive can be divided into: failure of intake, abnormal losses, failure of utilisation, increased requirements, and reduced growth potential.**
- **When considering organic causes, it is useful to look at whether there is persistent vomiting, gastro-oesophageal reflux, chronic diarrhoea or malabsorption.**
- **With a detailed physical examination and a few simple screening tests, a provisional diagnosis can often be made, but the child should be referred to a specialist if there is no weight gain despite dietary interventions or if serious disease is suspected.**

investigations should be deferred. Most of these infants will gain weight after counselling or a trial of feeding in hospital.

Organic causes

The organic causes of failure to thrive can be divided into:

- failure of intake (e.g. cerebral palsy, orofacial malformations)
- abnormal losses (e.g. vomiting, malabsorption)
- failure of utilisation (e.g. metabolic diseases, diabetes mellitus)
- increased requirements (e.g. chronic lung disease, chronic infection, cardiac failure)
- reduced growth potential (e.g. chromosomal abnormalities).

With a detailed physical examination and a few simple screening tests, a provisional diagnosis can often be made (see the box on this page).

Investigating particular causes of failure to thrive

Vomiting and gastro-oesophageal reflux

Hypertrophic pyloric stenosis

Persistent vomiting may cause weight loss through loss of fluids and nutrients. In the first weeks of life, hypertrophic pyloric stenosis may present with projectile vomiting, hypochloraemic alkalosis and dehydration. On examination, the enlarged pyloric sphincter muscle can often be palpated, or visualised by abdominal ultrasound examination.

Gastro-oesophageal reflux

In older infants, failure to thrive may result from gastro-oesophageal reflux with frequent regurgitation and feeding difficulties.[3] It can be difficult to distinguish between vomiting and effortless regurgitation. Nonregurgitative 'silent' reflux is not a cause of failure to thrive. The severity of gastro-oesophageal reflux can be assessed by 24-hour oesophageal pH monitoring. The presence of oesophagitis should be confirmed endoscopically. Barium studies are used primarily to identify anatomical abnormalities.

Food protein intolerance

Intolerance to cow's milk and soy protein may present with vomiting, distressed behaviour and failure to thrive.[4] The clinical presentation of these infants is very similar to that of infants with gastro-oesophageal reflux. Apart from a detailed dietary history, the definitive diagnosis relies on double-blind challenges with formula and with food.

Suggested initial approach to the child with poor weight gain

1. Carry out a detailed history and physical examination (including nutritional assessment).
2. Measure weight, height and head circumference. Plot current and previous growth parameters on a percentile chart and assess growth velocity.
3. If nutritional intake appears inadequate, arrange review by a dietitian or consider a trial of feeding in hospital.
4. Order screening tests for failure to thrive:
   - full blood examination
   - iron studies
   - liver function tests, serum albumin
   - coeliac disease serology (total serum IgA, antigliadin IgG and IgA, and antiendomysial IgA or tissue transglutaminase IgA)
   - urinalysis and culture
   - faecal microscopy and culture.

Table 1. Investigation of persistent vomiting

Provisional diagnosis	Investigations
Hypertrophic pyloric stenosis	Abdominal ultrasound Electrolytes and acid–base status
Gastro-oesophageal reflux	Oesophageal 24-hour pH monitoring Gastroscopy and biopsies Barium meal (if anatomical abnormality is suspected)
Malrotation	Plain abdominal x-ray and barium meal
Urinary tract infection	Urinalysis and culture
Raised intracranial pressure	Detailed neurological examination CT scan of the brain
Metabolic disease	Urine metabolic screen Acid–base status

Other causes of vomiting

Other causes of vomiting need to be considered (Table 1). Vomiting may be a presenting feature of urinary tract infections or, rarely, may indicate a metabolic problem. Surgical causes of vomiting present more acutely and generally do not cause persistent weight loss. Raised intracranial pressure should be suspected if vomiting occurs in association with headaches or other neurological features.

Table 2. Investigation of persistent diarrhoea

Provisional diagnosis	Investigations
Infective causes	Stool culture and microscopy Tests for viral pathogens (rotavirus and adenovirus) Microscopy for *Giardia* and *Cryptosporidium*
Fat malabsorption	Faecal microscopy (fat globules) Liver function tests Serum levels of fat-soluble vitamins Clotting profile
– Cystic fibrosis	Sweat chloride >60 mmol/L Chest x-ray
Carbohydrate malabsorption (osmotic diarrhoea)	Stool pH (<5.5) Faecal sugars positive (<0.25%) Osmotic gap in faecal fluid (>125 mOsm/L) Breath hydrogen testing (e.g. lactose) Duodenal disaccharidase levels (in biopsy specimen)
– Coeliac disease	Faecal microscopy (fatty acid crystals) Total serum IgA Antigliadin IgG and IgA antibodies Antiendomysial IgA antibody or tissue transglutaminase IgA Small bowel biopsy (if antibodies elevated or strong clinical suspicion)
Secretory diarrhoea	Stool electrolytes (sodium >70 mmol/L) Osmotic gap in faecal fluid (>50 mOsm/L)
Protein-losing enteropathy	Serum albumin and immunoglobulins Alpha-1-antitrypsin clearance in faeces Urinalysis (to exclude proteinuria)
Inflammatory bowel disease	Full blood count, erythrocyte sedimentation rate and serum albumin Faecal microscopy and culture Gastroscopy and colonoscopy

Chronic diarrhoea and malabsorption

Faecal microscopy is the key to the investigation of chronic diarrhoea (Table 2).[5] The presence of fat globules is associated with maldigestion or rapid intestinal transit, whereas fatty acid crystals indicate impaired small intestinal mucosal absorption, as in coeliac disease.

Infective causes

Although bacterial pathogens rarely cause longstanding weight loss in immunocompetent children, at least one stool sample should be sent for culture and microscopy. Parasitic infestation with *Giardia lamblia* (Figure 1) or *Cryptosporidium parvum* may cause persistent diarrhoea in young children, resulting in failure to thrive. The diagnostic yield for *Giardia* cysts from a single stool specimen is low, and examination of three stool specimens is recommended. Alternatively, if there is a strong likelihood of giardiasis, children can be treated empirically with metronidazole (Flagyl, Metrogyl, Metronide) or tinidazole (Fasigyn, Simplotan).

Coeliac disease

While sensitive and specific serological screening tests for coeliac disease are available, a definitive diagnosis can be established only by duodenal biopsy (Figures 2a to c and 3a and b). A gluten-free diet should never be instituted on the results of serology alone.[6,7] Most screening tests for coeliac disease rely

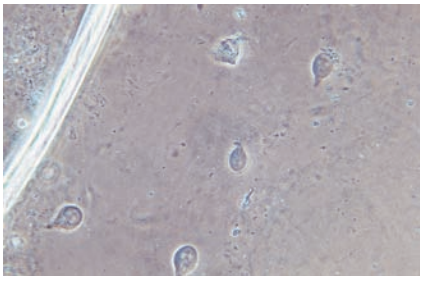


Figure 1. Trophozoites of *Giardia lamblia* in duodenal aspirate.

on the detection of IgA antibodies to gliadin, endomysium and tissue trans - glutaminase in the presence of ongoing gluten intake. These antibodies are absent in about 15% of patients who have selective total IgA deficiency, and a total serum IgA level should be included in the serological screening (Table 2). Although antigliadin IgG is a relatively nonspecific serological marker with a high false-positive rate, it is useful in identifying IgA-deficient individuals with coeliac disease.

Cystic fibrosis

Since the introduction of genetic newborn screening, most cases of cystic fibrosis are diagnosed in early infancy.[8] A small number of infants with unusual cystic fibrosis mutations will be missed by the screening process and will present later in life with poor weight gain, persistent chest infections and fat malabsorption. A high index of suspicion is required. The definitive diagnosis is made by sweat iontophoresis, which should be arranged through a paediatric cystic fibrosis centre. A sweat chloride level above 60 mmol/L is diagnostic.

Osmotic v. secretory diarrhoea

Infants with osmotic diarrhoea due to carbohydrate malabsorption commonly present with significant perianal excoriation from acidic stools. Nonabsorbed carbohydrates are fermented by gut bacteria to short chain fatty acids. The diarrhoea stops when the patients are fasted.

The osmotic gap in faecal fluid can be calculated as $290 - 2([Na^+] + [K^+])$. It is usually greater than 125 mOsm/L in cases of osmotic diarrhoea. Stool sodium concentrations above 70 mmol/L and an osmotic gap below 50 mOsm/L are suggestive of secretory diarrhoea.

In infants, the collection of liquid faeces can be achieved by turning a disposable napkin inside out and by applying a urine bag to prevent urine from mixing with faeces.

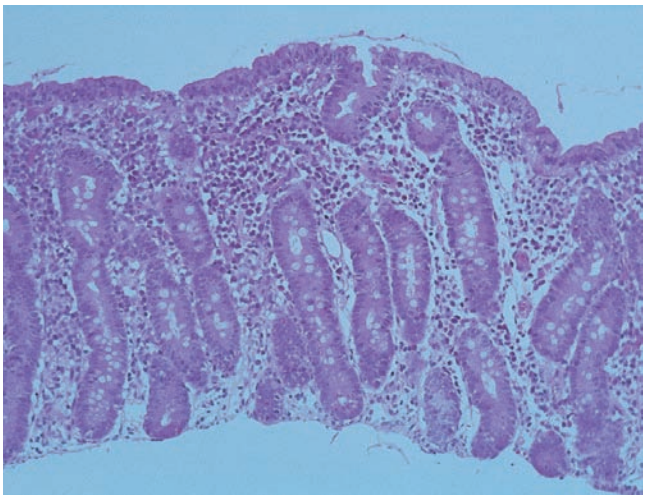
Common causes of osmotic diarrhoea include postenteritic lactose intolerance and coeliac disease. Secretory diarrhoea in childhood may be caused by infections (e.g. by *Cryptosporidium*), toxins, or rare congenital defects of intestinal electrolyte transport (e.g. chloride dia - rrhoea of infancy).

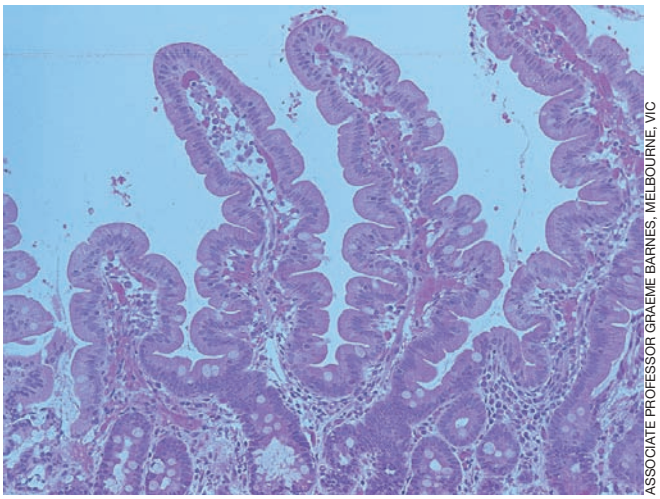
Inflammatory bowel disease

The incidence of inflammatory bowel disease in children is increasing. Children with Crohn's disease often present with significant weight loss, chronic diarrhoea, abdominal pain or perianal manifestations. In patients with colitis, faecal microscopy reveals white and red blood cells, and repeated stool cultures do not yield any bacterial pathogens.

Table 3. When referral is required

- No weight gain despite dietary interventions
- Suspected coeliac disease (antibody screen positive or strong clinical suspicion)
- Suspected cystic fibrosis
- Neurological abnormalities
- Suspected malignancy
- Suspected inborn error of metabolism
- Diabetic ketoacidosis (initial presentation)
- Suspected child neglect or abuse





ASSOCIATE PROFESSOR GRAEME BARNES, MELBOURNE, VIC

Figures 3a and b. Small bowel biopsy of coeliac disease. a (left). The small intestinal villous architecture is almost completely lost and the crypts are elongated. There is a dense inflammatory infiltrate in the lamina propria. b (right). The return of normal villi on a gluten-free diet.

The platelet count and erythrocyte sedimentation rate are usually elevated during acute exacerbations. Gastroscopy and colonoscopy with biopsies will establish the diagnosis.

Other causes of weight loss

There are many other causes of weight loss in childhood that are beyond the scope of this article. Young infants with inborn errors of metabolism may present with vomiting and failure to thrive. Common biochemical abnormalities include metabolic acidosis, hypoglycaemia or hyperammonaemia. These infants require urgent referral to a metabolic paediatrician. Other causes of weight loss include insulin-dependent diabetes mellitus, malignancies, and eating disorders such as anorexia nervosa. Early referral to a paediatric centre is essential for optimal management of these conditions (Table 3).

Conclusion

Failure to thrive develops when the high energy requirements of the growing infant are not met. When a child is investigated for poor weight gain, the growth pattern should first be assessed on a percentile chart. Nonorganic causes are common, and a detailed medical and dietary history should always be obtained. If inadequate kilojoule intake is likely, the response to dietary interventions should be assessed and further extensive investigations be deferred. Simple screening tests may identify children with a likely organic cause and associated deficiency states. MT

References

1. McCann JB, Stein A, Fairburn CG, Dunger DB. Eating habits and attitudes of mothers of children with non-organic failure to thrive. Arch Dis Child 1994; 70: 234-236.

2. Pugliese MT, Weyman-Daum M, Moses N, Lifshitz F. Parental health beliefs as a cause of nonorganic failure to thrive. Pediatrics 1987; 80: 175-182.

3. Hyman PE. Gastroesophageal reflux: one reason why baby won't eat. J Pediatr 1994; 125(6 Pt 2): S103-S109.

4. Hill DJ, Heine RG, Cameron DJS, Francis DEM, Bines JE. The natural history of intolerance to soy and extensively hydrolyzed formula in infants with multiple food protein intolerance. J Pediatr 1999; 135: 118-121.

5. Fine KD, Schiller LR. AGA technical review on the evaluation and management of chronic diarrhea. Gastroenterology 1999; 116: 1464-1486.

6. Troncone R, Maurano F, Rossi M, et al. IgA antibodies to tissue transglutaminase: an effective diagnostic test for celiac disease. J Pediatr 1999; 134: 166-171.

7. Heine RG, Catto-Smith AG. Antibodies in the diagnosis and management of coeliac disease. J Paediatr Child Health 1993; 29: 331-334.

8. Massie RJ, Olsen M, Glazner J, Robertson CF, Francis I. Newborn screening for cystic fibrosis in Victoria: 10 years' experience (1989-1998). Med J Aust 2000; 172: 584-587.